行政院所屬各機關因公出國人員出國報告

（出國類別：其他）

參加「美國中藥製藥協會第五屆國際研討會」

出國報告

出國人員：行政院衛生署中醫藥委員會

高級研究員 鄭毓璋

出國地區：新加坡

出國期間：九十年五月二十七日至三十日

報告日期：九十年六月十三日

目　　次

摘　　要

本次會議係為「美國中藥製藥協會」(American Chinese Pharmaceutical Association. USA) 主辦之第五屆國際研討會，會議主題為討論如何將亞洲中草藥帶入現代主流藥品世界，演講者包括有美國藥物食品管理等有相關專家，因此參加此次會議的主要目的為瞭解美國及其他國家中草藥管理規則與研究動態，作為未來推動台灣中草藥產業發展之依據與參考。行政院衛生署中醫藥委員會高級研究員鄭毓璋亦於五月二十九日在該會以「台灣中草藥研發現況與展望」(Recent Developments of Herbal and Traditional Medicines in Taiwan) 之題目進行演講，將台灣目前中草藥發展的情形，向與會各國人士報告，使其能對我們政府的政策、研究環境、生產技術、臨床試驗體系、與產業結構有進一步的瞭解，相信對未來促成國際合作，及延攬廠商到台灣投資、開發中草藥，或進行跨國性的中草藥臨床試驗有莫大的助益。

壹、目的：

本次會議係為「美國中藥製藥協會」(American Chinese Pharmaceutical Association. USA) 主辦之第五屆國際研討會，會議主題為討論如何將亞洲中草藥帶入現代主流藥品世界，演講者包括有美國藥物食品管理等有相關專家，因此參加此次會議的主要目的為瞭解美國及其他國家中草藥管理規則與研究動態，作為未來推動台灣中草藥產業發展之依據與參考。

另該會本亦邀請行政院衛生署中醫藥委員會張主任委員成國於五月二十九日在該會以「台灣中草藥研發現況與展望」(Recent Developments of Herbal and Traditional Medicines in Taiwan) 之題目進行演講。不過，由於預算審查問題，張主委最後不克成行，而由中醫藥委員會鄭毓璋高級研究員代表演講，使其他國家與會者，對目前台灣中草藥發展現況及政府相關政策與法規有更充份的瞭解，增加其未來與台灣合作或來台投資之意願，為台灣中草藥帶來更多商機。

貳、過程

此次三天開會期間均於新加坡 Orchard Hotel 進行，第一

天的會議主要是邀請一些學者、研究人員及廠商，報告目前中草藥的相關研究，包括臨床試驗、製程相關等項目。第二天的會議的議題則主要為各國中草藥發展現況，及未來中草藥發展的趨勢，包括新加坡香港、美國、及我國均有代表報告。第三天的會議則由各廠商介紹其公司， 為一種 Business Exchange 的模式。會場亦有 Poster 場地，供與會者發表其研究成果或作公司簡介。

參、心得

近幾來國際延燒著一股中草藥熱，與會的人員除來自美國、香港、新加坡外，亦包括菲律賓、泰國、印度等起步比較晚，或其技術較為落後之國家，大家莫不摩拳擦掌，努力挖掘自己或其他國家的傳統草藥寶藏，期能在國際中草藥市場揚眉吐氣，為國家帶來無窮的財富。

與會的人士一致同意，過去中草藥除了幾千年的服用經驗之外，多缺乏經由臨床試驗證明之統計學數據，再加上中草藥的成分複雜，品質的一致性較難掌握，造成中草藥臨床療效常常無法穩定再現，難以被現代西方醫學所認同，銷售對象大都侷限在台灣、中國大陸、日本、韓國、東南亞等華人市場，其他地區則只能以健康食品之名義行銷，無法擺脫傳統民俗療法的陰影。因此今天要發展中草

藥，就不應停留在過去的古籍有記載，或使用經驗階段，而是必需下定決心，設法將其現代化，提出讓科學家們信服的數據，樹立中草藥的有效性、安全性的新形象，如此才能達到國際化的目標，這也是過去幾年來各國政府一直努力的目標。

以香港為例，其具有深厚之經濟基礎，加上大陸做為其後盾，發展中草藥的潛力無窮。其工業署在 1995 年即透過「工業支援資助計畫」支持有關中草藥的研究項目，至目前為止已以超過壹億港幣，支持 21 個有關中草藥的研究項目，在多方面支持中草藥產業的發展，包括建立必需的基礎設施、改良中草藥生產技術，協助新產品開發、建立中草藥資料庫等，而其立法會更於 1999 年通過香港第一個監管中醫藥業的條例，內包括中醫師執業、中藥的製造、使用、販賣等，大幅提昇了香港整中藥產業水準。

而新加坡過去對中醫藥則採取放任態度，並沒有給予正式承認，不過隨著全球中草藥市場的蓬勃發展，自 2000 年 11 月 14 日，新加坡國會三讀通過了中醫師法案，其內容包括成立中醫管理委員會，建立中醫師、中藥註冊制度等內容。該法案的通過，說明新加坡政府進一步提高了對中醫中藥的重視，以及致力於提升中醫藥專業水準和保護病人利益與安全的決心。此外，新加坡政府已經前後兩次投

入共計約 12 億美元的鉅額資金，用於包括中成藥在內的生物工程的研究開發，再加上其本為全球醫藥原料重要產地及出口國，且為亞洲第一個成為 PIC/S (Pharmaceutical Inspection Co-operation Scheme 之國家，這些都為新加坡中草藥的發展奠定一個良好的基礎。

在美國方面，隨著 1994 年其保健食品健康教育法 (DSHEA, Dietary Supplement Health & Education Act) 通過後，其中草藥市場即大幅成長，而 FDA 更於 2000 年提出植物性藥品規範草案，為中草藥量身定做，使其在美國亦能以處方藥上市。草案內容強調中草藥藥品可以不是純化之化合物，並接受中藥複方的觀念，且鼓勵過去有人體使用經驗者，包括典籍記載、其他國家上市之中草藥，直接進入早期人體臨床試驗，減少對其臨床前安全性試驗數據的要求，不過在進入第三期人臨床驗或查驗登記時，則完全要比照西藥的標準辦理。這種前門寬後門窄的原則，實不僅考慮到中草藥的歷史背景，更可鼓勵更多人投入中草藥的開發，可以預期未來美國的中草藥產業一定更為蓬勃發展。

不過這次國際研討會，商業氣息較濃，雖然大會有安排一些如技術、臨床試驗的演講內容，但多為一般公司的研究成果，具有突破性發展或學術參考價值者較少，不過本

前國內尚欠缺對這些方法或圖譜之客觀標準，廠商亦缺乏獨立開發這些技術之能力，因此政府應儘速結合各項資源，如財團法人生醫、生技、製劑三大中心，建立如各項藥材或常用基準方之化學分析方法、指紋圖譜及生物活性試驗之平台技術等，供業界遵循及國外參考，為中草藥的科學化打通任督二脈。

另一方面我們都知道，一個產業必需有充沛的人才資源，才能有足夠的能量永續發展。以目前國內的環境來說，中央研究院李遠哲院長就曾直言不諱的指出人才的不足將會是台灣發展生技產業，包括中藥產業，的一大瓶頸。其他國家如香港、新加坡亦有相同問題。不過香港近幾年來有注意到這個問題，積極於各大學成立中醫藥相關科系，如香港浸會大學及香港中文大學就相繼於 1998 及 1999 開辦中醫學士學位課程，而其僱員再培訓局亦開設中藥配藥員的訓練課程，另香港政府亦積極從大陸引入中醫藥專才，以補其本身之不足。

反觀台灣，過去在國內中草藥一直處於弱勢，並不受到太多的重視，以至到目前為止，國內各大學中並無獨立之中藥系，設有中藥相關研究所者僅寥寥數家，而在中醫師培育上則僅中國、長庚、慈濟醫學院設有中醫系，每年能培養出的中醫藥人才相當有限，實無法提供未來中藥產業

的發展需要。從近年國內學術界研究中醫藥的主題、計畫主持人素質及數目，我們就可看出中醫藥研發人才的確有嚴重斷層存在，實有待更多對中藥有深入認識的年輕學者的投入，才有可能在未來對中草藥開發所遭遇的問題，做出突破。

而最近幾年來，政府大力推動的中藥臨床試驗過程可以用困難重重來形容，廠商送來的中藥臨床試驗計畫書常常慘不忍睹，與西藥相去一萬八千里，更有甚者，廠商無法瞭解審查委員的意見，雙方難以交集，從這些問題，我們亦可看出業界對有經驗的審查人員、主持醫師、試驗設計、統計、品管人才之需求。

雖然目前政府各相關單位常舉辦中醫藥的訓練課程，不過大多僅止於技術層面，對提昇整體產業的研發能力幫助有限，未來仍需鼓勵各大專院校成立中醫藥相關系所，以正規教育向下下扎根，並在教考制度上作適度鬆綁，積極從國外延攬有經驗的人才，才能為台灣中藥的發展打下一穩定的基礎。

附錄：大會手冊

THE 5TH ACPA INTERNATIONAL CONFERENCE

BRINGING ASIAN HERBAL AND TRADITIONAL MEDICINES TO THE MODERN MAINSTREAM PHARMACEUTICAL WORLD

• *May 28 – 30, 2001* •

Orchard Hotel, Singapore

POST-CONFERENCE WORKSHOP

May 31 – June 1, 2001

National University of Singapore, Singapore

FOREWORD

As President of the American Chinese Pharmaceutical Association (ACPA), and Principal Investigator of GEA-NUS Pharmaceutical Processing Research Laboratory (PPRL), Department of Pharmacy, National University of Singapore (NUS), we welcome you to the 5th ACPA International Conference.

ACPA was officially founded as a non-profit organization in December 1986. The organization now has members in North America and overseas representing several related disciplines: pharmaceutical science, pharmacy practice, and regulatory affairs. The original mission of ACPA is to promote the professional development and global networking for pharmacists and pharmaceutical scientists of Chinese heritage. To foster and nurture future pharmacy leaders of Chinese heritage, the organization has an annual scholarship program in existence since 1991, and assists in the development of student chapters at different universities. ACPA further defines its values through advancing excellence in pharmaceutical sciences and pharmacy practice, using venues such as regional conference and local seminars.

GEA-NUS PPRL was established in April 1997 in the Department of Pharmacy, Faculty of Science, NUS. This research laboratory is set up with support from the National Science and Technology Board, NUS, GEA (Aeromatic-Fielder) and the private sector. The objectives of GEA-NUS PPRL are to conduct research and development in pharmaceutical technology, to provide manpower training and to assist in process and product development for the pharmaceutical and allied industries. These objectives are geared towards meeting the needs of the local and regional industries and developing the research laboratory into a center of excellence for pharmaceutical technology research.

For the past year, our local and national organizing committees have been actively involved in developing an exciting program of scientific sessions for the 5th International Conference. In addition to the excellent scientific program, the committees have also provided the delegates with the opportunities to participate in the technology and product exchange forum. Hopefully you will find the conference scientifically stimulating, and the additional events both unique and enjoyable. Since our primary mission is to facilitate networking opportunities, we hope the conference will provide you with the time to not only meet colleagues, but to make new acquaintances as well.

Our special thanks to Dr. Keith Chan and the local and national organizing committees. These groups of dedicated individuals are to be congratulated in facilitating our excellent program for the conference. Please do no hesitate to contact any of the local organizers or us if you need assistance during the conference. Rest assured, we will all do our best to make your attendance both enjoyable and memorable.

Marina Y. Chang, R.Ph.
President
ACPA

Paul W.S. Heng, Ph.D.
Principal Investigator
GEA-NUS PPRL

ACKNOWLEDGEMENT

We would like to express our appreciation to the following individuals who worked very hard for this meeting:

Executive Committee
Marina Y. CHANG (Co-Chair), Paul HENG (Co-Chair), Keith CHAN, Winston TOWN, Van Doren HSU, Chester LAU

Local Organization Committee
Paul HENG (Chair), Lai Wah CHAN, Sui Yung CHAN, Celine LIEW, Tin Wui WONG, Jinsong HAO, Mei Yin WONG, Teresa KWOK, Judy SEOW, Wai Yee CHAN, Sze Nam CHEE, Wai See CHEONG, Li GU, Yudi JIN, Tuck Loong KWOK, Chin Chiat LEE, Huey Ying LEE, Xiaoman LI, Liang Theng LIM, Kang Teng ONG, Grace CHEN

Program Committee
Keith CHAN (Chair), Paul HENG, Marina Y. CHANG, Van Doren HSU, Shaw T. CHEN, Winston TOWN, Francis LAM, James SHIH, Shing Tzouk TSAI, Jeff QI

Post-Conference Workshop Committee
Paul HENG (Chair), Keith CHAN

Regional Committee
Winston TOWN (Chair, HK), Paul HENG (Singapore), Yvonne TAN (Malaysia), Garnpimol RITTHIDEJ (Thailand), Shing Tzouk TSAI (Taiwan), Keith CHAN (Outside of Asia)

Fundraising Committee
Keith CHAN (Co-Chair), Paul HENG (Co-chair), Winston TOWN

Official Travel Agents
BK Travel, Rockville, Maryland, U.S.A.
American Lloyd Travel Services Pte Ltd., Singapore

ACKNOWLEDGEMENT

We would like to thank the following companies and individuals for their generous support.

Corporate Sponsor

Andrx Pharmaceuticals, Inc
Brion Research Institute.
Colorcon
Development Center for Biotechnology
Dow Chemical Company
Eu Yan Sang International Ltd.
GloboAsia LLC
ISP Asia Pacific Pte Ltd
Niro (S.E.A.) Pte Ltd
Pharmaceutical Industry Technology Development Center
SunTen Pharmaceutical Company Ltd.
Walton Pharmaceutical Co. Ltd

Individual Donation

Keith Chan, Ph.D.
Jinn Wu, Ph.D.

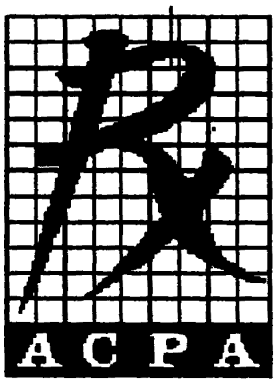
Exhibitor

Cerebos Pacific Ltd.
Colorcon/Dow Chemical Company
ISP Asia Pacific Pte Ltd
Rohm Pharma Polymers, Degussa Huls (SEA) Pte Ltd.
Schmetterling Associates
Sun Ten Pharmaceutical Company Ltd.

Advertisement

Cerebos Pacific Ltd.
Eu Yan Sang International Ltd.
M.E.I. Project Engineers Pte Ltd.
Nutri-Active Pte Ltd.
Tai Chuan Medical Trading Company Pte Ltd.

TABLE OF CONTENTS



PROGRAM

Program

SUNDAY – MAY 27, 2001

8:00 p.m. - 10:00 p.m.	**Welcome Reception**

MONDAY – MAY 28, 2001

8:00 a.m. - 9:00 a.m.	**Registration**
9:00 a.m. - 9:15 a.m.	**Opening Remarks** Marina Y. CHANG, R.Ph., 2001 President of ACPA Paul HENG, Ph.D, GEA-NUS PPRL
9:15 a.m. - 9:45 a.m.	**Special Presentation: Opportunities and Challenges for Traditional Chinese Medicine in the New Economy** CHAN Soo Sen, Senior Parliamentary Secretary, Prime Minister's Office and Ministry of Health, Singapore
9:45 a.m. - 10:15 a.m.	**Plenary Presentation: Bringing Asian Herbal and Traditional Medicines to the Modern Mainstream Pharmaceutical World: The Time is Now** Kuo-Hsiung LEE, Ph.D., University of North Carolina, U.S.A.
10:15 a.m. - 10:30 a.m.	**Coffee Break** (Set up poster and exhibition)

Session 1: How to Apply Modern Pharmaceutical Technology to Asian Herbal and Traditional Medicines
Moderators: Paul HENG, Ph.D. and Keith CHAN, Ph.D.

10:30 a.m. - 11:00 a.m.	**Production of Herbal Products by Direct Compaction** Yolande ANTHONY, Ph.D., ISP Asia Pacific Pte Ltd., Singapore
11:00 a.m. - 11:30 a.m.	**Continuous High Throughput Extraction** Ole KJAERGAARD, M.Sc., Niro A/S, Denmark
11:30 a.m. - 12:00 noon	**Application of Spray Drying Techniques in Herbal Product Manufacturing** Ole KJAERGAARD, M.Sc., Niro A/S, Denmark
12:00 noon - 1:00 p.m.	**Lunch, Poster and Exhibition**

Session 2:	Advances of Asian Herbal and Traditional Medicines - What Does That Mean to Modern Pharmaceutical World? Moderators: Kuan-Chih CHEN and Yvonne TAN, Ph.D.
1:00 p.m. - 1:30 p.m.	**Establishing Evidence in Chinese Medicine: Evaluating the Chinese Herbal Treatment of Irritable Bowel Syndrome** Alan BENSOUSSAN, M.Sc., University of Western Sydney, Australia
1:30 p.m. - 2:00 p.m.	**Use of Porcine Relaxin for the Treatment of Untreatable Diseases Such as Fibromyalgia** Samuel YUE, M.D., HealthEast Pain Clinics, U.S.A.
2:00 p.m. - 2:30 p.m.	**Efficacy and Safety of Ja Wai Ophiopogon Decoction in the Treatment of Allergic Asthma** Ching-Hsiang HSU, M.D., Ph.D., China Medical College, Taiwan
2:30 p.m. - 3:00 p.m.	**Pyrrolizidine Alkaloid Metabolism Induced Hepatotoxicity and Prevention of Such Toxicity by Herbal Medicines** Ge LIN, Ph.D., Chinese University of Hong Kong, Hong Kong
3:00 p.m. - 3:30 p.m.	**Coffee Break, Poster and Exhibition**
3:30 p.m. - 4:00 p.m.	**Strategy on the Research and Development of Herbal Medicine: An Example on the Development of Antidepressant Herb** Feng-Nien KO, Ph.D., Pharmaceutical Industry Technology and Development Center, Taiwan
4:00 p.m. - 5:00 p.m.	**Poster and Exhibition** Authors/presenters must be present during this time
7:00 p.m. – 11:00 p.m.	**Banquet** Goodwood Park Hotel

TUESDAY – MAY 29, 2001

8:00 a.m. - 9:00 a.m. **Registration**

Session 3: Regulatory Requirements in Bridging Asian Herbal and Traditional Medicines to the Modern Pharmaceutical World
Moderators: Keith CHAN, Ph.D. and Lai Wah CHAN, Ph.D.

9:00 a.m. - 9:30 a.m. **The GMP Inspection and Licensing System of Singapore**
Chong Hock SIA, M.Sc., Centre for Pharmaceutical Administration, Health Sciences Authority, Singapore

9:30 a.m. - 10:00 a.m. **Status of Herbal-and Traditional Medicines in Thailand**
Garnpimol C. RITTHIDEJ, Ph.D., Chulalongkorn University, Thailand

10:00 a.m. - 10:30 a.m. **Recent Developments of Herbal and Traditional Medicines in Taiwan**
Chung-Gwo CHANG, M.D., Committee on Chinese Medicine and Pharmacy, Taiwan

10:30 a.m. - 11:00 a.m. **Coffee Break, Poster and Exhibition**

11:00 a.m. - 11:30 a.m. **The Impact of Legislation on Chinese Medicine in Hong Kong**
Brad LAU, Ph.D., Hong Kong University of Science and Technology, Hong Kong

11:30 a.m. - 12:00 noon **Developing Herbal Medicines as New Drugs: Regulatory Approaches in the Draft FDA Guidance**
Shaw T. CHEN, M.D., Ph.D., Food and Drug Administration, U.S.A.

12:00 noon - 12:30 p.m. **Requirements for Registration of OTC Products in the U.S.**
Jacqueline LEUNG, R.Ph., U.S.A.

12:30 p.m. - 1:30 p.m. **Lunch, Poster and Exhibition**

Session 4:	**Bridging Asian Herbal and Traditional Medicines to the Modern Pharmaceutical World** **Moderators: Winston TOWN and Sui Yung CHAN, Ph.D.**
1:30 p.m. - 2:00 p.m.	**Herbal and Traditional Medicines - Will the Future be Clinical Driven or Evidence-Based?** Ming HU, Ph.D., Washington State University, U.S.A.
2:00 p.m. - 2:30 p.m.	**Development Center for Biotechnology's Experience in Toxicology for Herbal Medicines** Billy CHOU, Ph.D., Development Center for Biotechnology, Taiwan
2:30 p.m. - 3:00 p.m.	**Herbal Drug Interactions - Recent Development** Y.W. Francis LAM, Pharm.D., University of Texas Health Science Center at San Antonio, U.S.A.
3:00 p.m. - 3:30 p.m.	**Coffee Break, Poster and Exhibition**
3:30 p.m. - 4:00 p.m.	**Application of Modern Instrumentation (LC/MS/MS) in Herbal Product Quality Control: Case Study - Tien Ma** Jinn WU, Ph.D., XenoBiotic Laboratories, Inc., U.S.A.
4:00 p.m. - 4:30 p.m.	**Targeted Discovery of Steroidogenic Compounds in Traditional Herbal Medicines** Eu Leong YONG, MRCOG, Ph.D., National University of Singapore, Singapore

Closing Ceremony and Remarks (All Attendees)

4:30 p.m. - 4:45 p.m.	Marina Y. CHANG, R.Ph., 2001 ACPA President Paul HENG, Ph.D., GEA-NUS PPRL

WEDNESDAY – MAY 30, 2001 (HALF-DAY)

Business Exchange Forum between Herbal Companies, Manufacturers and Developers
Moderators: Winston TOWN and Tin Wui WONG, Ph.D.

9:00 a.m. - 9:15 a.m.	**J.S.S. College of Pharmacy, India**
9:15 a.m. - 9:30 a.m.	**M.E.I. Project Engineers Pte Ltd., Singapore**
9:30 a.m. - 9:45 a.m.	**Dow Chemical Company, Singapore**
9:45 a.m. - 10:00 a.m.	**Colorcon, Singapore**
10:00 a.m. - 10:15 a.m.	**Pharmaceutical Industry Technology Development Center, Taiwan**
10:15 a.m. - 10:30 a.m.	**Sun Ten Pharmaceutical Company Ltd., Taiwan**
10:30 a.m. - 11:00 a.m.	**Coffee Break**
11:00 a.m. - 11:15 a.m.	**Maywufa Enterprise Group, Taiwan**
11:15 a.m. - 11:30 a.m.	**Kinetana Inc./Hong Kong Herbal Pharmaceuticals Ltd., Canada**
11:30 a.m. - 11:45 a.m.	**Development Center for Biotechnology, Taiwan**
11:45 a.m. - 12:00 noon	**XenoBiotic Laboratories Inc., U.S.A.**
12:00 noon - 12:15 p.m.	**Sky Biohealth Solutions Inc., U.S.A.**
12:15 p.m. - 12:30 p.m.	**GloboAsia, LLC, U.S.A. and Hong Kong**
12:30 p.m. - 12:45 p.m.	**GEA-NUS Pharmaceutical Processing Research Laboratory, Singapore**

The 5th ACPA International Conference: Bringing Asian Herbal and Traditional Medicines to the Modern Mainstream Pharmaceutical World
Post-Conference How-To Workshop

May 31 - June 1, 2001
National University of Singapore
Lecture Theatre (LT) 31 (see map on page 8)

THURSDAY – MAY 31, 2001

8:00 a.m. - 8:45 a.m. **Registration**

8:45 a.m. - 9:00 a.m. **Opening Remarks**
Overall Objectives and Expectation of the Workshop
Paul HENG, Ph.D., GEA-NUS PPRL

9:00 a.m. - 12: 00 noon (2.5 hr + break) and 1:00 p.m. – 5:00 p.m. (3.5 hr + break)

Session 1: Pharmaceutical R&D and Business Essentials for Herbal and Traditional Medicines
Keith CHAN, Ph.D. (1.5 hr + Break)

1.1 The Route of Taking Herbal Medicines into the Global Healthcare System
Herbal drug products as food additives, dietary supplements, OTC, or prescription drugs; Pharmaceutical drug development and how herbal and traditional drug products fit in; Worldwide intellectual properties; How to maximize the business potential with pharmaceutical licensing; Putting it all together – a successful Asian business model

Session 2: cGMP Quality Issues and the Potential Solutions for Herbal and Traditional Medicines
Keith CHAN, Ph.D. (1.0+2.0 hr + Break)

2.1. Fundamental of cGMP
2.2. Non-drug specific cGMP compliance – Quality System, facility, personnel, procedures, documentation, equipment, validation, and software, etc.
2.3. Drug-specific cGMP compliance
  2.3.1 Chemistry – Raw materials, drug substance and drug product
  2.3.2 Manufacturing – Raw materials, drug substance and drug product
  2.3.3 Controls – Specifications for raw materials, drug substance, drug product and manufacturing process
2.4. FDA botanical drug product IND Filing – Putting it all together

Session 3:	**Botanical Drug Product: Modern Formulation Development and Stability Study Design for Herbal and Traditional Medicines** **Gan-Lin CHEN, Ph.D. (1.5 hr)**

3.1. Fundamental of formulation development
3.2. Control of botanical raw materials, botanical drug substance, excipients, and drug product
3.3. Stability study design for botanical drug products

FRIDAY – JUNE 1, 2001

9:00 a.m. - 12:00 noon (2.5 hr + break)

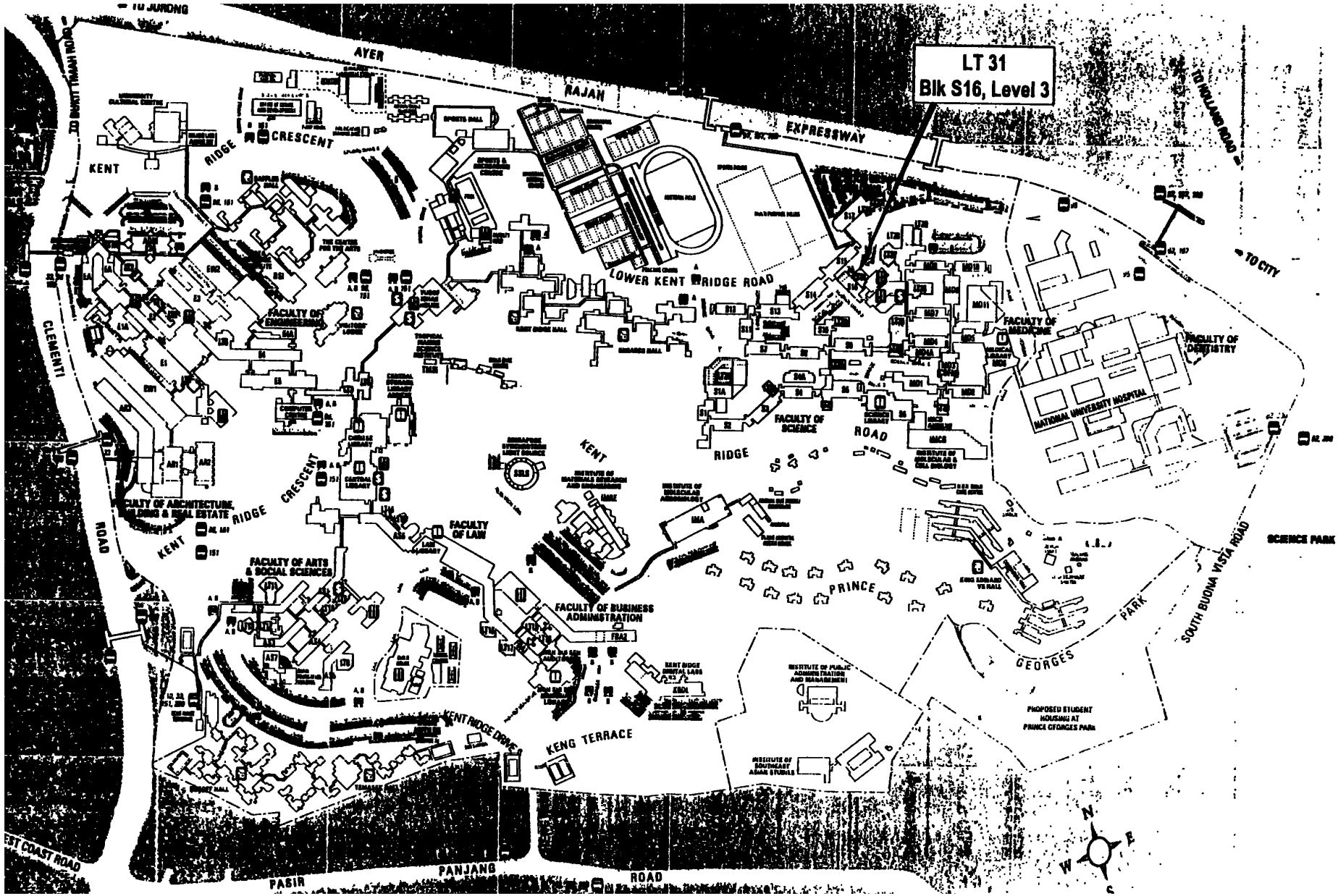
Session 4:	**Pharmacology and Toxicology Studies, GLP and Validation in Herbal and Traditional Medicines** **Billy CHOU, Ph.D. (2.5 hr + Break)**

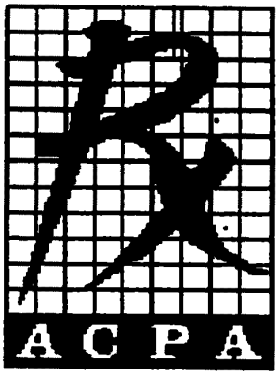
4.1. Fundamental of GLP and pre-clinical studies
4.2. Pre-clinical pharmacology and safety studies for botanical drug products
4.3. Toxicological study designs for oral, parenteral, and topical herbal and traditional drug products
4.4. GLP in non-clinical laboratories

1:00 p.m. - 5:00 p.m. (3.5 hr + break)

Session 5:	**How to Properly Design Clinical Studies for Herbal and Traditional Medicines** **Shaw T. CHEN, M.D., Ph.D. (3.5 hr + Break)**

5.1. Basic principles for proper design of clinical trial for botanical drug products of regulatory quality
5.2. Advice on Botanical IND submission – clinical perspective
5.3. A guide to evaluation of new botanical drug candidate for clinical development


LT 31
Blk S16, Level 3
TO JURONG
AYER RAJAH EXPRESSWAY
TO KALLANG ROAD
TO CITY
KENT RIDGE CRESCENT
KENT RIDGE ROAD
LOWER KENT RIDGE ROAD
CLEMENTI ROAD
FACULTY OF ENGINEERING
FACULTY OF ARCHITECTURE, BUILDING & REAL ESTATE
FACULTY OF ARTS & SOCIAL SCIENCES
FACULTY OF LAW
FACULTY OF BUSINESS ADMINISTRATION
FACULTY OF SCIENCE
FACULTY OF MEDICINE
FACULTY OF DENTISTRY
NATIONAL UNIVERSITY HOSPITAL
PRINCE GEORGES PARK
SOUTH BUONA VISTA ROAD
SCIENCE PARK
KENG TERRACE
KENT RIDGE DRIVE
PROPOSED STUDENT HOUSING AT PRINCE GEORGES PARK
WEST COAST ROAD
PASIR PANJANG ROAD
N
E
W
S



SPEAKER BIOGRAPHIES AND ABSTRACTS

SPECIAL PRESENTATION

Opportunities and Challenges for Traditional Chinese Medicine in the New Economy

CHAN Soo Sen
Prime Minister's Office and Ministry of Health
Singapore

BIOGRAPHY

Mr. Chan Soo Sen was born in Singapore on 1 October 1956.

He was educated in Catholic High School from 1963 to 1974, and was awarded Colombo Plan and President's Scholarships in 1975 to study Mathematics in the University of Oxford, United Kingdom. He graduated with a Bachelor of Arts (2nd Class Honours) degree in 1978.

After returning to Singapore, Mr. Chan completed his full-time National Service, and joined the Administrative Service in 1980. He started in the Ministry of Defence, and was transferred to the Ministry of Education in 1984.

In 1986, Mr. Chan was awarded a Post Graduate Scholarship by the Ministry of Finance to study Management Science in the University of Stanford, USA. He graduated with a Master of Science degree in 1987 and was posted to the Ministry of Home Affairs upon his return.

In 1992, Mr. Chan was chosen to be the founding Executive Director of the Chinese Development Assistance Council (CDAC). He set up CDAC Management from scratch, and put its various programmes on track.

In March 1994, Mr. Chan became the first Chief Executive Officer of the China-Singapore Suzhou Industrial Park Development Co. Ltd. (CSSD). He started up the physical construction, achieved good marketing results, and completed preparation work for infrastructure development.

On 1 April 1996, Mr. Chan became Business Advisor to EM Services, one of the major managing agents for the Town Councils.

Mr. Chan was returned unopposed as one of the six members of Parliament for the East Coast Group Representation Constituency (GRC) in the 1997 General Election.

On 25 January 1997, he was appointed Parliamentary Secretary, Prime Minister's Office and Ministry of Community Development. He resigned from CDAC and EM Services the same day.

On 3 June 1999, Mr. Chan relinquished the post of Parliamentary Secretary to the Minister for Community Development to become Parliamentary Secretary to the Minister for Health. He remained concurrently as Senior Parliamentary Secretary to the Prime Minister.

Mr. Chan is married with two sons. Away from work, he spends time with his family. He has keen interest in history, social studies, as well as current affairs. Mr. Chan is a Captain in National Service.

ABSTRACT

The use of traditional Chinese medicine (TCM) is gaining popularity worldwide. The holistic and personalised style of TCM practice distinguishes it from the high-tech but sometimes low-touch Western medicine practice. As good health is increasingly valued, the demand for TCM increases correspondingly.

However, TCM uses herbal plants and elements. Where it is grown, how it is harvested and processed is important. Hence the quality control of the production and manufacturing of TCM herbs becomes an increasingly important issue today. Coupled with that is the professional standard of the dispensers of TCM to ensure that the TCM products dispensed are of good quality.

The secret of success for TCM in the new economy must be good product, good formula, modern quality control measures and high dispensing professional standards.

PLENARY PRESENTATION

Bringing Asian Herbal and Traditional Medicines to the Modern Mainstream Pharmaceutical World: The Time is Now

Kuo-Hsiung LEE, Ph.D.
University of North Carolina at Chapel Hill
Chapel Hill, North Carolinas, U.S.A.

BIOGRAPHY

POSITION TITLE: Kenan Professor of Medicinal Chemistry
Director of Natural Products Laboratory
University of North Carolina at Chapel Hill (UNC)
Academician of Academia Sinica

EDUCATION:

Institution and Location	*Degree*	*Year Conferred*	*Field of Study*
Kaohsiung Medical College (Taiwan)	B.S.	1961	Pharmacy
Kyoto University (Japan)	M.S.	1965	Pharmaceutical Chemistry
University of Minnesota (Minneapolis)	Ph.D.	1968	Medicinal Chemistry
University of California (Los Angeles)	Postdoctoral Scholar	1968-70	Organic Chemistry

EMPLOYMENT:

1970-1974	Assistant Professor of Medicinal Chemistry, UNC
1974-1977	Associate Professor of Medicinal Chemistry, UNC
1977-1991	Professor of Medicinal Chemistry, UNC
1998-1999	Chair, Division of Medicinal Chemistry and Natural Products, UNC
1983-present	Director of Natural Products Laboratory, UNC
1992-present	Kenan Professor of Medicinal Chemistry, UNC

HONORS and AWARDS:

1978 Academy Fellow of the Academy of Pharmaceutical Sciences
Fellow of the American Association of Pharmaceutical Scientists
1988 Hollingsworth Faculty Scholar Award, UNC
Soine Memorial Award for Outstanding Contributions to the Field of Medicinal Chemistry Research
Kenan Professor, Endowed Chair, UNC
Dean's Special Research Award, UNC
Distinguished Alumni Award, Kaohsiung Medical College
Genelabs Achievement Award
The Lifu Academic Award for Chinese Medicine

1994 Fellow of American Association for the Advancement of Science
T.M. Tu's Science Award, Taiwan Association for the Advancement of Science
National Health Research Institutes Merit Award, Taiwan
1996 Academician, Academia Sinica
1996 Honorary Professor, Shanghai Institute of Materia Medica, Chinese Academy of Sciences
Editor's Award, Japan Oil Chemical Society
1999 Honorary Advisor, Chinese Medicinal Material Research Centre, The Chinese University of Hong Kong
1999 Honorary Professor, Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences
1999 Sir Edward Youde Memorial Fund Visiting Professorship Scheme Award, Hong Kong
Outstanding Achievement Award, University of Minnesota at Minneapolis
2000 Scientific Advisor, National Laboratories of Foods and Drugs, Department of Health, Taiwan
2000 Chairman, Committee for the Promotion of Chinese Herbal Medicine Industry and Technology, Ministry of Economic Affairs, Taiwan

CURRENT RESEARCH PROGRAMS:
New Drug Discovery and Medicinal Chemistry of the Bioactive Natural Products and Synthetic Analogs Including Antitumor, Anti-AIDS, Antimalarial, Anti-inflammatory, Anti-arthritis, and Antiviral Agents; Antifungal Antibiotics; Insect Antifeedants; Combinatorial Chemistry; and Chinese Medicine

PUBLICATIONS, PATENTS AND OTHERS:
More than 450 research articles in refereed journals
More than 30 patents
Delivered more than 280 invited lectures
Served as a member of the editorial advisory board for 15 journals

ABSTRACT

Herbal products, including Asian herbal and traditional medicines, have been used since antiquity as folk drugs and are now being used increasingly worldwide by the general population and studied rigorously by academicians and industries. Both Asian and Western medicine have contributed greatly to health and disease treatment. However, the two approaches differ in theory and practice, especially in the drugs they design and use.

Western medicine uses pure natural or synthetic compounds aimed at a single target while, Asian herbal and traditional medicines use processed crude multicomponent natural products – in various combinations and formulations aimed at multiple targets – to treat different symptoms according to a unique theory.

By applying advanced scientific technology, herbal medicines can be promoted both as dietary supplements and as a fundamental basis for modern drug discovery and development. For current benefits as dietary supplements, four criteria should be met: quality controlled GMP products, no undesirable side effects or toxicity, some proven beneficial effects, and patentable aspects. In the future, herbal products should be rigorously studied to provide proven efficacy and safety and to be developed as new drugs by one of three approaches. (1) active principles (bioactive compounds) approach, (2) active fractions approach, and (3) active prescription-based approach.

The above goals can be achieved through an iterative process of bioactivity-directed fractionation and isolation of natural lead compounds, chemical modification and improvement through structure-activity relationship, mechanism of action, drug metabolism, molecular modeling, and combinatorial chemistry studies, as well as best quality control, efficacy and toxicity determination, and clinical trials. From these studies, Asian herbal medicines can be brought to prominent positions as dietary supplements for health maintenance and as new medicines in the mainstream pharmaceutical market of the 21st century.

Production of Herbal Products by Direct Compaction

Yolande ANTHONY, Ph.D.
ISP Asia Pacific Pte. Ltd.
Singapore

BIOGRAPHY

International Specialty Products (ISP) is one of the world's premier specialty chemical companies, which develops and manufactures innovative products for customers in a diverse range of industries. Dr Yolande Anthony has been with ISP Asia Pacific Pte Ltd, Singapore since 1994. Prior to this position, she held various senior administrative posts in Singapore and was also Technical Manager, Centre for Drug Formulation Studies, University of Bath, UK from 1984-1990. She has also held various research positions in industry and government organizations in the United Kingdom.

She obtained her Ph.D in Pharmaceutics at the University of Bath, UK and has a B.Sc. (Hons) Microbiology from the University of Bristol, UK.

ABSTRACT

In recent years, there has been an increasing trend in the usage of herbal remedies. Herbal teas and extracts, medicinal wines and pills are some common examples of traditional herbal dosage forms. Other suitable techniques in processing herbal substances into various dosage forms for added consumer convenience are also being explored. Herbal materials may be formulated into granules and then further processed into capsules or tablets, the most common pharmaceutical dosage forms available today.

There are several techniques for producing granules. Granulation is a size enlargement process where small particles are converted into larger, physically strong agglomerates. The more widely used technique to produce granules is by the wet granulation process. A granulating liquid is used. High shear mixers and fluid bed processors are commonly used equipment associated with wet granulation.

Granulation can also be carried out without the use of a liquid binder (granulating liquid). Such techniques re-classified as dry granulation methods. Dry granulation includes slugging and roller compaction. In compaction, enlargement is followed by reduction where dry compacted materials are broken down into smaller granules. In addition, no granulating liquid is required.

Roller compaction is a continuous process that offers high-volume production, better process control and efficiency. Roller compaction is a useful alternative when the powder blends do not possess properties such as good flow, compressibility and minimal powder segregation, which are essential for direct compression into tablets. A homogenous blend of drug substance and excipients are compacted between two counter rotating rollers of a compactor to form sheets, ribbons or briquettes of compacted materials. The compacts are appropriately processed and finally used for tableting or capsule filling.

For moisture sensitive material, dry granulation offers many advantages. In the case of herbal tablets, the high content of natural polymer can adversely affect its tablet disintegratibility when prepared by wet granulation. Roller compaction confers many advantages on the preparation of herbal solid dosage forms.

This study is conducted to investigate the viability of compacting herbal substances using roller compactor technology. *Baphicacanthus cusia* (*isatis* root) was selected as a model herb for comparison with lactose, a widely used pharmaceutical excipient. The root was first milled into powder and subsequently compacted. The compacted materials were then granulated through a 1.25 mm aperture sieve and the granules were characterised. The effect of varying the concentration of two binders, Plasdone® K-25 and Plasdone® S-630 on the compactibility of these materials was also investigated. Preliminary results showed that direct compaction of herbal powders was feasible with optimisation of processing and formulation parameters.

Continuous High Throughput Extraction

Ole G. KJAERGAARD, M.Sc.
Niro A/S
Soeborg, Denmark

BIOGRAPHY

Ole G. Kjaergaard graduated from the Danish Technical University in 1967 with a M.Sc. in Chemical Engineering. After military service, he joined the Niro Atomizer Research & Development Department in 1969, specialising in design and performance of industrial solid/liquid extractors, spray dryers and fluid-bed dryers. He has been closely involved in all aspects of extraction and drying technology including mathematical modelling, pilot plant testing and commissioning of industrial units. For 12 years, he managed the pilot plant facilities of Niro Inc. (Maryland, Ú.S.A.) and Niro A/S (Copenhagen, Denmark). He is presently Process Design Manager in the Food Projects Division at the main office of Niro A/S in Copenhagen.

ABSTRACT

The Niro CONTEX™ features true continuous counter-current extraction:

The solids to be extracted are fed by gravity or metered by volume to the lower end of the elongated process-vessel and are transported through the extractor by means of two counter-rotating helicoidal screws with a controlled slip. The material passes in the form of two cylinders, rotating at about half the speed of the transporting screws.

The fresh extraction liquid enters the top-end of the slightly inclined vessel and flows by gravity down through the solid material as a controlled, submerged stream in the bottom half of the cross-sectional area, through the slowly rotating, on-coming solid material.

The speed of the screws is adjusted to give the desired residence time for the extraction of the solids. The amount of liquid is adjusted to give an optimum concentration of the extract, and finally the inclination of the vessel is adjusted to sustain the liquid flow.

The extract leaves at the lower end through a special, self-cleaning filter and a level-controlling reservoir. The extracted solids are slightly squeezed at the top end and discharged.

The process can easily be adjusted and automatically controlled. Scale-up from pilot plant tests is simple with liquid velocity as the only limitation. A high concentration extract and a high yield can be obtained simultaneously. The residence-time distribution of both solids and liquid is very narrow.

The solids are only submerged into the liquid half of the time in 10-15 passages of the lower part of the vessel. But as extraction is diffusion controlled, all the residence time is in fact used. The over-all efficiency equals that of a system with 3 to 5 ideal counter-current equilibrium/ separation stages.

The process has been successfully used for many beverages and pharmaceuticals extracted from all kinds of vegetable materials such as leaves, stems and roots. The solid material must be cut, milled, rolled or shredded as fine as possible to speed-up the extraction, however with a maximum of around 10% by weight passing 1 mm due to the built-in filter and in order to limit the resistance to the gravity-driven percolation of the liquid. Organic solvents can also be handled.

Commercial units with up to 2.7 m^3 active volume and capacities in the range of 500-1000 kg/h raw material are available, with solids residence times in the 1/2 to 2 hour range.

Application of Spray Drying Techniques in Herbal Product Manufacturing

Ole G. KJAERGAARD, M.Sc.
Niro A/S
Soeborg, Denmark

ABSTRACT

Spray Drying is a unique, direct one-step transformation of a liquid (with dissolved or suspended solids) into a dry powder.

The process is a convection type or "suspended particle" dryer as the solvent is removed by evaporation, using a large volume of drying gas for heat transfer and as vapour-carrying medium. The advantages of being a one-step, very low residence time and product-shaping drying process, makes it one of the preferred processes for food and pharmaceutical products in powder form. In some cases, spray drying is the only way to a dry product with sufficient preservation of all functional properties. The final product with tailored physical properties such as free-flow, re-wettability or coating and encapsulation-protection is obtained directly from the spray dryer.

The process involves the stages of:

- atomization of the liquid into small droplets by various mechanisms,
- contacting the spray with the hot drying gas in a suitably shaped drying chamber,
- evaporation under controlled low temperature and short residence time conditions,
- collection of the dry product from the drying chamber and exhaust air cleaning devices.

Depending on the properties of the solid and the specification of the final powder properties, the optimum combination of atomization principle, contacting pattern and temperatures can be selected.

Even the simplest, basic spray dryer design would be capable of producing a saleable powder, a powder for dry-mixing or for tabletting.

Spray dryers for heat sensitive food- and pharmaceutical products with more complex powder specifications often involve the more sophisticated designs including fluid-bed- or conveyor-belt- post-drying stages.

Modern spray dryers can be fully equipped with

- closed cycle inert drying gas loop for drying of flammable or expensive solvents
- fire- and explosion protection systems
- Cleaning-In-Place systems
- and any degree of automatic or computerised control system.

If necessary, the spray drying system can be built to any sanitary or sterile requirement and can be fully documented and validated.

Establishing Evidence in Chinese Medicine: Evaluating the Chinese Herbal Treatment of Irritable Bowel Syndrome

Alan BENSOUSSAN, M.Sc.
University of Western Sydney
Penrith South DC, NSW, Australia

BIOGRAPHY

Alan Bensoussan heads the Chinese Medicine Program at the University of Western Sydney, Australia. He has been in clinical practice in Chinese medicine for 18 years and is an active clinical researcher. Alan has attracted funding from industry, state health departments and the National Health and Medical Research Council. He acts in an advisory capacity for both government and industry, including the Complementary Medicines Evaluation Committee of the Therapeutic Goods Administration, and has served as a short-term consultant to the World Health Organisation. He sits on a number of relevant committees and boards, including the international editorial boards of *Complementary Therapies in Medicine* (Churchill-Livingstone), and *Focus on Alternative and Complementary Therapies* (Pharmaceutical Press, UK). He has published two books including a major government report on the practice of traditional Chinese medicine in Australia.

ABSTRACT

Background. Traditional Chinese medicine (TCM) is now used by a broad cross-section of the western community. However, despite its increased utilization, there is debate as to its evidence base. Few TCM trials have been performed in the West, and previous Chinese TCM trials have been perceived to lack methodological rigor.

Methods. A clinical trial was designed using a variety of approaches to promote methodological rigor whilst allowing the flexibility required in TCM practice. Irritable bowel syndrome (IBS) was selected as the disease focus, creating the possibility of tailoring TCM treatments to the variable clinical presentations of IBS. Patients were randomized to receive individually tailored treatment (n=38), a standard Chinese herbal formulation (n=43), or placebo (n=35) for 16 weeks. Patients, gastroenterologists and herbalists were all blinded as to treatment group.

Results. Both standard and individualized treatments were significantly more effective than the placebo treatment on all key outcome measures. However, this study failed to confirm the added value of tailoring treatments. Chinese herbal formulations individually tailored to the patient proved no more effective than the standard treatment on all measures. Nevertheless, the trial demonstrates it is possible to test individualization of treatment whilst adhering to conventional trial protocols.

Conclusions. Clinical trials can be designed that accommodate nuances of TCM practice. This study also shows Chinese herbal medicine may offer assistance to some patients with IBS and may prove as effective as current pharmaceutical approaches. Further validation of TCM interventions in required.

Full reference

Bensoussan A, Talley NJ, Menzies R et al. Treatment of irritable bowel syndrome with Chinese herbal medicine: a randomised controlled trial. *JAMA*. 1998; 280(18):1585-89

Use of Porcine Relaxin for the Treatment of Untreatable Diseases Such as Fibromyalgia

Samuel YUE, M.D.
HealthEast Pain Clinics
St. Paul, Minnesota, U.S.A.

BIOGRAPHY

Name: Samuel Ka-Sheng Yue, M.D.
Business Address: HealthEast Pain Clinic
559 Capitol Blvd.
St. Paul, MN 55103, USA
Phone: 612-232-2319
Fax: 612-232-2328
email: sky97@sprynet.com

Education
Augsburg College, Minneapolis, MN, USA: B.A. June 1967
University of the East Ramon Magsaysay Medical Center, Philippines: M.D. 1978

Hospital Appointments
Clinical Medical Director: HealthEast Pain Clinic, St. Paul, MN, USA, 1991-present

Certification
American Board of Anesthesiology, 1987

Licensure
State of Minnesota: Medicine and Surgery
State of Iowa: Medicine and Surgery

Presentations and Workshops 1991-2001
Numerous workshops and presentations in "Botulinum Toxin Use in the Treatment of Pain. Associated with Muscle Dysfunction".
Numerous workshops and presentations in " Relaxin: Its Role in the Pathogenesis of Fibromyalgia".

Patents and Investions
Patent No. 326,153 SKY Epidural Catheter for an ambulatory infusion pump. May, 1992.
Patent No. 5,551,424 Fetal Probe Apparatus. September, 1996.
Patent No. 5,612,051 Method of Treating Involuntary Muscle Dysfunction with Relaxin Hormone. March, 1997.
Patent No. 5,707,642 Method of Treating Fibromyalgia with Relaxin. January, 1998.
Inventor: PRECISE infusion pump.
Inventor: INFUSTHERM portable and disposable fluid and blood warming device through exothermal chemical reaction.
Co-inventor: Pulse Oximetry Fetal Monitoring Device.

Clinical Research
Clinical Investigator: A Multicenter, Double-Blind, Placebo-Controlled, Parallel, Graduated-Dose Clinical Trial of BOTOX® (Botulinum Toxin Type A) Purified Neurotoxin Complex for the Treatment of Chronic Low Back pain.
A Phase II Study of Safety and Efficacy of Subcutaneous Continuous Infusion of Recombinant Human Relaxin for 8 Weeks in Patients with Fibromyalgia.

ABSTRACT

Relaxin

- 6000 dalton insulin-like hormone.
- Known as the 3rd major pregnancy hormone.
- Also occurs in every woman's menstrual cycle as the third hormone besides estrogen and progesterone.
- Secretes from the ovaries in female and seminal tubule in male.
- 5 days after luteal phase in the menstrual cycle.
- Lasts 3-5 days and peaks at 80-100 picogram/mL.
- If conception occurs, the level goes up 10 times to 800-1000 picogram/mL and slowly decreases to 400-500 picogram at the 3rd trimester.
- In male the serum level is too low to be detected with the present tests.
- But is detectable in the semen - 200 nanogram/ejaculate.
- Porcine relaxin was an FDA approved drug from 1950-1972.
- Indications - Scleroderma, peripheral vascular diseases, PMS, cervical induction of labor and others.
- Taken off the market by FDA in 1972 for **lack of proof of efficacy** and not safety (Kefauver-Harris Drug Amendments 1962).
- Porcine relaxin is approx. **6-10** times more potent than human relaxin.
- Pregnant fibromyalgia patients report complete to good remission of their pain and associated symptoms.
- Return of their symptoms usually ½ month after delivery.
- Increase of symptoms 1 week before and during menstrual cycle.
- Increase of symptoms during and after menopause.

Hypothesis - Relaxin

- Clinical experience of porcine relaxin in treating fibromyalgia patients:
  - **60-70% success rate in female**
  - **20-30% success rate in male**

Relaxin Other Usage

- Hormonal replacement in menopause:
  - Hormone replacement when estrogen and progesterone did not alleviate all the symptoms.
  - The missing hormone of the menopausal women during replacement.
- Adjuvant for adult onset diabetes type 2.
- Porcine relaxin reduces the insulin requirement of insulin dependent diabetes by 30-40 %.
- Reduces oral antihypoglycemic agents by 40-50 %.
- Normalize glucose intolerance in hypo/hyperglycemic patients.
- Therefore porcine relaxin affects the **insulin resistance** of pre-diabetic and diabetic patients.

- Clinical observations suggest that porcine relaxin may also affect and prevent many of the complications associated with AODM.
- Other usage:
  - Many untreatable diseases seem to improve during pregnancy.
    - Multiple Sclerosis, Rheumatoid arthritis, Lupus, Parkinson's disease, Dystonia, and others.
  - Pregnancy Cx?
  - Osteoporosis and osteoarthritis?
  - Anti-aging?

Efficacy and Safety of Ja Wai Ophiopogon Decoction in the Treatment of Allergic Asthma

HSU Ching-Hsiang, M.D., Ph.D.
China Medical College
Taichung, Taiwan

BIOGRAPHY

EDUCATION:

9/1981- 6/1988	Chinese Medical College, B.S. in Medicine
9/1993- 6/1996	Graduate Institutes of Immunology & Microbiology, National Taiwan University, Ph.D. in Immunology

PROFESSIONAL EXPERIENCE:

6/1990-8/1993	Residency, Mackay Memorial Hospital, Taipei
9/1993-5/1996	Attending Physician in Pediatrics, St. Paul Hospital, Taiwan
6/1996-Present	Director of Pediatric Departments, God's Help Hospital, Taiwan
6/1997-Present	Associate Professor, Chinese Medicine Institute

BOARD CERTIFICATION:

1. Specialist of Pediatrics
2. Specialist of Neonatology
3. Specialist of Emergency Medicine
4. Specialist of Allergy and Clinical Immunology

PROFESSIONAL ACTIVITIES:

1. Member, The Society of Pediatrics
2. Member, The Society of Neonatology
3. Member, Infectious Disease Society of the Republic of China
4. Member, The Society of Ultrasound in Medicine
5. Member, The Formosan Medical Association

Summary of Research Experience

1. Establishment of an animal model for the study of atopic dermatitis
   I and my colleagues establish first animal model for atopic dermatitis induced by allergen.
2. Prevention and treatment of allergic disease by direct allergen-gene transfer
   I and my colleagues has successfully demonstrated that direct gene transfer (gene therapy) could treat and prevent IgE-mediated allergic diseases including atopic dermatitis and airway hyperreactivity. This is a major breakthrough in the treatment of allergic diseases.
3. To investigate the working mechanisms of tradition Chinese medicine in the treatment of allergic diseases.

ABSTRACT

Objective To investigate the benefits and adverse reactions of traditional herbal medicine Ophiopogon decoction in the treatment of allergic asthma.

Design Double-blind, placebo-controlled, randomized trial.

Patients One hundred and twenty patients between the age of 5 to 50 years with mild and moderate asthma.

Intervention Treatment with Ophiopogon-1 decoction, Ophiopogon-2 decoction, or placebo in the dose of 800 g/kg/day, administered twice daily for 4 months.

Main outcome measures Daily diary record of symptoms, supplemental bronchodilator and glucocorticoid treatment, changes of pulmonary function (forced expiratory volume in 1 second), changes of total and *Dermatophagoides pteronyssinus* -specific IgE, and side effects.

Results Ophiopogon-1 decoction was effective primary treatments for mild to moderate chronic asthma. Ophiopogon-1 decoction resulted in statistically significant reduction of symptom scores, systemic steroid dose, total IgE and specific IgE. In addition, STA-1 also improved significantly the pulmonary lung function FEV_1 as compared to placebo and Ophiopogon-2 group. All groups showed minimal side effects.

Conclusions Ophiopogon-1 decoction is effective therapy for mild to moderate asthma.

Pyrrolizidine Alkaloid Metabolism Induced Hepatotoxicity and Prevention of Such Toxicity by Herbal Medicines

Ge LIN, Ph.D.
Chinese University of Hong Kong
Shatin, Hong Kong

BIOGRAPHY

Qualifications

Ph.D. ***Drug Metabolism and Pharmacokinetics***
College of Pharmacy, University of Saskatchewan, Saskatoon, Canada, 1992

M.Sc. ***Natural Product Chemistry***
Department of Chemistry, University of Alberta, Edmonton, Canada, 1988

B.Sc. ***Pharmaceutical Sciences***
College of Pharmacy, China Pharmaceutical University, Nanjing, China, 1982

Main Research Interests/Fields of Specialism

1. Drug metabolism and pharmacokinetics; especially in metabolism-induced toxicity.
2. Investigation of Traditional Chinese Medicinal (TCM) herbs, including phytochemistry, developments of analytical and quality control methods, pharmacology, pharmacokinetics and metabolism of bioactive ingredients in TCM herbs.

Working Experience

1993-present	***Associate Professor (1997); Assistant Professor (1996); Lecturer (1993)*** Department of Pharmacology, The Chinese University of Hong Kong, Hong Kong
1992-1993	***Postdoctoral Fellow***, College of Pharmacy, University of Saskatchewan, Saskatoon, Sask., Canada
1988-1992	***Research Assistant***, College of Pharmacy, University of Saskatchewan, Saskatoon, Sask., Canada
1985-1988	***Research Assistant***, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada
1982-1985	***Assistant Lecturer***, Department of Traditional Chinese Medicinal Pharmacology, China Pharmaceutical University, Nanjing, P. R. China

Publications

Number of **patent** allowed	**1**
Number of **patent** applied	**3**
Number of **paper** published in peer-refereed international journals	**40**
Number of **paper** submitted	**7**
Number of **invited review article** submitted	**1**
Number of **abstract** published and presented in international conferences	**65**
Number of **invited speech**	**9**

Membership of Academic Societies:

- Member of International Society of Study of Xenobiotica (ISSX)
- Member of American Association of Pharmaceutical Scientist (AAPS)
- Member of American Chemical Society (ACS)
- Member of Hong Kong Pharmacology Society (HKPS)
- Member of Hong Kong Society of Mass Spectrometry (HKSMS)
- Member of Hong Kong Society of Traditional Medicine and Natural Product Research

Service to the Profession/Community:

- Fellow of Institute of Chinese Medicine, CUHK
- Fellow of Epithelial Cell Biology Research Centre, CUHK
- Member of Chung Chi Campus Environment Committee and Monitoring Sub-Committee of Campus Environment Committee
- Referee for international journals of *Phytochemical Analysis* and *Journal of Chromatography*
- Invited Supervisor for Ph.D. students at China Pharmaceutical University, P. R. China
- External Examiner of Ph.D. students at China Pharmaceutical University, P. R. China

ABSTRACT

Pyrrolizidine alkaloids (PAs) naturally occur in various plants and medicinal herbs. Many PAs are hepatotoxins and responsible for a serious health problem to livestock and humans worldwide. Hepatotoxic PAs are classified into two types: the retronecine-type and the otonecine-type. The mechanism of inducing hepatotoxicity for the former type PA has been extensively investigated and is believed to be due to the formation of reactive pyrrolic metabolites and covalent binding of such metabolites with cellular macromolecules in the liver. However, with respect to the otonecine-type PA, the mechanism of metabolism-induced hepatotoxicity is not understood yet.

Investigation into the otonecine-type PA induced hepatotoxicity and prevention of hepatotoxicity caused by both types of PAs has been carried out in our research group. Using clivorine, a representative hepatotoxic otonecine-type PA isolated from a traditional Chinese medicinal (TCM) herb, as the substrate, the hepatic metabolism of otonecine-type PA was investigated, and the unstable pyrrolic metabolites formed from clivorine were unequivocally identified. The results provide the firmest evidence to date to support that the mechanism of hepatotoxicity induced by otonecine-type PAs involves similar key metabolic steps as retronecine-type PAs in involving the formation of reactive pyrrolic metabolite(s) and covalent binding of such pyrrolic metabolite(s) to cellular macromolecules. This pyrrolic metabolite generated from otonecine-type PA likely arises *via* initial *N*-demethylation followed by ring closure to an unstable carbinolamine, which dehydrates spontaneously to a toxic pyrrolic metabolite.

PA-containing plants are widespread throughout the world and responsible for extensive poisoning of humans and livestock, investigation of the protection of PA-induced hepatotoxicity becomes more and more important. Our research team has also investigated the prevention of PA-induced liver damage by TCM herbs. In the present presentation, the prevention of PA-induced hepatotoxicity in male Sprague Dawley rats by two principal ingredients of liquorice, is also reported. Liver damage was produced by retrorsine, a retronecine-type PA. The effects of these two active ingredients of liquorice on PA-induced liver damage were then determined by both histological assessment and measurement of serum transaminase levels (i.e. ALT and AST). The results demonstrated that multiple-dose pretreatment with active liquorice components produced hepatoprotective effect against PA-induced liver damage in rats. However, a single dose pretreatment with these two active ingredients did not show such protection. Therefore, liquorice may have a potential role to play in protecting animals and humans against PA-induced hepatotoxicity when it is used appropriately. (This research project was supported by the research grant council of Hong Kong: Earmarked Research Grant CUHK 415/95M)

Strategy on the Research and Development of Herbal Medicine: An Example on the Development of Antidepressant Herb

Feng-Nien KO, Ph.D.
Pharmaceutical Industry Technology and Development Center
Hsi Chih City, Taiwan

BIOGRAPHY

5F, No. 101, Lane 169 Kang Ning St.,
Hsi Chih City, Taipei Hsien, Taiwan
Tel: (02) 2692-2103 ext. 132; Fax: (02) 2695-4538

Education:

Kaohsiung Medical College	B.S.	1983	Pharmacy
Pharmacological Institute, College of Medicine, NTU	M.S.	1987	Pharmacology
Pharmacological Institute, College of Medicine, NTU	Ph.D.	1990	Pharmacology

Professional Experience:

1991-1993	Lecturer, Pharmacological Institute, College of Medicine, NTU
1993-1998	Associate Professor, Pharmacological Institute, College of Medicine, NTU
1998-1998	Researcher, Planning Division, Pharmaceutical Industry Technology and Development Center
1998-1999	Deputy Chief, R & D Division, Pharmaceutical Industry Technology and Development Center
1999-present	Chief, R & D Division, Pharmaceutical Industry Technology and Development Center

ABSTRACT

Recently, herbal medicine plants may be a potential fast renewable source for new pharmaceuticals or nutraceuticals has attracted many pharmaceutical companies and scientists to join this venture. Traditional Chinese Medicine (TCM), has been used in Chinese for thousands of years, is a treasure for Chinese. It has been consumed by a large human population as herbal medicine, and their efficacy has recorded experientially or proven clinically. Pharmacological screening and evaluation of the activities of TCM against a specific target, in an experience- and literature-directed manner, can increase the potential for the discovery of new pharmaceutical and nutritional products.

Some of the traditional Chinese herbal medicines were classified and used as tranquilizers clinically. Although these herbal tranquilizers are usually used to treat insomnia, dreaminess, amnesia, palpitation, frightening and irritability, their actual effects on disease(s) were not well evaluated. In a preliminary screening test, elevated plus maze and tetrabenazine (TBZ)-induced hypothermia were used to study the possible anti-anxiety and anti-depression activities of these herbal tranquilizers.

One of the extract (PDCext.), derived from the Chinese herbal tranquilizers, alone had no effect on the body temperature, inhibited TBZ-induced hypothermia in a dose-dependent manner with an EC_{50} estimated to be around 0.5 g/kg. It also suppressed reserpine-induced hypothermia and ptosis dose-dependently. In contrast, PDCext. did not induce or inhibit apomorphine-caused climbing behavior in mice, possess 5-HT_{1A} agonistic activity or have effects in the elevated plus maze model. It neither inhibited the serotonin transporter directly and uptake of 5-HT in recombinant HEK-293 cells, nor potentiated the activity of 5-HTP in mice. However, PDCext. suppressed dopamine and norepinephrine uptake in recombinant CHO-K1 and MDCK cells concentration-dependently with EC_{50} values estimated to be 6.7 and 4.6 μg/ml, respectively. It is concluded that the possible anti-depression activity of PDCext. is mainly mediated by the inhibition of dopamine and norepinephrine reuptake.

The GMP Inspection and Licensing System of Singapore

SIA Chong Hock, M.Sc.
National Pharmaceutical Administration
Singapore

BIOGRAPHY

EDUCATIONAL QUALIFICATIONS

M.Sc. (Health Care Management), University of Wales, Swansea - 1997
B.Sc. (Pharmacy), University of Singapore - 1979

PRESENT POSITION

Deputy Director, Division of Manufacturing and Quality Audit, Centre for Pharmaceutical Administration, Singapore Health Sciences Authority

WORK HISTORY

Assistant Director, Good Manufacturing Practices & Licensing Unit, Singapore National Pharmaceutical Administration (1 April 1997 to 31 March 2001)

Acting Divisional Director, Drug Administration Division, Singapore National Pharmaceutical Administration (1998 to 2000)

Regulatory Pharmacist, Drug Administration Division, Pharmaceutical Department, Singapore (1990 to 1997)

Department of Pharmacy, Alexandra Hospital, Singapore (1987 to 1990)

Singapore Government Production Laboratories (1980 to 1987)

ACADEMIC AFFILIATION

Part-time Lecturer in Forensic Pharmacy, Department of Pharmacy, National University of Singapore (1995 to 2000)

Member, Board of Examiners, Singapore Pharmacy Board (1995 to 2000)

OTHER APPOINTMENTS

- Secretary, Quality Control Advisory Committee, Ministry of Health
- Chairman, Staff Well-Being Committee, National Pharmaceutical Administration
- Chairman, Legislation Task Force, National Pharmaceutical Administration (1 May 1999 to 31 July 1999)

- Member, Quality Assurance Advisory Committee, Singapore Productivity and Standards Board (PSB)
- Member, Technical Committee on Biological and Chemical Testing, Singapore Accreditation Council-Singapore Laboratory Accreditation Scheme (SAC-SINGLAS)

ABSTRACT

The Good Manufacturing Practices (GMP) and Licensing Unit of Singapore was formed in April 1997 within the National Pharmaceutical Administration (NPA) of the Ministry of Health. The principal function of the GMP and Licensing Unit is the inspection and licensing of manufacturers and importers/wholesale dealers of medicinal products (including traditional Chinese medicines) in accordance with current international GMP and GDP (Good Distribution Practices) standards respectively. The main objective of these inspection and licensing activities is to ensure that manufacturers consistently produce good quality medicines and the quality of the products is preserved down the supply chain from the manufacturers to the distributors, pharmacies, medical halls and other retail outlets.

Effective 1 January 2000, Singapore has become the first Asian country to accede to Pharmaceutical Inspection Co-operation Scheme (PIC/S). PIC/S comprises participating authorities with equivalent high standards of GMP inspection. Currently its members include the European Union countries, Australia, Canada and Switzerland. Earlier on in September 1999, the GMP and Licensing Unit was also certified to the ISO 9002 standard by the Singapore Productivity and Standards Board (PSB). With membership of PIC/S, Singapore is now in a position to pursue Mutual Recognition Agreements (MRAs) with other countries. The status of Singapore as a life sciences and pharmaceutical hub would be enhanced, and greater acceptance of the quality of pharmaceutical products manufactured and exported from Singapore can be expected.

The main challenges for the inspection and licensing agency (as well as for the industry) revolve around their ability to function in a knowledge-based economy, to ride on the wave of the life sciences revolution, and to respond to the rapidly-changing global environment. For the inspection and licensing agency, these challenges include :

(a) building up our capabilities in the field of GMP inspection for biologicals and biotechnology-derived medicinal products, Active Pharmaceutical Ingredients (APIs), herbal and traditional medicines and validation of computerised systems used in pharmaceutical manufacturing.

(b) possessing the ability to recruit and retained qualified and experienced GMP inspectors who are capable of auditing large and often complex pharmaceutical and biotechnology manufacturers, as well as a diverse group of smaller companies.

(c) levelling up the generic pharmaceutical, herbal and other traditional medicines industry in Singapore to meet international GMP, GDP and other quality system standards.

Status of Herbal and Traditional Medicines in Thailand

Garnpimol C. RITTHIDEJ, Ph.D.
Chulalongkorn University
Bangkok, Thailand

BIOGRAPHY

ADDRESS Faculty of Pharmaceutical Sciences,
Chulalongkorn University
Phayathai Road, Bangkok 10330, THAILAND
Telephone: (662) 218-8272, (662) 218-8276
Fax: (662) 218-8279
E-mail: rgarnpim@chula.ac.th

PROFESSIONAL EXPERIENCE

Jan. 1998 - Present	Chair, Dept. Industrial Pharmacy, Fac. Pharm. Sci., Chulalongkorn University, Thailand
Dec. 1993 - Dec. 1997	Associate Dean-Research Affairs, Fac. Pharm. Sci., Chulalongkorn University, Thailand
Dec. 1990 - Present	Associate Professor, Fac. Pharm. Sci., Chulalongkorn University, Thailand
Nov. 1985 - Dec. 1990	Assistant Professor, Fac. Pharm. Sci., Chulalongkorn University, Thailand
Mar. 1983 - Nov. 1985	Lecturer, Fac. Pharm.Sci., Chulalongkorn University, Thailand
Nov. 1980 - Sept. 1982	Research Assistant, School of Pharm. and Health Sci., St. John's University, New York
Jan. 1980 - Nov. 1980	Chemist, Ketchum Laboratories, New, York

RESEARCH INTEREST

1. Drug delivery systems
2. Chitosan as pharmaceutical excipient
3. Membrane Technology

RESEARCH PRESENTATIONS & PUBLICATIONS

About 40 articles

PROFESSIONAL EXPERIENCES

WHO'S National Consultant: Guideline on "Product Development Recommendations for Solid Dosage Forms" 1993-1994

Chairman, Conference of the 80th Anniversary of the Pharmaceutical Education in Thailand, June 1994.

Chairman, 12th Annual Symposium on Pharmaceutical Sciences, Thailand, December 1995.

WHO'S National Consultant: Guideline on "Product Development Recommendations for Liquid Dosage Forms" 1995-1996

Chairman, 13th Annual Symposium on Pharmaceutical Sciences, Thailand; December 1995.

Visiting Professor, Faculty of Pharmaceutical Sciences, Hoshi University, Japan, 1996

Co-chairman & Symposium secretary-general, 11th International Symposium on Microencapsulation, August 1997.

PROFESSIONAL MEMBERSHIPS

President, Controlled Release Society, Thailand Chapter (1996-present)
Treasurer, The Sigma Xi Society, Thailand Chapter, (1994- present)
Executive committee, International Microencapsulation Society (1997-1999)
Member, American Association Pharmaceutical Scientists, (1978- present)
Member, Pharmaceutical Association of Thailand under the Royal Patronage, (1976- present)
Member, Thai Society of Industrial Pharmacists, (1983-present)
Member, Rho Chi Honor Society (1979- present)

EDUCATION

Doctor of Philosophy (Ph.D.), Industrial Pharmacy, College of Pharmacy and Allied Health Sciences, St. John's University, Jamaica, New York. (Sept. 1979 - Sept. 1982)
Master of Science (M.S.), Pharmacotherapeutics, A&M Schwartz College of Pharmacy, Long Island University, Brooklyn, New York. (Jan. 1977 - May 1979)
Bachelor of Pharmacy (B.Pharm.), Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok. (June 1971 - April 1976)

ABSTRACT

Using of herbal and traditional medicine has been continually recorded since the early kingdom of Thailand in the thirteenth century. The first Thai Traditional Pharmacopoeia in the seventeenth century had included garlic, nutmeg, ginger, Siam cardamom and pepper vine. More than 1000 herbal medicines were stone inscribed in the nineteenth century along the corridor of Temple Po, which was the so-call first university in Bangkok. Since modernization or westernization invaded the country in the early twentieth century, the popularity of herbal medicine was drastically decreasing[1]. In 1999, the consumption of herbal medicine was only 1.35% of the total consumption of medicine. Thanks to the recent economy crisis in Thailand and the World Health Organization who recently has promote the use of herbal medicine in the national health care system in members' country that Thai herbal and traditional medicine have been brought back to attention.

In Thailand, 95% of consumed herbal medicines are used as crude drug, crude extract and semi-purified extract, of which 10-20 % are imported. Only 5% are used as purified constituents. The commonly used herbs are roselle, garlic, nutmeg, ginger, Siam cardamom, turmeric, asafetida pepper vine, elephant's apple, senna and lemongrass. Their efficacy is claimed including anti-inflammatory, diuretic, anti-emetic, anti-tussive, laxative, and lipid regulator. They are marketed in various forms such as powder, decoction, extract, granules, pellets, capsule ointment, lozenges and tablets.

Imported herbal medicines are mostly focused on health food products which are divided into two types, organic natural food and dietary supplement product. Both are claimed as nutraceuticals and phytoceuticals, respectively. The neutraceuticals are marketed as powder for reconstitution, tablet, granule and soft gelatin capsule whereas the phytoceuticals are tablet and capsule. Export of Thai spices and herbal products has reached 20 million US dollars / year. Most of them are exported as crude drug. The amount is considered very low compared to those from China, India or Zaire eventhough the climate and geography flavor growing herbal or medicinal plants. The main reasons are low content of active constituents, lack of

standardization, different species from the required ones, uncertain productivity and high price. Qualified herbal medicine should be produced through 5 processes, good agriculture practice, good harvesting practice, good manufacturing practice, good laboratory practice and good clinical practice. Even though Thailand is considered as an agriculture country, the first two processes have many variations and need to be scientifically controlled.

Although modern machine or equipment are now allowed to be used in the production of herbal products but most formulations and preparations are still traditional and using low technology. In 1998, more than 5000 formulations of herbal and traditional medicine were officially registered from 626 companies. Only about 10% of these companies manufacture their products following the GMP guideline whereas 85% of the manufacturers of modern medicine are GMP certified. Officially, synthetic chemicals cannot be incorporated in solid herbal medicine such as powder, granule, tablet, capsules or pellet. However, various herbal compounds are fortunately to have additive properties whether of disintegration, binding or lubricating. In liquid herbal preparations, only the benzoates are allowed to be added as preservatives in extract or decoction. Microbial contamination needs to be controlled for safety use of these preparations. The quality control of herbal medicine is very crucial. The determination of the claimed amount of active constituents is to assure the efficacy of the products. To date, 66 herbal medicines are being standardized. Several Thai compendia and textbooks have specifications on herbal medicine or chemical from herbal plants such as Thai Pharmacopoeia, Thai Herbal Pharmacopoeia, and Specification of Thai Medicinal Plants.

Hospitals under the public health care system have been promoted to use herbal and traditional medicine. Forty-seven types in various forms of preparation have been suggested. These includes ginkgo, shallot, guava, candle brush, pomegranate, safflower, soapberry, Indian snakeroot, heavy basil and Indian marsh fleabane. Several hospitals especially those in the rural area are now producing their own herbal medicine. Some even use them as alternative medicines such as Chaopaya Apaipubas Hospital uses capsule of *Cissus quadrangularis* Linn. instead of commercial anti-haemorrhoidal products.

Research and development on herbal medicine have been extensively conducted in universities and research institutions. However, most research work has emphasized on the finding and elucidating of new compounds. Only recently that studies on crude drug, crude extract and semi-purified extract are publicly accepted. These include garlic, *Andrographis paniculata* Nees, *Zingiber officinale Roscoe*, *Solanum trilobatum* Linn., *Zingiber cassumunar Roxb.*, and *Centella asiatica*. Moreover, various training courses, conferences and seminars on the production and application of herbal medicine are occasionally offered. Promotion from mass media also arouses the interest of people. National heritage and self-sufficiency become popular and in awareness. With cooperation from all sectors, Thai herbal and traditional medicine can be of full advantage.

Recent Developments of Herbal and Traditional Medicines in Taiwan

Chung-Gwo CHANG, M.D.
Committee on Chinese Medicine and Pharmacy
Taipei, Taiwan

BIOGRAPHY

Name:
Chang, Chung-Gwo, M.D. & C.M.D.

Business Address:
No. 6, Shuang Cheng St.
Taipei, Taiwan, R.O.C.
Tel: +886-2-25994326
Fax: +886-2-25994327
Mobile Phone: 0939084299

Education :

1974	China Medical College	M.D. & C.M.D.

Professional Experience:

1980~1983	Director	Department of Acupuncture, China Medical College Hospital
1981~1983	Director	Acupuncture Research Center, China Medical College
1983~1985	Superintendent	Kaohsiung Municipal Chinese Medicine Hospital
1986~present	Board Member Associate Professor	China Medical College
1988~present	Consultant	National Research Institute of Chinese Medicine
1989~present	Board Member & Secretary General	Li-Fu Foundation
1996~present	Board Member & Secretary General	China Traditional Medicine Research and Development Fund
1998~present	Chairman	Committee on Chinese Medicine and Pharmacy, Department of Health, Executive Yuan, Taiwan, R.O.C.

ABSTRACT

With liberalization of the global market, Taiwan needs to develop high-tech industry and puts great emphasis on originality to be able to cope with tough international competition. Due to the increase of population in favor of a natural lifestyle, the global market for Chinese herbal medicine has skyrocketed recently. Because Chinese herbal medicine is deeply rooted in our traditional culture, and because large amount of experience and documentation for its use have been accumulated here, therefore, we think Taiwan does have some advantage over western countries in developing and manufacturing Chinese herbal medicine. As a matter of fact, in 1995, the Executive Yuan of Taiwan announced its program for promoting biotech industry, and since then, some substantial measures have been taken. Subsequently, the Department of Economics has brought up a five-year project for technique development of Chinese herbal medicine industry in 2000. It is expected within the next five years, the government will devote much of its manpower and resources to this project. We hope, through all these efforts, we can build Taiwan as a high-tech island of Chinese herbal medicine and revitalize our sluggish high-tech industry.

Because of the complexity of their constitutes and big individual variations, the quality control of raw materials has always been a problem with Chinese herbal medicine, which often results in inconsistency of potency. The problem is further aggravated since about 90% of Taiwan's raw materials are imported from mainland China. Therefore, "how to maintain the quality of imported raw materials" becomes a big issue when we consider to further expand Taiwan's Chinese herbal medicine business. We understand, to resolve this, we have to utilize systematic management and modern technology, such as GAP, standardizing processing procedures and specifications, quantifying active or characteristic markers, to effectively monitor the quality of both raw materials and final products. So far, we have first work on raw materials step by step, and are establishing specifications and criteria for package, processing, microbial contamination, pesticide residue, and heavy metal content, etc. This year we have also set up a germplasm center for Chinese herbs, and urge the necessity of establishing a cGMP pharmaceutical factory for Chinese herbal medicine in Taiwan. Moreover, we are planning to set upoffshore quality control centers at major export cities of mainland China in the future for better control of raw materials,. We believe all these measure can eventually lay solid groundwork for our final goal, that is internationalization of Chinese herbal medicine.

In the past, the therapeutic effect of Chinese herbal medicine was always questioned by western doctors, due to lack of statistic data approved by clinical trials. Therefore, to help accelerate its global acceptance, the efficacy of Chinese herbal medicine has to be proved by clinical trials. At present, we have chosen several traditional and commonly used recipes of Chinese herbal medicine to verify their efficacy, and clarify their indication and contraindication through clinical evaluation. To encourage and facilitate manufacturers to invest in clinical study, we have also bulletined "Guideline on Examination and Registration of New Chinese Medicines" on July 29, 1998, which was further amended on October 20, 1999. In addition, from this year, we have financially supported hospitals to set up several clinical trial centers of Chinese medicine. Therefore, there will be more doctors and medical institutions to get involved in clinical evaluation of Chinese herbal medicine. We hope they can develop methods of clinical study, which not only scientifically show therapeutic effects but also retain philosophy of traditional Chinese medicine, and build the moment for further development of Chinese herbal medicine in Taiwan.

Besides promoting Chinese herbal medicinal products, we also encourage manufacturer to invest in health foods, plaster, and cosmetics developed form Chinese herbs. The time needed to bring these products into the market is rather short compared with a drug, but the potential markets for these products are huge. Hence, to help the industry in the process of developing these products, we are establishing guidelines on preclinical safety tests for plasters and cosmetics of Chinese herbs. We hope, by introducing these products into the market, the overall economic values of Chinese herbal medicine can be elevated, and the industry can gain some profits back to further develop their medicinal products.

Considering the major techniques of western drugs are controlled by western countries, the only possible way for Taiwan to develop pharmaceutical industry successfully is through Chinese herbal medicine. We believe that leading by government's strong promotion and policy, in conjunction with the efforts of industry and academia, the goal of internationalization of Chinese herbal medicine will be achieved in the near future.

The Impact of Legislation on Chinese Medicine in Hong Kong

Brad W.C. LAU, Ph.D.
Hong Kong University of Science and Technology
Clear Water Bay, Hong Kong

BIOGRAPHY

Addresses

- 17/A, 19 Village Road, Kam Shan Court, Happy Valley, Hong Kong
- 515, Meramec Station Road, St. Louis, MO 63021, USA

Education

- Northern Montana College, AA (Chemical Technology), 1971
- University of North Dakota, BS (Biology), 1972
- University of North Dakota, MS (Biochemistry), 1975
- University of North Dakota, Ph.D. (Biochemistry), 1979
- Washington University Medical Center, Fellowship Program in Clinical Chemistry, 1986-1988

Employment

- University of Chicago, Laboratory Assistant, Summer 1970
- University of North Dakota, Teaching Assistant, 1972-1974
- University of North Dakota, Research Assistant, 1974-1979
- US Department of Agriculture Human Nutrition Research Center, 1979-1982
- Syracuse University, Postdoctoral Fellow, 1982-1985
- Jewish Hospital, Washington University Medical Center, Research Fellow 1986-1988
- Sigma Diagnostics, St. Louis, USA, Senior Chemist, 1988-1993
- Hong Kong University of Science & Technology (HKUST), 1994-present

Awards

- State Board of Education Scholarship (State of Montana)
- Board of Higher Education Scholarship (State of North Dakota)
- Distinguished Young Investigator Award (1986), Academy of Clinical Laboratory, Physicians and Scientists

Professional Societies

- American Society of Biochemistry and Molecular Biology (1979)
- American Association for Clinical Chemistry (1986)
- Sigma Xi, The Society of American Scientists (1979)
- The North American Chinese Society for Clinical Chemistry (1986)
- Clinical Ligand Assay Society (1986-present), its Gateway Chapter, Board Member (1990-1992) & President-elect (1993)
- Drug Information Association (1997)
- Hong Kong Society for Traditional Medicine & Natural Product Research (1997)
- Modernized Chinese Medicine International Association (1999)

- Asia Anti-Aging Association (2000)

Experiences

- Subcommittee member, Chinese Medicine Council, Department of Health, Hong Kong Special Administrative Region Government, China (1997-present)
- Observer, WHO Conference of Traditional Medicine, Hong Kong (2000)

ABSTRACT

More than 75% of the population in Hong Kong take prescriptions from practitioners of the traditional Chinese medicine for the betterment of their well being as well as sicknesses. This "healthcare system" had been practiced in the past 150 years without much regulation or support from the former British colonial government. The quality of service was never scrutinized so long as there were no adverse effects reported in the public. Once the sovereignty Hong Kong returned to China in 1997, the new SAR Government decides to establish the legitimacy of Chinese medicine(s) through regulation (Department of Health) and development (Innovation & Technology Commission). In September, 1999 the Hong Kong Legislative Council formally passed the Draft of Chinese Medicine Ordinance which later established the Chinese Medicine Council to regulate the practice of CM practitioners and the use, manufacture and trading of Chinese medicines. The Chief Executive of the Hong Kong SAR Mr. Tung Che Wah proclaimed later in his second Policy Address that Hong Kong became the International Center of Chinese medicine(s) and CMs a value-added economy. More than HK$100 million were funded to tertiary institutes by the ITC in the past several years for the development of CMs.

The Chinese Medicine Council mapped out details of the ordinance for the CM practitioners in August 2000 and started to process the registration for the practitioners. After this ordinance is implemented, all practitioners who are not registered to the standards of the Department of Health are "listed practitioners" for a transitional period and deprive the privilege of prescribing certain listed CMs. Merchants and manufacturers of CMs will face stringent regulations once the details of ordinance for CMs are finalized in less than a year. Similar regulatory measurement for the western drugs such as GCP, GLP and GMP to guarantee safety, efficacy and stability will be applied to CMs registration.

It is conceivable that the quality of practitioners now might vary to a great extent after long years of neglect and lack of regulation in the past. Resentment is bound to surface no matter how lenient the new regulation is drafted. Registered practitioners will be a new breed of professionals qualified by stringent rules and education requirement, as under-qualified practitioners will be eliminated by choice in a matter of time. Likewise, the Chinese medicines industry will have to follow new guidelines to assure safety, efficacy and stability of their products through GMP and other quality-oriented practices. Huge expenditure of resources will be apparent to fulfil these requirements. The CMs industry now comes to the dilemma or crossroad of making CMs a sun-rising enterprise or a sun-setting business. It is not unique for CMs but genuinely correct across the board of pharmaceutics and nutraceutics businesses. One must follow the insurmountable tide of quality and make each product to the best of its standard to get good market coverage. Lest, one remains his status quo of inadequacy and loses his business to the qualified counterparts.

Developing Herbal Medicines as New Drugs: Regulatory Approaches in the Draft FDA Guidance

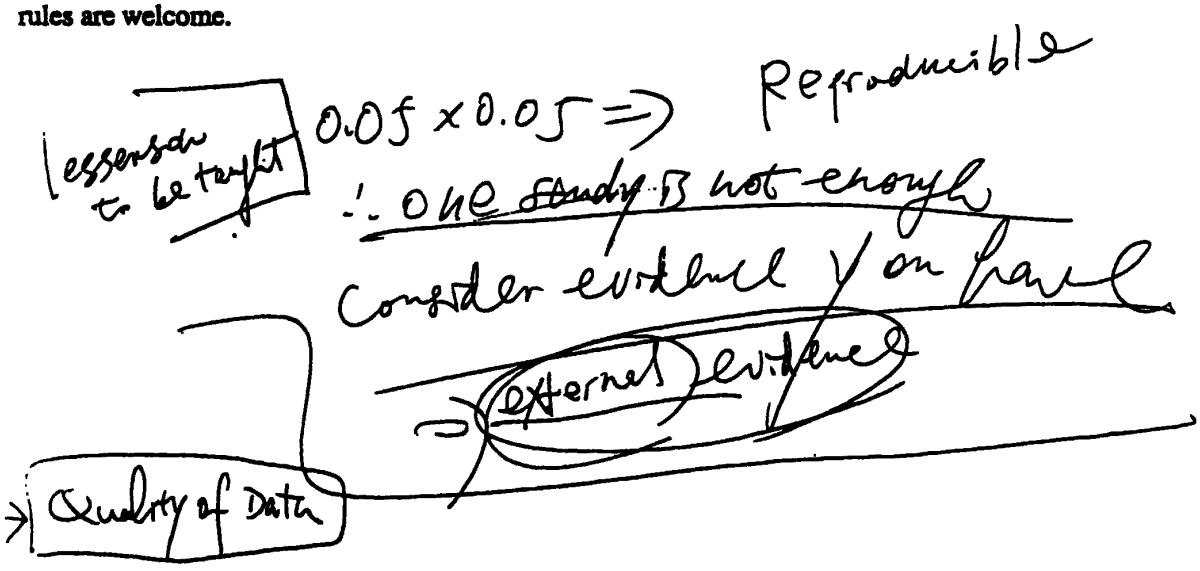
Shaw T. CHEN M.D., Ph.D.
Food and Drug Administration
Rockville, Maryland, U.S.A.

BIOGRAPHY

Dr. Chen was originally from Taiwan; he received his Ph.D. in Chemistry from Johns Hopkins, M.D. from University of Miami, and pediatric residency training from University of Minnesota. He is currently Associate Director, Office of Drug Evaluation V, Center for Drug Evaluation and Research, FDA, responsible for establishing a consolidated reviewing unit for botanical drug applications in the Agency. Prior to that, he was a Medical Team Leader at FDA's Division of Cardiorenal Drug Products, performing secondary clinical review of drug applications and supervising a group of medical reviewers and multidiscipline scientists. Recently Dr. Chen was on a sabbatical from FDA and served as the Lead Advisor to the Taiwanese government to help establish the Center for Drug Evaluation, or CDE, a modern drug review agency in the Pacific Asian region.

ABSTRACT

The US FDA has recently published a draft Guidance for Industry on developing botanical drug products, which will be described in this presentation. The agency is proposing to use previous uncontrolled human experiences, as the basis for presumed safety, to expedite limited early stage testing to assess the therapeutic potential of botanicals. Public comments on the proposed new rules are welcome.



Requirements for Registration of OTC Products in the U.S.

Jacqueline LEUNG, R.Ph.
Potomac, Maryland, U.S.A.

BIOGRAPHY

Ms. Jacqueline Leung obtained her Bachelor of Science degree in pharmacy from Loyola University, New Orleans, Louisiana. Upon graduation, she practiced pharmacy at the Turo Infirmary, Ochsner Foundation Hospital, and Columbia Hospital. In 1973, she joined the Drug Listing Branch at the Food and Drug Administration (FDA). She also worked briefly in the Division of Poison Control Center. Later, she was promoted to the position of Chief of the Drug Listing Branch. In 1994, she became the Deputy Director of the Division of Drug Labeling and Non-Prescription Drug Compliance in the FDA. She retired from the agency in 1998 after 25 years of service, during which she received numerous achievement awards. Under her leadership, the Drug Listing Branch received the Inspector General's Integrity award. Ms. Leung is a registered pharmacist in both Louisiana and Maryland.

ABSTRACT

The U.S. government is responsible for regulating drugs in the United States. Before 1973, it could not tell what drugs were commercially distributed except by periodic inspecting the registered establishments. The Food and Drug Administration (FDA) then asked the Congress to pass a law to obtain the information. The Congress passed the Drug Listing Act in 1972. The law became effective on February 1, 1973.

The Drug Listing Act of 1972 amended the Federal Food, Drug, and Cosmetic Act to require owners or operators of drug establishment engaged in the manufacturing or processing of a drug or drugs to do two things. First, register their establishment. Second, to list all their commercially marketed drug products with the FDA. Please note that dietary supplements are not classified as drugs. Therefore, they are not required to be listed with the FDA under the Drug Listing Act.

Let us look at "Who must list", "When to list", "How to list" and "Where to submit" the OTC drug information in the U.S.

Who must list?

All manufacturers, all repackers, all foreign firms that sell bulk or finished dosage forms to domestic firms, U.S. firms that export, and private label distributors.

When to list?

Within 5 days after beginning operation and the firm must update their product listings twice a year.

How to list?

Submit certain information on form FDA2657 and FDA2658.

The NDC number

Each product is uniquely identified using the NDC number. This number is a 10 digit code made up of three distinct segments. Each segment is separated by a dash. There are three allowable NDC configurations and a firm must use the same configuration for all of its products.

FDA requests but does not require that the NDC number appears on all product labels and labeling. However, when the NDC number is used on a label or in labeling, the NDC number must be shown in certain manner.

A firm must assign a new NDC number to a product when any change occurs in a product's characteristics that clearly distinguishes one product version from another.

Drug firms must submit imprint information of all oral dosage form for OTC drug products to the FDA.

Herbal and Traditional Medicines - Will the Future be Clinical Driven or Evidence-Based?

Ming HU, Ph.D.
Washington State University
Pullman, Washington, U.S.A.

BIOGRAPHY

Telephone: (509)-335-4184
Fax: (509)-335-0162
E-mail: minghu@wsu.edu

EDUCATION AND TRAINING

1978-1982 B.S. in Pharmacy-Shanghai First Medical College, Shanghai, The People's Republic of China.

1983-1988 Ph.D. in Pharmaceutics-College of Pharmacy, The University of Michigan, Ann Arbor, Michigan. (Advisor: Dr. Gordon L. Amidon)

1988-1990 Postdoctoral Training-Department of Pharmaceutical Chemistry, The University of Kansas, Lawrence, Kansas. (Mentor: Dr. Ronald T. Borchardt)

PROFESSIONAL EXPERIENCES

1990-1997 Assistant Professor of Pharmaceutics, College of Pharmacy, Washington State University, Pullman, Washington.

1997-present Associate Professor of Pharmaceutics, College of Pharmacy, Washington State University, Pullman, Washington 99164-6510.

REPRESENTATIVE PUBLICATIONS AND INVENTIONS

1. Passive and Carrier-Mediated Intestinal Absorption Components of Captopril. M. Hu and G. L. Amidon, *J. Pharm. Sci.*, 77(12), 1007-1011 (1988)
2. Use of the Peptide Carrier System to Improve the Intestinal Absorption of L-α-Methyldopa I: Carrier Kinetics, Intestinal Permeabilities, and In vitro Hydrolysis of the Dipeptidyl Derivatives of L-α-Methyldopa. M. Hu, P. Subramanian, H. Mosberg and G. L. Amidon, *Pharm. Res.*, 6(1), 66-70 (1989)
3. Transport of a Large Neutral Amino Acid in a Human Intestinal Epithelial Cell Line (Caco-2): Uptake and Efflux of Phenylalanine, M. Hu and R. T. Borchardt, *Biochim. Biophys. Acta*, 1135, 233-244 (1992)
4. Comparison of Uptake Characteristics of Thymidine and Zidovudine in a Human Intestinal pithelial Model System. M. Hu, *J. Pharm. Sci.*, 82, 829-833, (1993)
5. Mechanisms and Kinetics of Uptake and Efflux of L-Methionine in an Intestinal Epithelial Model (Caco-2). J. Chen, Y. Zhu, M. Hu, *J. Nutr.*, 124,1907-1916, (1994)

6. Development of a Novel Delivery System for Functional Enzyme: Application to Prolidase. PDA. M. Hu, *J. Pharma. Sci. Techn.*, 51(6), 238-241, (1997)
7. Morphological and Metabolic Characterization of Caco-2 Cells Expressing High Levels of cDNA-Derived Cytochrome P4503A4. M. Hu, Y. Li, B. W. Penman, S. M. Huang, K. Thummel, C. L Crespi, *Pharm. Res.*, 16, 1352-1359, (1999)
8. License Agreement Between WSU Research Foundation and GENTEST Corp.; Caco-2 Cells Expressing Human Cytochrome P-450 (Case #288)
9. Lipozyme: A Novel Delivery System for Functional Enzymes. Patent Pending.

ABSTRACT

Herbal and traditional medicines have been practiced for thousands of years in Asia, and remained an integral part of its health care system today. The basis for the established practice is often clinical driven, where certain practice (e.g., herbal combinations) is passed through generations within a family or by books, although the latter is not commonly done. The basis for Western or "conventional" medicine is hypothesis driven and is often well documented. The method for documentation tends to evolve with better technology and new knowledge. To protect possible economical gain associated with the progress of Western medicine, an elaborated intellectual property (IP) system is developed and rigorously protected. This IP system forms the basis for continued progress in Western medicines. In contrast, herbal and traditional medicines do not have nearly as much (if at all) IP protection and valuable treatment modality with proven clinical outcomes often gets lost because it is not in public domain. Lack of uniformity among the practitioners often invites further debate on the value of this traditional practices and herbal medicines. Therefore, traditional and herbal medicines have been called by Western media and scientists alike anything from "voodoo medicine" to "alternative and complementary medicine."

The future of herbal and traditional medicine will depend on if and how fast we can develop new methods and technologies to conduct hypothesis-driven studies to evaluate them. Initially, the majority of the work will be clinical driven, since numerous herbal products are available now and widely used, and there are urgent needs to determine their safety profile and effectiveness. Some evidence-based study that determines the mechanism of action will be conducted with government support, but the scope will be limited to most popular herbs. However, major and rapid advance in this area, which are resources intensive, will not occur unless a system of effective IP protection can be established by Asian governments in collaboration with various stake holders. Without proper IP protection, the future of herbal and traditional medicine in Asia will largely depend on how much government will spend in response to pressure from consumers who want to know more about them. In United States, The National Institutes of Health (NIH) was asked by Congress in 1998 to determine if herbal and traditional medicines work and whether they are safe to use. At that time, sales of herbal products were growing much faster than other medicines and a lot of people were using it. This year, NIH's National Center for Complementary and Alternative Medicine (NCCAM) will spend about 100 million dollars, a tiny sum compared to NIH's 25 billion dollar budget. However, this is 100 million dollars more than three years ago.

Hypothesis driven study is what has been used to determine the safety and effectiveness of pharmaceuticals and medical treatment procedures. However, methods commonly used in Western medicine and biomedical research often do not translate well into the study of herbal and traditional medicine. When studying raw herbs and/or processed herbal medicines, we often do not know what the active ingredients are and whether a particular ingredient is bioavailable. Adapting today's state of the art screening process to finding an active ingredient(s) in a single herb is tough enough and finding it/them in a "mixed-herbal soup" may be extremely challenging, and require significant amount of resources that herbal pharmaceutical houses and universities cannot afford. One solution is a government-sponsored center(s) where efforts are made to systemically catalogue the active ingredients in commonly used herbs provided by various stake holders, which are subsequently published or otherwise made available for a reasonable fee and a small royalty.

In conclusion, the future of herbal and traditional medicine will depend on the use of hypothesis driven research. The future will include IP law reform and increased government support. Asian governments must seek way to encourage Western governments to amend IP law so that potential economical gain is protected. New methods and technologies must be developed to serve the special scientific needs in the study of herbal and traditional medicines.

Development Center for Biotechnology's Experience in Toxicology for Herbal Medicines

Billy CHOU, Ph.D.
Development Center for Biotechnology
Taipei, Taiwan

BIOGRAPHY

Dr. Billy J. Chou received his DVM degree from National Taiwan University, and MS and Ph. D degrees from Kansas State University. He is a Diplomate of American Board of Toxicology with close to 30 years experiences in industry toxicology. He is Vice President of R&D for Development Center for Biotechnology (DCB) in Taiwan. At this capacity he manages 220 technical staffs in 8 core technologies to provide infrastructures and technical support for biotechnological and pharmaceutical products research and development.

Before he joined DCB he worked as the Program Director for National Toxicology Program at Pacific Northwest National Laboratories in U.S. During his tenure, he received and managed more than US$ 140 million grants and contracts from NIEHS. He studied more than 30 chemicals, which are important to the workplace and the environment. He also worked as a Senior Pharmacologist, Section Manager, Department Manger at Rhone Poulenc Rorer. He participated in the research and development of drugs in 11 therapeutic areas.

Dr. Chou has more than 200 papers, technical reports.

ABSTRACT

The toxicological studies conducted at DCB for botanical products are usually health food and herbal medicine products. The government has different regulatory requirements for these two products. Herbal medicines usually are non-traditional and require toxicity studies for drug approval. Health food product's sponsors are encouraged to find out which category of health food government may classify your product before toxicity studies package are designed. When conducting toxicity studies, the common problems we face usually are related to test articles. Because the proprietary nature of the products, information concerning identity, strength, purity, composition, stability, uniformity, etc. are lacking. The test articles are available either in solution, or powder form. Most of the powders will present you solubility and uniformity problems, it is difficult to provide large safety margin compare to recommended human dose. Large dose volume often necessitates split-dosing schedules and may cause more accidental death due to dosing errors. Test articles available in solutions sometime are organic solvent extraction products. The solvent toxicity very often complicates toxicity assessments of the herbal medicines. Very few ADME studies have been studied, detection and quantification methods development for marker components in bio-specimen matrices are very difficult to establish for complex mixtures.

Herbal Drug Interactions - Recent Development

Y. W. Francis LAM, Pharm.D.
University of Texas Health Science Center at San Antonio
San Antonio, Texas, U.S.A.

BIOGRAPHY

Y. W. Francis Lam is an Associate Professor of Pharmacology and Medicine at the University of Texas Health Science Center at San Antonio (UTHSCSA). He is also a Clinical Associate Professor and an endowed fellow of the College of Pharmacy at the University of Texas at Austin.

Dr. Lam received his undergraduate pharmacy degree in England and his Doctor of Pharmacy degree from the University of Minnesota, USA. His postdoctoral training included a residency at the University of Minnesota and a research fellowship at the University of California, San Francisco.

Dr. Lam currently serves as a member of the FDA Non-Prescription Drug Advisory Committee and the United States Pharmacopeia Pharmaceutical Analysis Expert Committee. He is the Director of the Advanced Pharmacological Evaluation Laboratory at UTHSCSA, which performs genetic evaluation of drug metabolism and response for clinical consult, as well as provides drug concentration determinations. Dr. Lam also is a Center Investigator and Pharmacokineticist of the NIDA Clinical Trial Center at the same institution. He is a fellow of the American Society of Consultant Pharmacists and Past President of the American Chinese Pharmaceutical Association.

Dr. Lam's research interests include ethnic and genetic differences in drug metabolism and response, mechanism and clinical implications of drug-drug interactions, as well as correlation of pharmacokinetics and pharmacodynamics in clinical pharmacology. His research scholarly activities include over 50 original publications and 60 abstracts; 7 book chapters contribution, and more than 55 national and international invited presentations. Dr. Lam has served as Program Project and Merit Research Program reviewer for both NIMH and the US Veterans Affairs' Medical Research Service.

ABSTRACT

Herbal medicines are being used by an increasing number of consumers and patients. Although data supporting efficacy are increasingly available, the safety issues remains largely under-studied. One particular concern regarding their use is potential drug interaction with concurrent prescription and non-prescription drugs. This is especially important, as patients tend not to report their clinicians of concomitant herbal product usage. This presentation will focus on recent reports of interactions involving the commonly used herbal products. The implications of herbal drug interaction for the consumers, clinicians, manufacturers, and the regulatory agencies will be discussed.

Application of Modern Instrumentation (LC/MS/MS) in Herbal Product Quality Control: Case Study - Tien Ma

Jinn WU, Ph.D.
XenoBiotic Laboratories, Inc.
Plainsboro, New Jersey, USA

BIOGRAPHY

Dr. Jinn Wu established XenoBiotic Laboratories, Inc. in 1987. He received a Ph.D. degree in Natural Product Chemistry from the College of Pharmacy, The Ohio State University, Columbus, Ohio in 1979. He was a postdoctoral research associate at the Department of Pharmacology, College of Medicine, The Ohio State University from 1979 - 1980. He obtained his B.S. degree in Pharmacy and a M.S. degree in Pharmaceutical Chemistry from the School of Pharmacy, National Taiwan University, Taipei, Taiwan in 1971 and 1975, respectively. He was a senior research chemist and research associate at FMC Corporation in Princeton, New Jersey from 1980-1987. Dr. Wu's areas of expertise are in pharmaceutical, agrochemical and biochemical product development, especially in bio-organic chemical analysis, drug assay, environmental chemistry, metabolism studies both in pre-clinical and clinical phases. His work at XenoBiotic Laboratories centers on assisting producers of pharmaceutical and agrochemical products to meet worldwide regulatory requirements for product registration. Currently he is a member of American Chemical Society (ACS), the American Society of Pharmacognosy (ASP), the International Society for the Study of Xenobiotics (ISSX), American Association of Pharmaceutical Scientists (AAPS), and a life-time member of the American Chinese Pharmaceutical Association (ACPA). He has published 44 scientific papers. In 1994, he was the receipient of The Jack L. Beal Postbaccalaureate Award, College of Pharmacy, the Ohio State University. He served as a consultant for NIH-NCI; as 2000-2001 Program Committee Chair for ACPA and has served as a Member of Board of Directors for Delta Pharmaceuticals, Inc.

ABSTRACT

The application of modern instrumentation such as liquid chromatography tandem mass spectrometry (LC/MS/MS) and other related detectors (i.e., PDA and/or ELSD) will be a pivotal part of consideration to control and improve the quality of herbal products. LC/MS/MS offers sensitivity, specificity, and reliability in both qualitative and quantitative analyses. Enormous publication using LC/MS/MS in bioanalysis demonstrated that the instrument is appropriate to apply in herbal medicine. Tien-Ma is a widely used medicinal plant which can be found in many herbal products such as Tien-Ma Wan. The quantitative determination of one of its major constituents, i.e., gastrodin, in wild-grown, cultivated, as well as in herbal products using LC/MS/MS has been developed. Pulverized Tien-Ma or Tien-Ma-Wan (500 mg) was extracted with 10.0 mL of methanol by ultrasonication for 30 min. The mixture was kept on the bench for approximately 24 hours, vortexed and centrifuged at 5000 rpm for 10 min. The aliquot (50 μL for Tien-Ma or 500 μL for Tien-Ma-Wan) of the methanol layer was combined with 5 mL of 0.01 M NH_4OAc in H_2O in a 10-mL volumetric flask, and adjust the volume to 10.0 mL with 0.01 M NH_4OAc in H_2O to give each sample solution. Samples were further diluted 2-fold in 0.01 M NH_4OAc in H_2O before injection onto LC/MS. A Waters HPLC 2690 Separation Module with TSK-Gel ODS-80TS column (2.0x150 mm, 5 μm) coupled with PE-Sciex Triple Quadrupole Mass Spectrometer Model API-365 in positive turboion spray (electrospray) mode was used. The mobile phases consist of 0.01 M NH_4OAc and 1% HCOOH in H_2O:CH_3OH (95:5) in isocratic elution at 0.4 mL/min and the run time is ~5 minutes. Different calibration methods, external standard curve, single and multiple standard addition to individual extracts, and single and multiple standard addition to mixed extracts, were developed to satisfy different purposes of usage of the quantitation method. Cultivated Tien-Ma showed higher gastrodin content than wild-grown samples. Three Tien-Ma-Wan products analyzed showed varied gastrodin content. One wild-growth Tien-Ma and one Tien-Ma-Wan showed extremely low levels of gastrodin. Detailed experimental conditions and results will be discussed.

Targeted Discovery of Steroidogenic Compounds in Traditional Herbal Medicines

YONG Eu Leong, MRCOG, Ph.D.
National University of Singapore
Singapore

BIOGRAPHY

Name: YONG Eu Leong, MRCOG, Ph.D.
Current Positions: Vice-chairman NUH Medical Board (Research)
Senior Consultant (since 1997) &
Associate Professor (Tenured 1997)
Department of Obstetrics and Gynaecology
National University Hospital, Singapore
Correspondence: Department of Obstetrics and Gynaecology
National University Hospital, Lower Kent Ridge Road
Republic of Singapore 119074.
Tel: (65) 772 4261
Fax: (65) 779 4753
E-mail: obgyel@nus.edu.sg

QUALIFICATIONS:

1980 Bachelor of Medicine, Bachelor of Surgery (MBBS), Singapore.
1987 Member of the Royal College of Obstetricians and Gynaecologists of the United Kingdom (MRCOG).
1987 Master of Medicine (M.Med) (Obstetrics & Gynaecology) - NUS
1992 Subspeciality Certification (Reproductive Medicine) RCOG (UK)
1994 Doctor of Philosophy, National University of Singapore (Ph.D)

AWARDS & SCHOLARSHIPS

1) MERIT Scholarship for Medical Studies NUS 1975
2) 12th Benjamin Henry Sheares Memorial Lecturer, OGSS, Singapore 1994
3) William Blair Bell Lectureship in Obstetrics and Gynaecology RCOG (UK) 1994,
4) National University of Singapore Outstanding Researcher Award. 7 October 1998. Presented by Vice-Chancellor, NUS.
5) National Award: Ministerial Citation for outstanding contribution in the research on molecular genetics of human fertility. Presented by Deputy Prime Minister Tony Tan, Singapore. NSTB Tech Month 1999.

PATENTS:

A method of modulating steroidogenic activity
Patent filed with US Patent and Trademarks Office. February 2000.
INTRO Ref :19/4/315

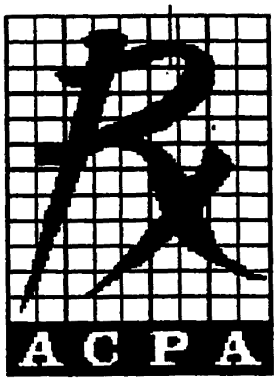
SELECTED PUBLICATIONS (Best of over 50 international publications):

1. Yong E L, Ng S C, Roy A C, Yun G, Ratnam S S. Pregnancy after hormonal correction of severe spermatogenic defect due to mutation in androgen receptor gene. *Lancet* (U.K.) 1994, 344; 826-827.
2. Ghadessy FJ, Lim J, Abdullah AAR, Panet-Raymond V, Choo CK, Lumbroso R, Tut TG, Gottlieb B, Pinsky L, Trifiro MA, Yong EL. Oligospermic infertility associated with an androgen receptor mutation that disrupts interdomain and coactivator (TIF2) interactions. *J. Clin. Inv.* (USA) 1999, 103, 1517-1525.
3. Dowsing AT, Yong EL, McLachlan RI, de Kretser D, Trounson A. Linkage between male infertility and trinucleotide expansion in the androgen receptor gene. *Lancet* (UK) 1999, 354, 640-643.
4. Ong YC, Wong HB, Adaikan G, Yong EL. Directed pharmacological therapy of ambiguous genitalia due to an androgen receptor gene mutation. *Lancet* (UK) 1999, 354, 1444-1445.
5. Lim J, Ghadessy FJ, AAR Abdullah, Pinsky L, Trifiro M, Yong EL. Human androgen receptor mutations disrupts ternary interactions between ligand, receptor domains and the coactivator TIF2. *Mol. Endocrin.* 2000, 14, 1187-1197.
6. Wang Q, Lu JH Yong EL. Ligand- and coactivator-mediated transactivation function (AF2) of the androgen receptor ligand-binding domain is inhibited by the cognate hinge region. *J. Bio. Chem.* 2001, 276, 7493-7499.

ABSTRACT

Many drugs in clinical use have originated from folk medicines and traditional herbal preparations. Androgenic and estrogenic substances (phytoestrogens) are present in many herbal and plant extracts, but their identification is difficult because current assays are imprecise, depending on measurement of weight changes in hormone-dependent tissues such as the castrated rat ventral prostate or caponised chicken combs. The recent cloning of androgen, estrogen and other members of the steroid/nuclear receptor superfamily of genes make possible new specific and sensitive bioassays for targeted discovery of steroidogenic substances. Our laboratory is a leading center for the study of androgen receptor mutations in the etiology of male & female infertility and prostate cancer. Over the last 10 years, we have identified dozens of androgen receptor mutations and polymorphisms that cause sexual ambiguity, male & female infertility, and prostate cancer.

Leveraging on our expertise in the molecular and cellular biology of androgen action, we embarked on a new research initiative to screen for testosterone-like and estrogen-like substances in traditional Chinese herbs. Our receptor studies have provided us with very sensitive and precise molecular tools for detecting minute quantities of any compound with testosterone-like effect. Screening of various herbs, described in Ancient Chinese Pharmacopoeia to improve the male principle or "Yang", has resulted in the identification and characterization of several very promising compounds with potent testosterone-like, estrogen-like or anti-hormonal activity. Such substances have wide potential utility as pro- or anti-fertility agents, for hormone replacement therapy, for treatment of hormone-dependent disorders such as uterine leiomyoma, endometriosis, polycystic ovarian syndrome, and as hormone antagonists for breast, endometrial and prostate cancers.



POSTER ABSTRACTS

Vasodilator Activity Guided Isolation Of *Centella Asiatica*

Sue Hay Chan, Amirin Sadikun, and M. Zaini Asmawi
Pharmacology Discipline, School of Pharmaceutical Sciences,
Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia
Tel: 604-6577888 ext 2226, Fax: 604-6586488, E-mail: suehay@tm.net.my

Centella asiatica is a creeping herb, widely distributed throughout the tropics. It can be eaten as a salad and claimed to have many medicinal values including the treatment of hypertension. In our previous work (1), the methanol extract of the plant was found to inhibit noradrenaline induced contraction in isolated rat aortic strip preparations. The results showed that it had vasodilator activity, which may explain its anti-hypertensive property. Therefore, vasodilator activity guided isolation was performed on the plant in an attempt to find a new anti-hypertensive drug.

The aqueous solution of methanol extract of *C. asiatica* was further extracted successively with petroleum ether, chloroform, and butanol and water. The extracts obtained were dried under reduced pressure before being tested again in the isolated rat aortic strip preparations. It was found that the chloroform extract 0.5 mg/ml caused the strongest inhibition (79.8±5.9%) on noradrenaline-induced contraction.

The chloroform extract was therefore, separated further into five different fractions (CF1, CF2, CF3, CF4 and CF5) via the conventional silica gel column chromatography method. The fractions obtained were individually examined in the isolated rat aortic strip preparations. Results showed that all the five fractions [(CF1 (0.13-0.5 mg/ml, CF2 (0.5 mg/ml), CF3 (0.13-0.5 mg/ml), CF4 (0.13-0.5 mg/ml) and CF5 (0.13-0.5 mg/ml)] invariably inhibited the noradrenaline-induced contraction of the aortic strips. The strongest inhibition was caused by fraction CF4 (0.5 mg/ml) where it produced almost total inhibition of the contractions (98.9±0.8%) as compared with CF1 (45.7±4.8%), CF2 (68.9±6.4%), CF3 (41.4±7.0%) and CF5 (33.3±7.5%).

C. asiatica, inhibited the log dose responses curves of aortic strips to noradrenaline in the non-competitive manner i.e. shift the log dose response curves of aortic strips to noradrenaline to the right and reduce its maximum responses. Since, the *C. asiatica* extract also non-competitively inhibited the log dose response curves of isolated paced left atria to isoprenaline (2), it suggested that the inhibition mechanism of action of the plant extracts is non-specific possibly by blocking the calcium channel.

REFERENCES

1. Chan, S.H., Harahap, H. & Asmawi, M.Z. (2000). 15th Scientific Meeting of the Malaysian Society of Pharmacology and Physiology, Kelantan. P19.
2. Chan, S.H., Asmawi, M.Z. & Sadikun, A. (2000), International Conference on Traditional/Complementary Medicine, Kuala Lumpur. P3.

Salvia Miltiorrhiza Induced Antioxidant Enzymes And Attenuate Myocardial Damage Following Myocardial Infarction In Rats

Julia Xin Yan Ji, Benny Kwong Huat Tan, Yi Chun Zhu[1], Annie Hsu, Wolfgang Liut[2] and Yi Zhun Zhu
Department of Pharmacology, Faculty of Medicine,
National University of Singapore, 10 Kent Ridge Crescent, Singapore 119260
[1]Department of Physiology, Shanghai Medical University, P.R.China
[2]Cardiovascular Research, Aveutis Pharma AG, Fraukfurt, Germany
Tel: (65) 2886810 (Mon.–Wed.), (65) 8743312 (Thurs.–Sat.),
Fax: (65) 2888326, E-mail: medp8140@nus.edu.sg; dr_Julia@oceanhealth.com

In the present study, we investigated (a) whether *SALVIA MILTIORRHIZA* (DanShen), a Chinese herb, was as effective as an ACE inhibitor (ramipril) in protecting the rat myocardium following myocardial infarction (MI); (b) the underlying mechanisms of the beneficial effects of DanShen on chronic heart failure following MI.

All rats were treated with DanShen or Saline or Ramipril for 1 week before ligation of the left descending artery to induce MI. The treatment was continued for another 2 weeks after MI. Morphological examination and antioxidant assays were performed after sacrificing the animals at the end of the treatment period.

Compared to Saline group, our results show that DanShen reduced: (1) the ratio of infarct size to the left ventricular size ($P<0.001$), total heart weight ($P<0.005$), left ventricular weight ($P<0.001$), right ventricular weight ($P<0.001$) to body weight. The similar results were observed in Ramipril-treated rats; (2) the oxidative stress from MI by increasing the activities of hepatic-antioxidant enzymes, including SOD ($P<0.001$), GSH-Px ($P<0.001$), catalase ($P<0.05$) and GST ($P<0.005$). However, Ramipril and Saline group did not show any antioxidant effects.

In conclusion, DanShen has similar cardioprotective effects following MI in rats as that of ramipril; its capacity for scavenging free radicals could be one of the important mechanisms in protecting the post MI myocardium.

Promising Herbal Composition For Presbyopia

Yanxue Li, Jiesheng Gao and Renjing Tu
Shenzhen Techtransfer Consulting Co. Ltd.,
206, 85 Taining Road, Shenzhen, Guangdong, P. R. China 518020
Tel: 86-755-5612997, Fax: 86-755-2891361, E-mail: rjt@chinatt.com

Presbyopia is a vision condition in which the crystalline lens of the eye loses its flexibility, which makes it difficult to focus on close objects. It is caused by a slow loss of flexibility within the human lens inside the eye. The cumulative effects of this flexibility loss are noticed around the age of 40, though some people become aware of it earlier and others later. Today, there are 1.5 billion presbyopes in a world comprising six billion inhabitants. Most importantly, that section of the population is growing faster than the total population. Presbyopia affects 100% of the population by age 50. There is no proven prevention for presbyopia. Wearing glass and surgery are the only options for the mass presbyopes to accommodate. Here we report the preliminary result of the human experiment of a herbal composition for treating presbyopia. The composition is an alcohol extraction of a number of herbals available in the Chinese Herbal Medicine market.

Table 1. Preliminary results of the clinical observation on the composition.

			Near vision test	
Patient	Sex	Age	Pre-	Post-administration
1	F	47	0.33	0.5
2	F	47	0.33	0.5
3	F	55	0.5	0.66
4	M	44	0.33	0.5
5	F	45	0.5	0.66
6	M	49	0.25	0.33
7	M	52	0.1	0.16
8	F	48	0.1	0.16
9	M	50	0.1(unclear)	0.1(clear)

Nine presbyopes, including 4 male and 5 females, were selected to orally take 30 ml of the alcohol extraction of the composition, two times per day for 6 days. The near vision tests were performed at pre and post composition administrations. The results are shown in the table 1 above. There was no abnormal effect complained and/or reported.

It is apparent that there is a need for further study to define its efficacy and safety in a scale-up and controlled clinical trials. The above result indicates that the herbal composition could be a promising candidate to develop a drug which is very much in need to be able to treat and/or control the progression of presbyopia. In the mean time, it may have the possibility to reduce the occurrence rate and/or time of cataract. It is observed that the composition is best for the presbyopes who are wearing near vision glasses within 2 years and with less than 150 degrees.

Anti-Inflammatory Activity Guided Isolation Of Some Malaysian Medicinal Plants

ChongYee Tan, Amirin Sadikun and M. Zaini Asmawi
Pharmacology Discipline, School of Pharmaceutical Sciences,
Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia
Tel: 604-6577888 ext. 2253, Fax: 604-6570017, E-mail: eeytan@yahoo.com

In an attempt to seek new, more potent, and less side effects anti-inflammatory agent(s) from plant origin, several Malaysian medicinal plants were screened for their ability to inhibit carrageenan induced hind paw oedema in rats. The plants studied were traditionally used to treat swelling (*Ageratum conyzoides*, *Lantana camara*, *Psidium guajava*), fever (*Ageratum conyzoides*, *Lantana camara*, *Psidium guajava*), pain (*Ageratum conyzoides*), and rheumatism (*Ageratum conyzoides*, *Lantana camara*), i.e. indications for the use of nonsteroidal anti-inflammatory drugs.

The plants were dried, pulverized, and extracted sequentially using non-polar to more polar solvents. The extracts obtained were evaporated to dryness under reduced pressure and kept in a bell jar until used. In this manner, hopefully the anti-inflammatory constituents of the plants had been concentrated in one of the solvents and made it more detectable when pharmacologically screened. Powdered *Ageratum conyzoides* (whole plants) were exhaustively extracted sequentially in a soxhlet extractor with petroleum ether, chloroform, and methanol. However, at the dose of 1 g/kg through the oral (*p.o.*) route, none of these extracts significantly inhibit carrageenan induced hind paw oedema in female rats.

While, powdered leaves of *Lantana camara* and the combination of other parts of the plant (flowers, stems, fruits) and leaves of *Psidium guajava* were macerated with warm methanol (45 °C). It was found that the inhibitory activity of the crude methanol extract of the leaves of *Lantana camara* (1 g/kg, *p.o.*) against carrageenan induced oedema in female rats was better than the same dose of methanol extract of the combined various parts of the plant. Oral administration of methanolic extract of the *Psidium guajava* leaves (1 g/kg) caused significant inhibition of carrageenan induced oedema in male rats. Therefore, the crude methanol extract of *Lantana camara* leaves and *Psidium guajava* leaves were fractionated into five fractions i.e. petroleum ether, chloroform, ethyl acetate, butanol and water fractions using solvent-solvent partition method. The chloroform fraction (1 g/kg, *p.o.*) of *Lantana camara* leaves was found to give the best inhibition of oedema in female rats compared to other fractions of the plant. On the other hand, three of the five fractions of *Psidium guajava* methanolic extract i.e. petroleum ether, butanol and water fractions (1 g/kg, *p.o.*) were found to significantly inhibit the carrageenan induced male rats hind paw oedema.

In general, this study concluded that, the relatively non-polar fraction of *Lantana camara* leaves extract, and non-polar and polar fractions of *Psidium guajava* leaves extract contain substance(s) with anti-oedema activity and have the potential to be used for treatment of inflammation and related diseases.

Evaluation of Reproductive Toxicity Of Dehulled Adlay In Rats

M.F. Yang, M.L. Wang, J.C. Lai, C.P. Wang and C.W. Chen
Development Center For Biotechnology, 103 Lane 169, Kang-Ning Street,
His-Chih City, Taipei County, Taiwan
Tel: 886-2-2695-6933 ext. 3227, Fax: 886-2-2695-3404, E-mail: cwcema@mail.dcb.org.tw

Animal studies have demonstrated that dehulled adlay have anti-tumor and immuno-regulatory effects. It has been used as dietary supplement in human for a long time, however, previous human use experience and ancient medical documents suggested that aldlay is not recommended for consumption by women with early stage of pregnancy. Because it may induce spontaneous abortion. The present study was designed to investigate the reproductive toxicity of dehulled adlay in Sprague-Dawley (SD) rats, this may provide an evidence to support the previous use experience observed in human. In this study, rats were dose fed on days 0-15 of gestation with different diets containing 0% (control group), 10%, 20% and 50% dehulled adlay with equal amount of dietary calorie content. The reproductive toxic effects were evaluated by different parameters, including maternal body weights, maternal food consumption, gravid uterus weights, number of corpora lutea, number of resorptions, number and sex of viable fetuses, number of implantation, individual fetus weight and external malformation. The results indicated that there were no significant differences in fertility, mean uterine weights, mean maternal food consumption, mean fetal weights, mean placental weights and post-implantation losses among control and treated groups. However, a trend of dose related pre-implantation losses was observed in this study. This finding indicates that adlay may affect the implantation of fertilized eggs in uterus which could be associated with the induction of spontaneous abortion in women with early stage of pregnancy.

The Chinese Herbal Extract CHS-7 Induces Cytotoxicity And Apoptosis In Several Cancer Cell Lines

Wee Sing Yeo, Benny K.H. Tan, S.H. Chan and Vincent T.K. Chow
Departments of Microbiology and Pharmacology, Faculty of Medicine,
National University of Singapore, 10 Kent Ridge Crescent, Singapore 119260

CHS-7 is an extract from a mixture of Chinese herbs used in traditional Chinese medicine for treating a range of cancers common in Singapore. The effects of CHS-7 on cell cytotoxicity, cell cycle progression and apoptosis in Jurkat, Raji, U-937 and P388D_1 cancer cell lines were investigated. CHS-7 was extracted with 80% ethanol, filtered, concentrated under reduced pressure, and freeze-dried to obtain the crude extract for quantification. The four cell lines and normal human leucocytes were seeded in triplicate at 2×10^6 cells per ml under the following conditions: untreated (control), treatment with CHS-7 at concentrations of 100, 50, 25, 12.5 and 6.25 μg/ml. After 24 hours, cell viability and cytotoxicity were assessed by flow cytometry via uptake of fluorescein diacetate and propidium iodide (PI) by viable and non-viable cells, respectively. Cell cycle progression and early apoptosis were analyzed at 24 hours by flow cytometry following PI and annexin-V-FITC staining, respectively. Further verification and qualitative study of apoptosis were performed using confocal and electron microscopy with annexin-V-FITC and uranyl acetate staining, respectively. Dose-dependent selective cytotoxicity against Raji, Jurkat, P388D_1 and U-937 cells, and an increase in the sub-G_1 apoptosis peak in the cell lines were observed. The LD_{50} values of CHS-7 crude extract against Raji, Jurkat, P388D_1 and U-937 were 24, 14, 11 and 10 μg/ml, respectively. Apoptosis in these cancer cell lines was demonstrated quantitatively and qualitatively by flow cytometric analysis, confocal and electron microscopy.

Prevalence Of Laxatives In Over-The-Counter Slimming Products

Hwee-Ling Koh, Aik-Jiang Lau, Li-Ching Nah and Soo-On Woo[1]
Department of Pharmacy, National University of Singapore,
10 Kent Ridge Crescent, Singapore 119260
[1]Centre for Analytical Science, Health Sciences Authority

The use of laxative for weight reduction is a form of eating disorder. Laxative induced diarrhoea does not significantly reduce absorption of food calories, while acute or chronic diarrhoea may result in serious injury or death. Although the presence of laxatives in food and slimming products is known, to date, there is no extensive study on the prevalence of laxatives in a wide range of slimming products. The main aim of the study was to assess the prevalence of laxatives in slimming products available in Singapore.

A total of 121 over the counter slimming aids (including Chinese Proprietary Medicine) were documented at 4 community pharmacies and a Chinese Medical Hall. The presence of laxatives was determined from the list of ingredients and by chemical analyses using High Performance Liquid Chromatography, Gas Chromatography-Mass Spectrometry and British Pharmacopoieal tests.

Of the 121 products, 103 products gave a complete list of ingredients, 7 did not give complete information on the ingredients while 11 products did not state the ingredients. 28 products claimed to contain laxatives. 11 products without any laxatives stated were analysed for sennosides (stimulant laxatives). All the 11 products tested positive for sennosides A and B. This study shows that at least 39 (32.2%) out of 121 over the counter slimming products available in Singapore may contain laxatives. 37 (94.9%) out of these 39 products either did not state the side effects of the laxative or claimed to produce no side effects at all. This study also provides analytical evidence of the presence of sennosides in some products that did not claim to contain laxatives or did not give any information about its ingredients.

In view of the prevalence of laxatives in slimming products and their potential adverse effects, the public and healthcare providers should be made aware of the potential presence of laxatives in slimming products and the associated adverse effects. Greater regulatory control over the labelling and inclusion of laxatives in such products is also necessary.

Screening Of Some Traditional Herbs For Antibacterial Activity

Teresa Swee Har Kwok, Lai Wah Chan and Paul Wan Sia Heng
Department of Pharmacy, National University of Singapore,
10 Kent Ridge Crescent, Singapore 119260
Tel: 65-8742656, Fax: 65-7791554, E-mail: phaangsh@nus.edu.sg

Many people from different cultures use traditional medicine, either on its own or in conjunction with western medicine. A wide selection of herbal remedies is available for treatment of a wide range of ailments. There is limited scientific investigation on the efficacies of these preparations.

A study was carried out to investigate some commonly used herbs for their antibacterial properties. Six herbs traditionally used in treating infections were selected. Their common names are Creat, Japan Honeysuckle, Midnight Horror, Common Plantain, Paku Padang and Rangoon Creeper. The dried form of these herbs is readily available from the local Chinese medical shops.

Extracts of these herbs were prepared for evaluating their antibacterial properties. The dried herbs were cut into small pieces and milled into powder. Aqueous extracts of the herbs were prepared by infusion or boiling in hot water. Alcoholic extracts were prepared by using methanol in the Soxhlet extraction system.

The antibacterial properties of these extracts were determined using the agar diffusion method. The test organisms employed were *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative). The antibacterial activities of the extracts were compared with two commonly used antibiotics, namely, penicillin G and tetracycline.

The extracts showed varying degrees of antibacterial activities. The aqueous and alcoholic extracts of Midnight Horror were found to be active against both test bacteria. The minimum extract concentration against *Staphylococcus aureus* for Midnight Horror was 38.6% w/v. The antibacterial components in Creat, extracted by methanol only, were also active against both test bacteria. Both aqueous and alcoholic extracts of Rangoon Creeper exhibited zones of sparse growth, indicating slight antibacterial activity. This was similarly demonstrated by the alcoholic extract of Japan Honeysuckle.

The results showed that only some of the herbs used in this study are potentially useful in the treatment of infections. The method of extraction is important in obtaining the antibacterial components in these herbs.

Microbiological Quality Of Chinese Proprietary Medicines Sold In Singapore

Aik Peng Yeo, T.R.R. Kurup and Lai Wah Chan
Department of Pharmacy, National University of Singapore,
10 Kent Ridge Crescent, Singapore 119260
Tel: 65-8743506, Fax: 65-7791554, E-mail: phaclw@nus.edu.sg

Although western medicine constitutes the mainstream of drug therapy in Singapore, traditional Chinese medicine continues to enjoy considerable popularity. Chinese proprietary medicines, which consist of traditional Chinese medicines formulated into various ready-to-use dosage forms, can be readily purchased from local Chinese medical halls without a prescription. Besides causing product spoilage, microbial contamination of these products may also result in hazards to health when they are consumed. Hence, the Ministry of Health of Singapore has established a set of microbiological standards to control the microbiological quality of these products.

A study was carried out to assess the microbiological quality of 28 products purchased from a Chinese medical hall. They consisted of various dosage forms for oral and topical administration. These products were appropriately processed for determination of microbial contents. Unspecified microorganisms, such as aerobic microorganisms, yeasts, moulds and enterobacteria, in the products were enumerated using the pour plate method. The presence of specified microorganisms, such as *Escherichia coli*, *Salmonella*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, in the products were detected using selective media.

None of the specified microorganisms was detected in any of the test products. However, the products were found to exhibit varying microbial counts. The pills generally showed the lowest counts, followed by the tablets and liquids. The ointments, creams and powders were contaminated to a larger extent. The capsules showed the highest microbial counts and all of them failed to comply with the microbial limits imposed. Non-compliance with the stated microbiological standards was due to the yeast and mould counts in almost all the cases. A number of the products, which failed to comply with the microbiological standards, were found to contain antimicrobial ingredients. Products consisting of plant parts generally showed higher microbial counts than those consisting of extracts. In addition, no significant correlation between product packaging and microbiological quality was observed.

It can be concluded from this study that the microbiological quality of Chinese proprietary medicines varied with the type of preparation and method of production. The presence of antimicrobial ingredients does not assure elimination of microbial contamination. It is therefore important to adopt good manufacturing practices in the production of Chinese proprietary medicines.

Formulation Factors For Film-Coated Herbal Powder Tablets

Charles R. Cunningham
Global Technical Manager, Colorcon, West Point, Pennsylvania, USA

Objectives. The benefits of film coating include providing a unique dosage identity, enhancing appearance, masking bitter tastes and improving tablet stability. One must, however, be cognizant that a dosage form that will be film coated should be robust enough to withstand the additional stress imparted by the film-coating process. Since most herbal powders have low potency, it is necessary to develop a formulation that will use a minimum level of excipients and still result in a tablet that will have the mechanical strength to ensure a sucessful film-coating process. Echinacea purpurea tablets that had been previously granulated with partially pregelatinised corn starch (Starch 1500®) and fumed silica exhibited very good mechanical strength but exhibited erosion on the tablet faces during the film coating process. Various types of microcrystalline cellulose were added to the granulated material to investigate their potential in reducing tablet erosion tendencies during the film-coating process.

Methods. The primary material used in the study was pre-granulated Echinacea purpurea powder (root and aerial parts) containing Starch 1500 and fumed silica. The three types of microcrystalline cellulose (MCC) direct blended with the herbal granulation were MCC 90 micron grade (Emcocel 90M, Penwest), silicified MCC 90 micron grade (Prosolv 90M, Penwest) and a low density MCC (Ceolus, Asahi Chem. Ltd.). The MCC was used at 20% of each formulation.

Each of the formulations, along with a control formulation with no MCC, were compressed using a 10-station rotary tablet press (Oval shaped tooling with logo). Tablet samples at varying compaction forces were tested for breaking force and friability. Tablet weight variation was also measured as an indication of the flowability of the powder blends. Tablet samples from each of the formulations were film coated in a side-vented coating pan using an aqueous film-coating system (Opadry®II, Colorcon) and evaluated for appearance.

Results. The addition of any of the MCC grades to the pre-granulated echinacea resulted in tablets with a > 20% increase in tablet breaking force over the control. The silicified MCC (Prosolv 90M) resulted in a 32% increase in tablet breaking force. The tablet weight variation for the control formulation and both 90 micron grades of MCC were less than 0.4% RSD. The addition of low density MCC (Ceolus) resulted in a higher 0.7% RSD indicating poorer flow characteristics. Samples of coated tablets from the control formulation exhibited erosion on the face of the tablet while the tablets where any of the MCC grades was used in the formulation the erosion was greatly reduced or eliminated.

Conclusions. While there were differences noted in the performance characteristics of each type of MCC used in the study, the addition of any of the types to the pre-granulated echinacea resulted in tablets suitable for use in the film-coating process.

A Study On Powder Compaction

S.N. Chee, L.W. Chan, Celine V. Liew, Yolande Anthony[1] and Paul W.S. Heng
Department of Pharmacy, National University of Singapore,
10 Kent Ridge Crescent, Singapore 119260
[1]ISP Asia Pacific Pte. Ltd., Singapore

There had been increased popularity and market for herbal remedies in recent years. Herbal teas, extracts, tablets and pills are some common examples of herbal dosage forms. Suitable techniques for processing of herbal materials into various dosage forms for added consumer convenience are also being explored. This preliminary study serves to investigate the feasibility of compacting herbal and pharmaceutical materials using roller compaction technology and the influence of binders on properties of the compacts.

Baphicacanthus cusia (*isatis* root), a common remedy for "heatiness" and Lactose 200M, a widely used pharmaceutical excipient, were selected as the materials to be compacted. The effect of two binders, Plasdone K25 and S630, on the compactibility of the *isatis* root and lactose was also studied. The milled herb or lactose, with or without a binder, was compacted using a roller compactor (Model L200/30P, Hosokawa Bepex) and subsequently broken into granules using an oscillating granulator (Erweka AR 401). The yield of the compacts and granules were measured and the size distribution of the granules was determined using sieve methods.

The preliminary results showed that compaction of herbal and pharmaceutical powders were feasible with optimisation of the roller compactor processing parameters. The addition of a binder at the concentrations used appeared to have some effect on the percentage yield of the compacts. The appearance of the compacts was affected by the nature of the binder used. The percentage yield of the granules, an indirect measure of the hardness of the compacts, was shown to be dependent on the formulation. Size distribution of the granules was influenced by the formulation parameters.

The findings provided further information on the potential use of roller compaction for compacting herbs, compounds or materials which could be further processed and used for capsule filling or tabletting.

Optimization And Formulation Of *Andrographis Paniculata* Nees Herbal Matrix Pellets

Siek Nee Choo, Yvonne Tze Fung Tan and Khiang Peh Kok
School of Pharmaceutical Sciences, University of Science Malaysia 11800
Penang, Malaysia
Tel: 604-6577888 ext 2207, Fax: 604-6570017, E-mail: Yvonne@usm.my

Optimization of inert pellet production was studied using two formulation variables: ratio of lactose to microcrystalline cellulose (MCC) and amount of moistening liquid, employing two different pelletization methods, namely, granulation and extrusion-spheronization. In the latter, the influence of two different types of extruders, ram extruder and cylindrical extruder, on the physical properties of pellets was also compared. The pellet properties were characterized using particle size distribution, geometric-weight mean diameter (d_{gw}), geometric standard deviation (S_g), percent yield in the size range of 0.80 to 1.25 mm, flowability, friability, hardness and shape of pellets. Results showed that either increasing amount of lactose or moistening liquid increased pellet size. Less amount of moistening liquid was required at high lactose content due to the hydrophilic behavior of lactose. Inert pellets produced by granulation method were soft, friable, of wider particle size distribution and non-spherical in shape. The highest percent yield was only 48% at its optimal ratio. Extrusion-spheronization method resulted in inert pellets of better physical properties, where ram extruder produced larger pellets than cylindrical extruder. The highest percent yield was about 70% using ram extruder and 95% using cylindrical extruder at an optimal lactose-MCC-moistening liquid ratio of 4.6: 6.4: 6.1. The feasibility of formulating matrix pellets containing *Andrographis paniculata* (Burm. f.) Nees (Acanthaceae) herbal medicine with the highest percent yield was subsequently investigated. The herbal matrix pellets were formulated by incorporating *Andrographis paniculata* Nees aqueous extract as the moistening liquid in the lactose-MCC mixture at the optimal ratio. The *Andrographis paniculata* Nees matrix pellets possessed some similar physical characteristics as the inert pellets. These characteristics were particle size distribution, d_{gw}, S_g, shape and flowability of the pellets. Nevertheless, the herbal pellets were found to be more friable and having uneven surface morphology. In conclusion, this study has provided a means of predicting an optimal formulation with some desired physical characteristics having good agreement between the inert and the herbal matrix pellets.

Eudragit Coatings For TCM And Herbal Medicines

A. Muthaiah* and Peter Wolff
Rohm Pharma Polymers, Degussa-Huls (SEA) Pte Ltd
2, Corporation Road, #06-03, Corporation Place (Lobby D), Singapore 618494

The typical properties of TCM and herbal medicines are usually of dark colors, have long or delayed disintegration time and high friability. Also the tablets containing oils (volatile and non-volatile) as active ingredients might be lost during storage. Hence, to improve these qualities, it is necessary to do a top coating for the herbal and TCM tablets.

To improve the qualities of the herbal and TCM tablets, the tablets are coated with different type of polymers such as Eudragit (methacrylic acid co-polymer), HPMC (hydroxypropyl methylcellulose) with viscosity 3, 5 and 6 cP's and modified HPMC. The herbal and TCM tablets coated with different types of polymers, such as, Eudragit *L*, Eudragit *E* and Eudragit *RD 100* gives a smooth and glossy appearance from a clear as well as pigmented coating. The dark color of the core tablets are covered with a minimum quantity of polymer (1.5 to 3.0% weight gain) due to its higher pigment binding capacity and it is up to 300% based on dry polymer without affecting or prolonging the disintegration time. Whereas, HPMC and modified HPMC coating requires higher amount of polymer (7.0 to 10.0% weight gain) due to its limitation on pigment binding capacity of only 20 to 50% based on dry polymer. This high weight gain of the HPMC coating prolongs the disintegration time as well as processing time. Other problems observed in the case of HPMC coated tablets were, sticking to the tongue, giving a slimy feeling in the mouth and color fading. The modified HPMC coating was not smooth and glossy. Hence, it is necessary to do a second coating with clear HPMC in order to make it glossy.

* Corresponding author

Formulation Of Alginate Beads For Binding With Copper Ions

Pei Yin Tan, Paul W.S. Heng and Lai Wah Chan
Department of Pharmacy, National University of Singapore,
10 Kent Ridge Crescent, Singapore 119260
Tel: 65-8743506, Fax: 65-7791554, E-mail: phaclw@nus.edu.sg

Presence of trace heavy metals, such as arsenic, copper, lead and mercury, in water has a significant impact on the ecosystem. These metals pollute the environment and produce harmful effects on living organisms. Such toxic metals are also found naturally in medicinal herbs used in Chinese medicines. Due to the process of concentration, extracts of these herbs often contain a relatively high level of heavy metals. When these products are consumed, the heavy metals may accumulate in the human body and cause adverse effects to health. It is therefore important to control the levels of these metals in the above products.

The aim of this study was to formulate a potentially useful product for the removal of heavy metals from water and extracts of medicinal herbs. Copper was used as a model heavy metal. Various methods of producing alginate beads were explored. The morphology of the beads was determined by microscopic examination. The stability of the beads in water and copper sulphate solution was also determined. Beads that remained intact after 15 minutes in the test media were considered as stable. The binding rates and capacities of the stable beads for copper were then evaluated. Atomic absorption spectroscopy was employed for the assay of copper.

The test products formulated included sodium alginate beads, calcium alginate beads and calcium alginate beads treated with sodium citrate. The morphology of the different types of beads was found to be significantly affected by the process and formulation variables. The sodium alginate beads were found to disintegrate rapidly in both water and copper sulphate solution. Comparison of the binding capacities showed that the calcium alginate beads treated with an optimal concentration of sodium citrate had the highest binding capacity. These beads are potentially useful for the removal of trace heavy metals from water and extracts of medicinal herbs.

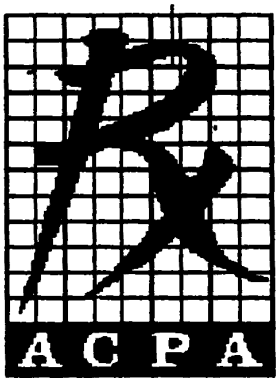
The Influence Of Particle Size Of Milled *Cocos nucifera* L. Fibers During Spheronization

Li Gu, Celine V. Liew and Paul W.S. Heng
Department of Pharmacy, National University of Singapore,
10 Kent Ridge Crescent, Singapore 119260

Herbs, in the form of a concentrated extract or as milled powder, may be incorporated into spheroids by spheronization. For incorporation using a milled powder form, the particle size and size distribution of the milled herb material may influence the spheronization process. *Cocos nucifera* L. fibers were used as a model for a fibrous herb material. After milling, the milled material was separated into different size fractions by sieving. It was found to have a wide size distribution, ranging from 1 mm to below 90 μm. Different size fractions, < 90 μm, 90-125μm, 125-180 μm and 250-355μm, of the milled material were tested for spheronization. Spheroids were prepared by adding the milled material into a microcrystalline cellulose (MCC) : lactose (1:3 ratio) blend using distilled water as the moistening liquid. The amount of milled material used was calculated as 1% of the total weight of MCC and lactose. Spheroid properties were rated by mean size, size distribution, yield and oversized part.

The study revealed that the particle size of the milled *Cocos nucifera* L. fibers affected the extrusion-spheronization process and the quality of the spheronized product. Spheronization using the 250-355 μm size fraction was not workable. The long fibrous particles could not be incorporated into the MCC:lactose spheroids. During spheronization, the long fibrous particles separated out from the MCC:lactose mass. The spheronized product consisted of MCC:lactose spheroids and long fibrous particles. This was attributed to the disparity in the particle sizes of the starting materials. The mean particle sizes of the lactose and MCC powders were comparatively much smaller than that of the fibrous particles in the 250-355 μm size fraction.

Spheronization was possible with the <90 μm, 90-125 μm, 125-180 μm size fractions. Characterization of these spheroid batches showed that there was no significant difference among them for mean spheroid size, size distribution, yield and oversized part. However, it was found there was a higher "between batch" variability for spheroids prepared using the 125-180 μm size fraction. In conclusion, herb materials must be milled down below a certain size before spheronization is possible. In this study, it was found that milled material with a mean size above 250 μm could not be spheronized. For spheronization, the particle size of the milled material should preferably be below 180 μm.



BUSINESS EXCHANGE FORUM ABSTRACTS

TIFAC Centre of Relevance and Excellence (CORE) in Herbal Drugs
J.S.S. College of Pharmacy, Ootacamund, Tamil Nadu, India.

J.S.S College of Pharmacy, Ootacamund, is presently the largest postgraduate and research institute in India imparting quality pharmaceutical education at diploma, degree, postgraduate and doctorate levels. The institution is affiliated to the Tamil Nadu Dr.M.G.R Medical University, Chennai and has been granted accreditation rating "GRADE A" (Excellent) by the National Board of Accreditation of All India Council for Technical Education, New Delhi.

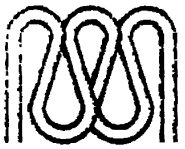
The TIFAC CORE in Herbal Drugs is supported by Pharmaceutical Industries and Technology Information, Forecasting and Assessment Council (TIFAC) of the Department of Science and Technology, under its programme "MISSION REACH" (Relevance and Excellence in Achieving New Heights in Educational Institutions) as a part of TECHNOLOGY VISION 2020 follow up document of the Govt. of India (more at: http://www.missionreach.net).

The primary purpose of the CORE, with its state of the art infrastructure, is to meet the specialized demands of the human resource requirements of the Pharmaceutical industries and organizations engaged in the development and standardization of herbal drugs and formulations in addition to undertaking research projects. The CORE would also document the traditional medical practices and medicinal plants to protect the heritage of India from piracy. The CORE is electronically linked with 90 other COREs in diverse areas of Science & Technology throughout India through land and V-Sat Connectivity. Situated in the heart of the Nilgiri Biosphere Reserve, the CORE has already interacted with the tribal population of the biosphere and identified and documented it's medicinal plants. The CORE is collaborating with several industries, universities, national and international organizations for developing herbal formulations, particularly in the antidiabetic, antihyperlipidemic, antiulcer, wound healing, antiinflammatory and antifertility, etc. The CORE is on the verge of launching collaborative programmes with The Uniformed Services University of Health Services, Bethesda, Maryland, USA. It has other tie-ups with the best brains within the country and abroad.

The college also has a Centre for Advanced Drug Research and Testing (CADRAT), where pharmacology and toxicology of drugs, production of tumour specific antibodies for drug targeting, design of drug delivery systems, stability testing, standardization of poly herbal formulations, bioavailability and bioequivalence studies in human volunteers are carried out.

The centre is committed to uphold the highest traditions of professional ethics, quality, and confidentiality. We invite Pharmaceutical Industries and the Institutes of Pharmacy the world over to participate in this world class CORE for their manpower training needs and research programmes.

For additional information, please contact: **Prof. M.J.Nanjan, Director / Programme Coordinator, TIFAC CORE in herbal drugs, J.S.S. College of Pharmacy, Ootacamund 643 001, Tamil Nadu, India. Tel: +91-423-447135/443393; Fax: +91-423-443394; E-mail: mjnanjan@yahoo.com**



M.E.I. Project Engineers Pte. Ltd.

(Company Registration No.: 197301079G)
21 Marsiling Industrial Estate Road 9 Singapore 739175
Telephone: (65) 367-1113 Telefax: (65) 367-1110
E-mail: meieng@singnet.com.sg Website: www.meiasia.net

Roland Wee, founder of *M.E.I. Project Engineers Pte Ltd*, was a former *Beecham Pharmaceuticals* engineer. He was involved in the design, construction, commissioning and maintenance of the first semi-synthetic penicillin plant in Singapore.

He established M.E.I. in 1973. Since then, M.E.I. has built up a track record of well-engineered and well-managed sophisticated projects in Singapore, China, Taiwan, Malaysia, Indonesia, Vietnam and India.

M.E.I.'s strength lies in the pool of qualified and dedicated engineers who have the ability to provide turnkey design, engineering, procurement, project management and construction services for life sciences and pharmaceutical projects. M.E.I. also adds value by participating in the clients' process technology development from the earliest stages.

M.E.I.'s mission is to help customers build their plants, factories and facilities they need in Asia. Turning new customers into repeat clients is our goal as they are a vital part of M.E.I.s' success. Our clientele includes many prominent *Fortune 500* companies.

In line with our business, M.E.I. is also involved in the design and construction of sophisticated teaching and pilot plant units for various educational institutes and multi-national companies in Singapore and the region. These are unique miniature plants, such as crystallisers, natural and forced circulation evaporators, flow visualisation, fluidisation, filtration and solid-liquid extractor units, heat exchanger test rig, centrifugal pump test rig, pump circuit operation rig and sedimentation operation rig. Each teaching unit demonstrates fundamental production concepts that a student or operator must understand. Experiments are designed to illustrate dynamic chemical processes. The aim is to prepare students and operators to deal with problems in real-world industrial processes.

M.E.I. will undertake the process plant design alone or in partnership with others in order to fulfil the clients' requirements. The company is certainly committed to provide any customer with the most comprehensive and tightly co-ordinated project within the budget and on time.

Dow Chemical Company

Tina Dasbach, Pacific Technical Director
Midland, MI, USA

My presentation will focus on a preliminary investigation to evaluate the use of hydroxypropyl methylcellulose (HPMC) and ethylcellulose (EC) as granulation binders with Ginkgo biloba extract. HPMC and EC have been effectively used as binders in solid oral dosage forms with a wide range of active ingredients. However, there has been little research published on the use of these polymers with herbal products. Both wet and dry granulations were prepared and evaluated in the study. Using an AERO-FLOW(R) apparatus, the flow properties of the granulations were measured and compared to the flow of the extract alone. Tablet physical data was also considered.

Method for Increasing the Compressibility of Herbal Powder Dosages

Charles R. Cunningham, Global Technical Manager
Colorcon, West Point, Pennsylvania, USA

Objectives

Due to inherent lack of compressibility, most herbal powder remedies are marketed in hard gelatin capsule form. Higher cost herbal extracts are often used in manufacture of tablets due to their higher potency and increased compactibility. By developing a process to impart increased compaction characteristics to the herbal powders, the increased manufacturing and cost efficiency of tablet compression versus that of capsule filling may be realised whilst avoiding the use of more costly herbal extracts.

Using Echinacea purpurea as a model, the goal of this study was to investigate fluid-bed granulation as a process to enhance the compressibility of the herbal material.

Methods

The materials used in the granulation study were Echinacea purpurea powder (root and aerial parts), partially pregelatinised corn starch (Starch 1500®) as the binder, Fumed silica (Cabosil®) and ambient temperature water as the granulation liquid.

The granulations were performed in a Glatt GPCG-3 fluid bed equipped with top spray. Trial 1 consisted of 95.0% echinacea and 5.0% Starch 1500 that was dispersed in water (6.0% w/w) and sprayed onto the echinacea powder. Trial 2 consisted of 92.5% echinacea, 5.0% Starch 1500, and 2.5% fumed silica where the Starch 1500 and fumed silica were dispersed together in water (6.0% w/w) and sprayed onto the echinacea powder. Both granulations were dried to 4.0% moisture content.

A 10-station rotary tablet press (9.5 mm standard concave tooling) was used to compress the granulations and a control sample of the untreated powder. The tablets were tested for breaking force, friability and disintegration time. The total phenolic compound levels present in the granulations and tablets were measured by HPLC to ensure that the granulation and tableting process did not affect the potency of the herb.

Results

The echinacea granulated with Starch 1500 produced tablets with a breaking force 53.0% higher than the straight herbal powder. When fumed silica was added to the Starch 1500 in the granulation liquid, the resultant tablets had a breaking force that was 76.0% higher than the powder and 49.0% higher than when Starch 1500 alone was used as the binder. Tablet friability was low for the granulated materials and the disintegration times were all less than 2 minutes. Tests for total phenolic compounds in the granulations and finished tablets showed little or no degradation.

Conclusions

The process demonstrated in this study can be used to produce herbal powder tablets that are sufficiently robust to withstand the mechanical stresses of packaging and transport and even the film-coating process.

Pharmaceutical Industry Technology and Development Center (PITDC)

5/F, No.101, Lane 169, Kang Ning St., HisChih City, Taipei Hsien, Taiwan
Contact: Mr. Shing Tzuok TSAI, General Manager
Tel: 886-2-2692-2103, Fax: 886-2-2695-4538
E-mail: pitdc@msl.hinet.net

PITDC is a non-profitable organization founded in 1993 with the joint effort of the Industrial Development Bureau under the Ministry of Economic Affairs and 45 pharmaceutical companies in Taiwan. The objectives of PITDC are to provide a communication channel between the government, the private sector and the academic sector and more importantly to enhance the technological aspect of the local pharmaceutical industry.

Over the last few years, PITDC had been conducting its own research and providing the following services:

- Developments of new pharmaceutical technology like new delivery system, formulation design, PK analysis and new analytical techniques.
- Research in scientific based Chinese herbal medicine in the area of analytical method, extraction method, standardization and new dosage forms. Research and development of traditional herbal formulations for new indications like anti-depressant, anti-anxiety, and in the treatment for arthritis and cough from pre-clinical through to clinical phases.
- Internationalization of domestically manufactured pharmaceutical products by upgrading the quality of existing products.
- Continue education and training programs in manufacturing, analytical workshops, regulatory affairs and intellectual property protection and licensing.
- Information services including literature and patent search and continuous update on global regulatory affairs.
- Assist pharmaceutical industry in establishing cGMP.
- Assist in technology transfer and collaboration with overseas companies.

The center will continue to work together with the private sector to improve on the quality of domestically manufactured drug products and to enhance the international image and competitiveness of the local pharmaceutical industry. It will continue its effort in the development of key technologies with special emphasis in Chinese herbal medicine.

Challenges in the 21st Century – Utilizing Western Science on Traditional Chinese Herbs

Herb C.G. Shen, CEO
Sun Ten Pharmaceutical Co. Ltd.
3F, No. 11 Roosevelt Rd., Section 2, Taipei, Taiwan
Tel: 886-2-2395-7070 ext. 115, Fax: 886-2-2321-3707
E-mail: jichen@sunten.com.tw

Sun Ten Pharmaceutical Company (ST) founded by Dr. Hong-yen Hsu in 1946. Over the past 50 years, we have committed to provide the most efficacious and safest herbal drugs to people around the world. "Ethical products and honest operation" has always been our mission at Sun Ten.

Sun Ten TCM Concentrated Herbal Extracts consist of over 260 Herbal Formulas and over 400 single Herbs in granules and some in tablet form. The quality control process starts from herb origin for its accuracy and safety. High Performance Liquid Chromatography (HPLC) is used for identification; both Gas Chromatographic Test (GC) and Atomic Absorption Spectrophotometric Test (AA) are used to assure that pesticides residue and heavy metals are all within safety range. In addition, our unique production process allows us to retain the essential oil of the herbs for added efficacy. As the result of years of hard work, our products have honored with lots of awards and recognized by various organizations. Our TCM Concentrated Herbal Extracts are currently adopted by numerous hospitals in Taiwan and sold in Japan, Australia, South East Asia and the US.

With the dramatic increase of interest in using herbs and phytomedicine worldwide, we are doubtless to join the stream with our half a century experience and expertise. In the past couple of years, ST has collaborated with various domestic and international research institutes for new drug and/or phytomedicine development. We have three US/PCT patents pending at present.

In order to offer the market a more cost-effective product, ST has recently developed a patent pending fermentation process to culture *Ganoderma Lucidum* and *Cordyceps sinensis*. For instance, wild *Cordyceps sinensis* is extremely rare and difficult to obtain. The conventional cultivation method for *Cordyceps sinensis* includes solid media stationary incubation, liquid media rotating shaking incubation, liquid-state fermentation, and submerged liquid-state fermentation. Unfortunately, these methods either require high capital investment due to high energy and waste output in the process or produce little H1A, which is proven to have pharmacological effects on immune system, renal function, and cardiovascular system. The solid state fermentation (SSF) we have developed requires low capital investment due to low energy and waste output. The base materials and media used are generally cheaper and simpler than other methods. In addition, the SSF medium generally contains low water content, which not only reduces the risk of contamination but also offers a favorable condition for fungal growth, because it resembles the natural habitats for fungi. Most of all, the kinds of fungi which can be propagated by SSF include, but not limited to, *Cordyceps sinensis*, *Trametes versicolor*, *Antrodia camphorata*, *Agaricus Blazei*, and *Ganoderma Lucidum*.

Maywufa Groups Introduction

Maywufa Enterprise
5F, No. 167 Fu Hsing North Road, Taipei, Taiwan
Tel: 886-2-27136621; Fax: 886-2-27152181

Maywufa Enterprise consists of a diversified group of companies specializing in healthcare and drug products research, distribution and logistics. It is the distributor of Rexall Sundown, Novartis and Japanese healthcare products in Taiwan. Maywufa also operates franchise drug stores distributed throughout Taiwan, medical laser device distribution and Laser Centre consultation, and consumer cosmetic product distribution through its subsidiary Pro Healthcare Int'l Co. Ltd. Three recent creations under Maywufa group are PhytoHealth Corporation, United Biotech Corporation and Walton Pharmaceutical Co. Ltd.

PhytoHealth Corporation was established in 1998, specializing in new drug development. It has already licensed in a number of promising drug candidates valued with a market capitalization of approximately US$ 600 million in the R&D pipeline and intends to have its first product approved for Asian markets as early as 2004. It is PhytoHealth's objective to continue to source for new drug candidates and seek co-development partners for its products. [Contact information: Fl. 7-5, No. 181 Fu Hsing North Road, Taipei, Taiwan, R.O.C. Tel: 886-2-25453697, Fax: 886-2-25140245; E-mail: tsjiang@yahoo.com]

United Biotech Corporation (UBC) was established in 1996 to develop botanical products, including several dietary supplements. One of them, called L.E.M. 1000, is an immunomodulator with the active components extracted from Lentinus Edodes Mycelium. Other products under development include an anti-fatigue drink and a cholesterol reducer. All of them are botanical products. Potential sales distributors or research partners are encouraged to contact the company. [Contact information: 1 Industry E. Rd. II, Suite 605, Science-Based Industrial Park, Hsinchu, Taiwan, R.O.C. Tel: 886-3-5783605 Fax: 886-3-5770875; E-mail: yachunwang@kimo.com]

Walton Pharmaceutical Co. Ltd. was set up in 1999 with a vision to distribute and market pharmaceutical product through its e-commerce platform. It is envisioned that Walton's technology platform will play a vital role and enhance the overall value for the whole group. [Contact information: Fl. 5-1, No. 167 Fu Hsing North Road, Taipei, Taiwan, R.O.C. Tel: 886-2-27187711, Fax : 886-2-27183887; E-mail: service@wthealth.com]

The Development Center for Biotechnology in Taiwan

Billy J. CHOU and Chiao-Wen CHEN
81 Chang Hsing Street, Taipei, Taiwan
Tel: 886-2-2732-5123 ext. 2109, Fax: 886-2-2732-5181
E-mail: bjchou@mail.dcb.org.tw

The Development Center for Biotechnology (DCB) is a non-profitable research and development organization established in 1984 to promote and to assist the development and nurturing of the biotechnology industry in Taiwan. There are four research and administration buildings with total 30,000 square meters of floor space. It has about 300 staffs and more than 60% of them have advanced degrees. Throughout the years DCB has built many core technologies and infrastructures, which are vital in developing biotechnology and pharmaceutical products. These centers of excellence are readily available resources for academic institutions and domestic industries. Through its five international liaison offices and domestic organization, DCB will seek promising inventions being developed by start-up companies worldwide. These new promising inventions will be nurtured in varied degrees by the 8 core technologies established at DCB. The nurtured inventions will then be partnered with local industries and investors for further development. In longer term, we hope these efforts will help the local industries produce profitable health products with global competitiveness. We hope the reinvestment of these profits to more products R&D will eventually reduce the need for continue government support.

G

GOH Lena
National University of Singapore, Singapore

GU Li
National University of Singapore, Singapore

GUO Dianwu
Minsheng Pharmaceutical Corp., China

GUO Jian-Wen
Chengdu University of Traditional Chinese Medicine, China

H

HAO Jinsong
National University of Singapore, Singapore

HARIANTO
PT Herlina Indah, Indonesia

HARUN Pramono
PT Soho Industri Pharmasi, Indonesia

HENG Paul
National University of Singapore, Singapore

HENI Ekasani R
PT Nufarindo, Indonesia

HINDRIANTO Lukas Lioe
PT Soho Industri Pharmasi, Indonesia

HSU Charleson C.S.
Brion Herbs Corporation, U.S.A.

HSU Ching-Hsiang
China Medical College, Taiwan

HSU Irene
Sun Ten Pharmaceutical Co. Ltd., Taiwan

HSU Van Doren
University of Maryland, U.S.A.

HU Ming
Washington State University, U.S.A.

HUANG Chia-Hsin
Center for Drug Evaluation, Taiwan

I

I Gusti Putu Bagus Diana Virgo
PT Kalbe Farma, Indonesia

J

JI Xin Yan, Julia
Ocean Healthcare (S) Pte Ltd., Singapore

JIN Yudi
National University of Singapore, Singapore

JUDI Indrawati Kusumajaya
PT Soho Industri Pharmasi, Indonesia

K

KALISTA Utama
PT Soho Industri Pharmasi, Indonesia

KAM Yin Fah
Eu Yan Sang International Ltd., Singapore

KJAERGAARD Ole
Niro A/S, Denmark

KO Feng-Nien
Pharmaceutical Industry Technology and Development Center, Taiwan

KOH Hwee Ling
National University of Singapore, Singapore

KOO Chee Kai
Kim Sin Medication Supply, Singapore

KUNG Patrick
PhytoCeutica, Inc., U.S.A.

KWOK Tuck Loong
National University of Singapore, Singapore

L

LAI Jung-Nien
National University of Taiwan, Taiwan

LAI Weng Fai
Centre for Pharmacutical Administration, Health Sciences Authority, Singapore

LAM-LIM Christina
Ocean Healthcare (S) Pte Ltd., Singapore

LAM Y.W. Francis
University of Texas Health Science Center at San Antonio, U.S.A.

LAU Brad W.C.
Hong Kong University of Science and Technology, Hong Kong

LAU Chester
Capital Health System, U.S.A.

LEE Chin Chiat
National University of Singapore, Singapore

LEE Echo
Sun Ten Australia, Australia

LEE Huey Ying
National University of Singapore, Singapore

LEE Kuo-Hsiung
University of North Carolina at Chapel Hill, U.S.A.

LEE Lynette
TCM Task Force Secretariat, Economic Development Board, Singapore

LEE Tat Leang
National University of Singapore, Singapore

LEE Tiak
HST Medical Pte Ltd., Singapore

LEUNG Jacqueline
U.S.A.

LEUNG Shawn
Hong Kong Institute of Biotechnology Ltd, Hong Kong

LEW Chang Ching
Gano Excel Enterprise Sdn Bhn, Malaysia

LI Haoran
Zhejiang University, China

LI Xiaoman
National University of Singapore, Singapore

LIEW Celine
National University of Singapore, Singapore

LIM Heng Moh
MOH Pharmaceutical Technologies Sdn Bhd., Malaysia

LIM Johnny
DAC Pharmalab Pte Ltd., Singapore

LIM Liang Theng
National University of Singapore, Singapore

LIM Lis Sa Elissa
National University of Singapore, Singapore

LIMUACO Olivia M
Centro Escolar University, Philippines

LIN Ge
Chinese University of Hong Kong, Hong Kong

LIN Tsung C.
EastWest Pharmaceuticals International, U.S.A.

LIOU Albert
Apex International Clinical Research Company Ltd., Taiwan

LUI Joseph
Hon Ding International Inc., U.S.A.

M

McCRAY John E.
Pan Pacific Pharmaceuticals, Inc., USA

MOK Darrel
Hog Seng Medical Hall, Singapore

MUTHAIAH A
Rohm Pharma Polymers, Degussa Huls (SEA) Pte Ltd., Singapore

N

NANJAN M.J.
J.S.S. College of Pharmacy, India

NEOH Ching Ching
Euro Chemo-Pharma Sdn Bhd., Malaysia

NG Siong Mui
Chun Chun Manufacturing Pte Ltd., Singapore

NG Toon Yaa
National University of Singapore, Singapore

NGOH Angeline Ai Hua
Yi Shi Yuan Pte Ltd., Singapore

O

ONG Beng Thai
Euro Chemo-Pharma Sdn Bhd., Malaysia

ONG Kang Teng
National University of Singapore, Singapore

ONG Yek Cheng
National University of Singapore, Singapore

ONO Hiroyuki
Cerebos Pacific Ltd., Singapore

P

PAN Fusheng
Huadong Pharmaceutical Institute, China

POH Swee Cheng
YSP Industries (M) Sdn Bhd, Malaysia

PU Songlin
Zheda-Tianmu Pharmaceutical Inc., China

R

RITTHIDEJ Garnpimol C.
Chulalongkorn University, Thailand

RUO Tsuen-Ih
MDS Pharma Services, Taiwan

S

SCHMETTERLING Dori
Schmetterling Associates, U.K.

SEAW Judy
National University of Singapore, Singapore

SHANG Zhicai
Zhejiang University, China

SHEN Herb C.G.
Sun Ten Pharmaceutical Co. Ltd., Taiwan

SHI Shirley
ISP Shanghai, China

SIA Chong Hock
Centre for Pharmaceutical Administration,
Health Sciences Authority, Singapore

SURESH B
J.S.S. College of Pharmacy, India

T

TAM Yun K
Kinetana Inc./ Hong Kong Herbal
Pharmaceuticals Ltd., Canada

TAN BT
Tengah Chinese Medical Hall, Singapore

TAN Eng Liang
PT Soho Industri Pharmasi, Indonesia

TAN Hooi Peng
Euro Chemo-Pharma Sdn Bhd., Malaysia

TAN Yvonne
Universiti Sains Malaysia, Malaysia

TANG Mun Hay
ISP Asia Pacific Pte Ltd., Singapore

TANG Like
Minsheng Pharmaceutical Institute, China

TEH Go Wai
Imexcel Sdn Bhd, Malaysia

TEO Eunice
Ministry of Health, Singapore

TING Ka Hua
Poh Guan Hong (1985) Sdn Bhd, Malaysia

TING Pao-Lien
Pharmaceutical Industry Technology and
Development Center, Taiwan

TOWN Winston
GloboAsia (HK) Ltd., Hong Kong

TSAI Shing-Tzuok
Pharmaceutical Industry Technology and
Development Center, Taiwan

TSI Daniel
Cerebos Pacific Ltd., Singapore

TU Renjing
Shenzhen Techtransfer Consulting Co. Ltd.,
China

W

WANG Shi
Inwe Technology Inc., China

WEE Roland
M.E.I. Project Engineers Pte Ltd., Singapore

WEN Kou-An
Sun Ten Pharmaceutical Co. Ltd., Taiwan

WIJONO Widjojo
PT Soho Industri Pharmasi, Indonesia

WONG Kwun Cheung
Farmacia Man Fong, Macau

WONG Mei Yin
National University of Singapore, Singapore

WONG Tin Wui
National University of Singapore, Singapore

WOO Soo On
Center for Analytical Science,
Health Sciences Authority, Singapore

WU Jinn
XenoBiotic Laboratories, Inc., U.S.A.

WU Tianxing
Hangzhou TechBank Technology Inc.,
China

X

XIAO James
Eu Yan Sang International Ltd., Singapore

Y

YANG Chih-Hsin
National Taiwan University Hospital, Taiwan

YANG John Po-Wen
Taiwan Sugar Corporation, Taiwan

YANG Thomas
Analytica, Taiwan

YAP Foo Chee
Sun Ten Pharmaceutical Mfg (M) Sdn Bhd., Malaysia

YAP Sook Peng
National University of Singapore, Singapore

YEO Calvin Wee Sing
National University of Singapore, Singapore

YEW Sei Ling
Skywide Medical & Health Food Trading, Singapore

YONG Eu Leong
National University of Singapore, Singapore

YU Kwun Chark, Samuel
Messrs. Victor Chu & Co., Hong Kong

YU Wei Min
ISP Shanghai, China

YUE May K.Y.
Sky Biohealth Solutions Inc., U.S.A.

YUE Samuel
HealthEast Pain Clinic, U.S.A.

YULIANI Dewi
PT Soho Industri Pharmasi, Indonesia

Z

ZAMAN Nuzhat
Kinetana Inc./ Hong Kong Herbal Pharmaceuticals Ltd., Canada

ZHANG Qi
Kemin Industries (Asia) Pte Ltd, Singapore

ZHANG Yonghua
Huadong Pharmaceutical Institute, China

ZHI Lifen
Hangzhou Pharmaceutical Bureau, China