NR-P-001

STUDIES ON THE EFFECTS OF DIFFERENT SYRINGES AND PERSONNEL APPLYING RADIOPHARMACEUTICALS IN THE CLINIC ON THE RESIDUEL ACTIVITY

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Introduction

The type of syringes and the volume of the patient doses of radiopharmaceuticals cause high residuel radioactivity in the syringes during application to patients. Therefore the investigation of the effects of syringes type and differences in volume and personnel on residuel radioactivity and adsorption were aimed.

Materials and Methods

Two types of syringes were chosen and the residuel activity left in 0.5 and 1.0 mL syringes after the application of different TcO-4 activities was investigated.

Commercial radiopharmaceuticals were injected to the patients by nurses and technicians. Then, radiopharmacist withdrew these radiopharmaceuticals to the syringes and emptied in-vitro and amounts of residuel activity were determined. The change of residuel activity was evaluted depending on the syringe, radiopharmaceutical kit and applicant types.

Results

The residuel activity reduced by 35- 45 % in the syringes with flat plungers as the decrease in the amount of radioactivity decreased when the volume was doubled but the radioactivity dose remained the same. The highest values were 15- 38 % in syringes with an elostomeric tip on the plunger.

When the injection of radiopharmaceutical kits were examined the residuel activities resulting from personnel application reached up to 10- 22 % whereas the application by radiopharmacist reduced this result.

Conclusion

Injection of radiopharmaceuticals needs special care. It is concluded that less care during injection or the preparation of radiopharmaceutical in syringes will cause decrease in the accuracy of the radioactive dose received by the patient and the residuel radioactivity in the syringes will cause and increase in the enviromental contamination.

NR-P-002

RADIOPHARMACY EXPRIENCE IN TURKEY

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Radiopharmacy covers the professional principles and practices of pharmacology and nuclear radiation in the preparation, dispending and control of radiopharmaceuticals used either in producing scans used for imaging, metabolic and functional studies of internal parts of the body for diagnostic purposes or in the treatment of patients with several diseases.

Radiopharmacy and education activities have started in 1993 officially. In this presentation, the current status of radiopharmacy has been discussed.

NR-P-003

99MTC-TRASTUZUMAB: A POTENTIAL RADIOPHARMACEUTICAL FOR THE EVALUATION OF THE OVER-EXPRESSION OF HER2 IN TUMORS.

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Trastuzumab (Herceptin®) is a monoclonal antibody produced by recombinant DNA technology that binds specifically to the human epidermal growth factor receptor-2- protein (also known as HER2). A consequence of the amplification of gene HER2 is an increase in the expression of protein HER2 in the surface of the tumour cells, which result in a constituently active receptor HER2. It has also been verified that Trastuzumab inhibits the proliferation of human tumour cells with over-expression of HER2.
The purpose of this study was to radiolabel Herceptin with 99mTc by a direct method, as a previous step to develop a therapeutic radiopharmaceutical.
The addition of 2-mercaptoetanol enabled the reduction of the disulphuric binds of the protein, and so obtaining 99mTc-S. The 99mTc-Herceptin was then prepared by the addition of 1mg of Herceptin to 35mg of HEDP, 3mg of SnCl2.2H2O and 1mL of 99mTcO4- (10- 20 mCi), waiting 15 minutes to 37°C. Radiochemical purity was controlled by: a) HPLC with a Protein-PaK SW 300 column and a isocratic program (buffer phosphate 0,01 M, pH 7,0 and flow 1 mL/min; two peaks at 9,9±0,1 and 10.6± 0.1min); b) ITLC-SG with NaCl 0,9% and acetone (Rf 99mTc-Herceptin = 0,0); c) EtOH:NH4OH:H2O (2:1:5) in ITLC-SG previously imbueded with BSA 5% (Rf Herceptin = 0,7-0,9). Purification was carried out by gel filtration in column PD-10 eluted with buffer phosphate 0.01 M, (pH 7.0). Biodistribution studies in normal male mice CD1 and blood and renal clearance in female wistar rats were performed.
The antibody was radiolabelling with radiochemical purity higher than 90%, showing stability for 3h. No uptake at thoracic level was detected. Blood elimination adjusted to a monoexponential model.
It was concluded that 99mTc-Herceptin could be prepared by direct method with a suitable stability and a biodistribution pattern which enable further studies.
Acknowledgments: To Roche for collaborating with Herceptin®; to IAEA for URU 12836 grant; CSIC and PEDECIBA-Química.

NR-P-004

COMPARATIVE STUDIES OF NOREPINEPHRINE OXIDATIVE DEAMINATION IN DIABETIC AND NON-DIABETIC HUMAN BLOOD VESSELS.

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The present work was undertaken to apply the radiochemical methods to the study of oxidative deamination of some neurotransmitors, particularly noradrenaline (NA), in human arteries of both non-diabetic and diabetic individuals in order to know if diabetes could have any influence in monoamines metabolism. We have evaluated the vascular alterations of human diabetic arteries by the quantification of monoamine oxidase (MAO types A and B) and semicarbazide-sensitive aminoxidases (SSAO).
To determine the best enzymatic conditions the method was applied using two incubation temperatures (24°C and 37°C) and also three pH of phosphate buffer (7.2, 7.4 and 7.6). These results directed the enzymatic activity for a incubation temperature of 37°C and pH phosphate buffer to 7.4. The MAO activities were determined using as specifics substrates, 3H-5-hydroxytryptamine (32,5 to 1000uM) for MAO A,14C-ß-fenyletylamine (5 to 160uM) for MAO B and 14C- benzylamine (50 to 1600uM) for SSAO. The Km and Vmax of each enzyme was also determineted.
The MAO A in non-diabetic vessels, showed a enhanced affinity and activity when compared with diabetic vessels.
Acording to the results obtained for MAO B affinity and activity values were similar for diabetic and non-diabetic vessels.

SSAO showed similar affinity for diabetic and non-diabetic vessels and activity appeared to be slightly greater in non-diabetic vessels than in diabetic.

From these results we can admit that arteries of non-diabetic patients mainly contain the isoform MAO A. The oxidative deamination is the same for MAO B in the two vessels and the SSAO activity is sligltly greater in non-diabetic vessels. This remarks could be the result of the deteriorated blood vessels walls of diabetic patients.

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NR-P-005

RADIOCHEMICAL DETERMINATION OF CATECHOL-O-METHYLTRANSFERASE ACTIVITY IN BLOOD VESSELS OF DIABETIC RATS.

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Catechol–O–methyltransferase (COMT) is the enzyme responsible for the O-methylation of catecholamines widely distributed in tissues from various mammalian species and with high levels of activity. The hypothesis that the COMT is related to diabetes is based on evidence that there are some changes in catecholamine metabolism in patients who suffer from obesity and diabetes mellitus. The study of COMT activity has been tested with human arteries and it allows obtaining reproductive results.

The aim of the present work is to determine the activity of COMT in vascular tissues of rat without and with diabetes, induced by Streptozotoxin (STZ) and related with acute (1 week) and chronic (1 month) effects on hyperglycaemia.
The blood vessels (aorta and cava vein) were obtained from normal and diabetic Wistar rats and were homogenized in phosphate buffer pH 7,4 and the COMT activity was determined by radiochemical method, using 3H- noradrenaline (0.4 to 12.8 μM) as the subtract in the presence of S-adenosylmethionine (0.5 μM). The reaction mixture contained MAO inhibitors (Monoamine Oxidase – enzyme responsible for deamination of catecholamines) clorgyline 10-4 M and (-) – deprenyl 10-2 M for MAO A and MAO B. Protein concentration was determinate by the modified method of Lowry.
The values of Km and Vmax for the substrate were determined by Woolf Hanes method, and were expressed in μmoles/L and pmoles/mg protein/ h to Vmax respectively and are in the diabetic vessels smaller in the diabetic tissues.
We also studied the noradrenaline (NA) contents trying to establish a correlation between the noradrenaline and the activity of COMT. The endogenous NA levels have been determinated by high pressure liquid chromatography with electrochemical detection (HPLC-EC) and this content are also smaller in the diabetic tissues.
With our results we can conclude that the increase of hyperglycaemia induce a decrease in the activity of COMT and also a decrease in the noradrenaline content.

NR-P-006

99MTC(V) AND 188RE(V) DIMERCAPTOSUCCINIC ACID (DMSA) QUALITY CONTROL: AN EVALUATION OF DIFFERENT SUPPLIERS AND LABELLING CONDITIONS.

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99mTc(V)-DMSA has been widely adopted as the imaging agent of choice, mainly for medullary thyroid carcinoma. Rhenium analogue 188Re(V)-DMSA has also been evaluated for targeted radiotherapy of cancer. After labelling procedure following species were reported: different isomers as anti, syn-endo and syn-exo, but also other species could be detected. Tumour uptake and renal excretion has also been described as very variable, being O2 bubbling an important condition to increase both parameters.

The aim of our study is to assess the species which are obtained from different labelling procedures, quality controls and suppliers.
Commercial kits from different suppliers were used to prepare 99mTc(V)-DMSA (Techi, Tecnonuclear, Mallinckrodt). In addition 99mTc(V)-DMSA was prepared from 99mTc(III)-DMSA kit, changing pH to 7,5 - 8,5. 99mTc (V)-DMSA was also exposed to O2 or air during 30 minutes. Besides, 99mTc(V)-DMSA was prepared from raw materials. 188Re(V)-DMSA was obtained as follows: 2 mg of DMSA were dissolved in bicarbonate buffer (0.5 M, pH 9), 0.4 mg SnCl2.2 H2O, pH 2, N2 purged and warmed 30 min at 37°. Radiochemical purity of 99mTc(V)-DMSA was controlled by: a) two HPLC techniques b) Whatman 3MM with NaCl 0,9%, acetone and butanol:acetic acid:water (3:2:3); c) electrophoresis on Whatman 3MM, pH = 3.6, 300v for 1 hour. 188Re(V)-DMSA was controlled in similar conditions.
Eventhough 99mTc(V) - DMSA was prepared with radiochemical purity higher than to 95%, different species were detected by HPLC, according to the supplier. Exposition to O2 or air did not seem to affect peaks distribution. The effect of pH showed that optimal complexation is achieved at 8.5 – 9.0 and the radiochemical purity is increased with the time of reaction.

Quality controls are essential in 99mTc(V) and 188Re(V)-DMSA preparation, in order to differentiate the species which are administered to the patient and predict possible in vivo behaviour.
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PB-P-001

PREVALENCE & GENOTYPING OF HEPATITIS-B VIRUS (HBV) IN HYDERABAD, INDIA

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Two billion people around the world (almost 1 out of 3 persons) have been infected with the hepatitis B virus. Many people recover and get rid of the virus, but 400 million people have been unable to get rid of and remain 'chronic carriers' of the virus. Hepatitis B is common in Asia, Southeast Asia, India, parts of Africa, South America, Eastern Europe, and the Middle East. In the United States there are more than one million Americans who have chronic hepatitis B infections. In the present study a detail prevalence and genotyping of Hepatitis-B Virus have been done to find out the percentage of people affected by the disease and an idea for the need of the latest drugs have been predicted to control the disease.

The serum sample from the patients was analyzed for the viral markers HBsAg, HBeAg, HBcIgM, and HBV DNA. This virus shares a common mode of transmission through parental route. This virus is responsible for both acute and chronic Hepatitis.

The prevalence of HBsAg was observed to be 145 (29%) out of 500 serum samples of patients collected at Center for Liver Research, Hyderabad, by performing PCR, RFLP and DNA sequencing analysis. By this we have established a classified method for HBV genome based on viral surface gene of asymptomatic HBV carriers (ASC). It was observed that 17(84%) of serum samples were genotype D1 where as the remaining shows genotype A. Cultural practices such as tattooing, body piercing etc, are the potential sources of spread of infection.

PB-P-002

POLYETHYLENE GLYCOL-GRAFTED NANOCAPSULES FOR SUSTAINED PROANGIOGENIC ACTIVITY OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)

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Aims- The sustained delivery of proangiogenic growth factors for therapeutic angiogenesis in diseased tissue is limited by lack of optimal delivery vehicles. We hypothesized that polyethylene glycol(PEG) surface modified poly (lactide) PLA nanocapsules of VEGF would sustain and enhance its proangiogenic effect.

Methods- Nanocapsules were formulated by interfacial polymer deposition following solvent displacement method. PLA-PEG copolymers were used at 20kDa chain length and PEG content (5-20% w/w of total polymer). The prepared formulations were characterized in terms of in vitro parameters- particle size, release rate, percent entrapment and cell culture studies.

Results- PEG-PLA-VEGF nanocapsules exhibited 72% encapsulation efficiency with a loading of about 180ng VEGF per mg of nanoparticles. Release profile demonstrated reduced burst release of 10% of VEGF from surface modified nanocapsules as compared to 35% release in case of non modified nanocapsules. Better sustained effects were observed with higher PEG content (20% w/w of polymer). It further exhibited sustained and nearly complete release over a period of nine weeks in bioactive form. This was also supported by cell culture studies with enhanced endothelial cell proliferation, migration and morphogenesis.

Conclusion- covalently attached PEG on the surface of nanocapsules can be used as an effective delivery system for growth factors to induce therapeutic angiogenesis.

PB-P-003

BENEFITS OF PHARMACEUTICAL BIOTECHNOLOGY INDUSTRY DEVELOPMENT: SELECTED CASE STUDIES AND LESSONS LEARNED FOR SERBIA AND MONTENEGRO

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The author, graduate of Pharmacy School at Belgrade University and currently completing a Masters degree in Bioscience Enterprise at the University of Cambridge, presents results of his recent original research into benefits of and key success factors for the national and/or regional development of pharmaceutical biotechnology sector. Analysis of two biotechnology sector development case studies - the United States' Massachusetts Biotechnology Corridor and the South African Cape Biotech - led to identification of: (i) key benefits of this type of development, such as boosts to economic growth, innovation, R&D, and entrepreneurialism, pharmaceutical and health discoveries and contributions to health outcomes, and overall society development; and (ii) key success factors for such development, including clear government strategy and regulation including measures to encourage development (e.g., tax incentives, information, cluster development, IP protection), existing scientific and industry base, commercialization infrastructure, access to capital and grants, and ability to attract and retain talent. Lessons learned from this analysis together with an original survey of key experts and stakeholders in the author's home country of Serbia and Montenegro, helped inform a future roadmap for such development in Serbia and Montenegro including the following key steps: creating a tailored and targeted national strategy and sequenced action plan based on the strategy, promoting entrepreneurialism through regulation and education, enabling private-public partnerships and strengthening the local scientific base and talent pool.

PB-P-004

DEVELOPMENT OF A METHODOLOGY TO MEASURE THE EFFECT OF DIVALENT CATIONS ON THE TRANSPORT OF CALCIUM BY THE PLASMA MEMBRANE CALCIUM PUMP.

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The plasma membrane calcium pump (PMCA) is a fundamental mechanism to remove Ca2+ from the cytoplasm of all eukaryotic cells. PMCAs, like all members of the superfamily of P-type ATPases catalyze the hydrolysis of ATP. There are four genes encoding mammalian PMCAs. The diversity of PMCAs is further increased by alternative RNA splicing that generates more than 20 different variants. At the protein and tissue level, the expression of many of these PMCA isoforms has been confirmed by detection with specific antibodies. The main cation transported by PMCA is Ca2+, although other divalent cations (C2+) also seem to be transported. However reports about C2+ transport are rather controversial. We reported here a method to measure the active transport of C2+ in inside-out vesicles prepared from human red cell membranes. Volume changes were followed recording the intensity of light scattered by a suspension of these vesicles which express mostly PMCA 4b.

Results obtained by this methodology showed that (a) it is possible to quantify the transport of Ca2+ measuring the slope of light intensity as a function of time; (b) the influence of drugs that could be inhibitors and activators of PMCA; (c) the transport of divalent cations like Zn2+, Ni2+,Ba2+, Sr2+, Pb2+ and (d) the competence among C2+ and Ca2+.These results show that the method is useful to assay the effect of C2+ different from calcium and drugs present in pharmaceutical preparations that are hazardous for human health. With grants of ANPCYT, UBACYT and CONICET.

PB-P-005

POLYETHYLENIMINE-BASED ANTISENSE OLIGODEOXYNUCLEOTIDES OF IL-4 SUPPRESS THE PRODUCTION OF IL-4 IN A MURINE MODEL OF AIRWAY INFLAMMATION

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Purpose. Interleukin-4 (IL-4) plays a crucial role as an inflammatory mediator in allergic asthma via inducing Th2 inflammation, IgE synthesis, and eotaxin. To develop an effective therapeutic agent which specifically inhibits production of IL-4, antisense-oligodeoxynucleotides (AS-ODNs) against murine IL-4 mRNA were generated and complexed with polyethylenimine (PEI) to maximize intracellular delivery.

Methods. AS-ODNs were generated against translation initiation region of murine IL-4 mRNA, and complexed with various concentrations of linear PEI. The efficacy of AS-ODNs/PEI complexes was tested by measuring IL-4 production in D10.G4.1 cell line in vitro and in a murine model of airway inflammation in vivo. The cellular cytotoxicity was tested by XTT incorporation assay, and the physicochemical properties of AS-ODN/PEI complexes were examined using atomic force microscopy (AFM) and DNase I protection assay.

Results. IL-4 AS-ODNs/PEI complexes were spheres with an average diameter of 98 nm and resistant to DNase I-mediated degradation. When compared to naked ODNs, IL-4 AS-ODNs/PEI complexes showed marked inhibition (33 fold increase as compared to naked ODNs) of IL-4 production in D10.G4.1 cells. Furthermore, IL-4 AS-ODNs/PEI complexes were effective in suppressing secretion of IL-4 in the bronchoalveolar lavage (BAL) fluid in an ovalbumin-sensitized murine model of airway inflammation.

Conclusions. These data demonstrate that complexation of IL-4 AS-ODNs with PEI provides a potential therapeutic tool in controlling inflammation associated with allergic asthma, and further presents an opportunity to the development of clinical therapy based on combination of multiple AS-ODNs of cytokines and/or signaling effectors involved in Th2 inflammation and eosinophilia.

PB-P-006

ENCAPSULATION OF DRUGS WITHIN YEAST CELLS ALLOWS INCREASED DELIVERY VIA THE ORAL ROUTE

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Oral drug administration is the most convenient route of drug delivery but drawbacks of administration of drugs via this route include poor adsorption in the gastrointestinal tract, degradation by gastric acidity and degradation by first-pass metabolism in the liver. Encapsulation of drugs can protect the drug from the harsh acidity of the stomach, releasing the drug further down the digestive tract where pH is neutral. Penetration of drugs, especially hydrophilic ones, across intestinal cells is controlled by tight junctions, which exist between cells forming a very effective barrier. Some encapsulation materials can enhance the penetration of drugs by reversibly open epithelial tight junctions, and thus increase drug transport.

Yeast cells can encapsulate and retain essential oils and therefore the aim of the present work was to investigate the ability of heat-killed yeast cells to both encapsulate and increase the permeation of model drugs through a cell monolayer using an intestinal cell culture system of Caco-2 cells. Visualisation of the drug transported across Caco-2 cells was carried out using fluorescent compounds and confocal microscopy in order to investigate the transport pathways. Immunofluorescence microscopy found revealed that the tight junction proteins ZO-1 and occludin were involved in the junction-opening process, also were the secondary messengers PKC and protein tyrosine phosphatase.

PP-P-001

COUGH MEDICINES FOR ACUTE COUGH IN BRAZILIAN MARKET

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Acute cough is a common symptom. Over the counters cough medicines (CM) are widely available in Brazil. The aim of this study is to analyse the CM registered in Brazil To make the identification of antitussive drugs possible, it was made a research in current literature of pharmacology and therapeutics. To find which antitussive drugs are registered in Brazil, it was made a research at the data base of Brazilian Sanitary Surveillance Agency (ANVISA). The clinical trials were searched in Medline and Cohcrane Library. In total, 109 antitussive drugs were identified being used in clinical practice. At ANVISA there were 62 drugs registered, in which 17 (27.4%) were single drugs , 7 (11.3%) 02 drugs' combinations (DC), 14 (22.6%) 03 DC, 12 (19.4%) 4 DC and 12 (19.4%) over 4 DC. Among the DC there were 08 (12,9%) herbal drug/herbal drug, 9 (14.5%) herbal drug/drug and 28 (45,2%) drug/drug. Considering the drugs registered there were 09 generic. The register of same drug by different manufacturers was found to the amount of 10. 2 of them have more than 20 registers without considering the different presentations of the medicine. The anatomical therapeutic chemical classification of the medicines was of 9.7% expectorants, 6.5% mucolytics, 1.6% opium alkaloid and derivatives cough suppressants, 9.7% other cough suppressants, 1.6%opium derivative and expectorant combination and 71% other cough supressant and expectorants combination. Randomized clinical trials were found for only 3 drugs registered in Brazil: bromexin, dextromethorfan and guaifenesin.. None clinical trials were found with DC. Systematic review published by Schroeder & Fahey, 2005 found no good evidence for or against the effectiveness of over the counter CM. The evidence regarding the effectiveness of CM available in Brazilian market is inconclusive. The high number of DC without clinical trials raise concern on their effectiveness and safety once these medicines have been sold without medical prescription

PP-P-002

PROFILE OF ADVERSE DRUG REACTIONS RELATED TO THE USE OF GATIFLOXACIN IDENTIFIED BY INTENSIVE SURVEILLANCE IN AN UNIVERSITARY HOSPITAL

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Fourth-generation fluoroquinolones are broad-spectrum antibiotics frequentely used to treat a wide variety of infections. Gatifloxacin is one of the newest and the most effective quinolones. This study intended to identify suspected adverse drug reactions (ADR) with gatifloxacin and establish their frequency; to describe the ADR identified and establish a causal relation. The research was an observational cross-sectional study realized from May 2003 to December 2005. The patients in use of gatifloxacin were identified by the drug distribution system of hospital pharmacy. In order to identify the ADR that ocurred during hospitalization, we analyzed the medical prescriptions and intercurrences reported on medical records. The algorithm of Naranjo was used to establish the imputability of ADRs. W.H.O. categories were used to assess the severity of suspected ADRs. The descriptive statistical analysis was performed using SPSS version 10.0 software. Approximately 6% of 379 patients presented at least one suspect ADR. The most frequently ADR were hypoglycemia (4.3%), cutaneous reactions (13%) and hyperglycemia (39.1%). The ADR was classified as possible (88.2%) and probable (11.8%). The gravity was moderate (41.2%) and mild (58.8%). The ADR identified were notified to the Brazilian Pharmacovigilance System. Related cases of hypoglycemia and hyperglycemia have been published in literature since 2002. These results of intensive surveillance made us aware of the possibility of problems with glucose control in any patient receiving gatifloxacin. We should make health professionals aware of this possibility .Additionaly, health professionals must file reports to the pharmacovigilance system when they notice unusual ADR. The knowdlege of the profile of ADR is very important to safety use. The intensive surveillance of hospitalized patient helps to know better the ADRs.

PP-P-003

UTILIZATION OF PARENTERAL DRUGS IN PAEDIATRIC UNIT OF AN UNIVERSITARY HOSPITAL: AN OBSERVATIONAL STUDY.

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Parenteral drug administration has clinical relevance in paediatric care. However the cost to health care system and the risks related to parenteral therapy should be evaluated. The purpose of this observational cross-sectional study was to analyse the utilization of parenteral drugs in a paediatric unit. The prescriptions issued to all patients of the paediatric unit over a three-week period were analized. Patients' age, sex and weight were recorded. From the patients in parenteral therapy, their drugs prescribed were recorded as well as their dosage form, doses, and route of administration. The descriptive statistical analysis was performed using SPSS version 10.0 software. A total of 75 patients were admitted, 56% were male. The age range most frequently was the infants. The length of hospitalization was over 20 days (24%), 6 to 10 days (21.3%) and less than 3 days (17.3%). Parenteral route was used to 56 (74.7%) patients, so 19 (25.3%) used other routes or did not use medicine. Intravenous route was used to 52 (92.99%) patients. The number of parenteral drugs prescribed ranged from 1 to 9 per patient; the average was 5. Overall, 47 different parenteral drugs were prescribed to 34 (60.7%) patients. The average of 5 drugs per patient requires more time of nursing team in activities related with drug administration. The reconstitution, administration, dilution and compatibility of intravenous drugs are important considerations, especially in children receiving multiple drug therapy. The pharmacist should give advice on this considerations to the nursing team. The high number of drug prescribed per patient raise concern about safety. The risks of adverse drug reaction increase with the number of drugs used. The pharmacist should stimulate conversion from parenteral to oral administration because it would not just decrease hospital costs but also, increase safety and improve the patients' quality of life.

PP-P-004

PHARMACOECONOMIC ANALYSIS OF MEDICAL COST OF TREATING SIDE EFFECTS OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

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Introduction: Gastrointestinal (GI) toxicity assosiated with non-steroidal anti-inflammatory drugs (NSAIDs) is still an important medical and socio-economic problem. Conventional NSAIDs are more often associated with risk of GI side effects than selective COX-2 inhibitors.

Methods: Data base for pharmacoeconomic analysis of the cost of treatment are based on the medical records of the patients treated at the Clinic of Gastroenterology, at the Military Medical Academy (MMA), who had endoscopically proven GI side effects in the period from 2001-2004. We applied the price list of MMA for 2005. The following data were used: the number of days spent in hospital, all analysis and diagnostic procedures used in treatment, medical therapy, recommended therapy on leaving the hospital. We excluded drugs used for treating the concomitant disease. For the evaluation of the medical costs, a cost-benefit analysis was applied.

Results: 90 patients, out of 580 examined records, had clinically tested side effects due to NSAIDs and 22 patients were advised not to use conventional NSAIDs. All 22 patients used both diclofenac and proton pump inhibitors, which causes the elevation of medical costs. Results of this study showed that the medical costs of treating GI side effects for one patient were 770 $. Costs of treatment for one patient were nearly the same as for the two-year use of coxibs.

Conclusion: It is better and cheaper for patients, who had proven GI side effects, to use selective COX-2 inhibitors instead conventional NSAIDs.

PP-P-005

A STUDY OF PRESCRIBING PATTERNS AND ERRORS OF ANTIBIOTICS IN A SAUDI HOSPITAL

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Background:
The term 'prescribing patterns' has been used extensively in studies to describe different aspects of the prescribing process. There are no standard definitions or methodologies for prescribing patterns or prescribing errors studies. The incidence of prescribing errors ranges between 0.5% and 18.8%.
Objective:
In this study we will address the prescribing patterns of antibiotics and the incidence of prescribing errors in a tertiary hospital and the potential relationship between them.
Methods:
A prospective study of all prescriptions in a three-month period (June to August 2003) in a tertiary hospital has been analyzed. The hospital provides both primary and secondary levels of care. Criteria used include frequency of selected prescribed drugs, average number of items per prescription, compliance to the hospital formulary, frequency of prescriptions for antibiotics and parenterals, generic prescribing and diagnosis. All prescribing errors were identified and documented. The incidence of prescribing errors was calculated by dividing the number of errors identified by the total number of prescriptions.
Results:
Total number of prescriptions for the three-month study was 24,404. Emergency Room (ER) and primary care have the highest number of prescriptions (37.1%). The average number of items per prescription is 2.1. The most prescribed drugs by primary care (25.3% errors), emergency are antibiotics (28.2 %), medicine (3.7), ophthalmology (22.3), gynecology (7.8), and pediatrics (17.8). The prescription errors were 13.6% in primary care and 22.3% in emergency department.
Discussions and conclusions:
Over 24000 prescriptions were included in this study. The incidence of prescribing errors was 18.8% the average number of items per prescription was 2.1. There was a relation between prescribing of antibiotics and prescribing of trade names ($p <; 0.01$), compliance to the hospital formulary ($p <; .001$), frequency of injection use ($p<;0.001$) and the incidence of medication errors and the average number of items per prescription.

PP-P-006

HERBAL FORMULATIONS PRESCRIPTION ANALYSIS

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Pharmaceutical formulations containing substances of herbal origin are registered as nutritients or medicines on our market in a great number. This analysis is limited only to the solid pharmaceutical formulations containing only substances of herbal origin (the analysis was not performed with the formulations containing vitamins and minerals).

The aim of this work was to determine the range of prescription and sale of these preparations in 'Tefarm' Pharmacy in Tešanj during time period of one year.

Complete monitoring of prescription and sales of herbal medicines was performed using the apothecary computer system. Since different pharmaceutical formulations are available, as well as different packages of the same preparation and instructions for use, single dose was established as one tablet or a capsule.

From the total number of herbal preparations sold, there have been 49,20% preparations for enhancement of cerebral circulation or 42 974 single doses; 22,42% for sedation; 13,40% for stimulating the immune system; 8,47% for enlarged prostate gland treatment; 2,95% for depression treatment; 1,79% for veins and 1,76% for purgation.

Considering the number of herbal preparations sold and possible interactions between them and the other medicines, it is necessary to establish systemic monitoring in herbal medicine prescription in order to avoid side effects caused by inappropriate use.

PP-P-007

QUALITY OF CARDIOVASCULAR DRUG PRESCRIBING IN CROATIA, 2001- 2004

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Objective: The purpose was to investigate the outpatient utilisation of cardiovascular drugs in Croatia, during the 2001-2004 period using the ATC/DDDs methodology and to investigate the relationship between the utilisation of particular drug groups and the number of hospital admissions.

Method: Data on outpatient drug utilization were obtained from Zagreb Municipal Pharmacy to calculate the number of DDD, and DDD per 1000 inhabitants per day (DDD/TID). Drug Utilization 90%(DU90%) method was used on the drug prescribing quality assessment . Data on hospital admissions were collected from the inpatient base kept at Zagreb Institute of Public Health.

Results: Total utilisation of cardiovascular drugs (group C), was between 402.9 DDDs/TID and 406.9 DDDs/TID) in Croatia during the 2001-2004 period. Agents acting on the renin-angiotensin system (C09) (121.3 DDDs/TID) and calcium channel blockers (C08) (87.5 DDDs/TID) accounted for more than 50% of drugs used for the treatment of hypertension in 2004. The great increase in the utilization was observed for statins (78.3%). A markedly increasing utilization was recorded for ACE inhibitors in combination with hydrochlorothiazide (HCTZ) (40.5%) and angiotensin II antagonists (278%). Comparison of DU90% segment between 2001 and 2004 revealed pentoxifylline and amiodarone to be absent, whereas cilazapril and ramipril in combination with HCTZ, bisoprolol, valsartan and losartan alone or in combination with HCTZ were added in 2004. On the other hand, DU90% segment still contained doxazosin and propafenone, which had no grounds in therapeutic guidelines. During the period of observation, total rate of hospital admissions for major cardiovascular events decreased by 17.2%.

Conclusion: The outpatient utilization of cardiovascular drugs was high during the 2001-2004 period. The utilization pattern was improved in 2004, showing a decrease in the number of hospital admissions for major cardiovascular events.

PP-P-008

DRUG UTILIZATION IN CROATIA IN 2004

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In Croatia, drug costs account for 15% of health care budget. In 2004, 7.5 prescriptions per insuree were issued, with highest consumption recorded in the >;65 age groups. According to the By-Law on Data and Reporting on Drug Marketing (Official Gazette 29/05), all corporations and physical persons involved in drug wholesale and retail are obliged to submit annual reports to the National Agency for Drugs and Medicinal Products, categorizing the drugs according to the Anatomical-Therapeutic-Chemical (ATC) classification. Data on outpatient and inpatient were collected and processed by the Zagreb Institute of Public Health. The number of defined daily doses (DDD) and number of DDD/1000 inhabitants/day were calculated from data on the size and number of drug packages.Prescription drugs accounted for 86.96% and over-the-counter (OTC) drugs for 13.04% of total utilization in DDD/1000/day, respectively. Inpatient drug utilization accounted for 3.06% and 5.8% of total drug utilization in DDD/1000/day. Group C drugs showed highest consumption with 250.45 DDD/1000/day. At the secondary level of ATC system, the group of vitamins (A11) had highest consumption, predominated by OTC products, followed by psycholeptics (N05), which was the leading group of prescription drugs with 74.33 DDD/1000/day, with benzodiazepines accounting for 75% of their utilization. Amlodipine showed highest utilization among prescription drugs, and simvastatin according to financial parameters. The highest utilization was recorded in the City of Zagreb, and lowest in the LikaCounty.In conclusion, drug utilization is too high in Croatia, frequently failing to follow the respective professional guidelines.

PP-P-009

UTILIZATION OF ANTIDIABETIC DRUGS OVER A 5-YEAR PERIOD (2001-2005) IN ZAGREB (CROATIA)

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Objective To describe quantitative and qualitative changes in the utilization of oral antidiabetic drugs (OADs) and insulins between 2001 and 2005.

Method Data on outpatient utilization in Zagreb were collected from Zagreb Pharmacy to calculate the number of defined daily doses per 1000 inhabitants per day (DDD/TID) using the WHO ATC/DDD methodology.

Results Total utilization of drugs used in diabetes decreased from 44.01 to 43.33 DDD/TID. Total utilization of insulins decreased by 4.5% (13.54 DDD/TID in 2004), whereas that of OADs increased by 3.4% (29.79 DDD/TID in 2004). During the 2001-2005 period, sulfonylureas (A10BB) and the biguanide metformin (A10BA02) were most frequently used among OADs, and intermediate-acting combined with fast-acting insulins and analogues(A10AD) in the insulin groups. While in 2001 gliblenclamide was the most often prescribed OAD (16.26 DDD/TID), its utilization decreased twice, whereas the utilization of metformin increased twofold in 2005 (6.58 DDD/TID). The utilization of the new agent repaglinide increased more than sixfold. Among insulins, the A10AD group retained the leading place. Human insulin predominated the overall utilization of all insulin groups. The utilization of the insulin aspart increased, whereas bovine and porcine insulins have not been used since 2001.

Conclusions The utilization pattern of OADs and insulins changed during the 2001-2005 period. The predominance of glibenclamide in the OADs utilization in 2001 was shared by glibenclamide and metformin in 2005.The utilization of repaglinide showed significant increase. Among insulins, bovine and porcine insulins disappeared, whereas the utilization of the insulin aspart increased.

PP-P-010

ANALYSIS OF FACTORS ASSOCIATED WITH DRUG-DRUG INTERACTION ON ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORS: RESULTS FROM THE NATIONAL AMBULATORY MEDICAL CARE SURVEY, 2003

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Objective: Our goal was to examine the impact of potential drug-drug interactions on Angiotensin Converting Enzyme (ACE) Inhibitors in the U.S. outpatient settings.

Methods: This project applied a secondary data analysis using the 2003 National Ambulatory Medical Care Survey (NAMCS) conducted by the National Center for Health Statistics. A series of descriptive analyses were performed to evaluate the prevalence of potential drug interaction. A multivariate logistic regression was developed to exam how patient and physician characteristics impact the presence of drug interaction. All analyses were used SAS statistical software with 0.05 alpha values.

Results : A total of 25,288 visits to office-based physicians were sampled from the NAMCS in 2003, representing 906.0 million visits in the U.S.. Based on the unweighted sample, ACE inhibitors prescriptions were examined in 734 visits (2.9% of the total visits). Benazepril encountered the highest prevalence rate for the drug Interaction (56.7%); following by Ramipril (55.1%), Lisinopril (47.8%), Enalapril (45.7%), and Captopril (45.5%). The results of multivariate logistic regression will be presented by Odds Ratio and 95% confidence interval to identify if any predictor variable is significantly associated with drug interaction.

Conclusion: The study reveals a very high prevalence rate (49.5%) of potential drug interactions with ACE inhibitor agents typically used for hypertension. These drug interactions can lead to morbidity or even mortality if appropriate clinical actions are not taken. From the safety viewpoint, there is the legal duty for physicians to pay greater attention to the choice of drugs, particularly for the patients with polypharmacy status. Consideration of patients' accessibility to pharmacists, the vigilant pharmacy services may attribute more success in monitoring potential drug interactions and making appropriate dosage and therapy adjustment.

PP-P-011

REASONS FOR DROPOUT FROM AN ARTERIAL HYPERTENSION CONTROL PROGRAM AT A GOVERNMENT-RUN HEALTH CENTER IN CAMPO GRANDE, MATO GROSSO DO SUL, BRAZIL

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One of the chief concerns in programs for the control of long-term diseases is the high rate of dropout from treatment. In Brazil, few studies have been conducted on the causes of this behavior and on the profile of noncompliant patients. To identify the reasons for dropout from treatment, as described by noncompliant patients enrolled in a hypertension control program at a health center in Campo Grande, MS, Brazil. A survey was conducted from June to July 2005 with noncompliant patients enrolled in the program and their responses were analyzed. Respondents claimed to have abandoned treatment because of lack of medication, adverse reactions, poor service to patients, and difficulties in transportation to the health center. Some patients declared having continued the treatment by other means (privately paid medical visits, purchase of medication with a previously filled prescription). Others stated not feeling any disease-related discomfort and thus not perceiving the need for treatment. A third group informed having replaced the drug treatment by diets and exercise, succeeding in stabilizing their arterial pressure. Respondents presented three major reasons to justify quitting the hypertension control program. The first one relates to the health center itself (poor service to patients, lack of medication, difficulty in making appointments); other respondents claimed that they do not need the medication, that it has side effects, or that they do not perceive any effects from it. Finally, another group claims to have reached health improvements with physical exercise and diet. Irrespective of the reasons given, patients with hypertension need to be monitored, and one of the strategies available for improving the rates of treatment success is the provision of pharmaceutical care.

PP-P-012

THE RESULTS AND PERSPECTIVES OF THE PHARMACOVIGILANCE PROGRAM OF RIO DE JANEIRO, BRAZIL

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Introduction: The Health Surveillance Center of Rio de Janeiro (CVS-RJ) together with the National School of Public Health have implemented the Pharmacovigilance Program with the objective to monitor adverse drug events, in accordance to the National Adverse Drug Event Monitoring Program coordinated by the National Health Surveillance Agency in collaboration with WHO. Methods: Description of the results of the Pharmacovigilance Program-RJ, from September 2005 to March 2006. Results: In March 2006, UNIFARJ had received 86 reports, 76% of which were suspect ADRs and 24% suspected pharmaceuticals defects. Reports were forwarded by hospitals (79%), industries (19%), community pharmacies (2%). Professionals who notified were pharmacists (79%), physicians (15%) and nurses (6%). Suspect ADRs were mostly observed in patients form 30 to 49 yrs (50%). Eleven percent of suspect ADRs were serious and 3% lethal. Eighty-three percent were classified as probable or possible ADRs. Reactions were mainly related to skin (26%), gastro-intestinal (13%) and general disorders (13%). Anti-infectives were related to 51% of cases. For the Program dissemination, flyers and folders were designed and distributed with information on report procedures. Two issues of the Pharmacovigilance Bulletin were published with the time frame. Conclusions: In 2005, the Pharmacovigilance Program of RJ was implemented. From 2006, the major aim is the consolidation of the Program. Main strategies are: broadened dissemination, training courses of staff, commitment of health professionals on the importance of notifying and the strengthening of institutional partnerships.

PP-P-013

PHARMACOECONOMIC STUDY OF ACQUIRING ANTI-HYPERTENSIVE DRUGS IN A METAL WORKS NEAR CAMPINAS THROUGH DATA OBTAINED THROUGH A PBM SYSTEM.

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Hypertension is a disease characterized by a rise in blood pressure and constitutes an elevated risk for cardiovascular diseases. The Pharmacy Benefits Management (PBM) manages benefits of access to drugs by reducing costs and motivating its rational use. The objective of this study is to verify if the PBM system can be used as a tool to supply information on the consumption of anti-hypertensive drugs, their use profile and indirect adhesion monitoring. During three months (April, May and June 2005) the drug consumption of a group formed by approximately 2500 employees of a metal works near Campinas was analyzed. This company subsidizes 70% of the cost of drugs to its employees. Of this total, 165 workers (6.6%) used anti-hypertensive drugs where 126 (76.36%) were males and 39 (23.64%) were females, totaling 675 drug cases prescribed. The active ingredients prescribed were as follows: 14.54% was enalapril where 45.7% was generic, 34.3% was similar and 20% were reference. The mean monthly treatment cost taking into account one pill per day was of US $ 8.56 ($ 18,50 reais) for the generic, US $ 10.56 ($ 22,82 reais) for the similar and US $ 14.29 ($ 30,86 reais) for the reference. If only generic enalapril was bought, the treatment cost would be reduced by 27.7% and the reduction would not only be greater because despite the subsidy of the company, 45.7% of the purchased enalapril is already generic. The economy made could be destined to anti-smoking campaigns, motivation of physical activities and others, contributing for improving the control of the disease.

PP-P-014

PRESCRIPTION OF CAPTOPRIL PRECEDING BLOOD PRESSURE ELEVATION IN HOSPITALIZED PATIENTS: A PILOT STUDY.

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Aims: To describe the results of a pilot study of evaluation of prescription of captopril preceding blood pressure elevation in hospitalized patients. Methods: This is a cross-sectional retrospective study, developed in a Brazilian college hospital. A chart-view was done by using a standard form. This pilot study included 50 hospitalized patients during the first semester of 2004 that had at least a prescription of captopril in case their blood pressure overshot a certain limit. For example: captopril 25 mg if blood pressure was =160x110mmHg. Results: The average age of the patients was 52,1± 18,5 years old. 30(60%) of the patients were female. The average of days of hospitalization was 21,7 ± 23,8. 45 (92%) of the patients were in surgical wards and 5 (8%) in medical clinic wards. Only 24 (48%) patients had hypertension and were under maintained antihypertensive drugs. Captopril was given to only 10 (20%) of the patients. 9(90%) of these patients had hypertension and used captropil through sublingual via. Conclusion: The data of this pilot study show the need of a more rational approach concerning the prescription of antihypertensive drugs in hospitalized patients. More conclusive data will be presented after the conclusion of this study.

PP-P-015

ANALYSIS OF THE ASSIGNATION OF THE MEDICINES FOR THE CLINICAL PEDIATRICS' NURSING TEAM AND THE POTENCIAL RISK OF DRUGS INTERACTIONS.

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The polypharmacy in pediatrics represents a potencial risk for the occurrence of drugs interactions (DIs). The aim of this study was identify potencial DIs from the assignation analysis carried through for the nursing team, of medicines prescribed to the pediatrics patients of the Unit of Clinical Pediatrics of a general Universit Hospital (HUB) in Brasília, Federal District, Brazil. One is about a cross-sectional study, analytical-descriptive, where they had observed 90 lapsings, in months of October of 2005 to February of 2006. Results shows that the biggest frequency of lapsings analyzed were of children between 4 to 11 years (46,6%), male (61%) and hospitalization diagnosis of imperfect osteogenisis (31,5%). The ATC classes more prescribed were nervous system (N) 40,2%, systemic antiinfectious (J) 16,5% and digestive system and metabolism (A) 16,5%. The most used drugs were Dipyrone (27,34%), Paracetamol (24,02%) and Dissodic Pamidronate (9%). In the evalution of assignation quality were found 14 potencials DIs, higher frequently between aminoglycosides x cephalosporins (14,5%) and cephalosporins x diuretics (14,5%). It was observed that 81% of assignation were carried through for the nurse, frequently in the schedules of 6 hrs (13,1%), 12 hrs (13,5%) and 22 hrs (11,8%). They been found some lapsings with drugs not approved for pediatric use (Captopril, metoclopramide and nifedipine). The concentration of medicines in schedules of service transition and nocturnal period, polypharmacy and the use of drugs not approved in pediatrics, they are factors that could unchain DIs undesirable.

PP-P-016

MEDICINE PRESCRIPTION PATTERNS AT THE URCAMP PHARMACEUTICAL ASSISTANCE NUCLEUS - BAGÉ, STATE OF RIO GRANDE DO SUL, BRAZIL

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The herein enclosed study intends to supply information on medicine prescription patterns as supplied by the Pharmaceutical Assistance Nucleus of URCAMP/RS [Southernmost Plains Area University], employing as reference prescription indices recommended by World Health Organization. The present is a descriptive-observational-retrospective study in which all prescriptions issued between the months of January and June 2005. As to the average number of drugs per medical prescription the bottomline achieved is 2.8 which is compatible with literature. Considering that within the network spanned by the SUS (Health Unified Service) all medical prescriptions are mandatorily filled in by generical drug denomination, the 80.4% prescriptional results achieved on generical drug denomination were satisfactory. As to prescriptions according to the Basic Listings the bottomline-achieved results of 83.7% point toward a general acceptation of same by health area professionals. As to the free dispensing of medicine, bottomline was 69.7% of all medicine prescribed, which is a cause for great concern under the medical-social viewpoint, as patients might be subjected to therapeutical failure due to product-access hampering. Most-prescribed therapeutical groups were dehypertensives, 17.17%; diuretics, 13.09%; antibiotics, 9.75%, and antiinflammatories, 8.21%. A systemic study of herein-presented indices is needed to monitor medicine-usage interaction with global health-care process and in the way scientific and medical communities interact with health service users in the selection of solutions that will involve pharmacological interventions.

PP-P-017

ANTIMICROBIAL EMPLOYMENT WITHIN FAMILY HEALTH BASIC UNITS FROM BAGÉ, RS [STATE OF RIO GRANDE DO SUL, BRAZIL]

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Abusive, indiscriminate usage of antimicrobial drugs is one of the causes pointed at for the emergence of growing antimicrobial-resistant-level microbial strains. Present day prescription practice characterization as assayed by studies among care dispensers in relation to their prescriptional habits belongs among such strategies that are adopted for the management of this public health problem. The herein study aims to study antimicrobial employment within Family Care Basic Units (UBSFs) located in the county of Bagé, Rio Grande do Sul state, Brazil, as well as the quantification of such prescriptions and differences presented between Winter and Summer dosages, plus the most-frequently-prescribed groups of antimicrobials identification, and the assessing of employment-pattern differences among the several evaluated health units. The present is a traversal-descriptive-observational-retrospective study, in which all medical prescriptions issued from the selected UBSFs between the months of July 2005 and January 2006. The present study is also representative as concerns the populations cared by the Family Health Program in the city of Bagé, Rio Grande do Sul state, Brazil. Global antimicrobial prescription prevalence was 14% during Winter months and 11% during Summer months. Amont such units that were observed, lowest and highest percentiles found were 7.3% and 17.5% on Winter as well as 7.7% and 20.9% on Summer. Most-often-prescribed antimicrobials in the two assessed periods were amoxycilyn and the sulfamethoxazol-trimetoprin association. Drug employment studies have become nowadays an important rationalization strategy on the use of pharmaceuticals.

PP-P-018

NEW DRUGS OF 2005 AND PUBLIC HEALTH NEEDS

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Background

The pharmaceutical market needs an effective medicines policy to provide drugs to care population diseases, to give access to these drugs, to improve rational use, and to avoid those non essential, unnecessary and dangerous. As a strategy of medicines policy, new drugs launched in market should be analyzed, verifying if they accomplish the above requirements and the public health needs.

Objectives

Identify and characterize all new drugs (New Chemical Entities- NCE) registered, in Brazil, in 2005.

Results

In the study period, 13 new drugs were registered: chlormadinone, bortezomib, otilonium bromide, palonosetrone, entecavir, epleronone, fosamprenavir, iloprost, nitazoxanida, cadotrile, terizidone, tigecicline and ximelagatrane.

These drugs will be used for part of country's population. There are diseases with public health interest like Malaria, Chagas disease, and Leishmaniosis that do not have new drugs introduced for it.

Conclusions

According to our findings, diseases of poor populations have not been treated with new drugs launched in the market.

PP-P-019

SPONTANEOUS ADVERSE DRUG REACTION REPORTING SYSTEM: CONTRIBUTION OF PHARMACISTS TO THE NATIONAL SYSTEM OF PHARMACOVIGILANCE IN BRAZIL

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Background: The National System of Pharmacovigilance, managed by Pharmacovigilance Unit, has faced since its creation a strong difficulty among health professionals, including pharmacists: the lack of tradition in reporting adverse events. Many strategies have been adopted to solve this problem, such as implantation of sentinel hospital and notifying pharmacy projects.
Aims: To describe contribution of pharmacists by evaluating suspected adverse drug reaction (ADR) reports sent by them to the Pharmacovigilance Unit during the year of 2004.

Methods: Only ADR reports sent by pharmacists were assessed. They were evaluated according to reporter institution and professional categories, patient sex and age, and therapeutic classes (ATC classification) corresponding to suspected drugs. Reports related only to medicine's deviation problems or ineffectiveness were excluded.

Results: During 2004 Pharmacovigilance Unit has received 1,890 reports, but only 1,253 (66,30%) were specifically about ADRs. From these, 745 (59,46%) reports were sent mainly by pharmacists, followed by physicians (19,47%). Most of the assessed report forms (85,91%) were sent by sentinel and volunteer hospitals. There were more female than male patients (53,02%). The most frequent patient age ranged from 0 to 10 years old (21,21%). The therapeutic classes frequently present were antibacterials for systemic use (25,80%), analgesics (10,18%), and antimycobacterials (5,68%). Serious ADRs corresponded to 161 reports (21,61%), according to WHO classification; seven patients have deceased.

Conclusions: Pharmacist contribution is significant to the National System of Pharmacoviglance; their reports corresponded to more than 50% of ADR reports in 2004. It is expected an increased number of non-hospital reports after widespread implantation of reporting pharmacy project started in 2005.

PP-P-020

ASSESSMENT OF ADVERSE DRUG REACTION REPORTS RELATED TO PEDIATRIC PATIENTS SENT TO PHARMACOVIGILANCE UNIT, BRAZIL

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Background: Few clinical trials select children as study population during a drug development, so adverse drug reactions (ADRs) related to pediatric patients become a concern to National System of Pharmacovigilance in Brazil. Lack of information about ADRs in children makes ADRs more difficult to be detected and reported by health professionals.

Aims: To describe the suspected adverse drug reactions in pediatric patients sent by spontaneous reporting system to the Pharmacovigilance Unit during the year of 2004.

Methods: Only ADR reports related to patients from 0 to 12 years old were assessed. They were evaluated according to reporter institution and professional categories, patient sex and age, and therapeutic (ATC classification) and system-organ (WHO-ART) classes corresponding to suspected drugs and reported ADRs. Reports without age information were excluded, as well as those related only to medicine's quality deviations or ineffectiveness.

Results: During 2004 the Pharmacovigilance Unit received 1,890 reports, but only 1,253 (66,30%) were specifically about ADRs. From these, only 248 (19,79%) reports related to pediatric patients. Most of the assessed report forms (90,73%) were sent by sentinel hospitals, and the pharmacists were the professional who reported more (72,98%). There were more male than female patients (52,82%). The most frequent patient age ranged from 0 to 1 year old (37,10%). The therapeutic classes frequently present were antibacterials for systemic use (29,58%) and psycholeptics (9,86%). The commonly reported ADRs were skin and appendages disorders (16,83%) and autonomic nervous system disorders (13,63%). Fifty-two (20,97%) reports revealed serious ADRs, according to WHO classification; two patients have deceased.

Conclusions: Assessing ADRs related to children is an important strategy, once Pharmacovigilance systems may monitor adverse events and disseminate information for

QP-P-001

DESIGN AND IMPLEMENTATION OF THE QUALITY CONTROL SYSTEM TO A NATURAL PHARMACEUTICAL PRODUCT

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Developing pharmaceutical products from natural sources pharmacist professionals find new challenges with the purpose of to obtain high quality products, difficult task when these medicines are administered by a route of complex administration that cause that their requirements are similar to those of an inyectable one. Due to the high requirements for this type of product, each manufactured lot is put under rigorous controls of quality. The present work approaches the design and implementation of a effective Quality Control System with views to guarantee reliable in the results of quality control of a natural pharmaceutical product, complimenting the validation and the uncertainty determination of all the analytical methods, the elaboration of new Reference Materials for the internal control of these tests, the mechanism to treatment of the results out specifications, the use of the statistical control like tools for the improvement of the system with the execution of control graphics that allow the monitory in the time and the tendency analyses among other essential aspects for the fulfilment of the Good Laboratory Practices following the actual specific ISO Guides. Key words: Natural pharmaceutical product, quality control, analytical method validation, and Reference Material.

QP-P-002

DEVELOPMENT OF AN INTERNAL REFERENCE MATERIAL OF PHOSPHOLIPIDS TO THE QUALITY CONTROL OF A NATURAL LUNG SURFACTANT

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The lung surfactants obtained of natural sources at the moment constitute effective therapeutic options for the treatment of the Neonatal Respiratory Distress Syndrome (NRDS). The biochemical composition of these exogenous surfactants presents rich in phospholipids, reason why in the control of quality of this type of product diverse spectrophotometric and chromatographic analytical methods for the identification, separation and quantification of these compounds are used. The present work approaches the design, obtaining and characterization of a Reference Material (RM) of phospholipids for its use as internal control of the chromatographic tests. Two sources of phospholipids of placenta and lung of a same specie were evaluated as raw material, being selected the second because it presented the components of interest, the one went that showed greater performance, smaller expense of organic solvent, and greater availability to acquire it. Three lots of RM were manufactured by means of the optimization of a flow that guaranteed the reproducibility of the process. The biochemical characterization of these three lots was carried out through of the use of analytical methods previously validated and using a comparison with pure standards of phospholipids from SIGMA shown that they comply with all the required quality indicators for this type of product for analytic uses. Key words: Quality control, phospholipids, Thin Layer Chromatography, and natural lung surfactant.

QP-P-003

VALIDATION OF ERYTHROMYCIN MICROBIOLOGICAL ASSAY - EMPLOYING AN ALTERNATIVE EXPERIMENTAL DESIGN

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The agar diffusion method, widely employed in antibiotic dosage, related the diameter of the inhibition zone with the dose of th substance assayed. It is interesting to adopt experimental planning, what may provide better results and an indication of the assay validity. The symmetric or balanced assays (2 x 2) as well as the ones with interpolation in standard curve (5 x 1) are the main designs used in the dosage of antibiotics. This works aims at proposing an alternative experimental design for erythromycin microbiological assay with the evaluation of the validation parameters of the method refereing to linearity, precision and accuracy. The design proposed (3 x 1) used 3 doses of standard and 1 dose of sample, being all the doses applied in a unique plate, aggregating characteristics of the 2 x 2 and 5 x 1 assays. The method adopted for erythromycin microbiological assay through agar diffusion was validated, what reveals its adequacy to linearity, precision and accuracy standards. Likewise, the statistic methods employed demonstrated their accordance with the method concernig the parameters evaluated. The 3 x 1 design proved to be adequate for the dosage of erythromycin, thus being a good alternative.

QP-P-004

THE ANNUAL PRODUCT REVIEW – A GOOD WAY IN IMPROVING THE QUALITY OF DRUGS.

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Aims:
Safety and efficiency are crucial to drugs. However, before taking the medicine, consumers are not able to immediately identify which one is of good quality. A pharmaceutic factory, therefore, must take actions to maintain their product's quality which can not depend on the market screening only. The annual product review, can help pharmaceutic factories monitor their products' quality before factories release them.
Methods:
Since 2005, the annual product review has been put into practice by FortDodge Animal Health (Division of Wyeth) in Taiwan. It consists of ten parts which are summary, batches reviewed, approved documents, stability data, analytical data, annual visual inspection, adverse drug reaction, recall/salvages, action and change history. The annual product reviews compare this year's data with that of last year. For each veterinary pharmaceutical product, we review all batch records and documents about their quality of former year. The reports should be kept in the factory.
Results:
We have finished six Annual Product Reviews in 2005 and are going to finish ten reports in 2006. Judging from the comparison between the reports of this year and those of last year, we not only realized whether follow-up actions were finished but also found out the discrepancy and the current trend. We terminated the repeating problems and took the right remedial steps to correct shortcomings. According to a statictics of the customer complaints in these three year, we found that the number of the customer complaints have reduced 10% after we started performing the annual product reviews.
Conclusions:
The annual product review in a pharmaceutic factory can be a reference when setting up formulas, specifications, SOPs and SOIs. When executed and aimed at products in the market properly, it can help factories prevent customer complaints and reduce the loss in recalling products. The annual product review is really good at improving the products' quality and customer satisfaction.

QP-P-005

ORIENTATION OF MEMBRANE-BOUND MELITTIN STUDIED BY A COMBINATION OF HPLC AND LSIMS

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Melittin is a hemolytic toxin peptide of the European bee Apis mellifera. It is demonstrated that the membrane bound melittin molecules present a certain structure of amphipathic helix (1~22 residues) but the orientation of the helical structure of melittin on phospholipid membranes is still controversial.

Combining high performance liquid chromatography with mass spectrometry, the membrane bound melittin is analyzed through the trypsin-digested products to obtain the orientation information of melittin.As melittin bound to the LUVs without transmembrane potentials, there exists the peaks of A8~21, A8~22 in the HPLC spectrum of tryptic digestion products of melittin. It indicates that Lys7 is exposed in the solution and can be attacked by proteases. This result provides a strong proof for the assumption that the α-helix structure of melittin lies flat on the membrane surface. As melittin bound to the LUVs with a negative transmembrane potential, there is no obvious A8~21 or A8~22 peaks in the HPLC spectrum of tryptic digestion products of melittin, but there existed relatively strong A1~23 peak group. The results indicate that Lys7 must be buried in the membrane and can not be attacked by proteases, while it is relatively easy for trypsin to access the proteolytic site at the C-terminal of membrane bound melittin. So it can be supposed that the α-helix structure of melittin does not lie flat on the membrane surface under the influence of the negative transmembrane potential, and the Lys7 is no longer exposed in the solution but inserted into the membrane. It can be supposed that (i) the α-helix structure of membrane bound melittin mainly adopts the orientation of lying flat on the membrane as melittin binds to LUVs without transmembrane potential; (ii) but as melittin binds to LUVs with negative transmembrane potential, the N-terminal of melittin inserted into the membrane and the α-helix structure of membrane bound melittin probably adopts the perpendicular orientation.

QP-P-006

SIMULTANEOUS LC DETERMINATION OF ATORVASTATIN AND FENOFIBRATE IN TABLETS

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A simple, precise and reproducible reverse phase high performance liquid chromatographic method has been developed for the simultaneous analysis of Atorvastatin and Fenofibrate in tablets. Separation was carried out in Phenomenex, Gemini C18 column (150x 4.6 mm. 5m), with the mobile phase consisted of 0.4% v/v triethyl amine (pH adjusted to 4 using dilute ortho phosphoric acid) : acetonitrile in the ratio 10: 90 % v/v. Detection of drugs were done at 245 nm and a flow rate of 1 ml/ min was used in the study. Mefenamic acid served as the internal standard. Calibration curves were linear in the range of 0.2 to 1 mg/ml and 4 to 20 mg/ml for Atorvastatin and Fenofibrate respectively. Correlation coefficient values were close to 1 proves good linear correlation between response factor and concentration. The elution order was atorvastatin (2.14 min), Mefenamic acid (2.87 min) and Fenofibrate (3.69 min). The Limit of Detection for Atorvastatin and Fenofibrate were found to be 5 and 6 ng respectively. Limit of Quantification were found to be 20 and 22 ng for Atorvastatin and Fenofibrate respectively. The precision of method was studied under intra day, inter day and repeatability studies. A low relative standard deviation value indicates that developed method has good precision. Recoveries of Atorvastatin and Fenofibrate were in the range of 98- 101 %, which shows that method is accurate and free from interferences and excipients present in formulation. The LC method was successfully applied to analysis of drugs in tablets and the estimated amount was found to be close to the labeled claim. System suitability studies and peak purity tests (Peak purity index values close to one) were performed. A complete statistical validation was also carried out proves the suitability of the method to analyze Atorvastatin and Fenofibrate simultaneously in tablets .

QP-P-007

PREPARATION AND EVALUATION ON THE SAFETY OF INTRAVENOUS EMULSION FOR GARLIC OIL

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OBJECTIVE To prepare intravenous emulsion for garlic oil and evaluate its safety. METHODS The intravenous emulsion for garlic oil was obtained by a high pressure homogenizer.According to the principle of SFDA and the Pharmacopoeia of the People's Republic of China (Edition 2005), the experiments of acute toxicity, hemolysis, vascular irritation, allergy and pyrogen were made. RESULTS The preparation was stable in quality. The particle size was 150.4±14.6 nm. The LD50of intravenous injection in mice was 184.1mg•kg-1. The preparation in different concentrations had no effects on hemolysis within 3 hours. There was no vascular irritation observed after 3 days of continuous intravenous injection of the emulsion. And the drug was free allergy and pyrogen. CONCLUSION The preparative technique is simple and reliable. The preparation is safe for injection.

QP-P-008

DETERMINATION OF CARBOCYSTEINE SYRUP SHELF LIFE BY ARRHENIUS METHOD .

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Carbocysteine has been currently used as a mucolytic agent in adjunctive therapy of respiratory tract infections. The pharmaceutical industry is responsible for quality, safety and efficiency of the product during its shelf life. Shelf life can be determinated through an accelerated stability study where the degradation of the drug is managed with the extrinsic factors.

According to Arrhenius, there is a relationship between temperature and chemical kinetic. The shelf life of carbocysteine syrup was determinated with the Arrhenius method. The syrup assay method has been validated. The linearity, precision, accuracy, detection limit, quantitation limit, selectivity and robustness were evaluated. The samples were exposed to drastic conditions at 40 °C, 50 °C, 60 °C and 70 °C just to accelerate the degradation. The results were analyzed with the Arrhenius equation and through the graphical method. The proposed shelf life of carbocysteine syrup was 240.9 days when the dosage form is stored in appropriated conditions, 25 °C. However difference was found between the proposed shelf life and the usual shelf life of this drug, this study has showed the presence of endogenous peaks that must be more evaluated to confirm or not the presence of degradation products. On the other hand, the assay for the measurement of carbocysteine may be applied to analysis of carbocysteine syrup in routine quality control and stability studies.

QP-P-009

TRANSFER OF ANALYTICAL METHODS FOR DETERMINATION OF ASSAY AND IMPURITIES IN PARENTERAL DOSAGE FORM

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The trend in pharmaceutical industry is globalization of pharmaceutical companies. To protect quality of the product, transfer of analytical methods is necessary. Method transfer is the process that qualifies Receiving laboratory to use an analytical test procedure. It has to ensure that the staff of the Receiving laboratory is well trained and qualified to run the method and obtain comparable results.

First of all methods should be validated. Validation experiments must be done according to appropriate regulatory guidelines for method validation and described in method validation report. Validation should be done on qualified equipment.

Once when method is validated, method transfer can begin. During pre-transfer stage, receiving laboratory has to review relevant documentation. After that, method transfer protocol can be written. It is the document that is agreed upon the Transferring and Receiving laboratories which outlines the requirements of the method transfer. It is consisted of purpose, scope, responsibilities, materials and methods references, experimental design, acceptance criteria and approval page.

When method transfer protocol is signed, analyses can be done.

Next step is writing of method transfer report that contains results obtained by both parties participating in the transfer, a discussion of the results, conclusion of the transfer testing and also approval page.

In this paper will be presented transfer of analytical methods for determination of assay and impurities in parenteral dosage form of Ondansetron Injections, 2mg/mL. After all analyses were done and results were compared, it was concluded that all results meet acceptance criteria and that Receiving laboratory is qualified to use this test procedure.

QP-P-010

HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC ASSAY OF BENZYL ALCOHOL AS A PRESERVATIVE IN TOPICAL FORMULATION

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Stability indicated HPLC method for determination of benzyl alcohol as a preservative in terbinafine HCl topical (cream) formulation is developed and validated. The method is based on the method for determination of terbinafine impurities in terbinafine hydrochloride substance published in Pharmaeuropa Vol.16, No.1, January 2004.

Benzyl alcohol is an antimicrobial preservative used in cosmetics, foods, and a wide range of pharmaceutical formulations, including oral and parental preparations, at concentration up to 2.0% v/v. In cosmetics, concentrations up to 3.0% v/v may be used as a preservative. Concentrations of 5% v/v or more are employed as a solubizer, while a 10 % v/v solution is used as a disinfectant.

Terbinafine HCl is a synthetic antifungal agent.

Chromatographic conditions: cream was dissolved in a mixture of acetonitrile, metanol and water in the ratio 50 : 25 : 25 with final concentration 0.5 mg/ml of benzyl alcohol and analysed on Agilent 1100 instrument with DAD detector (260 nm) on column RP-18, 250*4.6 mm. Mobile phase was mixture of 0.01M K2HPO4 and organic phase (acetonitrile/methanol 67/33 v/v).

Method was validated in terms of selectivity, linearity, accuracy, precision (measurement repeatability and intermediate precision), stability of standard and sample solutions and robustness. In conclusion, the method is suitable for tracking the content of benzyl alcohol in Terbinafine cream 1% during stability testing.

QP-P-011

COMPARISON OF CAPILLARY ZONE ELECTROPHORESIS (CZE) AND HIGH PERFORMANCE LIQUID CHROMATOGRAPHY METHODS (HPLC) FOR QUANTITATIVE DETERMINATION OF FEXOFENADINE IN DRUG FORMULATIONS

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The aim of our study was to develop a rapid, simple and robust quantitative procedure, validate, and compare CZE and HPLC assays with UV detection for the determination of fexofenadine in pharmaceutical formulation. Separations HPLC system were made on a Phenomenex C18 column (150 x 4.6 mm i.d, particle size 4 µm), using isocratic elution with triethilamine 1%:ACN:methanol (50:30:20 v/v/v) pH 3.2 as the mobile phase. The detector wavelength was 210 nm. The elution was performed at a flow rate of 1.0 ml/min and experiment conducted at 40° C. Capillary zone electrophoresis separations were performed in a fused-silica uncoated capillary (48.5 cm x 50 µm i.d., Agilent.) thermostated at 25°C. A voltage of 20kV was applied during analysis. The electrophoresis medium was 10 mM sodium tetraborate decahydrate 20 mM adjusted with sodium hydroxide to pH 9.3. Internal standard was nimesulide. The two methods allow direct and sensitive quantification of fexofendine and have been shown to have good sensitivity, linearity (r >; 0.999). The limits of detection and quantification were 0.002 and 0.05 µg.mL-1 for RP-HPLC and 0.3 and 1.0 µg.mL-1 for CZE, relative standard deviations (RSD) were 1.62 and 0.98% for CZE and RP-HPLC, respectively. The percentage recovery determined with CZE was 99.87% and with RP-HPLC was 99.8 %. The two methods (CZE and RP-HPLC) have been successfully validated and may be considered for routine analysis of fexofendine pharmaceutical formulation. Both methods exhibited satisfying validation results concerning sensitivity, linear range, detection limit, reproducibility, accuracy and precision (RSD<; 2%).

QP-P-012

SIMPLE AND RELIABLE HPLC METHOD OF ATENOLOL DETERMINATION IN PHARMACEUTICAL DOSAGE FORMS

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This work describes a new, fully validated, simple, rapid, selective, and sensitive HPLC method with diode array detection for the direct determination of Atenolol in pharmaceutical dosage forms without any ion-pairing agent on the mobile phase. A survey of literature has revealed several analytical methods for the determination of atenolol in dosage forms including high-performance liquid chromatography (HPLC) utilizing heptansulphonic acid, HPLC adopted by the United States Pharmacopoeia was based on the mobile phase containing heptanosulfonate as ion-pairing agent, which is very expensive.

The mobile phase employed was 10 mM ammonium acetate buffer (pH 7,0) and acetonitrile (80:20 v/v). The samples of 20 µl were injected onto Purospher Star® RP-18 (250 mm x 4.6 mm, 5 µm particle size) column, Shimadzu LC-20AT HPLC system, equipped with a model LC-20AT pump, oven for column model CTO-10AS. The flow rate was 0.8 ml.min-1. The retention time was 2.5 min for atenolol. The samples were detected at 275 nm. The assay was linear in the concentration range 125 – 375 µg.ml-1

The representative linear equation was y= 2E-07x – 0,0091, with a correlation coefficient (r=0,9989) highly significant for the method. The precision of the method was determined by repeatability (CV 0.88%) and intermediate precision (CV 0.96%.). The accuracy of the method was determined and the mean recovery was found to be 99.80% indicating an agreement between the true value and the value found. The HPLC method for the determination of atenolol in tablets was found to be simple, rapid, precise, accurate and sensitive. It was successfully applied to the analysis of atenolol pharmaceutical preparation in routine quality control.

QP-P-013

VALIDATION OF HPLC AND UV SPECTROPHOTOMETRY DETERMINATIONS OF CEFIXIME IN CAPSULES

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In this study two different methods, HPLC and UV spectrophotometry, are presented and validated for the determination of cefixime in capsules, a known antibiotic, with excellent efficacy in the treatment of urinary and respiratory infections. Cefixime was determined by HPLC method using a LiChrospher 100 RP-18 (5mm) column with mobile phase consisting of pH 7.0 potassium phosphate buffer - acetonitrile (90:10 v/v) at a flow rate of 0.4 ml.min-1. The concentration range was 5.0-35.0 mg.ml-1. The spectrophotometric UV method was performed in pH 6.0 potassium phosphate buffer in concentration range 2.0-10.0 mg ml-1. Both validated methods are linear, precise, accurate, sensitive and can be directly and easily applied to determination of bulk drugs and the pharmaceutical preparations of cefixime.

QP-P-014

IMPORTANCE OF THE EVALUATION OF THE FLOUR LIFE-OF-SHELF STRENGHTENED WITH FOLIC ACID IN THE PREVENTION OF DEFECTS OF THE NEURAL PIPE IN PELOTAS-RS

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Many scientific works point on the importance of the folic acid in the prevention of defects of the neural pipe. In the attempt of that the population improves the ingest of this vitamin has been praised the enrichment of flours so that if it obtains to prevent between 50 and 70% of the malformations of the neural pipe. Exactly thus, the rigorous control of these flours becomes necessary therefore, can occur losses during the manufacture processes and stockage. Factors as temperature, light, pH, oxidantes presence of catalysers and agents are responsible for the degradation of the folic acid being of this form, sufficiently useful the studies on the stability of the folic acid in flours, in the direction to guarantee the quality until the end of the validity stated period, to guide the producer in the necessary super dosage, for the production, and from the best conditions of packing, it has carried and storage. This study it has as objective to quantify the folic acid in existing flours of wheat in the market of Pellets, verifying if the levels of folic acid in wheat flours are in accordance with the levels praised in the legislation of the National Sanitary Monitoring Agency (ANVISA) and to evaluate the stability of the folic acid to the long one of the period of 4 months of validity of flours.

QP-P-015

QUALITATIVE AND QUANTITATIVE ANALYSIS OF THE FOLIC ACID COMMERCIALIZED IN PHARMACIES GALENICAS IN THE BAGE CITY

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In the present time Quality it is the word of order and it must be inherent to any product or rendering of services. For the skillful pharmacy it is not different, being the basic quality for its survival, the professional respect and the guarantee of a farmacological therapy effective for the patient. The skillful sector grew very and currently already it exists all about 5 a thousand pharmacies in the Brazil. However, which had not the conformity of some of the pharmaceutical establishments with demanded minimum standards of quality, the sector that in such a way suffers much preconception on the part from the population as on the part of the excessively professional ones of the health and, in many cases the industrialized medicine is considered of better quality. One becomes, therefore primordial the establishment of the conditions of the products gifts in the market is on the part of governmental institutions of fiscalization, particular universities or institutions that have capacity technique and physics for accomplishment of analytical techniques that guarantee the degree of quality of such products. This work carries through the study of the quality of the capsules of folic acid commercialized in pharmacies of manipulation of the city of Bage, tracing itself thus a parameter of quality between the same ones, having as reference the medicine industrialized commercialized with name of Folin, acquired in one would drug in the city of Bage. The necessity of external controls of quality of medicines was verified to prevent errors with medications and, to assist the population in the medication use with quality guaranteed

QP-P-016

EVALUATION OF THE QUALITY OF MALEATO OF ENALAPRIL IN INDUSTRIALIZED AND MANIPULATED PHARMACEUTICAL FORMS

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The medicine preparation compels to a rigorous verification how much it is possible, given to the moral and legal aspects related they, where any error can express risk for patient. Thus the pharmaceutical control of quality must guarantee the conformity of the medicine with the specifications that say respect to it, as well as its harmless and effectiveness. The guarantee of the service and product quality of health is evidenced mainly in chronic pathology where it has the necessity of the use of these products and services for long periods of time. The high blood pressure is one of the pathology of bigger prevalence in the world. In Brazil, high blood pressure, also, possesss high prevalence, for the control is used, in the treatment with preventives drugs. The useful medicines in the treatment of this pathology include chemical structures widely varied, being able to be classified in function of its mechanism of action. The enalapril is an example, therefore, it acts for diverse mechanisms. In this work they had been analyzed and evaluated the possible variations in the product quality that they possess as active principle the maleato of enalapril, as much in the industrialized pharmaceutical forms how much manipulated in the intention of assisting in the guarantee of the quality of available medicines the population, verifying itself it necessity of external controls of quality for attainment of minimum levels of quality of available medicines in the market.

QP-P-017

THE PRESERVATION OF THE FOLIC ACID IN THE PARBOLIZATION OF THE RICE

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The parbolization is an improvement method that increased more than of 4 for 20% of the total of rice consumed in Brazil in last the two decades. In this process it has increase of the nutritional value and the grains more present accented flavor and odor of the one than the polishing white rice. Recent studies disclose that the folic acid, essential vitamin of the Complex B, have important metabolic functions for maintenance of the health human being, mainly as cofactor of enzymes that synthesize the DNA and the RNA. Its scarce ingest of vitamins causes serious fetais illnesses, as defects in the closing of the neural pipe, and the best form to get this nutrient is through the ingest of foods the base of grains. In this work the texts of folic acid in grains of parboilizado rice are investigated and the effect of the operations of industrial improvement on the preservation of the folic acid in the attempt to trace a parallel enter the legal regulation proposal for the ANVISA of Brazilian flour blockhouse with folic acid x industrial improvement and guarantee of the product quality offered to the consumer acting together to the producers local of rice in the maintenance of title of greater center of rice producers of granted America Latin the city of Pellets. Importance of metodological alternatives in the evaluation of products for the guarantee of the final quality of these products is verified it and, of the legal adequacy of existing products in the market

IM-P-001

INCREASED PHOTODYNAMIC AND ANTIMICROBIAL ACTION OF METHYLENE BLUE INDUCED BY RED LED LAMPS EXPOSURE.

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Photodynamic therapy (PDT) is a technique that uses a photosensitizing compound, activated at a specific wavelength of visible light, to destroy a targeted cell via strong oxidizers that cause cellular damage, membrane lysis, and protein inactivation. One of the most well known photosensitizers is methylene blue (MB), which has photoeradication properties against microorganisms. Considering that the most disadvantageous aspect of PDT is the high cost of treatment that uses laser as light device, the objective of this paper is to propose the use of red LED lamps as an alternative to PDT, and to check their effectiveness against microorganisms using MB as photosensitizer. Assays with and without LED lamp exposure for 10, 20 and 30 minutes were carried out in plates containing Staphylococcus aureus (ATCC 26923), Escherichia coli (ATCC 26922) or Candida albicans (ATCC 90028) in Mullen Hinton Broth, with MB at concentrations of 10 to 200 mg/ml. The power of the LED lamps was 5mW, with maximum absorption at 660 nm (the same absorption region as MB). In the control groups (cultures without MB), no effect was observed with LED lamp exposure. MB without light induced a progressive inhibition of cell growth from 10 to 200 mg/ml, while with LED light exposure all cells were inhibited. In ten minutes of light exposure and 50 or 60 mg/ml of MB, the % of inhibition was 92.96% for S.aureus, 96.9% for E.coli and 93.33 % for C.albicans. The red LED lamp is a promising light device for PDT that can effectively inhibit bacteria and yeast growth.

IM-P-002

FREQUENCIES OF CYP2D6 *10 AND *14 ALLELES AND THE INFLUENCE ON THE METABOLIC ACTIVITY IN A HEALTHY HEALTHY CHINESE POPULATION

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AIM: To study the gene frequencies of CYP2D6 *10 and *14 alleles in a healthy Chinese population, and the influence of the two alleles one the metabolic activity of CYP2D6. METHODS: The CYP2D6*10 and *14 genotypes of 295 healthy Chinese subjects were determined by allele specific amplification established in our lab. The phenotypes of 131subjects were determined. RESULTS: There are 10 subjects with *14 allele, including a homozyguous for *14 allele. The gene frequency of *10 and *14 alleles were 55.8% and 1.8%, respectively. The metabolic ratio (MR) of dextromethorphan (DM) in 131 subjects was 0.032 ± 0.106. The MR of *1/*1, *1/*10, *10/*10, *1/*14, *10/*14 and *14/*14 group were 0.007 ± 0.012, 0.009 ± 0.010, 0.042 ± 0.029, 0.065, 0.14 and 1.186, respectively. The MR of homozygous for *14 group, which is found in a poor metabolizer(PM), was higher than those of *1/*1, *1/*10 or *10/*10 groups (P<;0.001). CONCLUSION: The CYP2D6*10 and *14 allele have great impact on the metabolic activity of CYP2D6, and CYP2D6*14 allele may be the cause of the PM in Chinese subjects.

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