HPS-P-005

EVALUATION OF TPN UTILIZATION FOR PATIENTS WITH RENAL INSUFFICIENCY

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Aims: To evaluate the outcome of TPN for renal insufficiency and to enhance patient safety. Methods: 1. To select ESRD under hemodialysis, chronic renal insufficiency, and acute renal failure as the key words. 2. During the period of Oct. 2003 and Dec. 2004, under the key words of diagnosis, to screen and monitor concurrently all adults on TPN. 3. Data collected from intranet e-Hospital and medical records. 4. To evaluate and analyze the data via an Excel worksheet. Results: 22 patients (18M, 4F) aged 42-89.6 y/o (mean 69.1) with mild (3) to severe renal insufficiency (moderate 7, advanced 6 ESRD/failure 6) and under HD(16), CVVH (1), CAVH (1). 91% of NPO cases (22) was malnutrition. TPN indicated for UGI bleeding (41%), perioperation, chemotherapy, small bowel resection and so on. CPN-B2 G2 Nutriflex Aminomix and A2 formula were used to provide RDA TEE in 22.7% cases and RDA dextrose in 100% cases to keep 95.5% cases with normal level (NL) blood sugar. RDA amino acid provided in 86.4% cases. BUN and CrSr elevated in all cases. RDA fat provided in 72.7% cases to keep NL TG. Hyponatremia (18.2%), hypernatremia (4.6%), and hypokalemia (9.1%) occurred sporadically in 22 cases with RDA Na+ and K+. Hypochloremia occurred in 5% RDA CL- cases (20) and in 100% cases without CL-. Hypocalcemia (5.3%) occurred in 19 cases with RDA Ca++. Hyperphosphatemia occured in 41% cases. Hypomagnesemia occured inTPN without Mg++. Complication rate was 13.6%. Liver enzyme, bilirubin, BUN and CrSr elevated obviously. 68.2% patients expired and 32% survived. Conclusions: Mortality rate is high in renal insufficiency, outcome evaluation will improve nutritional status and enhance patient safety.

HPS-P-006

CHANGES OF CALCIUM HOMEOSTASIS IN BRAIN UNDER THE INFLUENCE OF HYPOKINESIA AND GABA

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Hypokinesia (HK) as a risk factor promotes development of cerebrovascular disturbances. Ca2+ is the most common signal transduction agent that controls many aspects of cellular function. Abnormal calcium homeostasis is usually thought to lead to neuronal death through rather complex degenerating processes.
The effects of HK and γ-aminobutyric acid (GABA) on free Ca2+ ions influx rate into the cells and its distribution between the subcellular fractions have been investigated in rat brain neurocytes. Male mature white rats were used. HK was modeled in individual small cages. Contemporary radioisotope method for 45Ca2+ labeled ions influx rate measurement was used. Our results evidence that the Ca2+ ions influx rate increases. It is very important to note that the entered Ca2+ ions are mainly accumulated within the mitochondrial fraction of neurocytes thus promoting irreversible damage of the cells. Our morphological investigations revealed worsening of the state in brain tissue, especially blood-brain barrier permeability increases with formation of perivascular edema, neuropycnosis, glial nodules, loss of capillary net in brain tissue. Our experiments show that administration of GABA prevents movement of Ca2+ ions into the neurocytes. On the other hand GABA inhibits worsening of the morphological picture of the brain tissue in conditions of HK and manifests expressed cerebroprotective effect.

HPS-P-007

ROLE OF THE CLINICAL PHARMACIST IN THE MANAGEMENT OF PATIENTS WITH HEART FAILURE

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Introduction: Chronic heart failure is a common clinical condition with high morbidity and mortality. The aim of this study was to explore clinical pharmacists' accounts of their management of patients with heart failure and identify the perceived obstacles to diagnosis and management.
Methods: We conducted this qualitative study using semi-structured interviews in 31 clinical pharmacists. The interviews were based on a schedule of open questions based on the literature on diagnosis and management of patients with heart failure. Transcriptions of the audiotaped interviews were independently analysed by two researchers and analysis was based on open coding using a constant comparative approach.
Results: Clinical pharmacists suspect heart failure when patients present with breathlessness or ankle edema. Obstacles to diagnosis were mentioned by most clinical pharmacists and included lack of facilities for appropriate investigations and lack of time and expertise. Obstacles to management included lack of time, high cost of drugs, difficulty with diagnosis, selection bias towards younger patients and not having the confidence to initiate angiotensin-converting enzyme inhibitors.
Conclusions: Although symptoms of heart failure are not sufficiently specific for diagnosing patients with heart failure, many clinical pharmacists recommend treating people with suspected heart failure on the basis of symptoms and signs alone. This study has identified many obstacles to the diagnosis and management of heart failure that may explain why patients are inadequately managed. Specific implementation strategies need to be tailored to overcome these obstacles.

HPS-P-008

EFFECTS OF THE CONCENTRATION OF PARENTERAL NUTRITION WITH AND WITHOUT GROWTH HORMONE ON BODY COMPOSITION IN GASTROINTESTINAL (GI) SURGERY PATIENTS

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BACKGROUND: Protein loss is an inevitable consequence of major surgery which is associated with post-operative (PO) impaired immunity and increased morbidity and mortality. Growth hormone (GH) has powerful anabolic effects which are hypothesized to potentiate the effects of parenteral nutrition (PN) in maintaining the PO body composition (BC). AIMS: A randomised, controlled, double-blind study was carried out to determine the effects of ½ PN+GH, ½ PN-GH, Full PN+GH, or Full PN-GH on patients' BC following major GI surgery and whether lower nitrogen and calorie PN input is satisfactory in maintaining BC. METHODS: 43 major upper GI surgery patients were randomised into one of the 4 groups continuously from PO day 1 to 14. The Full PN provided 0.2g N/kg/day & 65% of the non-protein calories as lipid whereas the ½ PN provided 0.13g N/kg/day & 52% of the non-protein calories as lipid. GH/placebo (16 IU/day) was administered subcutaneously. Changes in BC were measured as changes in TBN, body fat (BF), total body water, and potassium. RESULTS: 35 of the 43 patients completed the study. The ½ PN-GH group (n=11) lost TBN (p=0.001) and MM (p=0.005) but not BF. The Full PN-GH group (n=9) maintained TBN, MM (p=0.050), and BF. The ½ PN+GH group (n=8) maintained TBN and BF but lost MM (p=0.038). The Full PN+GH group (n=7) maintained TBN and MM but lost BF (p=0.018). Statistical analyses indicated that concentration of PN input (p=0.031) and not GH had a significant effect on TBN/MM. CONCLUSION: In the PO setting, GH has a more significant effect on BC if administered with a higher strength PN input. In addition, higher strength PN input is more important than GH in preserving TBN/MM.

HPS-P-009

THE EFFECT OF CIGARETTE-SMOKING TO CLINICAL DATA OBTAINED FROM CITIZEN EXAMINATION

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Object
At the annual meeting of the Pharmaceutical Society of Japan in March 29, 2004 , we presented that there are the correlation between Smoking Index and clinical laboratory data of WBC or Hemoglobin. The aim of this study was to assess the effect of cigarette-smoking to clinical laboratory data.
Method
We asked about Cigarette-Smoking usage to the 697 people of who take citizens examination at Kume clinic, and lived in Fuchu-city, Tokyo, Japan. Smoking Index was calculated in each people. All data were obtained in individual people. The correlation of smoking index and clinical laboratory data was assessed.
Result
The study comprised 769 data of people (272 male and 497 female) who visted Kume clinic. Never-smoker were 537 person (125 male and 412 female), active-smokers were 136 person(77 male and 59 female), former-smoker wer 96 person(70 male and 26 female). It was shown a relationship between WBC, Hemoglobin, or hematocrit and smoking index.
Conclusion
We showed that the cardiovascular risk is going to get higher with Smoking Index.

HPS-P-010

UNAFFORDABLE DRUG PRICES: THE MAJOR CAUSE OF NON-COMPLIANCE WITH HYPERTENSION MEDICATION IN GHANA

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INTRODUCTION: The HIV/ AIDS epidemic in Sub Saharan Africa appears to divert attention, care and resources from all other diseases. In Ghana, the prevalence of hypertension has been reported as increasing. A major concern is that many patients may not have access to standard hypertension medications. In this study we evaluate access to hypertension medicines in Ghana and search for the reasons for non-compliance with hypertension medication. METHODS: Patient interviews were conducted on all new patients attending the hypertension clinic at Komfo Anokye teaching hospital between December 2001 and April 2002. Data were collected from 128 hypertension patients RESULTS: 119 of the 128 interviewed patients (93%) did not comply with their medications. 114 (96%) of the non-compliant patients cited unaffordable drug prices as the main reason for non-compliance. CONCLUSIONS: Non-compliance with hypertension medication is a major problem in Ghana. Unaffordable drug prices appear the major cause. Effort should be made both locally and internationally to improve access to medications for chronic diseases in developing countries.

HPS-P-011

DEVELOPMENT AND ASSESSMENT OF A COMPUTERIZED PRESCRIPTION ALERT SYSTEM

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Medication errors may result in adverse drug events, increase the workload of health care professionals, and deplete medical resources. Many studies have demonstrated that CPOE with medication alerts may reduce medication errors.
This study developed a real time medication alert system in original computerized order entry system at the outpatient department. The impacts of medication alert system on physician's prescribing practices were evaluated. A prospective before-after comparison was carried out to assess the effects of the alert system in reducing the rate of prescribing and transcribing errors. After two months of intervening medication alert system in practice, we conducted questionnaire survey to evaluate the user's satisfaction. During the study, 0.74% of prescriptions triggered the alert. Fifty nine percent were overridden among the alerted prescriptions. The major reason to override the drug alert was 'justification of patient's condition'. In comparison with pre-intervention period, the prescribing and transcribing error rate dropped from 0.20 per 1000 prescriptions to 0.12 per 1000 prescriptions(P<0.001)after intervention. The results of questionnaire survey revealed that over 60% of physicians, pharmacists and clerks agreed with the criteria appropriality of the medication alert system. More than 90% of users had confidence on the alert system to reduce medication errors.
In conclusion, computerized order entry with medication alert is an effective tool for modifying physician prescribing practices and substantially decreases the rate of prescribing and transcribing errors. Overall, users are satisfied with the medication alert system.

HPS-P-012

THE MANAGEMENT OF INTRAVASCULAR CATHTER-RELATED INFECTION

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Currently,many kinds of fluid cather such as central venous catheter,CVC and intravenous catheter,IVH are used for the therapy of critically ill patients. Unfortunately,these devices are associated with a number of complications among which infection predominates,CVC.
Catheter-related infection,CRI is a major cause of patient morbidity and mortality.
I'll present the practice in the Saiseikai Matsusaka Hospital about the vein catheter of nutrition support therapy related infection CRI and the role of the pharmacist in the infection control team and the nutrition support team.

HPS-P-013

MULTI-DRUG RESISTANCE GENE MUTATION (MDR-1) : ROLE IN DETERMINING INTERPATIENT VARIABILITY IN SERUM DIGOXIN LEVEL

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Aim:outlining different MDR-1 genotypes(gtp) present in a group of Egyptian patients(pts), assessing the role of different MDR-1 gtp in affecting digoxin serum levels (DSL), studying the effects of different gtp on DSL and on pts' clinical outcome.Methods:37 Egyptian pts suffering from congestive heart failure(CHF) were chosen.Pts were selected to have non-significant variability in their demographics and pretreatment clinical data. 2 venous blood samples were drawn from each pt after reaching steady state condition:1st one for DNA genotyping, 2nd one for serum digoxin assay.Results: 20 pts showed DSL within the therapeutic range,12 pts showed DSL below minimum effective concentration, 5 pts showed DSL over maximum safety concentration, with a significant difference between the 3 groups.MDR-1 genotyping revealed 10 pts carrying the homozygous mutant TT gtp, 27 pts carrying the heterozygous mutant CT gtp, with no pts showing the wild CC gtp. A significant lower levels in mean DSL was found in pts carrying the TT gtp than in those carrying the CT gtp. A significant relation was found between different MDR-1 gtp and outcome of CHF pts, where in the 15 pts who showed significant improvement, 14 carried the CT gtp (i.e. had DSL within the therapeutic range), while 1pt carried the TT gtp. In pts with limited improvement the 2 gtp were equally prevalent.In those who showed no improvement, 4 pts showed the TT gtp, whereas 1 pt showed the CT gtp.Conclusion: Characterization of variations in the MDR-1 gene is an important tool for individualizing doses of drugs that are of its substrates. Identification of MDR-1 gtp was found useful in predicting therapy outcome.

HPS-P-014

SAFETY EVALUATION FOR LONG-TERM ORAL AMIODARONE ADMINISTRATION AT A TEACHING HOSPITAL IN TAIWAN

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Aim:To evaluate the monitoring rate and the frequency of LFTs and TFTs for amiodarone-treated patients, and to interpret results if such monitoring was done. Also to evaluate the drug interaction between amiodarone and digoxin or warfarin.
Method:A patient database of the 435-bed hospital was used to identify outpatients who take oral amiodarone for at least 6 months. A retrospective analysis of medication profile and lab data was performed to identify drug interactions and abnormal lab values. Patients' charts were reviewed to confirm findings. All data were analyzed by the descriptive statistics.
Results:Of 60 patients with age of 68±10.82(mean±SD), 31 patients are male and 29 patients are female. They took amiodarone for 24±17.54 months at the daily dose of 169±80.83 mg. The rate of LFT is 65% at the baseline and 65% after 8.5±5.81 months of therapy. The rate of TFT is 5% at the baseline and 22% after 13.7±11.53 months therapy. All patients' baseline LFTs were normal, but 25% of LFTs were above UNL after therapy. All patients' baseline TFTs were normal, but two patients developed hypothyroidism afterward. Seven patients took digoxin at the same time, but only one patient's dosage was adjusted based on the digoxin level. One patient developed digoxin-related toxicity with nausea and vomiting. Two patients took warfarin with amiodarone, and the dosage was adjusted based on INR.
Conclusion:Elevated LFTs and hypothyroidism exist after long-term amiodarone therapy.Clinical evaluation and periodic monitoring is the key to prevent those toxicities. Digoxin-related toxicity is noticed;therefore, the health care professionals need to be cautious about this combination.

HPS-P-015

UTILIZATION OF THE ANTIMICROBIAL DRUGS IN THE CLINICAL HOSPITAL

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Excessive drug use in Croatia requires continuous professional following of the utilization of the most prescribed and expensive drugs.The aim of the study was to analyse antimicrobial drugs utilization at our hospital according to the ATC.Drug consumption data help us determine the most prescribed groups in order to propose cost saving options.
This was a retrospective study,conducted at our 1160 bed tertiary care hospital in the year 2004.A group of antimicrobial drugs was analysed (ATC-J),which makes 20% of the overall drug consumption.In this class,J01 medicines for the treatment of systemic bacterial infections make 86,33%.Beta-lactamic antimicrobials-penicillins,ATC-J01C,make 24% of this consumption(amoxicillin/clavulanate is the most prescribed medicine at our hospital and makes 69,57% of this group).The other beta-lactamic antimicrobias-J01D make 44,1%,followed by J01X group with11,5%,quinolones J01M with 8,5%,aminoglycosides J01G with 6,3% and macrolides/lincomycins J01F with 5,1%. In group J01D, cephalosporins-J01DA make even 73,5%(cephuroxime is the third most prescribed medicine,which makes 30,2% of that subgroup),and group J01DH-carbepenems with 26,5%(meropenem makes 85,2% of the group).
Based on this analysis,we can conclude that significant cost saving effects and prevention of bacterial resistance is possible by defining measures for the rational use of J01C group of medicines,especially amoxicillin/clavulanate.The same applies for the J01DA,with the use of cephuroxime.Carbapenems are reserve antimicrobials and their use depends on the results of antimicrobial tests performed for each patient.

HPS-P-016

CLASSIFICATION OF THE IDENTIFIED MEDICATION RELATED PROBLEMS (MRPS) IN RECENTLY DISCHARGED ELDERLY PATIENTS USING THE PCNE SYSTEM

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Introduction:Although there's no universal classification of MRPs, classification of it is important when assessing the effectiveness of pharmaceutical care services.There are a variety of ways in which MRPs can be classified.One of the recently developed systems is the PCNE system which was developed by the Pharmaceutical Care Network Europe.
Aim & Method:61 Patients recently discharged from the hospital received structured pharmaceutical care & a second 61 patient group received normal discharge procedure provided by the hospital.Both groups were monitoring for MRPs patients suffered post hospital discharge.The identified problems in both groups were classified according to PCNE system.The basic classification has 6 primary domains for problems, 6 for causes & 5 for interventions.
Results:A total of 240 problems were reported during the 1st home visit, 56% were assigned for the control group. The percent of the identified MRPs in this group increased to 63% during the 2nd visit. Intervention group had 106 problems (44%) during the 1st visit and this number decreased to 37% during the 2nd visit. Side effects were the main problem (19%) during the 1st visit followed by insufficient awareness of the health & disease (18%). The opposite was true for the control group. The total number of identified problems was significantly lower for the intervention group during the 2nd visit.
Conclusion:The PCNE system was chosen because of its ability to classify both causes and interventions related to the identified problems. Also, it's more detailed in pinpointing a broad range of problems due to large numbers of sub-categories included in it.

HPS-P-017

A HOSPITAL BASED DISCHARGE MEDICATION REVIEW SCHEME: HOMER TRIAL

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Introduction:The HOMER trial recently identified an increased readmission rate & number of GP visits with a reduced quality of life in elderly patients who had received a community pharmacist domiciliary medication review.
Method:122 elderly patients to be discharged from the Hospital were randomised into a control or active group.A hospital-based liaison pharmacist counselled patients in the intervention group concerning their medication prior to discharge.Detailed summaries of discharge medication were sent to the GP & community pharmacist.All patients were visited at home by the same pharmacist at 2 & 6 weeks post discharge.Compliance, quality of life (QoL) & medication knowledge were assessed. For the intervention group medication related problems (MRPs) were identified & resolved by liaison with the GP & hospital.
Results:Compliance was higher in the intervention group in both visits.Knowledge was also better. A wide range of MRPs were identified & the total number tended to be lower in the intervention group for 1st visit.The identified ADRs tended to be greater in the intervention group.QoL tended to be higher or no different in the 6 parameters of the NHP. There was no significant difference in readmission at 6 months.
Conclusion:The high compliance rates in both groups couldn't be an explanation for the readmission rates. However, the tendency for increased ADR reported may support the fact that patients had better understanding of their illness, prompting increased help seeking behaviour.Liaison pharmacist familiar with the medical history of the patient may reduce the complexity of care so that decreases admission and increases Quality of Life.

HPS-P-018

DECISION-MAKERS VIEWS OF ACCESS TO HIGH COST MEDICINES (HCMS) IN PUBLIC HOSPITALS IN AUSTRALIA.

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OBJECTIVE: To investigate the perceptions, concerns and attitudes of decision-makers regarding access to HCMs in public hospitals.
METHODS: In-depth, semi-structured interviews were conducted with public hospital senior managers, directors of pharmacy and senior medical doctors in a Sydney Area Health Service. Interviews were audiotaped and transcribed verbatim.
RESULTS: Twenty-four in depth semi structured interviews were conducted. Data analysis identified several categories, which were collated into, inter – related themes (tension, rationing, and equity). The central theme was tension between funding models, equity of access and budget constrains. Decision-makers perceived the current health care system funding model as obstacle to equity of access to HCMs. They were concerned that there were inequities in decisions for individual patients depending on public or private sector hospital status. The majority of respondents identified problems in access to HCMs, and the ethical dilemmas they faced when decided if an HCM should be available, however they had difficulty in identifying solutions. Respondents described that, besides safety, effectiveness, efficacy and cost, ethical principles should be borne in mind when deciding whether a HCM should be available in a public hospital. Most wanted a transparent, accountable, evidence-based decision-making process.
CONCLUSION: The results of this study suggest that decision-makers were concerned about the equity of access to HCMs in public hospitals. They were concerned regarding the process for decision-making and the outcomes of these decisions.

HPS-P-019

CONSUMPTION OF CYTOSTATIC DRUGS ATC L IN CLINICAL HOSPITAL OSIJEK

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Cytostatic drugs and immunomodulators ATC-L participate in overall drug consumption with 21,1% in our hospital. The purpose of the study was to analyze consumption according to ATC classification for the group of drugs L and to point out which subgroups, drugs and wards participate the most and to suggest cost saving options.
Clinical Hospital Osijek has 23 clinics/wards and fourteen of them use this group of drugs. Oncology participate with 60%, internal clinic with 26% and neurology with 11%.
Antineoplactics L01 make 70%, hormone-related drugs L02 1%, immunostimulators L03 28,5% and immunosupressives L04 0,5%. Analisys of the group L01 shows that alkylating agents participate with 4,4%, antimetabolites with 7,7%, plant alkaloids with 34,9%(93,7% of that subgroup make paclitaxel and docetaxel), antitumor antibiotics with 20,8%(epirubicin makes 74,3%) and miscellaneous antineophatics drugs with 32,2%(trastuzumab 22,9%,irinotekan 20,9%, imatinib 13,8%). Analisys of the group L03 shows that 95% of the costs make 5 drugs (interferon beta-1b with 29,2%, pegisterferon alfa-2a with 25,3%, interferon alfa-2a with 21,4%, interferon beta-1a with 10,7% and interferon alfa-2b with 8,4%). Treating of maligant disease requires integral care for the patient, including doctors,pharmacists,nurses,social workers and other professions.Patient should be an active participant,not just the object of the therapy. Therapy guidelines,defined protocols and continuous education of all participants are essential for the rationalization and effective outcome of medical treatment.

HPS-P-020

CONTINUOUS CONTROL OF DRUG USE – A CONCEPT OF RATIONALIZATION OF DRUGS CONSUMPTION

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Clinical Hospital Osijek has 23 clinicals/wards, 19 with beds and all support services. In 2004 we had 392 828 inhabitants/day and, according to financial report for 2004, costs for medicines and other supply material made 20,1% of overall hospital costs. Medicines participated with 9,5% and supply material with 10,6%.
In this work drug consumption was analysed according to ATC classification. By pointing out groups of medicines with significant part in overall consumption and wards that use them, it is possible to recognize mistakes and remove them.In our hospital, ATC group B makes the most significant participation (32,7%), followed by ATC J with 21,1% and group J with 20%. In group B subgroup B05 makes 43,7% and 73,5% of that makes B05B-intravenous solutions (B05BB-electrolytes infusions make 73%, B05BA-glucose and amynoacid solutions 24%). In group L three clinics/wards make significant part (oncology 60%, hematology 26% and neurology 11%). In group J subgroups J01C and J01D make the most of financial costs. This group of drugs is continuously analysed for the reason of possible irrational use and developing bacterial resistance.
Optimizing drug use and adequate education, recognizing irregularities and correcting them is essential for each health care programme. By preventing overuse of drugs and polipragmasy, noticing adverse drugs reactions and decreasing duration of hospitalization made by drugs side effects it is possible to reduce costs of healthcare without limiting patient rights.

HPS-P-021

EFFICIENCY OF GENE DELIVERY ON HEPATOMA CELLS WITH POLYPLEX AND TERNARY COMPLEX

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Aimes: The aimes of this study is to investigate the efficiency of plasmid DNA (pDNA)/polyethyleneimine (PEI) complex (polyplex) and pDNA/PEI/polyanion complex (ternary complex) as gene delivery vectors in a human hepatoma cell line HepG2.
Methods: pDNA encoding luciferase gene was complexed with PEI at various charge ratios. It awa also complexed with both PEI and polyanion, such as carboxymethyl cellulose sodium salt (CMC), sodium alginate (SA) and poly-L-aspartic acid sodium salt (PAA). The cultured HepG2 cells were incubated at 37 oC for various transfection times in the presence or in the absence of fetal bovine serum (FBS) and albumin. Thereafter the cells were lysed for luciferase activity quantum by a luminometer.
Results: When HepG2 was incubated with naked pDNA, luciferase activity was not detected. Polyplex, however, showed high transfection activity. The polyplex prepared at a nitrogen/phosphate ratio (N/P ratio) of +8 showed the highest luciferase activity. The luciferase activity was clearly depending on the transfection time and the incubation time. Various ratios of the polyanions added to the polyplex prepared ternary complex at a N/P ratio of +8. pDNA/PEI/PAA complex showed high transfection activity although a decreased activity was observed with pDNA/PEI/CMC and pDNA/PEI/SA complexes.
Conclusions: Efficient gene transfection in HepG2 cells was achieved by polyplex and ternary complex on the optimal conditions.

HPS-P-022

REVIEW AND ANALYSIS OF MEDICATION ERROR-INDUCED ADVERSE DRUG REACTIONS

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Objective: Preventable adverse drug events (ADEs) are commonly associated with medication errors. Besides, lots of hospitalized patients suffer from renal insufficiency, which is ignored frequently in clinical settings. Therefore, patients are under the potential risk for adverse drug reaction (ADRs) occurrence or even death. An automatic reporting system for ADRs and medication errors provides institutions an opportunity for self-inspection this dilemma. The purpose of this study is to evaluate the cause-effect relationship between adverse drug reactions and medication errors. Methods: From January 2003 to December 2004, all ADRs were extracted from a teaching hospital in southern of Taiwan. Results: Total 122 ADRs were reviewed. Thirty cases (30/122, 25%) were defined as medication error-related ADRs. Reasons for causing these events were as follows: non-performed dosage adjustment based on patient's renal function (19/30, 63.3%), drug-drug interactions (4/30, 13.3%), noncompliance (4/30, 13.3%), and overdose (3/30, 0%), respectively. Especially, 18 out of 19 non-performed dosage adjustment based on their renal function cases occurred in elderly. Conclusions: For medication safety use purpose, we suggest that a patient-specific creatinine clearance calculation or a computerized dosage adjustment warning system should be implanted for reducing or preventing these adverse events in the future.
Key words: Adverse drug events, medication errors, renal insufficiency, adverse drug reaction, elderly

HPS-P-023

AUTOMATING HANDLING OF GOODS WITH AN AUTOMATED STORAGE MACHINE

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Tornado is an automated storage machine installed in 2001 at the central hospital pharmacy, CSA, at Great Southern Hospital in Stockholm, Sweden. Tornado consists of two units with mobile shelves where restricted products are set aside on special shelves and can only be accessed by having an additional security clearing and a password. Castor can handle both traditional shelves as well as automated stock deposits.

The purpose of developing Castor was to simplify and increase efficiency when delivering goods to customers from both in-patient wards and out-patient wards. Castor collects automatically all information from an underlying system. By scanning goods labels, stock place labels and client labels we secure that the right products are delivered to the right customers.

Our experience shows that a combination between Castor and Tornado is the most efficient, generates rationalizing, is economically justified and also ergonomically developed. Castor even supplies a more secure handling compared to today's system, no errors has been detected since startup in September 2003, because the control system for bar codes is built-in, starting from receiving the goods at the pharmacy to gathering products for client distribution. Higher efficiency has also been achieved by automating several work elements through Castor. Due to more compact storing of products in Tornado a better use of the stockroom has also been achieved. For us at CSA, Castor has increased the production by 44.1% in a year. A solely use of the Tornado resulted in improved quality and handling but not at high increase in productivity as combined with Castor.

HPS-P-024

TOTAL PARENTERAL NUTRITION SUPPORT FOR PRETERM INFANTS

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Aim: This study evaluated the total parenteral nutrition (TPN) prescription at the Pediatric Intensive Care Unit (PICU) at Chang Gung Memorial Hospital, Taiwan, to identify the logic of its prescription and thereby improve the quality of infant TPN.
Method: A review was performed of all PICU preterm infants supported with parenteral nutrition solutions between January 1 and June 30 2004. The TPN prescriptions and other relevant data from electronic medical records were gathered via the hospital's website and analyzed by retrospective longitudinal study.
Results: Fourteen preterm infants (9 male, 4 female), between 25–36 weeks old, were administered TPN for 4–45 days. The percentage of cases that met the recommended daily allowance and requirements (RDA) were as follows: 86% for individual dextrose; 93% for amino acid; 100% for lipids; 93% for total calories; 93% for calcium; 100% for phosphorus; 79% for sodium; and 14% for potassium. During nutrition support care, 86% and 79% of these cases had normal serum calcium and phosphorus levels, respectively, and 21% and 64% of the cases showed decreased serum sodium and potassium, respectively.
Conclusion: Administration of parenteral nutrition to the infant has decreased morbidity but has been associated with the development of complications. Thus, it is necessary to closely monitor nutritional values obtained by biochemical examination. When there is an electrolyte imbalance, a pharmacist can promptly suggest that a doctor adjust electrolyte content in infusion fluids. Monitoring the laboratory data support can prevent complications and achieve rationality, suitability and validity of care.

HPS-P-025

TWO-YEAR COMPARISON OF ANTIMICROBIAL SPECTRA

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Aims: In vitro activities of antibiotics against common bacterial isolates were analyzed. Susceptibility rates were collected from all adult patients during the period from 2003 to 2004. First, 2004 data were compared with antimicrobial spectra in the 34th edition of the Sanford guide to antimicrobial therapy. Second, susceptibility rates from 2003 and 2004 data were compared to determine chronological changes.
Methods: Disk diffusion tests were performed.
Results: The susceptibility rate of Staphylococcus aureus to oxacillin was lower than that in the Sanford guide. Ampicillin showed a decreased potency against Enterococcus faecium, H. influenzae, E. coli and Proteus vulgaris. Enterococcus faecium and H. influenzae to ampicillin were lower than the 2003 data. Piperacillin showed a decreased potency against E. coli, Aeromonas hydrophilia and Bacteroides fragilis. Aeromonas hydrophilia and Bacteroides fragilis to piperacillin were lower than the 2003 data. Cefepime showed a decreased potency against Enterobacter aerogens and Serratia marcescens. The susceptible rate of Enterobacter aerogens declined from 100% (2003) to 25% (2004). That of Serratia marcescens declined from 63% to 14%. Erythromycin showed a decreased potency against gram-positive organisms.The susceptibility rate of Acinetobacter baumannii to ceftazidime, ciprofloxacin and cefepime were only 17%, 15% and 19%, respectively.
Conclusions: Inappropriate uses of extended spectrum antibiotics promote the development of drug resistance. Knowledge of antimicrobial susceptibility is useful to design strategies that maximize therapeutic efficacy of drugs and minimize emergence of resistance.

HPS-P-026

QUALITY IMPROVEMENT OF PHARMACY PRACTICE IN ALEX.UNIV.HOSPITAL &RESULTING CLINICAL AND FINANCIAL OUTCOMES

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Before 2002,hospital pharmacist role involves dispensing of medications without medication related care with limited pharmacist educational activities.
As for 2002,delivery of pharmaceutical care services is diff.units: 1-oncology. 2-haematology&bmt. 3-i.c.u. 4-toxicology.
These services include:
-medical chart review,reporting drug interactions,avoiding adverse reactions and medication errors.
-proper cytotoxic drugs handling&disposal
-educational activities for patients &working staff
-monitoring of poisons in bld. Using viva.
*outcomes includ:
1-clinical(related to the quality of life of the pt.&optimising dose with lower possible side effects
2-financial(saving medication cost)
3-documentary(full documentation of pt. Data)
4-sharing in international trials(alimta)
*future plans include : tpn unite , pharmacokinetic lab.,
Clinical pharmacies in all hospital departments
We have the power to be the best in our career with open budget &we can believe that what we made in only 3 years is something to be proud of &others in arabian world can have benifits from this still young experience &we can get more experience by international participation

HPS-P-027

THE RESEARCH OF HIGH RISK DRUGS SAFETY REGULATION IN REGION HOSPITAL

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gh Risk Drugs Safety Regulation' is a quite high standard. All the specialists ncerned can not accept any kind of mistake to occur. In this study, the achieving rate the former measure (Comparison Group) and the later measure (Experimental roup) is a little bit different, it is 87.39% and 100% separately. However, the wrong dicine rate of the two groups is all 'zero'. It means that all the pharmacists and nursing ff are doing very careful job and carry out medicine-safety strictly. It is nothing to do h the education and training.

HPS-P-028

MULTICENTRE, MULTINATIONAL DISTANT LEARNING POST-GRADUATE DIPLOMA/MASTERS DEGREE IN CLINICAL PHARMACY

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A new Irish MSc/Higher Diploma in Clinical Pharmacy course by distance learning is expanding the range of options for pharmacists in Ireland and elsewhere who wish to acquire post-graduate qualifications in clinical pharmacy. Previously Irish-based pharmacists who wanted to undertake further studies in clinical pharmacy by distance learning had to look to courses outside the country and this has been the case in many other countries also.

This new course is innovative in many respects. It is a joint collaboration between the School of Pharmacy, University College Cork (www.ucc.ie) and the Centre for Advanced Clinical Therapeutics (www.cact.ie) based in St James's Hospital, Dublin, Ireland. It is the first distance learning clinical pharmacy course in Europe to utilise teleconference tutorial sessions to complement course materials. Extensive use is also made of Internet and email to teach and communicate.

In terms of content this MSc/Higher Diploma clinical pharmacy course represents a move away from rote-book learning into the application of knowledge in real-life situation. Students are also encouraged to think about their contribution to the broader healthcare system. As well as providing comprehensive training in clinical pharmacy, covering all major therapeutic areas, the course also aims to equip students with skills and knowledge necessary to develop new pharmacist-led services in their hospitals. Reflecting the strong multidisciplinary focus within the course, the module leaders who run the teleconference tutorial sessions, include senior clinical pharmacists, medical consultants, health economists, biostatisticans and clinical nutritionists.

HPS-P-029

CHOOSING PRESERVATIVES FOR CARBOHYDRATE-CONTAINING ORAL GEL PRESERVATION

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Purpose: Glucose and sucrose-containing (15% each) oral gels were formulated, intended for managing the phase I of hypoglycaemia in patients suffering from type II diabetes mellitus. Cellulose derivatives were used as gelling agents: 3.5% sodium carboxymethylcellulose (NaCMC), 2.5% hydroxypropylmethylcellulose (HPMC) and 2.25% hydroxyethylcellulose (HEC). As the preparations contain 30% carbohydrates in a hydrosoluble oral gel, we tested which preservative and in what concentration should be utilized for obtaining a product of a satisfactory microbiological quality (category 3A according to Ph.Eur IV), with a minimum shelf life of 60 days.
Methods: pH value was determinated by potentiometry, directly immersing the pH-meter electrodes into the samples. Biological appropriateness was tested by applying 0.1 ml of each sample with a sterile syringe onto blood agar and Sabouraud agar, smearing it with a sterile loop, and incubating for 48 hours at 370C.
Results: No bacterial strains were detected in non-preserved samples, however in each of them fungal strains were identified: Penicillium in NaCMC and HEC, Candida in NaCMC and HPMC and Verticillum in HPMC. Measured pH values of the samples are as follows: NaCMC, 7.3; HPMC, 4.6, and HEC 5.8. Samples were made containing 0.1% parabens, which maintains best antimicrobial activity in the pH 4 to 8 range, where our samples pertain. Testing for biological appropriateness was performed on days 1, 30 and 60 after manufacturing and no bacterial or fungal strains were isolated.
Conclusion: Parabens content of 0.1% is sufficient for preserving oral hydrogels containing carbohydrates, if NaCMC, HPLC or HEC are used as gelling agents.

HPS-P-030

EFFECT OF TANNINE UPON THE STABILITY OF UNGUENTUM CONTRA PERNIONES

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Formulae magistrales et reagentis(FM 79) prescribe contents including tannine and ichthamol, in the procedure of manufacturing Ung. contra perniones.
AIM: test effect of tannine on preparation quality and stability, depending on the way tannine is admixed into the base.
METHOD
Sample manufacturing: a) procedure prescribed by FM 79; b) mixture of water-free lanoline and vaseline is made. Tannine is dissolved in water and admixed to the base. Further procedure is identical to the original one; c) procedure is identical to b); only the tannine solution is admixed after all the other active substances are admixed.
change follow-up: performed organoleptically and microscopically.
RESULTS
a) sample has good spreadability and homogenous structure. b) grainy structure is formed on skin, drops of non-emulsified water with dissolved tannine are detected, c) on application upon skin, sticky grains are formed. Coalescents, aggregates and areas of 'free' water are seen.
DISCUSSION
Method a): tannine is suspended in the base; dissolution is delayed, achieving acid medium for incompatibility reaction with ichthamol. If tannine is first emulsified into the mixture of anhydrous lanoline and vaseline (method b), reaction between tannine and ichthamol will have slower rate, and if tannine is added in the end (method c), instantaneous reaction between ichthamol and tannine disables emulsification, forming 'free' water areas and an instable emulsifier layer on contact surface of two phases.
CONCLUSION
Incompatibility between tannine and ichthamol does exist and is the cause of poor spreadability of Ung. contra perniones. Destabilization rate depends on technological procedure.

HPS-P-031

ASIRIN USE AND RECOMMENDATION FOR PATIENTS WITH DIABETES AT A MEDICAL CENTER IN EASTERN TAIWAN

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Aims The American Diabetes Association has recommended aspirin therapy for the diabetic individuals since 1997. However among 3790 diabetic patients treated at a medical center in eastern Taiwan, from January to June 2004, only 232 (6%) received additional aspirin therapy. To promote the aspirin therapy for patients with diabetes, our study examined the practices and the use of aspirin therapy for hospitalized patients in this medical center. Method→The study consisted of hospitalized diabetic patients, who have at least one diabetes-related ICD-9 code (250.x) or receive at least one hypoglycemics during January-March 2005. Recommendations for aspirin therapy (100mg/day) were pharmacy-directed intervention via physicians. The compliance and the effectiveness were examined and analyzed with SPSS program. Results→A total of 921 patients with diabetes were identified. 55 patients had been given aspirin therapy and 21 patients were intolerable to aspirin. Aspirin therapy was then recommended to a total of 844 patients during clinical intervention; 701(83%) accepted and were given daily aspirin. 655 discharged patients continued to receive aspirin therapy, and then 35 of 46 outpatients had accepted follow-up telephone intervention for the use of aspirin.Conclusions→A pharmacy-directed intervention increased prophylactic aspirin therapy in patients with diabetes from 6% at baseline to 83% at the end of the study. Most clinicians agree aspirin as an important treatment for patients with preexisting coronary disease. This intervention provided appropriate assistance to clinicians for the prevention of many cardiovascular events and deaths.

HPS-P-032

EFFECT OF A COMPUTER ALERT SYSTEM ON PRESCRIBING PRACTICE AND QUALITY OF HEALTH CARE IN A PAKISTANI TEACHING HOSPITAL

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Study assesses the impact of an inpatient Computerized Physician Order Entry (POE) system on prescribing practices. Department of Pharmacy Services developed a system in collaboration with Information Technology of the Aga Khan University Hospital that alerts the dose adjustment when physician enters the order of drugs requiring the renal adjustment for patients whose serum creatinine is inappropriate. A six-month Pre & Post system modification data of calls on Drug Information Center was compared to see the impact. Before the system modification 420 calls were logged for renal dose adjustment in six months. After system modification number was increased to 1100 calls in six months that shows a 2.6 times increase in physician's alertness for adjusted dose. Similarly as the Physician enter the order for Vancomycin or Meropenem, the system displays the restriction policy approved by Pharmacy & Therapeutic Committee. A one-month pre and post system intervention data of the number of prescription was generated through system to see the impact. Before intervention 264 prescriptions of vancomycin were recorded in all wards of hospital. This number was reduced to 166/month after the intervention. This shows a 1.6 times decrease in vancomycin prescribing. In this regard hospital saved US $ 78933 (1 US $ = 60 Pak Rs.) /month. Similarly for meropenem the prescription numbers dropped to 70 from 166/month. This shows a 2.4 times decrease in the meropenem prescribing and in this regard the savings were US $ 10298 (1 US $ = 60 Pak Rs.) /month. POE powered by decision support alert systems is an effective tool for improving physician prescribing practices and quality of health care.

HPS-P-033

FACILITY DESIGN FOR MANUFACTURE OF CELL THERAPY PRODUCTS

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U.S. medical centers and hospitals manufacturing cell and gene therapy products, including products for clinical trials, are required by the Food and Drug Administration to follow current Good manufacturing Practice (cGMP) regulations. This provides assurance that there is consistency between lots and that adequate controls are in place to assure the safety, efficacy and potency of the product. These regulations also apply to the facilities and equipment in which the product is produced. Although these requirements are clearly identified, similar requirements are still under discussion in Europe. It should be noted that US-FDA does allow for a sliding scale of GMP compliance depending on the phase of clinical study---with validation and document completed during Phase 3 or commercial product. This allows for a reduction in costs of manufacture and handling of the product in its early studies. The design of these facilities for manufacture should be based on their intended use. Materials of construction, heating, ventilation and air conditioning (HVAC) systems; both for containment and product protection; aseptic processing area requirements; biosafety levels; gowning practices, multiuse issues and environmental monitoring will be discussed with emphasis on ex vivo transduction of patient's cells and possible vector preparation if needed. GMP requirements in Europe with those in the U.S. will be compared and discussed.

HPS-P-034

A STUDY ON THE USAGE OF DRUGS THAT AFFECT THE RENAL FUNCTION OF CRITICALLY ILL PATIENTS

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AIMS: Alterations of renal function are constantly associated with decreased in renal blood flow, renal mass and creatinine clearance. These changes have a major impact on patient management in particular with respect to drug therapy.
METHODS: This retrospective study was conducted to review the usage of drugs that affect renal function, the relationship between the drugs and creatinine clearance and the degree of dose adjustment practice in the critically ill patients. Forty-two subjects (n=42) have been enrolled in the study. Drugs that known to cause increase in renal function will be classified as positive effect drugs whilst drugs that are known to deteriorate renal function will be classified as negative effect drugs.
RESULTS: Creatinine clearances of the subjects were higly reduced in both affecting drugs usage. The effects of positive effect drugs on improving the renal function and the effect of negative effect drugs on further deteriorating the renal function of the ICU subjects were not significantly showed any pattern. Dosage modifications of antibiotics among renal dysfunction patients in this studied were not being performed optimally based on established references.
CONCLUSIONS: The effects of drugs on the renal function were unpredictable, thus, close monitoring of renal function for critically ill patients with multiple drugs therapy is needed.

HPS-P-035

CONSUMPTION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN MILITARY MEDICAL ACADEMY IN BELGRADE IN THE PERIOD OF 2001-2004

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Introduction: Nonsteroidal antiinflamatory drugs (NSAID) are indicated for pain and ...ss in inflammatory reumatologic diseases, the short-term management of pain in ...arthritis and for acute pain, inflammation and fever in various conditions. NSAIDs ...frequently used in our hospital. The aim was to measure utilisation of NSAID in ...ary Medical Academy in Belgrade, for the period from 2001 to 2004.
Material and methods: NSAID utilisation was analysed using the ...ATC methodology. We included NSAIDs with the ATC code M01A. The annual ... of DDDs was used to categorise the NSAIDs consumption. It was DDD/100 ...ays. Results: We had 40.77 DDD/100 bed-days in 2001, 41.36 DDD/100 bed-... 2002, 36.64 DDD/100 bed-days in 2003 and 35.41 DDD/100 bed-days in 2004. ...ac was the most frequently used drug, with the DDD% 87.74% in 2001, 78.02% ...74.50% in 2003 and 70.43% in 2004. It is also the cheapest drug. Ibuprofen, the ...ug regarding GI toxicity, was not the most prescribed. No coxibs have been ...
...ow that consumption of NSAIDs has reduced from 2001 to 2004. This is ...c trend, in the light of serious adverse effects which could be caused by ...d use and use of large daily doses of NSAIDs. The coxibs are new and ...e drugs. The DDD price for celecoxib is 35 times higher than DDD price for ...
Conclusion: We should reduce the use of nonselective NSAIDs and follow ...in use of selective COX2 inhibitors.

Keywords: non-steroidal anti-inflammatory drugs, drug consumption

HPS-P-036

EVALUATION OF THE DIGOXIN TOXICITIES RELATED TO SERUM DIGOXIN CONCENTRATION IN A MEDICAL CENTER IN TAIWAN

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Aims:
To evaluate the incidence of digoxin related toxicities in variant digoxin serum concentrations.
Method:
This retrospective chart review was conducted from September 2004 to December 2004. Patients who checked serum digoxin concentrations(SDCs) during this period were all included. We divided our patients into 5 groups:SDC less than 0.5 ng/ml, 0.5 to 0.99 ng/m, 1.0 to 1.49 ng/ml, 1.5 to 2.0 ng/ml and greater than 2.0 ng/ml. We evaluated the association between SDCs and digoxin related toxicities. The digoxin related toxicities include : premature ventricular contractions, second or third atrioventricular block, sinus bradycardia<60 beats/min, nausea, vomiting, anorexia, diarrhea, weakness and headache. The digoxin related toxicities are defined as disappearance after a week of digoxin withdrawal or dose reduction.
Result:
There were 192 patients included in our evaluation. Of the 192 patients, 29 patients had SDCs greater than 2.0 ng/ml and 19 patients had SDCs of 1.5 to 2.0 ng/ml. In the group of SDC greater than 2.0 ng/ml, 21 patients had digoxin related toxicities (72.41%, n=29), but in the group of SDC of 1.5 to 2.0 ng/ml, just 6 patients had digoxin related toxicities (31.58%, n=19).
Conclusion:
According to the preliminary result, a greater proportion of patients who had higher SDCs had higher rate of Digoxin related toxicities. This evaluation is still ongoing and will be finished on 30th April 2005.

HPS-P-037

HEALTH INSURANCE IN FLUID MANAGEMENT OF FRACTURED EXTREMITY

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Objective: This retrospective study discusses a routine work about the fluid management of Diagnosis-Relate-Groups fractured cases in the regional hospital. There are extensive views to the whole national health insurance system.
Materials and Methods: There were totally 6017 cases, during January-2000 and December-2003, accepted orthopedic operation. The Diagnosis-Relate-Groups cases were about 5902 (98%) people, the rest 115 (2%) cases got more severe condition, combined trauma and poor nutrition. The blood samplings were done before and after the operation. Replacement of prior fluid losses based on known electrolyte composition of the body fluid, serum electrolyte measurement, and clinical assessment of intravascular volume status.
Result: In Diagnosis-Relate-Groups cases, there was no obvious change of electrolyte. Average maintenance fluids were 1988.67 ml (1000-3000 ml/day) and maintain urine output of 0.5-1.0 ml/kg/hour (1000-1500 ml) reasonable. Hyponatremia were the most common condition in the non-Diagnosis-Relate-Groups cases. The Asia infectious crisis, severe acute respiratory syndrome (SARS), was a major influence about the hospital data and prolongs hospital days (from March-2002 to December-2002).
Conclusion: Majority cases need the routine fluid input for intra-vascular dosage but the severe cases need the exactly fluid support for life saving even the nutrition support. The medical budget expenses year by year, the government must reasonably formulate the procedure to keep the quality of the health care. But it is very hard work.

HPS-P-038

INTRODUCTION OF A RE-CHECK METHOD TO ENSURE ACCURACY OF POWDERED DOSAGE FORMS OF TRADITIONAL CHINESE MEDICINES PRIOR TO DISPENSING

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Purpose: The aim of this study is to introduce the use of a re-checking process to assure accuracy of powdered dosage forms of traditional Chinese medicines compounded prior to dispensing to patients within the Out-Patient Department (OPD) at our hospital. The objective of this process is to assure improvements in patient safety and achieve potential reductions in dispensing errors.
Method: A pre-weighed checking card was designed as a tool in this process. The checking card was designed to assist the pharmacist to ensure that the correct weight of the mixed CCM was assured during the last step of the compounding process prior to dispensing. Using the checking card, the pharmacist will re-examine the mixed CCM by total weight compared with the total weight of the package. If there is a ±2% variation in the weight of the CCM, the prescription is re-dispensed correctly with the correct amounts, before being dispensed to the OPD patient.
Results: Following a ten-month study with the re-checking process, it was found that the rate of prescription errors detected was 0.023%. The errors were traced to pre-packing processes and the delivery or weighing steps in the dispensing processes.
Conclusion: Preliminary findings suggest the need to re-check or re-examine the dispensing of traditional Chinese medicines powdered dosage form prescriptions for accuracy in some or all medical dispensing clinics or hospitals. These steps would potentially enable healthcare professionals to verify that patients are receiving the right drug at the right dose.

HPS-P-039

THE COMBINED IMPACT OF PREVENTION CATEGORY AND CO-PAYMENT TIER ON STATIN NON-ADHERENCE AND DISCONTINUATION

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The objectives of this analysis were to determine if statin non-adherence and discontinuation rates differ between levels of a combined prevention category/co-payment tier variable. The electronic medical and pharmacy records of managed care enrollees age 18 to 64 who filled at least 2 statin prescriptions during the study period were reviewed; n = 2,881. Patients were categorized as secondary or primary prevention based on published risk criteria and were further stratified to groups with monthly co-pay tiers of <$10 or $10-20. Patients with cumulative multiple refill-interval gap (CMG) >10% were considered non-adherent. Discontinuation was defined as cessation of refills prior to the end of available claims data. Chi-square and Cox proportional hazard were used to analyze non-adherence and discontinuation, respectively. In bivariate analysis, a significant difference in non-adherence was observed across the prevention category/co-pay tier variable. Non-adherence in secondary/<$10, secondary/$10-$20, primary/<$10, and primary/$10-$20 were 50%, 61%, 53%, and 63%, respectively. Secondary/<$10 patients were least likely to discontinue statin therapy (significantly < primary/<$10). Though not statistically different, secondary/<$10 trended toward lower discontinuation rates than secondary/$10-$20 and primary/$10-$20. Co-payment tier appears to have a significant impact on non-adherence and discontinuation rates, particularly in the secondary prevention population in whom the benefits of statins are most important. Strategies such as benefit based co-payment systems may be indicated in order to mitigate the negative impact of co-payment in the highest risk patients.

HPS-P-040

A TRADITIONAL HERBAL MEDICINE SHO-SAIKO-TO AFFECTS EXPRESSION AND FUNCTIONAL ACTIVITIES OF PEPT1 AND MRP2 IN CACO-2 CELLS

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Aim: It has been known that many kinds of herbal medicines can cause pharmacokinetic interactions with synthetic drugs. We have already demonstrated that Sho-saiko-to (SST), a commonly prescribed herbal medicine, upregulates MDR1 leading to the increased activity of MDR1. The purpose of this study is to clarify the effects of SST on the other transporter proteins PEPT1 and MRP2 in Caco-2 cells.
Methods: Caco-2 cells were cultured according to the conventional method and exposed to SST in the culture medium for 1, 2, 7 and 14 days. The levels of PEPT1 and MRP2 mRNA in the cells were determined with the real-time PCR procedure. The uptake experiments of radiolabeled Gly-Sar and methotrexate in the cultured cells were carried out to evaluate the functional activities of PEPT1 and MRP2, respectively.
Results and Discussion: It was confirmed that SST exposure did not change the viability of the cells at all. In the expression level of PEPT1 mRNA, 50% to 100% increase was observed by 1- or 2-day exposure to SST, while there is no significant change in the cells treated for 7 or 14 days. Uptake amounts of Gly-Sar were significantly increased by SST exposure for 1 or 2 days, indicating the increased activity of PEPT1. On the other hand, enhancement of MRP2 mRNA expression was observed only in 14-day exposure. In this exposure condition, the uptake of methotrexate was also increased by 50%, meaning the reduction in the activity of the efflux transporter MRP2.
Conclusions: These results indicate that SST can upregulate PEPT1 expression, resulting in the enhanced function, and that SST has the induction effect on MRP2 expression.

HPS-P-041

DRUG INFORMATION LABELING ON PRESCRIPTION MEDICINE BAG

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Introduction: The objectives of this study were to advance patient-centered pharmaceutical care and provoke the ideal drug information labeling on prescription medicine bag. Method: This is a prospective study. The layout of the bag is 18.6cm width x 20.3cm long. All labeling text items and description are presented in both Mandarin and English; the new font size is 25% larger and neatly printed. Total labeling items included the bag number, patient name and history number, administration dosage, drug name, appearance, clinical uses, other instructions, physician, pharmacists, division, date & time, expiration date, duration and quantity, and additional information. Result: The satisfactory resulted an 11% (74-85%) increased from February to May of 2004 and 13% (74-87%) increased in August when compared with the previous edition. The total time spending on communication between clinical staffs and patient counseling were decreased. About 1.6 staff pharmacist or an average 3,328 working hours or NTD $2.32 millions salary saved could be transferred and focused on clinical pharmaceutical services. Discussion: The automated labeling system serves in helping pharmacists to minimize handwriting omissions and most importantly to dispense accurately. All labeling descriptions are carefully deliberated and weighed on the relative importance between patient safety and treatment efficacy. Conclusion: Taipei VGH is the pioneer healthcare institute to implement the bilingual labeling innovation significantly facilitated our foreign friends and native citizens in properly taking their medications.

HPS-P-042

THE USAGE EVALUATION OF CELECOXIB

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Aims:
Base on a medical center medication usage data, analyzing gastrointestinal, renal and cardiovascular system adverse reaction associated with long term use of celecoxib. Also compared those information found from literature research and our hospital data to establish the usage guideline for celecoxib.
Methods:

Record blood urea nitrogen, serum creatinine, hemoglobin, and hematocrit data changed before and after celecoxib used for rheumatoid arthritis patients from our rheumatologic clinic. Other data recorded include the time for adverse reaction occurred, patients' past medical history, concurrent medication used and treatment of adverse reaction occurred during study period.
Results:

During study period (Jan. 2003 to Feb. 2005), we found 854 rheumatoid arthritis patients use celecoxib. Adverse reaction were seen in 84 patients: 72 (8.43%) cases related to gastrointestinal system, 6 (0.7%) cases related to renal system and 4 (0.5%) cases related to cardiovascular system. The dose and using period of celecoxib and incidence for gastrointestinal adverse reaction are irrelevant. For those patients have past medical history of peptic ulcer are easier to have recurrent peptic ulcer after taking celecoxib.
Conclusion:

Base on this evaluation, the adverse reactions related to renal and cardiovascular systems are not very often. With normal dosage and within 2 years usage of celecoxib can still be safe. But safety of higher dose and longer period usage still need more data to evaluate.

HPS-P-043

DESIGNING DOSE REGIMEN FOR TEICOPLANIN BY USING NOMOGRAM

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[Aims] Teicoplanin (TEIC) is one of the glycopeptide antibiotics and has been very useful to cure Methicillin-resistant Staphylococcus Aureus (MRSA) infection in Japan. Since TEIC has a long-term half life, many reports suggested that 400mg of TEIC should be administered twice in the first day as a loading dose to quickly increase its level up to therapeutic range (10-20 μg/mL). But there are little reports about the lasting dose for the following days. In this study, we established nomogram to determine the lasting dose of TEIC and evaluated its usefulness by simulation analysis.
[Methods] Nomogram was estimated by values of creatinine clearance according to the Dettli-Cockcroft-Gault formula and population parameters of 'Teicoplanin TDM analysis support software Ver 1.2'. The serum levels of TEIC were measured by fluorescence polarization immunoassay.
[Results] We simulated trough levels of TEIC by using the parameter of 20 patients who had been treated with TEIC. Using by nomogram as a lasting dose for each patient, the simulated trough levels of TEIC in 15 patients were within the serum level of 10-20 μg/mL, but no more than 20 μg/mL in any patients. The lowest trough level among other 5 patients was 7.3 μg/mL.
[Conclusions] The maintained serum levels of TEIC in most patients were simulated within 10-20 μg/mL, which is an effective level, by using our nomogram. Therefore, our nomogram was very useful to determine the dose of TEIC as a lasting dose for most of MRSA patients.

HPS-P-044

NONOLIGURIC ACUTE RENAL FAILURE ASSOCIATED WITH CELECOXIB

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OBJECTIVE: To report a case of nonoliguric acute renal failure associate with celecoxib therapy.
CASE SUMMARY: A 71-year-old woman with underlying hypertension, recent multiple infarctions with right hemisphere, chronic renal insufficiency, and gouty arthritis was treated with aspirin, allupurinol, magnesium, seenoside, enalapril, celecoxib. Ten days after celecoxib 200 mg/day initiating therapy; she developed nonoliguric acute renal failure include increased serum potassium, and serum creatinine at least two-fold. Celecoxib was discontinued. Renal function improved, but had not returned to baseline.
DISCUSSION: Patients considered at high risk for acute renal failure, such as those treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, hypovolemia, the elderly, and patients with congest heart failure, diabetes mellitus, hypertension, and chronic renal insufficiency. Only one case of nonoliguric acute renal failure have been reported after fourteen days therapy with celecoxib. But renal function had not returned to normal after 30 days.
CONCLUSIONS: Selective cyclooxygenase-2 inhibitor celecoxib may causing reversible, nonoliguric, acute renal failure, or hyperkalemia, especially in high risk patients. Although renal function improves after discontinuation of celecoxib, but it may not return to baseline.

HPS-P-045

SUSPECTED WARFARIN RELATED INTRACRANIAL HEMORRHAGE

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OBJECTIVE: To report a case with intracranial hemorrhage (ICH) related to warfarin therapy.
CASE SUMMARY: A 49-year-old woman who had been taking warfarin therapy for underlying rheumatic heart disease, and replaced prosthetic heart valve include mitral and aortic valve 10 years ago. She was sent to emergency department with suffered nausea, vomiting, seizure attacked, and unconsciousness. She was found to have a right frontal hematoma with 30mm in diameter on brain computed tomography (CT). Her international normalized ratio (INR) was 2.37 on admission. Warfarin was stopped and anticoagulation was corrected with fresh frozen plasma and vitamin K therapy. Further evaluation by CT angiography and no vascular abnormality. She was discharged restard warfarin after two weeks who recovery completely was treated with support care and had not surgical intervention.
DISCUSSION: Mechanical valve prosthesis patients who required intensive long-term anticoagulant therapy, and keep INR in 2.5-3.5. Anticoagulants treatment increases the risk of ICH 8-10 fold. Among patients given anticoagulant therapy during longer periods, the annual risk of ICH was 1% to 2% and mortality rate was 44% to 68%. Management of anticoagulant-related ICH requires cessation of anticoagulants, administration of vitamin K.
CONCLUSIONS: Patients with mechanical heart valve had been suffered ICH maybe maintaining the INR between 2.0-2.5 and needed strict monitor.

HPS-P-046

HYPOALBUMINEMIA IN PATIENT OF TRAUMATIC COMPARTMENT SYNDROME.

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Background: We have recently discovered that postoperative complications of compartment syndrome related to hypoalbuminaemia.
Objective: The study was performed to elucidate the risk factors and complications of the patients who received the operation in order to release traumatic compartment syndrome.
Materials and Methods: This is a retrospective study. From January-2000 to December-2002, we have collected 4392 cases of fractured limb treated with open reduction and internal fixation. There were 615 cases received further fasciotomy due to acute compartment syndrome. Before and after the operation, the blood samplings of the patients were routine taken for the albumin level, the electrolytes, and blood cells count.
Results: Most of patients suffered from hypoalbuminaemia with average level of 2.9 ±0.43 (from 1.8 to 3.9) g/dl in the cases who received further fasciotomy. Beside the prolong hospital days, there were complications noted after the operation of fasciotomy including delayed wound healing (52%), ilius (10%), urinary tract infection (5%). The improved conditions of the patients were noted including ordinary activity, subsided of edema of the patients who received intravenous human albumin for nutrition support after the operation.
Conclusion: Once the major operation done with massive body fluid lose, the albumin level of the human blood could have fallen below the standard level. The parenteral nutrition support to the patients with the human albumin seems play an important part of the recovery of the healing.

HPS-P-047

EVALUATION FOR PRESCRIBING PATTERNS OF MAJOR DEPRESSION PATIENTS IN A MEDICAL CENTER

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Aims: The study was to evaluate the prescribing patterns of antidepressants in a Medical Center.
Methods: Data were derived from the Psychiatric department in a medical center. The study included all outpatient users of antidepressants in the Psychiatric department in a medical center from October 1, 2003 to March 1, 2004.
Results: There were 888 patients in the research of the study. Paroxetine was the most used antidepressant (45%). 49.5% the patients stopped his first antidepressant in 1 month, The percentages of patients who had continuously used his first antidepressant for 4 months and 6 months, were 23% and 20.7% respectively. The range of effectively continuous treatment rate (ECTR) of the antidepressants was 9.4~66.7%. The averages of defined daily dose (DDD) of the antidepressants were all smaller than 1.00, except fluoxetine (1.13) and venlafaxine (1.17). The DDD (0.27) of trazodone was the lowest of all. The reason that illness was not improved, for patients to stop continous using first antidepressant of trazodone was the secondary high (22.7%) among all.
Conclusion: There was not significantly different among the ECTRs of antidepressants, except bupropion (9.4%, $P < 0.05$). We suggest that the doctors may increase the dose of trazodone in major depression patients to improve the efficacy of treatment.

HPS-P-048

FACTORS INFLUENCING THE HEALING OF PRESSURE ULCERS

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Purpose: There are many reports on risk factors for formation of pressure ulcers. However, there are few studies of factors influencing the healing process of an existing pressure ulcer. The aim of this study is to explore factors relating to the prognosis of existing pressure ulcers.
Method: Hospitalized patients in whom pressure ulcers had occurred after hospitalization were enrolled in this study. Patients were classified into two groups: one group consisted of patients whose pressure ulcer had improved for 3 months (the improved group), and another group consisted of the remaining patients (the unimproved group). Their pressure ulcers were evaluated by scoring depth, exudate, size, inflammation, granulation tissue and the necrotic tissue of lesions (the DESIGN score). The DESIGN score, laboratory data, and active daily life (ADL) score were collected before and after formation of the pressure ulcer.
Results and Discussion: The factors influencing the healing of pressure ulcers were the ADL score, route of nutrition intake, serum cholesterol level and hemoglobin level. The mean cholesterol level of patients in the unimproved group before formation of the pressure ulcer was statistically lower than that in the improved group. This suggests that a patient's cholesterol level before formation of a pressure ulcer may be a prognostic indicator of healing of an existing pressure ulcer.
Conclusion: Pressure ulcers may be expected to repair poorly in patients whose cholesterol level is lower than the normal range. Pharmacists should concentrate on the care of pressure ulcers in association with other caregivers.

HPS-P-049

TO STUDY THE INTEGRATION OF COMPUTERIZED-SYSTEM FOR KNOWLEDGE MANAGEMENT IN A MEDICAL CENTER

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Aims: In order to create the advantaged competition of hospitals, it is important to know how to manage the knowledge of pharmaceutical cares. It is necessary to set up and computerize the program of pharmaceutical standard procedures. The program will help the Bureau of National Health Insurance to decrease the cost in medications and increase the quality of patient care.
Methods: During January to October 2004, we designed the program of pharmaceutical standard procedures and used Visual Foxpro to design document center of pharmaceutical cares. The categories include drug utilization evaluation(DUE), total parenteral nutrition(TPN), therapeutic drug monitoring(TDM), drug information service(DIS), patient education and consultation in diabetes and renal transplantation, medication errors, database of drug information, updated clinical experiences, evaluation of serum creatinine clearance and dosage adjustments.
Results: During September to December 2004, pharmacist interventions of all the pharmaceutical cares categories are 1584 entries in the document center. These include DUE 1001 entries, TPN 61 entries, TDM 156 entries, DIS 134 entries, education and counseling of diabetic patients 206 entries and medication errors 26 entries. We estimated that these pharmaceutical interventions may have the potential to save about NT$ 2405998.81 on medications. The system is user friendly and easy to perform search and analysis in the database for pharmaceutical cares.
Conclusions: The system serves not only a great resource for pharmacists acquiring information from others but also a useful pharmaceutical intervention tool associated with medication cost saving.

HPS-P-050

PRIOR INSPECTION INJECTION COMPOUNDING OF MEDICINES DUTIES IN IMCJ

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Aims:
Injection duties in IMCJ use Automatic Injection Medical Dispenser basically. After a doctor inputs prescription, a pharmacist compounds it, and a nurse confirms mixture injection. And it is administered to a patient last. When the doctor inputs anticancer drug or poison, prior inspection by the pharmacist is done in the process as part of the malpractice prevention. We report on it.
Method:
A normal prescription is published with the input of a doctor, and data are transmitted promptly, and automatic compounding of medicines with Automatic Injection Medical Dispenser is done. However, the prescription is not to be compounded without prior inspection by a pharmacist when anticancer agent or poison was prescribed. When anticancer agent and poison of a high risk prescribed, it evade accident by a pharmacist inspects using technical knowledge in refer to information on the patient and a protocol of chemotherapy. A prescription is published after the prior inspection of a pharmacist, and a pharmacist compounds the medicine. After that mixture and administrations of a medicine are enabled.
Result:
For a drug treatment by a doctor, the pharmacist who is an expert of medicine is concerned with prior inspection duties I think that we can contribute to reasonable use of medicine and security of safety for a patient thereby.
Consideration:
Now a pharmacist does prior inspection in some injection medicines in IMCJ.
However, all problems are not solved by a current method. I analyze contents and the number of inquiry and we want to do the duties aim at more and more improvement of prior inspection and measures of prevention of accident in future.

HPS-P-051

CLINICAL TRIAL INFORMATION MANAGEMENT BY DATABASE SOFTWARE ACCESS(?)

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Background
In the clinical trial business of Japan, which contains secretarist business, Clinical Research Coordinator(CRC) business and investigational medical products management, etc., there is huge information and a lot of essential documents are needed to manage it.
Aims
We report on the improvement of information management by the database software Access in IMCJ.
Methods
We had input the essential information to the database of the software Access,which made the retrieval and the extraction of the clinical trial information easy.
Input information)
Institutional Review Board(IRB)
Protocol title, Principal Investigator, Information of the pharmaceutical company, etc.
CRC business
Patient information, Schedule management, etc.
Investigational medical products management
Delivery and return, Appropriate use, etc.
Result
We were repeatedly inputting same information to the computer for managing a lot of documents before. However, we were able to retrieve and extract promptly necessary information by using the database. And creation of IRB document , CRC business and progress report of clinical trial were managed efficiency. In addition, the investigational medical products management was improved accuracy.
Conclusion
Using the database reduced the amount of the clinical trial work.
Moreover, we were able to arrange necessary information efficiently and speed of preparing work was improved. We should take part in the reliability of the clinical trial and the safety of the patients based on those information in the future.

HPS-P-052

COMMUNITY AQUIRED BACTEREMIC PNEUMONIA DUE TO METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS--A CASE REPORT

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Aim:
To present a case of community acquired methicillin-resistant staphylococcus aureus (MRSA) bacteremic pneumonia successfully treated with linezolid.
Case summary:
A 15 y/o girl was previously healthy except a past admission history of pneumonia when she was 5-6 y/o. This time she was referred from another hospital where CXR showed RML, RUL, and RLL pneumonia patch, sputum and blood culture all showed MRSA.
After admission, chest X-ray revealed consolidation with air-bronchogram over LUL, LLL & RLL. The laboratory data confirmed that influenza B Ab & PCR (+). Bone scan reported with no definite abnormal finding. We used linezolid for the MRSA infection control. The patient still got intermittent fever, productive cough with yellowish and blood stained sputum, mild shortness of breath. After linezolid treated 12 days, fever subsided and discharged on day 18.
Discussion:
Several retrospective studies appear to show an advantage of linezolid over vancomycin to treat MRSA infections. In this case, we use linezolid earlier to treat this patient's multiple lobe pneumonia that prevent from severe complications such as require intubation, chest tubes for drainage of pleural effusion.
Conclusion:
Because of increasing concerns about the efficacy of vancomycin, linezolid may be a better choice for MRSA pneumonia including nosocomial and community acquired.

HPS-P-053

AN EVALUATION OF THE CLINICAL PHARMACY REPORTS PUBLISHED IN THE PHARMACEUTICAL SOCIETY OF CHINA-TAIWAN'S ANNUAL CONFERENCE ABSTRACT BOOK FROM 1998 TO 2004

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Aims: From 1998 to 2004, the Pharmaceutical Society of China-Taiwan held annual conferences that accepted reports from pharmacists and related professions. Thus making it possible to evaluate all of the structure and contents of the published abstracts, and to analyze and reflect the development of clinical pharmacy in Taiwan.
Methods: Over the 7 year period, a total of 276 abstracts were reviewed, including the academic background of the authors and the content details of the articles. Data Management was performed using the Microsoft Access Program.
Results: The no. of reports increased from 7 in 1998 to 107 in 2004.The % of papers relating to clinical pharmacy forum increased, whereas those relating to experimental research decreased. In the beginning the reports focused mainly on pharmacokinetics, therapeutics and drug utilization review. However the parameters of research and discussion were later widened to include case reports, adverse drug reports, pharmacoepidemiology, medication error, therapeutic drug monitoring and service quality. Furthermore, there was a trend towards producing results and conclusions based on more and more sophisticated statistical methodology. Hospital pharmacies that had their own affiliated colleges of pharmacy had a better opportunity to perform research work than those without. Another observable tendency was that non-pharmaceutical postgraduate institutes and government departments worked together in cooperation to produce more in-depth papers.
Conclusion: Our findings show that clinical pharmacy is both flourishing and diversifying in Taiwan; and that both the quantity and the quality of annual publications are clearly rising.

HPS-P-054

DRUG USE EVALUATION OF INSULIN GLARGINE IN A [illegible] MEDICAL CENTER

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Aims:The hospital's Pharmacy and Therapeutics Committee has [illegible] treatment guideline of insulin glargine in August 2004. The aim of this [illegible] measure and assess the safety and efficacy of insulin glargine.
Methods:This study was conducted from September 2004 to March 200[illegible] pharmacists reviewed each prescription and clinical record according to the [illegible] Data collection and outcome assessment were based on the glycosylated [illegible] (HbA1C), fasting plasma glucose (FPG), nocturnal hypoglycemia, and cost-[illegible]
Results:A total of 76 patients (10 type 1, 66 type 2 diabetes) were enrolled [illegible] patients, 25% (3 type 1, 16 type 2 diabetes) were evaluated during a 12-week [illegible] consecutive insulin galrgine treatment. Compared with previous therapy [illegible] glargine treatment produced significant reduction in FPG level (p=0.002). [illegible] FPG level less than 140 mg/dl were achieved in 63.2% of patients with insulin [illegible] compared with 10.5 % before insulin glagine therapy. The target HbA1C level [illegible] 8% were achieved in 15.6% of patients with insulin glargine compared wi[illegible] before insulin glagine therapy, there was no significant improvement in mean [illegible] value (p=0.059). The cost of new treatment is higher than the conventional [illegible] however the new treatment reduced incidence of nocturnal hypoglycemia by 20[illegible]
Conclusions:From this study insulin glargine appears to be more effective in co[illegible] FPG and causes less nocturnal hypoglycemia than conventional therapy. We will [illegible] conduct a long-term project for further evaluating the cost-effectiveness and q[illegible] life with insulin glargine therapy.

HPS-P-055

THE DRUG UTILIZATION FOR PATIENT WITH COPD IN TAIWAN

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Aims:To reveal the drug use pattern of COPD patients in Taiwan and to evaluate the use of anti-tussives which are not recommended in some countries because of it's lacking well documents and evidences.
Methods:Using the claims data files of ambulatory care expenditure by visits(CD) and details of ambulatory care orders(OO) from the Taiwan National Health Insurance(NHI) Research Database of 2003, we analyzed the pattern and extent of the medication used in COPD patients (ICD-9-CM code:496) from a total of forty-two thousands systematic randomized patients. The drug codes of the merged CD and OO files were translated into their drug names using the drug file and grouped by the pharmacological system released from the NHI.
Results:The COPD patients visited more than 3 times in this year were included, which consisted a total of 1,244 patients, 0.349% cases from the whole claims database, with a mean age (SD) of 74.3(11.0) years. The pharmacological groups were respiratory smooth muscle relaxants(66.5%), sympathomimetics (58.6%), anti-tussives(56.1%), expectorants(20.5%), adrenals(20.0%), mucolytics(19.3%), anti-cholinergics(14.0%), anti-inflammatory agents(12.9%), and common cold preparations(7.7%) respectively. Commonly prescribed anti-tussives comprising of its group were dextromethorphan, glycyrrhiza extract and potassium creosolsulfonate, benzonatate, platycodon extract, codeine, ephedrine.
Conclusions:A considerable reimbursement for the anti-tussives used in COPD was reported in this study. Since its clinical outcome has not been fully documented, drug use guideline could be established by the NHI to cope with the limited budget for the health insurance resource.

HPS-P-056

THE UTILIZATION PATTERN OF THE THERAPEUTIC DRU[illegible] MONITORING IN TAIWAN – A 7-YEAR REVIEW FROM 1997 [illegible] 2003

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Aims:Through years of clinical experiences of Therapeutic Drug Monitoring(TDM) nowadays a growing clinical routine for the hospital pharmacy practice in Taiwa[illegible] aimed to review the ambulatory utilization pattern of the TDM from 1997 to 2003.
Methods:All the TDM items based on 3 major research data files: the registrie[illegible] ambulatory care expenditures by visit and the details of ambulatory care orders [illegible] the 7 year period from the Taiwan National Health Research Institute, were access[illegible] analyzed. These files are systematic sampling files representing 0.2% of the [illegible] database.
Results:During this period, a mean total of 2,385,397.6 cases and 231.6 TDM [illegible] claims data per year were determined. About 63.8% TDM were ordered in [illegible] centers. The frequency and the reimbursement of TDM increased about 1.5-fold a[illegible] fold respectively within this period. Though the reimbursement covered 29 items [illegible] 12 was identified in the database that cyclosporine(21.1%), carbamazepine(17.7%) phenytoin(16.6%) were at the most. The most frequently prescribed TDM drugs theophylline 21,917.7 prescription/year., digoxin 1909.6 and carbamazepine 1[illegible] however, the proportion of their TDM was extremely low. The patient who cyclosporine and FK-506 performed a TDM at least once a month and these two have obviously tended to increase every year in comparison with the other items.
Conclusions:Only the TDM of the immunosuppressants were frequently ordered [illegible] appears that some items i.e. amitriptyline, theophylline and lithium were ignored b[illegible] clinicals. Thus, TDM should be re-announced its importance in the Taiwan h[illegible] society.

HOSPITAL PHARMACY SECTION - POSTER SESSION

HPS-P-057

IMPACT OF A PHARMACY INTERVENTION FOR PHYSICIANS TO IMPROVE PROPHYLACTIC TREATMENT OF CIO

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Aim:The numerous side-effects associated with long-term corticosteroid treatment. Corticosteroid-induced osteoporosis (CIO) is the most serious side-effects which remains underdiagnosed and often inadequately managed. The objective of this study is to assess the effect associated with a pharmacy intervention aimed at physicians in order to improve the CIO-prophylactic treatment in a medical center in northern Taiwan.
Methods:The research using medical records of 1,432 patients from both the inpatient and outpatient populations who were receiving corticosteroid therapy for the period of April to November 2002. The impact of the pharmacy intervention was measured 6 months thereafter by changes in CIO-prophylactic-treatment prescribing behavior.
Results:Among all the 1,432 patients , only 430 patients (30.0%) used corticosteroids for up to 3 months were receiving CIO-prophylactic-treatment before pharmacy intervention. Review of ICD-9-CM diagnostic coding showed an osteoporotic patient population of 300, of whom only 204 (68%) received treatment: 906 patients (63.3%) needed to receive prophylaxis; 810 patients (56.6%) warranted bone densitometry evaluation. As a result of pharmacy intervention, 430 (30.0%) patients were increased to 693 (48.5%) patients receiving CIO-prophylactic-treatment.
Conclusions:The involvement of pharmacists in the team of care-providers can ensure that drugs are used safely and effectively. It is indeed laudable that this research has consequently been able to effectively improved quality of patient care and concluded that extension of pharmacy intervention from a focal level to district and even national level is worthwhile.

HPS-P-058

POINT OF CARE PHARMACIST; AN INNOVATION TOW BETTER PATIENT CARE BY PHARMACIST.

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Objective: To determine the quantitative impact of Point of Care Pharmacist i a medical care unit. Background: Pharmacist is an active member of multidi team, but is being underutilized in a country like Pakistan. The study has been to determine the quantitative impact of point of care pharmacist in a ter hospital of Pakistan. Methods: A pharmacist was selected on the basis of his achievements and the feed back from his supervisor. Pharmacist was credentia supervision of Clinical Pharmacist. Pharmacist was then placed inside w collaboration of ward management staff. Findings: Over 6months there w interventions by pharmacist with an average of 113permonth. Cost saving thousand rupees has been documented with an average of 251thousand ru month. There was a gradual decrease in number of interventions show improvement in physician order entry by the presence of pharmacist inside ward were 580 queries replied during 6months with an average of 88 per month. An of 6 drug food interaction has been identified with a total of 35 in 6months. T nursing sessions has been taken by pharmacists on different topics. 35missed dos been identified with an average of 6/month. 22 ADRs have also reported.Conclusion: Pharmacist can play a vital role in management of hospi patient. Once placed inside ward, Pharmacist can contribute extra to better management and cost reduction. Study also shows an improvement in the phy order entry by the presence of pharmacist inside ward.

HPS-P-059

IMPACT OF COLLABORATIVE EFFORT BY PHARMACIST AND NURSES ON PATIENT CARE

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Objective: To determine the impact of a collaborative approach of Pharmacist and Nurses in prevention of missing doses and reportage of ADR.
Background: Disease state management is a latest concept introduced in the health care system. Pharmacist is already involved in multidisciplinary clinical rounds in our hospital. To improve the patient care different problems were identified where nurses and pharmacist can work together for the betterment of patient care. Two major areas were targeted, study also been designed to determine the impact.

1. Missing dose
2. Adverse Drug Reaction Reporting

Methodology: A pharmacist and nurse were appointed to check the medication bins of the patient after administration time of all the doses that is 1130 am at medicine ward, an extra dose was checked against medication administration sheet of the nurse and the missed doses were identified and administered where possible. Nursing staff of medicine ward were encouraged to report ADRs and the collective effort results in increase reportage of ADR.
Results: Total of 35 missed doses has been identified in a period of six months, the number decreased gradually, that shows a gradual improvement in the practice. Number of ADR reported increased from 1 per month to an average of 4 per month during 6months.
Conclusion: Collaboration between nurses and pharmacists can result in better patient care.

HPS-P-060

HEALTH INSURANCE IN FLUID MANAGEMENT OF FRACTURED EXTREMITY

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Objective: This retrospective study discusses a routine work about the fluid management of Diagnosis-Relate-Groups fractured cases in the regional hospital. There are extensive views to the whole national health insurance system.
Materials and Methods: There were totally 6017 cases, during January-2001 and December-2003, accepted orthopedic operation. The Diagnosis-Relate-Groups cases were about 5902 (98%) people, the rest 115 (2%) cases got more severe condition, combined trauma and poor nutrition. The blood samplings were done before and after the operation. Replacement of prior fluid losses based on known electrolyte composition of the body fluid, serum electrolyte measurement, and clinical assessment of intravascular volume status.
Result: In Diagnosis-Relate-Groups cases, there was no obvious change of electrolyte. Average maintenance fluids were 1988.67 ml (1000-3000 ml/day) and maintain urine output of 0.5-1.0 ml/Kg/hour (1000-1500 ml) reasonable. Hyponatremia were the most common condition in the non-Diagnosis-Relate-Groups cases. The Asia infectious crisis, severe acute respiratory syndrome (SARS), was a major influence about the hospital data and prolongs hospital days (from March-2002 to December-2002).
Conclusion: Majority cases need the routine fluid input for intra-vascular dosage but the severe cases need the exactly fluid support for life saving even the nutrition support. The medical budget expenses year by year, the government must reasonably formulate the procedure to keep the quality of the health care. But it is very hard work.

HPS-P-061

THE TECHNOLOGY APPLIED TO IMPROVE THE QUALITY OF DISPENSATION BY UNIT DOSE

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The amount spent on medication in our ambience is considered the second section of expenditure of all Hospitals; so that a method for reducing and improving the quality of dispensation is looked upon

The aim is to show how methods of dispensation by Unit Dose of tablets and liquids with the adequate technology and area can achieve an improvement in the quality and cost reduction.

The methodology is based in the incorporation of technology : d-blister machine, double disk tablet packaging, liquid packaging and new plant.

Analyzing the processes we see that the average speed by manual
d-blisting method versus the automized is 50 % greater. The performance increases to the double with the double disk machine.

In the case of liquids a 36.3 % savings on the monthly cost was seen.

The plant was designed for the pharmacy's needs, with delimited areas reaching the conditions for each process.

We achieved a greater service and quality for patients and an important economical impact.

In conclusion technology alone isn't the fundamental issue but it's important to reach the objective.

HPS-P-062

QUALITY IMPORVEMENT OF HOSPITAL PHARMACY PRACTICE &MEDICAL SAFETY MANAGEMENT IN ALEXANRIA UNIVERSITY TEACHING HOSPITAL

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Health care environments worldwide are changing dramatically towards the delivery of high quality,cost effective patient care.At Alex.University Teaching Hospital,the role of pharmacists as legally responsible dispensers of medications (without medication-related care with limited pharmaceutical educational activities)has expanded in the recent 3 years to embrace the additional challenge of patient care.This was associated with the implementation of a postgraduate Pharm.D.Program at the Faculty of Pharmacy,University of Alexandria .The outcome of changes in pharmacy practice in four departments,namely Oncolgy.Hematology,ICU and Toxicology was monitored.Changes include establishment of a sterile area for the handling and dispensing of cytotoxic drugs by trained pharmacists,establishment of a computer-based documentation system,reviewing patint medical charts,reporting drug interactions,adverse drug reactions and medication errors,providing drug information to patients and other members of the health care teamwithin an educational activity framework and tonic&drug monitoring using VIVA apparatus.Positive outcomes include reduction in medication errors,improvement in nursing services,improved medication cost effectiveness translated as considerable financial savings,which collectively led to improved therapeutic outcomes and patient quality of life.Such charges motivated the Department of Pharmacy and hospital pharmacists to extend patient care services to the TPN unite and Therapeutic drug monitoring lab.&Clinical Pharmacies in all hospital departments.

HPS-P-063

USE/NON-USE OF HORMONE REPLACEMENT THERAPY IN THE CONTEXT OF WOMEN'S MENOPAUSAL EXPERIENCE.

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Aims : To investigated the decision-making about use/non-use of hormone replacement therapy (HRT) in the context of women's menopausal experience.
Methods : Interviewed 22 women age 49-61 years with natural menopause from northern Thailand. Data collected from June to December 2002.
Results : A total of 9 (40.9%) women were currently being treated with HRT. A total of 8 (36.4%) women were not being treated with HRT and 5 (22.7%) women had been treated with HRT in the past. The reasons for starting treatment for alleviating menopausal symptoms, to prevent osteoporosis and physician offered it. The reasons for not taking HRT included the following : never had menopausal symptoms, the physicians never offered it, lacking of knowledge about HRT, fear of cancer, allergic symptoms and menstruation recurrence. The reasons for discontinuation was unbearable side effects, being bored in taking the hormone, taking the hormone for a long time, forgetting to take treatment and don't want to pay for the medications
Conclusions : Most women who used HRT are under government health welfare. The women of low social status and low educational level tended to use HRT without participate in making decision about the use/non-use of HRT. On the contrary, the women with high social status and high educational level were more likely to participate in decision-making about use/non-use of HRT. The result of this study suggest that health service providers should provide information about benefits and adverse effects of HRT and a women must be able to make decision about the use/non-use of HRT.

HPS-P-064

USE/NON-USE OF HORMONE REPLACEMENT THERAPY IN THE CONTEXT OF WOMEN'S MENOPAUSAL EXPERIENCE.

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Aims : To investigated the decision-making about use/non-use of hormone replacement therapy (HRT) in the context of women's menopausal experience.
Methods : Interviewed 22 women age 49-61 years with natural menopause from northern Thailand. Data collected from June to December 2002.
Results : A total of 9 (40.9%) women were currently being treated with HRT. A total of 8 (36.4%) women were not being treated with HRT and 5 (22.7%) women had been treated with HRT in the past. The reasons for starting treatment for alleviating menopausal symptoms, to prevent osteoporosis and physician offered it. The reasons for not taking HRT included the following : never had menopausal symptoms, the physicians never offered it, lacking of knowledge about HRT, fear of cancer, allergic symptoms and menstruation recurrence. The reasons for discontinuation was unbearable side effects, being bored in taking the hormone, taking the hormone for a long time, forgetting to take treatment and don't want to pay for the medications
Conclusions : Most women who used HRT are under government health welfare. The women of low social status and low educational level tended to use HRT without participate in making decision about the use/non-use of HRT. On the contrary, the women with high social status and high educational level were more likely to participate in decision-making about use/non-use of HRT. The result of this study suggest that health service providers should provide information about benefits and adverse effects of HRT and a women must be able to make decision about the use/non-use of HRT.

HPS-P-065

REVIEW OF ORAL HYPOGLYCEMIC AGENTS OF HOSPITAL IN TAIWAN

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Objective: Type 2 diabetes mellitus is a common disease, affecting as much as 20% of elderly population. The total annuals costs of treating type 2 diabetes were 11.5% in Taiwan. We investigate the current status of use oral hypoglycemic agents (OHA) of hospital in Taiwan. Discuss the rationality of use OHA. Methods: Retrospective method was used. ICD-9 code 250 was caught by our computer system. Included criteria were diagnosis, which is type 2 diabetes, and took the OHA, which for a month period. Use insulin alone was excluded. The rationality was reviewed and analyzed. Results: The total number of selected cases was 1057. Every patient was given 1.64 kinds of OHA on average. The rates of use kinds of OHA were 43.2% (462, one drug), 49.7% (530, two drugs), and 7% (75, three drugs). The absurdity orders had 2 cases (0.19%) and 35 cases (3.2%), which associated with dosage and contraindication. Conclusions: Two patients with type 2 diabetes were combined therapy with 2 sulfonylurea agents. Most patients with type 2 diabetes will eventually require combination therapy with 2 or more agents to maintain glycemic control. Combining an insulin secretagogue (i.e. sulfonylurea or meglitinide) and an insulin sensitizer (i.e. metformin or glitazone) capitalizes on unique mechanisms of action and results in significant HbA1c lowering. Two insulin secretagogues (i.e. sulfonylurea) combining are not recommendation. If patient is unable to achieve glycemic control, insulin therapy is an appropriate consideration and should be added to oral agents. The others 35 cases were prescribed metformin (31), Diamicron (3), and rosiglitazone (1).

HPS-P-066

APPROPRIATE USE OF DRUG INFORMATION THROUGH THE INTERNET

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We conducted studies on organizing drug information and a system to offer such information, as well as methods to provide information included in the package insert for medicinal products. Specifically, the studies focused on electronic processing of information for the service system, the use of the Internet, and centralization of information. In 1998, a 'group to establish a format to offer information for correct use of pharmaceutical products' was instituted.
Method - In the more specialized area, the information contained in the package insert for medicinal products was electronically processed. During this process, an acronym, SGML/DTD (Standard Generalized Markup Language/Document Type Definition), was selected for the aforementioned system. Considering the overwhelming demand and usefulness of the information at the clinical setting, a study was also conducted on the feasibility of offering it as a PDF (Portable Document Format) file.
Results -The information in the package insert can be searched by generic name, trade name, or therapeutic category. At the moment (February 2005), 11,768 products (expressed in the number of sheets in the package insert, PDF 11,591 sheets) are registered in the system.
Conclusions - The 'Drug Information Offering System' (http://www.pharmasys.gr.jp/, available since May 31, 1999) is a system that supplements the conventional information sources for those involved in medical services and employed at medical facilities (such as physicians and pharmacists). The use of the Internet means accurate and rapid dissemination of information uniformly without favoring any specific geographic areas.

HPS-P-067

DRUG-RELATED PROBLEMS IN THE INTENSIVE CARE UNIT

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The patient care in intensive unit is multidisciplinary. These patients usually received treatments with enteral feeding tube. Drug therapy may be complicated in these cases. The aim of this study is to estimate the active interventions by pharmacists.

From July 2002 to March 2005, this study on drug-related problems (DRPs) was retrieved through chart review in the medical ICU, of an 800-bed medical center. The DRPs are divided into two parts. General DRPs: appropriate indication, efficacy, safety and compliance. And enteral feeding DRPs: change of dosage form, interactions between drugs and enteral feeding tube, or nutrition formulas, and the patients themselves.

With a total of 399 DRPs, the major problems were related to drug safety (168 events, 42.1%) and efficacy (172 events, 43.1%). Regarding dosage adjustment in the renal and hepatic insufficient patients and unsuitable dosage form, there were 182 events (45.6%) and 104 events (26.1%), respectively; and the acceptance rate was 81.0%. The unsuitable crushed drugs for enteral feeding found in 143 events, and the acceptance rate is 81.8%. The major recommendations (128 events, 89.5%) were the change of dosage form. Our interventions may prevent the detrimental results of the increased dissolution rate (63 events, 44.1%), side effects, and the destroyed active components.

Dosage form selection and appropriate administration methods recommended by pharmacists were crucial in patients with enteral feeding tube. The pharmacists' main recommendations favored dosage adjustments and avoidance of unsuitable dosage form. The pharmacists played an important role on the patients care in the intensive unit.

HPS-P-068

ANALYSIS OF AN ADVERSE DRUG REPORTING SURVEILLANCE

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Aim: Both the effective spontaneous reporting of adverse drug reactions (ADRs) and the rapid identification of possible drug safety hazards are important to pharmacovigilance. This study is describing an current electronic ADR-reporting system involves several approaches in which care-providers are encouraged to report adverse events via the outpatient system, inpatient system, nursing system and the pharmacy system. In addition, clinical pharmacists will monitor and reply the reports routinely through this reporting system, and it will be recorded on the patient's chart.
Method: The number of reports had been collected two years before the system was implemented in 2002 and also two years thereafter. Besides, the classification such as majority damage of organ system, treating methods and patient outcomes were analyzed.
Result: There were 614 cases had been reported after the system was implemented during 2002-2003, compared with only 124 cases without the system during 2000-2001. The majority damage of organ system were Skin(32%), CNS(14%), CV(12%), Blood(12%), Hepatic(9%), Renal(8%). Most of the treating methods were discontinuing treatment(33%), discontinuing treatment plus antidotes(26%), shifted to other agents(13%), shifted to other agents plus antidotes(11%). The patient outcomes were classified as symptoms improved(62%), shifted to outpatient(30%), symptoms unimproved(5%), non-ADR report(1%), expired(1%), expired due to underlined disease(1%).
Conclusion: The electronic ADR-reporting system is a technology being used to find a new way of improving signal generation procedures and enhanced methods for optimizing the collection of spontaneous reports.

HPS-P-069

IMMEDIATE PHARMACIST'S INTERVENTION TO PHYSICIAN'S PRESCRIPTION OF FLUOROQUINOLONES WITH ANTACIDS

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Fluoroquinolones is a broad spectrum of antibiotics with good antibacterial effect to different organisms including G (+) and G (-) bacteria, anaerobe, Chlamydia, mycoplasma, legionella and beta-lactam-resistant organisms.
The oral absorption and tissue penetration of fluoroquinolones are good. However its bioavailability including absorption, area under the curve (AUC), C max, Tmax and drug urine output may decrease significantly when administrated with di- and trivalent cations containing antacids. In such conditions, the reduction of bioavailability can potentially lead to treatment failure and development of quinolone-resistant strain.
In our retrospective study, 128 out-patient department patients who took levofloxacin/ofloxacin were included. In this study, 82 persons took levofloxacin/ofloxacin with antacids (such as aluminum and magnesium contained in antacids) simultaneously; another 46 patients took levofloxacin/ofloxacin 2 hours before or without antacids administration. Prescription accuracy rate increased from 35.9%(46/128) to 64.2%(70/109) ($p<0.05$,X2 test) after immediate pharmacist's intervention for one month. Prescription accuracy rate was 58.6 %(65/111, $p<0.05$) and 54.5 %(55/101, $p<0.05$) in 3rd and 6th months, respectively in spite of pharmacist's intervention withdrawal after one month.
Conclusion: Immediate pharmacist's short term intervention could significantly promote efficacy of fluoroquinolones utilization in patients. The role of pharmacist in the intervention of drug prescription can indeed improve the quality of medical care.

HPS-P-070

PROVIDING QUALITY INFORMATION TO CHEMOTHERAPY PATIENTS

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Introduction : Generally, patients receiving chemotherapy for the first time are anxious about possible strong adverse reactions because anticancer agents show severe adverse reactions in comparison to other drugs. For this reason, it is important to provide quality information to alleviate their concerns.

Methods : We prepared a leaflet about chemotherapy to provide the information that patients wanted based on the results of questionnaires to 45 patients involved in chemotherapy treatment. During the period January 2003 through June 2004, 44 patients were asked to evaluate these leaflets.

Results : We found that 100% of the patients understood the information about chemotherapy and 95% were satisfied with the relevant information about the adverse reactions of chemotherapy.

Conclusions : These results suggest that the use of information leaflets by a pharmacist can improve patients' understanding of chemotherapy and can alleviate their concern about adverse reactions of anticancer agents.

HPS-P-071

A SIMPLE INITIATION SCHEDULE OF ORAL WARFARIN TO PREDICT THE SUBSEQUENT CLINICAL RESPONSE IN THE MANAGEMENT OF THROMBOEMBOLISM

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Abstract: Warfarin is an oral anticoagulant for the treatment of thromboembolism. However, it is inconvenient for the clinical evaluation. During initial treatment, the international normalized ratio (INR) response has to be monitored frequently, until a stable dose-response relationship is obtained. This study was aimed to design a simple warfarin initiation schedule and established the relationship of the initial INR and maintenance doses of warfarin during the follow-up period. The study included 46 in-hospital patients with deep vein thrombosis (28), pulmonary embolism (9) ,atrial fibrillation with stroke (7) or others(2), with age ranging from 26 to 90 years,12 patients were excluded from the study due to they had prior warfarin treatment or baseline INR > 1.2 or loss of followed up in clinic. Patients were initiated with 5 mg warfarin daily for 3 days (day 1 to day 3). The INR was measured on day 4. The subsequent dose of warfarin was given according to the data of INR and patients were discharged with the maintenance dose and measurement of INR was performed at least 1 week later. (Table 1)

Measurement of INR at day 4 and clinical follow-up (F/U)

No of patient (Day 4)	INR Mean dosage of warfarin(mg) (mean ± SD)
8	1.33-1.49 4.82 ± 0.31
12	1.54-2 4.37 ± 0.76
6	2.12-2.5 5 ± 1.1
4	2.59-2.98 2.32 ± 0.22
4	3.03-3.76 2.5 ± 0

According to this study, about 82 % patients (28/34) could achieve the therapeutic level of INR (2.0-3.0), no complication was noted. In conclusion, this simple initiation schedule of oral warfarin to predict the maintenance dose is safety, and effectively.

HPS-P-072

INCIDENT REPORTS IN A PHARMACY DEPARTMENT

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Patient safety is a very important issue. To improve it, sharing incident reporting and learning from it is recognized to be an effective approach. In the current report, we reviewed the events associated with the practice in a pharmacy department.

We classified the types and evaluated the consequence and the likelihood of recurrence of the events by using the Safety Assessment Code (SAC) scoring system from January 2000 to December 2004 in an 800-bed medical center, with 3,500 outpatient prescriptions per day. Incident that ranks a SAC 1 represents highest risk and SAC 4 means lowest risk. For the potential events, the assigned severity is based on the most likely worst consequence.
There were 27 reports within 5 years, the incidence of actual adverse events was 37% and that of potential events or close calls was 63 %. Of the actual adverse events, 40% were belonged to SAC 2, 50% with SAC 3. In the potential events, the incidence of SAC 1 to SAC 4 was 23.5%, 41.2%, 29.4% and 5.9% respectively. Error rate due to poor staff performance was 74%, and the other 26% might be attributed to system problems.

The information gained from the reports may serve as a guide for determining appropriate procedures to improve patient safety, moreover it should not be used for accountability.

HPS-P-073

PRESCRIPTION DRUG USE IN PREGNANCY IN TAIWAN

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Aims: The purpose of this study was to provide information on the prevalence of the use of prescription drugs among pregnant women in Taiwan.
Methods: A retrospective study was conducted with the use of a database of two hundred thousands random subjects offered by The National Health Research Institute (NHRI). The sampling period was from 1997 through 2002. ATC classification and the US FDA risk classification system were used for evaluation. Gestational duration was assumed to be 270 days, with three 90-day trimesters of pregnancy. The due day was separated from the 3rd trimester and analyzed independently.
Results: During the study period, 9622 deliveries (from 7703 pregnant women) were identified that met the study criteria. A total of 120468 medications was prescribed during pregnancy, of which 60924 (50.6%) had US FDA risk classification with 0.93% as category A, 55.36% as category B, 9.66% as category C, 30.52% as category D, and 3.52% as category X. The three most frequently prescribed drug classes were antacid and drugs for treatment of peptic ulcer & flatulence (17.16%), cough & cold preparations (13.28%), and analgesics (10.18%).
Conclusions: Our finding that almost one half of the prescription medications during pregnancy belonged to categories C, D, or X. Many of these drug uses such as the systemic use of tetracyclines and iodinated glycerol should be avoided.

HPS-P-074

MEDICATION USE IN PEDIATRICS BY NON-PEDIATRICIANS

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China Taiwan

Aims: To evaluate the prescription appropriateness including drug choices and doses for pediatric patients cared by non-pediatricians.
Methods: A retrospective study was conducted in a general teaching hospital from July through September in 2004. All pediatric inpatients aging 12 years or less not cared by the pediatricians were included. They were mainly cared by the General Surgery, Orthopedics or Otorhinolaryngology.
Results: A total of 57 cases was available for evaluation. Four medications were found to have the highest dosing guideline noncompliance rate, they were gentamicin, acetaminophen, cephalexin and cefuroxin with noncompliance rate of 100% (18/18), 66.7% (10/15), 57.1% (57.1%) and 55.6% (5/9) respectively. Medications not approved for pediatric use were also found in the study.
Conclusions: Our finding that dosing guideline noncompliance was commonly seen in pediatric patients cared by non-pediatricians, especially in the use of antibiotics and acetaminophen.

HPS-P-075

DATA ANALYSIS OF THERAPEUTIC DRUG MONITERING OF THEOPHYLLINE IN A TEACHING MEDICAL CENTER IN TAIWAN

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Backgrounds
Theophylline has been placed as a second line bronchodilator as a result of expanding usage of ß2 agonist for the treatment of bronchial asthma and COPD. Theophylline is now prescribed in low-dose as an anti-inflammatory agent. Nevertheless, the therapeutic monitoring of theophylline serum level is still actively performed for inpatient in our hospital. This evaluation is performed to see if the practice of theophylline serum level monitoring is properly and we would like to look for a cut-off dose that beyond this dose doctor can safely prescribe this potentially toxic drug without routinely follow up the serum level.
Methods
A list of adult in-patients who had a serum theophylline level checked during 2005/1/1-2005/2/28 was selected. We reviewed the patients chart based on the list and collected patients' basic information, daily dose of theophylline used, sampling time, serum level, and drug interactions. The cut-off dose of theophylline was analyzed by ROC curve.
Results
181 patients were evaluated. 64% of them (116) were over 60 years old. 17% of the samples were collected at inappropriate time. 35% of the interpretable data were below 5 mg/L. Daily dose of theophylline under 270 mg were related to a serum level below 5 mg/L with a sensitivity of 88.5% and specificity of 77.8%.
Conclusions
The data of this evaluation suggest that pharmacist had a responsibility to educate related medical personnel about the proper sampling time of theophylline. Patients over 60 years old with no other factors affecting theophylline clearance may be given a daily dose under 270mg safely with no need of checking theophylline level regularly.

HPS-P-076

ACTIVITY AND GENOTYPE OF THIOPURINE S-METHYLTRANSFERASE(TPMT) RELATED TO ADVERSE REACTIONS IN LEUKEMIC CHILD PATIENTS UNDER THE MAINTENANCE THERAPY WITH 6-MERCAPTOPURINE(6MP)

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Aim: Activity and genotype of TPMT were studied to explain cause of severe adverse reactions in leukemic child patients under the maintenance therapy with 6MP.
Methods: Three patients(3, 4 and 14 y.o.) with acute ALL participated in this study after the informed consents were obtained, whereas one patient(15 y.o.) with ML participated these except genotype analysis. Maintenance therapy was started with 6MP at 50, 60 or 75 mg/m2. Activity of TPMT in red blood cell(RBC) was measured according to the reported method. Genetic polymorphism of TPMT was distinguished by the allele specific PCR, PCR-RFLP and the direct sequencing methods. The concentration of 6MP and its metabolites in RBC was also determined by HPLC method.
Results and Conclusions: Present study included 2 ALL patients who suffered from serious vomiting shortly after the maintenance therapy with 6MP and were obliged to discontinue the medication. TPMT activities in these patients tended to be lower than those in other two patients who did not experience any severe adverse reactions. Genotype of TPMT with both relatively low activity in two patients and high activity in one patient was distinguished as the wild type (TPMT*1), and any of known mutations (TPMT*2, *3A, *3B, *3C, *6) were not detected at all. Discontinued patients could resume low dose maintenance therapy accompanied with monitoring of 6MP and its metabolites in the RBC. Therefore, the estimation of TPMT activity may lead to a primary prediction to avoid severe adverse reactions in the maintenance therapy with 6MP. In addition, adjunct monitoring of 6MP and its metabolites may assist better dose adjustment.

HPS-P-077

THE GENERAL SITUATION OF ORPHAN DRUGS USAGE IN TAIWAN

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Aims:
Rare disorders refer to those conditions that affected small numbers of individual. Drugs used to treat these disorders are commonly referred to as 'orphan drugs'. Usually those drugs are not easily obtained and the quantity is limited. In order to smoothly providing these medications, government's involvement for integrating those orphan drugs supply is very important. This research founded by Bureau of Pharmaceutical Affairs, Department of Health, Executive Yuan, Taiwan, R.O.C. collected orphan drugs used items and quantity in every hospital in Taiwan from 2001 to 2004. Base on the result of this evaluation, government and medical personnel can have an idea to distribute orphan drugs and to conduct further studies. At the end of our study period, a formulary of orphan drugs used in Taiwan was published to provide as a reference.

Methods:
In order to collect information and publish formulary, we ask hospitals, Bureau of National Health Insurance, Foundation of Rare Disease and pharmaceutical companies to provide orphan drugs they used or other related information base on Bureau of Pharmaceutical Affairs' help.

Results and Conclusion
Until March 2005, government announces total 120 classes and 140 types of rare disorders since the Rare Disorders Prevention and Treatment Act put into practice. The total number of rare disorders patients reported to Bureau of National Health Insurance is 1747. Base on our survey, there are 76 items of orphan drugs included. Within those drugs, Anagrelide, Tetrahydrobiopterin, thalidomide and Kelfer are used most often.

HPS-P-078

USE OF PRESCRIPTION-REFILL RECORDS TO ASSESS PATI… COMPLIANCE IN TAIWAN

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Aim: Lack of compliance with prescribed medication regimens contribu… preventable patient morbidity. The purpose of this study is to understand th… behavior of patient and to know which factors contribute to the poor com…
Methods: This study was a longitudinal survey. In a period of five months (… October, 2004), we used prescription-refill records from a computerized pre… database in FEMH to assess patient compliance and evaluated the factors a… with compliance. Compliance was defined as refill within the days' supply … refill-due date.
Results: A total of 7,568 out-patients were enrolled in this study. The mea… subjects was 58.67 ± 14.84 years. The patient groups were almost equally dist… men (n=3,657, 48.3%) and women (n=3,911, 51.7%). We found compliance wa… to patient's age, prescription day and clinic service. In our survey, 5667 patient… were refilled on time. The study revealed higher compliance was in pati… increased age (0-19 years old: 61.1% v.s >80 years old: 80.8%, p<0.001). 3512… (78.9%) with 28-day of prescription refilled scheduled, and 2223 patients (73.2… day of prescription refilled scheduled (p < 0.001). Meanwhile, the patients fo… surgical and psychiatry services had better compliance than others.
Conclusion: Under the attention of Taiwanese government encouraging … prescribe refill prescription, the compliance was still quite low. Therefore, p… can play important role in educating patients to use medications more corr… safely.

HPS-P-079

ASSESSMENT OF MEDICATION ERRORS IN A MEDICAL CENTER UNDERGOING INTEGRATED PHARMACIST EDUCATION

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Aim: To identify the factors contributing to medication errors that occurred in a 3500-bed medical center which executing integrated pharmacist continued education program in order to examine the ability of detecting medication errors reported by the pharmacists through an electronic reporting system.
Method: The reported medication errors had been collected during January 2004 to January 2005. The causes of these medication errors were also been classified and evaluated.
Result: There were totally 15876 medication errors have been reported. The causes of these medication errors are multi-factorial including physician prescribing errors(40.4%), physician key-in errors(17%) and mistakes of control drug management(42.6%). Among the 6420 physician prescribing errors, it can be classified as wrong drug(21.4%), improper dosage(54.1%), drug-drug interactions(19.4%), wrong administration route(4.6%) and others(0.52%). Among those 2700 physician key-in errors, there were wrong units(11.6%), improper quantities(42.9%), wrong drug(16.7%), improper dosage(5.3%), improper therapeutic period(7.9%), wrong administration route(7.7%), wrong frequency(0.3%) and others(7.6%). In addition, there were 1923 medication errors reported about contraindication in renal insufficiency patients who need to discontinue the current therapy or need to adjust the dosage among all of the medication errors.
Conclusion: Pharmacists play an important role in preventing medication errors. Both effective education and reporting system will allow for the identification of processes that introduce the potential for errors and will lead to an open discussion about improving the quality of patient care.

HPS-P-080

STUDY OF NSAIDS USAGE PATTERN AFTER VIO…

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Aims:To reveal non-steroidal anti-inflammatory drugs (NSAIDs) use pat… in Kaohsiung Veterans General Hospital (KVGH) after Rofecoxib (Vioxx…

Methods:Using the claims data files of ambulatory care expenditure fr… Database of 2004, we analyzed the pattern and extent of these patients … for pain relief.

Results:The 59,443 patients with a NSAIDs prescription in our practice … with a mean age (-SD) of 52.3 (22.1) years. The subgroups were non-C… drugs (63%), COX-2-selective drugs (37%) respectively. Ceoxx… NSAIDs comprising of its group were Diclofenac Pot. (22%)- Piroxicam… Etodolac (13%). However, only Celecoxib market increased up 8% in t… (Q4) than Q3.

Conclusions:After Vioxx's withdrawal, these patients taking Vioxx coul… COX-2-selective drugs more than non-COX-2-selective drugs.

HPS-P-081

EFFECTS OF IMPACT (JAPAN) ON PERIOPERATIVE INFLAMMATORY AND IMMUNE RESPONSES IN PATIENTS UNDERGOING MAJOR SURGERY FOR CANCER

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Preoperative nutritional support is a potentially beneficial strategy to improve perioperative morbidity. To investigate the influence of preoperative administration of arginine-, n-3 fatty acids- and RNA-enriched supplement (Impact, Japan) on inflammatory and immune responses in patients undergoing major surgery for cancer, we measured plasma levels of n-3 fatty acids (eicosapentaenoic acid, decosahexaenoic acid, linolenic acid and docosapentaenoic acid), n-6 fatty acids (linoleic acid, arachidonic acid, etc.), thromboxane B2, prostaglandin E2, inflammatory markers, nutritional markers and cytokines. Patients were classified into two groups; supplement group received 1 L/day of Impact (Japan) for 5 days before surgery, control group received an ordinary diet without Impact (Japan) before the operation. Blood samples were collected 5 days before operation at the starting point of supplementation, and on postoperative days (PODs) 0, 1, 3 and 7. After taking the supplement, n-3 fatty acid family and rapid turnover proteins significantly increased on POD-0, while the levels of thromboxane B2 and n-6 fatty acids significantly decreased on POD-0. On POD-0 only, inflammatory markers (CRP and alpha 1-acid glycoprotein) in supplement group were lower compared with the control group. Supplement group showed remarkably low levels of polymorphonuclear leukocyte-elastase on POD-1 and POD-3, and interleukin-8 on POD-3. Oral administration of a supplement enriched with n-3 fatty acids for 5 days before surgery would bring an improvement of perioperative inflammatory and immune responses as well as nutritional state in cancer patients.

HPS-P-082

THE QUALITY CONTROL OF CLINICAL PHARMACOKINETIC SERVICE

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Aims
To develop the indicators to measure the outcomes assessment of TDM and the contribution of clinical pharmacokinetic service.

Methods:
The five indicators to evaluate the outcomes assessment of TDM service were developed. The five indicators were: (1) timing of specimen collection, (2) timing of interpretation of TDM result by pharmacist, (3) dosage regimen adjusted by pharmacist, (4) physicians' action taken according to TDM interpretation, and (5) clinical impact on patient care. They were then used to evaluate the outcomes assessment of daily routine TDM cases that were provided clinical pharmacokinetic service by clinical pharmacists. A total of 364 TDM cases were included during 4-month period in a 1600-bed ward at the Tri-Service General Hospital.

Results:
Of 364 TDM cases, 282 cases (77%) was correct time for specimen collection. 307 cases (84%) whose timing of interpretation of TDM result by pharmacist were within 24 hours. The dosage regimen need to be adjusted was 298 cases (82%). 226 cases (76%) of the 298 dosage regimen adjusted cases were physicians' action taken according to TDM interpretation. 245 cases (82%) of the 298 dosage regimen adjusted cases were improvement in clinical condition.

Conclusions:
Outcomes assessment is an important component of the evaluation of therapeutic drug monitoring and the contribution of clinical pharmacokinetic service. The indicators in this study have provided a tool for monitoring the quality of therapeutic drug monitoring.

HPS-P-083

INVESTIGATING CUSTOMERS' EXPECTANCY AND SERVICE QUALITY OF OUT-PATIENT DEPARTMENT IN THE HOSPITALS BY QFD

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Objectives: To investigate the expectancy and the weighting on the quality of OPD (out-patient department) pharmacy services of the three parties: pharmacy administrators, pharmacists, and patients, and then try to propose the related information for further actions on the improvement of service quality.Methods: We utilize the technique of QFD (quality function deployment) to evaluate the service quality and customers' satisfaction on OPD pharmacy. First, clarify the variables of OPD patients' demand and expectancy on the pharmacies by personal interview. Then investigate the customers' satisfaction and weighting on each variables by questionnaires. Finally we construct the matrix from two dimensions: patients' needs and the quality improvement activities that the pharmacy administrator plans to implement. According to the analysis of this matrix, the priority of service quality improvement activities can be decided.Results: The total QFD construction of OPD pharmacy was well-interpreted by following the steps of QCC (quality control circle). QFD also provided some advantages rather than the traditional way of customers' satisfaction survey.Conclusion: The results of the present study can be as the references to someone who wish to provide further excellent quality of pharmaceutical services.

INDUSTRIAL PHARMACY SECTION - POSTER SESSION

IPS-P-001

DEVELOPMENT OF METRONIDAZOLE COLON SPECIFIC DRUG DELIVERY SYSTEMS

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The ability of matrix, multilayer and compression coated tablets of metronidazole to reach the colon intact has been investigated in vitro using pectin as a carrier.
Matrix tablets containing various proportion of pectin in absence and presence of certain excipients were prepared by direct compression and wet granulation techniques.
Multilayer tablets were prepared using 50-100 mg of pectin matrix tablet of metronidazole.
Rapidly disintegrating metronidazole core tablets were also prepared and were compression coated with pectin.
The effect of coat: core ratio as well as the incorporation of 10% chitosan in pectin coat on drug release was investigated.
Results of in vitro release studies using conditions simulating the pH and times likely to be encountered during transit to colon indicated that matrix and multilayer tablets liberated 50-75% and 32-61% drug respectively in the physiological environment of stomach and small intestine.
On the other hand, coats consisting of pectin alone protected the cores from premature release when a high coat: core ratio (5:1) was used. Within 5 hours ,the release was less than 1%.
In presence of chitosan protection occurred at lower coat: core ratio (3:1).
Selective delivery of metronidazole to colon can be achieved using pectin or pectin-chitosan mixture in the form of compression coated tablets.

IPS-P-002

BIOAVAILABILITY OF DESMOPRESSIN FROM A SUPERPOROUS HYDROGEL BASED DRUG DELIVERY SYSTEM

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The purpose of this study was to evaluate the bioavailability of desmopressin formulated in a superporous hydrogel based drug delivery system without and with N-trimethyl chitosan (TMC), an absorption enhancer, in juvenile pigs.
Six female pigs, average body weight of 30 kg, were operated to insert a silastic carnula at the jugular vein for blood sampling. One week after the surgery, the pigs were given desmopressin formulated in a superporous hydrogel based drug delivery system without and with TMC via oral administration in enteric coated hard gelatin capsule. To determine the bioavailability (F) values, desmopressin solution was also given to the pigs intravenously. Blood samples were taken from the cannulated jugular vein and subsequently analyzed by radioimmunoassay.
Peroral administration of 10 mg desmopressin formulated in a superporous hydrogel based drug delivery system without and with TMC resulted in the F values of 0.42 ± 0.06 and 0.63 ± 0.41% (mean ± SD), respectively. Administration of desmopressin superporous hydrogel without and with TMC showed Tmax of 80.0 ± 34.6 and 160 ± 64.6 min, respectively, and Cmax of 2,481.3 ± 715.1 and 2676.5 ± 1266.3 pg/ml, respectively. The insignificant effect of TMC, an additional absorption enhancer, on bioavailability parameters of such drug delivery system may be attributed to the short opening of most tight junctions by the effect from the superporous hydrogel.
The designed delivery systems appeared to possess very promising prospects for the development of effective oral dosage forms of peptide drug desmopressin.

IPS-P-003

EFFECT OF ZETAPOTENTIAL, PARTICLE SIZE AND OTHER PHYSICOCHEMICAL FACTORS ON STABILITY OF NIOSOMES

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Methotrexate niosomes were prepared by lipid layer hydration method using chloroform: ethanol combination using span 60 surfactant in 1:1 molar ratio with cholesterol with
15-micromolar quantity of DCP. The niosomes of Methotrexate prepared were studied for zeta potential, particle size, and leakage of drug through the niosomes on storage at room temperature and at refrigeration temperature.

The stability of niosomes were studied for 6 weeks. There is increase in vesicle size of the niosomes noted and there was a change from 1micrometer to 40 microns. The zeta potential was measured using pH 7.4 buffer. The stable niosomes were found to be range between 38 mv to 45 mv. There was a change in the zeta potential upon storage and at the end of the 6 week the zetapotential was found to be in the range of 60mv-70mv. The scanning electron microscopy studies showed that there was a uniform shape and size of the vesicles seen. Up on storage there was coalescence noted with nonuniformity in the shape with increase in vesicle size. The poly dispersity index was increased upon storage.

The stability of niosomes is crucial factor and the physicochemical factors decide the stability of niosome.

IPS-P-004

COMPLEXATION OF CELECOXIB AND MELOXICAM WITH 2-HYDROXY PROPYL BETA-CYCLODEXTRIN USING DIFFERENT TECHNIQUES

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The effect of hydroxypropyl ß-cyclodextrin (HPB) on the aqueous solubility and dissolution of celecoxib and meloxicam was investigated. Solid complexes were prepared by freeze drying, evaporation, and kneading. Various ratios of drug to HPB were prepared ranging from 1:1 up to 1:10. The resulting complexes were characterized using differential scanning calorimetry (DSC), infrared spectroscopy (IR), and scanning electron microscopy. Solubility and dissolution profiles were also determined. Dissolution media included water, 0.1N HCl with or without tween 80 and buffer at pH 7.4. In vitro studies showed that the solubility and dissolution rate of celecoxib and meloxicam were significantly improved by complexation with HPB. DSC, IR and electron microscopy examinations also demonstrated clear differences between the parent drugs and the complexes. Solid dosage forms incorporating these complexes in presence of pvp showed better performance than drug alone. The dosage forms made from solid dispersions prepared by the solvent evaporation technique gave the highest improvement in dissolution rate and efficiency. This work has demonstrated that the formation of solid complexes of insoluble drugs with HPB can be applied to produce dosage forms that could lead to better bioavailability of the insoluble drug.

IPS-P-005

PREPARATION, CHARATERIZATION AND EVALUATION OF METHOTREXATE LIPOSOMES

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Aim: To prepare, characterize and evaluate Methotrexate liposomes for oral drug delivery.
Method: The Methotrexate liposomes were prepared using various ratios of Dimiyristoyl phosphatidyl cholin(DMPC),Soya lecithin, cholesterol with various weight ratios of the drug using lipid layer hydration method to get multilamellar and unilamellar liposomes. Both multilamellar vesicles and unilamellar vesicles were characterized by SEM analysis for their surface characteristics, zeta potential for surface charges and particle size analysis using Malvern Mastersizer. A short term stability studies was conducted for 2 months at 4oC and at room temperature (25oC).
Results: DMPC liposomes showed a better entrapment than Soya lecithin liposomes. Both MLVs and ULVs showed uniform particle size distribution. The zeta potential was found to be satisfactory. Drug release from liposomes was in a biphasic manner with an initial fast release within 3 hrs and then an equilibrium state. SEM analysis showed a smooth outer surface.
Conclusion: Thus MLVs ULVs can be prepared for oral drug delivery for the drug Methotrexate. Final formulations were prepared after lyophilizing the selected liposomes in the form of dry syrup. The stability of liposomal methotrexate can be enhanced by using in the form of dry syrup.

IPS-P-006

NIOSOMAL UREA GEL-ADJUVANT TREATMENT OF PSORIASIS

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Aim: To prepare niosomes of urea by various methods.To incorporate urea niosomes in chitosan gel and to study release pattern of urea. To conduct HRIPT test of urea niosomes to study the irritation and sensitization of the gel on human skin.

Method: The Urea niosomes were prepared using various spans such as span 20, span 40, span 60, span 80 in combination with cholesterol by lipid layer hydration sonication and Trans -membrane pH gradient method. The dried film was rehydrated with 7.4 buffer solution. The hydrated solution was kept at 60/c with occasional shaking and niosomes thus prepared. The niosomes were characterized for particle size analysis, entrapment efficiency and in vitro release. Then a gel was formulated using chitosan as polymer. The skin irritation test, 'Repeated insult patch test protocol' (RIPT) was performed on human volunteers to study the cumulative irritation and or allergic contact sensitization potential of a test material.

Results & discussion: Trans -membrane pH gradient methods produced 45% entrapment of the urea. The span 40,1:1 molar quantity with cholesterol gave 70% release was seen in 24 hours from the gel formulation. 1%,1.5%,concentrations of chitosans gave good urea gel and did not produce any irritation on the human volunteers by RIPT method.

Conclusion:The span 40,1:1 molar quantity with cholesterol gave better release compare to other surfactants.. Various concentrations of chitosan urea gel did not produce any irritation on the human volunteers by RIPT. This urea gel can be used as adjuvant treatment in psoriasis as well as in cosmetic area.

IPS-P-007

PHARMACOKINETICS AND ANTILEISHMANIAL ACTIVITY OF AMPHOTERICIN B ENCAPSULATED LONG CIRCULATING LIPID NANOSPHERES

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Amphotericin B lipid nanospheres (LN-A) and long circulating lipid nanospheres (LN-A-PEG) were prepared by Amphotericin B with Distearylphosphatidylethanolamine-Polyethylene glycol (DSPE-PEG) (57.6 mg), egg lecithin and cholesterol were dissolved in soybean oil, heated to 70°C on a water bath. Glycerol, sucrose and sodium oleate were dissolved in sufficient amount of distilled water and the aqueous phase was added to the oil phase at the same temperature (70°C). A coarse emulsion was prepared by homogenization at 6000 rpm for 3 minutes was subjected to ultrasonication using ultrasonicator. The blank lipid nanosphere formulation (LN-PEG) was prepared in a similar manner without drug. The formulations were sterilized by autoclaving at 121oC. The pharmacokinetics of LN-A and LN-A-PEG were compared to the amphotericin B deoxycholate (Fungizone). The same dose of each formulation (5 mg/kg) of amphotericin B was injected in the male wistar rats via tail vein. Plasma samples were collected after 5, 10, 15, 30 min and 1, 2, 4, 6, 8, 16 and 24 h after the injection. Amphotericin B showed biphasic disposition. The pharmacokinetics of LN-A and LN-A-PEG were significantly different with high AUC0-t, and lower clearance than that of fungizone. The peak plasma concentration of LN-A-PEG was approximately 4 and 2.5 folds higher than fungizone and LN-A. Antileishmanial activity of LN-A and LN-A-PEG was assessed in BALB/c mice infected with Leishmania donovani AG83 for 60 days. A single dose (5 mg/kg) of LN-A and LN-A-PEG was injected intravenously. Mice were sacrificed after 15 days of treatment with fungizone, LN-A, LN-A-PEG and Leishman Donovan Unit (LDU) is counted.

IPS-P-008

ASSESSMENT OF PHARMACEUTICAL QUALITY AND ANTIFUNGAL ACTIVITY OF MICONAZOLE NITRATE CREAMS MARKETED IN EGYPT

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Miconazole nitrate (MCZ), a sparingly soluble antifungal agent is marketed in Egypt as topical cream and oral gel. This post-marketing surveillance study was conducted to assess the in-vitro performance and antifungal activity, against C. albicans, of three local brands of MCZ cream in comparison to the innovator product Daktarin ® (two batches each). Creams were tested for: drug content both chemically (two-phase titration) and microbiologically (turbidimetry), pH, spreadability, shape and size of MCZ crystals in the cream and in-vitro drug release. A modified USP dissolution apparatus 5 (paddle over disk) and agar diffusion technique were compared for testing drug release. Results of drug content obtained chemically ranged from 95.2 to 100 % and those obtained microbiologically ranged from 125.4 to 153.6 %, due to interference of preservatives. In-vitro release results obtained over 8 hours (under sink condition) ranged from 2.2 to 10.8 % compared to 17.3 & 20.5 % for Daktarin ® (samples analyzed by HPLC). Inhibition zone diameter ranged from 15.6 to 19.8 mm compared to 25.4 & 26.3 mm for Daktarin ®. The size and shape of MCZ crystals in different creams proved major determinants of drug release. Inter-batch variability was generally low. Antifungal activity in terms of inhibition zone diameter could be correlated linearly with cumulative % MCZ released after 8 hrs ($r = 0.983$) and with in-vitro release rate in $\mu g / cm^2 . hr^{0.5}$ ($r = 0.982$). In conclusion, products tested vary widely in their in-vitro performance and antifungal activity. Both of the in-vitro release and agar diffusion tests proposed are equally useful in estimating drug release from creams.

IPS-P-009

ASSESSMENT OF PHARMACEUTICAL QUALITY OF OMEPRAZOLE CAPSULE PRODUCTS MARKETED IN EGYPT

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Omeprazole, a poorly soluble, acid labile, lipophilic drug, is marketed as enteric coated pellets in capsules. Generic products available in Egypt show more than 4-fold price difference. This work is a post-marketing surveillance study to compare the in-vitro performance (using validated HPLC methodology) of 7 local omeprazole generics relative to the innovator's product. Tests performed include drug content, content uniformity, USP drug release test for enteric coated articles and a modified release test (involving pre-exposure to pH 4 buffer rather than 0.1N HCl). Products were subjected to an accelerated stability study under ICH conditions (40°C and 75 % relative humidity) for 3 months.

Results indicate that 6 generic brands passed tests for drug content & content uniformity. All brands passed the USP drug release test (% release at 45 min. ranged from 91.5 to 114.6) despite different release rates as judged by t 90. The modified release test which better simulates in-vivo conditions proved more discriminative (% release at 45 min. ranged from 22.8 to 96.1). Stability data indicate that after 3 months storage, drug content of 3 generics remained above 90 % with only one brands maintaining drug release above 75 % and showing similar stability to the innovator's. Chemical degradation of omeprazole resulted in darkened pellets and amber glass bottles provided more protection than blisters, strips or plastic bottles.

In conclusion, omeprazole capsule products in Egypt show wide variation in in-vitro performance and the modified release procedure could be recommended as a discriminative test for omeprazole release from enteric coated articles.

IPS-P-010

MODULATION OF TENOXICAM RELEASE FROM HYDROPHILIC MATRIX: MODULATOR MEMBRANE VERSUS RATE CONTROLLING MEMBRANE

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Aim: to study the release pattern of tenoxicam from hydroxypropyl methylcellulose (HPMC) through the restriction of the releasing surface by addition of membrane layer. Also to explore the membrane layer is a rate controlling or modulator layer. Methods: Twelve devices were constructed based on bilaminated films which produced by a casting/solvent evaporation technique. The drug-HPMC layer was covered by drug free membrane layer composed of a mixture of HPMC and ethylcellulose (EC). Devices were evaluated for thickness, drug content, water absorption capacity and drug release. The films were evaluated for thickness, appearance, folding endurance and transparency. The influence of membrane layer composition and thickness on drug release pattern was studied. Results: The release of drug from HPMC matrices without the membrane layer was fast and follows diffusion controlled mechanism. Except four devices, the release of drug from other devices becomes linear with time (zero order) and extended for long time especially when thickness and the ratio of EC was increased in the membrane layer. Conclusions: changing the geometry of drug layer by addition of membrane layer and changing its composition and thickness plays an important role in determining whether the membrane layer is rate controlling (ie. control drug release and no change in its release mechanism) or modulator membrane (ie. control drug release and change its release mechanism).

IPS-P-011

PREPARATION, CHARACTERIZATION AND EVALUATION OF SOLID LIPID NANOPARTICLES CONTAINING TENOXICAM

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Solid lipid nanoparticles (SLN) were prepared using tenoxicam as a model drug according to a 23 factorial design, at two levels of lipid and surfactant concentration. The SLN were prepared by the modified high shear homogenization and ultrasonic method using Cumpritol and cetyl palmitate as lipids, and poloxamer 188 as surfactant. The prepared SLN were characterized using DSC, X-ray diffraction, and zeta potential and were evaluated regarding particle size, drug encapsulation efficiency and in-vitro drug release. The DSC and X-ray studies showed that the prepared SLNs showed less orderly arrangement of crystals, which was favorable for increasing the drug loading capacity. The encapsulation efficiency of tenoxicam within the SLN was in the range 83-88% for the prepared SLN formulations. Zeta potential studies revealed the stability of the SLN preparations as indicated by the negative charges obtained for all the preparations, which ranged from -11.7 to -35.0 mV. Particle size analysis showed that mean particle size of the prepared SLNs was in the range of 256- 392 nm. The particle size decreased at the higher level of surfactant used. The obtained results from the in-vitro release studies revealed that SLNs could be used as modified release formulations for tenoxicam over a period of 12 hours.

IPS-P-012

LIPOSOMAL DIBUCAINE DELIVERY SYSTEM: DEVELOPMENT AND CHARACTERIZATION

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Formulation of local anesthetics in controlled delivery systems provides safer and more effective anesthesia. The aim of this study was to develop a liposomal dibucaine base (DB) local anesthetic delivery system. DB-loaded multilamellar vesicles (MLVs) with different characteristics were obtained by varying lipid composition, drug loading, induced charge and pH of the hydration buffer. Liposomes were characterized for morphology, size, entrapment efficiency (EE) and stability including leakage stability. Results indicate that amongst formulations tested, negatively charged liposomes with the lipid composition phosphatidyl choline: cholesterol: dicetyl phosphate 7:6:1 and drug: lipid ratio 90mg: 300mg prepared with pH 9 hydration medium showed good in vitro characteristics in terms of EE (~ 90%), sustained drug release (~ 20% in 12 hrs) and low burst effect. However, they exhibited relatively poor leakage stability. A delivery system was prepared by incorporating negatively charged DB-loaded liposomes in a 2% HPMC gel base. Gel formulations were assessed in vitro for drug leakage stability and in vivo using the pin prick test in Guinea pigs. Incorporation of liposomes in the gel enhanced their leakage stability. Release characteristics of the liposomal gel could be modulated by combining different proportions of free and liposomal DB. The in vivo performance of a combination gel provided a superior local anesthetic profile (fast onset and prolonged duration of action) compared to a non-liposomal DB gel and a liposomal gel formulation with no free drug added. The DB liposomal gel developed offers great potentials as a local anesthetic delivery system.

IPS-P-013

LIPOSOMAL 5-FLUOROURACIL FOR TOPICAL DRUG DELIVERY

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Effective topical therapy with 5-fluorouracil (5-FU) requires sustained availability of the drug at a minimum effective concentration in deeper skin layers with minimal systemic absorption. A liposomal 5-FU delivery system may fulfill such requirements although it presents formulation challenges because of the drug hydrophilicity and low molecular size. In this study, 5-FU was incorporated in multilamellar vesicles (MLVs) and stable plurilamellar vesicles (SPLVs) of different lipid composition and charge to modulate entrapment efficient (EE). 5-FU-loaded liposomes were characterized for morphology, size, EE, release kinetics, stability including leakage stability and skin permeation through rabbit skin. Negatively charged 5-FU SPLVs exhibited good biopharmaceutical attributes in terms of appearance, size (~0.32μ), EE (~44%), release rate (~80% in 12 hrs), with ~31 fold increase in dermal retention of the drug. However, they showed poorer leakage stability relative to neutral liposomes. 5-FU-SPLVs were subjected to freeze drying with different cryoprotectants to improve their stability. This was achieved maximally with trehalose. A liposomal gel was prepared by incorporating trehalose-freeze dried 5-FU SPLVs in 2% hydroxypropyl methylcellulose gel. The gel showed good short term storage stability (one month at 4oC) with maximum drug release of ~65% in 12 hrs and reduced burst effect. Incorporation of liposomal 5-FU in the gel base in different physical forms (fresh dispersion, freeze dried powder as such or after reconstitution) did not affect the release characteristics. The liposomal gel prepared offers promises as a 5-FU topical delivery system.

IPS-P-014

TRANSDERMAL DELIVERY OF NAPROXEN FROM ENHANCED NIOSOMES

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The study investigated the effect of fatty acid side chain in Span on the transdermal delivery of naproxen (model drug) from niosomes and monitored the effect of penetration enhancers when incorporated in niosomes. Niosomes were prepared from surfactant and cholesterol at 2:1 molar ratio. This was hydrated with 10% v/v ethanol in water to produce total lipid concentration of 50 mg/ml. The control was saturated aqueous drug solution. Full thickness skin prepared from the ventral side of freshly excised rabbit ears was mounted on vertical Franz diffusion cells. To ensure sink conditions, ethanol-water (30% v/v) was employed as a receptor. At different time intervals after occlusive application of the tested formulations, samples were taken from the receptor compartments and replaced with fresh receptor fluid. These were analyzed for drug content by HPLC. The steady state transdermal flux of naproxen was increased by 2.9, 2.7 and 1.3-fold after incorporation in Span 20, 40 and 60 niosomes, respectively. Employing Span 20 the effect of enhancers was tested. Incorporating menthol in niosomes augmented the niosomal skin drug delivery and increased the drug flux by 4.1-fold when incorporated at 20% w/w. In contrast, incorporating oleic acid in niosomes did not augment the skin drug delivery with the transdermal flux values being decreased by increasing oleic acid concentrations. Phase separation was visually evident for niosomes containing high concentrations of oleic acid. In conclusion, the fatty acid chain of surfactant can affect niosomal skin drug delivery and incorporation of menthol in niosomes can further enhance transdermal drug delivery.

IPS-P-015

ALBATIN® IN HEALING HIPERPIGMENTATED SKIN

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Besides already known substances (hydrochinon, lactic, kojic, AHA acids...) a new substance named Albatin® is also used in hiperpigmentated skin treatment and for skin lightening. It is used as an inhibitor of melanogeneseis in lightening products, against age spots, and spots caused by long sunlight exposure. It is stable in pH 3-9, and the recommended concentration is 0.5–1.5%. It can be formulated without restriction into the aqueous phase of a gel, an emulsion or a solution. The substance is not cytotoxic, phototoxic, photosensitive, skin irritating. The mechanism of action is quite different from that of other skin lighteners. It does not act as inhibitor of tyrosinase, but contributes to melanogenesis inhibition, directly stabilizing DOPAchrome through inhibition of DOPAchrome tautomerase.

The paper gives account of the therapeutic observation of patients with circumscription hyperchromic dermatosis (CHD), where Albatin® was used as depigmentation product. Hydrogels with Albatin® concentration of 0.5% and 1.5% were produced, and thirty patients with different CHD (chloasma, melasma, Lentigo solaris, Lentigo senilis, ephelides, berlock dermatitis etc.) were treated and observed. The age of patients was 18-26 years. In the course of two months, therapeutic results were evaluated and recorded by medical checkup once in fifteen days. Besides depigmentation effects, the appearance of some possible contraindications (irritation and itch) was also observed. Astonishingly good results were obtained in ephelides therapy, good results in berlock dermatitis therapy, and poor results in solar and senil dermatitis therapy. Best results were obtained by 1.5% concentration.

IPS-P-016

AMOXICILLIN AND IBUPROFEN: DRUG INTERACTION, BACTERIOLOGICAL , CLINICAL AND PHARMACOKINETICS STUDY. PART 1. COMBINED THERAPY FOR TREATMENT OF HUMAN BACTERIAL INFECTION.

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It was found that ibuprofen(IBU)influences the complex immune system to overcome a bacterial infection and possesses antibacterial activity,thus,its formulation with amoxicillin(AMX)in the same dosage form(capsule)worth to be studied.The aim of this combination is to obtain a higher antibacterial activity and increase patients' compliance.AMX and IBUphysical mixture at ratios1:1and2:1were subjected to in-vitro examination for possible interactions using IR,UV scanning,DSC,TLC,results confirm absence of interaction.Effect of IBU on the antibacterial activity of AMX against certain bacterial species was investigated.The results showed that IBU potentiate the antibacterial activity of AMX towards certain micro-organisms.Sixteen A-I capsule formulations were prepared using a fractional factorial design (1/8)of 27and tested for powder content characteristics and dissolution testing which showed that neither drug affect the dissolution proces of the other.Data treatment and statistical analysis was performed.The chosen formulae; F4 and F15 were subjected to clinical study on 25 patients divided into 2 groups,one was treated with A-I capsules,the second was given AMX capsules.Data collected include;age, diagnosis,body temperature,total white blood cell count(W.B.C.),kidney and liver functions. Statistical analysis of W.B.C.data by using paired t-test revealed that there was a significant difference between before and after treatment and between AMX and A-I at $p<0.001$.There was no effect of sex on the percent decrease in W.B.C.at $p<0.05$.Thus,A-I combination proved to posses a higher clinical efficacy and microbiological activity than AMX alone.

IPS-P-017

PROMISING ALTERNATIVE CARRIERS TO LACTOSE MONOHYDRATE FOR CROMOLYN SODIUM DRY POWDER INHALATION

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To date, most Dry Powder Inhalation (DPI) rely on a-lactose monohydrate as the carrier of choice. However, interactions with many drugs with immunological and allergic problems were reported

In this study, Coarse sieved fractions (63-80 µm) of lactose, glucose, anhydrous lactose, avicel PH 101, spray dried lactose, mannitol and sorbitol have been evaluated as alternative carriers for cromolyn sodium (CS) that possess the positive aspects of lactose but overcome the above mentioned drawbacks. Their physicochemical properties (particle size, initial water content, microscopic optical image and moisture sorption capacity) were analyzed. Carriers that showed suitable physicochemical properties for use in DPIs (glucose and sorbitol) were further used to prepare CS-coarse carrier binary mixtures. Ternary drug carrier mixtures were also prepared adopting two strategies. The first one includes the addition of micronized carrier particles in different ratios to coarse carrier CS-binary mixture. In the second one, micronized aerosil 200® as a high adsorbing material was premixed with CS before the addition of coarse sorbitol in a trial to overcome its detected high moisture sorption capacity. Finally all formulations were tested for their in vitro aerosol deposition using a twin stage impinger

The results revealed that, no significant difference ($P<0.05$) between the fine particle fractions(FPFs) of CS delivered from mixtures containing lactose (36.05±1.5%), glucose (35.00±1.2%)and sorbitol (33.33±1.2%)

This suggests that glucose & sorbitol are promising carriers for DPI where they possess acceptable aerodynamic properties and able to deliver CS efficiently as lactose

IPS-P-018

DRUG CHECKING SYSTEM FOR THE SAFETY OF UNIT DOSE DRUG DISTRIBUTION SYSTEM—PRIMARY REPORT

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More attention had been placed on the topic of drug safety for patients in the past few years. In order to preserve the medication safety for hospitalized patients and prevent unnecessary and unknown source of human error, it is critical to implement an automatic drug dispensing system with Bar code Point-of Care (BPOC)1 which provide pharmacists the latest patient drug profiles with wireless connection, and also serves as an important tool to check drug names, dosages, doses, appearance and even the name of patients for nursing staffs during medication administration.

Therefore, we are actively discussing and communicating with the firm responsible for automatic dispensing machine on issues as re-integrating of dispensing protocol and updating the designs of the hardware and software. As for the pharmaceutical service and nursing procedures, a wireless updating system is designed for pharmacists when preparing prescription furthermore the system is adapted for nurses to administer and verify medication at patients' beside in order to minimize error-prone and unknown source of human mistakes.

IPS-P-019

ENHANCEMENT OF DISSOLUTION RATE OF ACYCLOVIR BY COMPLEXATION WITH HYDROXYPROPYL ?-CYCLODEXTRIN USING DIFFERENT TECHNIQUES

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Aiming to increase the water solubility of the poorly soluble drug, acyclovir, complexes of the drug with hydroxypropyl ß-cyclodextrin (HPßCD) were prepared. Complexes between the drug and HPßCD were prepared as physical mixtures and lyophilized forms. Phase solubility study was performed in phosphate buffer saline at concentrations 5, 10, 15 and 20% HPßCD. The complex was evaluated using differential scanning calorimetry (DSC), X-ray diffraction and thermal gravimetric analysis (TGA). The solubility studies showed that HPßCD-drug complexation was of the A(L) type, of stochiometric ratio 1:1. This was confirmed by the continuous variation method. DSC studies shows that a complex existed between acyclovir and HPßCD as indicated by the disappearance of the characteristic endothermic peak of acyclovir. X-ray diffraction revealed the acyclovir existed in an amorpheus state in the lyophilized inclusion complex. In-vitro release studies revealed enhanced dissolution of the poorly soluble drug when complexed with HPßCD (1:2). Such enhancement was more pronounced in the lyophilized form of the complex than the physical mixture.

IPS-P-020

PREPARATION AND EVALUATION OF RAPIDLY DISINTEGRATING TABLET IN THE ORAL CAVITY BY THE DRY GRANULATION AND COMPRESSION METHOD -AVAILAVILITY OF POWDERED CELLULOSE AS AN EXCIPIENT

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Introduction

A rapidly disintegrating tablet is known to be a form that can be swallowed easily because it is deformed by sputum in the human oral cavity. In this study, the tablet was prepared by the dry granulation and compression method using powdered cellulose (PC) as main excipients. Powdered cellulose is expected to be good for not only compressibility but also disintegration due to its swelling property. It also has the advantage of lower cost compared with other excipients such as microcrystalline cellulose.

Experimental

Batches contained some model drugs and PC, lactose (Lac), L-HPC as excipients were compressed to flakes by a roller compactor, then the flakes were crushed and sieved to granules. The granules were added to sucrose fatty acid esters (SE) as a lubricant and AEROSIL (AERO) then compressed to tablets by a rotary tableting machine. The tablets were evaluated mainly by tensile strength and disintegration time.

Results and Discussion

The rapidly disintegrating tablet containing PC were successfully prepared. Fluidity of the granules were improved and the tensile strength of tablets became higher using 0.1% AERO. As the amount of SE addition were increased, the tensile strength became lower and the disintegration time became later, but from the pressure transmission ratio, the optimal amount was 1~2%. The advantage of using PC was that it had very good compressibility and disintegrated faster after blending with L-HPC rather than using L-HPC alone. A disadvantage was that the evaluations on sensory test worsened as the amounts of PC increased, although this was improved by using saccharides such as Lac-

IPS-P-021

THE PHARMACEUTICAL MANUFACTURING OF CRUDE DRUG POWDER ~THE EFFECT OF SOME DISINTEGRANTS ON THE PHYSICAL PROPERTIES OF THE TABLET~

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Introduction
Crude drugs are very useful for health but these powders show various forms and properties that can become difficult to deal with qualities due to poor fluidity, strong adhesiveness and highly fibrous. Therefore we studied the pharmaceutical manufacturing of crude drug powder by the dry compacting method.

Experiment
Granules: Crude drug powders were mixed with a/some excipient, for example lactose or Micro Crystalline Cellulose (MCC), and compressed by a roller compactor into a flake form then the flakes were milled to produce granules. The physical properties of these granules were examined.
Tablets: The granules were compressed by a single or rotary tableting machine with a disintegrant, Kollidon CL and some binder, such as HPC, MCC and so on. The physical properties of these tablets such as tablet hardness, disintegration time and dissolution rate were examined.

Results and Discussion
As a result, tablets without a disintegrant showed a low hardness level below 1.0kgf and a long disintegration time over 1hr., but tablets with a disintegrant showed a lower hardness and shorter disintegration time. To increase the hardness, a binder, for example HPC or MCC, was added and the effect examined. Then the hardness was increased and the disintegration time was only slightly longer.
Furthermore, the optimal mixture ratio of binders and disintegrants was derived by multiple regression analysis.
This suggests that the formulation of tablets with ideal physical properties can be easily determined and that using these results allows the quantitative and rational manipulation of tableting.

IPS-P-022

COMPARATIVE EVALUATION OF MATRIX AND MINIMATRIX TABLETS OF CHLORPHENIRAMINE MALEATE

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Aim:To design extended release matrix and mini-matrix tablets of a water soluble model drug Chlorpheniramine maleate(CPM) using two native polysaccharides -xanthan gum(XG) and locust bean gum(LBG).
Methods: Granules of CPM were prepared by wet granulation technique using 50% of the polysaccharides comprising of XG and LBG in different ratios of 1:1, 1:2 and 1:3.Avicel PH101 was used as the diluent ,alcoholic solution of either PVP K-30 or Ethyl cellulose(EC) as the binder . Matrix tablets were prepared by compressing 150mg of the granules on 8mm punches and Mini-matrix tablets on 4mm punches.The tablets were evaluated for their physical parameters and drug content. The in vitro drug release of the tablets was studied in 500ml of distilled water. Drug release data was fitted in the zero order, first order and Higuchi models.
Results : The drug release was extended upto eight hours for mini-matrices and upto 10 hours for matrix tablets.The drug release from mini-matrices followed first order kinetics whereas the release from matrix tablets followed zero-order kinetics.
Conclusions: The present study suggests that the matrices and mini-matrices of XG-LBG could be successfully used in extending the release of a water soluble drug like CPM.

IPS-P-023

STABILITY TESTING OF SILDENAFIL TABLETS

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Stability testing of Sildenafil tablets is performed as part of the drug development program.
During the stress test of Sildenafil tablets assay (HPLC), impurities (HPLC), water and appearance were tested. It was shown that the product is chemically stable, however significant physical changes were observed after exposure to high humidity.
Within the formal stability study, samples of Sildenafil tablets 25 mg, 50 mg and 100 mg in two types of packaging are tested: OPA/Al/PVC/Al blisters (packaging A) and PVC/PVDC/Al blisters (packaging B). Formal stability study is performed in line with ICH guidelines. Assay, impurities, dissolution, disintegration, hardness, appearance and microbiological quality are monitored.
After the first six months of stability testing the results obtained with samples in two types of packaging were compared. The samples in packaging B have shown slightly greater changes in physical parameters (water, disintegration, hardness, appearance), than the samples in packaging A. However, since all of the obtained results complied with the specification requirements, it was concluded that both types of packaging provide adequate protection for Sildenafil tablets. Therefore, the more economical type of packaging, PVC/PVdC/Al blisters, was chosen as the final packaging for Sildenafil tablets.
Up to now, 24 months of stability testing is completed. The obtained results confirm adequate chemical, physical and microbiological stability of Sildenafil tablets in the proposed packaging. According to CPMP Note for guidance on declaration of storage conditions (CPMP/QWP/609/96/Rev 1) no labelling regarding storage conditions is required.

IPS-P-024

PREPARATION AND EVALUATION OF SOLID DISPERSION FOR NITRENDIPINE-AEROSIL SYSTEMS USING MELT-MIXING METHOD

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Introduction
Nitrendipine (NTD), a dihydropyridine calcium channel blocking agent, is used to treat a variety of cardiovascular disorders. Due to its low aqueous solubility (about 2μg/mL), leading to the poor absorption of nitrendipine after oral administration, we prepared solid dispersions of nitrendipine to improve its dissolution rate and solubility.
Experiment
Solid dispersions (SD) of NTD were prepared by the melt-mixing method using fine silica particles having different particle size and specific surface area (Aerosil) as carriers. The physicochemical properties and dissolution properties of SDs were investigated.
Results and Discussion
Powder X-ray diffraction and differential scanning calorimetry evaluation showed that NTD in SDs was dispersed in the amorphous state when treated by the melt-mixing method. Fourier Transformation IR Spectroscopy obtained with SDs indicated the presence of hydrogen bonding between the secondary amine groups of NTD and silanol groups of silica particles. For NTD-Aerosil 200FAD (1:5) SD, specific surface area and water adsorbed amount on the surface of SD particles at 0.4 relative pressure were 223 times and 20 times that of original drug crystals respectively. The dissolution property of NTD in SDs was remarkably improved regardless of the grade of Aerosil. For NTD-Aerosil 200FAD, 300CF, 380 (1:5) SDs, at the end of dissolution test (60min) the concentration of NTD were 28, 27, 22 times that of original NTD crystals respectively. The rapid dissolution rate from SD was attributed to the amorphism of drug, improved specific surface area and wettability than original drug crystals.

IPS-P-025

PREPARATION OF SOLID DISPERSION FOR PRANLUKAST HYDRATE AND HYDROXYPROPYLMETHYLCELLULOSE SYSTEM USING A TWIN SCREW EXTRUDER

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Introduction
The solid dispersion method, by which a drug is dispersed in a carrier to makeit amorphous, is one of the pharmaceutical approaches most commonly employedto increase bioavailability of poorly water soluble drugs. A pressurization/kneading/extruding method using a twin screw extruder is one of the methods used to facilitate solid dispersion. This extruder, originally designed as an extraction/ casting device for polymer alloys in the plastic or food industry, can be used formare and continuous production of solid dispersion.
Materials and methods
In the present study, we prepared solid dispersion of Pranlukast hydrate(ONON) as a model drug and Hydroxypropylmethylcellulose(TC-5E) as the carrier using a twin screw extruder. Additionally, we investigated improvement of the solubility of the drug by changing the extrusion conditions, operation temperature and the kind and quantity of additive liquid. The degree of solid dispersion obtained was evaluated and the crystallinity, solubility and interaction between drug and carrier were compared with those of preparation made by the co-grinding method and physical mixing.
Result and discussion
The extrusion pressure increased as the operation temperature decreases,but there was no change in the crystallinity of ONON. However, the solubility of solid dispersion produced under higher pressure was better than that of preparations produced under lower pressure. Therefore, the solubility could be improved by selecting an appropriate extrusion temperature, and the solubility of ONON was improved by changing the kind and quantity of additive liquids.

IPS-P-026

DESIGN AND IN-VITRO EVALUATION OF ALGINATE HYDROGEL PARTICLES OF GLICLAZIDE FOR ORAL CONTROLLED RELEASE: EFFECT OF POLYMER TYPE.

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Gliclazide,an effective antidiabetic drug, entrapped within gel microbeads using sodium alginate and systems containing mixtures of sodium alginate and various polymers were obtained by Orifice-Ionic gelation method. encapsulation efficiencies, bead size and drug release profile were evaluated. Increase in encapsulation efficiencies for the alginate beads from 69, to 76 and 84% were observed with the increase in drug ratio (sodium alginate: drug, 1:1, 1:3, and 1:5). The encapsulation efficiencies obtained for the gel beads in presence of different polymers were not affected significantly, except systems with xanthan gum where encapsulation efficiencies increased to 76% and systems with eudragit RL 30D and eudragit RS 30D decreased to 57 and 47% respectively. Also, increase in polymer concentration from 10 to 20% of total alginate polymer concentration had no effect on the encapsulation efficiencies. The majority of the studied systems showed no effect on the drug release except for xanthan gum that decreases the release significantly. Gel microbeads size distribution with and without polymers was approximately similar. However, increasing drug to polymer ratio increases beads size significantly. The morphological observations showed that the gel microbeads were spheroid with a homogenous distribution of the drug in the microbeads. From the previous work we can conclude that type, concentration of polymer, drug concentration and drug ratio to polymer, have effect on the characteristics of gliclazide hydrogel particles.

IPS-P-027

EFFECT OF VARIABILITY OF PRIMARY ACTIVE MATERIAL ON THE PERFORMANCE OF CARBAMAZEPINE GENERIC PRODUCTS

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The influence of the variability of primary active material on the dissolution behavior of carbamazepine (CBZ) generic products was studied using commercially available CBZ from different suppliers.
The differences between the commercial samples were determined by differential scanning calorimetry, X-Ray powder diffraction, hot stage microscopy, scanning electron microscopy, and dissolution rate.
The CBZ samples varied in their crystal modification or polymorphism, exhibiting different morphology, particle size and size distribution, all of which led to irregular dissolution behavior and affected short and long-term stability of the products.
The variations of the crystal properties are most likely due to the differences in the crystallization processes used by the different manufacturers of the drug.
The variability of the morphological properties was suggested to be due to the different conditions used in the manufacture and/or due to grinding.
The dissolution profiles of both, bulk powder and tablets, varied significantly from sample to sample. Furthermore, the mechanical properties were also influenced by the variability in the crystal modifications of the different samples.
The differences of primary active material were best described by powder dissolution profiles of bulk drug samples.
Conclusion: In order to maintain the quality of the final product either the characteristic properties of the drug have to be determined or a pretreatment has to be selected to eliminate the previous history of the active ingredient.

IPS-P-028

A NOVEL APPROACH TO THE PREPARATION AND SCALE UP PRODUCTION OF PENTOXIFYLLINE CONTROLLED RELEASE TABLETS: I. PREPARATION AND EVALUATION

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Aim: The purpose of this study was to prepare 600 mg pentoxifylline tablet formulation with acceptable controlled release (CR) profile and to scale it up to a pilot level.
Experimental: Tablets were prepared using wet granulation (WG), direct compression (DC) and hot melt (HM) techniques. The prepared formulae were subjected to various physicochemical and physicomechanical testing to determine the most appropriate formulation with an acceptable CR profile. Factors affecting the release profile either related to the formulation (content and type of gum, tablet hardness, granules particle size and tablet surface area/shape) or the production technique (Method of preparation, type of granulating fluid and thermal treatment) were studied. Formulae showed satisfactory CR profiles were subjected to scale –up production up to 20 kg per batch.
Results: Seven formulae prepared by WG technique, two prepared by DC technique and one by hot melt technique showed satisfactory CR profiles. Water, as a granulating agent, showed superior CR behavior compared to isopropyl alcohol. Decreasing the granule particle size and the tablet surface area improved the CR behavior. Scaling-up the previous formulae affected the release profiles dramatically. Only three formulae prepared by WG technique gave acceptable profiles.
Conclusion: Pentoxifylline CR tablets using wet granulation technique and water as granulating fluid with low granule particle size and either xanthan gum or HPMC E4 as gum type matrix and low tablet surface area gave satisfactory formula with acceptable CR profiles comparable to the innovator product.

IPS-P-029

ELECTRICAL MUSCLE STIMULATION AS NEW METHOD FOR ENHANCED TRANSDERMAL DELIVERY OF TENOXICAM IN PATIENTS

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Aim: To investigate the accessibility of AB Tronic fitness device (electrical muscle stimulator) for the transdermal delivery of tenoxicam in patients. Methods: Tenoxicam gel was prepared by dispersing 1% of carbopol 940 in a mixture of water and propylene glycol with drug (2%) and then neutralized with triethanolamine and adjust pH to 7.4. Fifteen human patients, suffering from stiff and painful shoulder, were participated in this study under supervision of a physician and divided into three groups. Tenoxicam gel was applied to each patient shoulder in three different ways: method I) add gel to first group only (passive transport, PT); method II) add gel to second group and then applying AB Tronic device (1pulse/second) for 10 minutes; method III) for third group applying AB Tronic device (1pulse/second) for 10 minutes then removes the device and then adds gel. Results: Pain and stiffness was relieved in the following decreasing order: method II > method III > PT. The pharmacokinetic parameters and area under the curve were calculated from blood levels of the drug reveals that method II showed higher AUC than method III than PT. Conclusion: Addition of gel and then applying AB Tronic device was the most interesting way for the application, where lag time was markedly reduced suggesting a faster penetration of drug into the skin and relieve pain.

IPS-P-030

FORMULATION, PHARMACOKINETICS AND CLINICAL EVALUATION OF NICARDIPINE HYDROCHLORIDE SUSTAINED RELEASE FLOATING TABLETS

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The aim of this study is to evaluate the prepared floating tablets of nicardipine HCl (NC)and determination of its pharmacokinetic parameters and hypotensive effect compared with a standard commercial capsules.Three hydrophilic polymers;NaCMC, HPMC and Avicel in combination with CO2 generating mixture(NaHCO3and anhydrous citric acid in the ratio of 1:1)were used in the compounding process.The tablets'rate of water uptake, floatation performance and dissolution rate were evaluated.Two chosen formulae(the first consists of 25:25:100mg of NaCMC: HPMC:Avicel while the second of 75:75mg of HPMC:Avicel per matrix)were subjected to pharmacokinetics and bioavailability studies which showed that both floating tablets had lower Cmaxand longer Tmax and Frel% of 87% and 119.4% compared to the conventional capsule.Clinical study was conducted on 16 male hypertensive patients,using formula of higher Frel% value and the conventional reference capsule for comparison,the obtained data showed that both evoked a hypotensive effect after 60 minutes and continued for 3 and 7hr for the capsule and the tablet respectively.The significant acute hypotensive maximum effect(Emax)were 10.85+0.141and 9.87+0.359mmHg with a tmaxof 2 and 6hr respectively.The mean values of the decrease in blood pressure at each interval for each administration were evaluated by ANOVA one way statistical analysis showing no significant difference between the prepared tablets and the conventional capsules at p<0.05.Sustained release effect of NC floating tablets was achieved which could increase patient compliance due to the reduction in vasodilatation-related effects such as flushing, headache, and peripheral edema.

IPS-P-031

DEVELOPMENT OF PECTIN/CHITOSAN MATRIX TABLETS FOR COLONIC DELIVERY OF DEXAMETHASONE.

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Aim: Development of pectin:chitosan (P:C) based matrix tablets for colonic delivery of dexamethasone. Methods: Pectin and chitosan were mixed in different ratios viz 2:1, 6:1and 10:1 P:C. In vitro release studies were done in pHs 1.2, 5.5, 7.4 and 6.8. The tablets were investigated concerning the % matrix erosion, the % water uptake and the unconstrained swelling behavior. In vivo evaluation was carried out in the cecum of conscious male rats with and without antibiotic treatment. Results: Tablets prepared with pectin only, failed to retain the drug enough period to reach the colon as 100 % of the drug was released after 4hrs. On the other hand, the addition of chitosan retarded the drug release. An inverse relationship was found between % drug released and % chitosan incorporated in the tablet. The 2:1 P:C tablet released 20% of its drug load after 5 hours before it reaches the colonic pH (6.8). The kinetic analysis of the release data showed variability in the order of drug release depending on the % of chitosan and the pH. The 2:1 P:C matrix tablet with the lowest rate of erosion and water uptake and the largest gel layer thickness, as well as the highest drug protection, was selected for in vivo studies which confirmed the ability of this matrix to deliver most of its dexamethasone content in the colon. Conclusion: The addition of chitosan to pectin was necessary to achieve colonic drug delivery of dexamethasone when formulated as matrix tablet. The optimum ratio of P:C was found to be 2:1.

IPS-P-032

PECTIN/CHITOSAN COMPRESSION COATED DEXAMETHASONE TABLETS FOR COLONIC DELIVERY: AN IN VITRO IN VIVO EVALUATION

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Aim: The preparation of compression-coated tablets containing dexamethasone in the core by dry coating with either pectin alone or pectin:chitosan (P:C) mixture for colonic delivery. Methods: The P:C mixture was used in the following ratios: 2:1, 6:1 and 10:1.The coat was applied into 3 layers to give different coat:core (c:c) ratios viz 1:1, 2:1 and 3:1. The in vitro release of the tablets in a gradient pH. In vivo evaluation was done in the cecum of conscious male rats with and without antibiotic treatment. Results: Pectin alone was unable to protect the tablet core from premature release even with 3 coating layers. Addition of chitosan to pectin offered better tablet protection. The formula with 2:1 P:C coat and 3:1 c:c ratio showed maximum drug protection. The dexamethasone release exhibited always an initial lag period followed by a stage of controlled drug release. The mechanism of release was complex as it was dependent on P:C and c:c ratios except in case of 2:1 P:C where the order of drug release was by diffusion at all coating levels, indicating that the number of coats had no effect on the mechanism of drug release at this P:C ratio. The formula with 2:1 P:C coat and 3:1 c:c ratio was subjected to further in vivo studies. The coat undergoes biodegradation in the presence of colonic microflora of the rat leading to higher drug release than in vitro. Conclusion: The addition of chitosan with pectin increased its protection ability until it reaches the colon. A successful colonic controlled drug delivery was achieved with 2:1 P:C at 3:1 c:c. Results were more prominent after in vivo studies as the colonic microflora plays a major role in drug release.

IPS-P-033

MEASUREMENT AND EVALUATION OF THE ADHESIVE FORCE BETWEEN FINE PARTICLES BY THE DIRECT SEPARATION METHOD AND THE INFLUENCE OF ELECTRIFICATION

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A new apparatus was developed to measure the adhesive force between particles with a high resolution of approximately 2nN. The force was measured directly by pulling the particles with a contact needle. Also, the separation processes were observed with a 3CCD camera during the measurement. Here, the adhesive force of six kinds of pharmaceutical particles and glass beads were measured, and the effects of moisture, shape and triboelectrification of the particles on the force were investigated. In the case of moisture adsorptive particles, the force of adhesion increased rapidly with the moisture content under high relative humidity. In the case of moisture non-adsorptive particles, the force was affected by particle shape and triboelectrification. The adhesive force of particles having sharp corners was greatly affected by triboelectrification at the corner of the particles. So, the distribution of triboelectrification affects the adhesive force of the particle. The adhering of finer particles to the surface such as lactose caused an increase in the distance between particles, and a marked decrease in adhesive force. A knowledge of the adhesive force of particles and factors influencing the force is of advantage to development of new drugs, for instance, dry powder inhaler, and to prevent pharmaceutical manufacturing troubles.

IPS-P-034

PREPARATION AND EVALUATION OF CHITOSAN MICROSPHERES OF DILTIAZEM HYDROCHLORIDE

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Microspheres of diltiazem hydrochloride were prepared by spray drying and solvent extraction technique using biodegradable and biocompatible polymer chitosan. Prepared formulations by both the methods yielded microspheres with good encapsulation efficiency, further an increase in the stirring rate, concentration of an emulsifier and temperature were found to reduce the particle size. The release of drug from the microspheres was found to follow biphasic pattern, including initial burst effect followed by slower release. Formulations were found to have no interaction with the excipients used in the formulation. SEM studies revealed that chitosan microspheres were spherical when prepared by solvent extraction method and appeared shriveled when prepared by spray drying irrespective of drug polymer ratio; further surface folding was also seen. The mechanism of drug release was studied by fitting the data into Korsemeyer peppas and Higuchi Model, according to which the formulations were found to follow fickian diffusion releasing the drug upto 12h. Thus prepared formulations by both the methods were found to be promising interms of successfully extending the release of diltiazem hydromchloride

IPS-P-035

FORMULATION AND EVALUATION OF ACYCLOVIR OCULAR INSERTS

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A common cause of blindness in developed countries is due to Herpes Simplex Virus(HSV) Type I infections.
Acyclovir ,selectively inhibits the replication of this virus .Therefore, it deemed necessary to develop Acyclovir formulations of prolonged ocular residence time. This can be achieved via development of ocular inserts.
Acyclovir inserts were prepared by casting method using polyvinyl alcohol (PVA) and methylcellulose (MC) mixtures .Inserts were subjected to the following studies:
in vitro release, water absorption capacity(swelling index) , effect of different additives(osmotic , viscosity imparting and hydrophobic agents) on drug release as well as differential scanning calorimetry (DSC).
Results showed significant increase in drug release from all formulations except in presence of hydrophobic agents which decreased the release significantly.
Increase in release was partially attributed to the presence of the drug in amorphous form as confirmed by DSC studies.
Statistical analysis of data was performed through Student t-test.
The best fit of release data for most formulae was obtained using Higuchi equation, although relaxation of polymers caused a slight deviation from Fickian diffusion. Release from some inserts was controlled by zero order mechanism.
Swelling index (using diameter method) of all the formulations did not exceed 25%.
In conclusion, polymeric ocular Acyclovir inserts are easily prepared; the rate and pattern of drug release can be modified using different additives.
This would ensure long residence time, better patient compliance, suitable drug level at target site and consequently less side effects

IPS-P-036

FORMULATION AND EVATUATION OF ACYCLOVIR OPHTHALMIC GELS

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Acyclovir, an antiviral agent, is successfully used to treat localized and systemic HSV infections. Commercially, it is available as tablets, suspension , ophthalmic ointment and skin cream.
ophthalmic ointment is applied 4-5 times daily causing side effects and poor patient compliance.
The aim of this study is the formulation of Acyclovir gels in a way to reduce the frequency of application, ensuring better bioavailability and patient compliance.
Acyclovir gels were prepared using three different concentrations of each of the following polymers: Methylcellulose (MC), sodium alginate, Carbopol, Chitosan, Hydroxypropylmethylcellulose (HPMC) and Hydroxyethylcellulose (HEC).
Formulations were subjected to release and rheological studies, differential scanning calorimetry (DSC) and Infrared (IR) analysis on drug, polymers and physical mixtures (1:1).
Results showed higher release rate with the lowest polymer concentration used.
Rheological studies indicated that the incorporation of drug into the polymer base increased the viscosity except for HPMC and Carbopol.
No interactions between drug and gel bases occurred as confirmed by DSC and IR studies.
Storage decreased the viscosity of all gel formulations except in case of sodium alginate. It also reduced the release rate for all formulations except for gels prepared with chitosan.
From the results obtained, we can conclude that good and prolonged release of the drug from gel formulations compared to ointment would ensure better bioavailability and patient compliance.

IPS-P-037

IMPROVED BIOAVAILABILITY OF CELECOXIB WITH SMEDDS

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Objective: The objective of the present investigation is to develop and optimize self-microemulsifying drug delivery system of poorly water-soluble drug celecoxib and to improve its oral bioavailability.
Introduction: SMEDDS is isotropic mixture of oil, surfactant and cosurfactant, when introduced in
GI fluid, which rapidly disperse to form particles of nanosize range enhancing absorption and GI permeation. SMEDDS is very good approach to overcome dissolution limited release of poorly water-soluble drugs. In the present investigation celecoxib has been chosen as a poorly water-soluble drug (6.18+0.23□g/ml). SMEDDS of celecoxib has been developed and optimized on the basis of particle size.
Experimental: Different oils, surfactants and co-surfacants were screened for the development of SMEDDS based on saturation solubility study. Approximate limit were set based on pseudoternary phase diagram. SMEEDS was optimized with the help of 23 factorial design. Analytical method of celecoxib was developed on HPLC both for human and rabbit plasma. In-vivo study in rabbits of optimized formulation was carried out.
Result and Discussion: Optimized system was found to be self-emulsifying in 10 sec with optimum viscosity and surface tension and with Particle size of 230nm. In vitro dissolution of optimized batch showed more than 95% release in 10 min. In-vivo study has shown enhanced oral bioavailability of SMEDDS compared to marketed preparation.
Conclusion:-Celecoxib capsule in SMEDDS was successfully developed to overcome dissolution limited release and hence enhance adsorption of the drug through GIT.

IPS-P-038

DEVELOPMENT OF A MICROBIOLOGICAL SPF DETERMINATION METHOD

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A microbiological method for SPF determination is validated as a simple quality control tool for assessing the photoprotective effect during sunscreen product development. Sunscreen preparations were applied as a continuous film on a UV- transparent membrane (2mg/cm2) covering nutrient agar plates on which E. coli was spread. Plates were irradiated by a UV lamp for different exposure times. After overnight incubation, colonies were counted and the decimal reduction time (DRT) determined. The method was validated by assessing the effect of selected experimental variables on DRT using a market SPF 12 product as standard and by correlating the DRT for a variety of commercial sunscreen products with their SPF values (ranging from 12 to 100). The method was then tested as a quality control tool by assessing the influence of formulation variables on the photoprotective effect of a series of O/W emulsion lotion formulations with different composition.
The method proved valid for detecting changes in the photoprotective effect of the standard product as a result of modifying experimental conditions. It proved also valid for ranking market sunscreen products according to their protective effect. Equally important, the method could successfully detect the change in the photoprotective effect of a sunscreen test formulation as a function of concentration of the sunscreen agent, benzophenone-3 and the synergistic photoprotective effect produced by combining this agent with chemical and physical sunscreen agents. An additional advantage was the ability of the method to detect the effect of physicochemical interactions on photoprotection provided by the test formulation.

IPS-P-039

BENZOPHENONE-3 SOLID LIPID MICROSPHERES : DEVELOPMENT AND IN VITRO CHARACTERIZATION

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Effective photoprotection by sunscreen products implies sustained availability of the sunscreen agent(s) to the outer layers of the skin in an effective concentration. Sunscreen controlled delivery systems offer promises in this respect. The aim of this study was to develop a controlled delivery microsphere system for the lipophilic sunscreen agent benzophenone-3 (BZ-3) with optimum pharmaceutical attributes. Microspheres (MS) were prepared using carnauba wax (CW) by a melt solidification technique. A full factorial design (24) was used to assess the combined effects of four independent variables (BZ-3:CW ratio, type and concentration of emulsifier and emulsification speed) on MS in vitro characteristics (particle size, drug loading, incorporation efficiency, and % drug release at 1 hour) as dependent variables. BZ-3 loaded MS of size ranging from 50 to 85 µm were obtained with more than 90% yield. Maximum drug loading and incorporation efficiency were 39% and 100% respectively. Drug release occurred according to combined first order and Higuchi kinetics and ranged from 34 to 84% at 1 hour.
All independent variables tested did affect MS in vitro characteristics. Statistical data obtained were used for the selection of MS formulations with optimum in vitro characteristics. These MS were incorporated in a W/O cream base. The protective effect of the cream against UVB radiation was assessed using two in vitro SPF spectrophotometric methods and a microbiological method developed in our laboratory. Combined results indicate that the sunscreen MS developed exerted a prolonged photoprotective effect which was potentiated by the microsphere carrier system.

LABORATORIES AND MEDICINES CONTROL SERVICES SECTION - POSTER SESSION

LMCS-P-001

COMPARATIVE STUDY OF AMOXICILLIN-SULBACTAM WITH OTHER FOUR ANTIMICROBIAL AGENTS IN VITRO.

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Aims: To evaluate the antibacterial activity of amoxicillin-sulbactam compared with other four antimicrobial agents in vitro.
Methods: The antibacterial activity of amoxicillin-sulbactam against clinical isolated strains were compared with amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanic acid and ceftriaxone.Minimal inhibitory concentrations were determinated by use of agar dilution method.
Results: The susceptible rate of amoxicillin-sulbactam against gram positive bacilli strains was 91,28%, higher than those of amoxicillin and ceftriaxone. The susceptible rate of amoxicillin-sulbactam against Escherichia coli, Klebsiella pneumoniae and Proteus mirabilis was 81,28%, 84,12% and 100%, similar with those of amoxicillin-clavulanic acid,ampicillin-sulbactam and ceftriaxone,higher than that of amoxicillin. The susceptible rate of amoxicillin-sulbactam against Enterobacter cloacae was 84,23%, higher than that of amoxicillin significantly and better than other two agents containing beta lactamases inhibitors and ceftriaxone.The antimicrobial activity of amoxicillin-sulbactam against common clinical isolated bacterial strains was better than that of amoxicillin, especially to beta lactamases positive strains.
Conclusions: Amoxicillin-sulbactam is an effective antibiotic containing beta lactamases inhibitor and a powerful antimicrobial agent for clinical bacterial infections especially to Enterobacter.

LMCS-P-002

LITHUANIA'S OFFICIAL MEDICINES LABORATORY'S FUNCTIONS, TASKS AND PERSPECTIVES IN PREVENTION OF LITHUANIA'S PHARMACEUTICAL MARKET FROM REJECTED MEDICINES AND PHARMACEUTICAL SUBSTANCES

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Aims:
This work involves the activity of LT-OMCL in 2001-2003. The main questions are:
» Does LT-OMCL fully perform its functions, which are indicated in its official regulations?
» How does LT-OMCL prevent Lithuania's pharmaceutical market from rejected medicines and pharmaceutical substances?
» Which drug defects were found?
» What are the perspectives of LT-OMCL?
Methods:
The work refers to:
1. Statistical data of LT-OMCL activity in 2001-2003.
2. The survey of reliable sources of information OMCLs activities in other countries.
Results:
1. The average number of investigated samples per year in all given period is: 7130 made by pharmaceutical industry, 2424 made by pharmacies and 9554 of total samples.
2. The average percent of defects found per year in all given period is: 0.14% of samples made by pharmaceutical industry, 0.20% of samples made by pharmacies and 0.16% of total samples.
3. There was almost no biological profile investigations performed in LT-OMCL in all given period.
Conclusions:
The most effective ways to optimize LT-OMCL work and to guarantee the best prevention of Lithuania's pharmaceutical market from rejected medicines and pharmaceutical substances are:
1. To make the LT-OMCL investigation project for the next year considering to the data of the last year LT-OMCL investigations and rejected medicines and pharmaceutical substances.
2. To expand variety of investigated drug forms.
3. To perform more modern biological profile analysis methods.

LMCS-P-003

IMPROVING REGULATORY REACH AND CAPACITY: DEVELOPING A NATIONAL REGULATORY PROJECTION SCHEME

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The Tanzania Food and Drugs Authority (TFDA) has implemented a six-zone regulatory administrative structure in the 21 governmental regions to coordinate and focus programs into a more manageable structure. The zonal centers provide a focus for training, collection of TFDA program data and regulatory extension by incorporating on a part-time basis other governmental health workers to perform on behalf of TFDA compliance assessments. Any out of compliance findings are then referred to the TFDA for follow-up and action. The TFDA has appointed a desk officer who among other duties is to liaise with the zonal centers ensuring good flow of information. For the pharmaceuticals control segment the training is focused on raising awareness on product quality attributes, performing structured product physical examinations, and inspecting both public and private drug dispensing outlet facilities. In addition a selected group of health workers were trained on Minilab® drug quality screening procedures to manage testing sites serving the various zones. An overview and current status of this effort will be presented.

LMCS-P-004

PROFICIENCY TESTING AS A TOOL TO ASSESS THE PERFORMANCE OF VISUAL TLC QUANTITATION ESTIMATES

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Thin-Layer Chromatography (TLC) has been used as a separation tool for an array of analytical applications. For example, TLC visual detection test procedures to assess pharmaceutical product quality has been included in a very convenient kit concept developed by the German Pharma Health Fund (GPHF) called the Minilab®. The Tanzania Food and Drugs Authority (TFDA) has established a drug product screening program using the Minilab® testing technology. All of the inspectors who participated in this program are pharmaceutical technicians or pharmacists who have had prior laboratory training in volumetric procedures. Prior to performing the screening procedures the inspectors completed a one-week training program after which each of the inspectors was sent with a Minilab® to perform the product screening tests at various locations in the country. As a part of the TFDA Quality Assurance (QA) program a proficiency test procedure was established to provide assurance that the Minilab® screening tests were being competently performed. The results of the first proficiency test indicated that most inspectors had difficulty discerning the differences of substandard products. A performance qualification test set was developed to reinforce the inspectors ability to discern the differences and their performance on a second proficiency test was markedly improved. It is important to include proficiency testing into the Minilab® implementation plan to provide an added measure of confidence in these screening tests and to identify additional training needs or other interventions to assure quality performance.

LABORATORIES AND MEDICINES CONTROL SERVICES SECTION - POSTER SESSION

LMCS-P-005

QUALITY ASSURANCE: INSPECTION TRAINING

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The flow-chart decision tree standard operating procedures and forms were used to develop a training manual, daily study guides, and examination materials for a one-week inspection training program, which includes inspection of import documents, compliance with labeling requirements, physical examination of products, etc., and outlines procedures for inspection at both ports-of-entry and dispensing outlets. In addition, a one-week Minilab-based screening test training program was developed for inspectors to field-test products to assess their quality. These programs were initiated in October, 2002 and have been fine-tuned in subsequent presentations. An overview of this program discussing successes and problems will be presented.

LMCS-P-006

DETERMINATION OF BENZOIC AND SALICYLIC ACID IN WHITFIELD'S OINTMENT BY DERIVATIVE SPECTROPHOTOMETRY

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Whitfield's Ointment contained 6% benzoic and 3% salicylic acid. Benzoic acid has a long history of use as an antifungal. Salicylic acid also possesses fungicidal properties and is used topically in the treatment of fungal skin infections.
A second-order derivative spectrophotometric method was suggested for the simultaneous determination of benzoic and salicylic acid in Whitfield's Ointment.Benzoic acid was measured at 289nm and salicylic acid at 304nm (peak-baseline). Validation of the method confirmed that linearity concentration range lies between 20-60 □g/ml for benzoic and 10-30□g/ml for salicylic acid. The corresponding regression equation was: 2D289 = 0,00004 + 0,00004□c (r = 0,9999), for benzoic acid and 2D304 = - 0,00002 + 0,00007□c (r = 0,9992), for salicylic acid. LOD was 3 □g/ml and 0,857 □g/ml ; LOQ was 10 □g/ml and 2,857 □g/ml for benzoic and salicylic acid, respectively.
The validity of the method was tested by an assay of benzoic and salicylic acid in Whitfield's Ointment. The mean value of the content of benzoic acid was 5,898% (98,30% of the labeled claim) and of the content of salicylic acid was 3,049% (101,63% of the labeled claim).
The developed method is suitable for fast and reliable identification and quantification of both components.

LMCS-P-007

QUALITY ASSURANCE: ESTABLISHING STANDARD OPERATING PROCEDURES

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The Tanzania Food and Drugs Authority compliance decision tree provides structure for inspectional standard operating procedures (SOPs) and reporting forms. The SOPs and forms outline how to conduct and record the examination of products and premises to determine their compliance or non-compliance with the laws and regulations. To establish standard operating procedures (SOPs), the following steps were taken—

- Each inspectional function was defined and reviewed together by a group of key managers and experienced inspectors.
- Step-by-step procedures on what actions are required to achieve each decision point were discussed and documented.
- These step-by-step procedures were developed into SOP format, and checklists were prepared to guide inspectors through the SOP process.

An overview of this process will be presented.

LMCS-P-008

QUALITY ASSURANCE: THE DRUG INSPECTION AND TESTING PROGRAM

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The Government of Tanzania has enacted legislation and regulations to help assure the quality of pharmaceutical products available in the market. To help improve market compliance, a ranked inventory of requirements and policies was prepared to guide all stakeholders. This inventory was used to develop a flow chart compliance decision tree, which directs the inspection process to regulatory decision points. These process revisions were presented at a stakeholders' workshop for wholesalers and importers to make them aware of the changes in regulatory expectations. Following the initial workshop in Dar es Salaam, the Minister of Health formally launched the new inspection program, in October 2002. Subsequently stakeholders' workshops have been conducted throughout the country to apprise them of the legal requirements and possible regulatory actions to be taken for non-compliance. The decision tree will be presented.

LABORATORIES AND MEDICINES CONTROL SERVICES SECTION - POSTER SESSION

LMCS-P-009

SIMULTANEOUS DETERMINATION OF SOME ANTIFUNGALS AND CORTICOSTEROIDS IN BINARY MIXTURES BY UV-SPECTROPHOTOMETRIC AND CHEMOMETRIC METHODS

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This work is concerned with the simultaneous determination of econazole nitrate (EZ)-triamcinolone acetonide (TA) and miconazole nitrate (MZ)- hydrocortisone (HC) in binary drug mixtures without previous separation by two different techniques . The first technique is the application of the derivative spectrophotometric methods, where the mixture of EZ-TA was determined using the first derivative of the ratio spectra . EZ can also be determined using the second derivative spectrophotometry . The mixture MZ-HC was also assayed for MZ using second derivative spectrophotometry and the first derivative of the ratio spectra. HC can be alternatively determined in binary mixture with MZ using the first derivative spectrophotometry.
The second technique is based on the application of different chemometric methods , namely classical least squares(CLS) calibration model , partial least squares(PLS) and principle component regression (PCR) models . These models were used after their validation for the prediction of the concentration of the analyzed drugs in their mixtures.
The validity of the proposed methods was further assessed by applying standard addition technique. The obtained results of the suggested methods agreed statistically with those obtained by the official methods.

LMCS-P-010

SEPARATION AND VALIDATION OF FIVE PRINCIPAL ALKALOIDS IN OPIUM AND OPIUM TINCTURE BY GRADIENT REVERSED-PHASE HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY-PHOTODIODE ARRAY DETECTION

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The separation of five alkaloids (morphine, codeine, thebaine, papaverine, noscapine)in opium and opium tincture samples has been achieved on a reversed- phase octadecyl column by gradient high-performance liquid chromatography-photodiode array detection. The multiple linear gradient program was started at 12% acetonitrile in potassium dihydrogen phosphate buffer to elute morphine, then hold at 16% acetonitrile to elute codeine, then hold at 22% acetonitrile to elute the remained three alkaloids. Heptane-1-sulfonic acid sodium salt was used as ion pair reagent to increase the resolution between morphine and morphine N-oxide. All of the peaks of five alkaloids in opium and opium tincture samples have good peak purity. The sample preparation was simplified by heating with methanol to removed flocculent precipitate of plant fragments in opium. The method validation involved system suitability, specificity, linearity, accuracy, precision, detection limit and quantitation limit.

LMCS-P-011

SALIVA AND SERUM LITHIUM MONITORING IN HOSPITALIZED PATIENTS AND A POSSIBILITY TO DSUBSTITUTE SALIVA FOR SERUM

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ABSTRACT

Aim of work
The aim of our study was to compare results of lithium ions concentration from two body fluids saliva and serum.
Methods
Lithium concentration was determined in saliva and serum of 25 patients treated with lithium carbonate (3x 300 mg) Jadran, Galen Laboratory Rijeka. Saliva and blood were taken 2 and 12 hours after the last dose. Lithium ion determination was done using the dry-slide technology Vitros 250 Analyser (Ortho Clinical Diagnostic) and atomic absorption spectrometry (AAS) method Perkin Elmer 403. At the same time samples of blood and saliva were determined with these methods, which showed a high level of correlation.
Results and discussion
The mean difference between serum and saliva was statistically significant for p<0.05 using t student test. The saliva/serum ratio after 12 hours was 1.24 +/- 0.269, while after 2 hours it was 2.15 +/- 0.179 using dry-slide technology; after 12 hours it was 1.22 +/- 0.314, and after 2 hours 2.17 +/-0.170 by AAS method.
At saliva we got Ki = 0.02□[1]h and half-life of saliva was t1/2 = 34.6 hours. For serum half-life was t1/2 = 24 hours, which means that the lithium ions elimination is slower from saliva than from serum. That is the reason why probably the concentration in saliva is higher than in serum.
Conclusion
The lithium elimination is a two-compartment pharmacokinetic model, where saliva and salivary glands are an important part of the compartment. At a certain point in medical treatment, it could be expected to use controlled determination of lithium ions in saliva and in serum as control.
Key Words: Lithium, Serum, Saliva.

LMCS-P-012

VITROS DRY SLIDE TECHNOLOGY METHOD FOR THE DETERMINATION OF LITHIUM IONS IN HUMAN SERUM

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ABSTRACT

Aim of work
The medical treatment with lithium preparations demands the determination of the lithium ions concentration 12 hours after the last dose when the excretion of lithium ions has already started. The aim of work was to compare lithium ions concentration analyzed by dry-slide technology Vitros 250 Analyser (Ortho Clinical Diagnostic), atomic absorption spectrometry (AAS) method Perkin Elmer 403 and ion-selective electrode (ISE) potentiometry AVL 9181.
Methods
The Vitros 250 Analyser consists of a colorimetric end-point reaction where the crown ether chromophore binds the lithium in the sample; the resultant dye complex is measured using reflectance spectrophotometry at a wave-length of 600nm after 2.5 minutes at 37° C. We analyzed lithium ions in 23 serum specimens of patients after oral administration of lithium carbonate (3x 300mg) Jadran, Galen Laboratory Rijeka by dry-slide technology, AAS and ISE methods.
Results and discussion
The precision of dry-slide technology, variation coefficient (CV) varied from 2.45 to 4.64 %. The reproducibility of the method determined CV to be from 0.60 to 1.81% over a ten-day period. The accuracy of the assay in the concentration range examined was from 3.60 to 6.12%. The limit of detection was 0.20 mmol/L.
Conclusion
The Vitros dry slide technology gave a good coefficient of correlation (r) with AAS and ISE method. Dry slide technology is a practical method of interest in the therapeutic monitoring of patients receiving lithium salts. It may also be an useful alternative or it could even change other methods such as AAS.
Key Words: dry slide technology, AAS, ISE and lithium.

LABORATORIES AND MEDICINES CONTROL SERVICES SECTION - POSTER SESSION

LMCS-P-013

DETERMINATION OF LACIDIPINE IN THE PRESENCE OF ITS ACID DEGRADATE BY DERIVATIVE,UV-SPECTROPHOTOMETRY AND COUPLED HPTLC DENSITOMETRY

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Two sensitive and selective spectrophotometric and coupled HPTLC-densitometric methods have been established for determination of Lacidipine in the presence of its acid degradate .Derivative,UV-spectrophotometric techniques were carried out by measuring the absorbance of (¹D) at 271.2nm,(¹D) at 285nmand(¹DD) at 229.6nm.The concentration range was 5-30 µgml-1 for the three techniques, with the corresponding mean accuracies of 100.118± 0.743,99.41± 0.946 and 99.59± 1.04 respectively.
For coupled HPTLC-densitometry;the separation was done on silica gel plates(10x20cm) with H2O:methanol:30%NH3(4:6:0.05,v/v) as the mobile phase,developing time was 20min ,Rf =0.52 and scanned at 240nm.The concentration range was 5-60µg/spot,with the mean accuracy of 99.615±1.4315.
The results obtained were statistically compared with those obtained by the company method.
The degradate was confirmed by IR and mass-spectrometry.

LMCS-P-014

SOLUBILITY OPTIMIZATION AND FORMULATION OF NIMESULIDE INJECTION

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AIM: The aim of the study was to solubilize nimesulide a water insoluble analgesic, anti-inflammatory and antipyretic drug by the use of physiologically compatible hydrotropes and to attempt their injectable formulation and evaluations.
METHODS: UV method was selected for the analysis of nimesulide in solubilized systems. For solubility enhancement hydrotropic solubilization method was proved to be successful for nimesulide in the study, using sodium benzoate (SB), sodium-o-hydroxy benzoate (SS) and sodium-p-hydroxy benzoate (SP). Physical parameters like viscosity, relative density, conductivity, diffusion study, interaction study, pH study, refractive index, gel study etc was done.A greater solubilization capacity was noted for SB than SS and SP, which has been explained on the basis of possible steric factor. The solubility determination was carried out at 25□2oC and 37□2oC.
RESULTS AND CONCLUSIONS: The solubility increased up to 93 times at 37□2oC in sodium benzoate (25% w/v solution) solution while upto 87 times at 25□2oC in sodium benzoate (20% w/v) solution. The solubilizing power of different hydrotropes could be ranked as. SB > SS > SP.
Formulation was prepared with sodium benzoate (20%) using Sodium metabisulphite (0.1%) and EDTA (0.1%) as antioxidant and chelating agents. Physical and chemical stability study was conducted and found that injection with sodium benzoate was stable for 108 days.

LMCS-P-015

RP-HPLC METHOD FOR ASSAY OF FOLIC ACID IN CHEWABLE TABLETS

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Introduction:Folic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)-methyl]amino]benzoyl]-glutamic acid, is a member of the vitamin B group. Folic acid is reduced in the body to tetrahydrofolate, which is a coenzyme for various metabolic processes.

Methods: The chromatographic system consisted of a Shimadzu LC-10ADvp pump, a Rheodyne 7725 injector with a 20 µl sample loop and a Shimadzu SPD-10AVvp UV-VIS detector. Separations were performed on a Purospher® STAR RP-18 endcapped column (150mm x 4,6mm; 5µm) at room temperature using 0.1 M sodium acetate : acetonitrile (940:60 V/V), adjusted to pH 5.7 with acetic acid as mobile phase. Flow rate was 1.0 ml/min. UV detection was performed at 254 nm.

Results: The aim of this work was to find optimal conditions for HPLC method determination of folic acid in chewable iron and folic acid tablets. Each chewable tablet contains 350 µg (mcg) of folic acid and iron(II)hydroxyde polymaltose complex equivalent to 100 mg elemental iron. Validation of applied method was carried out by determination of linearity range, accuracy, precision (repeatability, reproducibility). The sensitivity of method was demonstrated with determined LOD and LOQ for active components.

Conclusion: The obtained results show that applied HPLC method may be used for determination of folic acid in chewable iron and folic acid tablets.

LMCS-P-016

DETERMINATION OF LACIDIPINE IN THE PRESENCE OF ITS ACID DEGRADATE BY DERIVATIVE,UV-SPECTROPHOTOMETRY AND COUPLED HPTLC DENSITOMETRY

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Abstract
Two sensitive and selective spectrophotometric and coupled HPTLC-densitometric methods have been established for determination of Lacidipine in the presence of its acid degradate .Derivative,UV-spectrophotometric techniques were carried out by measuring the absorbance of (1D) at 271.2nm,(2D) at 285nmand(1DD) at 229.6nm.The concentration range was 5-30 µgml-1 for the three techniques, with the corresponding mean accuracies of 100.118±0.743,99.41±0.946 and 99.59±1.04 respectively.
For coupled HPTLC-densitometry;the separation was done on silica gel plates(10x20cm) with H2O:methanol:30%NH3(4:6:0.05,v/v) as the mobile phase,developing time was 20min ,Rf =0.52 and scanned at 240nm.The concentration range was 5-60µg/spot,with the mean accuracy of 99.615±1.4315.
The results obtained were statistically compared with those obtained by the company method.
The degradate was confirmed by IR and mass.

MILITARY & EMERGENCY PHARMACY SECTION - POSTER SESSION

MEPS-P-001

RATIONAL AND COST EFFECTIVE USE OF PROTON PUMP INHIBITORS

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ABSTRACT

Title: Rational and cost-effective prescription of protein pump inhibitors (PPIs) in the Armed Forces Memorial Hospital-Kenya.
Objective: (1) To determine the relationship between prescriptions for PPIs and gastro-intestinal conditions
(2) To compare the usage of different PPIs and cost implications.
(3) To compare the pattern of PPI prescriptions with the recommendations of the National Institute of Clinical Excellence.
Design: Retrospective, cross-sectional study evaluating the utilization of PPIs.
Setting: Armed Forces Memorial Hospital-Kenya
Subjects: Dispensed PPIs for 104 patients from the hospital pharmacy over eight consecutive weeks (15 January to 15 March 2004).
Results: 67 patients (64.4 %) had no appropriate upper gastro-intestinal tract Investigations and 52 patients (75.4%) did receive trial of H2 – antagonist therapy before
commencement of a PPI. The major indication for use of PPIs in the study patients were gastro- oesophageal reflux in 68 patients (65.4%), peptic ulcer disease in 19 patients (18.3%), NSAID induced ulcer in 9 patients (8.7%) and non-ulcer dyspepsia in 8 patients
(7.7%). 81 patients (77.9%) were treated at a cost below Kshs 5000. In only 45 patients (43.3%) did prescriptions comply with the NICE guidelines. Clinical indication that failed highly in meeting the guideline was gastro esophageal reflux disease.
Conclusion: Drug utilization data indicate high costs that were incurred as a result of not using the guidelines. Many patients were put on PPI without any investigations. These findings explain the irrational use of these drugs and associated hospital expenditure.

MEPS-P-002

ASSESSMENT OF RISKS ASSOCIATED WITH SHORT-TERM USE OF MEFLOQUINE IN CANADIAN FORCES MEMBERS : A DESCRIPTIVE CROSS-SECTIONAL STUDY

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Methods
Medical records of Regular Canadian Forces personnel who served in Somalia between 1992 and 1993 were reviewed by trained data extractors. All health effects recorded during treatment with mefloquine were assigned ICD-10-CA codes. Data extractors also noted if the effect has been reported with mefloquine, and rated the severity of the effect. Cohen's kappa was calculated to determine concordance between extractors, and descriptive statistics used to report the health effects seen.

Results
The majority of the 1413 subjects identified were male (96%). A total of 5019 adverse health effects were recorded in the medical records, most of which were mild in severity. At least one adverse effect which could potentially have been related to mefloquine was reported in 39.2% of subjects. Of the adverse effects recorded, 21 were classified by the data extractors as major (18 affecting the nervous system and 3 cardiovascular system effects). These results are consistent with those reported in other populations.

Conclusions
The results of this study have been applied to guide development of policies governing the provision of chemoprophylaxis for subsequent military missions. In particular, resources have been allocated to formalize the counselling provided to members regarding antimalarials and the prevention of malaria.

MEPS-P-003

A CANADIAN FORCES CERTIFICATION PROGRAM FOR NON-TRADITIONAL HEALTH CARE PROVIDERS

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Background
In contrast to provincial health care systems, the Canadian Forces (CF) relies heavily upon alternative professionals to provide heath care in challenging environments. Medical Technicians (Med Techs) provide non-prescription (OTC) medications to CF members to manage both minor self-limiting illnesses and urgent or emergent conditions.
Purpose
To develop an evidence-based process to assess the competency of Med Techs to supply selected OTC medications safely and appropriately.
Process
Existing provision of medications policies were reviewed. Following an extensive literature review, the policy framework was reconfigured to meet the CF's unique needs. A decision was made by consensus to apply a model allowing delegation of tasks defined in the Med Tech scope of practice. A certification examination was used as a screening tool to ensure that Med Techs have maintained their competence to supply OTC medications.
Output
A variable option multiple-choice examination was developed based on critical decisions required of Med Techs in this practice area. Components of the examination process include: development of an exam blueprint therapeutic; defining the scope of practice definition; development of questions by Med Techs and expert item writers; establishing a pass standard using modified Angoff method pass standard; rigorous psychometric analysis
Conclusions
A valid examination is now used to assess the competency of CF Med Techs to supply OTC medications. The exam identifies those who have maintained their competency, and highlights those who require additional assessment, educational or training to demonstrate such competency.

MEPS-P-004

UPDATING AND TENDENCIES OF BIOAVAILABILITY (BA) AND BIOEQUIVALENCE (BE), REGULATORY ASPECTS IN URUGUAY AND THE LATIN AMERICAN REGION.

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The use of Generics, the responsibility assumed at the time of interchanging medicines with the efficiency and safety which must be given to the patient in his treatment, lead to necessity of having regulations according to the reality of the country and the International Norms.
OBJETIVES:
* Revision of the regulatory aspects of BA and BE of the medicines in Uruguay and tendencies in the region within the frame of harmonization and integration programs promoted by PAHO.
* Analysis of the impact of the generic prescription and pharmaceutical substitution; and the need to demand BA and BE studies within the regulatory practice in our country.
METHODOLOGY:
* QMS Documents
* Guidelines for the FDA Industry
* UE Norms
* Norms in regions
* Documents issued in Conferences of the PAHO
* National Bibliography
CONCLUSIONS:
I)The PAHO has strongly developed the concept of 'generics' in the region in order to make medicines accessible, but national authorities have faced certain failures regarding this issue. In the pharmaceutical market there are a number of 'similar ones', which have been interchanged and it is unknown whether they are equivalent or not. At the Military Hospital, medicines are traditionally interchanged based on costs.
II) The costs of the BA and BD studies should be no obstacle
III) There is a Regulation Project on the rational use of medicines in Uruguay which has as its main objective to know the degree of interchange of the different medicines, with the premise that the GMP are the basis of assurance of the quality. The implementation of this practice is still in process.

MILITARY & EMERGENCY PHARMACY SECTION - POSTER SESSION

MEPS-P-005

HOW CANADIAN FORCES (CF) PHYSICIAN ASSISTANTS (PA) MET THE MEDICATION NEEDS OF CF MEMBERS.

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Background
The CF has an obligation to provide quality health care to CF members often in very distinctive settings. Unlike most health care systems the Canadian Forces (CF) relies heavily upon unique heath care providers such as Physician Assistants (PAs). PAs provide care, including prescription medications to CF members for urgent emergent conditions where a delay in treatment would be harmful. CF members in operational settings need medications provided in a safe and effective manner by a competent provider.

Objective
To develop an evidence-based process to assess the competency of PAs to provide selected medications safely and appropriately.

Methods
In order to assess competency, a variable option multiple-choice, critical decision, key question type examination was developed. Steps involved in this process included: exam blue print development (disease states/therapeutics); scope of practice (SOP) definition; question development by practicing PAs and expert item writers according to practice-based blueprint; modified Angoff methodology utilized to set the pass standard; psychometrical analysis prior to release of results

Conclusion
A validated examination is now used to assess the competency of PAs to provide prescription medications. This exam is used to identify those who have maintained their competency, and to highlight those who require additional assessment, educational or training to demonstrate such competency.

MEPS-P-006

PHARMACIST-MANAGED, PHYSICIAN-DIRECTED MANAGEMENT OF ALLERGIC RHINITIS IN THE CANADIAN FORCES – A TRIAL

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Canada

Background
According to the 2000 Canadian Forces Health and Lifestyle Information Survey, 21% of male and 32% of female Canadian Forces (CF) members suffer from allergic rhinitis (AR).

Objective
To evaluate the impact of pharmacist-managed care on the quality of life of AR patients in the CF.

Study Design
CF members with a confirmed diagnosis of AR who presented to sick parade, physician appointments or a base pharmacy at 4 CF bases between September 2003 and December 2004 were included in the study. Patients at the 2 control bases received standard pharmacist care while patients at the 2 treatment bases received enhanced pharmacist care including: monthly follow-up consultations, detailed counselling and modification of medication therapy via a collaborative prescribing protocol. As the primary outcome, study participants completed the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ(S)) at 4 week intervals, patients were followed for 12 weeks.

Results
Ninety-two patients were recruited (39 control, 53 intervention). Results indicate that CF members receiving enhanced care from pharmacists report a clinically-significant improvement in allergy symptoms and related RQLQ(S) scores at week 4. These improvements were sustained for the entire study period. Patients receiving enhanced pharmacist-managed care showed a more rapid progression to clinically relevant improvements in emotional and non-eye/nasal symptoms versus the control group.

Conclusion
Regular interaction with a pharmacist over a 12-week period, where counselling can be provided and pharmacotherapy adjusted, appears to positively impact AR symptoms and quality of life.

MEPS-P-007

ROLES OF THROMBOXANE A2 IN OLEIC ACID-INDUCED LUNG INJURY

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Japan

[OBJECTIVES] Acute respiratory distress syndrome (ARDS) is a severe lung injury with hypoxemia.We are trying to elucidate the mechanism of ARDS and to find candidate drugs against the disease, by using an animal model, oleic acid (OA)-induced lung injury. Although precise mechanism of ARDS is not clear, thromboxane A2 (TXA2) is suggested to play an important role. On the other hand, participation of TXA2 in the OA-lung injury is unclear. Therefore, we examined the participation of TXA2 in the OA-lung injury. [RESULTS] An intravenous injection of OA to guinea pigs caused hypoxemia, and an increase in TXB2, a stable metabolite of TXA2 in bronchoalveolar lavage fluid (BALF). Both ozagrel, an inhibitor of TXA2 synthetase and EPC-K, an inhibitor of phospholipase A2, prevented the hypoxemia and the increase in TXB2. OA injection induced hyperpermeability of pulmonary blood vessels and also induced an increase in macrophages and neutrophils in the BALF, while eosinophiles and lymphocytes were not increased. The expressions of mRNAs of chemokines which activate macrophages and neutrophils were increased with OA, but those of chemokines that activate eosinophiles were not increased. Ozagrel inhibited the expressions and the increase in macrophages and neutrophils in the BALF. RAW264 cells derived from macrophages released TXA2 with an application of OA.[DISCUSSION] These results suggest that an increase in TXA2 in the lungs induced by OA, facilitates the expressions of mRNAs of chemokines, which leads to an activation and infiltration of macrophages and neutrophils into alveolus.

PI-P-001

EFFECT OF ATP-SENSITIVE POTASSIUM CHANNEL MODULATORS ON INDOMETHACIN-INDUCED GASTRIC LESIONS

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Mechanisms like decreased gastric mucosal blood flow, increased motility, acidity and apoptosis have been proposed for the pathophysiology of indomethacin-induced gastric lesions (IIGL). It seems probable that ATP-sensitive potassium (KATP) channels have a regulatory effect on them. AIM: Investigation of the effects of KATP channel modulators, nicorandil as a channel opener and glibenclamide as a channel antagonist, on IIGL. METHODS: Gastric lesions were induced by injection of indomethacin (40 mg/kg s.c.). Nicorandil (2 and 10 mg/kg i.p.) was given to 2 groups and a third group recieved glibenclamide (6 mg/kg i.p.). Another 2 groups recieved glibenclamide, concomitantly, with either doses of nicorandil. Nicorandil and glibenclamide were always given thirty minutes and one hour, respectively, before indomethacin.The rats were killed 5 hours after indomethacin and the stomachs were removed. Macroscopic gastric lesions in each stomach were measured and the ulcer index and preventive index was calculated. RESULTS: Indomethacin produced ischemic lesions in 96% of the rats with an ulcer index of 20.4. Nicorandil protected by up to 51.2% against indomethacin-induced lesions and glibenclamide aggravated the lesions by 55.1%. CONCLUSION: 1)Nicorandil has an ulcer-protective action which is,assumingly,completely attributable to its KATP channel opening action. 2) It is suggested that antagonism of KATP channels is an important pathway for tissue injury by noxious agents and that KATP channel antagonists may play a permissive role in damage produced by other ulcerogens.
3) KATP channel openers may prove to be important candidates for developing new effective anti-ulcer drugs.

PI-P-002

MAKING EFFORTS TO PROMOTE CLINICAL PHARMACY BETTER IN ROMANIA

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Romania

AIMS: To develop the hospital pharmacy as a service system where the patient can meet professional pharmacists and get advice about medication usage in an easy and inspiring way.
METHODS: A new style for drug dispensary as well as drug information service have been implemented for the outpatients.
RESULTS:
1. Pharmacy was reconstructed completly into a patient-centered service. The dispensary was changed from 'window style service' to 'counter style service', wich is so called face-to-face service for the patients.
2. The individual drug list is proved to help the patients to understand the whole medicines treatment and the cost of every medicine.
3. The drug usage labeling is combined with a simple oral explanation to make sure that patients can follow the important usage directions exactly.
4. Specialized counseling pharmacists are available to answer the special questions based on each patient's disease history and background.
5. The 'Drug usage booklet' is delivered for recording the medication history and informing patients severer adverse effects and drug interactions with some precautions. This is especially useful for the elderly patients with chronic diseases.
CONCLUSIONS: The concept of pharmaceutical care has been prevailing accepted in Romania for many years. Our practice has been promoted by many hospital pharmacies, and will contribute to improve rational use of medicine in Romania.

PI-P-003

PHARMACOGENOMICS AND PHARMACEUTICAL CARE

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Pharmacogenomic is relatively new science. The complete sequencing of the human genome will result in improved understanding of the role of genes in disease and drug response. Genetic profiling will become an integral part of the prescription process whereby drugs will be prescribed based on a patient,s genotype. Pharmacists will need to understand the concepts and promise of pharmacogenomics in order to adapt to the demands of genotype-based prescribing.
The aim of this presentation is to emphasize how pharmacogenomics might influence pharmaceutical care in the future. The surge of interest in pharmacogenomics stems from growing knowledge that individual responses to drugs vary considerably. We are consider the potential benefits of pharmacogenomics to pharmaceutical care in the future like as :

- more powerful medicines
- better, safer drugs the first time
- more accurate methods of determining appropriate drug dosages
- improvements in the drug discovery and approval process and
- decrease in the overall cost of health care.

Impact of pharmacogenomics will be allow medical practitioners and pharmacist to avoid the prescription of drugs to non-responders or those patients who are predisposed to adverse reactions. Pharmacogenomics aims to provide the right prescription immediately for the maximum benefit of the patient. Pharmacist are likely to be key players in the dispensing of drugs based on an individual,s gene profile.

PI-P-004

PHARMACEUTICAL EXPENDITURES IN ARMENIA

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Pharmaceutical expenditures are very different depends on countries. There is no official data about drug spending in Armenia. The aim of this work was to study the situation on pharmaceutical expenditures and to develop appropriate recommendations.
Methods: documents review; collecting information from records and the National Statistical Service; interviewing key staff.
Analysis of the State Budget shows that the sums planned for medicines centralized procurement were very low (about a half of USD per capita) for the period up to 2003 when it is sharply increased reaching almost 2.2 US dollar in per capita terms. Since 2004 public drug expenditures again twice decreased. Real expenditures were always less than planned. Private expenditures are also sharply increased since 2002, and the trend is kept. The private expenditures made up 7 USD per capita without taking into account shadow economy. Drug donations were significantly reduced since 2000.
Comparison demonstrates that pharmaceutical expenditures in Armenia are very low. In the OECD on average, the public pharmaceutical expenditures in 1996 was 137 USD per capita, in developing countries it is usually less than 30 USD, and only in 38 countries it is less than 2 USD. This leads to the situation when many patients lack access to essential medicines. Recommendations on increasing public pharmaceutical expenditures and other strategies for improving affordability of medicines were presented to the Ministry of Health. Access to information should also be amended. Accountability and transparency mechanisms have to be introduced.
This work was supported by the OSI – with the contribution of the IPF of OSI-Budapest.

PI-P-005

QOL OF PATIENTS WITH UNIPOLAR MAJOR DEPRESSIVE DISORDER WITH SOME SELECTED ANTIDEPRESSANTS.

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India

Aim: To assess the changes in Quality of life (QOL) of patients with unipolar major depressive disorder receiving either single or combination of selected antidepressant drugs.

Method: The study was open labeled, prospective study conducted over a period of nine months at the department of psychiatry of J.S.S.Medical College Hospital, Mysore. Total five drug groups were selected. The different drug groups were i.e. citalopram, sertraline, dothiepin, citalopram in combination with dothiepin and sertraline in combination with dothiepin group. Patients of either sex who were diagnosed as having unipolar major depressive illness as per DSM-IV criteria and patients who gave their written consent to participate in the study were included in the study. Institutional Human Ethical Committee of J.S.S. College of Pharmacy, Mysore, has approved the study. WHO-BREF Quality of Life questionnaire was used to assess the quality of life.

Results: Among all the five drug groups, statistically significant ($p<0.05$) improvement in quality of life at the end of 8 weeks was seen in sertraline plus dothiepin combination compared to other groups.

Conclusion: Improvement in quality of life scores of patients with unipolar major depression was found in all the study groups. The maximum improvement in quality of life scores was seen with sertraline plus dothiepin group followed by citalopram group.

PI-P-006

COMPARATIVE STUDY OF SAFETY AND EFFICACY OF SOME SELECTED ANTIDEPRESSANTS IN UNIPOLAR MAJOR DEPRESSIVE DISORDER

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Aim: To assess and compare the safety and efficacy of selected antidepressants and their combinations in unipolar major depressive patients.

Method: The study was open labeled, prospective study conducted over a period of nine months at the department of psychiatry of J.S.S.Medical College Hospital, Mysore. Total five drug groups were selected. The different drug groups were i.e. citalopram, sertraline, dothiepin, citalopram in combination with dothiepin and sertraline in combination with dothiepin group. Patients of either sex who were diagnosed as having unipolar major depressive illness as per DSM-IV/ICD-10 criteria and patients who gave their written consent to participate in the study were included in the study. Institutional Human Ethical Committee of J.S.S. College of Pharmacy, Mysore, has approved the study. Hamilton rating scale for depression – 17 items and somatic symptom questionnaire were used to assess the efficacy. Udvalg for Kliniske Undersogelser side effect rating scale was used to assess the safety.

Results: Results of this study showed that citalopram was most efficacious drug ($p<0.05$) showing 93% reduction in HAM-D scores and 98% reduction in somatic symptoms followed by sertraline plus dothiepin combination. Upon assessment of safety parameter study showed that citalopram was safest drug with only decrease in salivation as an ADR while sertraline plus dothiepin combination showed maximum number of ADRs.

Conclusion: All the study drugs were effective in treating unipolar major depression. The results suggest that citalopram was found to be most efficacious and better tolerated drug among all the study groups.

PI-P-007

ANTIMICROBIAL DRUG RESISTANCE (AMR): AN INCREASING CONCERN FOR TREATMENT FAILURE

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The devastating effects of HIV infection, tuberculosis, malaria, and many other infectious diseases, especially in resource-poor countries, has led to local, regional, and international public efforts in the prevention and treatment of infectious diseases. However, the scale of infections diseases is changing rapidly because of emerging infections and AMR. AMR results in increased morbidity, mortality and costs of health care. AMR has been observed since the 1940s with penicillin resistant Escherichia coli and Staphylococcus aureus. Resistance has also been detected in both gram-positive and gram-negative organisms immediately after the introduction of penicillin. Recently, more and more pathogens are showing multiple drug resistance. Examples are multiple drug-resistant Mycobacterium tuberculosis (MDR-TB), penicillin-resistant Streptococcus pneumoniae, fluconazole-resistant Candida, methicillin-resistant S. aureus (MRSA), vancomycin-resistant Enterococci (VRE) and more recently, vancomycin-resistant S. aureus (VRSA) with reduced susceptibility to vancomycin. Given the spectacular increase in the incidence of multiple drug-resistant organisms and the growing resistance transfer from one organism to another, we will certainly witness pathogens for which there are no antibiotic solutions. Both prescribers and patients should appreciate and understand the problem and the magnitude of AMR. Therefore, appropriate infection control measures designed to curb the problem of AMR should also include the development and dissemination of drug information in relation to AMR.

PI-P-008

MARKETING STRATEGIES TO INCREASE CONSUMER AWARENESS OF IMPROVED ACCESS TO MEDICINES IN UNDERSERVED POPULATIONS

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Three models for improving access to medicines through use of private sector drug sellers have been implemented under the SIAM Program. The goal of these initiatives was to improve overall access to medicines; with access being defined as geographic accessibility, affordability, availability and acceptability of quality drug products and services. In each initiative, strategies were implemented to address access gaps. Substantial marketing efforts were needed to inform consumers of the changes taking place.

Key marketing messages for consumers were defined using input from stakeholders and consumers. These included: 1) only buy medicines from drug sellers that are properly trained, licensed, and regulated; 2) recognize the dangers posed by buying medicines of unknown quality; 3) understand how to take your medicine; and 4) know what to expect from drug dispensers, including good service and a fair price.

The facilities involved with these initiatives are in rural areas with limited service availability. As a result, this limited the usage of some traditional marketing strategies and alternative, culturally-adapted marketing strategies were employed. These included re-branding or re-naming old facilities, extensive radio and billboard campaigns, elaborate program launches, public skits and presentations, traveling road shows, and 'word of mouth' promotion.

Preliminary data collected for the final evaluation of the project indicate these strategies have played a major role informing people of the improved access. The strategies used have been key to the successful implementation and will be critical for continued expansion to other regions of the countries.

PI-P-009

MAXIMIZING THE IMPACT OF DONOR INITIATIVES FOR INCREASING ACCESS TO MEDICINES

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Aims: Coordination of donated funds and commodities is a key step to ensuring uninterrupted and rational commodity disbursement within an underdeveloped country. Making this information readily available for program management, especially those donor programs dealing in drugs and supplies used in the prevention, diagnosis, and treatment of HIV/AIDS, is essential. The introduction of a shared, Web-enabled database has facilitated this access.
Methods: MSH collaborated with Synergy International Systems using their Intelligent Data Manager™ software to create the Commodities Tracking Tool (CTT). The database, which currently focuses only on HIV/AIDS drugs and supplies, is being used in countries targeted by the U.S. President's Emergency Plan for AIDS Relief where MSH has a presence. Piloting of the tool was done with data from the Haiti program.
Results: Use of the CTT depends heavily on good coordination of data gathering efforts in-country, as was discovered during the experience in Haiti. Based on the results of the pilot phase, use of the tool allowed the donor organization and the Ministry of Health to help answer the questions of what is coming into Haiti, how much is coming in, and where the gaps are in drug supplies for national treatment programs. Knowing the answers to these questions will help to more appropriately redirect donor initiatives to maximize public health impact.
Conclusion: A Web-enabled database is an effective way to share information about donor initiatives. As the database grows, it is hoped that more donors will see the CTT as a valuable source of information and opt to include their program funding information.

PI-P-010

BOT-PLUS: THE SANITARY KNOWLEDGE DATA BASE : INNOVATIONS

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Aims:
For more than twenty years, the Database of the General Council has served the information needs of pharmacists in Spain. Advances in the pharmaceutical world have led the Council to consider the continous updating of its computing tools in order to meet current requirements and those which might arise in the short and medium term. This has been the origin of the new Database of the General Council BOT Plus.
Methods and results:
In order to meet the needs of the pharmaceutical sector, BOT-Plus incorporates a series of advantages over its previous version:

• New information blocks:
- Pharmaceutical care: permits the development of Pharmaceutical Care.
- Pathologies: information referring to illness and their treatment
- Medicines for animal use.
- Herbal Medicines: information on more than 200 active principles and over 600 products.
- Homeopathy.

• Foreign medicines: correspondences between Spanish and foreign medicines.

• Incorporation of multimedia contents: annexe documents that enrich the information (technical files, information files for the patient, documents from the magazine Panorama, etc.).

• Searches and lists: direct and fast gathering of the most common lists of various types of medicines required by the pharmacist in his daily labour.

Conclusion:

BOT-PLUS constitutes an essential element for developing the pharmacotherapeutic monitoring of the patient, thereby improving the rational use of medicines.

PI-P-011

USE OF PHARMACEUTICAL MANAGEMENT SOFTWARE IN RESOURCE-LIMITED SETTINGS

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Aims: Resource-limited countries rarely have adequate infrastructure to manage pharmaceutical procurement, inventory, and distribution effectively. They also lack ready access to resources needed to build this capacity. Low-cost software, specific to their needs, is required.
Methods: MSH, in collaboration with 3i Infotech, created software to address this gap. ORION@MSH incorporates pharmaceutical supply best practices for resource-limited settings and is comprised of six interlinked modules spanning from accounting to warehousing. This software was successfully piloted at the Pharmaceutical Procurement Service of the Organization of Eastern Caribbean States (PPS/OECS) and St. Lucia's Central Medical Store in May 2004 and then rolled out to six other island nations over the following 14 months.
Results: In order to effectively integrate new software into a site where old or no software currently exists, many conditions must be understood and met beforehand. Some key items: 1) buy-in and agreement from the sites regarding the effort required from local resources and its provision, 2) clear understanding how the program operates and changes required (both in the software and in the processes of the beneficiary) to ensure maximum benefit, and 3) available and accessible support for the clients. User response (both from the managerial and support levels) is positive.
Conclusions: Affordable pharmaceutical management software built on best practices for resource-limited environments is a sustainable alternative that countries can consider in building their pharmaceutical management infrastructure.

PI-P-012

IMPORTANCE OF INFORMATION IN HERBAL MEDICINES USAGE

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Herbal medicines are used in traditional treatment but there are lack of evidence in efficacy, toxicity and safety. Despite potential risk, monitoring of side effects is still developing.
According with this well- timed and precise information about herbal medicines became an imperative. Usage of herbal medicines is very important for patient because it makes symptoms easier in minor illnesses. How to make this more safety? Generally, this treatment requests high level of health education and social status thus the role of community pharmacist is significant.
The aim was to emphasize importance of precise and well-timed information for usage of herbal medicines.
In this work, we presented examples of herbal drug which efficacy is confirmed in controlled pharmacology and clinical trials, and examples of some herbal medicines side effects and interactions. The exact examples of information that community pharmacist give at dispensing are shown. Data Base and Report of Adverse Effects are used.
We emphasize that Instruction for usage for herbal medicine has to be in concordance with SPC but adjusted for patients.
Today, knowing of existence of side effects, interactions and cautions with herbal medicines it is very important to include them in Instruction for usage.
Analyzing results, we concluded that responsibility of community pharmacist is enlarged while dispensing herbal medicines. The difference of giving complete information in community pharmacy and in Instruction for usage is significant.
To make this service more professional, the importance of communication, counseling and continuing education have to be stressed in permanent education of pharmacist.

PI-P-013

APPLICABILITY OF INFORMATION PROVIDED BY A DRUG-INFORMATION CENTRE (DIC) FOR COMMUNITY PHARMACY DAILY PRACTICE

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Portugal

Aims: To evaluate if the information provided by CEDIME (DIC) is useful for community pharmacists and applicable to their daily practice.
Methods:
Study design: descriptive cross-sectional study
Period of data collection: data will be collected over a one-month period (April 2005)
Tools for data collection: information will be collected through telephone interviews performed by an independent person, registering such information on a data collection sheet. This information will be entered into a database specifically developed for the purpose of the study. Checking data entering will be performed prior to its analysis as a means to ensure validity.
Study participants: all community pharmacists calling CEDIME for pharmacotherapy-related queries will be included in the sample, when agreeing to participate (until 48 hours later). Data analysis: Variables allowing concluding on daily applicability (main outcome) will be evaluated by descriptive statistics. Bivariate analysis will be used to explore the association of socio-demographic data, origin of the query (e.g. patient request) with the main outcome of the study.
Results: will be available for the congress.
Discussion: we believe these studies are important to detect improvement opportunities in order to better align theory and practice.

PI-P-014

DEVELOPMENT OF DRUG INFORMATION DATABASE FOR NONPRESCRIPTION DRUGS AND SUPPLEMENTS

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From the viewpoint of the proper use of nonprescription drugs and supplements, we have developed a drug information database for nonprescription drugs and supplements with drug interaction check system. This database is set up by using the Microsoft® Access 2002 for Windows. There are a total of eight tables: drug information, ingredients, product information, drug interactions, contraindications, and therapeutic category. Each table is linked mutually by using the Japanese Article Number (JAN) Code and generic name. The up-to-date data required to develop the database were taken from resources such as 'Japan Self-Medication Database Center', 'The Medical Information System Development Center', 'Japan Pharmaceutical Information Center', and 'Hansten and Horn's Drug Interactions (Facts and Comparisons)'. The degree of drug interaction were classified into three levels: avoid combination, avoid unless benefit outweighs risk, and monitor.
The database consists of 14,003 items of nonprescription drugs and 19,210 items of prescription drugs and 179 ingredients of supplements. A total of 2,096 drug interactions are showed: 875 of nonprescription-nonprescription interactions, 1094 of nonprescription-prescription interactions, 44 of nonprescription-supplement interactions, 83 of prescription-supplement interactions. Sixty-two ingredients are found in both supplements and drugs (prescription and nonprescription), whereas 218 ingredients of nonprescription drugs contain contraindication when used as prescription drugs. In conclusion, we consider our database to be a useful tool for the proper use of medications and for the promotion of self-medication.

PI-P-015

THE CONSUMPTION OF INSULIN PREPARATIONS IN THE REGION OF BANJA LUKA FROM JANUARY 2002 TO DECEMBER 2004

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The aim of this research was to present the increase of insulin dependent diabetes mellitus in the region of Banja Luka, the area with population of almost 300000 people. The research was made in Apotekarska Ustanova Banja Luka from January 2002 to December 2004, using the data from 18 pharmacies. This is the only institution where patients can get the preparations of insulin on a prescription.
According to the contract with the RS Health Fund, the data and prescriptions of insulin preparations since 2002 have been taken separately from other medicines. The data included Novo Nordisk preparations, the only one on this market permitted by the RS Health Fund. They were compared by years and types.
We found that the number of used insulin preparations had been 11342 in 2002, 13230 in 2003 and 14232 in 2004. According to these results almost 5% of population are insulin dependent. The results also revealed that the use of insulin preparations had significantly increased from 2002 to 2003 of 16,65% and of 7,57% from 2003 to 2004.
Genetic factors, inpropriate nutrition and stress can be the causes of this increase, but the post traumatic syndrom specific for this region even years after the war is probably the leading factor.
Considering a large number of registrated patients and probably more uncovered cases, we constantly pay attention how to prevent the further development of this illness by having the workshops among the pharmacists and continuous education among the patients.

PI-P-016

USE OF INTERNATIONAL PHARMACEUTICAL PRICE COMPARISON INFORMATION

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United States of America

Aim: Access to a central, independent, updated source of comparative pharmaceutical price information should greatly facilitate procurement of medicines of assured quality for the lowest price.
Method: The International Drug Price Indicator Guide provides an indication of pharmaceutical prices on the international market. Updated annually and published by Management Sciences for Health (MSH) in collaboration with the World Health Organization, the Guide contains a spectrum of prices from pharmaceutical suppliers, international development organizations, and government agencies. The latest edition of the Guide contains prices for more than 900 pharmaceuticals, contraceptives, and vaccines. The Guide, in English, French, and Spanish, is available in print, on CD-ROM, and through the MSH Electronic Resource Center (http://erc.msh.org).
Results: A 2004 survey of more than 50 users of the International Drug Price Indicator Guide found that 68% of them use the Guide for comparing prices recently obtained from suppliers and 42% use it to plan their budget or tender. Sixty-four percent of the survey respondents stated that they do not have access to any other source of comparative international price information. Of the survey respondents, 44% said that using the Guide has contributed to better acquisition prices or other savings for them, with half saving 11-30%.
Conclusions: Access to independent comparative price information assists in price negotiations, in locating new supply sources, and in assessing the efficiency of local procurement systems.

PI-P-017

TO PROMOTE THE PATIENT SAFETY THROUGH A RADIO PROGRAM-'HOW TO BE A WISE PATIENT'

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Aim:
People in Taiwan are not only seeing doctors more than they really need to, but also taking too much over-the-counter (OTC) medicine and so-called healthy food supplements. It is important to educate people understanding the danger of that, and the right approach to use non-prescribed medicine. To achieve this goal, we must help people learning the correct ways to use the OTC medicine and understanding the food supplements that are advertised everywhere in Taiwan. We will covey the message that the patient is the centre in medical practice, patients and their relatives should be educated and informed thoroughly to assure patients' safety.

Method:
Playlets, which introduce patient's safety to the audience of all ages and backgrounds, were aired on the News Channel of the Broadcasting Corporation of China (BCC). The scripts were written by junior pharmacists and reviewed by experienced senior pharmacists, doctors and professors. The scripts were posted on websites of BCC and CKF foundation.

Result:
Short plays of 2 to 3 minutes were aired at noon or dusk on weekdays. A total of 66 playlets were aired within three month span. The subjects are, but not limited to, counterfeit medicines, differentiating exaggerated advertisements of medicine and healthy food supplements, storing medicine properly, asking questions regarding to your medicine, and being a participating patient.

Conclusion:
In a society bombarded by all kinds of OTC medicines and healthy food advertisements, it is important for pharmacists to educate the general public through mass media to be 'wise patients'.

PI-P-018

PHARMACEUTICAL JOURNALS IN SERBIA

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Any profession, but especially pharmacy is abundant with the information which are meaningful to colleagues and patients. In our country several Journals are published, of which some are strictly professional and some mainly popular, such as:

ARCHIVES OF PHARMACY, founded in 1950. and published bimonthly by the Serbian Pharmaceutical Society (YU ISSN 0004-163). It publishes the papers in Serbian with summary in English, based on original research, as well as general reviews.

APOTHECARY PRACTICE, published monthly by Pharmaceutical Chamber (ISSN 1451-1827). It presents the news from Pharmaceutical Chamber, details from the pharmacy practice, review of new books and news in pharmacotherapy.

PHARMACY, monthly Journal for popular medicine and pharmacy, published by BB-Soft. It is distributed to the individuals free of charge to the private-owned Pharmacies.

INFORMANT, Journal published monthly by BB-Soft assigned to the Pharmacies-members of the Serbian Society of Private Pharmacies.

PI-P-019

FREE CONSULTATION PHONE CENTRE AS A SOURCE OF INFORMATION ABOUT RATIONAL USE AND CHOICE OF MEDICINE FOR CONSUMERS AND SPECIALISTS

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Background: According to the data of investigations made in Yerevan among 7200 medicine consumers, 55% of medicine consumers lack information about rules of medicine use because of refusing to visit a specialist before taking medicines or buying the medicine without leaflet. 82% of medicine consumers are unaware of possible minimization of medicine expenses by using generics.
Aims: Create an available source of information about the rules of rational choice and use of medicines for Yerevan population.
Methods: We created a free consultation phone center (the staff of which includes licensed doctors and pharmacists) with an informational base including the rules of safely using the medicines, registered in Armenia and an opportunity of filtering generics by active substance.
The spread of information about phone center was realized by means of providing policlinics and pharmacies with posters, as well as by means of mass media.
Results: In the period of October 1, 2004- March 1, 2005 (150 days) there were 9981 calls. 55% (5549 calls) needed information about the rules of medicine use, 42% (4202 calls) were interested in different generics registered in Armenia. Of 4202 calls for generics 38% (1597 calls) were made by doctors or pharmacists.
Conclusions: We created and developed free phone consultation center that can be an effective source of information about rational choice and use of the medicines for medicine consumers, as well as for specialists.

PI-P-020

PATIENT INFORMATION ADMINISTRATE SYSTEM FOR A PHARMACIST-YAKUREKI-

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We use a tool saying 'Administration guidance and recording sheet of medication history' routinely to promote proper usage of medicine at a Japanese community pharmacy. We call a popular name 'YAKUREKI'.
YAKUREKI is a paper media which made to a patient individual by pharmacist as record of at community pharmacy, and a full name of the patient, an address , products names are specified. And this is made when pharmacist fills a prescription, hands products to a patient, and consults about medication.
This YAKUREKI was carried out since separation system-Bungyo- was introduced to Japan, but the contents, the purpose, the format changed with promotion of Bungyo.
Now administration of YAKUREKI in pharmacist duties is evaluated as required duties as a medical worker.
In other words contents and information of YAKUREKI are necessary indispensibility so that a pharmacist achieves a duty as a medical job.
Therefore a tool of this YAKUREKI was introduced and tried to analyze a point of revision of YAKUREKI which it continued having been lasted for at my community pharmacy for about 10 several years and a change of YAKUREKI after process and revision of revision.
I think that the result that they are analytical show a change of a social role of a pharmacist and a change of consciousness to the patient and a change of consciousness to a pharmacist of the patient.
I propose that the system of the patient information administrate duties that using YAKUREKI is a very effective system for promotes patient-centered medical care, and for approach a distance of a pharmacist and the patient.

PI-P-021

COCAINE USE IN METHADONE PATIENTS IN THE HEALTH SERVICE EXECUTIVE, NORTHERN AREA DUBLIN, IRELAND

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Ireland

Aims: To examine the use of cocaine among methadone patients in the Health Service Executive (HSE) Northern Area Dublin, Ireland. Methods: A survey was carried out on 851 patients receiving methadone treatment for opiate addiction. Patients reported the incidence and frequency of cocaine use. Results: Data showed that 77 % of the participants had a history of cocaine use. Of these, a significant percent, 34%, represented cocaine use within the last month, with 12% reporting a daily frequency of use. Of all the patients surveyed, 72% were receiving a daily dose of methadone of 60 mg or greater. Examination of the data from one of the largest Drug Treatment Centres surveyed, D1, showed that the participants had a cocaine incidence of 68 %, with 29% having used cocaine within the last month. Of these participants, 50% were in the 20-29 years age range. The survey showed that 71% of the participants who had used cocaine in the last month were receiving a daily dose of methadone of 60mg or greater. Conclusions: The survey concluded that cocaine abuse is emerging as a problem in the Irish drug scene among opiate users receiving methadone treatment in Dublin City. The figure of cocaine use observed in this survey is an important indicator of the level and extent of cocaine use in methadone patients and is valuable from a public health perspective in order to assess needs, and to plan and evaluate education, prevention, treatment and harm reduction services.

PI-P-022

PREVALENCE OF CANNABIS USE AMONG METHADONE PATIENTS IN THE ADDICTION SERVICES OF THE HEALTH SERVICES EXECUTIVE (HSE), NORTH AREA DUBLIN, IRELAND

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Aims: To examine the use of cannabis among methadone patients in North Dublin. Method: A survey was carried in 869 methadone patients of six drug treatment centres of North Dublin. Results: Prevalence of cannabis use among the participants was high at 83% and was consistent across all drug treatment centres (78-88%). Of the participants using cannabis, 42% reported a daily frequency of use and 19% reported using cannabis once or twice weekly. A high proportion of the participants surveyed, 46%, were receiving a medium to high dose of methadone (70-100mg) daily. The prevalence of cannabis use was not found to be related to the methadone daily dose received by the participants. A high incidence of cocaine use was previously shown in the same population of patients suggesting a high level of poly-drug use among these patients. Conclusions: The survey showed that the majority of methadone patients were using cannabis, with a high proportion of the patients using it on a daily basis. Although cannabis is perceived as a safe drug, it is known to have both acute and chronic health effects and does produce dependence.

PI-P-023

INFORMATION ON TRAVEL HEALTH

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Information on travel health empowers individuals to understand prevention and management of health conditions that can occur when travelling. The aim of the study was to develop and evaluate a travel health information booklet to be distributed from community pharmacies.

A booklet was prepared to present information on travel health. A self-administered questionnaire was developed to determine the knowledge of participants on travel health before and after the use of the booklet. The questionnaire was administered to 433 adults recruited from shopping localities (test 1). The booklet was presented to the participants after test 1 was completed and they were asked to complete the questionnaire again 15 days after reading the booklet (test 2).

Out of the 433 participants who participated in test 1, 96% (414) had traveled at least once and 13% (56) claimed that they had a health problem during travel. The majority (68%, 293) do not seek advice on travel health prior to traveling. Participants (98%, 425) were aware of the methods to prevent HIV infections. Knowledge about Hepatitis A and Hepatitis B infection was lower with only 21% (93) and 39% (168) respectively having the correct knowledge. Test 2 was completed by 323 participants (75%). There was an overall significant improvement in the knowledge reported (p=0). Participants (79%, 256) assessed the booklet as useful, understandable, well presented and informative.

Few persons seek advice on travel health. The presentation of a booklet on travel health creates an awareness on health travel in prospective travellers who can then seek advice from the pharmacist.

PI-P-024

GUIDES TO HELP COMMUNITY PHARMACISTS IN HIV/AIDS AND STDS COUNSELING

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Introduction: Sexually transmitted diseases (STD) are a major public health issue. According to estimates of WHO, 70% of those infected by STDs in Brazil do not seek for treatment. Community pharmacies are an important site where people seek for primary health services. The purpose of this work is to develop and test guides to help both pharmacists and pharmacy-sales-person in community pharmacies.
Methodology: The guides were developed based on previous ones published by Brazilian Ministry of Health, updated by a multidisciplinary team – pharmacists and physicians. The guides were distributed and evaluated in a course on HIV/AIDS and STDs in community pharmacies, which was attended by both pharmacists and pharmacy-sales-persons.
Results: It was produced the two guide's that include information about: The impact of STDs; their clinical issues and measures to prevent and control; the importance of community pharmacies in public health system; pharmacists responsibilities and counseling in STDs; patients' instructions about use of drugs in STDs; useful websites. It was held a course attended by 78 persons. Out of these, only 19 answered the questionnaire. The guides are 'very good' for 16(84%) and 'good' for 3(16%).
Conclusion: It was possible to develop the guides using the proposed methodology and to verify the opinion of their users. Limitations of this study include: evaluation of the guides by few people. In this moment is in processing the evaluation if the course, combined with the guides, change the current practices in community pharmacies. These results will be in the congress.
Thanks: To UNESCO, to CFF and to SES/DF.

PI-P-025

AIMING AT EXCELLENCE IN ADOPTING AND USING DRUG GENERIC NAMES

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Introduction: Drugs are identified by many names and codes, according to their developing status and use. This causes confusion over the pharmaceutical chain, including harm to users of drugs and loss of money due to market of a same drug with different names. Considering this situation, Brazilian authorities have adopted regulations to harmonize the generic names of the drugs.
Objectives: Describe regulations approved in Brazil to harmonize the generic drug names.
Methodology: Search and describe regulations approved in Brazil to harmonize the generic drug names, specifying their role in a system to adopt generic names in the Portuguese language.
Results: Six officially adopted regulations related to drug nomenclature were identified: 1. the Portuguese drug nomenclature rules; 2. the English – Portuguese translation rules; 3. the labeling regulation; 4. the database that stores drug nomenclature approved, their synonyms, English names and C.A.S. registry number; 5. the Brazilian Nonproprietary (generic) Names Official list and 6. the resolution to update, to correct and to delete official generic drug names.
Conclusion: In recent years, regulations approved can help users, professionals and the Brazilian government to use the same drug name over the pharmaceutical chain. That can avoid misunderstanding, promote rational use of drugs and reduce unnecessary costs and loss of time. The last mentioned regulation links all the other five ones, building a professional framework that can lead to an excellence in adopting and using generic drug names. Further works should study the correct use of generic names over the pharmaceutical chain.

PI-P-026

USING SELECTIVE SEROTONIN RECEPTOR INHIBITOR IN PREGNANT WOMEN AND NURING MOTHERS

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Atmic depression has became a modern disease, and it involed a great number of you women. We try to figure out the influence of ssri for them, especially they are in the s of planning parenthood. We hope that every patient will have a thoughtful suggesti form pharmacist. Methods: we collected the results of several clinical trials, form 20 to 2004. Results: although no evidence aproved the teratogenic effects in appearance newboen, we still need more research followed to assess the mental difference children. For those mothers who has taken ssri during pregnancy, we remind them attend to the withdrawal syndrome of their babies. Until now , we may say that few ssri is absorbed by infant from breast-feeding, the safety of using ssri in breast-feedi infant is more than we estimated before. But we still suggest that some ssri of hig protein-binding rate should have a bigger clinical trial. Not only star the administrati of ssri, but also stop the treatment of ssri, we strongly recommend the parmacist and t patient of depression, to judge the benefits of treatment of ssri with the clinician.

PI-P-027

A NEW METHOD TO PROVIDE DRUG INFORMATION BY '2D-BARCODE' WITH CAMERA PHONES

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[aims] Over 75% percent of mobile phones in Japan are camera phones which enable new services based on QR-code (2D-barcode) input leading to a variety of new transactions. Patients, for example, use their camera phones to take a printed a QR code and automatically access a corresponding website. Using this technology, patients are accessible to information on their prescribed drugs.
[methods]
Firstly, we made a database on representative medicines in Japanese as well as English. The database consist of following elements on each drugs. 'What is this medicine used for?' 'Usage of this medicine' 'When you forgot to take the medicine?' 'When you take too much medicine ?' 'What is the adverse reaction ?' 'Symptoms that require attention' 'Essential information you should tell your doctor' 'The government established code name of the drug'. QR codes corresponding to prescribed drugs for patients were printed on drug container, so that patients scan a QR code and access the specific drug website.
[results and conclusions]
Some people may stop taking their medicine, take a lower dose, or skip doses if they are having side effects. To avoid these medication errors, it is important to give the information not only by paper but also digital information. We could establish a new drug Information system using '2D-barcode' with camera phones. Although the QR code is a JIS Standard as well as an ISO standard, it is only widely used in Japan. For foreigners in Japan, we are also able to provide English instructions on prescribed drugs.

PI-P-028

HOPADOM HAUTE NORMANDIE 76000 ROUEN – FRANCE REGIONAL HEALTH NETWORK FOR THE COORDINATION OF KEEPING SICK PEOPLE AT HOME.

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France

AIM
To allow patients who have reduced physical and mental autonomy to be taken care of a home whatever their age or illness by their usual medical staff.
METHOD
Thanks to public finance by the « Fond d'Aide à la Qualité des Soins de Ville » (quality health care in town aid fund) run by the « Unions Régionales des Caisses d'Assurance Maladie » (grouping of regional National Health agencies) and by regional donations for the development of networks run with the help of the regional hospital departments. Hopadom has set up a team of co-ordinators and social workers to help patients who want to stay at home as well as people from the medical field specialised in hospital and town medicine. The association provides material and human resources necessary for health care at home while continuing the different types of health care, social help and psychological help needed by the patients. Its operation and data management are ran via Hopadom's Internet site.
RESULTS
25% of the patients are under 60, 30 % are over 80 and 42 % of them suffer from cancer. The association gives free health care. Hopadom, an independent neutral association, guaranties quality, safety and impartiality to the patients.
CONCLUSION
Hopadom, an organisation whose aim is to take care of sick people at home is an answer to those who want to be taken care of at home. It also fulfils a need to reduce the number and the duration of hospital visits as well as organizing patients return home after being in hospital and the doctors visits to the patients home.

PI-P-029

CHARACTERIZATION OF KNOWLEDGE AND ACCESSIBILITY OF SELF-MEDICATION USE IN UNDERGRADUATE STUDENT: A TEACHING PROVINCE

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Aims
To design appropriate drug information service of self-medication for undergraduate student
Methods
Questionnaire was designed and approved by specialists (compriesd of 4 sections: personal data, self-medication use, information accessibility and general knowledge test of self-medication use). The approved questionnaire was handed to a random sample of undergraduate student in a teaching province, Northern of Thailand.
Results
One hundred and fifty questionnaires were completed. Mean age (SD) of respondents was 21.43 (2.06) years old, 70% were female and 77.4% lived in dormitories. Result presented 93.3% were using self-medication. Most of self-medication uses were analgesics (87.3%), cosmetics (52.7%), first aid kit (46.7%) and home remedies (44.7%). The most of provided self-medication place was community pharmacy (90%) and only 38.7% were absolute recovered of chief-complaint. More than 50% agreed the most of drug information resources were television broadcast and community pharmacist and 68.7% preferred television broadcast for their most convenient accessibility. Most of drug information demands were primary health care medication and home remedies. An average score (SD) of general knowledge test was 14.78 (5.53) out of 28. Recommendation, adverse drug reaction and administration of drug use were particular topics of less right score.
Conclusions
Drug information service of self-medication use should be included recommendation, adverse drug reaction and administration. Television broadcast and community pharmacist are generally agreed the most drug information resource. Further study of self-medication use in other provinces is characterized.

PI-P-030

THE PHARMACIST'S ROLE IN WRITING THE BASIC GUIDEBOOK FOR RATIONAL PHARMACOTHERAPY

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Synthesis of pharmaceutical, pharmacological and therapy attitudes with the application of key information for health-care professionals, is rising the drugs knowledge level and enhancing the pharmacotherapy. Clinical pharmacy, clinical pharmacology and pharmacological information technology are the sources for the advancement of pharmaceutical and medical practice.
Project development survey of writing an operative Pharmacotherapy Guide which makes the practical pharmacotherapy easier in accord with the latest scientific and expert achievements.
The book was made at the Pharmacy Institute of Serbia. The data were collected from reference sources: relevant literature official positions of the regulatory organs, doctrinaire positions, expert opinions, and manufacturers' data.
The methodology has been adjusted to the international classification which provides keeping up with the main pharmacoepidemiological parameters. Up-to-date information and attitudes have been cited for the essential medicines; there has been made a more detailed description for new ones. In its supplements there were given abridged information from the field of pharmacokinetics, pharmacognosy, toxicology and other related disciplines.
There are brief, scientifically verified and practical information gathered in it. Commitment of the multi-disciplinary team of health experts is opening a space for a higher level of cooperation between pharmacists and doctors.
This book was reviewed very well by the health-care public imposing the need it to be published annually. With this study, we are emphasizing the very significant role of pharmacists in creating a rational pharmacotherapy.

PHARMACY INFORMATION SECTION - SHORT ORAL PRESENTATIONS

PI-O-001

HOW WELL DO UK ADULTS UNDERSTAND MEDICINE PICTOGRAMS?

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Patients' ability to understand information about medicines is crucial for safety and effectiveness. Rates of illiteracy mean that written information alone cannot meet patients' needs. Medicine pictograms are an alternative, but may be culturally sensitive. Previous testing has used large pictograms which are impractical for conventional information formats.
Study aims were:
to compare two sets of pictograms (from the USA and RSA) for understandibility by UK adults.
to examine the effects of pictogram size and repeat presentation on understandability among older adults.
In the first part of the study, 160 adults (aged 17–83) saw 10 pictograms, and gave their interpretation. In the second, 67 adults (aged 65–96) were randomly assigned to see 10 small or large pictograms. After giving their interpretation they were told the meaning. One week later they saw the same pictograms and gave their interpretation.
The pictograms for the 10 different instructions and warnings showed great variation in interpretation rates (7.5% to 90%), with few significant differences between the US and South African versions. Only 3 were understood by 85% or more. Pictograms performed significantly better if they were larger and at the second presentation.
Pictograms have the potential to help patients to understand information. This study shows that some existing pictograms are not easily interpreted and that testing is needed before their implementation. A reduction in their size to allow incorporation into conventional written formats may cause additional problems for patients.

NB I would be happy to submit this paper as a poster if an oral presentation is not possible.

PI-O-002

DEATHS AND USE OF CNS DEPRESSANTS IN COMBINATION WITH ASTHMA MEDICATIONS

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Background: Deaths from chronic lower respiratory diseases, of which asthma is one, remains the 4th leading cause of death in the United States. Sedatives and tranquilizers are still being prescribed to asthma patients despite knowledge of death-associated risks in asthma: hormonal/circadian differences, sideeffect of sedatives/tranquilizers, antihistamines, gender-related prevalence of underlying causes of death (i.e. men more often diagnosed with chronic bronchitis; women more often diagnosed with asthma), time of death, nocturnal asthma, melatonin contraindication.

Methods: Data from 2002 MarketScan Commercial Claims and Encounter Database (Medstat Group, Inc). Claims and prescription drugs for 5.6 million enrollees under age 65 were evaluated as part of employer-sponsored benefit plans for 45 large employers in all 50 states.

Results: 170.8 million individuals < 65 years enrolled in employer-sponsored benefit plans. 92,502 individuals took concomitantly asthma medication plus CNS-depressants for at least 30 days. Asthma medication combined with tranquilizers, sedatives, antipsychotics, and/or benzodiazepines was associated with odds of death 97% higher compared to any other asthma-CNS-depressant combination. Any asthma-CNS-depressant combination for 110-132 days was 45.4% more likely to lead to death compared to 30-40 days. Men taking asthma medications plus any combination type had twice the death rate compared to women. Men and women age 45-64 taking any asthma-CNS-depressant combination had 3 times the death rate compared to those ages 18-44. Persons taking = 4 combinations at once were > 3.5 times more likely to be hospitalized.

Conclusions: Further studies are required to clarify how combination of asthma medications and CNS depressants taken simultaneously contribute to death in asthma patients.

PI-O-003

DIFFERENCES IN LABELING PRACTICE OF OTC BETWEEN JAPAN AND OTHER COUNTRIES

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[Objective] In various countries, OTC medicine labels play an important role in providing information for consumers. However, OTC labeling regulations differ based on the laws of each country. We surveyed to what extent consumers consider labeling practices to be important in Japan and other countries.
[Method] The labelings of painkillers, antacids, and antihistamines from Japan, the U.S., Britain, Australia, and France were compared. In addition, a survey of Japanese consumers' perceptions of OTC labels was conducted.
[Results] In Japan, only ingredients, directions, and warnings are provided on labelings based on a Pharmaceutical Affairs Law. On the other hand, the FDA has detailed regulations regarding labeling, including drug interactions with prescription drugs and warnings for consumers with pre-existing conditions. Moreover, labeling in the U.S. has been standardized for all OTC medicines(Drug Facts Label). In Australia, where OTC medicines are graded into two categories, a labeling system delineating a medicine as a 'Pharmacy Medicine' or a 'Pharmacist Only Medicine' exists. In addition, in Australia, a priority is given to package inserts over outside box information. The content of the labeling differed in Britain depending on the medicine and the maker. In France, labels are extremely simple even in the case of Rx-to-OTC medicines.
From our recent survey, Japanese consumers are becoming more concerned about adverse reactions and drug interactions of OTC medicines.
[Conclusion] From our study, it has become obvious that there is much need for improvement in Japanese labeling requirements.

PI-O-004

IDENTICAL TABLETS FROM THE SAME COMPANY – BUT DIFFERENT NAMES AND INFORMATION

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Medicine is not only active substance and pharmaceutical formulation. Information is an indispensable component.
Some companies market tablets that are pharmaceutically identical under different brand names.
• Rofecoxib (until 2004) as Vioxx® for treatment of osteoarthritis, and as Vioxx ACB, Vioxxakut®, Vioxxalit®, Vioxxdolor® for treatment of acute pain.
• Bisoprolol fumarate as Emconcor® for angina pectoris and hypertension, and as Cardicor®, Emconcor® CHF, Concor®COR for heart failure.
• Bupropione as Zyban® for smoking cessation and Wellbutrin® for depression.
• Fluoxetine as Prozac® for depression and Sarafem® for premenstrual dysforic syndrome.
Not only do they differ in indication for use. The patient information/package inserts are also different.
Doctors, nurses, pharmacists, and patients get confused.
Generic substitution is difficult, because the package inserts have different texts, and do not cover the same indications.
Sometimes original brand names are stigmatised, so it is difficult to use them for other indications.
☺
Regulatory authorities should be very restrictive in allowing a company to use more than one brand name on a medicine.
When such permission is given, it should be demanded that
- Information in formularies and package insert should not differ significantly.
- The second brand name should be generic

PHARMACY INFORMATION SECTION - SHORT ORAL PRESENTATIONS

PI-O-005

IMPACT OF USE OF PDAS ON DRUG REGULATORY EFFORTS

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United States of America Tanzania United States of America

Aims: Collection of correct and timely drug inspection and testing data is critical in drug regulation. Tanzanian Food and Drug Authority (TFDA) field inspectors require ready access to TFDA's drug marketing authorization database and need to efficiently collect and submit inspection data.
Methods: Together with Management Sciences for Health, the TFDA devised and implemented a system using personal digital assistants (PDAs). The first steps consisted of defining standard operating procedures for inspections, data entry, and data transfer and identifying setting up a method for the monthly data transfer (both for data collected by inspectors to the TFDA and updated drug authorization lists to inspectors from TFDA). Concurrently, the TFDA mounted an effort to ensure the currency and accuracy of its drug authorization database. Existing paper-based forms used for inspection and postmarket surveillance were then programmed into a PDA-ready format to guide inspectors through the data-gathering process.
Results: Over the past eight months, inspectors have used PDAs to gather data. The program has allowed them to expand the number of premises visited, helped increase accuracy of data entry, and provided a mechanism for getting more timely and definitive information to the TFDA for regulatory action. Results show a decrease in time needed to perform inspections and enter data, a significant reduction in data entry errors, and the ability to create reports quickly.
Conclusions: Coupled with appropriate support from management, the use of PDAs can serve as an effective tool for building and maintaining regulatory efforts.

PI-O-006

DEVELOPMENT OF THE FIRST CLINICAL CLASSIFICATION OF DRUGS USED DURING LACTATION.

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The infant is recognized as the unintended recipient of drugs administered to the lactating mother. While a letter classification exists for drug use during pregnancy, a similar one is not available for lactation. Our objective was to create a classification system, to collect and evaluate available drug data, and to apply our classification on the collected data. Drug information on more than eleven hundred drugs were collected from primary, secondary, and tertiary resources. Data included drug excretion in breast milk, reported adverse effects on the infant, as well as the compatibility of the drug with breast-feeding. The classification represented each drug with two letters and two symbols. The first letter indicated compatibility with breast-feeding which was denoted by C (Compatible), I (Incompatible), or U (Unknown). The second letter indicated excretion in breast milk which was denoted by e (excreted), n (not excreted), or u (unknown). Four symbols (*, **, #, and ##) indicated potential adverse effects and their severity on both the infant and the lactation process. Fifty seven percent of the drugs evaluated were compatible and 22% were incompatible with breast-feeding; data on the remaining 20% were unreported. While 18% of the drugs evaluated were excreted in breast milk and less than 1% were not excreted; data on the remaining 81% were unreported. The presented data, simplified in a readily attainable pattern, may offer a valuable and quick initial source of information for the healthcare provider. Data will be continuously updated in the authors web site which may allow for timely updates as well as feedback by researchers and clinicians worldwide.

BB-P-001

CMAX/AUC FOR DEMONSTRATING THE BIOEQUIVALENCE OF TWO DRUG PRODUCTS CONTAINING LEVODOPA-BENSERAZIDE

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For evaluating the bioequivalence of two drug products, both the rate and extent of absorption of the two products are expected to be the same within a statistical tolerance. For the rate of absorption, Cmax is often used, an ambiguous measure of the absorption rate for also being affected by the extent of absorption. In the present work we assessed the feasibility of Cmax/AUC for demonstrating the bioequivalence of two drug products containing Levodopa-Benseraside for registration purposes.
An open, randomized, 2-period crossover study with 1-week washout interval between doses was conducted in male healthy volunteers. Blood samples were taken at pre-determined times up to 8 h after oral dose and assessed for levodopa by HPLC. Parametric analysis on log-transformed pharmacokinetic data were performed.
The percentage geometric mean ratios and 90% CI of Test/Reference were 105.1 % (76.3-144.7 %) for Cmax, 102.2 % (80.5-129.7%) for Cmax/AUC, 102.9 % (90.1-117.5%) for AUClast and 102.7% (89.9-117.4%) for AUCinf, respectively.
AUC but not Cmax demonstrated bioequivalence between the two formulations evaluated considering the 80-125 % interval defined by the US-FDA. However, the percentage Cmax ratios were found to be between 80-125%. Moreover, equivalence of the two drug product absorption rates could be declared as the 90% CI for the percentage ratio of Cmax /AUC was found to be between 75-133% as previously recommended by others (Endrenyi L., 1991).
Thus it is concluded that the test formulation of Levodopa-Benseraside is bioequivalent in terms of both rate and extent of absorptionto the reference drug product.

BB-P-002

RAPID AND SELECTIVE ANALYSIS OF CLOZAPINE IN HUMAN PLASMA USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY AND ULTRAVIOLET DETECTION

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A rapid high performance liquid chromatographic method has been developed for the determination of clozapine in human plasma. A simple extraction step with acetonitrile was done. The analysis was performed on a C18 (3.9 x 150 mm) reversed phase analytical column with the wavelength fixed at 280 nm. The mobile phase consists of methanol-water-triethylamine, 70:30:0.05 (v:v:v), flowing at a rate of 0.6 ml/minute, using celecoxib as an internal standard. Calibration curves were linear in the range of 20-300 ng/ml and the lower detection limit was 5 ng/ml. The intra-assay and inter-assay precision as well as recovery and reproducibility values were satisfactory. The developed method was used to compare between two commercially available products of clozapine in 24 healthy volunteers.

Keywords: clozapine, HPLC, plasma, bioequivalence.

BB-P-003

THE DEVELOPMENT OF A NEW METHOD FOR THE DETERMINATION OF RACECADOTRIL IN HUMAN PLASMA BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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A simple, rapid, specific high performance liquid chromatographic assay of racecadotril in human plasma has been developed. The method is based on extraction by precipitation with acetonitrile and reversed phase chromatography using a C18 (3.9 x 150 mm) analytical column and UV spectrophotometer detection at 230 nm. The mobile phase consists of acetonitrile:phosphate buffer [65:35 (v/v), flowing at a rate of 1 ml/minute]. Methyl paraben was used as an internal standard. The assay was linear in the concentration range of 100-1000 ng/ml, and the lower limit of detection was 30 ng/ml. Within-day and between-day precision expressed by relative standard deviation as well as recovery and inaccuracy were calculated and were within permitted limits. Blood levels have been measured with good precision in 24 healthy volunteers following the administration of 120 mg of racecadotril powder in water. This method was applied to study the bioequivalence of two commercial products using a two way open randomized cross-over design.

Keywords: racecadotril, HPLC, plasma, bioequivalence.

BB-P-004

COMPARATIVE BIOAVALABILITY STUDY OF FORMULATED AND MARKETED GLIMEPIRIDE

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Eight formulas of glimepiride capsules were prepared by changing the weights of additives used. Results of in-vitro study revealed that no interaction was found between the drug and the selected additives. Moreover, the results of in-vitro dissolution indicated that there were two formulae showing better dissolution than the others. The marketed glimepiride tablet 2 mg (Amary, Aventis) and the best two formulae were subjected to a random cross over bioavailability study in 6 healthy human volunteers with one week wash out period. After administering oral single dose, blood samples were collected over a period of 12 hours and were analyzed by HPLC. Pharmacokinetic parameters of the formulated capsules were Cmax 1.4, 1.3 µg/ml, tmax 2.5, 2.5 hr, and AUC0-8 7.71, 8.15 µg.hr/ml respectively, while the marketed tablets produced Cmax 1.5 µg/ml, tmax 2.5 hr, and AUC0-8 9.9 µg.hr/ml. Statistical evaluation of measured pharmacokinetic parameters using ANOVA revealed insignificant differences between the two formulae as well as the marketed tablets ($p>0.05$). This indicated that the marketed tablets and formulated capsules are bioequivalent

BB-P-005

LPS-INDUCED INFLAMMATION ALTERS THE DISPOSITION OF FEXOFENADINE IN THE ISOLATED PERFUSED RAT LIVER.

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AIM: To examine the effect of bacterial lipopolysaccharide (LPS) on the pharmacokinetics of fexofenadine (an OATP and P-gp substrate) in the isolated perfused liver. METHODS: Male SD rats were divided into 4 groups (n=4): 1 control group and 3 treatment groups. Inflammation was induced in the 3 treatment groups by either 5, 2.5 or 1mg/kg i.p. of E.coli LPS in sterile saline. The control rats received an equivalent volume of saline (1ml/kg). At 24h following treatment, the rats were euthanased, the liver isolated and perfused with fexofenadine (initial concentration = 2000ng/ml). Perfusate samples were collected at times 0, 1, 3, 5, 10, 15, 20, 25, 30, 40, 50 and 60mins. Bile samples were obtained at 10min intervals and the liver collected at the end of the perfusion. All samples were stored at -4°C until analysis with HPLC. Clearance of drug from the perfusate, biliary clearance (CLb), and the final liver:perfusate (L:P) and bile:liver (B:L) concentration ratios were determined. Statistical evaluation was conducted using the student's t-test. RESULTS: Significant ($p<0.05$) differences from the controls were observed in all treatment groups. This was most marked in the 5mg/kg LPS treatment group where CL = 0.024 (+/- 0.002) ml/min; CLb = 1.25 (+/- 0.20) ml/min; L:P = 44 (+/- 11); and B:L = 17 (+/- 2) compared with controls where CL = 0.040 (+/- 0.004) ml/min; CLb = 2.70 (+/- 0.48) ml/min; L:P = 88 (+/- 14); and B:L = 30 (+/- 4). CONCLUSIONS: Clearance from the perfusate and into the bile was reduced following treatment with LPS. The changes in the L:P and B:L ratios suggest that the reduced clearance is due to down regulation of both canalicular and sinusoidal transport.

BB-P-006

FACTORS AFFECING ATENOLOL BIOAVAILABILITY IN NORMAL VOLUNTEERS

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Atenolol is a widely used beta-blocker which has bioavailability of less than 50%. The objective of this research was to investigate the effect of dose, modification of gastric pH and food composition on atenolol bioavailability in normal volunteers. Our results demonstrated that the bioavailability of atenolol was dose independent in the range of 50-100 mg. Also, administration of atenolol with alkaline antacid solution significantly reduced atenolol bioavailability which was reflected by the 20% reduction of atenolol AUC and 40% reduction in its Cmax. The results also demonstrated that administration of atenolol after eating fat-rich meal resulted in significant delay in atenolol absorption. The tlag increased from 0.55 ± 0.31 hr to 1.04 ± 0.35 hr and tmax from 2.86±0.94 hr to 3.57±0.65 hr. Also, the bioavailability of atenolol was significantly reduced by administration after fat-rich meal. The AUC decreased from 5760± 732 ug-hr/L to 4179±777 ug-hr/L and the Cmax from 552.3 ± 160 ug/L to 415.7 ± 88.5 ug/L. Administration of atenolol after protein-rich meal also affected the rate and extent of atenolol absorption significantly. The tlag increased from 0.55 ± 0.31 hr to 1.58± 0.68 hr and tmax from 2.86±0.94 hr to 5.26±1.31hr, while the AUC decreased from 5760± 732 ug-hr/L to 3377±1082 ug-hr/L and the Cmax from 552.3 ± 160 ug/L to 255.6± 45.8 ug/L. The effect of fat-rich meal and protein-rich meal explained by delayed gastric emptying and reduced atenolol dissolution. Based on these results, it is advisable not to take atenolol with food or with beverage to decrease the variability in absorption and hence atenolol therapeutic effect.

BB-P-007

IN VITRO AND IN VIVO STUDIES ON RECTAL SUPPOSITORIES CONTAINING ACEMETACIN

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Acemetacin, a non-steroidal anti-inflammatory drug with analgesic and anti-inflammatory properties, is glycolic acid ester of indomethacin. Metabolic studies of acemetacin suggest that the drug is rapidly absorbed orally and hydrolized by the liver to produce indomethacin as its major active metabolite. Currently acemetacin is used orally for the treatment of arthritis and rheumatic diseases in capsule from.

The aim of this study was to formulate acemetacin suppositories with lipophilic (Suppocire AIM and Witepsol H15) and hydrophilic bases (PEG 1500 and a blend of PEG 1500 : PEG 400 (90:10, (w/w)) and to evaluate in vitro drug release from this formulations. Suppository formulations were prepared by the melting technique to contain 60 mg of acemetacin. In vitro release studies were performed with dynamic membrane diffusion method using a dialysis tube and acemetacin was assayed by spectrophotometrically at 318 nm. Based on the in vitro studies, the release of drug increased in the following order: Suppocire AIM > PEG 1500 > Witepsol H15 > PEG1500 : PEG400. According to in vitro release study results, the formulation showing the highest the drug release was selected for further in vivo evaluations. Suppositories containing 10 mg/kg as acemetacin were adjusted to fit the anatomical size of rats rectum. In vivo studies were performed with Sprag-Dawley rats. The amounts of acemetacin and indomethacin its active metabolite in plasma were analyzed by high-performance liquid chromatography with diode array detector. Comparative studies were run with acemetacin suspension given orally.

BB-P-008

FORMULATION AND BIOLOGICAL EVALUATION OF GLIMEPIRIDE - CYCLODEXTRIN - POLYMER SYSTEMS

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Glimepiride is one of the third generation sulfonylureas used for treatment of type 2 diabetes. Poor aqueous solubility and slow dissolution rate of the drug lead to irreproducible clinical response or therapeutic failure in some cases due to subtherapeutic plasma drug levels. Consequently, the rationale of this study was to improve the biological performance of this drug through enhancing its solubility and dissolution rate. Inclusion complexes of glimepiride in ß-cyclodextrin (ß-CD), HP-ß-CD, DM-ß-CD and SBE-ß-CD, with or without water soluble polymers (HPMC, PVP, PEG4000, PEG6000) were prepared by the kneading method. Phase solubility diagrams revealed increase in solubility of the drug upon cyclodextrin addition showing Ap type plot indicating high ordered complexation. In the dissolution study of binary systems, DM-ß-CD complex showed highest dissolution rate. All the ternary systems utilizing ß-CD or HP-ß-CD showed higher dissolution efficiency compared to the corresponding binary systems. This result indicates that these polymers enhanced glimepiride complexation in these cyclodextrins. Conversely, these polymers didn't enhance dissolution of drug complexes in DM-ß-CD or SBE-ß-CD. The hypoglycemic effect of the most rapidly dissolving ternary system of glimepiride -HP-ß-CD- PEG4000 was evaluated after oral administration in diabetic rats by measuring plasma glucose levels. The results indicate that this ternary system enhanced significantly the biological performance of the drug. In conclusion, the association of water soluble polymers to glimepiride-CD systems would lead to reduction in the dose of glimepiride as well as in the amount of cyclodextrin utilized.

BB-P-009

AMOXICILLIN AND IBUPROFEN: DRUG INTERACTION, BACTERIOLOGICAL , CLINICAL AND PHARMACOKINETICS STUDY. PART 1. COMBINED THERAPY FOR TREATMENT OF HUMAN BACTERIAL INFECTION.

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Amoxicillin (AMX)–ibuprofen(A-I)physical mixture(1:1and2:1)were subjected to in-vitro examination for possible interactions using IR,UV scanning,DSC,TLC,results confirm absence of interaction. Effect of ibuprofen (IBU) on the antibacterial activity of AMX against certain bacterial species was investigated.The results showed that IBU potentiate the antibacterial activity of AMX towards certain micro-organisms.Sixteen A-I capsule formulations were prepared using a fractional factorial design (1/8) of 27 and tested for powder content characteristics and dissolution testing which showed that neither drug affect the dissolution process of the other.Data treatment and statistical analysis of data was performed.The chosen formulae; F4 and F15 were subjected to clinical study on 25 patients divided into 2 groups,one was treated with A-I capsules,the second was given AMX capsules.Data collected includesage,diagnosis,body temperature,total white blood cell count (W.B.C.),kidney and liver functions.Statistical analysis of W.B.C.data by using paired t-test revealed that there was a significant difference between before and after treatment and between AMX and A-I at p< 0.001.There was no effect of sex on the percent decrease in W.B.C.at p< 0.05.A-I combination proved to posses a higher clinical efficacy and microbiological activity than AMX alone.

BB-P-010

AMOXICILLIN AND IBUPROFEN: DRUG INTERACTION, BACTERIOLOGICAL , CLINICAL AND PHARMACOKINETICS STUDY. PART2. PHARMACOKINETICS OF AMOXICILLIN AND IBUPROFEN ADMINISTERED ALONE AND IN COMBINATION.

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Studying the pharmacokinetics and reactivity of amoxicillin(AMX) and ibuprofen(IBU)in plasma required an analytical method for their simultaneous determination.A simple,rapid,specific and reliable HPLC assay is described using a mobile phase of acetonitrile:water(50:50)v/v,pH 3.5,UV detection at 230nm.Regression analysis for the calibration plot for plasma standards obtained on 3 different days indicated excellent linearity(r>0.999).Quantification of AMX and IBU from a single oral dose was conducted on 4 different drug formulations(A,B,C,D)in a latin square crossover design involving sixteen male adult volunteers. Formulation A(A-I capsules chosen formula(F15)AMX500mg+IBU400mg),formulation B(AMX500mg),formulationC(IBU 400mg),and formulation D(reference products of AMX capsules and IBU tablets).Criteria used to assess this pharmacokinetic study were:Cmax,Tmax,AUC(0-24),AUC(0-),AUMC(0-24),AUMC(0-),t1/2el,KelMRTandFrel%.CmaxofAMX,from formulations A and D were 19.95+1.83 and 18.23+1.291 □g/ml.While Cmaxof IBU for formulations A,D and C were 14.49+0.492,15.57+0.910 and 16.54+0.709 □g/ml respectively.Formulation A showed a greater values of AUC(0-),AUMC(0-),for AMX and IBU,than when each drug was administered alone.The MRT of AMX and IBU in formulation A were significantly higher than those of formulations B,C and D.Frel% of AMX from formulations A and B were 110.21+5.077% and 94.28+7.739%.While that of IBU in formulations A and C were 213.56+7.030% and132.04+5.685%.The data were analysed statistically according to one way ANOVA representing a significant difference between formulations A, B and D,for AMX, and between formulations A,C and D,for IBU, at p>0.001.

BB-P-011

THE PREPARATION OF FAMOTIDINE ORALLY DISINTEGRATING TABLETS.

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Elderly people, children, and most disabled patients often suffer swallowing difficulties, thus, the demand for rapidly disintegrating tablets (RDT) has been growing fast. The problem concerning most of orodispersible tablets is to achieve an optimal balance between their physical strength and stability and their rapid disintegration when placed in the oral cavity.
In this work, to make RDT with sufficient mechanical integrity as well as rapid disintegration, Ac- di- sol as superdisintegrant, Avicel PH102 as binder, Mg stearate as lubricant, and mannitol or lactose as diluents were formulated. Sixteen tablet formulations were prepared according to a full factorial experimental design to investigate the effects of these excipients on the formulation of directly compressed orodispersible tablets.
Tablet properties such as tensile strength, in-vitro disintegration, wetting time, dissolution and mouth dissolving time were determined and compared for the prepared formulae. A selected formula was then evaluated in-vivo compared to conventional tablets. For the prepared formulations, the tensile strength ranged between 94.64 and 27.45 N/cm2, while the in-vitro disintegration time ranged from 12 minutes to 23 seconds. The preparations showing tensile strength above 52 N/cm2 and in-vitro disintegration time less than 2 minutes were selected for further investigations. All showed wetting time less than 56 seconds, mouth disintegration time of less than 40 seconds, and drug release in 15 min. ranged from 75.4 to 100.17%. In conclusion, RDT with acceptable hardness and desirable disintegration properties could be prepared within the obtained optimum region.

BB-P-012

PREPARATION AND EVALUATION OF TIMOLOL MALEATE NANOPARTICLES FOR OCULAR DRUG TARGETING.

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Nanoparticles (NP) are known to increase the efficacy and/ or to reduce the toxicity of drugs, thus attracted interest in the last decade. Timolol maleate-loaded ocular nanodispersions were prepared by a new technique based on salting-out process between two completely miscible solvents. Eudragit S-100 used as the nanoparticles- forming polymer while polyvinyl alcohol (PVA) was selected as the protective colloid and stabilizer agent to stabilize both the emulsification process and the final dispersion. The influence of changing PVA concentration on the ocular NP prepared was evaluated through drug loading capacity, particle size analysis, morphological characters examination, and drug release profile. A selected formula was then evaluated in-vivo compared to conventional eye drops. The results indicated an increase in the drug loading efficiency with the increase in PVA concentration; the loading of timolol into nanoparticles prepared using PVA concentrations higher than 1% exhibited a linear relationship with a correlation coefficient of 0.998. Regarding the NP size, increasing the concentration of the hydrocolloid (PVA) in the external aqueous phase led to a consequent decrease in the particle size of the produced nanoparticles. Formulation of timolol maleate- loaded nanodispersion resulted in significant improvements in the maximum intra-ocular pressure reduction effect, the time of maximum response and the duration of the IOP reduction effect of timolol maleate when compared to control conventional eye drops. In conclusion, preparation of ocular nanoparticles colloidal dispersion to achieve a controlled release of timolol maleate proved to be of promising potential.

BB-P-013

FORMULATION AND EVALUATION OF FELODIPINE IN SOFTGELS WITH SOLUBILIZED CORE

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Felodipine, an antihypertensive and antianginal calcium channel antagonist, is considered to be water insoluble (about 1mg/L) and only 15% bioavailable. In this study softgels, with solubilized- drug core, were used to improve the solubility of felodipine. Drug solutions were prepared using both cosolvency and micellar solubilization.

The optimum dielectric constant (DEC) for maximum drug solubility was first determined using dioxane/ water mixtures of different proportions. The optimum DEC was found to be 16.3, so felodipine was dissolved in either glycerin/ PEG400 mixture or propylene glycol (PG)/ PEG400 mixture (containing 90% & 80% PEG respectively). The drug solutions were filled in softgels, which were subjected to dissolution testing & evaluated for their drug content, weight uniformity & moisture absorption behavior.

Dissolution tests revealed a significant improvement of felodipine dissolution characteristics using cosolvency. After 90 minutes, more than 95% of the drug was dissolved from softgels containing solutions.

To study the effect of micellar solubilization on felodipine dissolution parameters, three different surfactants were investigated (0.5% sodium lauryl sulfate (SLS), 0.5% CTAB & 10% Tween80). All surfactants were found to increase the rate of felodipine dissolution where the time required for 100% drug dissolution was 60, 45 & 45 minutes for Tween, SLS & CTAB in glycerin/PEG & 75, 60 & 45 minutes for Tween, SLS & CTAB in PG/PEG respectively.

It could be concluded that felodipine softgels succeeded in enhancing the rate & extent of dissolution of such insoluble drug.

BB-P-014

ENHANCED BIOAVAILABILITY OF THE LUTEOLIN OF ARTEMISIA AFRA PLANT MATERIAL IN THE VERVET MONKEY (CHLOROCEBUS AETHIOPS).

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Aim: To investigate the bioavailability of luteolin contained in an aqueous extract of Artemisia afra to ascertain the influence of plant matrix on flavonoid absorption. Methods: A freeze-dried aqueous extract of A. afra was prepared and evaluated for luteolin content by validated HPLC assay. In a two-period cross over design bioequivalence study, six healthy vervet monkeys received, on two different occasions, the equivalent of 1mg luteolin/kg body weight of luteolin or A. afra aqueous extract via oral route (gastric tube). Blood samples (2ml) were drawn at 0, 15, 30, 60, 120, 240 and 360 min after administration and hydrolysed, extracted with ethyl acetate and assessed for luteolin using HPLC assay. From the luteolin plasma concentration vs. time data AUC0-360, AUC0-inf, Cmax, Tmax and Kel were calculated and bioequivalence assessed applying individual ANOVA analysis on the ln-transformed data of AUC0-360, AUC0-inf, and Cmax, point ratios and 90% CI of the ln-transformed data. Results: The aqueous extract of A. afra contained 2.5ug luteolin / mg plant material. The AUC0-inf, Cmax and Kel for luteolin pure and in A. afra were: 20.34 ± 4.524 and 37.69 ± 3.049 µg/mL.min; 140.8 ± 20.15 and 258.8 ± 9.735 ng/ml and 96.59 ± 51.19 and 63.33 ± 14.28/min, respectively and the point ratios and 90% CI for AUC0-inf and Cmax 188.8 (CI = 163.6 – 217.8%) and 185.3 % (CI = 163.9 – 209.5%), respectively. Conclusion: The bioavailability of luteolin was better in A. afra aqueous extract than in pure form suggesting that either plant matrix constituents improved the absorption of luteolin or luteolin was better absorbed in the plant (i.e. glycoside) form.

BB-P-015

RAPID DETERMINATION OF CLOBAZAM AND DESMETHYLCLOBAZAM IN HUMAN PLASMA BY HPLC

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Aim: The study was designed to develop a rapid HPLC method using Chromolith TM column for sensitive determination of clobazam (CLB) and its main metzbolite N-desmethylclobazam (NDCLB/IS) in human plasma with an acceptable LOQ for pharmacokinetic studies.

Methods: The chromatographic apparatus consisted of a low-pressure gradient HPLC pump, a UV detector and an online degasser, all from Knouer (Berlin, Germany). Chromatographic separation was achieved with a ChromolithRP-18e (100x4.6mm) column (Merck, Darmastadt, Germany). A mixture of a phosphate buffer (pH 3.5; 10 mM)-acetonitrile (70-30, v/v) was delivered at 2 ml/min. UV detector was set at 228 nm.

The plasma samples (0.5 ml) were extracted with 1.5 ml toluene after addition of 20 □l alprazolam (internal standard). The mixture was vortex and centrifuged at 10000 rpm (1 min each). The organic layer was evaporated under a gentle stream of nitrogen and reconstituted in 150 □1of mobile phase and a 100 □1 aliquot was injected on to the HPLC system.

Results: The regression equations showed intercepts of -0.0135 and 0.0297, slopes of 0.0004 and 0.0076, and r2 of 0.9988 and 9986 for CLB and NDCLB respectively. The mean intra and inter day reproducibility was shown to be less than 10% for both compounds (n=5).

The limit of quantitation (LOQ) of the method as signal/noise of 5 was equal to 25 and 10 ng/ml for CLB and NDCLB respectively. Each complete run time lasted 3.5 minutes.

Conclusion: The developed method is applicable in Pharmacokinetic and bioequivalence studies.

BB-P-016

THE PHARMACOKINETICS OF RIBAVIRIN IN TAIWANESE

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As a broad-spectrum antivirus agent, ribavirin is used in treating hepatitis C combined with interferon-a. Pharmacokinetics of ribavirin has been reported in papers, but there are many differences, such as T1/2 of ribavirin varies from 37h to 100h. Besides, no pharmacokinetic data about ribavirin in Taiwanese was found, either. This study was to provide pharmacokinetics of ribavirin in Taiwanese. 22 healthy volunteers (Female=9, Male=13) were enrolled in this study. 600mg ribavirin (Rebetol®) was given with 240 mL of water orally. Blood sample was taken from 0 to 372 h after dosing. Plasma concentration of ribavirin was assayed by LC/MS/MS. Pharmacokinetic parameters were determined by non-compartment model. The results were as following: Ribavirin was fast absorbed with the Tmax and Cmax were 1.42 h and 791.15 ng /mL which agreed with published data. The clearance was 22.43 mL/hr. The AUC0-t and AUC0-8 were 22827.19 h•ng/mL and 28274.78 h•ng/mL. The T1/2 was 176.96 h, significantly longer than it used to be known. This showed the extended blood sampling time was necessary in studying ribavirin pharmacokinetics because of its easily accumulation in erythrocytes. Higher absorption extent was obtained resulted from the AUC0-t / AUC0-8 ratio (81%). The CV% was 22.42% in average for all pharmacokinetic parameters showed no major individual variation was among Taiwan residents. Based on this study, no significant difference in the absorption rate of ribavirin is between Taiwanese and Caucasian. However, with different study design and better analytical sensitivity, longer half-life and higher absorption extent were obtained in the study.

BB-P-017

BUCCAL SILYMARIN LIPOSOMAL DELIVERY SYSTEM: PREPARATION AND INVESTIGATION APPLYING FACTORIAL DESIGN

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Silymarin, a natural lipotropic agent of low bioavailability from oral products, is prepared in a buccal liposomal delivery system. Silymarin liposomes were prepared using lecithin/cholesterol mixtures. Additives were explored in a full 2(3) factorial experimental design regarding drug entrapment efficiency. Additives used to optimize liposomal product were also investigated for their optimal concentrations considering release properties and in vitro permeation and absorption through chicken cheek pouch.
The results showed an optimal liposomal performance at 7:4 lecithin to cholesterol molar ratio. Decrease in entrapment efficiency with increasing cholesterol content was observed. Tween 20 or Tween 80 decreased the entrapment efficiency after 0.5 molar ratios. Positively charged liposomes showed superior entrapment efficiency over neutral and negatively charged liposomes. The product containing lecithin, cholesterol, stearyl amine and Tween 20 in molar ratios 9:1:1:0.5 gave the best drug absorption and permeation. It showed steady state permeation through chicken pouch for 6 hours.

BB-P-018

COMPARATIVE IN VITRO RELEASE OF KETOPROFEN FROM COMMERCIAL GEL FORMULATIONS THROUGH SILICONE MEMBRANE UTILIZING EUROPEAN PHARMACOPOEIA AND FRANZ DIFFUSION CELLS

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Three commercially available ketoprofen gels, from the United Kingdom, France and South Africa were used in these diffusion experiments. The purpose of this study was to evaluate the in vitro release of ketoprofen from these gels and to compare the release profiles using two different diffusion techniques, Franz diffusion cells and those of the European Pharmacopoeia (EP).
The diffusion cells of the EP were immersed in 1l of receptor fluid maintained at 32°C and stirred at 100 rpm. Silicone membrane was used which was cut to size to cover the aperture. One millilitre of receptor fluid was withdrawn at intervals sufficient to generate a release profile. Jacketed Franz cells maintained at 32°C were also utilised for this experiment. At pre-defined times the cells were emptied and refilled with pre-warmed receptor solution. The receptor solution used for both techniques was 0,2M phosphate buffer solution at pH 6.8. All runs were performed on five replicates for both techniques. The receptor fluid was analysed for ketoprofen using hplc.
The best release profiles observed were for the French and SA formulations using the EP cells. Next were the release profiles for the French and SA gels using the Franz diffusion cells. The UK formulation showed a very low release profile using both diffusion techniques. On examination it was found that the French and SA formulations were very elegant gels which spread evenly whereas the UK formulation was very thick and sticky and did not spread well. It is interesting to note that for all three formulations, the Franz diffusion cells always produced a lower release profile than that obtained from the EP cells.

BB-P-019

EVALUATION OF DOUBLE-PEAK PHENOMENON OF GLICLAZIDE AFTER ORAL ADMINISTRATION TO HEALTHY VOLUNTEERS

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The pharmacokinetics (PK) of gliclazide after oral administration in healthy volunteers was studied. The concentration-time profiles after administration of 80 mg Gliclazide exhibited a double-peak phenomenon in some of the volunteers (in test product n=6, in reference product n=10). This phenomenon was not seen clearly in the mean concentration-time profiles. The time between the two peaks was different in volunteers. We concluded that the mechanism underlying the double-peak phenomenon is due to either enterohepatic recirculation or two sites of absorption of gliclazide in the healthy volunteers. This is the first report of double peaks for oral gliclazide in healthy volunteers. The double-peak phenomenon caused by the hypothesized mechanism may have important therapeutic effects. The double-peak phenomenon was also seen in the decrease of blood glucose level (dBGL) in pharmacodynamic (PD) studies.

BB-P-020

A NOVEL APPROACH TO THE PREPARATION AND SCALE UP PRODUCTION OF PENTOXIFYLLINE CONTROLLED RELEASE TABLETS:II. BIOEQUIVALENCE STUDY

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Aim: The bioequivalence of a single 600-mg doses of pentoxifylline, newly formulated controlled release tablets, (Treatment A) and Trental® tablets (Treatment B) were evaluated in a crossover study in 12 healthy volunteers under fasting conditions.
Experimental: In vitro dissolution profiles were determined for the new formulation and Trental® at 100 rpm using USP paddle (apparatus II) employing simulated gastric fluid and simulated intestinal fluid. Twelve healthy volunteers received single oral doses of each formulation with a washout period of one-week in a randomized double blind, crossover study. Concentrations of pentoxifylline in plasma were measured by high-performance liquid chromatography. Typical ANOVA for crossover studies was applied to the area under the plasma concentration versus time curve (AUC) and the maximum concentration (Cmax) and the log transformed data. Bioequivalence of the two formulations in each comparison was assessed using the 90% confidence intervals (CI). In vitro dissolution profiles were also characterized and compared with corresponding human bioavailability study results.
Results: No statistically significant difference was found in the mean bioavailability parameters between Treatments A and B. The ratio of the mean bioavailability parameters and the logarithmically transformed AUC0-inf and Cmax values of treatment A over those of Trental® was calculated to be within the acceptable limit of 0.80-1.20 and 0.80-1.25, respectively. There was a good correlation between the in vitro and in vivo results.
Conclusion: These two products were bioequivalent and can be considered interchangeable in medical practice.

BB-P-021

COMPARISON OF THE IN VITRO RELEASE OF KETOPROFEN FROM EXTEMPORANEOUSLY PREPARED GELS CONTAINING DIFFERENT CONCENTRATIONS OF CARBOPOL

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There are a large number of proprietary topical ibuprofen formulations on the market, but in South Africa there is only one topical gel formulation available. The purpose of this study was to evaluate the in vitro release of ketoprofen from three extemporaneously prepared topical gel formulations containing different concentrations of carbopol (Ultrez 10NF) and compare the release with that produced by the commercially available formulation. All formulations contained 2.5% ketoprofen.
Jacketed Franz cells maintained at 32°C were utilised for this experiment, each being replicated five times. Silicone membrane was cut to size to cover the aperture. The receptor solution used was 0,2M phosphate buffer solution at pH 6.8. At pre-defined intervals sufficient to generate a release profile, the cells were emptied and refilled with pre-warmed receptor solution. The fluid was analysed for ketoprofen by hplc and cumulative release curves were plotted.
The formulations containing 1.5% and 2.0% carbopol produced virtually identical release profiles. The commercial gel produced a slightly higher release profile but it was very similar to the carbopol formulations. The gel containing 1% carbopol produced a much higher release profile than the other formulations. This is because gelling did not appear to be complete when using 1% of carbopol, whereas using 1.5% and 2.0% resulted in an elegant gel formulation with release profiles very similar to the commercially available formulation.

BB-P-022

RAPID INTRANASAL DELIVERY OF METOCLOPRAMIDE HYDROCHLORIDE: EFFICACY AND SAFETY OF VARIOUS ABSORPTION ENHANCERS AND PHARMACOKINETIC EVALUATION

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Aims: Evaluation of efficacy and safety of different absorption enhancers used in the preparation of nasal solution (NS) of metoclopramide hydrochloride (MPC HCl), and determination of pharmakinetics parameters of the drug in the formula containing the safest enhancer. Methods: Different enhancers viz: sodium deoxycholate (SDC), sodium cholate (SC), chitosan low and high molecular weight (CS L, CS H), protamine sulphate (Prot) and poly – L – arginine (Pol arg) were evaluated as nasal absorption enhancers for (MCP HCl) in anaesthetized rats. The safety of enhancers was assessed in vitro using human erythrocytes lysis experiment and in vivo by leaching of bilogical markers: total protein and enzyme lactate dehydrogenase (LDH) from the rat nasal epithelium. Furthermore, the pharmacokinetics of the MCP HCl in the NS with higher apparent first-order absorption rate constant (K app) and better safety, were evaluated in rabbits and were compared to those obtained after intravenous (IV) and peroral administrations. Results: Based on the obtained K app. the enhancers were ranked as follows: SDC> SC> CS H> CS L> Poly arg > Prot > control (no enhancer). SC proved to be a safe enhancer with < 15 % hemolysis and insignificant protein and LDH leaching (P<0.05). This same NS has a Tmax of 23.3min. compared to 50 min in case of the oral drug solution while the AUC 0-□ were 506.1, 434.9 and 278.7 □g/ml.min for IV, NS and oral solutions respectively. These values corresponded to absolute bioavailabilities of 87.21 and 55.61 % for the nasal and per oral solutions respectively. Conclusion: MCP HCl NS containing SC represents a successful approach for achieving a rapid control of emesis.

BB-P-023

COMPARATIVE IN VITRO RELEASE OF KETOPROFEN AND IBUPROFEN FROM COMMERCIALLY AVAILABLE TOPICAL GELS FROM THREE COUNTRIES

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The purpose of this study was to compare the diffusion rates of ketoprofen and ibuprofen from commercially available topical gels manufactured in three different countries (France, United Kingdom and South Africa) using the diffusion cells described in the European Pharmacopoeia (EP). The gels contained either 2,5% ketoprofen or 5% ibuprofen.
The diffusion cells of the EP (5 replicates) were immersed in 1l of receptor fluid maintained at 32°C and stirred at 100 rpm. Silicone membrane was used which was cut to size to cover the aperture. One millilitre of receptor fluid was withdrawn at pre-determined time intervals sufficient to generate a release profile. The receptor fluid was not replaced. Both ketoprofen and ibuprofen were determined in the receptor fluid using hplc.
The ibuprofen formulations showed the highest diffusion rates. This is probably due to the fact that there is more ibuprofen than ketoprofen present in the formulations. Another factor is that the ibuprofen molecule is smaller than ketoprofen. The French and UK products showed very similar release rates, with the SA formulation displaying a much lower diffusion rate. In the case of the ketoprofen formulations, the French and SA formulations displayed the highest diffusion rate and were almost identical, with the UK formulation displaying a much lower diffusion rate. The formulations manufactured in France and the UK were imported into South Africa in the hand luggage of one of our investigators to reduce any temperature fluctuations. This is another example of formulations from different countries showing different release rates of the active ingredient.

NRP-P-001

IMPLEMENTATION OF A INTERNAL MONITORING PROGRAMME IN OCCUPATIONALLY EXPOSED WORKERS

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Radionuclides incorporation may occur as a result of diverse activities; these include the work associated with the different stages of nuclear fuel cycle, the use of radioactive sources in medicine, scientific research, agriculture and the industry. In many countries, legal regulation exists that establishes the form in which incorporation studies must be performed, but in Uruguay these kind of studies had not been implemented up to now. Nevertheless within the framework of an ARCAL Project (International Atomic Energy Agency collaboration with Latin American Governments), based on the Safety Guides of the AIEA, a pilot program was implemented by our group. The target group were occupationally exposed staff from Nuclear Medicine Services (both public and private). This program initially was circumscribed to a reduced group of 9 volunteers. The pilot program was followed during 1 year, assessing biweekly internal activity of thyroid using a NaI (Tl) scintillation probe associated with a EG&G Ortec spectrometer. The measures were performed during 15 minutes to determine 131I and 99m Tc and urine samples were collected the same day.
Incorporated doses were estimated using specific software provided by the IAEA.
Internal contaminations were found and correction actions were taken. The pilot program is being extended to 20 workers and its generalisation to the whole population involved in Nuclear Medicine Services is being considered by national nuclear regulatory authorities. Different procedures must be revised in order to improve safe management of the radiopharmaceuticals.

NRP-P-002

EVALUATION OF 188RE-SN RADIOPHARMACEUTICAL SAFETY FOR RADIOSINOVECTOMY

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The 188Re-Sn is a radiopharmaceutical used with therapeutic purposes in patients wit rheumatoid arthritis (AR) or hemophilic joint disease. The procedure consists o intraarticular administration of the radiopharmaceutical, keeping the treated join immobilized and in rest during 72 hs. 188Re is a suitable beta-emitting radionuclid with a maximum energy of 2.12 MeV and a 155 KeV gamma emission that enable scintigraphic image acquisition to follow leakage from the administration site. The ai of the study was to evaluate the safeness of a radiosinovectomy treatment for the patien the family and the staff. The protocol was previously approved by the Committee o Ethics of the University Hospital. Four patients with informed consent received th treatment (three young hemophilic patients and one adult woman with AR) Radiopharmaceutical leakage was assessed for blood and urine samples during 72 hrs b a solid scintillation counter NaI(Tl) (crystal of 3'x3'). Radioactivity at one meter o distance from the knee, measured with a portable detector, was registered. Scintigraphi images (0, 24, 48 and 72 hrs) in a SOPHA SDX gamma-camera were acquired. A maximum of 11 % by urine elimination was determined, and 8% of administered dos was found in blood after the 72 hrs. The activity registered at 1 m of distance wa always below the recommended limits. Scintigraphic images did not show significan levels of activity, except in the injection site.
Radiosinovectomy with 188Re-Sn is a safe procedure, from a radioprotection point o view, for the patient and the involved staff.
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PB-P-001

STABILITY OF INSULIN IN PLGA NANOPARTICLES AFTER COMPLEXATION WITH PROTAMINE

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Aims: To investigate the effect of complexation on the stability of insulin in biodegradable nanoparticles of poly (D, L-lactic-co-glycolic acid) (PLGA). Methods: Bovine insulin was incorporated into PLGA nanoparticles by a solvent evaporation and a solvent diffusion method following its complexation with protamine. A stability-indicating high performance liquid chromatography (HPLC) method was developed and validated for analysis of insulin in the presence of nanoparticle matrix materials. Insulin loading in nanoparticles was determined by the HPLC assay after solvent extraction using acetonitrile:0.01M HCl (1:2, v/v). The stability of insulin within nanoparticles, in PBS (pH 7.4, containing 0.05% sodium azide and 0.2% BSA), and in extraction solvent was evaluated by HPLC at both the room temperature and 37 0C. Nanoparticles were also characterised for morphology, particles size and surface charge. The in vitro release of insulin from particles was investigated in PBS. Results: HPLC analyses indicate that insulin is very unstable in acidic solution and high temperature increases the speed of insulin degradation. However, in PBS, less than 1% increase of insulin degradation was detected after 3 days and about 2% increase in degradation products after 7 days storage at 37°C. The investigation of insulin-loaded PLGA nanoparticles after 7 days of release study at 37°C showed no significant insulin degradation occurred within nanoparticles compared to that of the control (insulin solution). Conclusion: Our study suggests that the formation of insulin-protamine complexes can effectively stabilize insulin, leading to the higher stability of insulin in PLGA matrix.

PB-P-002

SKIN PENETRATION OF BIODEGRADABLE POLYMERIC MICRO/NANOPARTICLES

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Aims: To establish the relationship between physicochemical characteristics of micro- and nanoparticle formulations and particle skin penetration. Methods: Rhodamine 6G (R6G) was chosen as a model drug and as a fluorescence label. Micro- and nanoparticle carriers were prepared from two different types of polymers. Hydrophilic particles were manufactured from chitosan (CS) by a coacervation method and hydrophobic particles were made of poly (D,L-lactic-co-glycolic acid) (PLGA) by both solvent evaporation and solvent diffusion methods. The mean particle size and zeta potential were determined by the Malvern Zetasizer 3000HS. Morphology of particles was characterized by FESEM. The in vitro release of R6G from particles was investigated in PBS. The penetration and distribution of nanoparticles in human skin were investigated by using Franz's cells and skin cryosectioning. The skin sections were examined under a fluorescence microscope. Results: Characteristics of CS particles such as size and charge were determined by the charge ratio of oppositely charged polymers whereas the size of PLGA particles was influenced by the method of preparation. Fluorescence images of skin penetration samples indicated that only hydrophobic PLGA particles showed significant penetration into the skin while hydrophilic CS particles did not show any penetration. Size of PLGA particles played an important role on permeation. Microparticles with size above 7 μm remained on the skin surface but nanoparticles (<1 μm) showed penetration into the viable epidermis and dermis of skin. Conclusions: This work suggests that both the nature and size of particles influence their skin penetration.

PB-P-003

PARTIALLY BENZYLATED DECAPEPTIDE OF POLYASPARTIC ACID TO REDUCE AMPHOTERICIN B TOXICITY

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Polyaspartic acid (PAA) has been extensively studied to protect renal toxicity of aminoglycoside antibiotics both in vivo and in vitro. However, PAA has not been examined if it has similar effect on the nephrotoxicity of amphotericin B (AmB). As a new method to reduce renal toxicity of AmB, we synthesized partially benzylated decapeptide of PAA and examined self-aggregation status along with acute toxicity of AmB after interaction of the drug with the polymer. Transmission electron microscopy of AmB solution after the interaction showed nano-sized spherical micelles with mean diameter of about 20 nm. Molar absorptivity of AmB after the interaction was significantly higher than that of AmB only, indicating low degree of self-aggregation of the drug. In acute toxicity test, all of the six mice survived seven days in 6 mg/kg AmB as of the drug interacted with the polymer, and only one mice died in 8 mg/kg dose. In contrast, AmB without the interaction was very toxic showing only one and three mice survived in 3 and 2 mg/kg dose, respectively. Mechanism for the reduced toxicity is unclear at present, but it appears that the micelles of AmB and the partially benzylated decapeptide of PAA get around the acute tubular damage in kidney.

PB-P-004

GENE TRANSFER SYSTEM INTO HUMAN PLACENTAL CELLS BY FIBER-MODIFIED ADENOVIRUS VECTORS

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[Purpose] Aim of this study was evaluate the ability of fiber-modified adenovirus (Ad) vectors, which can be effective in cells lacking the coxsackievirus and adenovirus receptor (CAR), to transduce human trophoblast cell lines used as in vitro models of human placenta.
[Methods] Human trophoblast cell lines, JEG-3, JAR and BeWo cells were used. Ad vectors, wild-type Ad-L2, Ad-RGD(HI)-L2 containing an Arg-Gly-Asp motif, Ad-K7(C)-L2 containing a 7-tandem lysine motif and Ad5/35 containing a chimeric Ad type 5 and 35 fiber protein were prepared. Luciferase gene was used as a reporter gene. For Ad-mediated gene transduction into cultured cells, the luciferase production was measured after culture of cells with vector particles for 48 h.
[Results and Discussion] Compared to the amount of luciferase produced by wild-type Ad-L2, Ad-RGD(HI)-L2 had the largest infectious potential and mediated 8-fold the amount of luciferase in JEG-3 cells, 14-fold in JAR cells and 77-fold in BeWo cells. Ad5/35 vector had greater gene transfer efficiency than wild-type Ad-L2 in three trophoblast cell lines (1.8-fold in JAR cells, 5-fold in BeWo cells and 6-fold in JEG-3 cells). Thus, Ad-RGD(HI)-L2 can be a potential tool for gene transfer into human trophoblast cell lines. Furthermore, Ad5/35 is a promising vector for mediating efficient gene transfer into human trophoblast cells which expressed CD46 of receptors for Ad5/35.

PB-P-005

IN SEARCH OF ACTIVE AZATYROSINAMIDE METABOLITES AS ANTI-ANGIOGENESIS AGENTS

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HPW98-1, asynthesized in this laboratory, showed inhibitory activities on the growth of human colon, pancreatic and prostate cancer cells. It also demonstrated anti-angiogenesis effect in nude mice with VEGF-induced angiogenesis. As this compound exhibited short half-life, it is suspected that the antitumor activity might be resulted from its possible metabolites. Therefore, the investigation of bioactive metabolites was conducted in this study. HPW98-1 was orally administered to Wistar rats. Two phase II metabolites, namely HPW071×001 glucuronide and HPW071×004 glucuronide / sulfate were identified from rat urine by LC/MS/MS analysis. Three phase I metabolites, namely HPW071×001, HPW071×002 and HPW071×003, were identified by hydrolysis of the urine samples with glucuronidase or sulfatase. The metabolites were chemically synthesized for the evaluation of cytotoxic activity on HL-60 human leukemia and SW480 human adenocarcinoma cancer cell lines.All three metabolites exhibited anti-angiogenesis effect in mice, with HPW071×001 showing highest activity at a low dose (10 mg/kg, oral), indicating its potential as an antitumor agent.

PB-P-006

FORMULATION OF A FAST-DISSOLVING KETOPROFEN LYOPHILIZED TABLET AS A NOVEL DOSAGE FORM

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To improve the solubility and dissolution rate of poorly water-soluble ketoprofen, a novel fast-dissolving tablet of ketoprofen was developed using freeze-drying techniqu Enhancement of solubility of ketoprofen was obtained by preparing its lyophilized tabl (LT) with highly water-soluble carrier materials consisting of gelatin, glycine, a sorbitol. Results obtained showed that the solubility of ketoprofen in its LT was nearly times greater than the solubility of the plain drug and 2 times greater than the solubili of its physical mixture (PM). Results obtained from dissolution studies showed that L of ketoprofen significantly improved the dissolution rate of the drug compared with t PM and the plain drug. More than 95% of ketoprofen in LT dissolved within 5 m compared to only 45% of ketoprofen plain drug dissolved during 60 min. Initi dissolution rate of ketoprofen in LT was almost tenfold higher than that of ketoprofe powder alone. Differential scanning calorimetry (DCS), X-ray powder diffraction, a scanning electron microscopic (SEM) analysis revealed that amorphous drug w dissolved in the carrier matrix of the LT.

PB-P-007

SIMPLE AND RAPID EFFICIENT METHODS FOR REGENERATION OF ARTEMISIA ANNUA L.

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Artemisia annua L., an important medicinal plant of the family Asteraceae contains an antimalarial, artemisinin. However, the relative low yield (0.01-0.6%) of artemisinin in A. annua greatly limits the commercialization of the drug. This work aimed to apply plant tissue culture techniques for high-frequency shoot regeneration in A. annua. In vitro efficient method for shoot organogenesis of A. annua L. were obtained from culture in different media to evaluate the frequency of regeneration. The result in variation of NAA, BA, 2,4-D and Kinetin was observed when stem segments culture for 4 weeks on Murashige and Skoog (MS) medium supplement with combination of NAA (0.05-1.0 mg/l) and BA (0.5-1.0 mg/l) and then transferred onto hormone-free MS medium for 8 weeks for rooting. MS medium supplement with NAA 1.0 mg/l and BA 1.0 mg/l mostly stimulated shoot formation and regeneration. In order to study effect of MS with only TDZ, the highest percentage of shoot formation (100% with >50 shoots/explant) was found when stem segments culture for 2 weeks on MS medium with TDZ 0.1 mg/L and then transferred onto hormone-free MS medium for 8 weeks. Combination of TDZ with NAA and BA concentration in different ratio were performed to obtain high frequency of shoot formation (75% with 3 shoots/explant) when stem segments culture for 4 weeks on TDZ 0.1 mg/L and BA 1.0 mg/L and then transferred onto hormone-free MS medium for 8 weeks. Finally the suitable conditions of three experiments could be the basal for genetic transformation with Agrobacterium tumefaciens.

PB-P-008

RELEASE STABILITY OF 5-FLUOROURACIL LIPOSOMAL CONCENTRATES, GELS AND LYOPHILIZED POWDER

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Possible leakage of 5-fluorouracil from stable plurilamellar vesicles was monitor during storage of the liposomal concentrates, gels and lyophilized powders. Changes release profile of dibucaine were taken as indicator of instability. Release profiles we obtained using the dialysis technique for a freshly prepared liposomal concentrate, gel reconstituted lyophilized powder (zero time) and storage for one, two and four weeks well closed tubes at 4 0C for the liposomal concentrate or gel and at 25 0C for liposom lyophilized powder.

Aiming at increasing stability of 5-fluorouracil liposomal dispersion, freshly prepar liposomal concentrates were directly incorporated in hydroxypropyl methylcellulose ge Stability release profiles of liposomal gels and concentrates indicated a significa increase in stability of liposomal formulations.

Also, lyophilization increases the shelf life of liposomes by preserving it in a dry form a lyophilized cake to be reconstituted immediately prior to administration or dire incorporation into a final dosage form. Release and physico-chemical stability studie showed superior potentials of the lyophilized product after reconstitution in comparis to concentrate and gel forms.

It could be concluded that lyophilization of liposomes loaded with a water-soluble dr such as 5-fluorouracil could significantly increase the stability of the liposomal vesicle and decrease leakage from it.

PB-P-009

DEVELOPMENT AND VALIDATION OF A DRUG RELEASE RATE TECHNIQUE FOR HYDROPHILIC AND HYDROPHOBIC DRUG ENTITIES IN LIPOSOMAL DISPERSIONS AND GELS

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The development, evaluation and validation of a method for determining the rate of hydrophilic and hydrophobic drug entities release from different types of liposomal dispersions and gels using a dialysis method are described. Dibucaine base and 5-fluorouracil were used as model drugs for a hydrophobic and hydrophilic drug respectively. Aliquots of liposomal dispersions were dispensed into dialysis bags of fixed length and size. The dialysis bags were fitted on the tablet dissolution tester paddle by attaching a stainless steel part to allow fixing the dialysis bags to it. The dialysis bag was attached horizontally fully stretched to the paddle, which was then immersed in the tablet dissolution tester beaker containing the release medium. The bag was fully immersed under the surface. Control bags were prepared and tested along with the liposomal dispersions. In case of liposomal gels, a known weight of each gel formulation was filled in stainless steel cups. The surface of the gel was made flat; the cups were fitted with the dialysis sheet by a rubber band and fixed at the bottom of the beakers of the tablet dissolution tester filled with the release medium. The paddles were positioned in the beakers of the tablet dissolution tester under the surface of the dialysis medium. Release rates were affected by the rate of rotation of the pebbles of the tablet dissolution tester, temperature, and volume of release medium. The method was reproducible and precise. The method applied was proved to evaluate the in-vitro drug release from hydrophilic and hydrophobic drug entities from liposomal dispersions and gels.

PB-P-010

OCTAARGININE-MODIFIED ENVELOPE-TYPE NANO PARTICLES FOR EFFICIENT AND SAFE GENE DELIVERY

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Protein transduction domains (PTDs) like TAT, penetratin and VP22 peptides are promising devices for efficient cellular uptake of associated peptides, proteins and other bioactive molecules. These peptides share the presence of several arginine residues in their sequences and it was shown that the arginine residues play an important role in the internalization. Here, we used the octaarginine (R8) peptide as an optimized arginine rich peptide to achieve high intracellular delivery of relatively large drug carriers such as liposomes.
We prepared R8-modified liposomes (R8-Lip) using a simple procedure in which the peptide is attached to a stearyl moiety that acts as an anchor to the lipid surface of the liposomes. The cellular uptake and intracellular trafficking of the R8-Lip were examined using confocal microscopy and flow cytometry.
R8-Lip were extensively internalized into cells mainly in the form of intact vesicles as judged by confocal microscopy. The presence of cell surface proteoglycans was found to be important for cellular binding and internalization. R8-Lip were internalized using different endocytic pathways depending on the density and the topology of the peptide on the liposomal surface. Furthermore, condensed DNA particles coated with a lipid envelope modified with R8 were highly internalized and were not subject to high lysosomal degradation. The R8-modified nano particles produced highly efficient transfection activities with a minimum cytotoxicity. The virus-like core-shell structure developed here is highly promising for gene therapy.

PB-P-011

A STATISTICAL MODEL-BASED APPROACH TO PLATFORM COMPARISONS AND MICRO ARRAY QUALITY ASSESSMENT

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The ideal platform comparison is a disciplined, statistical approach based on a model of platform behavior. We use an ANOVA model which describes the variability in the measured transcript as a combination of the variability of the platform, sample, replicates and transcripts. This approach has the significant benefit of providing estimates of the relative contribution to variability of each component in a system. In addition the analysis is objective and avoids the over-conservative behavior of intersecting lists. For such an analysis the dataset must consist of the same samples run in replicate on different platforms and the same transcripts should be detected by all the platforms. This model can be extended to include additional quality control variables such as different operators, different reagent batches, and different manufacturing batches. This approach allows the investigator to systematically identify and quantify all sources of variability in a micro array experiment.

PB-P-012

THE USE OF BIODEGRADABLE LACTIDE- CO-?-CAPROLACTONE FOR CONTROLLED DNA GENE DELIVERY

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The success of gene therapy is largely dependent on the development of safe and effective systems that deliver DNA for sufficient time to target cells. Non-viral delivery systems, such as biodegradable polymeric microspheres have been increasingly proposed as alternatives to viral vectors.

In this study, w/o/w double emulsion solvent evaporation technique was adapted for the preparation of controlled release Calf thymus DNA microspheres using two lactide copolymers with varying viscosities and lactide residues namely (D,L-lactide-co-glycolide) PLGA (50/50) (RG502) & poly(D,L-lactide-co-?-caprolactone) PLCL(75/25).

The prepared microspheres were evaluated for their surface morphology, average particle size, DNA loading efficiency and their release pattern in phosphate buffered saline pH 7.4. Agarose gel electrophoresis (AGE) and Differential scanning calorimetry (DSC) were applied to assess DNA structural integrity.
The Electron microscopy revealed that, DNA microspheres were round, spherical and smooth with average particle size of 3.1and 4.2 µm and entrapment efficiencies of 53.09% & 60.55% for PLGA and PLCL respectively. AGE and DSC showed no additional bands or extensive smearing and no significant change in DNA melting temperature. This would prove that lactide copolymer is an efficient polymer system for DNA protection. Both polymers successfully controlled DNA release for 7 days with more delayed pattern (30.2%) and low initial burst release (9.2%) from PLCL than PLGA (65.2% & 29.4%) respectively.

The physicochemical properties of microspheres are greatly affected by the lactide residue, viscosity and lactide copolymer composition used.

PB-P-013

SENNOSIDE A AND SENNOSIDE B PRODUCTION BY HAIRY ROOTS OF SENNA ALATA (L) ROXB.

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Senna alata (L) Roxb. (Family Leguminosae) is known to contain anthraquinone glycosides including sennoside A and B which act as purgative properties. Recently, hairy root cultures were useful for the production and biosynthesis of plant secondary metabolites in many plant species because of biochemical stability and rapid growth rate. In the process of our study on the production of sennoside A and B from *S. alata*, we established hairy roots of *S. alata* and described the effect of culture conditions for the formation of sennoside A and B.

Hairy roots of *Senna alata* transformed with Agrobacterium rhizogenes, strain ATCC 15834 were induced and grown in half strength of Murashige and Skoog (MS) medium. Yellowish hairy roots of *S. alata* generated from the wounded sites after 2 weeks of inoculation on half-strength MS medium containing 500 mg ml-1 cefotaxime. The time course study of the growth of hairy roots was carried out by using the shaking culture, and sennoside A and B contents were quantified simultaneously by ELISA using anti-sennoside A and sennoside B monoclonal antibodies. Hairy roots cultured on half-strength MS medium containing 5 % (w/v) sucrose under dark condition mostly stimulated the growth of hairy roots and increased the concentration of sennosides A and B yielding 168.94□4.20 and 34.16□3.64 ug g-1 dry wt, respectively.

In conclusion, the hairy root cultures of *S. alata* on hormone-free half-strength MS medium containing 5% (w/v) sucrose under the dark condition is the optimum condition for producing sennosides A and B by the shaking culture system.

SIG PHARMACOEPIDEMIOLOGY/PHARMACOECONOMICS - POSTER SESSION

PP-P-001

KNOWLEDGE ON DRUGS USED TO TREAT ASTHMA

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Aims : To compare knowledge on drugs used to treat asthma between teenagers (aged less than 20) and adults (aged 20 to 45 years).
Methods : Participants were recruited by community pharmacists who identified among their clients those who were aged 12 to 45 years, had had a previous diagnosis of asthma and were using a short-acting beta 2 agonist more than three times a week or an inhaled corticosteroid. We interviewed participants by telephone to obtain information on the medications they used to treat their asthma and on their knowledge on short-acting beta 2 agonists and on inhaled corticosteroid using a four item questionnaire. We computed a score for each class of drugs by adding one point for each correct answer. Mean scores were calculated for teenagers and for adults. Differences between the two groups were assessed using Student's t tests.
Results : A total of 220 individuals were included (57 (25.9%) teenagers and 163 (90.1%) adults). In all, 195 (88.6%) said they were using a short-acting beta 2 agonist. Adults had a higher mean score (2.84) than teenagers (2.39) (p-value = 0.001) for the knowledge on these drugs. Similar results were observed among the 156 participants who reported using an inhaled corticosteroid (adults mean score = 2.69; teenagers mean score = 2.16; p-value = 0.005).
Conclusion : In this population, knowledge on drugs is not optimal. Pharmacists could help improve asthma control by educating asthmatic people on their medication, in particular teenagers.

PP-P-002

EVALUATION OF A CLINICAL PHARMACOKINETICS MONITORING SYSTEM

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Background: Concentrations of some drugs appear to have inappropriate indications or suboptimal timing, particularly in the inpatient setting. The appropriate use of pharmacokinetic drug monitoring, particularly in conjunction with a clinical pharmacokinetic monitoring (CPM) service, is both efficient and cost-effective. Objective: The aim of this study is to evaluate the effectiveness of a computerized CPM system which was implemented in a medical center. Indicators of medication outcome were collected prior to and after the CPM system was introduced. Methods: The drug Digoxin is representative and being evaluated in this study. Several objective indicators were used to estimate cost-effectiveness of this CPM. Results: After introducing the CPM system, day intervals of abnormality in serum concentration are significantly reduced by 3.53 days/patient. Average length of stay significantly decreases after the CPM, from 32.13 to 27.92 days in average. The cost of laboratory blood test can be saved is US$33.27/patient. In addition, the cost of toxicity therapy was found significantly reduced by US$9.68/patient (US$23.76/patient vs. US$14.08/patient; p<0.05), due to reducing the use of Lidocaine, Phenytoin and anti-diarrhea drugs. Similarly, significant reduction was found as US$9.42/patient (from US$22.82/patient to US$13.41/patient; p<0.05) for the cost of combined therapy in the over-optimal group. Conclusion: This study provides the evidence for the implementation of the CPM system is meaningful in pharmaceutical care that can improve quality of patient care as well as enhance patient safety.

PP-P-003

PHARMACOEPIDEMIOLOGICAL STUDIES IN ANIMAL BITES: WHAT DO THEY SHOW?

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AIMS: The goal of our pharmacoepidemiological studies was to following the multiple problems concerning the prophilaxy, therapy and pharmacoeconomics problems caused by animal bites.
METHODS: Patients who were diagnosed having animal bites during July to December 2004 were included. It was studied and statistical analysed some different aspects: medico-pharmaceutical, medico-veterinary, the protection of environmental medium and pharmacoeconomics related to cases of animal bites.
RESULTS: A total of 261 patients were included. There were 152 patients (58,2%) with bites produced by dogs, 69 patients (26,4%) bitted by cats and 83 patients (31,8%) bitted by wild animals.The common interest in human and veterinary phisycians was to avoid rabies. The medico-pharmaceutical problems concerning the complex treatment, a local care of the wounds and a general therapy such as: immunizations, prophylactic antibioticotherapy, in easy cases with Cephotetan and Clindamicin, in severe cases with Ampicillin and Clindamicin. The costs of the wound careness are different, varying from 5 EU to 1500 EU.
CONCLUSIONS: In the light of these results, the prevention on animal bites depends on education and civilisation, pharmacoepidemiology and public health services, echological environmental protection.

PP-P-004

FLUOROQUINOLONES CONSUMPTION IN CLINICAL EMERGENCY HOSPITAL OF CRAIOVA

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AIMS: Excessive use of fluoroquinolones contributes to the development of antibiotic resistance and increase hospital costs. The aim of this study is to evaluate the impact of the fluoroquinolones controlled use on the consumption and the bacterial susceptibility.
METHODS: The study was performed between May 2003 and December 2004 and screened prescriptions of Ciprofloxacin, Ofloxacin, Norfloxacin and Pefloxacin. The following data were collected, recorded and analised using Epi-info software:
- consumption of antibiotics in euros, number of day of treatment
- clinical data (duration of therapy, administration route, germs, resistance).
- pharmacist interventions.
RESULTS: The consumption of fluoroquinolones decreased between 2003 and 2004 (18%) but increased in 2004 (3%). 5757 patients were enroled in this study. The main medication used were Ciprofloxacin (40%) and Ofloxacin (39%). Oral therapy represented 64% of cases. Fluoroquinolones were used for infection treatment (50%), empiric therapy (38%) or prophilaxis 918%0. Most frecquent germs were Escherichia coli (35%), Pseudomonas aeruginosa (14%) or Staphilococcus aureus (11%). Susceptibility to fluoroquinolones remain high (92%-82%-80%). Patients were treated for urinary tract infections (48%), respiratory tract infections (20%), bone or joint infections (7%). In 6,3% of cases, pharmacist interventions led to change the route of administration, to replace fluoroquinolone by another one or by another antibiotic.
CONCLUSIONS: The controlled use led to a large decrease of consumption during the first 6 month, a slowing down was observed after, probably due to the turn-over of resident phisician.

PP-P-005

DISCORDANCE OF UPPER RESPIRATORY TRACT INFECTION DIAGNOSIS AND TREATMENT BASED ON TAIWAN'S NATIONAL HEALTH INSURANCE DATA

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Background: Pharmacoepidemiologic study using administrative data relies on the correct classification of diagnosis. In Feb. 2001, the Bureau of National Health Insurance (BNHI) in Taiwan started a new policy for controlling antibiotic usage in upper respiratory tract infections (URI). However, lack of explicit definition of URI could induce bias in policy evaluation.

Objectives: This study investigates patterns in antibiotics prescription for URI using different classification of diagnosis to assess the potential impact on policy evaluation.

Method: The study draws its data from 6,284,760 outpatient visit claim records for 2002 from Taiwan's BNHI. Two definitions of URI were used in this study: single diagnosis (ICD9 code=465) and extended diagnosis (ICD9 code=461,463,464,465,466) of URI. Different definitions of diagnosis were hypothesized to reflect discordance in antibiotic prescribing rate and pattern.

Results: Contrast to the hypothesis, similar proportion (16.59% vs. 16.87%) of antibiotic prescriptions using different URI definitions fell outside of published guideline. The prescribing patterns were also identical. Variation was only shown in percentage of each antibiotic category. Cephalosporins (39.39% vs. 36.50%, p<0.001), penicillins (34.77% vs. 31.13%, p<0.001), and clindamycin (13.86% vs. 20.15%, p<0.001), were the most common prescribed antibiotics in both comparison groups.

Conclusion: A lack of appropriate definition of URI was shown in this study. Evidence-based prescribing evaluation using administrative data and followed policy implication should not be performed unless coding classification of diseases is improved.

PP-P-006

PATIENT PERCEPTION ON TREATMENT FOR ACNE

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The aim of the study was to investigate the perception of patients regarding treatment o acne.

Patients attending for a consultation with a dermatologist and who had been receivin treatment for at least 4 months were asked to participate. Patients were interviewe using a questionnaire intended to analyse patients' perception with regards to treatmen and occurrence of side effects. The Acne Disability Index (ADI) was administered. Dat was analysed using Microsoft Excel, and Anova and t-tests were carried out.

The severity of acne for the 53 participants (26 males, 27 females; mean age 20 years age range 13-38 years) was: 10 mild, 30 moderate, 13 severe. Treatment for acn included: topical treatment- 13, systemic antibiotics- 4, oral isotretinoin-21, both or and topical treatment- 15. The majority of patients described the degree of improvemen as moderate (22) and slight (18). Thirty-nine patients found their treatment expensiv Occurrence of side effects did not affect the quality of life for 34 patients. Patients wit severe acne were willing to pay either 125 -250 Euro (50%) or more than 250 Eur (50%) for a hypothetical cure. Patients with mild to moderate acne were willing to pa 25-125 Euro (28%), 125-250 Euro (50%) and more than 250 Euro (22%) (p<0.05).

Participants feel that their treatment is expensive, the side effects experienced affec their quality of life and the improvement is only moderate slight. However patients ar willing to spend more money for a hypothetical cure and the amount of money they ar willing to pay varies proportionately with the severity of acne.

QP-P-001

SIMULTANOUS DETERMINATION OF MICONAZOLE NITRATE AND TRIAMICINOLONE ACETONIDE IN A TOPICAL PREPARATION BY LIQUID CHROMATOGRAPHY

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Miconazole nitrate is an antifungal agent. It is applied as 0.2% cream in the treatment of fungal infections of skin and nails. Triamcinolone acetonide is also applied topically as a 0.1% cream or ointment for treatment of various skin disorders.Combination of the two drug substances is applied in the formulation of a pharmaceutical topical preparation incorporating methyl paraben sodium and propyl paraben sodium as preservatives. Most of the reported chromatographic methods for determination of miconazole nitrate and triamcinolone acetonide are either dealing with each drug in separate or in different combinations. In this work, we determined simultaneously both active ingredients together with both preservatives by a validated gradient elution chromatographic method. Analysis was conducted on a C18 column (10um) with a mobile phases, (A) acetonitrile -methanol (80 - 20), and (B) 20mM ammonium acetate, with a programmable gradient elution at a flow rate of 1.0 ml.min-1 , and at a detection wavelength of 238 nm. The method was validated to linearity, precision, accuracy and selectivity. Correlation coefficient (r2) were 0.9998, 0.99998, 0.99997, 0.99995 in the ranges of 5-50 ug.ml-1 , 0.53-5.3ug.ml-1 , 0.9-9.0ug.ml-1 and 0.22-2.2ug.ml-1 for miconazole nitrate, triamcinolone acetonide, methyl paraben sodium and propyl paraben sodium, respectively. Recoveries of the method ranged from 99.82% to 100.88% for miconazole nitrate and from 99.76 to 100.46% for triamcinolone acetonide in the range of 80-120% of the labeled claim. Recoveries for methyl paraben sodium and propyl paraben sodium were ranged from 100.66% to 100.97% and from 100.36% to 100.90%, respectively.

QP-P-002

QUANTITATIVE ANALYSIS OF ESTROGEN DERIVATIVE RESIDUE IN POLIOMYELITIS VACCINE BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY WITH FLUORESCENCE DETECTION

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A quantitative HPLC-fluorescence method for estrogen derivative residue in poliomyelitis vaccine was developed and validated. Sample pretreatment included ethyl acetate extraction and solid-phase extraction on a C18 column. LC separation was performed on a column of Zorbax SB C18 (150 mm × 4.6 mm id, 5 mm of particle size), a fluorescence detector at an excitation wavelength of 280 nm and an emission wavelength of 310 nm, and a mixture of methanol-phosphorus acid 10 mM (7:3) as mobile phase with a flow rate of 1.0 ml/min. Identification and quantitation were based on retention time and fluorescence intensity, respectively. Limits of detection and quantitation (LOQ) had values of 1.17 and 3.91 ng/g, respectively. Linearity was obtained with an average coefficient of determination (R2) higher than 0.997, over a dynamic range from the LOQ value up to 65 ng/g. The recoveries of estriol, estron and estradiol from poliomyelitis vaccine were in the range of 93.5 to 96.3%.

QP-P-003

CHEMOMETRIC AND CHROMATOGRAPHIC METHODS FOR SIMULTANEOUS DETERMINATION OF ISOPROPAMIDE IODIDE, DIPHENYLPYRALINE HYDROCHLORIDE AND PHENYLPROPANOLAMINE HYDROCHLORIDE IN PHARMACEUTICAL MIXTURES

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General chemometric methods are outlined for the use of orthogonal polynomials for unequal intervals (OPU) to eliminate interferences in multi-component spectrophotometric analysis. The methods are useful when the absorption spectra of the analytes show considerable overlap. The unequal interval wavelengths are selected according to the shape of a specified segment on the absorption curve, thus the optimum values of the calculated OPU coefficients reflect exactly the fine structure of the absorption curve for each analyte in the mixture. The work utilized those coefficients in two approaches. The first involves matrix calculation for a number of source equations equal to the number of analytes in the mixture, a method named the unique orthogonal polynomials for unequal intervals (U-OPU method). In the second the OPU is applied under least squares approach, a method termed LS-OPU method. In the latter the number of source equations exceeds the number of mixture components. The mathematical explanation behind the methods is presented. The methods are illustrated by analyzing a mixture of isopropamide iodide, diphenylpyraline hydrochloride and phenylpropanolamine hydrochloride. In addition, an HPLC method was developed for resolving such ternary mixture using a 250mmX4.6mm C-18 column. The mobile phase is a mixture of acetonitrile and 0.025M NaH2PO3 (60:40v/v) containing 0.1% sodium lauryl sulfate and 0.1% triethylamine (pH 3.5), flow rate 1ml/min, with UV detection at 223nm and ambient temperature. The proposed methods were successfully applied to the determination of the drugs in their capsules. The results obtained are statistically compared.

QP-P-004

FORCED DEGRADATION - A SUITABLE METHOD FOR THE SYNTHESIS OF IMPURITIES IN LIFE SAVING DRUGS

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AIM:A state of absolute purity of any pharmaceutical substance is almost impossible, but approached as closely as possible.The US FDA drafted guidance states that all related impurities of the drug are to be identified, characterized, qualified and studied for its impact on safety and stability of its products.A standard is thus needed to:
1.Detect impurities in drug
2.Decide the presence/absence of degradation/related substances
3.Standardize the impurity substance
4.Control strength/ potency of Active Pharmaceutical Ingredient.
Such official impurity reference standards are costly and not freely available in Asian market.Hence, an economical method for producing these impurities, which can be used as working standards, is designed.
The drugs selected for the study are Glibenclamide and Nifedipine.
METHODS:Hydrolysis of Glibenclamide produced BP Impurity-I while carbomylation of Impurity-I gave BP Impurity-II. Nitrosophenyl pyridine and Nitrophenyl pyridine analogs of Nifedipine were synthesized using two basic reactions: oxidation and reduction.Exposure of dilute solution of drug to visible light can also be used, but is a slow process. The synthesized impurities were purified by specialized techniques of recrystallization & column chromatography.
RESULTS AND CONCLUSIONS: The synthesis of Glibenclamide and Nifedipine impurities have been successfully carried out and process-standardized. The purity (99-99.9%) of the substances was checked by TLC, HPLC and characterized by physical, chemical and spectral analysis (Elemental, NMR, Mass, IR, UV).
ACKNOWLEDGMENT: Thanks are due to Deputy Drug Controller (WZ).

QP-P-005

SPECTROPHOTOMETRIC AND SPECTROFLUORIMETRIC METHODS FOR THE DETERMINATION OF FLUVOXAMINE MALEATE WITH NINHYDRIN IN DRUG FORMULATION

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Two sensitive and selective spectrophotometric and spectrofluorimetric methods have been developed for the determination of Fluvoxamine maleate in pure form and in pharmaceutical preparation. The methods are based on the reaction of the primary amino group of the drug with ninhydrin in N,N\ - dimethyl formamide (DMF) medium producing a blue colored complex measured spectrophotometrically at 600 nm and the first derivative value (peak to peak) at 553 and 646 nm. The fluorophore exhibits excitation □max at 308 nm and emission □max at 624 nm. The composition of product was found to be 2:1 (Reagent: Drug). The reaction obeys Beer's law over the ranges of 15-55 and 10-50 μg/ml for the absorption and first derivative measurement and over the ranges of 0.1-0.5 μg/ml for spectrofluorimetric method. The detection limits were found to be 4.36, 2.37 and 0.04 μg/ml for the spectrophotometric and spectrofluorimetric methods, respectively. The proposed methods have been applied successfully to the analysis of the drug in tablet form. No interference was observed from common pharmaceutical adjuvant. Statistical comparison of the results with the reference method showed excellent agreement which indicated no significant difference in accuracy and precision.

QP-P-006

ENZYME KINETIC ANALYTICAL METHOD FOR ANGIOTENSI CONVERTING ENZYME INHIBITOR DRUGS DETERMINATIO IN PLASMA USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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Based on enzyme kinetic principle, angiotensin converting enzyme inhibitor drugs plasma, demonstrated by captopril and enalapril were determined via the analysis hippuric acid, the product of reaction between hippuryl-histidyl-leucine and resid angiotensin converting enzyme from drug inhibition. The developed high performan liquid chromatographic technique consists of C18 column and the mixture of acetonit and 40 mM phosphate buffer with sodium dodecylsulfate at the pH of 2.3 as the mob phase operated at the flow rate of 1 ml/min. The detector wavelength was 228 nm. T sensitivity of the method for enalapril as enalaprilat was 3 ng/ml or 10 ng/ml captopril in plasma. Acceptable accuracy as average %bias was –0.45% for enalapril and 0.27% for captopril. The %RSD of intra-day and inter-day precision for enalapril and captopril were all within 9%. Since none endogenous interference was detecte supporting the specificity of this method. The stability of plasma enalaprilat a captopril at laboratory temperature were10 and 5 h and at frozen temperature (- 48o were 30 d and 14 d, respectively. Plasma enalapril could be restored within two freeze thaw cycles while only one cycle for captopril. However, the processed analytes we still stable within the autosampler at 0oC up to 40 h. This developed method w successfully used for analyzing plasma sample from twelve volunteer subje throughout 14 h after administered enalapril tablets.

QP-P-007

APPLICATION OF DERIVATIVE RATIO SPECTROPHOTOMETRY AND PARTIAL LEAST SQUARES PLS TO THE DETERMINATION OF DISSOCIATION CONSTANTS.

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Dissociation constants of some compounds have been determined using (i) derivative ratio spectrophotometry, (ii) multivariate methods using absorbances and absorbance ratio data. For the PLS method, the training set was constructed by computation using a general formula UAa + DAb where U+D= 1 and Aa and Ab are the absorbances of the completely dissociated acidic and basic forms. Teorell buffer solutions were used. At a given pH, any of the studied compounds behaves as a mixture of two components (dissociated and undissociated forms). Accordingly, first and second order ratio spectrophotometry have been applied to obtain the dissociated and undissociated concentrations at different pH values. Substituting in the Henderson equation, the pKa values were obtained. Using the same principle PLS has been applied to obtain the concentrations at different pHs.

Compound	Reported pKa	1D	2D	PLS
Theophylline	8.6	8.60	8.61	8.61
Chlorpheniramine	4.0	4.00	4.02	4.01
Trimethoprim	7.2	7.23	7.25	7.26
Paracetamol	9.5	9.53	9.50	9.51
Chlorzoxazone	8.0	8.13	8.09	8.10
Benzoic acid	4.2	4.15	4.18	4.17

QP-P-008

APPLICATION OF CHEMOMETRICS, PLS, TO SECOND-ORDER DERIVATIVE SPECTROPHOTOMETRIC DETERMINATION OF BENZENE AS IMPURITY IN ETHANOL AND ISOPROPYL ALCOHOL.

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Benzene is assayed as an impurity in ethanol, I and isopropyl alcohol, II at a level of ppm using GC methods (B.P. 2004) . The multivariate method of analysis (PLS) ha been applied to develop a rapid, simple and direct spectrophotometric method for thi purpose. Second-order derivative data has been recorded for I and II in 5 cm and 1 cm path lengths, respectively against water as blank over the wavelength range 240 – 29 nm at 1nm intervals. Training sets containing benzene in I and II have been constructe over the concentration range 1.2 to 3.6 ppm at 0.4 ppm increments. Absorbance an second order-derivative data have been recorded. Applying PLS for both data revealed that using second-order derivative readings was more appropriate than using direct absorbance data as a quantitative measure of benzene as impurity. Validation set prepared to contain benzene in I and II over the concentration range 1.4 to 3.4 ppm a 0.4 ppm increments were similarly measured and chemometrically treated. Mean percentage recoveries were found to be 99.93±0.67% and 100.41±1.22% for benzene i I and II, respectively using PLS. Four different samples of I and II containing variable amounts of benzene as impurity have been analyzed using second-order derivative PLS method. The same samples were determined using the tangential graphical technique applied to second order derivative curves (B.P. 1998) as a reference method. The amount of benzene in I and II were found to range from 1.36 to 2.51 ppm and 1.38 to 2.53 ppm , respectively using the official method.
The PLS method gave results ranging from 1.37 to 2.47 ppm and 1.34 to 2.48 ppm for I and II, respectively.

QP-P-009

DETERMINATION OF OMEPRAZOLE, LANZOPRAZOLE AND PANTOPRAZOLE IN PRESENCE OF THEIR ACID- INDUCED DEGRADATION PRODUCTS USING DERIVATIVE- RATIO SPECTROPHOTOMETRY AND PARTIAL LEAST SQUARES METHODS.

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Omeprazole I, lanzoprazole II, and pantoprazole III, have been determined trically in presence of their acid-induced degradation products using (i) first and second order-derivative ratios and (ii) PLS applied to absorbance and absorbance ratio data. Laboratory prepared mixtures of the intact compounds with the corresponding acid induced degradation products were prepared in 0.1M NaOH to contain 2.0 to 65% degradation product and measured over the wavelength range 220 – 340 nm at 2nm intervals. The derivative ratio, first and second order methods as well as the PLS method applied to absorbance ratio and absorbance data gave mean percentage recoveries 99.9 ± 0.30, 100.0 ± 0.23, 100.1 ± 0.33, and 99.9 ± 0.25 for I, respectively; and 100.1 ± 0.36, 100.2 ± 0.31, 100.3 ± 0.32, and 100.1 ± 0.29 for II, respectively; and 100.4 ± 0.28, 100.1 ± 0.45, 100.3 ± 0.36, and 100.3 ± 0.31, for III, respectively. The PLS method when applied to absorbance ratio data to give concordant results to absorbance data expresses its specificity to the investigated compounds I, II, and III.

Capsules of I (Gastrazole, 20 mg), II (Lanzor 15 mg) and tablets of III (Controloc 40 mg) have been analyzed using the proposed methods. Mean percentage found from the labeled were 100.5 ± 0.36, 100.8 ± 0.4, 100.5 ± 0.33 and 100.7 ± 0.35, for I, respectively; 98.6 ± 0.43, 98.6 ± 0.48, 99.0 ± 0.45 and 98.9 ± 0.35 for II, respectively; and 100.3 ± 0.46, 99.9 ± 0.43, 100.0 ± 0.33 and 100.0 ±0.39 for III, respectively. The PLS method is fast, easy simple and do not require any prerequisite. It is a one step calculation.

QP-P-010

POLAROGRAPHIC AND VOLTAMMETRIC CHARACTERISTICS OF A-OXO-?-BUTYROLACTONE-ARYLHYDRAZONES-DETERMINATION OF SULFA DRUGS THROUGH JAPP-KLINGEMANN REACTION

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The electrochemical behavior of a-oxo-?-butyrolactone arylhydrazones in aqueous solutions was studied by differential pulse polarography (DPP) at dropping mercury electrode (DME), differential pulse voltammetry (DPV) at hanging mercury electrode (HMDE) and cyclic voltammetry (CV). The adsorptive stripping characteristics at HMDE were also considered. a-Oxo-?-butyrolactone arylhydrazones are formed as a result of Japp-Klingemann coupling transformation reaction of 2-acetylbutyrolactone (ABL) with diazotized aromatic amines. In this study, sulfadiazine (SD) and sulfamethoxazole (SMX) were used as models of aromatic amines. Analogous study on sulfas-azo derivatives formed after diazo-coupling reaction with ethyl acetoacetate (EAA) was also of interest. Similar features in electrochemical characteristics of hydrazono- and azo- compounds were demonstrated. In aqueous acidic solution, the reduction of azomethine center of a-oxo-?-butyrolactone arylhydrazones and azo center of sulfas/EAA-azo derivatives (pH> 4) occurs in one 2e/2H+ reaction step, to give the corresponding hydrazo group. The redox system of either compound is irreversible. Based on the study performed, DPP, DPV and adsorptive stripping voltammetric (ADSV) methods were evaluated for determination of SD and SMX in pharmaceutical preparations. Further, SMX was determined in plasma and urine samples, spiked with clinically relevant levels, through voltammetric measurements of a-oxo-?-butyrolactone arylhydrazone. Real analysis of female urine samples was also done.

QP-P-011

DETERMINATION OF ARISTOLOCHIC ACID IN CHINESE MEDICINAL FORMULAS CONTAINING MU TUNG, FANG JI, XI XIN BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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Some herbs Mu Tung , Fang Ji , Xi Xin which always to be mistakem another species plants that contain aristolochic acid . The aristolochic acid can induce progressive fibrosing interstitial nephritis had been obvious.To ensuring patient's safety of using medicine, we investiged the commonly used traditional Chinese medicinal formulas that contain Mu Tung, Fang Ji and Xi Xin, carried in the pharmacy of certain medical center, to determine whether these formulas contain aristolochic acid. We selected 22 commonly used traditional Chinese medicinal formulas and randomly inspected 5 batches for each formula. The samples were analyzed by high performance liquid chromatographic on a silica gel RP-18 reversed-phase column and detected at 254 nm with 2% acetic acid--acetonitrile (55:45, v/v) in 0.8ml/min. The HPLC method can separate aristolochic acids I, II clearly within 30 min and all samples didn't find the aristolochic acids. We use photodiode array detector to further confirm the reality of existence of the aristolochic acids. It is useful to develop an effective system for monitoring the quality of traditional Chinese medicinal formulas in hospital.

QP-P-012

OPTIMIZATION OF HPLC METHOD FOR SIMULTANEOUS ANALYSIS OF NIACIN, ANHYDROUS CAFFEINE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN AND THIOCTIC ACID IN PHARMACEUTICAL PREPARATION

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This study was going to offer an improvement proposal about the simultaneous analytical method for niacin(NA), anhydrous caffeine(AC), pyridoxine hydrochloride(PH), riboflavin(RF) and thioctic acid(TA) in solution and capsule preparation by high performance liquid chromatography. For assay of solution and capsule preparation containing NA, AC, PH, RF, TA, chromatography was performed under gradient condition using a mixture of acetonitril-5mM sodium 1-heptane sulfonate with 0.1% phosphoric acid as mobile phase into UV 211 nm. Separations were performed on Capcellpak C18 column (5□, 4.6x250mm) and flow rate was 1mL/min. Under above conditions the retention time of NA, AC, PH, RF, TA was 6.500, 10.820, 11.684, 13.453 and 30.880min, respectively. This new proposed method was validated following the analytical performance parameters, i.e. linearity, precision, accuracy and system suitability, required by the U.S. Pharmacopoeia (USP) and the international conference on harmonization (ICH) guidance. Using development method, commercially available preparations (solutions and capsules) were assayed and all of the results were within their drug specification for assay. Due to their simplicity and accuracy, this method is suitable for the compendial method.

QP-P-013

DEVELOPMENT OF SIMULTANEOUS ANALYTICAL METHOD BY HPLC FOR THE COMPONENTS IN HERBAL MEDICINE PREPARATION 'GUPHUNGJIBODAN'

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The purpose of this study is the development of a simultaneous analysis for the components in herbal medicine preparation 'Guphungjibodan' using high performance liquid chromatography without derivatization. 'Guphungjibodan' should contain not less than 90.0% of the labeled amounts of geniposide(GS) in Gardeniae Fructus, paeoniflorin(PF) in Paeoniae Radix, ephedrine(ED) in Ephedrae Herba, baicalin(BC) in Scutellariae Radix, total berberine(BB) in Coptidis Rhizoma and Phellodendri Cortex, glycyrrhizic acid(GA) in Glycyrrhizae Radix, decursin(DS) in Angelicae Gigantis Radix according to Korean Pharmaceutical Codex (KPC), but each component has individual identification and quantification method. Simultaneous analysis using high performance liquid chromatography for contents assay of GS, PF, ED, BC, BB, GA and DS has been developed and validated. Sample preparation was extracted and individual standard was prepared using methanol. The simultaneous separation of GS, PF, ED, BC, BB, GA and DS was achieved on reversed-phase C18 column (Capcellpak C18, 5Ω, 4.6x250mm) with acetonitrile gradient system from 5% acetonitril to 70% acetonitril in 5mM sodium 1-hexane sulfonate with 0.1% phosphoric acid as mobile phase into UV 254 nm. According to this method, all of the compounds showed good results in linearity, precision, accuracy and recovery. This method was successfully applied to the identification and quantitative analysis of all compounds, except for the PF and ED in Guphungjibodan were mixed other ingredients, as revealed by the UV spectrum.

QP-P-014

SCREENING OF THE MECHANICAL PROPERTIES OF THERMOREVERSIBLE MUCOADHESIVE PHYSICAL HYDROGELS USING TEXTURE PROFILE ANALYSIS AND ARTIFICIAL NEURON NETWORKS

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Aim. Based on the assessment of mechanical properties, texture profile analysis(TPA assisted by artificial neurons network(ANN) are used to select the optimum thermoreversible hydrogel formulation intended for mucosal application.

Methods. Aqueous solutions of different concentrations of thermoreversible polymers pluronicF127 (F127) and pluronicF68 (F68) with or without the mucoadhesive polymer carbopol 934P (CP934P) or polycarbophil (PC) were prepared. Their gelatio temperatures were determined using the inverted test method. Three replicates from eac free flowing liquid formulation were kept at 34°Ca0.5 for 30 minutes prior testing t allow gelation. TPA was then performed where 2cm diameter cylindrical acrylic prob was twice compressed into each formulation at 34°C to 5.0mm depth, at pre-test spee of 5.0mm/s, test and post-test speed of 1.0mm/s, and recovery period of 15s between th 2 compression cycles. From the resultant force-time curve, values of hardness adhesiveness and cohesiveness were determined and analysed using ANN.

Results. Formulation with optimum mechanical properties appeared to be tha containing F127/F68/PC of concentrations 15.0/25.0/0.1 (%w/w) where the values o hardness, adhesiveness, and cohesiveness were 2.03 N, 7.20 Nmm, 1.06 Nmm respectively. These properties were negligible for formulations not gelling at bod temperature. PC proved to play a considerable role in cohesiveness (relative importanc 83%, R2 0.946 and MSE 0,001).

Conclusion. Combined TPA-ANN has shown its efficiency in screening mechanica characteristics of thermoreversible hydrogel formulations to obtain the most suitabl candidate for mucosal application.

SIG NATURAL SUBSTANCES - POSTER SESSION

NS-P-001

NOVEL SORBICILLINOID DERIVATIVES FROM THE MARINE FUNGUS TRICHODERMA VIRIDE ASSOCIATED WITH THE CARIBBEAN SPONGE AGELAS DISPAR

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The fungus Trichoderma viride isolated from the Caribbean sponge Agelas dispar, collected on Dominica, was mass cultivated and found to produce four novel sorbicillinoid polyketide derivatives, trichodermanone A-D and the trichopyranone. In addition to these compounds two known hexaketide derivatives, epoxysorbicillinol, vertinolide and three known dodecaketides trichodimerol, bisorbigiquinolide (trichotetronine), and bisvertinol, were isolated. Finally, a known fungal metabolite, 2-furancarboxylic acid was obtained. The structures of all compounds were determined by interpretation of their spectroscopic data (1D and 2D NMR, MS, UV and IR). Total extract and all compounds except 2-furancarboxylic acid have DPPH radical savenging effects (12.5, 43.8, 15.5, 37.2, and 23.8 % respectively at 230 µmol/L), with epoxysorbicillinol, vertinolide, and trichodimerol being also able to inhibit peroxidation of linolenic acid (17.8, 5.2 and 19.9, respectively at 164 µmol/L). Epoxysorbicillino showed moderate HIV-1 reverse transcriptase inhibitory activity (63.8 % at 200 □g/mL). All compounds and the total extract except 2-furancarboxylic acid were tested for their estrogenic, antitumor and antimicrobial effects and no significant activities were observed.

NS-P-002

ANTIMICROBIAL AND ANTIFUNGAL ACTIVITY IN LABURNUM ANAGYROIDES L.

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AIMS: To make evident the antimicrobial and antifungal effect of ethanolic extract of the species Laburnum anagyroides L. (Leguminosae), golden chain, against human pathogenic microbes
METHODS: The flowers,leaves, bark and seeds of the species Laburnum anagyroides L. air-dried were ground into fine powders and extracted in a Soxhlet extractor with 90% ethanol. The ethanolic extract at concentrations 83,25% were tested using filter paper discs sterils impregnated with 100microg extract. It was assessed sensibility/resistance of bacterial strains derived from 50 pathological biological samples ; taken from subjects living in community or hospitalized. The investigated species are follows: Escerichia coli, Staphylococcus aureus methicilin sensitive and resistant, Staphilococcus epidermidis, Streptococcus pyogenes, Klebsiella, Enterobacter aerogenes, Salmonella choleraesuis, Proteus mirabilis, Candida albicans. The extracts were tested using classic diffusimetric method Kirby-Bauer and observing area of microbial growth inhibition (mm) on specific solid mediums. Reading was done by comparison with standard strains and using in the same time antibiotics from standard medical pouch (Becton-Dickinson).
RESULTS: It was observed an antibacterial activity from different parts of the plant. Thus, extracts from seeds and flowers was efficiently on Gram positive cocci. The leaves and bark's extracts were efficiently on Enterobacteriaceae and Candida albicans.
CONCLUSIONS: The antimicrobial and antifungal activities of the ethanolic extract can be used in association with classic antimicrobial and antimicotic drugs therapy for a sinergic effect.

NS-P-003

IN VITRO EVALUATION OF ACACIA NILOTICA PODS FOR ANTI – HIV ACTIVITY

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INTRODUCTION
Traditional and folklore medicines play an important role in health services. Ayurveda, the traditional medicinal system of India provides remedial treatment for a variety of disease conditions. Rational design of novel drugs from traditional medicine offers new prospects in modern healthcare. Our current research work is an effort towards finding a cheaper and safer option in alternative medicine to existing HIV therapy.
OBJECTIVE
The present study aims at screening the extracts of the pods of Acacia nilotica (Family: Mimosaceae) for potential anti - HIV activity. The methanol and water extracts of the ripe pods of Acacia nilotica were used in this study.
METHODS
The anti - HIV activity of these extracts was measured in terms of their effects on viral infection and replication in-vitro. Infection was measured by the microtiter syncytium formation assay. Replication was measured by virus-associated Reverse Transcriptase activity. The H9 cell line was used for the infectivity assay and for virus-associated Reverse Transcriptase inhibition.
RESULTS
The methanol and water extracts of Acacia nilotica exhibited a dose related inhibition of the enzyme Reverse Transcriptase. The methanol and water extracts exhibited a 98.32% and 99.07% inhibition of Reverse Transcriptase.
CONCLUSIONS
The extracts of the pods of Acacia nilotica possess a statistically significant inhibitory activity against the novel enzyme Reverse Transcriptase. These results provide a rationale for further studies on isolation of active principles and pharmacological evaluation of Acacia nilotica pods.

NS-P-004

PHYTOCHEMICAL INVESTIGATION AND PHARMACOLOGICAL SCREENING OF TAGETES ERECTA LINN FOR NEPHROTOXICITY

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AIM: To evaluate Tagetes erecta Linn ethanolic leaf extract for nephrotoxicity
Method: Gentamicin and Cisplatin induced nephrotoxicity models are used.
Results:
In traditional system of medicine the juice extracted from the leaves of Tagetes erecta Linn was reported to be useful in treating Nephrotoxicity.
Gentamicin induced Nephrotoxicity
Gentamicin 60mg/kg.b.w/day for 13 days s.c in rats induced acute renal failure. This was evidenced by significant increase in blood urea nitrogen (BUN) and Serum creatinine levels (SCL). Which persisted even after 10days of cessation of therapy. Treatment with ethanolic extract after Gentamicin induced damage caused a marked decrease in BUN & SCL. The co-administration of the extract also showed the same effect indicating its protective activity.
Cisplatin Induced Nephrotoxicity
At 5mg/kg i.p Cisplatin induced renal injury . Extract treated groups showed decrease in BUN levels however no change in SCL levels. In curative regimen decrease in BUN and SCL were observed however in preventive regimen no change in SCL levels.
Conclusion:
Phytochemical investigation revealed the presence of flavonoids, phytosterols and triterpenoids. There may be chances of flavonoids will help in BUN & SCL levels. From the above results Tagetes erecta leaf proves tobe bonificial in the management of nephrotoxicity.

NS-P-005

ORGANOCHLORINE AND ORGANOPHOSPHORUS PESTICIDES IN VARIOUS HERBAL TEAS

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Due to its beneficial effects, different herbal teas are recommended and widely consumed all over the world. Anyhow, some literature data reported increased levels of pesticides in certain tea species, green tea being one of them.
The current study was undertaken to determine organochlorine and organophosphorus pesticides in 5 domestic herbal teas originated from the wild and field production in Serbia (Urticae folium, Hyperici herba, Thymi herba, Rosae fructus and Hibisci flos) and 2 imported teas (black indian tea and green tea). The herbal samples were purchased randomly from a local pharmacy.
Samples of herbal teas were extracted and purified according to Ph.Yug.V procedure, and the content of 18 organochorine and 15 organophosphorus pesticides was determined by GC/MS (apparatus Shimadzu QP 5050).
None of the investigated herbal teas contained increased organochlorine or organophosphorus levels. The obtained results were even under the level of detection for organochlorine (0.01 mg/l) and organophosphorus compounds (0.005 mg/l).
We can conclude that examined herbal teas fulfill the requirements for pesticides content given by our Drug Law (Ph. Yug. V), as well as standards given by European Union.

NS-P-006

A NEW HERBAL COLORANT FROM INDIAN PLANT

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OBJECTIVE: Colors have always been an essential constituent of pharmaceutical and food products. With the course of time approved synthetic colorants are coming under scientific and regulatory scrutiny for their toxicity and other reasons, thus developing the need for alternatives to these synthetic colorants. The use of organic plant materials as a source of colorant is now inclining due to varied reasons like cost effectiveness, safety, ease of availability, eco friendly nature and wide applications. The objective of our project was to develop new herbal colorant, having above characteristics, which can replace yellow colored synthetic colorants like tartrazine.
METHOD: The new colorant was obtained from flowers of Indian origin plant Butea. This paper describes about the raw material retrieval, its pretreatment and optimized novel extraction procedure for getting high yield. The most important part of the project is the extraction procedure using hydro-alcoholic solvent rendering a high yield with batch to batch reproducibility. The color was characterized using spectrophotometry and chromatographic methods. It was assessed for its stability and toxicity. Applications of this newly developed colorant were studied in different formulations like liquids dosage forms-syrup, elixir and solid dosage forms like tablets, granules, granules to be reconstituted and for coloring the coating solutions.

RESULTS AND DISCUSSIONS: Our studies have revealed that this new herbal colorant is safe and can be easily obtained with high yields economically. The color is also sufficiently stable thereby indicating that this can be a better substitute for yellow synthetic colors and dyes.

NS-P-007

EXTRACTION AND CHRACTERISATION OF THE POLYSACCHARIDES IN SCAPHIUM SCAPHIGERUM G.DON

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Nowaday many polysaccharides from plants have been showed interested properties. The glucomannan from Konnyaku inhibit cholesterol and sugar absorption to human intestine and has been us as dietary fiber. The fruit of Scaphium scaphigerum is rich with polysaccharide and has been used as food and traditional medicine for anti-inflammation. This study aims to extract the polysaccharides from the fruits of Scaphium scaphigerum and characterization of sugar component in the crude extracted. The fruits of Scaphium scaphigerum have been extracted by three methods; extracted with boiling water, extracted with cold water and extracted with organic solvent and then boiling water. The three crude extracts were further purification by sepharose 6B gel filtration chromatography and DEAE column chromatography. The elution profile of the polysaccharides from three extraction methods were similar. Extract obtained by using organic solvent and boiling water give the most percent yields and good appearance. Characterization of the polysaccharides has been perform by hydrolyze the polysaccharides and identify sugar composition comparison with standard monosaccharide thin layer chromatography and gas chromatography. The sugar compositions are major monosaccharide which found in pectin. The detail of the structure and bioactivity study will be performing later.

NS-P-008

POSSIBLE RISK OF DRUG INTERACTIONS CAUSED BY HEPATIC ENZYME REGULATORS FROM DAILY FOODS

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The purpose of this study is to address the risk related to the effects of food on pharmacokinetics in drug development. We had successfully screened the potential inhibitors and enhancers from 62 food components. Highly hitting rate of CYP450 and UGT modulating ability was found for these pure food components. For UGT2B7, HUCHE011, HUCHE002 and HUCHE025 were the most potent components to reduce the activity of UGT2B7, which are contained richly in onions, parsley, oranges and orange juice. It was found that 30 grams of raw onions, 15 grams of oranges, 36 grams of bottled lemon juice or 7 grams of tangelo juice will greatly reduce the activity of UGT2B7 range from 36% to 100%. For CYP3A4, HUCHE015, HUCHE019, HUCHE059 and HUCHE060 were the most potent components to reduce the activity of CYP3A4, which are contained richly in tea, chocolate, red wine and grapes. It was found that 7.3 mg of green tea leaves, 27 mg of oolong tea leaves, 485 grams of dark chocolate or 763 grams of red wine will greatly reduce the activity of CYP3A4 range from 40% to 90%. For CYP2D6, HUCHE066 was the most potent component to reduce the activity of CYP2D6, which is contained richly in tea, fennel, parsley and cranberries. It was found that 200 grams of dry green tea leaves, 300 grams of fennel leaves or 1200 grams of cranberries will greatly reduce about 86% of the activity of CYP2D6. Possible high risk is concluded that many foods uptake in daily life will possess the potential to affect the absorption and metabolism of drugs metabolized by CYP450 or UGT, such as simvastatin, nalbuphine, carvedilol and so on.

NS-P-009

PHARMACOGNOSTICAL,PHYTOCHEMICAL AND HEPATOPROTECTIVE ACTIVITY OF ZIZIPHUS OENOPLIA (L.) MILL.

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A detailed study of a folklore medicinal plant in India – Ziziphus oenoplia (L.) Mill, has been carried out. Detailed phytochemical tests were carried out on different extracts obtained from the aerial parts of the plant. Extracts were obtained using six different solvents of increasing polarity. Prior to this, standard physicochemical constants – ash value,total ash ,acid insoluble ash,water soluble ash,sulphated ash were determined.Extractive values of ethanol and water soluble extractives are determined. Estimation of crude protein was also carried out.Qualitative organic analysis was also performed. There are no reports of study on the methanolic extract of aerial parts of the said plant. Following the extraction using methanol, fractionation , isolation was attempted. Indepth detailed analysis of the compound obtained by subjecting it to HPTLC, IR ,UV analysis, NMR spectral analysis and mass spectroscopy, RUTIN was identified.Further to the isolation from the aerial parts, methanolic extract was subjected to acute oral toxicity studies and hepatoprotective activity.All those had proper ethical committee approval.Hepatoprotective activity was carried out using the carbon tetrachloride challenge method and silymarin was the standard.Biochemical parameters – SGOT,SGPT,ALP, total protein content and bilirubin were determined.Histopathological studies were also carried out.Analysis of the result shows significant hepatoprotective action when compared with standard as determined by subjecting result to ANOVA test .
To conclude methanolic extract of aerial parts of the plant contains rutin and has significant hepatoprotective activity.

NS-P-010

PHARMACOLOGICAL STUDY OF TRADITIONAL CHINESE MEDICINE- DANG-GUI-SHAO-YAO-SAN

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Dang-Gui-Shao-Yao-San (DGSYS) is a mixture of medicinal herbs, which has long been used in the traditional Chinese medicine for treating anemia and ovulary disorders. Its preparation comprises Angelicae sinensis (Oliv.) Diels, Ligusticum chuanxiong Hort, Paeonia lactiflora pall, Poria cocos (Schw.) Wolf, Atractylodis macrocephala Koidz and Alisma orientalis (Sam.) Juzep. The present study examined the anti-superoxide formation, free radical scavenging and anti-lipid peroxidation activities of DGSYS by xanthine oxidase inhibition, cytochrome C system with superoxide anion releasing by fMLP or PMA activating pathway in human neutrophils, and Fe-Cl2-ascorbic acid-induced lipid peroxidation effects on lipids in rat liver homogenate, respectively. DGSYS showed anti-superoxide formation and free radical scavenger activity in a concentration-dependent manner. It also inhibited PMA- but not fMLP-induced superoxide anion releasing from human neutrophils. These antioxidant actions of DGSYS showed beneficial cytoprotective effect against lipid peroxidation in rat liver homogenate, human platelet aggregation induced by AA and ADP, and mitomycin C-mediated hemolytic in human erythrocytes.

NS-P-011

ANTIOVULATORY ACTIVITY OF AQUEOUS EXTRACT OF DAUCUS CAROTA LINN. SEEDS IN ALBINO MICE.

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Aims
Carrot or Daucus carota Linn. Seeds (family : Umbelliferae) have been known as 'Garbhapatakara' in Ayurveda, the ancient system of Indian medicine, which means 'causing abortion'. The present study includes preparation of aqueous extract of carrot seeds and its evaluation for antiovulatory activity.
Methods
The aqueous extract was prepared by refluxing the dried, powdered seeds with distilled water for 8 hours. The extract was administered intraperitoneally to albino mice at 10 mg/kg and 20 mg/kg for 15 days and the estrous cycles were observed daily for 30 days. The activity was compared with control group and vehicle control group animals which showed normal estrous cycles.
Results
The aqueous extract (at doses of 10mg/kg and 20mg/kg body weight) arrested the estrous cycle at diestrous stage on 7th and 5th day of dose administration respectively indicating antiovulatory activity. This activity was found to be reversible as the cycles returned to normal pattern after the treatment has been stopped. The aqueous extract indicated presence of tannins, saponins, proteins, steroids and reducing sugars.

Conclusion
The aqueous extract of carrot seeds showed significant antiovulatory activity in mice at 10mg/kg and 20mg/kg body weight. The activity was found to be reversible in action.

NS-P-012

IN-VITRO ANTIMICROBIAL ACTIVITY OF BARK OF ACACIA NILOTICA LINN.

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Aims
The bark of the plant Acacia nilotica Linn. (Family: Mimosaceae), commonly known as 'babbul' has traditionally been used since ancient days as a 'chewing stick', for maintenance of oral hygiene. However its antimicrobial activity, with emphasis on dental microflora has not yet been reported. The present study aims at in-vitro antimicrobial activity of Acacia nilotica Linn.
Methods
Dried powdered bark of Acacia nilotica Linn. was extracted successively with various solvents. These extracts were studied for antimicrobial activity against various gram positive and gram negative bacteria, Candida albicans, and organisms isolated from tooth tartar of dental patients.
Results
Acetone extract was found to exhibit maximum activity with a Minimum Inhibitory Concentration (MIC) of 2.5 mg. 100 mg of acetone extract showed antimicrobial activity comparable to that of the standard used, Chloramphenicol-100mg. The extract was found to exhibit greater zones of inhibition for some of the cultures isolated from tooth tartar than the standard antimicrobial agent. Preliminary physochemical screening of acetone extract revealed presence of tannins, phenolic compounds, flavonoids, reducing sugars and carbohydrates. TLC profiles and HPTLC fingerprinting were developed for the extract and the numbers of peaks obtained were recorded.
Conclusion
Acetone extract of bark of Acacia nilotica Linn. possesses good antimicrobial activity against dental pathogens confirming the traditional claim.
Acknowledgements
Hi-Media Laboratories Ltd, Mumbai.
Nair Dental College, Mumbai.

NS-P-013

EVALUATION OF HEALTH PRODUCTS USED BY THE CANADIAN FORCES HEALTH AND LIFESTYLE INFORMATION SURVEY RESPONDENTS

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Objectives
To identify the patterns of natural health product (NHP) use among Canadian Forces (CF) members. The secondary objective was to compare NHP use with first language (English/ French), gender, age, marital status, education, rank, duration of service, Non NHP medication use, chronic conditions, weight (Body Mass Index BMI), and self reported health status.

Methods
A cross-sectional survey of CF members was performed and all 6,841 respondents to version B of the CF 2000 Health and Lifestyle Information Survey (HLIS) were included in the study. Descriptive statistics, using SPSS software, were determined for the demographics of the study sample and the frequencies of health products use. Odds ratios and 95% confidence intervals were determined for the association between the independent and dependent variables. A logistic regression analysis was done for independent characteristics associated with health products use.

Results
Data from the 6,841 respondents was analyzed: mean age was 37.2 years (7.52) with the majority of respondents rating their health status (41.3%) as very good. Of the respondents, 44.1% used health products on a regular basis and 2134 (31.2%) used a NHP in the previous two days.

Conclusions
CF members, in common with the general population, utilize the full range of NHP. All CF health care providers need to be knowledgeable about NHP and be able to provide accurate information to their patients. Further follow up studies should be conducted to determine where CF members obtain their NHP and from whom they obtain information on NHP.

NS-P-014

THE STUDY OF ANTISEPTIC EFFECTS IN ADONIS VERNALIS L.

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Adonis vernalis L. belong to Ranunculaceae family and consist several famous species that all of them have medicinal uses. This plant compounds are useful in fever, cough, epilepsy, asthma, spasm and rheumatism.
In this research, the plant organs (vegetative organs: leaves, stems and roots) and generative organs (flowers and fruits) was desiccated and powdered, separately. The powders were sterilised by Tindalization method. Then we prepared ethanolic, methanolic 80% and aqueous extracts. The study of antiseptic effect was evaluated by diffusimetric Kirby-Bauer method, adopted by N.C.C.L.S., USA, on six microorganisms (Staphilococcus aureus, Staphilococcus epidermidis, Enterobacter aerogenes, Klebsiella pneumoniae, E. coli, Candida albicans)
The results showed that aqueous extract had not any antimicrobial effect. Extract of generative organs showed antimicrobial effect more strongly than vegetative organs extracts. The antiseptic effect of mentioned plant on Gram positive bacteria was greater than Gram negative bacteria. In comparative with Amikacine antibiotic, inhibitory areole diameter of this plant extracts approximately was corresponded.

NS-P-015

EFFECTS OF THYMOL, A NATURAL PRODUCT, ON IONIC CURRENTS IN PITUITARY GH3 CELLS

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Drugs with the opening of potassium (K+) channels, causing hyperpolization of cell membrane, possess a clinical potential. The large-conductance Ca2+-activated K+ (BK) channel is highly selective for K+. Activation of this channel is Ca2+ and voltage dependent. We here investigated the effects of thymol, a natural product, on ion currents in pituitary GH3 cells. The patch-clamp technique was used to investigate the effect of thymol (100 μM) in these cells. Thymol reversibly stimulated Ca2+-activated K+ current with an EC50 value of 75 μM. In cell-attached configuration, application of thymol to the bath increased the activity of BK channels. BAPTA (1 mM) attenuated thymol-stimulated channel activity. In inside-out configuration, thymol exposed to the intracellular face of excised patches did not modify the single-channel conductance of these channels, however, it did enhance the channel activity. Neither menthol (100 μM) nor ringerone (100 μM) had any effects on BK-channel activity, while AAPH (100 μM) suppressed it significantly. The stimulatory actions of thymol on Ca2+-activated K+ currents may be associated with the underlying cellular mechanisms through which it affects neuronal or neuroendocrine functions.

NS-P-016

REPRESENTATION OF RARE AND PROTECTED PLANTS SPECIES IN MONTENEGRO WITH SPECIAL CONSIDERATION ON MEDICINAL AND AROMATIC PLANTS AND THEIR USE IN FOLK MEDICINE

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The aim of this research was to represent a unique and reach flora of Montenegro and trusted folk medicine, which is used in cases of self-medication for centuries. Montenegro have rich flora with more than 3000 species. Surface of 13812 km2 with more than 3000 species represent one of richest flora in Europe continent.
Special signet to our flora gives lots of endemic, endemoreliceous, rare, medical, aromatic and honeyed plants. In Montenegro flora there is 220 endemic spices of Balcanic peninsula and southeast Dendrids.165 taxons are with locus classicus in Montenegro. Republic of Montenegro has protected 50 endemic, rare and jeopardized spices and 25 of them are described like medicinal and aromatic plants and are used in folk medicine for variety of indications for centuries.

NS-P-017

INVESTIGATION OF MUTAGENICITY EFFECTS OF CARUM CARVI

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Introduction
A considerable number of mutagenes have been shown to be carcinogenic. Therefore it is useful to detect mutagenes through simple, rapid tests such as the Ames test1. Carum carvi is one of the herbal plants widely used in Iranian traditional medicine. In this paper, the mutagenic activity of this plant is investigated using the Ames test.
Materials and Methods
Cerum carvi was collected in Spring and dried in the proper conditions. Seeds of Carum carvi were then extracted with ethanol. Afterward ethanolic extracts were concentrated in the vacuum. In order to complete the extraction, different solvents were used2. The classic protocol described by Maron and Ames (1983) was adopted for the mutagenicity test. Tester strains of Salmonella typhimurium were TA97, TA98, TA100 and TA 102. These strains contain mutations in the histidine operon, so that they can not synthesize histidine. They also have additional mutations which increase the sensitivity of the system. Different samples were incorporated on plates containing agar in both the presence and absence of mammalian liver extract (S9), with tester strains. After incubation for 2 days the number of revertant colonies were counted and compared with control plates.
Results and Conclusion
After analysis of the results, it was observed that plant extracts have no mutagenicity effects in the Ames plate system.
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NS-P-018

REDISCOVERY OF POTENTIAL OF HONEY IN SKIN DISEASES AND ITS CHARACTERISATION

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Aim is to present a comprehensive review on types, sources, composition and properties of honey, which reveals its potential as therapeutic agent. Also to compile methods of evaluation like HPLC and enzyme activity determination; explore areas yet open for investigation such as HPTLC and to present the use of Honey on acne, pimples and eczema on the basis of study on 120 volunteers.
Ayurveda and Unani systems of medicine mention Honey to have antibiotic, wound healing and nutritive properties. Worldwide various official standards are available for honey. There are two streams of thought regarding whether to have an expiry date for honey or not. Authors have tried to compile this data. In this regard thought is given to presence of hydrogen peroxide, HMF (hydroxymethyl furfural) and high sugar content in honey.
Methodology: Topical effect of honey with cinnamon and Rubia Cardifolia was studied by the authors on 60 candidates each, which showed that cinnamon-honey combination had faster and better effects. This combination showed effect in the ratio of 20:45:35 in terms of fair:good:excellent, whereas Honey-Rubia Cardifolia showed effect in the ratio of 20:35:45. The pimples, acne and even eczema subsided to a large extent in both combinations, with a bit of improvement in complexion with Rubia Cardifolia combination.
Authors feel that various data of evaluation available combined with HPTLC analysis can give universal reference standard protocol for honey. The promising results of honey with cinnamon and Rubia Cardifolia on acne and eczema makes the author state that potential of Honey in various medicinal areas should be rediscovered and brought into practice.

SIG INDIVIDUALIZED MEDICINES - POSTER SESSION

IM-P-001

CLINICAL INVESTIGATION OF SILYBUM MARIANUM SEED EXTRACT (SILYMARIN) TREATMENT IN TYPE II DIABETIC PATIENTS

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Introduction: The free radical production and consequently metabolic oxidative stress disorder is hallmark of chronic disease particularly in uncontrolled hyperinsulinemic type II diabetic patients. Inhibition of free radical production, its neutralization or correction of oxidative metabolic abnormality in diabetic patients following antioxidant therapy may influence the glycemic control.

Aim: The present study was designed to investigate the efficacy of silymarin treatment with known antioxidant property on glycemic control in type II diabetic patients.

Methods: A 12 month randomized double blind clinical trial was conducted in 80 non-insulin dependent diabetic patients in two well – matched groups. One group (n=48) received 200mg silymarin tablet 3 times a day plus standard therapy, while the control group (n=32) received placebo plus standard therapy. The patients were visited every two month and glycosylated hemoglobin (HbA1c), fasting blood glucose, total cholesterol, LDL and HDL, triglyceride, SGOT and SGPT levels were determined at the beginning, after four month and at the end of the study.

Results: There were significant decrease in HbA1c, fasting blood glucose, total cholesterol, LDL, SGOT and SGPT levels in silymarin treated patients as compared to placebo group.

Conclusion: In present study the silymarin treatment to hyperglycemic type II diabetic patients for twelve months improved glycemic as well as lipid profile.

Key words: Silymarin, Herbal medicine, Antioxidant, Type II diabetes.

IM-P-002

CEFUROXIME VERSUS AMOXYCILLIN IN TREATMENT OF URINARY TRACT INFECTION IN CHILDREN

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AIMS: To investigate the clinical effect of parenteral Cefuroxime (CFX) and Amoxycillin (AMX) in children admitted to hospital for infection of urinary tract.
METHODS: 34 children (age 2 to 13 years) were selected for this study. The clinical criteria for selection were: fever, bacteriuria assessed by bladder puncture, positive C reactiv protein reaction. 20 subjects were treated with CMX and 14 with AMX (there were no intergroup differences in relation to age distribution or clinical data). The duration of the treatment was 7 days.
RESULTS: The etiological agent was Escherichia coli in 32 cases, there was 1 Enterobacter strain and 1 Streptococcus aureus strain. The treatment was considered good in 15 from 20 cases and fair in 4 from 20 cases in the CFX group. It was good in 10 from 14 cases, and fair in 4 from 14 cases in the AMX group.There was one culture of E.coli resistant to CFX and 12 from 34 cultures resistant (as well as 4 intermediate) to AMX. Although the study protocoll was initially randomised 10 of the AMX resistant cases appeared in the CFX group.
CONCLUSIONS: We conclude that although the results bear evidence of equal clinical response, the Cefuroxime appears superior to Amoxicillin, because of the higher incidence of AMX resistance.

IM-P-003

PREDICTION CYA DOSAGE IN KIDNEY TRANSPLANTATION USING DATA OBTAINED FROM FIRST DOSE

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Cyclosporin A (CyA) a selective and potent immunosuppressive intensively metabolized by the liver cytochrom P450 iso-enzymes M17 is the most important metabolite with 10% of CyA activity. The therapeutic level is highly variable so high risks of organ rejection/ toxic effects are existed. The common methods of TDM are trough level, AUC method and single concentration measurement other than trough level, all suffer either having a weak relationship to total drug exposure or not feasible to daily clinical use.
AIMThe aim of present study is to experience an individual dosage adjustment applicable in clinical centers.
METHOD510mg/kg CyA was orally administered to eight kidney transplant candidates 12 hrs before and 12 hrs after transplantation . The serum concentration of CyA and M17 were determined spontaneously by developed HPLC method at room temperature. The concentration/time profile for both, CyA and M17 was evaluvated.
RESULTSThere was very poor correlation using Cmax, AUC and Cmax/AUC M 17 against dose (r2 = 0.03, 0.3 and 0.12 respectively). The AUC M17/ AUC CyA against mid point CyA concentration approached plateau in patients over 60 kg the ratio of AUC M17/AUC CyA in female was higher than those in male, 0.33 and 0.19 respectively. Finally there was a good correlation between concentrations at 8, 10 and 12 hrs with AUC inf. of CyA.(0.9, 0.96, & 0.90), and M17, 0.78, .80 & 0.70 respectively.
CONCLUSIONThe calculated steady-state concentration using parameters obtained from 8, 10 and 12 hrs level following CyA first administered dose. AUCM17/AUCCyA above 0.50 would be considered as high metabolism so dose reduction is not recommended.

IM-P-004

ESTROGENIC AND UTERINETONIC ACTIVITY OF SIDDHA FORMULATION AMURI

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Aim : To evaluate the estrogenic and uterine tonic activity of Amuri in invivo and invitro experimental models.
Method: Estrogenic activity was studied in normal and ovariectomized rats, Amuri was administered orally for a period of 21 days. The parameters studied in both invivo models includes change in uterine weight, histometric changes of uterus. The effect was also studied on normal and regular estrous cycle . Invitro studies with amuri non-primed, estrogen-primed and amuri pretreated uterus were carried out to findout whether it possess any oxytocin like activity.
Results:Administration of Amuri in normal rats significantly increased the uterine wt, diameter of uterus and thickness of endometrium. Amuri treatment in ovariectomized rats didnot show any change in uterine wt. The rats from both control and treated groups showed normal estrous cycle and produced significa nt contractile response on non-primed, estrogen primed and amuri treated rat uterus when exposed invitro.
Conclusion: Siddha formulation Amuri proves to be beneficial in the management of gynaecological problems . Hence it justifies its traditional claim.

IM-P-005

PREVENTION OF REINSTATEMENT OF FEAR MEMORY BY CANNABINOIDS

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The treatment of choice for a number of anxiety disorders is exposure therapy. However, successful reduction of fear through exposure is often followed by a return of fear which poses a challenge for both research and clinical practice. Reinstatement, the recovery of fear that occurs when the subject is exposed to the unconditioned stimulus (US) after extinction, is one possible source of relapse. Here we show that pre-training administration of CB1 agonists WIN55212-2 or HU210 impaired fear memory measured with fear-potentiated startle while pre-testing application had no effect. The effects of WIN55212-2 and HU210 were blocked by AM251, a specific CB1 receptor antagonist. CB1 receptor agonists also blocked re-consolidation when applied after memory reactivation and facilitated conditioned stimulus (CS) alone-induced extinction of fear memory. Using a protocol to induce reinstatement of fear memory, we found that WIN55212-2-induced amnesia did not recover after a reminder shock. The absence of recovery was not attributable to permanent damage to the amygdala in WIN5521-2-treated rats because they could be re-trained. Taken together, these results suggest that CB1 agonists may be useful for the treatment of patients with inadequate reaction to potentially dangerous situation (e.g. patients with phobia or with posttraumatic stress disorders). More importantly, patients taken CB1 agonists may be less likely to relapse following successful completion of treatment.

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