

HONG KONG PHARMACEUTICAL *JOURNAL*

VOL 19 NO 1 Jan - Mar 2012 ISSN 1727-2874



News & Short Communications

Impact of Pharmacist Counseling Service on Blood Pressure Control of Borderline Hypertensive Patients

A Pilot Implementation of Decentralized and Automated Dispensing System by Omnicell – from Challenging to Benefit Realization

Immunization in Hong Kong

Emergency First Aid for poisoning and for Alkaloid Poisoning in Particular

Method Development for the Colorimetric Determination of Total Alkaloids in Herbal Medicine

Turtle Shell Extract as a Functional Food and Its Component-based Comparison among Different Species

Hong Kong Pharmacy Conference 2012

Road Traffic (Amendment) Ordinance 2011: Briefing Seminars for Transport Trades in March 2012

PSHK Forensic Lectures

Avonex™/ Prolia® Injection/ PRADAXA®

Hong Kong Pharmaceutical Journal: For Detailed Instructions for Authors



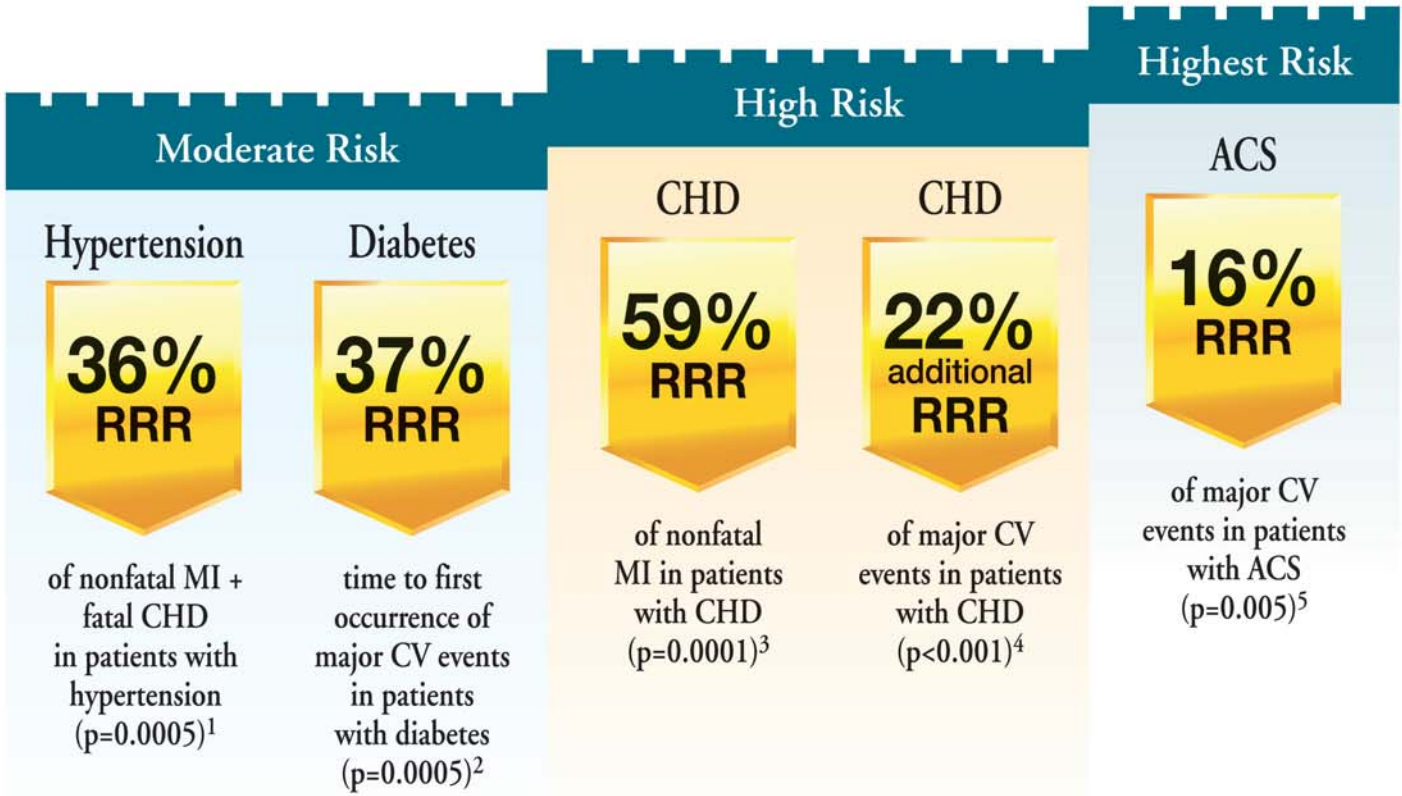
*The Pharmaceutical Society of Hong Kong
The Practising Pharmacists Association of Hong Kong
The Society of Hospital Pharmacists of Hong Kong*



LIPITOR
atorvastatin calcium – crystalline form

Power to do more

More Evidence across More Patient Types



References: 1. Sever PS, Dahlöf B, Poulter NR, et al; for the ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-lipid lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet*. 2003;361(9364):1149-1158. 2. Colhoun HM, Betteridge DJ, Durrington PN, et al; on behalf of the CARDS investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet*. 2004;364(9435):685-696. 3. Athyros VG, Papageorgiou AA, Mergouris BR, et al. Treatment with atorvastatin to the national Cholesterol education Program goal versus 'usual' care in secondary coronary heart disease prevention: the GREEK Atorvastatin and Coronary-heart-disease evaluation (GREACE) study. *Curr Med Res Opin*. 2002;18(4):220-228. 4. laRosa JC, Grundy SM, Waters DD, et al; for the Treating to New Targets (TNT) investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med*. 2005;352(14):1425-1435. 5. Cannon CP, Braunwald E, McCabe CH, et al; for the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med*. 2004;350(15):1495-1504. **Detailed information is available upon request.**



Pfizer Corporation Hong Kong Limited

16/F., Stanhope House, 738 King's Road, North Point, Hong Kong

Tel: (852) 2811 9711 Fax: (852) 2579 0599

Website: www.pfizer.com.hk



HONG KONG PHARMACEUTICAL JOURNAL

VOL 19 NO 1 Jan - Mar 2012 ISSN 1727-2874

EDITORIAL COMMITTEE

Editor-in-Chief	CHEUNG, Hon-Yeung
Managing Editors	CHEUNG, Mary TSANG, Warren WONG, Johnny TAI, Candy
Secretary	YUNG, Gloria
Treasurer	KWAN, Wanda
Business Manager	
Section Editors	
Pharmacy Education & Practice	CHONG, Donald CHAN, Timothy
Drugs & Therapeutics	LEUNG, Wilson
OTC & Health	CHEUNG, Foster
Pharmaceutical Techniques & Technology	CHEUNG, HY TONG, Henry
Herbal Medicines & Nutraceuticals	CHEUNG, HY WONG, Helen
Society Activities	CHAN, Ivy
New Products	PANG, Bobby LEE, Ken

Representatives from SHP

EDITORIAL ADVISORY BOARD

Prof. CHAN, Hak-Kim	Prof. CHANG, Pong
Prof. CHERN, Ji-Wang	Prof. CHIANG, Chiao-Hsi
Dr. CHING, Wei-Mei	Prof. CHO, Chi-Hin
Prof. CHOW, SS Moses	Prof. HUI, SC Sarah
Prof. LI, CH Paul	Prof. LI, Wan-Po Alain
Prof. LEE, An-Rong	Dr. MORGAN, Rae M.
Dr. TIAN, Hui	Prof. YANG, Chin-Hsin David
Prof. O'TOOLE, Desmond K	Prof. LEE, Hon-leung Vincent

The Hong Kong Pharmaceutical Journal, the publisher, the editorial board and the respective member societies are not responsible for the completeness and accuracy of the articles and advertisements contained in the Hong Kong Pharmaceutical Journal. The Journal will not be liable to any damages to persons and properties. Readers are advised to approach the respective authors and advertisers for information in case of doubts.

Copyright © 2010 by Hong Kong Pharmaceutical Journal

All rights reserved. No part of this publication or its supplement may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the Publisher.

All communications and enquiries should be directed to:

**The Secretary, Hong Kong Pharmaceutical Journal,
G.P.O. Box 3274, General Post Office, Hong Kong**

For all enquiries regarding advertisement, please contact:

Ms Gloria Yung (Tel. 9552 2458) at the following email address:
hkpjadv@gmail.com

INSTRUCTIONS FOR AUTHORS

The Hong Kong Pharmaceutical Journal is a journal of the pharmacists, for the pharmacists and by the pharmacists. Submissions are welcome for the following sections:

- Pharmacy Education & Practice
- OTC & Health
- Medication Safety
- Society Activities
- Drugs & Therapeutics
- Pharmaceutical Techniques & Technology
- Herbal Medicines & Nutraceuticals
- New Products

Comments on any aspects of the profession are also welcome as Letter to the Editor.

There is no restriction on the length of the articles to be submitted. They can be written in English or Chinese. The Editorial Committee may make editorial changes to the articles but major amendments will be communicated with the authors prior to publishing.

It is preferable to have original articles submitted as an electronic file, in Microsoft Word, typed in Arial 9pt. Files can be sent to the following address:

e-mail: editor@hkpj.org

**address: G.P.O. Box No. 3274,
General Post Office,
Hong Kong**

For detail instructions for authors, please refer to the first issue of each volume of HKPJ.

Editorial

CHEUNG, Hon-Yeung

5

News & Short Communications

Warning on Orally Consumed Product Containing Banned and Undeclared Western Drug Ingredients	6
Commencement Notice for the Regulation of Health Claims of Orally Consumed Products Gazette	6
Alert on Aconitum Alkaloid Poisoning	6
Recall of Allopurinol-Teva Tablets	6
Warning on Slimming Product Found with Banned Drug Ingredients	7
Contaminant in Drinking Water Linked to Mental Illness	7
Recall of Two Unregistered Pharmaceutical Products	7
Suspension of Use of Chinese Herb Mislabeled as "FlosCampsis"	7
Another Three Cancer Cures Added to the Subsidized Drug List by Hospital Authority	8
Arsenic Present in Organic Brown Rice Syrup	8
Woman Arrested for Allegedly Selling a Slimming Product with Undeclared and Banned Drug Ingredients	8
Woman Died of Legionnaires Disease after Dental Visit	8
Recall of MylifeTMPura® Blood Glucose Strips in France	8
Results of Hong Kong Chinese Materia Medica Standards (Phase IV) Announced	9
Import into China by Travelers or by Mail of Raw Bird's Nest and Material Medica Derived from Animals Banned	9
Market Boom for Generics and Biosimilar Drugs in Europe	9
Total Recall of Albumex 5 and Albumex 20 Infusion	9
Coca-Cola and Pepsi Caramel Color Is Carcinogenic	10
Results of Registration Examination for Pharmacists Announced	10
Low-dose Hormone Combo for Menopause Symptoms Approved by FDA	10
China to Help TCM Extends Global Reach	10
Lower Citalopram Dose Needed in Older Patients	11
Total Recall of Carboplatin Injection (Ebewe)	11
Man Arrested for Allegedly Selling Unregistered Pharmaceutical Products	11
Neurotoxin Found in Shark Fins	11

Pharmacy Education & Practice

Impact of Pharmacist Counseling Service on Blood Pressure Control of Borderline Hypertensive Patients	12
LEE, Vivian WY; CHAN, Belinda MC; CHEUN, Ken TK; SO, Renwick KH; YU, CM	
A Pilot Implementation of Decentralized and Automated Dispensing System by Omnicell – from Challenging to Benefit Realization	16
YUNG, Kit-Man; TAM, Ka-Ming; TSE, Pascal; WONG, Kei	

Drugs & Therapeutics

Immunization in Hong Kong	20
TSE, Kit-Ying; CHAN, Hoi Lam	

Emergency First Aid for poisoning and for Alkaloid Poisoning in Particular	25
O'Toole, Desmond Keith; CHEUNG, Hon-Yeung	

Pharmaceutical Techniques & Technology

Method Development for the Colorimetric Determination of Total Alkaloids in Herbal Medicine	28
CHEUNG, Hon-Yeung; BAIBADO, Joewel Tarra; CHAN, Gallant GL; ZHANG, Zhi-feng	

Herbal Medicines & Nutraceuticals

Turtle Shell Extract as a Functional Food and Its Component-based Comparison among Different Species	33
LI, Lin-Qiu; CHEUNG, Hon-Yeung	

Society Activities

Hong Kong Pharmacy Conference 2012	38
Road Traffic (Amendment) Ordinance 2011: Briefing Seminars for Transport Trades in March 2012	39
PSHK Forensic Lectures	40

New Products

Avonex™ (Biogen Idec (Hong Kong) Limited)	42
Prolia® Injection (GlaxoSmithKline)/ PRADAXA® (Boehringer Ingelheim)	44

Aims and Scope of the Journal

Hong Kong Pharmaceutical Journal: For Detailed Instructions for Authors	45
--	----



Eu Yan Sang

關懷始於1879

結合兩大靈芝精華 功效更勝一籌



破壁靈芝
孢子粉

高倍濃縮
+ 靈芝子實體
提取物

特效全靈芝
「破壁」孢子
Extra Strength
Lingzhi Cracked Spores

加入
靈芝子實體
提取物
精華二合一
Lingzhi Sporophore Concentrate is added!

每盒 60 粒膠囊
CAPSULES
PER BOX

有效活性成份

蘊含多種微量元素及
極高的活性孢子脂質成份

無農業污染

通過重金屬及農藥殘餘測試

品質監控

符合GMP標準及
ISO9001:2008認證

余仁生特效全靈芝破壁孢子結合整株靈芝的精華，由療效極高的破壁靈芝孢子粉及高倍濃縮的原木赤靈芝精華(子實體提取物)兩種成份精製而成，比一般市面的單一靈芝孢子成份產品含更豐富的靈芝多醣及三萜類元素，更有效調節人體免疫力，對改善人體多個系統功能起了更強更全面的功效!

余仁生特效全靈芝破壁孢子所選用的一級原木赤靈芝均參照GAP規範管理在天然無污染的生長環境下栽種，通過重金屬和農藥殘留測試，確保靈芝及孢子的純度及有效性，是靈芝產品中的極品。

顧客服務熱線：(852) 2544 3308

Healing a Wound with the Right Remedy and Error Free Medication



The Hong Kong Pharmaceutical Journal has entered its 19th Volume by this year, 2012. It is a year to be filled with lots of changes, uncertainties and maybe even turmoil in Hong

Kong and elsewhere. There will be many political elections which will mean transition of power in many countries. One of the recent hot issues in the mass media in Hong Kong was definitely the election of the Chief Executive (CE) of the Hong Kong Government SAR. Whether it was guessing who would be the CE aspirants or who would win the election attracted many people's attention. From the very beginning of the official launch of the campaign for the post of CE last October, no one would expect that the two candidates from the establishmentarian camp would fight each other so severely that from time to time someone would unexpectedly blow the whistle in relation to the integrity of the opponent. Certainly the campaign resulted in a series of shocks to the whole society. But we have witnessed the facts and sensed the pain not only pouring upon the two candidates but also for many people involved. Lurking suspicion is always damaging between people. For the majority of Hong Kong citizens, we were hurt too as long as we care about the harmony of the society. This is probably the price for a democratic election even though it was a small-circle exercise. This election reminds us whoever wants to be a public figure in an open society, you must be clean. Otherwise, you won't have a chance to be entrusted with power.

Fortunately, right after the election, Mr. LEUNG Chun-Ying, the Chief-Executive-elect, immediately declared that **there is no more a Tang or Leung camp but only a Hong Kong camp**. He also suggested we look forward and work together for Hong Kong. His speech was so touching and hopefully could bring about reconciliation with Mr. Henry Tang. **We sincerely hope that it can be realized and Mr. Leung should honor what he has said by taking a few steps forward to heal the wounds in the coming months.**

Straightly speaking, what we have seen in this CE election actually represents two different approaches to the deep social conflict that has spread and worsened in Hong Kong in the last two decades, but we prefer to remain blissfully unaware of what is going on. Mr. Tang was merely representing the extension of the current rule-by-the-rich, the tycoons and the conservatives, while Mr.

Leung was representing the long wish for change from the poor, the exploited and the moderate reformers. In other words, it is the privileged and the rich verses the exploited and the poor. This situation is almost the same in many other places and that explains why there are so many demonstrations and uprisings in many countries in the last couple of years because people have lost their patience.

Perhaps on a more mundane level, people should ask themselves what is the cause of the rift between the rich and the poor? Was Hong Kong really in such a state of blissful equilibrium 50 years ago, when there was as much inequality and far worse social deprivation than today? Until the answers to some key questions are found, it is quite impossible to give the correct remedy to the problems that people are facing.

This is exactly the same when a substance is to be prescribed to a patient for treatment of a disease or for nourishing the body. Before it can be used, sufficient background information about its biological effects as well as its qualitative and quantitative determination is necessary. Without this information, it is dangerous and risky to prescribe the substance as a cure. Chinese medicines have been used for thousands of years, yet many of them have not been systematically characterized or standardized using contemporary methodologies. The official release of Volume IV of the Hong Kong Chinese Materia Medica Standards announced by the Department of Health exemplifies the concerted efforts between the Hong Kong government and scholars from six local tertiary institutions. Although it merely covers the standardization of 36 commonly used herbs, at least these people have made some contributions to the modernization of Chinese medicines (p.9). In page 28, a more specific example about the determination of total alkaloids in herbs is described by Cheung and his associates. As many alkaloids have potent biological activities while being present in minute quantities, their assays, in many cases, are quite difficult. This article describes an alternative and easy method that could overcome the problem of alkaloid determination for quality control of herbs.

Apart from the determination method, an article in the Drugs & Therapeutics Section on the emergency treatment of alkaloid poisoning is included in this issue (p.25). This is a topic which we as pharmacists in our daily pharmacy practice, may be asked about or come across. The article on "Immunization in Hong Kong", which was written by Tse & Chan, is quite informative for persons who are unfamiliar

with the immunization schemes in Hong Kong. Indeed, there is quite a lot of free information and government-sponsored services available for eligible people. The authors have raised a few ideas about how pharmacists in Hong Kong could make their contribution in this healthcare work. Hence, it is worthwhile for all pharmacists to read and to think about.

Healing a disease does not simply rely on therapeutics alone but it also requires a good working spirit and system. In the Pharmacy Education and Practice Section of this issue, two working teams have thrown together their experiences and ideas on what a good medication practice would be in their daily work. Lee *et al.* share how borderline hypertensive patients are benefited by a counseling service that has been initiated by her and her associates (p12) while Yung *et al.* share with us how a decentralized and automated dispensing system was designed and installed in their hospital. The authors commented that nursing efficiency and patient safety were significantly enhanced since this electronic control system was introduced (p16). Both articles reveal that **advancement and new breakthroughs could only be made if we dare to try.** Certainly, it requires everyone's participation and contribution.

However, like the sky that may be raining sometimes, things are not always right. During the last three months, we have been told of a number of malpractices during drug manufacturing and of illegal sales of products containing some unregistered drugs or the wrong material medica. The situation of malpractice by people seems to be deteriorating. News associated with recalls or being caught doing the wrong thing has been frequently heard. Some of the representative news is reprinted in the News and Communication Section of the current issue for readers' reference. It is not difficult to conclude that the majority of recalls were attributed to the sales of health products containing some banned or undeclared drug ingredients while a few cases were due to some mistakes introduced during manufacturing. Whatever the cause, they may be harmful to the user and, therefore, they were ordered to be removed from the shelves by the authorities or on a voluntary basis by the manufacturer. **Nevertheless, let us always look forward and work together to build a prosperous Hong Kong.**

Cheung Hon-Young
 Editor-in-Chief
 11th April, 2012

Warning on Orally Consumed Product Containing Banned and Undeclared Western Drug Ingredients

Date: January 11, 2012

The Department of Health (DH) appealed to members of the public not to buy or consume an oral product, "TangBaoKouFuYiDaoSuJiaoNang", as it has been found to contain three undeclared Western drugs, one of which is a banned item in Hong Kong. The product is not a registered pharmaceutical product or a registered proprietary Chinese medicine in Hong Kong. The appeal followed DH's receipt of notification from the Hospital Authority about a 69-year-old man with diabetes

mellitus admitted to hospital on 26 December 2011 because of dizziness, nausea and vomiting. He had a history of consuming the above product. Investigation found that he suffered from hypoglycemia and renal failure. The patient was treated and discharged on 30 December 2011.

Results from the Government Laboratory revealed that the product contained the Western medicines metformin and glibenclamide, and a

banned drug, phenformin. All three drugs are hypoglycaemic agents. Improper use of hypoglycaemic agents may cause low blood sugar, which in serious cases, can be fatal. Metformin and glibenclamide are prescription drugs, meaning that they should be used under medical supervision. Phenformin, because of the possibility of causing fatal lactic acidosis, has already been banned in Hong Kong since 1985.

Source: www.chp.gov.hk

Commencement Notice for the Regulation of Health Claims of Orally Consumed Products Gazette

Date: January 13, 2012

The Secretary for Food and Health makes notice to commence the provisions related to the control of health claims of orally consumed products under the Undesirable Medical Advertisements (Amendment) Ordinance 2005. The Notice is gazetted today (January 13). It

proposes to commence the extension of the prohibition/ restriction on advertising orally consumed products for six groups of health claims from June 1, 2012. The Undesirable Medical Advertisements Ordinance (Cap 231) (UMAO) was first enacted in 1953 with the purpose

of protecting public health through prohibiting/restricting advertisements which may induce the seeking of improper management of certain health conditions.

Source: www.chp.gov.hk

Alert on Aconitum Alkaloid Poisoning

Date: January 13, 2012

It was reported that on December 28, 2011, a 35-year-old Chinese male developed symptoms and signs compatible with aconitum alkaloid poisoning, including perioral numbness, shortness of breath and palpitations. He

went to the Mainland on the same day and subsequently sought emergency care from United Christian Hospital on December 30. It was reported that the man had consumed some Chinese herbal medicines for health maintenance

prescribed by a registered Chinese medicine practitioner stationed in Po Yan Tong Medical Company, a licensed Chinese herbal retailer in Sai Wan before developing the symptoms.

Source: www.chp.gov.hk

Recall of Allopurinol-Teva Tablets

Date: January 16, 2012

A batch of Allopurinol-Teva Tablets 100mg (registration number: HK-57739; batch number: 1580211) has been withdrawn from the shelf on quality grounds as black substances were found on some tablets in two blisters of the product. Official investigation results showed that

no fungal elements were found. The report from the Government Laboratory revealed that the black substances, which adhered on the surfaces of some tablets, bear similar features as used hydrocarbon oil. Hydrocarbon oil might be used in equipment for the production

of tablets. The affected batch was manufactured by Teva Pharmaceutical Works Private Ltd Co. in Hungary. A total of 22,965 boxes had been imported into Hong Kong and were supplied to HA, local pharmacies and private doctors.

Source: www.chp.gov.hk

Warning on Slimming Product Found with Banned Drug Ingredients

Date: January 19, 2012

Through its surveillance network, DH found the slimming product named "FAT 2 AND 1 BURNERS III" offered again for sale on the Internet. The Government Laboratory confirmed that the product contained sibutramine and phenolphthalein. Sibutramine is a Part I

poison and was once a western medicine used as an appetite suppressant. Since November 2010, products containing sibutramine have been banned by the Pharmacy and Poisons Board because of the increased cardiovascular risk. Phenolphthalein is another banned

drug. It was used previously for treating constipation, but has been banned for its cancer-causing effect. The spokesman of DH Department urged people not to purchase products of unknown or doubtful composition.

Source: www.chp.gov.hk

Contaminant in Drinking Water Linked to Mental Illness

Date: January 30, 2012

Exposure to tetrachloroethylene (PCE) has been shown to cause mood changes, anxiety and depression in people who work with it. PCE readily crosses the blood-brain barrier and has a high affinity for the

lipophilic tissues in the central nervous system. A study published recently online in *Environmental Health* reveals that prenatal and early childhood exposure to the organic solvent, PCE may raise the risk

of certain psychiatric illnesses, particularly bipolar disorder, post-traumatic stress disorder and schizophrenia.

Source: www.medscape.com

Recall of Two Unregistered Pharmaceutical Products

Date: February 1, 2012

Allways (Germany) Medicine Ltd. Allways was instructed by the Department of Health (DH) to recall from the consumers two unregistered pharmaceutical products namely Centiplex-B Tab (HK-58444) and Abacod Cod Liver Oil Cap (HK-59342, 100's and 300's) as the products bear unapproved labels and render them unregistered. The matter came to light

upon the DH's investigation into a public enquiry about the products.

Investigation reveals that Allways is the product registration certificate holder of the two products. However, the two unregistered products were sold to local pharmacies by W&S International Medicine Ltd (W&S) which is an unlicensed

pharmaceutical product trader. According to information obtained so far, Allways had not authorized any person to import and sell Centiplex B-Tab and Abacod Cod Liver Oil Cap 300's. Allways imported unlabeled cod liver oil cap 100's and transferred them to W&S.

Source: www.chp.gov.hk

Suspension of Use of Chinese Herb Mislabeled as "FlosCampsis"

Date: February 3, 2012

The Department of Health (DH) appealed to the public who have bought the Chinese herb "FlosCampsis" from a licensed retailer, Cheong Kee Medicine Co in Yen Chow Street, Sham Shui Po, to stop using the product immediately as mislabelling might have occurred, such that what was dispensed could be another herb, FlosDaturaeMetelidis.

The precautionary alert is considered indicated as the latter is a known poisonous herb.

The suspicion arises as the DH investigates a suspected Chinese herbal poisoning incident notified by Queen Elizabeth Hospital earlier on today. A 27-year-old Chinese male

developed some symptoms compatible with anti-cholinergic poisoning, including palpitations and dilated pupils, after taking herbal medicines including "FlosCampsis" purchased from the above retailer. The patient's condition stabilized after hospital treatment.

Source: www.chp.gov.hk

Another Three Cancer Cures Added to the Subsidized Drug List by Hospital Authority

Date: February 9, 2012

The Hospital Authority expanded its drug list, adding three drugs used for treating rectal cancer, multiple sclerosis, pancreatic cancer and bladder cancer.

In future, the patients need not pay for the drugs on their own. Mr Cheung Wai-lun, Director of Cluster Services, Hospital Authority, said that 23,000 patients are

expected to benefit after the drug list is expanded.

Source: Sing Tao Daily

Arsenic Present in Organic Brown Rice Syrup

Date: February 16, 2012

Organic brown rice syrup, a sweetener used in many organic foods including cereal bars and baby formulas, may be a hidden source of arsenic, according to a new study published in *Environmental Health Perspectives*. Dartmouth College researchers tested commercial products

containing the syrup and compared them with other similar products without the sweeteners. They found that the former contained arsenic levels 20 times greater than the later. Because the risk of certain cancers or heart disease are said to be slightly elevated in drinking

water with a certain level of arsenic, consumers should be cautious and reduce their exposure to these items as much as they can.

Source: http://www.nlm.nih.gov/medlineplus/news/fullstory_122036.html

Woman Arrested for Allegedly Selling a Slimming Product with Undeclared and Banned Drug Ingredients

Date: February 17, 2012

A 30-year-old woman was arrested in a joint operation by the Police and the Department of Health (DH) at Sham Shui Po for suspected illegal sale of one box of Lexsci Fat Rapid Loss Capsule, which is

a slimming product with undeclared and banned drug ingredients. The operation followed laboratory test findings today that revealed that the slimming product, which had been obtained earlier from

an Internet auction website during DH's surveillance operation, were found to contain sibutramine, phenolphthalein.

Source: www.chp.gov.hk

Woman Died of Legionnaires Disease after Dental Visit

Date: February 17, 2012

An Italian woman is dead after having dental surgery and contracting Legionnaires' disease, also known as Legionellosis. The woman, who was 82, contracted Legionnaires' disease at her

dentist's office. Testing on the woman's home and the dental office showed that the infection came from the dentist's office water supply. Despite treatment with Cipro, a powerful antibiotic, the woman

quickly developed septic shock and died two days after her diagnosis. This is the first reported case of legionnaire infection via medical service.

Source: www.abcnews.go.com › Health

Recall of MylifeTMPura® Blood Glucose Strips in France

Date: February 22, 2012

The Department of Health (DH) drew the public's attention to the recall of certain lots of a blood glucose test strips in France. The affected product is MylifeTMPura® (box of 100's) manufactured by Bionime Corporation. The test strips may give falsely high blood glucose readings.

Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) about the recall. According to AFSSAPS, the problem came to their notice when several reports of overestimation of blood glucose levels were received. Further investigation revealed that the problem was due to the accidental opening of the unsealed vials of the test strips during transportation from the

distributor in France to the pharmacies. As the test strips are very sensitive towards air exposure, they may lose their performance, giving falsely high readings. The manufacturer has since then, taken preventive action by sealing all the vials with a protective film.

Source: www.chp.gov.hk

Results of Hong Kong Chinese Materia Medica Standards (Phase IV) Announced

Date: February 23, 2012

The Department of Health (DH) officially launched the reference standards on safety and quality for 36 commonly used Chinese Materia Medica (CMM) in Phase IV of the Hong Kong Chinese Materia Medica Standards (HKCMMS).

The 36 herbs are Arctii Fructus, Arsenicum, Arsenolite, Artemisiae Annuae Herba, Atractylodis Rhizoma, Aurantii Fructus, Aurantii Fructus Immaturus, Calomelas, Cinnabaris, Cistanches

Herba, Cnidii Fructus, Corni Fructus, Corydalis Rhizoma, Curculiginis Rhizoma, Curcumae Longae Rhizoma, Dictamni Cortex, Ecliptae Herba, Fritillariae Hupehensis Bulbus, Houttuyniae Herba, Hydrargyri Oxydum Rubrum, Hydrargyrum Chloratum Compositum, Isatidis Folium, Isatidis Radix, Orpiment, Peucedani Decursivi Radix, Peucedani Radix, Polygoni Cuspidati Rhizoma et Radix, Realgar, Schisandrae Chinensis Fructus, Schisandrae Sphenantherae

Fructus, Schizonepetae Spica, Scrophulariae Radix, Scutellariae Barbatae Herba, Smilacis Glabrae Rhizoma, Sophorae Flavescentis Radix and Stephaniae Tetrandrae Radix.

The standards for these 36 CMMs will be put into use for a trial period of 12 months, starting from April 2012, upon completion of all briefing sessions for traders and laboratories.

Source: www.chp.gov.hk

Import into China by Travelers or by Mail of Raw Bird's Nest and Material Medica Derived from Animals Banned

Date: February 27, 2012

CUBILOSE, a type of bird's nest considered a delicacy in China, cannot be brought in by travelers or mailed into the country, according to a newly amended list of prohibited items. The list, jointly

issued by the Ministry of Agriculture and the General Administration of Quality Supervision, Inspection and Quarantine, has 16 categories of banned animal and plant products. Compared with the

previous list issued in 1992, the new list has a broader range of banned products, such as leaf tobacco and genetically modified food.

Source: Ming Po

Market Boom for Generics and Biosimilar Drugs in Europe

Date: March 1, 2012

According to Frost & Sullivan's report, Generic Pharmaceuticals Market — A Global Analysis, pharmaceutical products worth \$150 billion will go off patent between 2010 and 2017, which will propel the generic-drugs market from revenues of \$123.85 billion in 2010 to an estimated \$231 billion by 2017. However, as competition intensifies, generic drug manufacturers will need

to carefully consider their product segments and the appropriate time for market launch. Companies will also have to deal with increasingly harsher cost cutting measures from governments and healthcare service providers.

The global biosimilars market earned revenues of around \$172 million in 2010, but this is estimated to jump to \$3987

million in 2017, with the industry growing at a compound annual growth rate of approximately 56.7%. According to Frost & Sullivan's Analysis of European Biosimilars Market report, impending patent expiries are expected to provide impetus to the market development of several new biosimilars.

Source: Pharmaceutical Technology Europe, Vol. 24(3)

Total Recall of Albumex 5 and Albumex 20 Infusion

Date: March 8, 2012

A licensed drug wholesaler, Hong Kong Red Cross Blood Transfusion Service (HK Red Cross), was told to recall all Albumex 5 Infusion 12.5g/250ml (HK-58570) and Albumex 20 Infusion 10g/50ml (HK-58571), due to quality issue. DH received notification from the HK Red Cross that they were informed by the product manufacturer in Australia, CSL Limited, that some of the Albumex products were found contaminated with ethylene glycol after

a follow up investigation of a small leak of ethylene glycol (in late January 2012) in a pasteurization vessel used in the manufacture of the products.

Albumex 5 Infusion and Albumex 20 Infusion, containing human albumin, are used for shock or in plasma exchange. They can only be sold on prescription and under the supervision of pharmacists at registered pharmacies. Ethylene glycol is a substance used to control

temperature during the manufacturing process. Toxic effects of ethylene glycol include CNS effects similar to ethanol, anion gap metabolic acidosis, and acute renal failure. Toxicity due to ethylene glycol occurs acutely and delayed effects beyond 72 hours would not be expected. Safety assessment of the products is being investigated by the Australian regulatory authority.

Source: www.chp.gov.hk

Coca-Cola and Pepsi Caramel Color Is Carcinogenic

Date: March 10, 2012

High levels of a chemical that causes tumors in animals were found in Coca-Cola Co. and Pepsi Co. Inc. sodas, according to a consumer advocacy group pressing U.S. regulators to ban a color additive. The chemical 4-methylimidazole was found in Coca-Cola, Pepsi Cola, Diet Coke and Diet

Pepsi and is part of caramel coloring used in the beverages, according to a study released on March 5 by the Center for Science in the Public Interest. The group petitioned the U.S. Food and Drug Administration in February to ban the ammonia-sulfite coloring, which is found in most colas.

4-Methylimidazole (4-MI) is used in a various processes, including manufacturing of dyes, pharmaceuticals, and rubber, as well as a byproduct of food fermentation.

Source: www.businessweek.com/news/2012-03-05/

Results of Registration Examination for Pharmacists Announced

Date: March 12, 2012

The Pharmacy and Poisons Board of Hong Kong announced today (March 12) the results of the Pharmacists Registration Examination held in December 2011. There were 82, 76 and 90 candidates sitting for examinations in "Pharmacy Legislation in Hong Kong", "Pharmacy Practice" and "Pharmacology"

respectively, with corresponding passing rates of 39 per cent, 88.2 per cent and 8.9 per cent.

In addition to meeting other requirements prescribed by the Board, any pharmacy graduate outside Hong Kong intending to be registered as a

pharmacist in Hong Kong is required to pass the above three subjects. The Board conducts its Registration Examination twice a year, normally in June and December.

Source: www.chp.gov.hk

Low-dose Hormone Combo for Menopause Symptoms Approved by FDA

Date: March 12, 2012

The FDA has approved 0.25-mg drospirenone/0.5-mg estradiol, a low-dose hormone combo to treat moderate to severe hot flashes, night sweats and moderate to severe symptoms of vulvar

and vaginal atrophy in menopausal women. Approval was based on findings from a randomized trial, which showed that compared with women receiving placebo, those receiving the

combo had a statistically significant reduction in frequency and severity of the symptoms.

Source: Medscape.com

China to Help TCM Extends Global Reach

Date: March 14, 2012

China plans to open more Confucius Institutes to teach traditional Chinese medicine overseas and promote the Eastern medical science, Deputy Minister of Health Wang Guoqiang said on March 12.

"TCM, particularly its preventive aspect, is very well received abroad, regardless of nationality or ideology," Wang told China Daily in an interview. To

date, there are more than 350 Confucius Institutes and 500 Confucius Classrooms in 101 countries and regions, official statistics showed.

Two Confucius Institutes are specially dedicated to teaching TCM - at the Royal Melbourne Institute of Technology in Melbourne, Australia, and London South Bank University. Source reveals that the third institute is being setup in the United

States. On June 20, Vice-President Xi Jinping inaugurated the TCM Confucius Institute in Melbourne, saying it opened a new window for foreigners to learn about Chinese culture. At present, such institutes are committed mainly to spreading Chinese culture, with a focus on TCM, rather than training TCM doctors, Wang said.

Source: China Daily/Asia News Network

Lower Citalopram Dose Needed in Older Patients

Date: March 28, 2012

The use of normal dosage of a selective serotonin reuptake inhibitor, Citalopram (*Celexa*, Forest Laboratories) is discouraged in patients with certain conditions because of the risk of QT prolongation. FDA warns that

the maximum recommended dose of citalopram is 20 mg per day for patients with hepatic impairment, patients who are older than 60 years, patients are CYP2C19 poor metabolizers, or patients who are taking concomitant cimetidine

or another CYP2C19 inhibitor, because these factors lead to increased blood levels of citalopram, increasing the risk for QT interval prolongation and torsades de pointes.

Source: www.medscape.com

Total Recall of Carboplatin Injection (Ebewe)

Date: March 29, 2012

The Department of Health (DH) today endorsed the recall of Novartis Pharmaceutical (HK) (Novartis), a licensed drug wholesaler, of all batches of its Carboplatin 10mg/ml Injection (Ebewe) (registration no: HK-43913) from shelf as part of a multinational effort to curb quality failure in the product. Carboplatin injection is indicated for the treatment of various cancers. It can only be sold on prescription and under the

supervision of pharmacists at registered dispensaries.

Novartis notified that the above product's Austrian manufacturer, EbewePharma, decided to recall the product as a precautionary measure because precipitates were identified in several batches of samples retained routinely as part of good manufacturing practice. According to EbewePharma,

the precipitates were likely from either the active drug ingredient or its degradation products. Further, preliminary assessment indicated that the precipitates were probably results of stability issues, although the root cause remained to be identified.

Source: www.dh.gov.hk/english/press/2012/120329-2.html

Man Arrested for Allegedly Selling Unregistered Pharmaceutical Products

Date: March 30, 2012

A 53-year-old man was arrested in a joint operation by the Police and the Department of Health (DH) at Mongkok for suspected illegal sale of two boxes of cold and flu medicine manufactured by Taisho Pharmaceutical Co., Ltd., which were unregistered pharmaceutical products. The operation followed laboratory test

findings that revealed that the cold and flu medicine, which had been obtained earlier from an Internet auction website during DH's surveillance operation, was found to contain paracetamol, which is a western medicine and is used for the management of pain and fever. Although the side effects are usually mild, taken in

high dosage may result in liver damage. Sale of an unregistered pharmaceutical product is an offence under the Pharmacy and Poisons Ordinance. The maximum penalty is a fine of \$100,000 and two years' imprisonment.

Source: www.dh.gov.hk/english/press/2012/120330-2.html

Neurotoxin Found in Shark Fins

Date: March 30, 2012

A study conducted by Dr. Deborah C. Mash revealed that a high amount of a neurotoxin, β -N-methylamino-L-alanine (BMAA), was found in fin clips from sharks in Florida waters. The concentration of BMAA in the shark fins

is a cause of concern as it may link to neurodegenerative diseases, including Alzheimer's disease, amyotrophic lateral sclerosis (ALS) and parkinsonism dementia. BMAA, which is produced by cyanobacteria (a blue green algae), is a

threat to people who are having long term exposure to it in fresh water systems. The toxin can be bioaccumulated in nerve cells and causes neurodegeneration.

Source: Medscape.com

Impact of Pharmacist Counseling Service on Blood Pressure Control of Borderline Hypertensive Patients

LEE, Vivian WY^{a*}; CHAN, Belinda MC^{a*}; CHEUN, Ken TK^{a*}; SO, Renwick KH^{a*}; YU, CM^b

^a School of Pharmacy, Faculty of Medicine, Chinese University of Hong Kong, Shatin, N.T., Hong Kong SAR, China

^b Division of Cardiology, Department of Medicine and Therapeutics, Faculty of Medicine, Chinese University of Hong Kong, Shatin, N.T., Hong Kong SAR, China

(* Corresponding author)

ABSTRACT

Objective: To investigate the clinical impact of pharmacist counseling service in borderline hypertensive patients. **Methodology:** This was a 9-month, open, prospective trial. Borderline hypertensive patients attending the outpatient hypertension clinic were recruited in this study. They were assigned to meet the pharmacists before usual physician consultation. Enrolled patients received hypertension education, drug compliance checking and lifestyle modification during two face-to-face interview sessions. A telephone follow up was arranged in between the interviews. At the end of the study, mean blood pressure was compared with baseline as the primary outcome. Secondary outcomes included compliance rate, drug-related problems identified and pharmacist interventions provided in the study. Patient satisfaction was also surveyed. **Results:** After 9 month study period, 47 patients completed the study. Mean systolic and diastolic blood pressure declined by 2.81 mmHg and 1.94 mmHg respectively. The results were not statistically significant when compared with the baseline blood pressure. Percentage of patients achieving the blood pressure goal was 39% with statistical significance ($p < 0.05$). The mean compliance rate was increased from baseline $83.16 \pm 30.52\%$ to $93.44 \pm 18.38\%$ at the end of study ($p=0.017$). A total of 588 pharmacist interventions were made. Most patients agreed pharmacist service was useful and

could help them manage their health problems. They generally agreed pharmacist had the best role for drug counseling. **Conclusion:** Patients with borderline hypertension may not be sensitive to pharmacist counseling service for blood pressure control. However, pharmacist interventions significantly improved drug compliance. Most patients welcomed pharmacy service in the management of hypertension.

Keywords: *borderline hypertension, clinical pharmacy, patient counseling and compliance*

INTRODUCTION

Hypertension is one of the most prevalent chronic diseases worldwide.⁽¹⁾ Inadequate control of hypertension can lead to many complications including cardiovascular, renal and optical diseases.⁽¹⁾ However, many patients are not aware of hypertension since it is asymptomatic before complication manifestations. In Hong Kong, about 20% of adults are hypertensive,⁽²⁾ and a study conducted locally showed about 75% of hypertensive patients had inadequate blood pressure (BP) control ($>140/90$ mmHg).⁽²⁾

Noncompliance with prescribed antihypertensive regimens has been known to be one of the reasons of suboptimal BP control.⁽³⁾ The most significant factors in noncompliance are a lack of knowledge about prescribed drugs and their side effects, and a lack of understanding about the consequences if a prescribed drug regimen is not

followed.⁽⁴⁾ Therefore, patients' knowledge and awareness of hypertension play important roles to achieve successful BP control. It is essential for patients to receive clear information about both the risks associated with uncontrolled hypertension, and the benefits expected from anti-hypertensive treatments and therapeutic lifestyle changes. Possible drug-related adverse effects also have to be explained. Physicians, with no doubt, should be involved in this educational process. However, they may not have enough time in the busy outpatient setting. In fact, patient management time constraint has been identified to be one of the barriers to the effective management of patients with uncontrolled hypertension.⁽⁵⁾ This is particularly true in the busy outpatient setting in Hong Kong with such a large patient load. Pharmacists, as drug professionals, are thus in a very good position to help optimize BP control by providing patient education and enhancing drug compliance. Various studies demonstrated that clinical pharmacy services can have a significant impact on compliance and patient satisfaction, and thus on drug therapy outcomes.⁽⁶⁻¹⁵⁾ The objective of our study was to investigate the clinical impact of pharmacist counseling service among borderline hypertensive patients.

METHODOLOGY

It was a 9-month, prospective, open-labeled study conducted in the outpatient hypertension clinic at the Prince of Wales Hospital (PWH) from August 2008 to May 2009. Eligible subjects were under

the usual physician follow ups in addition to counseling service by pharmacists. Patients were eligible in the study if 1) they were diagnosed with essential hypertension with borderline BP control in 2 consecutive clinic visits during the past 6 months (defined as systolic BP 140-150 mmHg and/or diastolic BP 90-100 mmHg in 2 visit records, or one clinic visit with controlled BP [$<140/90$] while the other with uncontrolled BP [$>140/90$]) and, 2) they were receiving one or more antihypertensive drugs and followed up regularly at the hypertension clinic for at least 6 months. Patients were excluded if they were under 18 years old, pregnant, were not able to communicate verbally, had secondary hypertension with underlying causes, hypertensive emergency, diabetes mellitus, or were enrolled in other clinical trials.

During the recruitment period, pharmacists were provided with the patients' list one week prior to the follow up dates by the head nurse. Eligible patients were invited to participate in the study when they attended the hypertension clinic before they met the physician. Demographic data included age, gender, past medical history, history of hypertension, anti-hypertensive regimen, baseline BP were collected from medical charts or the Hospital Authority's Clinical Management System (CMS). All patients' data were recorded on an individual patient assessment form. Other relevant informations such as laboratory data, social history, readings of home BP measurement and concomitant use of over-the-counter medications and herbal agents were recorded. Each pharmacist who participated in the study followed a standardized protocol throughout the study to ensure consistency of interventions and services provided to each patient. All pharmacist interventions performed were documented.

We used comparative method on the same group of patients on their baseline and final BP. The result was paired to each other and pair t-test was used to estimate sample size. We assumed the mean difference of decrease in BP to be 10 mmHg, and the standard deviation to be 20 mmHg based on previous study conducted locally.⁽¹⁶⁾ The number of patients to be enrolled was estimated on the basis of statistical power of 90% ($\beta=0.1$), with an error of 5% ($\alpha=0.05$). As a result, 44 patients were targeted based on the sample size calculation tool.⁽¹⁷⁾

Patients were interviewed twice (assuming a 3-4 month separation between follow-ups) by pharmacists during the study period. In each follow up, patients were seen by the pharmacists prior to physicians. Blood pressure measurement was done by the trained healthcare assistants before the interview with automatic BP monitor (Manufacturer: A&D; Model: TM-2655P). During the interview, pharmacists assessed their drug compliance, educated on lifestyle changes (benefits of exercises, diet modification, home BP monitoring, and smoking cessation) and evaluated if there was any side effect related to the patients' drug regimen. Brief information about hypertension including BP goal, complications of uncontrolled hypertension, benefit of BP decrease and the associated cardiovascular disease risk modification were discussed. Educational leaflets published by the Hospital Authority about hypertension were also provided. Leaflets covered classification and definition of hypertension, hypertension-related complications, drug treatment options and their potential side effects.

Any observed drug-related problems were documented. During the assessment, patient's compliance on each drug was evaluated. The pharmacist asked the patients to describe their regimens by drug dosages (number of pills), frequencies (number of doses), and number of pills taken at different times of the day. Patients were asked whether they had missed any dosage, changed their regimens in terms of doses, frequency and timing, or had drugs left over. We defined patients as compliant with a drug if they remembered their prescribed regimen correctly and complied with it for at least 80% of time.⁽¹⁷⁾ Their overall compliance rate was calculated as the total number of prescribed hypertensive drugs divided by the number of hypertensive drugs that the patient was compliant with and was expressed as a percentage.⁽¹⁷⁾ For example, a patient who complied with all prescribed drugs had a compliance score of 100%, while one complied with only two out of four drugs had a compliance score of 50%.

In the second follow up, pharmacists followed up on any drug-related problems identified previously. A telephone follow up was conducted in between the first and

second follow up. Pharmacists mainly focused on problems identified in the previous visit or provided advice in case of drug-related queries arose. A checklist was used to make sure important and necessary areas were covered in the telephone follow-up. At the end of the study, patients received a satisfaction survey to assess their satisfaction on this clinical pharmacist service.⁽¹⁶⁾

Demographic data including age, gender, history of hypertension, anti-hypertensive regimens, and baseline BP were collected. The primary outcome was the absolute BP change between the BP measured before and after the study period. Secondary outcomes included the mean difference in compliance rate and any potential drug-related problems identified, pharmaceutical interventions made as well as patient's satisfaction towards our service would also be documented.

Blood pressure change throughout the study was analyzed by Student's paired *t*-test. Proportion of patients achieving the JNC7 BP goal was analyzed by McNemar test (used for paired proportions). Compliance rate difference, which was not usually normally distributed, was analyzed by Wilcoxon test. Descriptive statistics was used to describe identified drug-related problems, pharmacist interventions and patient satisfaction survey. Statistical significance was taken at the 5% level and the test was two-tailed. Data would be analyzed using SPSS version 17 (Chicago, USA).

RESULTS

A total of 67 patients were enrolled in the study. However, 20 patients dropped out from the study due to lost to follow up; the date of second follow up was not within the study period; patients were referred to another clinic, excluded due to diagnosis of diabetes on the day of first interview, and passed away. Therefore, 47 patients completed the study. The mean age was 60.45 ± 13.73 years old. Over 60% of them were males. The study cohort was on an average of 2.19 ± 0.97 types of hypertension medications. The mean baseline systolic and diastolic blood pressures were 138.28 ± 18.26 mmHg and 78.15 ± 12.15 mmHg respectively. Baseline compliance

rate was 83.16 ± 30.52 %. The 4 most commonly prescribed blood pressure lowering medications were beta-blocker (66%), calcium channel blockers (44.0%), angiotensin converting enzyme inhibitor (ACEI) (36.2%) and diuretics (36.2%). Others included angiotensin receptor blocker (ARB) (14.9%), alpha-blocker (14.9%), methyldopa (6.4%) and hydralazine (4.3%).

At the end of the study, the mean reductions in SBP and DBP were 2.81 ± 18.17 mmHg and 1.94 ± 10.07 mmHg respectively. Both of them did not show statistical difference (p > 0.05). However, when we excluded the patients who initially presented with controlled BP (SBP<140 mmHg and DBP<90 mmHg) in the first interview and performed a subgroup analysis to investigate the BP difference, the results were statistically significant (p < 0.05). The mean reductions in SBP and DBP were 11.96 ± 16.94 mmHg (p = 0.003) and 4.91 ± 11.05 mmHg (p = 0.044) respectively. In addition, among the patients not at goal in the first interview, 39.1% of them (9 out of 23) were able to achieve the JNC VII goal after our study period (p=0.004). In addition, the mean compliance rate was increased from baseline 83.16 ± 30.52% to 93.44 ± 18.38% at the end of study (p=0.017). A number of drug related problems were identified and a total of 588 interventions were done (Table 1). The most common problem identified was related to adverse drug reactions. Patients were reminded to discuss with physicians regarding such potential adverse drug reactions. According to the

Pharmacist intervention	N (%)
Possible adverse drug reaction	
♦ identification and advice given	18 (3.1)
♦ referral to doctor	8 (1.4)
Drug compliance	
♦ compliance assessment	134 (22.8)
♦ correct the compliance	64 (10.9)
Lifestyle modification	
♦ diet	68 (11.6)
♦ exercise	68 (11.6)
♦ smoking cessation/alcohol consumption	69 (11.7)
Education	
♦ drug knowledge	76 (12.9)
♦ disease knowledge	67 (11.4)
Drug interactions	
♦ drug/herb interactions	3
♦ drug/drug interactions	5
Pharmacotherapy suggestion	
♦ duplication of drug class identified	3
♦ dosage choice/drug dosage recommendation	5
Total	588

patients' satisfaction survey performed during the last follow up, patients were satisfied with our service and had positive feedbacks (Table 2). They mostly agreed that the pharmacist was the most suitable person to provide drug counseling.

DISCUSSION

Studies demonstrated that additional clinical pharmacy service can improve disease outcomes in hypertension.⁽⁶⁻¹¹⁾ However, patients who received additional care by pharmacists in this study did not achieve a better BP control. However, our findings did not show the clinical significance in the management of borderline hypertensive patients. Borderline hypertension is not usually attended when compared with stage 1 and 2 hypertension classes. Other pharmacist-involved hypertension programs showed positive results were mainly focused on patients with

uncontrolled hypertension.^(4,14,19) In contrast, our patients had a relatively stable and controlled disease state. Fifty-one percent of subjects had achieved controlled hypertension at the first interview. Therefore, the effect of pharmacist intervention was not as prominent as compared to other overseas studies. We therefore performed a subgroup analysis in patients who were not at BP goal at the first interview. In these patients, our pharmaceutical service was able to achieve a significant reduction of 11.96 mmHg and 4.91 mmHg in SBP and DBP, respectively. The result was comparable to the overseas studies. The BP reduction achieved was clinically meaningful, as a 10 mmHg reduction in SBP was able to achieve 36% lower stroke risk, 24% lower ischemic heart disease risk in Asian hypertension patients.⁽²⁰⁾ After the study period, our intervention helped 39.1% of these patients to achieve the JNC VII BP goal.⁽²¹⁾ In our previously published data, the

Questions	N (%) (total 48)
1. Overall, are you satisfied with pharmacist counseling?	
Very satisfied	15 (31)
Satisfied	32 (67)
No comment	1 (2)
Dissatisfied	0
Very dissatisfied	0
2. Do you understand drug and disease knowledge educated by the pharmacist?	
Completely understood	22 (46)
Mostly understood	25 (52)
Understood half of the content	0
Mostly not understood	1 (2)
Totally not understood	0
3. Do you think pharmacist education is useful?	
Very useful	15 (31)
Useful	31 (65)
No comment	2 (4)
Very un-useful	0
Totally un-useful	0
4. Do you agree pharmacists can help you better manage your health problems?	
Totally agree	10 (21)
Agree	32 (67)
No comment	5 (10)
Disagree	1 (2)
Totally disagree	0
5. Would you like to spend more time to receive counseling from pharmacists?	
Strongly willing	11 (23)
Willing	27 (56)
No comment	8 (17)
Unwilling	2 (4)
Totally unwilling	0
6. Do you agree such pharmacist service be promoted to other patients with hypertension?	
Totally agree	16 (33)
Agree	30 (63)
No comment	2 (4)
Disagree	0
Totally disagree	0
7. Do you agree pharmacist has the best role to provide drug counseling?	
Totally agree	17 (35)
Agree	27 (57)
No comment	4 (3)
Disagree	0
Totally disagree	0

incidence of cardiovascular events in patients with inadequately controlled hypertension was positively related to the extent and duration of BP deviation from treatment goals. Furthermore, pharmacist counseling services helped patients to achieve a better compliance rate of 93.44% from a baseline of 83.16% ($p=0.017$). Compliance was believed to be one of the causes for resistant hypertension.⁽²¹⁾ In the current study, the most commonly prescribed drug class was beta-blockers. First line treatment for hypertension recommended by the JNC VII guidelines and the ALLHAT study⁽²³⁾ was thiazide diuretic. Calcium channel blockers and ACEI are preferred treatments in the ANBP-2⁽²⁴⁾ and ASCOT-BPLA.⁽²⁵⁾

There were a number of limitations in our study. Firstly, small sample size was due to high dropout rate. Future studies involving a greater sample size might be necessary to draw a significant result of pharmacist counseling service on BP control. Secondly, the current study has no control group to perform unpaired analysis. Thirdly, the long term impact of pharmacist intervention cannot be observed due to a short study period. It usually takes a few years for patients with uncontrolled hypertension to develop complications such as stroke or myocardial infarction. Finally, the reduction of BP may not be solely due to pharmacist interventions but change of BP lowering drug management.

CONCLUSION

This study suggested patient with borderline hypertension may not be as sensitive to additional pharmacy counseling service although improvement of BP control was observed. Drug compliance was significantly improved after pharmacist intervention. Careful allocation of pharmacy resources should be considered for the management of borderline hypertensive patients when resources are scarce.

ACKNOWLEDGEMENT

This study was supported by the School of Pharmacy, The Chinese University of Hong Kong. All authors declared that there was no conflict of interest during the study and the preparation of the manuscript.

Author's background

LEE, Wing Yan Vivian is currently Associate Professor in the School of Pharmacy and Assistant Dean (Student Affairs), Faculty of Medicine, Chinese University of Hong Kong. Both **CHAN, Belinda MC** and **CHEUNG Ken TK** are pharmacists at the Department of Health of Hong Kong. **SO, Renwick KH** is currently a pharmacist at the Prince of Wales Hospital, Hospital Authority, Hong Kong. **YU, CM** is currently Professor and Head of the department of medicine and therapeutics and Assistant Dean (External Affairs), Faculty of Medicine, Chinese University of Hong Kong. At the time of this study, Ms. Belinda M.C. Chan, Mr. Ken T.K. Cheung, and Mr. Renwick K.H. So were students of the Master of Clinical Pharmacy Programme, School of Pharmacy, CUHK. Corresponding author's email address is vivianlee@cuhk.edu.hk.

References

1. Kearney PM, Whelton M, Reynolds K, et al. (2005). Global Burden of Hypertension: Analysis of Worldwide Data. *Lancet*, 365: 217-223.
2. Cheung BM, Law FC, Lau CP (2002). The rule of halves applies in Chinese hypertensive patients. *Am J Hypertens*, 15:209A.
3. Burt VL, Whelton P, Rocella EJ, et al. (1995). Prevalence of hypertension in the U.S. population: results from the third national health and nutrition examination survey, 1988-1991. *Hypertension*, 25:305-313.
4. Vivian EM (2002). Improving blood pressure control in a pharmacist-managed hypertension clinic. *Pharmacotherapy*, 22(12):1533-1540.
5. Susan A, Pablo Lapuerta, Bruce D, et al. (2002). Physician-Related Barriers to the Effective Management of Uncontrolled Hypertension. *Arch intern Med.*, 162:413-420.
6. Sczupak CA, Conrad WF (1977). Relationship between patient-oriented pharmaceutical services and therapeutic outcomes of ambulatory patients with diabetes mellitus. *Am J Hosp Pharm*, 34:1238-1242.
7. Carmichael JM (1995). Do pharmacists need prescribing privileges to implement pharmaceutical care? *Am J Health-Syst Pharm*, 52:1699-16701.
8. Alsuwaidan S, Malone DC, Billups SJ, et al., for the IMPROVE Investigators (1998). Characteristics of ambulatory care clinics and pharmacists in veterans affairs medical centers. *Am J Health-Syst Pharm*, 55:68-72.
9. Carter BL, Malone DC, Valuck RJ, et al. (1987). The IMPROVE study: background and study design. *Am J Health-Syst Pharm*, 55:62-67.
10. Lip GY, Beevers DG (1997). Doctors, nurses, pharmacists and patients -- the rational evaluation and choice in hypertension (REACH) survey of hypertension care delivery. *Blood Pressure*, 6(suppl 1):6-10.
11. Walneia ADS, Juan CYT, Gun BM, et al. (2007). Effect of pharmaceutical care on blood pressure control and health-related quality of life in patients with resistant hypertension. *Am J Health-Syst Pharm*, 64(18):1955-1961.
12. Lee VWY, Chu KKY, Lam SSK, et al. (2010). Impact of Pharmacist Intervention on Cardiovascular Risks Management in Hypertensive Type 2 Diabetic Patients in Primary Care Setting. (Presented at the Hong Kong Pharmacy Conference 2010)

13. Borenstein JE, Graber G, Salliet E, et al. (2003). Physician-pharmacist comanagement of hypertension: a randomized, comparative trial. *Pharmacotherapy*, 23(2):209-216.
14. McConnell KJ, Zadvomy EB, Hardy AM, et al. (2006). Coronary artery disease and hypertension: outcomes of a pharmacist-managed blood pressure program. *Pharmacotherapy*, 26(9):1333-1341.
15. Erickson SR, Slaughter R, Halapy H (1997). Pharmacists' ability to influence outcomes of hypertension therapy. *Pharmacotherapy*, 17(1):140-147.
16. Winnie Chan Kit Yu (2007). A study of Pharmacist's Impact on the Blood Pressure Control in Patients with Uncontrolled Hypertension. Paper presented and published at School of Pharmacy, Chinese University of Hong Kong.
17. Sample size calculation. http://department.obg.cuhk.edu.hk/researchsupport/Sample_size_CompMeanIndependent.asp [accessed May 11, 2009]
18. Wu JYF, Leung WYS, Chang S, et al. (2006). Effectiveness of telephone counseling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomized controlled trial. *British Medical Journal*, (333):522.
19. Paul E. Bogden, Robert D. Abbott, Pam Williamson et al. (1998). Comparing standard care with a physician and pharmacist team approach for uncontrolled hypertension. *J Gen Intern Med*, 13:740-745.
20. Lawes CM (2003). Blood pressure and cardiovascular disease in the Asia Pacific region. *J Hypertens*. 21(4): 673-675.
21. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. <http://www.nhlbi.nih.gov/guidelines/hypertension/>. [Accessed April 9, 2009]
22. Lee VWY, Chan THW, Ko TTL, et al. (2008). Clinical Outcome of Hypertension Management-A Five-Year Observational Study. *Journal of Medical Economics*, 11(1):101-118.
23. The ALLHAT officers and Coordinators for the ALLHAT Collaborative Research Group (2002). Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs. Diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA*, 288: 2981-2997.
24. Dahlof B, Sever PS, Poulter NR, et al. (2005). ASCOT Investigators. Prevention of Cardiovascular Events with an Antihypertensive Regimen of Amlodipine adding Perindopril as required versus Atenolol adding Bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial- Blood Pressure Lowering Arm (ASCOT-BPLA): A Multicentre Randomised Controlled Trial. *Lancet*, 366: 895-906.
25. Wing LM, Reid CM, Ryan P, et al. (2003). Second Australian National Blood Pressure Study Group. A Comparison of Outcomes with Angiotensin-Converting Enzyme Inhibitors and Diuretics for Hypertension in the Elderly. *N Eng J Med*, 348: 583-592.

A Pilot Implementation of Decentralized and Automated Dispensing System by Omnicell – from Challenging to Benefit Realization

YUNG, Kit-Man^{a*}; TAM, Ka-Ming^b; TSE, Pascal^c; WONG, Kei^d

^a Pharmacist, Pharmacy Department, St. Teresa's Hospital, 327 Prince Edward Road, Kowloon, Hong Kong

^b Senior Analyst Programmer, Information Technology Services Department, St. Teresa's Hospital, 327 Prince Edward Road, Kowloon, Hong Kong

^c Chief Information Technology Officer, Information Technology Services Department, St. Teresa's Hospital, 327 Prince Edward Road, Kowloon, Hong Kong

^d Chief Pharmacy Officer, Pharmacy Department, St. Teresa's Hospital, 327 Prince Edward Road, Kowloon, Hong Kong

(* Corresponding author)

ABSTRACT

A pilot project of decentralized automated dispensing system by Omnicell has been implemented in a medical ward M5B of St. Teresa's Hospital since May 2011. An electronic active drug list (ADL) interfaced with Omnicell cabinet was also introduced to ensure a reconciled medication profiles for patients. The objectives of the pilot project were improving nursing efficiency and patient safety. In conclusion, the pilot project was successful and aspects for further development were identified.

Keywords: *decentralized and automated dispensing system, Omnicell, electronic active drug list, patient safety, HL7*

INTRODUCTION

Traditionally, inpatient medications are dispensed by centralized distribution systems. Pharmacy processes (i.e. data entry, drug pick, verification) the medication orders received from wards and finally dispatches the dispensed medications back to the ward. St. Teresa's hospital (STH) is a private general hospital and all patients are self-financed. Nurses have to review the continued medication order every three days in order to avoid unnecessary orders. Since the maintenance medications are not available at the point of care, nurses always need to order surplus to avoid running out of drugs at administration times. As a result, nurses have to handle a lot of drug returns when patients are discharged.

As a vicious cycle, the pharmacy has to handle repeat orders every three days and manage drug returns from the ward as well. In addition, every ward has a list of ward stock medications which aims to shorten the time to receiving drugs for administration. However, nurses have to dispense those ward stock items from several designated cupboards without guiding directions and restrictions. Hence, this increases the likelihood of medication selection errors, especially with sound-alike, look-alike items.

In order to enhance nursing efficiency and patient safety, a pilot project of a decentralized automated pharmacy system by Omnicell has been implemented in a medical ward M5B since May 2011. Additionally, an electronic active drug list (ADL) interfaced with Omnicell cabinet was also introduced to ensure a reconciled medication profiles for patients. Patient ADL is maintained by nurses, pharmacists and doctors collaboratively. Lessons learnt from project initiation, preparation and implementation are discussed and the way forward for further improvement is identified.

CONCEPT OF DECENTRALIZED AND AUTOMATED DISPENSING SYSTEM

Automated dispensing systems are typically installed in hospitals on patient care units, and are connected via a real-time interface to the hospital's Pharmacy Information System in order to maintain control over drug dispensing. Their major advantage lies in allowing nurses to obtain medications for inpatients at

the point of care. User identification (password/ fingerscan) is required for the users to get access to the system, the patients for whom medications are removed, and provide usage data to the hospital's financial department for the patients' bills (Fig. 1).

Omnicell medication dispensing cabinets are locked systems that are loaded with the medications. The stocked medications are kept in the compartmentalized cabinets. At the appropriate dosing time, nurses can logon with username and fingerprint or password to retrieve patients' medication profiles from the cabinet computer and remove medications by following the guiding lights to the specific drug storage location. The new system provides increased control and accountability over dangerous drugs and floor stock medications in patient care areas.

BACKGROUND OF WARD M5B

M5B is a 47-bed medical ward. We chose M5B as the pilot ward as it is one of the wards with high workload. Therefore, we could challenge the system with high activity in addition to the new workflow. In the pilot study, we installed a 2-cell Omnicell cabinet station in M5B, accommodating over 90% of formulary injectable drugs which need to be dispensed based on past usage records.

CONCEPT AND APPLICATION OF ACTIVE DRUG LIST (ADL)

In a close-loop drug distribution system, nurses should only administer

New Workflow with ADC

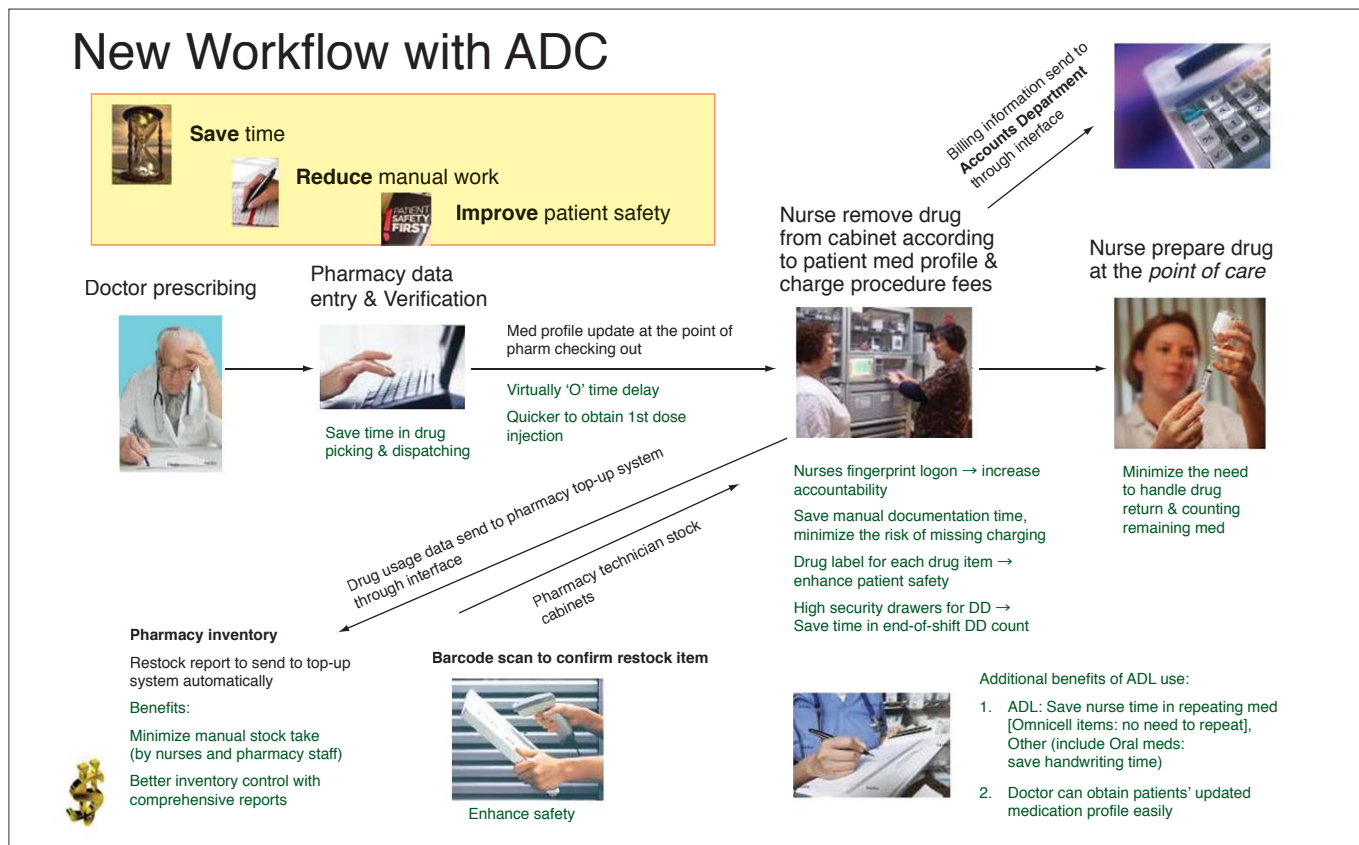


Figure 1: New workflow with automated dispensing cabinet (ADC) and benefits

medication-orders that have been verified by pharmacy except in emergency situations. Therefore, an ADL is essential for ensuring drugs administered by nurses are prescribed by physicians and reviewed by pharmacists. Currently, electronic inpatient medication order entry (MOE) is still not available in our hospital. We make use of the dispensing records to construct a drug list (medication profile). Attending doctors are responsible to review the 'active' drug and make orders to 'continue', 'discontinue' and 'add new drug'. Nurses are responsible to update the ADL according to doctors' instructions. The active drugs are clearly presented in ADL so that doctors can get their patients' complete medication profiles easily. It is ultimately beneficial for doctors who are taking care of patients intended for long-stay; patients who are on multiple drugs and those who are consulting multiple doctors.

PREPARATION OF IMPLEMENTATION

The kick-off project meeting was held in January 2011. It was a 5-day meeting which involved two experts from Omnicell, Mr. John Rosen and Mr. Dean Martin, representatives from vendor Deltason,

pharmacy, nurses and the IT department. In the kick-off meeting, we defined the objectives and timeline of the projects. Omnicell and vendor representatives were provided with ward site visit and the current STH drug distribution system and the nursing practices were explained. Mr. John Rosen helped us understand the database structure requirement and also the operation of Omnicell console. Mr. Dean Martin, who is a pharmacist from Australia, helped us develop the policies and procedures for ADC use in STH.

Follow-up meetings were held in March and May respectively for interface testing, cabinet setup and finalization of policies and procedures.

RISK AND PROJECT MANAGEMENT

As defined in the PMBOK 2008, projects are temporary endeavours undertaken to create unique project, services or results. Project management is the application of knowledge, skills, tools and techniques to project activities to meet project requirements. In the real world, project development is risky in nature; therefore, risk management is managing and mitigating the risks.

Even though the technology of decentralized automated dispensing is very mature and widely adopted in US and many European countries, STH is the innovator in using this technology in Hong Kong. Similar to many health-related IT projects, we are facing some common risks in project implementation such as delivery, business impact, business support, technology and project management, etc. Among all of them, achieving successful change management is the most challenging. On top of the general resistance to change, the application of health IT increases the accountability on all staff, especially nursing, which can make them reluctant to use. Because nurses are one of the major stakeholders in the project, the project team made great efforts to increase their knowledge, acceptance, and comfort with the technology.

In order to increase the users' acceptance, nurse representatives actively participated in requirement collection process. The Chief Nursing Officer and all senior nursing officers were invited to express their concerns and opinions on the new system. User requirements were collected and prioritized throughout the preparation and implementation process. The

involvement of M5B ward-in-charge nurse as a project governance committee member also ensured there was efficient communication among nurses, Pharmacists and the IT department.

SYSTEM TRAINING

Hands-on training was provided to pilot ward nurses and pharmacy staff immediately before the system Go-Live. Eight training sessions were conducted by Mr. John Rosen and representatives from Deltason. In training sessions, the general operation and functions of cabinets were demonstrated. The trainers also resolved many users' concerns and questions immediately in an interactive way. Participants had a chance to understand the benefits of the system and be more confident in the use of the new system within their own clinical environment.

CHALLENGES FROM IT ASPECTS

Apart from hardware support, the IT department played a crucial role in developing interfaces in Health Level Seven (HL7) standard to allow the Omnicell server and STH computer systems to communicate.

Health Level Seven International (HL7) are the global authority on standards for interoperability of health information technology. Even though HL7 standards are very common within and among healthcare organizations

internationally, it is a new experience to integrate STH hospital information systems (HIS) with a third-party application. Therefore, IT has done research on HL7 standards before interface development. It is understood that HL7 version 2 is just an interchange standard but not an interoperability standard. HL7 version 2.3.1 was selected because it is commonly used in Hong Kong. For this project, a new Gateway has been built to exchange HL7 messages between Omnicell server and HIS applications. Several information systems of STH have also been revamped in order to make them exchange data in HL7 standards. In addition, the IT department has developed a new module in Nursing service system that allow nurses to maintain the ADL. They also provided training to nurses on the new applications.

DISCUSSION

Benefits of ADC use in term of saving nurses' time

The instant benefit of using the ADC is the shortening of time between making new order to pharmacy and receiving drugs back from pharmacy for administration (i.e. reduction in prescription turn around time). There is virtually 'zero' time lag for receiving the continued doses. Nurses can also save manpower in documenting the procedure fee charging on the system electronically. When removing medications from cabinets, the procedure fee can be captured and billed to patient's account electronically.

Since all dangerous drugs are locked in high security bins individually and all transactions are accountable and traceable with a recorded witness, and inventory counts confirmed on each access, no cycle count is required during each shift handover. In addition, the ADC can free nurses' time in triweekly stock taking, requisition and ward stock expiry date checking. As the cabinet stocked medications can be available at the point of care, the implementation of ADC greatly eliminates the process of drug return and saves much time for both nursing and pharmacy staff.

In term of patient safety, the ADC reduces ward stock drug dispensing errors through the application of the guiding light directed removal and safety principles involved in defining drug locations within the cabinet.

Feedback from users

A survey on the nurse satisfaction level with the use of the ADC was conducted in late July (60 days after system go live). In the trial, thirty nurses had participated in using the ADC and twenty-five (83.3%) completed questionnaires were received. From the results, most of the nurses agree that the ADC is easy to use and they feel satisfied in general (Figure 2). Because the cabinet medication profile is updated immediately once the pharmacist validates the prescription, it greatly reduces the time taken to administer the first dose of injectable drugs.

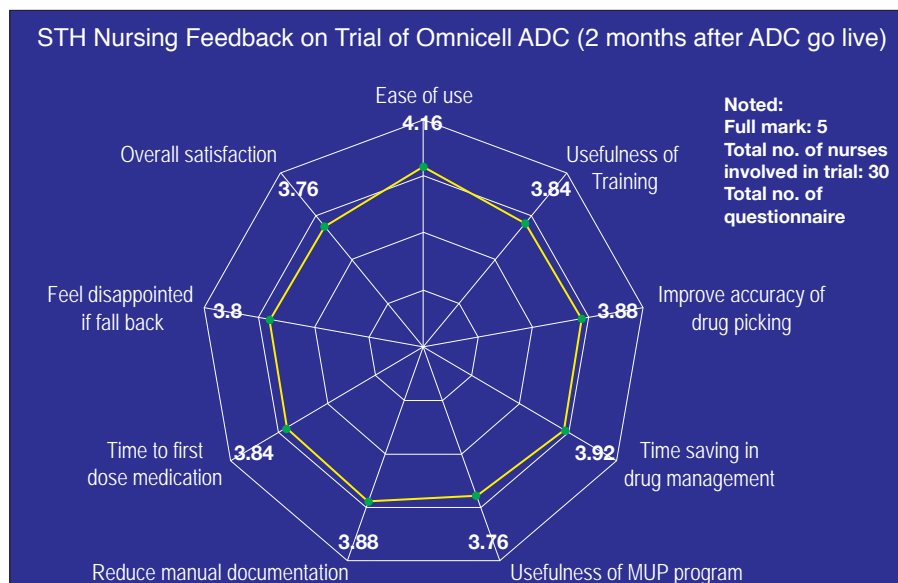


Figure 2: Results of STH Nursing Feedback on Trial of Omnicell ADC (2 month after ADC go live)

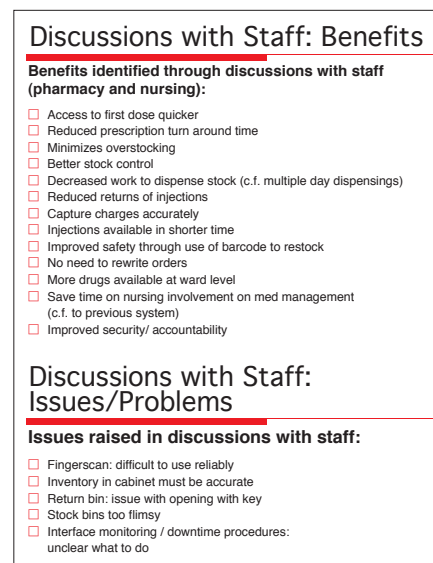


Figure 3: Summary of discussions with staff. Benefits and issues/problems

There is also support from nurses that the application of active drug list (ADL) has reduced the manual process of repeating doctors' drug orders and greatly reduced the chance of transcribing errors. However, before profile-based dispensing implementation, nurses still have to work to update the medication profile.

During post installation review (24th-29th July 2011), Mr. Dean Martin interviewed nursing and pharmacy staff (end users). The benefits and issues/problems associated with ADC uses were discussed (Figure 3).

Benefits of ADC use in term of improving pharmacy inventory control

The inventory monitoring function of Omnicell system has enhanced the efficiency of the restocks process and cabinet inventory control. Every cabinet stocked item has a unique item code. The PAR/Restock/Critical low levels of each item are defined in the Omnicell console. Once the stock level hits the restock level, restock order is created and sent to STH top-up system at a scheduled time. In addition, critical low or stock-out alerts will continue to be sent to pharmacy

stock-keeper directly. A pharmacy technician picks the items according to the restock pick list and affixes restock barcode labels to the verified items. With the Omnicell SafetyStock barcode feature, a pharmacy technician has to scan the restock barcode label to confirm correct bin during restocking.

Moreover, the inventory management is enhanced through review of electronic usage transactions and alerts. The regular review of inventory reports e.g. PAR vs usage report provides reference to pharmacy for optimizing the stock level of cabinet items in order to prevent overstock/under-stock.

Further improvement

In the pilot, we only stocked non-refrigerated injectable items in cabinets. We propose to add oral drugs in the future when unit dose package techniques are introduced. Moreover, we would utilize Omnicell Flexi-lock technology to link refrigerated items with the ADC in the future.

In order to improve the accuracy of patient drug profile, the interface for pharmacy data entry will be revamped. Pharmacy will be able to update and

reconcile the patient drug profile more proactively though profile-based dispensing.

Most of the benefits discussed in the pilot cannot be quantified because the baseline information before implementation had not been captured. In the subsequent ADC installations, baseline information (e.g. turnaround time, total dispensing time, and cost capture for ward stock administration) should be collected for further analysis.

CONCLUSIONS

The pilot project has been successful since the ADC and ADL use have improved nursing efficiency and patient safety. The acceptance of ADC use by nurses is high because it is easy to operate. ADC enhances patient safety by guiding nurses' drug selection in a more controlled manner. It frees nurses' time from tedious manual documentations to perform their clinical services. Patients benefit from receiving their first dose of medication with minimal time delay. Inventory control is optimized by regular analytical reports review to reduce drug expenditure resulting from overstocking. In the pilot, aspects for further development are identified.



世衛建議，消炎噴鼻劑
是紓緩鼻敏感**最有效**的藥物¹⁰

• 直接到達患處 • 對付問題根本*

Avamys™ 鼻眼適™ 一噴鼻舒適^{1,1-5}

美國FDA及香港衛生署認可
2歲或以上適用¹⁰

- 無睡意¹，每天一次¹，24小時有效
- 噴霧幼細，減少倒流問題¹
- 直達鼻腔，同時紓緩鼻、眼敏感症狀¹
有效改善鼻塞、流鼻涕、打噴嚏、鼻癢、流淚水、眼紅、眼癢

* 8小時起效¹ • 問題根本=鼻敏感引起的鼻膜發炎



香港鼻敏感
市場銷售
No.1



Avamys™ 鼻眼適™ 消炎噴鼻劑乃
醫生處方藥物，詳情請向醫生或
各大Rx藥房註冊藥劑師查詢。

*AVAMYS and 鼻眼適 are trademarks of the GlaxoSmithKline group of companies.
資料來源：1. Nakano W et al. Allergy 2007; 62:1078-1084. 2. Kaiser HB et al. J Allergy Clin Immunol 2007; 119:160-163. 3. Martin RG et al. Allergy Asthma Proc 2007; 28(2):216-225. 4. Batten P et al. J Allergy Clin Immunol 2007; 119(Suppl 1):S211-10. 5. Vassar M et al. Allergy Asthma Proc 2008; 29:313-321. 6. Berger WE et al. Expert Opin Drug Deliv 2007; 4(6):689-701. 7. Avamys prescribing information, Hong Kong. 8. Veramyst prescribing information, U.S. 9. HCAP Sales Data, Topical Nasal Preparation, (BIA), Systemic Nasal Preparation(018) and Systemic Antihistamine (BNA), January-August 2011. 10. Bouquet J et al. Allergy 2008; 63(Suppl. 16): 8-160

Immunization in Hong Kong

TSE, Kit-Ying^a; CHAN, Hoi Lam^{b*}

^a Hong Kong Sanatorium and Hospital, 2 Village Road, Happy Valley, Hong Kong SAR, China;

^b Pfizer Corporation Hong Kong Limited, 16/F, Stanhope House, 736 King's Rd, North Point, Hong Kong SAR, China (* Corresponding author)

ABSTRACT

Vaccines are an effective means to prevent diseases. Several trends can be observed in the development of vaccines in the 21st century. Various government funded immunization schemes are in place in Hong Kong and eligible citizens can enjoy free or subsidized immunization. Pharmacists are expected to have knowledge on vaccines and immunization programs; however local information resources are often limited or the access to them are unfamiliar. Pharmacy-based vaccination is currently being practiced in some countries, which may become a trend in immunization delivery in the future.

Keywords: Vaccine, vaccination, immunization, immunization programme

INTRODUCTION

Vaccines are biological preparations which enhance a person's immunity to a specific disease.⁽¹⁾ An agent that resembles a disease-causing microorganism is contained in either a live or inactivated vaccine. When the vaccine is administered to the human body, the immune system recognizes the agent as foreign, destroys it and "remembers" it. When the body encounters the disease-causing microorganisms later, fast recognition and destruction of them becomes possible.

Since its invention by Edward Jenner in late 17th century,⁽²⁾ vaccines have become an important method of reducing infections and diseases. Immunization with smallpox vaccine has caused the successful global eradication of fatal smallpox infection.⁽³⁾ The control of polio virus infection has

been successful with the worldwide implementation of the polio vaccination programme.⁽⁴⁾ Emerging and re-emerging infectious disease have made the role of immunization an increasingly important focus in preventative health. New possibilities in vaccine development such as new targets, combinations and novel routes of administration have helped to feed such a demand. Therefore, pharmacists have the responsibility to keep themselves familiar with the latest vaccination technologies, available vaccines and immunization programmes.

DISCUSSION

21st Century vaccination

The vaccine market is an ever changing environment. Compared to the vaccines in early days, we can observe several new trends in vaccine development.

Adolescents and adults have displaced infants and children as the major market of vaccines.⁽⁵⁾ Aggressive pediatric immunization programmes are still a health priority worldwide to eradicate polio, mumps, pertussis, measles and other diseases. However, in year 2007, adult vaccine sales increased slightly but significantly overtook pediatric sales.⁽⁶⁾ Vaccinations for adults with influenza vaccine, human papillomavirus (HPV) vaccine and traveller vaccines have become an important contributor to the vaccine sales. Adults are now considered as the driver for vaccine market growth.

Combination vaccines which target multiple diseases are becoming more common in many parts of the world.⁽⁵⁾ Pentavalent vaccines are available in many parts of the world. Also, hexavalent combinations containing diphtheria, tetanus, pertussis, H. influenza type b, hepatitis B and inactivated polio vaccines

have already been approved and marketed. In Hong Kong, the Childhood Immunization Programme (CIP) implemented by the government also includes the diphtheria, tetanus, acellular pertussis & inactivated poliovirus combination vaccine and measles, mumps & rubella vaccine.⁽⁷⁾

The routes of immunization are being extended to many nonparenteral methods.⁽⁵⁾ A new live, attenuated influenza vaccine administered intranasally to cause both systemic and local responses has been registered in Hong Kong. Aerosol, oral and transcutaneous vaccines have also been developed to reduce the invasiveness of immunization while maintaining the effectiveness of vaccines at the same time.

The purpose of immunization has been confined to the prevention of infectious diseases.⁽⁵⁾ However, vaccinations against various noninfectious diseases are being developed. Vaccines can become a very useful means to prevent or treat many kinds of diseases. A lot of effort has been made in the development of cancer vaccines which contains proteins and peptides from cancer antigens.⁽⁵⁾ Cancer prophylaxis for people with inherited carcinogenic mutations may be possible in the future. Active immunization against angiotensin II is a new strategy against high blood pressure.⁽⁸⁾ Alzheimer's disease can possibly be controlled by immunization against amyloid protein.⁽⁵⁾

Technology advancement also allows safer and more effective immunization. In recent years, there have been new findings suggesting that sex and pregnancy differences may affect the immune response as well as the occurrence of adverse effect to the vaccines.⁽⁹⁾ Women were found to have

a greater humoral immune response and more adverse reactions to vaccines when compared to men. However, sex-specific effects in vaccine efficacy and safety are usually not documented. To initiate a better immunization programme, the effects of sex and pregnancy on immune responses need to be further understood.

When more new vaccines are developed, pharmacists, as the primary healthcare providers, should know the emerging trends so as to deliver correct and up-to-date information to the patients and customers who make the enquiries.

Immunization scheme in Hong Kong

There are several free vaccination programme or subsidy schemes conducted by Hong Kong Centre of Health Protection.

The Childhood Immunization Programme (CIP) is provided by the Family Health Service of the Department of Health which offers free vaccinations to children from newborn to their primary 6.⁽⁷⁾ It protects children from ten

infectious diseases, including hepatitis B, diphtheria, tetanus, measles, mumps and rubella. From 1 September 2009 onwards, pneumococcal vaccine has been introduced into the Childhood Immunization Programme. The Scientific Committee on Vaccine Preventable Diseases (SCVPD) under the Centre for Health Protection has recommended the use of 13-valent pneumococcal

conjugate vaccine (PCV13) in the CIP of Hong Kong. PCV13 is expected to replace PCV10, which is currently being used, by the end of 2011.⁽¹⁰⁾

The Government Vaccination Programme (GVP) provides free seasonal influenza vaccination and pneumococcal vaccination to eligible people.⁽¹¹⁾ People such as healthcare

AGE	IMMUNIZATION RECOMMENDED
Newborn	B.C.G. Vaccine Hepatitis B Vaccine - First dose
1 month	Hepatitis B Vaccine - Second dose
2 months	DTaP-IPV Vaccine - First Dose Pneumococcal Vaccine - First Dose
4 months	DTaP-IPV Vaccine - Second Dose Pneumococcal Vaccine - Second Dose
6 months	DTaP-IPV Vaccine - Third Dose Pneumococcal Vaccine - Third Dose Hepatitis B Vaccine - Third Dose
1 year	MMR Vaccine (Measles, Mumps & Rubella) - First Dose Pneumococcal Vaccine - Booster Dose
1 1/2 year	DTaP-IPV Vaccine - Booster Dose
Primary 1	MMR Vaccine (Measles, Mumps & Rubella) - Second Dose DTaP-IPV Vaccine - Booster Dose
Primary 6	dTap-IPV Vaccine - Booster Dose
DTaP-IPV Vaccine: Diphtheria, Tetanus, acellular Pertussis & Inactivated Poliovirus Vaccine dTap-IPV Vaccine: Diphtheria, Tetanus, acellular Pertussis (reduced dose) & Inactivated Poliovirus Vaccine	

Vaccination programme	Characteristics of the programme	Persons with free or subsidized vaccination provided by the Government
Childhood Influenza Vaccination Subsidy Scheme (CIVSS)	Subsidise HK\$80 per dose of influenza vaccine given to children eligible under the Scheme	Children between the age of 6 months and less than 6 years; or attending a kindergarten or child care centre in Hong Kong.
Childhood Immunization Programme (CIP)	Offer free vaccinations to children from newborn to their primary 6	* Please see the above vaccination schedule
Elderly Vaccination Subsidy Scheme (EVSS)	Subsidise HK\$130 per dose of seasonal influenza vaccination and HK\$190 per dose of pneumococcal vaccination given to eligible elders by private medical doctors enrolled in the Scheme	Hong Kong residents AND aged 65 years or above
Government Vaccination Programme	Provide free seasonal influenza vaccination to eligible people	<ul style="list-style-type: none"> Residents of RCHes & RCHDs (under Residential Care Home Vaccination Programme) Healthcare workers of RCHes & RCHDs (under Residential Care Home Vaccination Programme) Community living persons aged 65 years or above with chronic illness attending public clinics Community living persons aged 65 years or above receiving CSSA CSSA recipients aged below 65 years with chronic illness attending public clinics In-patients under HA : hospitalized patients (including paediatric patients) with chronic illness, infirmary psycho-geriatric, mentally ill and mentally handicapped units/wards Paediatric out-patients with chronic illness or on long-term aspirin Healthcare workers working in DH, HA or in the public service Poultry workers or workers who may be involved in poultry-culling operations Children between the age of 6 months and less than 6 years from families receiving CSSA Pregnant women receiving CSSA Pig farmers / pigslaughtering industry personnel
	Provides free pneumococcal vaccination to eligible elders aged 65 or above	<ul style="list-style-type: none"> Residents of RCHes & eligible residents of RCHDs (under Residential Care Home Vaccination Programme) Community living persons aged 65 years or above with chronic illness attending public clinics Community living persons aged 65 years or above receiving CSSA In-patients under HA : hospitalized patients aged 65 years or above with chronic illness, infirmary psychogeriatric, mentally ill and mentally handicapped units/wards

CSSA: Comprehensive Social Security Assistance; DH: Department of Health; EHCs: Elderly Health Centers; EVSS: Elderly Vaccination Subsidy Scheme; GOPCs: General Outpatient Clinics; GVP: Government Vaccination Program; HA: Hospital Authority; MCHCs: Maternal & Child Health Center; PDQA: Professional Development and Quality Assurance; RCHDs: Residential Care Homes for Persons with Disabilities; RCHes: Residential Care Homes for the Elderly; SCVPD: Scientific Committee on Vaccine Preventable Disease; SOPCs: Special Outpatient Clinics; SPP: Special Preventive Programme
(adapted from http://www.chp.gov.hk/en/view_content/17980.html)

workers, poultry workers, pregnant women, people living or working in personal care institutions, elderly aged 65 or above with chronic illness or receiving Comprehensive Social Security Assistance, can receive free seasonal influenza vaccine for year 2010/11 from respective service providers from 1 November 2010. Free pneumococcal vaccination is also offered to eligible elders aged 65 or above to prevent hospitalization, and to reduce complication and mortality caused by pneumococcal infection.

Elderly persons aged 65 years or above living in the community who are not eligible for the free vaccination may go to private doctors enrolled in Elderly Vaccination Subsidy Scheme to receive seasonal influenza vaccine with Government subsidy of \$130 and pneumococcal vaccine with Government subsidy of \$190.⁽¹²⁾ Children between the age of 6 months and less than 6 years may go to private doctors enrolled in the Childhood Influenza Vaccination Subsidy Scheme to receive seasonal influenza vaccine with Government subsidy of \$80.⁽¹³⁾

If citizens are recommended to have immunization but are not eligible under the free or subsidy programmes, they should have the vaccination at their family doctor for personal protection. Apart from the vaccines included in the programmes, other vaccines for protection against certain infectious diseases are available at private doctors. For example, people should consult their family doctors for chickenpox vaccine, Haemophilus influenzae type b vaccine, meningococcal vaccine, hepatitis A vaccine and rotavirus vaccine if they want a more complete health protection.

Working pharmacists should constantly check the updates posted on the website of the Center for Health Protection to equip themselves with sufficient knowledge on local vaccination programmes which can facilitate their interaction with patients.

Information resources for pharmacists

Pharmacists, being primary health professionals, are expected to advocate, facilitate and provide health education to the public. With the increasing popularity of various kinds of vaccines and higher level of public awareness on personal health, pharmacists need to handle more

enquiries on immunization. Access to reputable and reliable local information resources about immunization is essential. However, they may not be widely accessed or known by our professional body.

The website of Center for Health Protection provides information of the vaccination scheme in Hong Kong. Details of immunization programme for different age groups, pregnant women, healthcare workers and workers in the poultry or pig-farming industry are uploaded to the website. Moreover, the summaries of various communicable diseases in Hong Kong, recommendations to the general public, institutions and businesses, education resources, and safety updates of vaccines are also available on the website.



Figure 1. Website of Centre for Health Protection. (http://www.chp.gov.hk/tc/view_content/17980.html)

The Travel Health Service of the Department of Health provides information on travel-related diseases, list of affected areas, travel health advice and traveller vaccines. The information is available on its website (<http://www.travelhealth.gov.hk/cindex.html>) and at the two Travel Health Centres situated in Wan Chai and Cheung Sha

Table 3. Online overseas resources about vaccines

Center for Disease Control and Prevention (US)	http://www.cdc.gov/vaccines/default.htm <ul style="list-style-type: none"> • Immunization Schedules • Recommendations and Guidelines • Vaccine Administration and Storage & Handling • Requirements and Laws • Vaccination Records • Information for Specific Groups of People • Information for Travelers • Vaccines & Preventable Diseases • Publications • Vaccine Safety & Adverse Events • Research and Development • News and Media Resources • Calendars and Events • Education & Training for Providers • Programs & Software/Tools • Statistics & Surveillance • Partners' & Related Sites
Department of Health (UK)	http://www.dh.gov.uk/en/PublicHealth/Immunisation/index.htm <ul style="list-style-type: none"> • Latest News • Key Documents • Immunization Usefulness Links • Vaccine Uptake Survey
Health Protection Agency (UK)	http://www.hpa.org.uk/ <ul style="list-style-type: none"> • Infectious Disease Topics • Publications • Products and Services • News Centers • Events and Professional Trainings
Department of Health and Aging (Australia)	http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-communic-1 <ul style="list-style-type: none"> • Communicable diseases control • Communicable diseases information
Public Health Agency of Canada	http://www.phac-aspc.gc.ca/im/index-eng.php <ul style="list-style-type: none"> • Canadian Immunization Guide • Immunization Competencies • Immunization Registries • Immunization Schedules • Influenza • National Advisory Committee on Immunization (NACI) • National Immunization Strategy • Travel Vaccines • Vaccine-Preventable Diseases • Vaccine Safety
Centers for Disease Control, R.O.C. (Taiwan)	http://www.cdc.gov.tw/mp.asp?mp=1 <ul style="list-style-type: none"> • News • Health topics • Programs & Campaigns • International Cooperation • Statistics & Analysis • Publication

Wan. These centers provide services including health risk assessment, health education, vaccinations and medications that travelers might need while travelling abroad.

These internet resources may not provide enough clinical information on each individual vaccine. There is a lack of comprehensive local resources on specific vaccine. Pharmacists often have to refer to the primary resource from overseas databases and the reports and updated news by overseas health authorities. The table below shows some examples of useful overseas resources on vaccines.

Frequently asked questions about vaccination

Pharmacists may come across some people or patients who enquire about vaccination. Here are some of the frequently asked questions and the brief answers.

Why are there boosters for some types of the vaccines? Booster doses should be given at specific intervals to maintain the immunity which may decrease with time after some types of vaccination.

Where should the children receive the immunization service included in the government CIP? Children from birth to 5 years of age can get immunized at any Maternal and Child Health Center of the Department of Health. The Department of Health also arranges inoculators to visit primary schools to provide school children free immunization. Parents may also bring their children to private doctors for vaccination.⁽¹⁴⁾

Under what circumstances are people not suitable for vaccination? Special arrangement for immunization is needed under certain circumstances. People should seek medical advice before receiving immunization if they have the following conditions.

- History of serious reaction to a previous vaccine
- History of severe hypersensitivity to any substance
- Immunodeficiency conditions:
 - Congenital immunodeficiency
 - Leukaemia, cancer
 - Chronic disease with long term treatment, e.g. chemotherapy or taking corticosteroids.⁽¹⁴⁾

What will be the adverse reactions after immunization? The adverse effects to various vaccines are different. Healthcare professionals should refer to the package insert for the specific reactions. Dizziness, low-grade fever, injection site pain and swelling are the mild and common reactions after immunization. The pain and fever can be relieved by self-administration of paracetamol. However, if the reactions persist, like for more than 24 hours, or become worse, the immunized individual should consult the doctor.⁽¹⁴⁾

Rarely there are severe adverse reactions such as convulsion and severe allergic reaction after immunization. Immunized individuals should be admitted to the Accident and Emergency Department immediately if they have difficulty in breathing, rapid pulse, skin rash and shock after vaccination. Such reactions should be recorded for future reference to take necessary precautions before other vaccinations.⁽¹⁴⁾

When is the appropriate time to receive seasonal influenza vaccine? The seasonal outbreak of influenza usually occurs from January to March in Hong Kong. To ensure protection against seasonal influenza, the vaccine should be taken at least 2 weeks before the outbreak for immunity to develop. People should get immunized before mid-December every year.⁽¹⁵⁾

New trend in vaccination: administration of vaccines by pharmacists

In recent years, pharmacists are getting involved in immunization as immunizers. In the United States, changes in pharmacy practice laws have allowed pharmacists to administer vaccines at non-traditional sites such as pharmacies and it has been recognised as a method to increase vaccination rates. Pharmacists are legally authorized to deliver influenza and pneumonia vaccinations in some areas in the US.⁽¹⁶⁻¹⁸⁾ The American Pharmacists Association has adopted guidelines for pharmacy-based immunizations through a national certificate training program for pharmacists and other training providers include National Community Pharmacists Association (NCPA) and Centers for Disease Control and Prevention (CDC).^(16,19) Pharmacists have to learn about vaccines, adverse reactions, emergency issues, legal and regulatory issue and practice the injections before

giving immunizations to the public.⁽¹⁶⁾ Vaccination by pharmacists can effectively raise the immunization rate because pharmacy-based immunization is convenient. People can get immunized at the community pharmacies at any time and do not need to make an appointment for vaccination at the clinics. This advantage is especially obvious in the rural areas where clinics may not be accessible and clinic hours may be restricted and have been willingly accepted by patients.⁽²⁰⁻²²⁾

This represents an evolving and changing practice role of the pharmacist combined with an increasing public health need. Apart from the US, pharmacy-based immunization services have started to develop in Australia,⁽²³⁾ as well as in the UK.⁽²⁴⁾ Although pharmacists in Hong Kong are not authorized to administer vaccinations at the moment, the efforts in improving vaccination rates amongst adults via pharmacist-managed vaccination programs represents a recognition of the role of pharmacists in providing primary healthcare. If pharmacy-based vaccination is implemented in Hong Kong in future, a comprehensive training programme must be in place.

CONCLUSIONS

The ever-growing demand of immunization for various types of communicable diseases has caused the rapid need to develop more vaccines. The Hong Kong Government offers several immunization programmes to its citizens, especially the children and elderly who are at risk of having serious infections. Pharmacists should equip themselves with sufficient resources, be aware of updates to the local immunization schemes and keep up with clinical knowledge of immunization in order to achieve effective patient education and interactions. Several reputable references are available from Hong Kong and overseas which pharmacists can easily refer to in their daily practice. New trends in immunization practices such as the administration of vaccines by pharmacists may potentially impact our role as health care providers. Pharmacists have a responsibility to keep themselves familiar with the latest vaccination technologies, available vaccines and immunization programmes in order to provide the best care to the community.

Author's background

TSE Kit Ying Helena was a pharmacy intern working in Hong Kong Sanatorium & Hospital. Her email address is: helena_0124@hotmail.com **CHAN Hoi Lam** is currently the Associate Manager - Medical Affairs of Pfizer Hong Kong. For more information about this article, please contact her through her email address: hoilam.chan@pfizer.com

References

1. What are vaccines? News Medical. <http://www.news-medical.net/health/What-are-Vaccines.aspx> Accessed May 10, 2011.
2. The Life of Edward Jenner. Edward Jenner Museum. <http://www.jennermuseum.com/edwardjenner.html> Accessed May 10, 2011.
3. Statue commemorates smallpox eradication. WHO website. http://www.who.int/mediacentre/news/notes/2010/smallpox_20100517/en/index.html Accessed May 10, 2011.
4. Global Polio Eradication Initiative - April 2010. WHO website. http://www.afro.who.int/index.php?option=com_content&view=article&id=2290&Itemid=2669 Accessed May 10, 2011.
5. Stanley A Plotkin. (2005). Vaccines: past, present future. *Nature Medicine*, 11(4): S5-11
6. Carlson B. (2008). Adults now drive growth of vaccine market. *Genetic Engineering & Biotechnology News*, 28(11): 22-3.
7. Childhood Immunisation Programme. Centre of Health Protection website. http://www.chp.gov.hk/en/view_content/17982.html Accessed May 10, 2011.

8. Ola Samuelsson, et al. (2008) Vaccination Against high blood pressure: a new strategy. *The Lancet*, 371:788-9.
9. Klein SL, et al. (2010) The Xs and Y of immune responses to viral vaccines. *Lancet Infectious Disease*, 10(5): 338-49.
10. Press release. New pneumococcal vaccine recommended for children immunisation programme. Centre of Health Protection website. <http://www.chp.gov.hk/en/content/116/23024.html> Accessed May 10, 2011.
11. Centre of Health Protection. Government Vaccination Programme 2010/11. Who is it for and when is it available?
12. Elderly Vaccination Subsidy Scheme. Centre of Health Protection website. http://www.chp.gov.hk/en/view_content/21839.html Accessed May 10, 2011.
13. Childhood Influenza Vaccination Subsidy Scheme. Centre of Health Protection website. http://www.chp.gov.hk/en/view_content/17984.html Accessed May 10, 2011.
14. Child Health: Immunisation. Family Health Service, Department of Health website. http://www.fhs.gov.hk/english/health_info/class_topic/ct_child_health/ch_immunisation_j1.html Accessed May 10, 2011.
15. Centre of Health Protection. Frequently Asked Question on Seasonal Influenza Vaccine. Available at http://www.chp.gov.hk/files/pdf/faq_gvp_eng.pdf Accessed May 10, 2011.
16. Scott A. (2009). Vaccination by pharmacists: New York pharmacists train to give flu and pneumonia shots. *Drug Topics*, 153(3):.

17. Krysten A. Modrzejewski. (2003). Pharmacists' involvement with vaccinations leads to preventive health care role. *American Journal of Health-System Pharmacy*, 60:1726-1728
18. Sharya Vaughan Bourdet, et al. (2003) Effect of a pharmacist-managed program of pneumococcal and influenza immunisation on vaccination rates among adult inpatients. *American Journal of Health-System Pharmacy*, 60:1767-1768.
19. Khalid M. Kamal, et al. (2003). Impact of the American Pharmacists Association's (APhA) Immunisation Training Certification Program. *American Journal of Pharmaceutical Education*, 67(4):124.
20. Emily M. Ambizas. Value of Community Pharmacist. Available on http://www.pssny.org/documents/pdfs/leg_docs/rphvalue_whitepaper.pdf. [Accessed June 22, 2011]
21. Annie Wong, et al. (2003). Pneumococcal vaccination in hospitalized elderly patients: role of the pharmacist. *Pharmacotherapy*, 23(2)
22. David T. Bearden. (2005) Statewide impact of pharmacist-delivered adult influenza vaccinations. *American Journal of Preventive Medicine*, 29(5):450-452.
23. Position statement on immunisation in pharmacies. Pharmaceutical Society of Australia website. <http://www.psa.org.au/site.php?id=3672>. [Accessed May 10, 2011]
24. Mary Francis, et al. Vaccination services through community pharmacy: a literature review. Public Health Wales. Available at [http://www2.nphs.wales.nhs.uk:8080/pharmaceutical/phtdocs.nsf/c944d98bdffc718802570050043d5cd/b16d4a1e2295dcbf802577830030f109/\\$FILE/Vaccination%20services%20through%20community%20pharmacy%20v1a.pdf](http://www2.nphs.wales.nhs.uk:8080/pharmaceutical/phtdocs.nsf/c944d98bdffc718802570050043d5cd/b16d4a1e2295dcbf802577830030f109/$FILE/Vaccination%20services%20through%20community%20pharmacy%20v1a.pdf). Accessed May 10, 2011.

CE Questions Answer for 184-S3(D&T)

Drug Administration in Enteral Tube Feeding

1. A 2. D 3. D 4. B 5. A 6. C 7. C 8. A 9. C 10. B



MSc in Clinical Pharmacy*

This is a 2-year part-time programme in HK delivered through face-to-face and distance learning. Tutorials / workshops are run by visiting academics from the University of Sunderland, U.K. The degree is awarded by the University of Sunderland.

Programme Features:

- Updated specialist modules
- Realistic project workload for timely completion
- Training in research skills
- High and timely completion rate

Teaching and Assessment:

- Teaching is conducted through lectures, tutorials, seminars and group work. Project work is required on a topic relevant to patients' needs from the students' area of study.
- Assessment is mainly by examination and coursework, including reports, seminar presentations, case studies and project report (dissertation).

Entry Requirements:

A minimum of lower second class honours degree in pharmacy (or equivalent) and registration as a pharmacist in Hong Kong. BPharm graduates from countries that do not normally award honours may also apply, provided they are registered as a pharmacist in Hong Kong. The programme is open to both hospital and community pharmacists.

Application Deadline: May 31, 2012

BSc (Hons) Pharmaceutical Science*

This programme is a 2-year top-up degree offered in part-time mode of study in Hong Kong. The BSc (Hons) Pharmaceutical Science is to be awarded by the University of Wolverhampton, UK. The programme aims to produce high quality pharmaceutical science graduates with the generic, subject-specific and transferable knowledge and skills suited to a career in the pharmaceutical industry or other related laboratory based scientific discipline.

Programme Features:

- a 24-month part-time undergraduate programme
- it covers the area of pharmaceutical science including pharmacology, pharmaceutical design and manufacture, biopharmaceutical, methods of analysis, quality assurance and delivery of pharmaceutical substances
- an articulation part-time programme for graduates of HKU SPACE Advanced Diploma in Pharmaceutical Science and HKIVE Higher Diploma in Pharmaceutical Technology (Western Medicine)

Teaching and Assessment:

- Teaching is delivered via face-to-face lectures, laboratory sessions and tutorials.
- Assessment includes a combination of examinations and coursework including laboratory reports, in-class assignments, quizzes, projects, dissertation etc.

Entry Requirements:

Applicants should hold either:

- Advanced Diploma in Pharmaceutical Science awarded by HKU SPACE; or
- Higher Diploma in Pharmaceutical Technology (Western Medicine) awarded by the HKIVE (Chai Wan)

Application Deadline: June 29, 2012

Enquiries: ☎ 3762 0096 📠 2151 0720 ✉ sheri.ip@hkuspace.hku.hk

* These are exempted courses under the Non-Local Higher and Professional Education (Regulation) Ordinance. It is a matter of discretion for individual employers to recognize any qualification to which these courses may lead.

<http://hkuspace.hku.hk/>
enquiry@hkuspace.hku.hk

ENROLMENT CENTRES
HKU Campus • Admiralty • Northpoint • Causeway Bay • Kowloon Bay • Mei Foo
HKU SPACE is a non-profit making University Company Limited by Guarantee.

Emergency First Aid for poisoning and for Alkaloid Poisoning in Particular

O'Toole, Desmond Keith; CHEUNG, Hon-Yeung*

Research Group for Bioactive Products, Department of Biology & Chemistry, City University of Hong Kong, Hong Kong SAR, China.

(* Corresponding author)

ABSTRACT

Poisoning due to ingestion of a range of chemicals and natural toxic materials requires swift responses to help the victim of poisoning. The general approach to handling these kinds of poisonings are reviewed and then the particular problem of alkaloid poisoning discussed. Poisoning of certain plants containing a naturally occurring alkaloid substance requires prompt action to minimize the poisonous effect on a patient. Although each type of alkaloid may have its own specific antidotes, they may not be immediately available. Tannic acid or a cup of strong tea could be used as the universal antidote. Besides, activated charcoal in liberal doses could also be a choice to eliminate the poisons from the body.

Keywords: *alkaloid poisoning, first aid, tannic acid, tea, activated charcoal, universal antidote*

INTRODUCTION

A poison is a substance that causes death or harm if it is swallowed or absorbed into the body.⁽¹⁾ It could be a chemical or toxins produced by living organisms including microbes, animals or plants.

Food poisoning is one of the most commonly known illnesses. It occurs after eating at picnics, restaurants, school cafeterias or large social functions. In most cases, one or more people may become sick within two to six hours of eating some food or drink because the food has been contaminated with certain types of bacteria, parasites, viruses, or toxins.⁽²⁾ However, food poisoning does not necessarily originate only from contaminated food. Sometimes it is due to consuming some confusing poisonous materials, such as poisonous fungi,⁽³⁾ or due to improper preparation of the puffer fish (fugu).^(4,5)

When a therapeutic substance is improperly taken at a wrong time or dosage or a combination of both, it can also cause poisoning.⁽⁶⁾ For example, when a person takes a larger-than-prescribed dose of barbiturates or combines the barbiturates with alcohol even at the proper dose, it can lead to a coma and death. Sometimes if a drug is taken on an empty stomach it may result in severe pain or strong reactions.⁽⁷⁾

Whatever the poison is, based on

the biological responses, the poison is classified into one of the following types; namely, the corrosive poisons, the narcotic poisons, the irritant poisons and the excitants. The last three types of poison are also known as the non-corrosive poisons. Although treatment for each kind of poisoning may be different, the common practices of handling a poisoned patient are about the same.

COMMON PRACTICES OF HANDLING NON-CORROSIVE POISONING⁽⁸⁾

First of all, cases of poisoning can be recognized by certain well-defined symptoms occurring soon after the act of eating or drinking. The training of a doctor or a pharmacist should cover the knowledge of antidotes for every kind of poison, and accordingly their services should be sought if poisoning is suspected. Information about the patient conveyed to the practitioner should be as accurate as possible, in particular the suspected kind of poison to be treated, so that the most appropriate antidote can be determined. As a first step, the lips and tongue of the patient must be examined. If they are not marked so as to appear seared or have white markings, this suggests that a non-corrosive poison has been consumed, and so special handling for corrosive poisoning is not required.

While awaiting the arrival of the doctor, no time must be lost to prevent the further action of the poison in the system, and this can first be done by diluting or removing as much as possible of the poison so as to arrest the progress of the poison. Dilution may be brought about by giving a copious draught of a bland, soothing (demulcent) drink, which will also ease the pain and alleviate irritation. The remedies in the home which are most likely to be at hand are milk, beaten egg, oil from tinned sardines (unless sardines are suspected as the cause of ptomaine poisoning), olive oil, cod-liver oil, flour and water, weak tea, warm water, barley water, thin gruel (congee), linseed tea, or a small dose of castor oil. Depending on the individual case, these remedies can be used as a diluting agent.

TREATMENT FOR NON-CORROSIVE POISONING⁽⁸⁾

Non-corrosive poisoning can be best treated by giving an emetic to promote vomiting, which is less painful and more

effective if the poison has been diluted with a demulcent drink such as those already mentioned.

The most convenient emetic method is to tickle the back of the throat with a feather, which can be done without risk of choking an unconscious patient who is not in a fit condition to swallow a liquid emetic such as a tablespoonful of salt in half a pint of lukewarm water, or a teaspoonful of mustard in half a pint of warm water, or a tablespoonful of an ipecac preparation (although there are doubts about its usefulness) or thirty grams of zinc sulfate in a tea-cupful of warm water.

As mentioned above, under the category of non-corrosive poisonings there are three types of poisons, each of which should be handled in slightly different ways, in addition to the general treatment just described.

1. The narcotic poisons are those which induce torpor, which gradually becomes deeper, until unconsciousness merges into death. Such poisons include chloroform, ether, the many preparations of opium, sometimes known as laudanum chlorodine, paregoric, syrup of poppies, morphia lozenges, Godfrey's cordial, infant soothing syrup, pain-killer, and many cough medicines. Symptoms of narcotic poisoning may be recognized by unconsciousness, a cold and clammy skin, a feeble and slow pulse, a dark line along the middle of the tongue, and by the contraction of the pupils of the eyes to a pin point.

The chief aim must be to get rid of the poison by vomiting, and then to fight against the increasing stupor by trying to keep the patient awake. Strong coffee should be given to the patient, who should be made to walk up and down, supported by one or two helpers, while another helper occasionally dashes cold water on the patient's face, or flicks the patient's chest and face with a wet towel. Slapping the bare soles of the feet with a slipper is useful when the patient is unable to be walked about the room, and if the breathing threatens to stop, artificial respiration must be applied. If medical aid is not forthcoming, and the patient is deeply unconscious, an attempt should be made to wash out the stomach. This is done by taking a clean piece of rubber gas tubing, and passing one end as far as possible down the gullet. A funnel is then put into the other end, the tube and funnel held upward and warm water

poured gently into the funnel until it is full to overflowing. The free end of the tube is then lowered and the stomach empties by syphon action.

2. The irritant poisons are of a metallic nature, and include arsenic, phosphorus, tartar emetic (potassium antimony tartrate), sugar of lead (lead acetate), corrosive sublimate (mercuric chloride), and copper sulfate.

The effect of such poisons may be recognized by a metallic taste in the mouth, running eyes and nose, pain in the pit of the stomach, vomiting, and violent purging. Such cases are treated according to the general directions, but the administration of oil must be avoided in a case of phosphorus poisoning. After vomiting ceases the patient's strength must be kept up by giving the patient stimulating beverages.

3. The excitants give rise to mental excitement followed by delirium or convulsions. The most common poisons of the class are belladonna with its alkaloid atropine, henbane and its extracts, woody nightshade, poisonous fungi, laburnum seeds, prussic acid contained in laurel leaves and almond essences, and strychnine, which may be recognized by its effect on the sufferer's back, which is bent inwards.

If the patient is not strongly convulsed an emetic is given, otherwise cold water is splashed over the face, and the patient is kept in a dark room.

4. Alcoholic poisoning. – The symptoms of this form of poisoning include coma, seizures, slow breathing and hypothermia (low body temperature). The general treatment for poisoning is followed, but vomiting is promoted, there is no attempt to dilute the alcohol, the patient is kept covered, and when consciousness returns the patient should be given a hot drink.

SPECIAL TREATMENT FOR CORROSIVE POISONING⁽⁸⁾

During the examination of the lips and tongue of a patient, if they are seared and white markings are present, then a corrosive poison is likely to have been taken, and the following special treatment is required.

Corrosive poisonings are attributed to strong acids and alkalis, such as vitriol (sulphate salts of various metals), spirits of salt (HCl), aqua fortis (nitric acid (HNO₃)), carbolic acid, and oxalic acid among the acids; and caustic soda, potash (soluble potassium salts), and lime among the alkalis. The symptoms of this type of poisoning are intense burning pain from mouth to stomach, the inside of the mouth appears blistered or covered with loosely-hanging white skin, the voice is hoarse, and the pulse feeble, and the patient retches. The vomited food matter contains whitish flakes or shreds, which

turn black. In such a case, an antidote should be given promptly. Fortunately, acids and alkalis neutralize each other, so that alkaline poisons can be neutralized with doses of a weak acid, such as vinegar, or lemon-juice and water, in the proportion of two tablespoonfuls to half pint of water. Acid poisons can be neutralised by the consumption of an alkali, such as a tablespoonful of magnesia, bicarbonate of soda, or common whiting in half a pint of water, or with ordinary lime water. In oxalic acid poisoning, potash, soda, and ammonia must be avoided, and only magnesia, whiting, or lime water should be used.

On no account must an emetic be given. With cases of corrosive poisoning there is always the risk that during retching the stomach may press against the diaphragm and rupture its weakened walls, which would result in peritonitis.

TREATMENT FOR ALKALOID POISONING

Many people often consume plants or Chinese medicines thinking they are natural substances and they are not poisonous. It is true in general; yet, as is well known, some botanical components are extremely poisonous. As a pharmacist and paramedical health caretaker, it is important to know the symptoms in cases of alkaloid poisoning and other kinds of poisoning. The initial treatment consists in chemical destruction or obstruction and subsequent evacuation of the toxic material. While each alkaloid, when taken by mouth, requires its own special antidote, if any is known, the following general procedure and drugs can be applied.

If a person is suspected of overdosing on any alkaloid that can cause death from overdose one should call an ambulance immediately and take the following actions:

1. If possible, positively identify the noxious agent the patient has overdosed on and give this information to the ambulance operator.
2. Remove the noxious agent from contact with the patient.
3. Keep the patient on their back with the head tilted back so that the airway of the patient remains open. If the patient vomits turn the patient's head to the side and assist the patient in removing the vomitus from the mouth. An unconscious or near-conscious person should be placed on their abdomen, head turned to one side and tongue pulled forward.
4. If the patient is conscious and has a gag reflex then it is fine to give him water or milk. The way to test a person's gag reflex is to apply pressure to the back of their tongue. Normally they will gag when you do this.
5. Give 2-4 glasses of water immediately but milk can be substituted.
6. Induce vomiting immediately by giving 1-2 tablespoonfuls of salt in a full glass of warm water, or a tablespoon of

mustard in warm water, or have the patient place their index finger far back on the tongue and stroke from side to side. Vomiting should also be induced after each dose of the antidote. Caution: with strychnine, strongly caustic, or corrosive poisons, DO NOT induce vomiting.

7. Give the patient the Universal Antidote as shown below.
8. Get medical attention as soon as possible. Do not interrupt the above procedures.

Paramedics who respond to this sort of incident are, in most cases, only minutes away and should have been trained and equipped to handle these sorts of emergencies.

UNIVERSAL ANTIDOTE FOR ALKALOID POISONING

When alkaloids have been swallowed, give 0.6 to 2.0 gm of tannic acid in a half glass of warm water immediately, followed by another glass of water; or give strong black tea, or potassium permanganate (1:5,000 solution) as an alternative. When a specific antidote is not available, give one teaspoon to one table spoon of activated charcoal in liberal doses. If the nature of the poison is unknown, give repeated doses of 15 gm of the following mixture or a like mixture, stirred in half a glass of warm water as the universal antidote for alkaloid poisoning.

- Pulverized, activated charcoal (burnt toast as an alternative) - 2 parts
- Tannic acid (strong black tea as an alternative) - 1 part
- Magnesium oxide (milk of magnesia as an alternative) - 1 part

A poison control kit for first-aid emergency use, containing ipecac syrup and the activated charcoal is possibly available in some pharmacy stores. Never give oils, fats, or alcohol; tannin (tannic acid powder or common black tea) precipitates most alkaloids (as well as certain toxic glycosides and many metals). However, the precipitates could dissolve in the acidic gastric juice. Hence, the antidote should be given with an alkaline substance, such as sodium carbonate or bicarbonate, milk of magnesia, or the like, which neutralize acids. Stomach contents can then be removed by vomiting or with a stomach pump.

Iodine in the form of tincture of Iodine diluted, or Lugol's Solution (iodine with potassium iodide) could also be given as a general antidote. But the precipitates may dissolve in alkaline juices in the intestines, so to hurry the poison through the bowels if vomiting or a stomach pump is not possible to rely on, a purgative should be administered.

According to Stedman's medical dictionary, the "universal antidote" described above is considered ineffective, except for the activated charcoal which absorbs and obstructs alkaloids. However, it could be very dangerous to

administer. If the victim is drowsy any vomitus could end up in the lungs which could result in death. But quick removal from the stomach is desirable.

EXAMPLE OF ALKALOIDS POISONING: - PYRROLIZIDINE COMPOUNDS

Background

Pyrrrolizidine alkaloids are a large, varied class of naturally occurring, stereochemically diverse monoesters, diesters and macrocyclic diesters of 1-hydroxymethyl-7-hydroxy-1,2-dehydro pyrrolizidines (e.g. esters of the diastereoisomeric necine bases heliotridine and retronecine) or their N-methylated, ring opened (otonecine) analogues.⁽⁹⁻¹¹⁾ These alkaloids and their N-oxides occur as natural components of many herbal preparations, cooking spices and honey, and can contaminate food crops (e.g. cereals) and animal-derived food (e.g. milk, eggs) destined for the human food supply.^(10,12) (See associated foods below.)

In vivo, the esterified dehydro pyrrolizidine alkaloids form hepatic, didehydro pyrrolizidine metabolites (i.e. dihydro pyrrolizine esters) that are hepatotoxic and can be pneumotoxic, genotoxic and carcinogenic.^(10,11,13) Although pyrrolizidine alkaloid intoxication is a rare toxicosis, it can be caused by consumption of plant material containing these alkaloids. The plants may be consumed as food, for medicinal purposes, or as contaminants of other agricultural crops. Cereal crops and forage crops are sometimes contaminated with pyrrolizidine-producing weeds, and the alkaloids find their way into flour and other foods, including milk from cows feeding on these plants.

While hepatic N-oxidation of pyrrolizidine alkaloids is a recognised detoxifying mechanism in mammals,^(14,15) it has been shown that orally ingested N-oxides of the pyrrolizidine alkaloids can have hepatotoxicity similar to that of the parent free base alkaloids due to reduction in the alimentary tract prior to absorption.⁽⁹⁾ Furthermore, Molyneux *et al.* showed that, in calves, intra-ruminal infusion of riddelliine-N-oxide alone, at the same rate as calculated for a toxic dose of the whole plant, resulted in toxicity on a par with the whole plant.⁽¹⁶⁾ By contrast, they also showed that infusion of the riddelliine free base, again at the rate calculated for a toxic dose of the whole plant, was not toxic. However, others have shown that, given intravenously, or studied in vitro using liver microsomes, the N-oxides are less toxic than the parent free base alkaloids.

Poisoning symptoms

Most cases of pyrrolizidine alkaloid toxicity result in moderate to severe liver damage. Gastrointestinal symptoms are usually the first sign of intoxication, and consist predominantly of abdominal pain

with vomiting and the development of ascites. Death may ensue from 2 weeks to more than 2 years after poisoning, but patients may recover almost completely if the alkaloid intake is discontinued and the liver damage has not been too severe.

Diagnosis

Evidence of toxicity may not become apparent until sometime after the alkaloid is ingested. Early clinical signs include nausea and acute upper gastric pain, acute abdominal distension with prominent dilated veins on the abdominal wall, fever, and biochemical evidence of a dysfunctional liver. Fever and jaundice may be present. In some cases the lungs are affected; pulmonary edema and pleural effusions have been observed. Lung damage may be prominent and has been fatal. Chronic illness from ingestion of small amounts of the alkaloids over a long period proceeds through fibrosis of the liver to cirrhosis, which is indistinguishable from cirrhosis of other aetiology.

Associated foods

Many plants from the Boraginaceae, Compositae, and Leguminosae families contain well over 100 hepatotoxic pyrrolizidine alkaloids. Pyrrolizidine poisoning due to the consumption of the alkaloid-containing plants as food, contaminants of food, or as medicinals has occurred.

Most result from the use of medicinal preparations as home remedies. However, intoxications of animals grazing on pasture sometimes occurs in areas under drought stress, where plants containing alkaloids are common. Milk from dairy animals can become contaminated with the alkaloids, and alkaloids have been found in the honey collected by bees foraging on toxic plants. Mass human poisonings have occurred in other countries when cereal crops used to prepare food were contaminated with seeds containing pyrrolizidine alkaloid.

Prevention

Avoiding the plants containing the substances is the only way of prevention. However, these plants are not normally consumed in a European diet.

Risk populations

All humans are believed to be susceptible to the hepatotoxic pyrrolizidine alkaloids. Home remedies and consumption of herbal teas in large quantities can be a risk factor and are the most likely causes of alkaloid poisonings.

CONCLUSION

Death or sickness caused by a toxic substance either intentionally for the purpose of murder or suicide, or unintentionally due to accidental contact or

consumption have increased significantly in recent years. Unlike the period prior to 1940, of all the recent casualties most were not attributed to alkaloid poisoning. Nevertheless, poisoning due to alkaloids still repeatedly happens and most alkaloid poisonings are recoverable if prompt first aid is given. Pharmacists should be knowledgeable about these kinds of poisonings so they can give advice on the right antidotes to use for alkaloid poisoning so that a poisoned life may be rescued.

ACKNOWLEDGEMENTS

This paper has drawn substantially on the material published at chestofbooks.com/food/household/Woman-Encyclopaedia, see reference 8 below.

Author's background

O'Toole, DK, is an Australian. He holds a BSc and MSc degrees from Qld University in Microbiology and Food Microbiology. He was awarded a PhD in 2001 from Griffith University on factors affecting the quality of milk and dairy products. Dr O'Toole has appeared as an Expert Witness in a number of court cases in Hong Kong involving food and microbiology. He has extensive experience with practical aspects of food production and has been an active member of committees that have developed standards for microbiological testing for the Dairy Industry. **Dr CHEUNG, HY** is associate professor of pharmaceuticals in the City University of Hong Kong. His email address: bhonyun@cityu.edu.hk

References

1. Hornby AS (2004). *Oxford Advanced Learner's English-Chinese Dictionary*, 6th Ed. Publisher: Oxford.
2. <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0002618/> (reviewed: January 10, 2011 and accessed on March 3, 2012)
3. <http://familydoctor.org/familydoctor/en/diseases-conditions/food-poisoning/mushroom-poisoning.html> [accessed on March 3, 2012]
4. Centers for Disease Control (1996-05-17). Tetrodotoxin Poisoning Associated With Eating Puffer Fish Transported from Japan. *Morbidity and Mortality Weekly Report* 45(19):389-412.
5. Noguch T, Arakawa O (2008). Tetrodotoxin – Distribution and Accumulation in Aquatic Organisms, and Cases of Human Intoxication. *Marine Drugs*, 6(2):220-242.
6. CASSIDY S, HENRY J (1987). Fatal toxicity of antidepressant drugs in overdose. *British Medical Journal*, 295:1021-1024.
7. Fleisher D, Li C, Zhou Y, Pao L, Karim A (1999). Drug, Meal and Formulation Interactions Influencing Drug Absorption After Oral Administration: Clinical Implications. *Clinical Pharmacokinetics*, 36(3):233-254.
8. <http://chestofbooks.com/food/household/Woman-Encyclopaedia-1/How-To-Treat-Cases-Of-Poisoning.html#zzz1rGbwzPLC> [accessed on March 3, 2012]
9. Mattocks AR (1986). Chemistry and toxicology of pyrrolizidine alkaloids. *Academic Press*: London.
10. International Program on Chemical Safety (IPCS) (1988). Pyrrolizidine alkaloids. *Environmental Health Criteria* 80. WHO, Geneva.
11. Wiedenfeld H, Roeder E, Bourauel T, Edgar J (2008). Pyrrolizidine alkaloids. *Structure and Toxicity*. V&R Unipress, Bonn University Press: Göttingen.
12. Edgar JA (2003). Pyrrolizidine alkaloids and food safety. *Chemistry Australia*, 70:4-7.
13. Fu PP, Xia Q, Lin G (2004). Pyrrolizidine alkaloids – genotoxicity, metabolism enzymes, metabolic activation, and mechanism. *Drug Metabolism Review*, 36:1-55.
14. Jago MV, Edgar JA, Smith LW, Culvenor CCJ (1970). Metabolic conversion of heliotrine based pyrrolizidine alkaloids to dehydroheliotridine. *Molecular Pharmacology*, 6:402-406.
15. Miranda CL, Chung W, Reed RE, Zhao X, Henderson MC, Wang JL, Williams DE, Buhler DR (1991). Flavin-containing monooxygenase: a major detoxifying enzyme for the pyrrolizidine alkaloid senecionine in guinea pig tissues. *Biochemical Biophysical Research Communications*, 178:546-552.
16. Molyneux RJ, Johnson AE, Roitman JN, Benson ME (1979). Chemistry of toxic range plants. Determination of pyrrolizidine alkaloid content and composition in *Senecio* species by nuclear magnetic resonance spectroscopy. *Journal of Agriculture and Food Chemistry*, 27:497-499.

Method Development for the Colorimetric Determination of Total Alkaloids in Herbal Medicine

CHEUNG, Hon-Yeung^{a*}; BAIBADO, Joewel Tarra^{a,b}; CHAN, Gallant GL^a; ZHANG, Zhi-feng^{a,c}

^a Research Group for Bioactive Products, Department of Biology and Chemistry, City University of Hongkong, 83 Tat Chee Avenue, Hongkong SAR, China (* Corresponding author)

^b Iloilo Doctors' College, College of Sciences & Nursing, 5000 West Avenue, Molo, Iloilo City, Philippines

^c Ethnic Pharmaceutical Institute of Southwest University for Nationalities, Chengdu 610041, Sichuan, China

ABSTRACT

Herbal plants contain many bioactive components that are responsible for their bioactivities. These compounds are very complex and closely related in structure making them difficult to isolate qualitatively and quantitatively. Numerous studies have demonstrated that isosteroidal alkaloids are the major active components in medicinal plants. However, the content of individual alkaloid components vary among species and the content of any potential marker is present at very low level (less than 0.01%) so that it can not be quantified by High Performance Liquid Chromatography (HPLC). It was found that using a specific marker for the assay is not an ideal choice for many herbs. Hence, the total alkaloid content was used as an index for the quality control of the herb. The aim of this study was to optimize an acid-dye colorimetric method for the quantitative determination of the total alkaloids in herbal medicines. The method developed shows good reproducibility and high reliability. This quantitative method is useful for the quality control of herbal medicine with low alkaloid content.

Keywords: Herbal medicine; Total alkaloids; Colorimetric method; Acid-dye; Quality control

INTRODUCTION

Alkaloids are secondary metabolites in plants that are complex but closely related in structure. A certain herb may contain many similar alkaloids. However, their contents may not be high enough

to be determined. The quantity may be so low that it cannot be assayed individually. Shams *et al.* (2009) reported that vincristine and vinblastine alkaloids in *Catharanthus roseus* L. Don are as low as 0.001 and 0.002% respectively.⁽¹⁾ Among wild morning-glory species (*Ipomoea* spp.), the range of the total ergot alkaloids is between 0.0029% to 0.0059%.⁽²⁾ The scopolamine alkaloids in *Atropa belladonna* were found to be as low as 0.00168 (% dry wt).⁽³⁾

On one hand, the amount and type of bioactive isosteroidal alkaloids varies among different *Fritillaria* species and the content of potential marker alkaloid(s) may be lower than 0.01%, which is the criterion set down by the committee of the Hongkong Chinese Materia Medica Standards (HKCMMS) for the selection of marker compounds for the quality control of herbs.⁽⁴⁻⁵⁾ To extract and produce sufficient quantities of a purified bioactive component, the quality of raw herb is a determining factor. Thus, it is necessary to determine the alkaloid contents at the start. Hence, this study aims to optimize a simple and reliable quality control method for herbal medicines with low contents of active alkaloids. The reported colorimetric

determination of total alkaloids in this study has also been endorsed and adapted as the assay method for *Fritillaria* spp. in Phase III of the Hong Kong Chinese Materia Medica Standards (HKCMMS) in 2010.⁽⁶⁾

MATERIALS AND METHODS

Apparatus and reagents

The UV absorbance of alkaloid-dye adducts was measured with a Hitachi U-2810 UV-Vis spectrophotometer (Lab Recyclers, Inc., Gaithersburg, America). Potassium biphthalate, bromothymol blue, dichloromethane, ammonium hydroxide, ethanol, ethyl acetate, anhydrous sodium sulfate were purchased from Shenzhen Zhongyuan Chemical & Glass Instruments Company (China). Peimisine (purity >98%) was purchased from Hai Chan Biotechnology Limited (Hong Kong). Seven batches of *Fritillaria ussuriensis* Bulbs (FUB) were purchased or collected freshly from various cities/counties in China in May 2007. Details of their origin are listed in Table 1. All collected samples were authenticated by Prof. Wang Qiuling (Beijing University of Chinese Medicine, Beijing, China).

Table 1. Source Information and Total Alkaloid Content of Different Batches of *Fritillaria ussuriensis* bulb

Batch No.	Sample ID	Source	Amount±SD (%w/w)
1	FUB 01-01	Tonghua, Jilin	0.2426±0.0056
2	FUB 03-01	Baishan, Jilin	0.2826±0.0081
3	FUB 04-01	Tieli, Heilongjiang	0.2516±0.0036
4	FUB 05-01	Heilongjiang	0.2826±0.0081
5	FUB 06-01	Jilin, Jilin	0.2826±0.0081
6	FUB 07-01	Northeastern, China	0.2246±0.0079
7	FUB 08-01	Heilongjiang	0.2840±0.0108

Initial procedure for the acid-dye colorimetric method

The colorimetric method for determination of total alkaloids is based on the conjugation reaction between total alkaloids in sample extracts and bromothymol blue, forming colored alkaloid-dye adducts which can be measured quantitatively with a UV spectrophotometer. The initial colorimetric method was carried out according to the method described by Liu & Xie (1995) with minor modification.⁽⁷⁾ Peimisine was selected as a standard as it is a typical active alkaloid in *Fritillaria* spp. and the average content is slightly larger than 0.01% (Table 2). Briefly, 2 mL of 0.2 M potassium biphthalate buffer solution (pH 5.0) and 2 mL of 0.001 M bromothymol blue solution were transferred into a 50-mL separating funnel containing 8 mL of standard solution or sample extract in dichloromethane. Then, the mixture solution was shaken vigorously and allowed to stand for 10 min. The number of partitionings of the sample solution in bromothymol blue dye with dichloromethane was investigated. The partition steps were repeated from one to four times. Subsequently, the dichloromethane layer was collected and filtered into a 10-mL volumetric flask. Filtrates were combined in the same 10-mL volumetric flask, to which was added dichloromethane to make up a total volume of 10 mL. After standing for 30 min, the UV absorbance of the solution was measured at 410 nm. The absorbance of the solution was diluted if necessary to give an absorbance value in the range from 0.2 to 0.8.

Optimization of sample extraction

Extraction solvent

To a 0.5 g sample of powdered FUB in a 50-mL centrifugal tube was added 1 mL of ammonium hydroxide and it was left for 30 min under room temperature. Then, 10 mL of five solvents, namely dichloromethane, dichloromethane/methanol (4:1, v/v), methanol, ethanol or ethyl acetate, was added into the centrifugal tube, respectively, for the later comparison of their extraction capabilities. After sonicating for 30 min, the above mixture solution was filtered and filtrate was evaporated to dryness.

The dried extract was further dissolved in 10 mL of dichloromethane. One mL of the dissolved sample extract was taken out and added with another 7 mL of dichloromethane for the determination of total alkaloids according to the method described above.

Extraction method

One mL of ammonium hydroxide was added to half gram of powdered FUB sample in a 50-mL round bottom flask and left to stand for 30 min at room temperature. Ten mL of dichloromethane/methanol (4:1, 128 v/v) was added into the round bottom flask. Then, an extraction method applied including sonication (for 30 min or 60 min) or refluxing (60 or 120 min) was adapted. After extraction, sample solutions were further processed according to the procedure described in the preceding paragraph on the optimization of extraction solvent.

Soaking time in ammonium hydroxide

One mL of ammonium hydroxide was added to half gram of powdered FUB sample in a 50-mL round bottom flask and left to stand for 30 or 60 min at room temperature. The following steps were the same as mentioned above while using dichloromethane/methanol (4:1, v/v) as the extracting solvent and refluxing (120 min) as the extraction method.

Optimization of the ratio of dye to sample extract

To ensure the homogeneity of the analyte, all the sample extract needs to be collected and analyzed as only one mL of sample extract was taken out for the analysis in previous experiments and all the sample extract re-dissolved in dichloromethane (total in 10 mL) should be used. Accordingly, the ratio of dye to sample extract needs to be optimized. Briefly, 0.5 g of sample was extracted with dichloromethane:methanol (4:1). After soaking in ammonium hydroxide for 30 min and subsequent 120-min refluxing, the extract was dried and re-dissolved in 8 mL of dichloromethane. Different amounts of sample extract (corresponding to 0.125, 0.25, 0.375 and 0.5 g sample used) were then partitioned with three concentrations of the dye (0.001, 0.0025 and 0.005

M), respectively, for later colorimetric analysis as mentioned above.

Investigation of the effect of residual water

As the remaining water present after the partition of sample extract with dye might interfere with the absorbance of the sample-dye solution, anhydrous sodium sulfate was used to remove the residual water in the dichloromethane layer to see the possible influence from residual water. In brief, the dichloromethane layer was collected in a test tube containing 0, 2 or 4 g of anhydrous sodium sulfate. The solution was shaken and filtered to a 25-mL volumetric flask for subsequent colorimetric analysis.

Validation of optimized method

Calibration curve

Two mg of peimisine was dissolved to 10 mL of dichloromethane in a volumetric flask as a stock of standard solution (standard stock). The calibration curve was prepared using 0.2, 0.4, 0.8, 1.0 and 1.2 mL of standard stock solution, which were then supplemented with 7.8, 7.6, 7.2, 7.0 and 6.8 mL of dichloromethane and processed accordingly.

Reproducibility, repeatability and recovery

The reproducibility test of the method was examined by analyzing five replicate standard solutions of 16 mg/L peimisine. The repeatability test was carried out through the measurement of five replicates of the same batch of *Fritillaria* sample (Table 3). To evaluate the recovery test of the developed method, five replicates of *Fritillaria* samples spiked with 0.7 mg of peimisine were measured with eight times dilution. Concentrations of the analytes were calculated from the established calibration curve.

Application to *Fritillaria* spp. samples

Briefly, 0.2 g of each 20 Beimu sample was soaked in 1 mL of ammonium hydroxide solution for 30 min. It was then extracted using 120 min reflux with the addition of 10 mL of dichloromethane/methanol (8:2v/v) solution. After evaporation, the extract was dissolved in 8 mL of dichloromethane for subsequent colorimetric analysis. The colorimetric method for determination of alkaloids described by Liu & Xie, 1995⁽⁷⁾ was adapted with minor modifications. Peimisine was selected as a standard as it is a typical active alkaloid in *Fritillaria* with the average content of slightly

Table 2. Results of the marker selection assay in the determination of components of FUB using HPLC

	Compound A	Compound B	Pingbeimine A 3-acetate	Peimisine
Mean	0.005	0.0054	0.0099	0.0163
RSD	44.00909	30.62562	60.5193	90.67995

larger than 0.01% (Table 2). Briefly, 2 mL of 0.2 M Potassium biphthalate buffer solution (pH 5.0) and 2 mL of 0.0025 M Bromothymol blue solution were transferred into a 50 mL separating funnel containing 8 mL of standard solution or sample extract in dichloromethane. Then, the mixture was shaken vigorously and stood for 10 min. Subsequently, the dichloromethane layer was collected and filtered into a 10 mL volumetric flask. Filtrates were combined in the same 10 mL volumetric flask, and were added with dichloromethane to make up a total volume of 10 mL. After standing for 30 min, the UV absorbance of the solution was measured at 410 nm (UV 1201 UV-Vis Spectrophotometer; Shimadzu). The absorbance of the solution was diluted by 5 (if necessary) to give an absorbance value from 0.2 to 0.8.

RESULTS

Optimization of the number of partitionings

When comparing the influence of the number of partitions on the partition efficiency (Fig. 1A), it is clear that three partitionings with dichloromethane was enough to extract total alkaloids as the content of total alkaloids reaches a stable level. Thus, three partitionings was adapted in the succeeding experiments.

Optimization of extracting solvent

The extraction yield of total alkaloids with different solvents including dichloromethane: methanol (4:1), dichloromethane, methanol, ethanol and ethyl acetate is displayed in Fig. 1B. The contents of total alkaloids were calculated through the calibration curve of peimisine, and the extraction efficiency of total alkaloids from FUB samples with different solvents was evaluated using the parameter amount (%) which was calculated as total alkaloid weight (equivalent amount of peimisine) percentage of the sample. By comparing extraction efficiency of different solvent systems, it was found that dichloromethane: methanol (4:1) was the most effective system for the extraction of total alkaloids of FUB samples. Therefore, dichloromethane: methanol (4:1) was chosen as the extracting solvent in the optimized method.

Optimization of extraction method

The performance of different extraction methods (30 or 60 min sonication,

60 or 120 min reflux) is shown in Fig. 1C. It is clear that using 120-min reflux as the extracting method gave the highest extraction efficiency of total alkaloids in FUB. Thus, 120 min reflux was selected as the extraction method in the optimized method.

Optimization of soaking time in ammonium hydroxide

In Fig. 1D, no significant difference was observed when samples were treated with ammonium hydroxide for 30 and 60 min, respectively, indicating that 30-min deposition time is enough for the sample solution to reach stable absorbance.

Optimization of the ratio of dye to sample extract

As shown in Fig. 2A(a), when bromothymol blue was at the concentration of 0.001 M, the absorbance of the sample-dye solution increased linearly with the sample amount initially and decreased at the point of 0.375 g of FUB sample. It might be due to the inadequacy of the bromothymol blue dye present in the alkaloid-dye reaction. When the concentration of the dye was increased to 0.005 M, the absorbance did not

increase proportionally to the amount of sample used Fig. 2A(b). This might be attributed to the interference with absorbance of the sample-dye complex caused by the redundancy of the dye. While the concentration of bromothymol blue lowered down to 0.0025 M Fig. 2A(c), the absorbance of the complex rose linearly. Through correlating the absorbance of the solution on the basis of the calibration curve of initial acid-dye colorimetric method (data not shown), the amount of total alkaloids determined by this method exhibited a good linear relationship with the amount of sample ranged from 0.1 to 0.5 g Fig. 2A(d). The result indicated that 0.0025 M was a proper concentration for bromothymol blue used in the optimized method.

Removal of residual water in sample-dye solution

The result of Fig. 2B showed that after the addition of anhydrous sodium sulfate (ASS), the absorbance of blank dichloromethane fluctuated a lot, and a similar phenomenon was observed for the sample extract. The absorbance of the solutions decreased substantially after the addition and the maximum absorbance of the solution also shifted

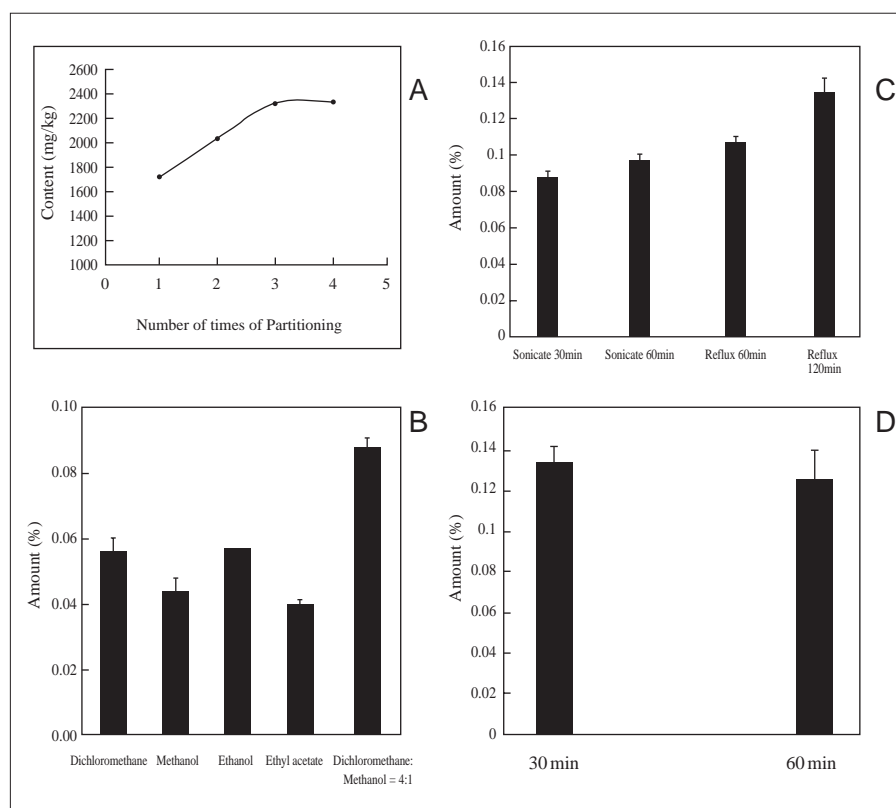


Figure 1. Method development for determination of total alkaloids in *Fritillaria* samples. **A** = Efficiency of extraction using an increasing number of partitioning. **B** = Extraction efficiency of total alkaloids with different solvents. **C** = Extraction efficiency of total alkaloids with different extraction methods. **D** = Extraction efficiency of total alkaloids from FUB samples with 30 or 60 min after the addition of ammonium hydroxide to the sample. (Each set of data or column represents the mean \pm SD of five independent experiments)

to different wavelengths. On the other hand, direct measurement of UV absorption for the blank dichloromethane and sample-dye solution without the addition of ASS gave a more reproducible and stable reading with consistent UV maximum absorption. Therefore, the organic layer could be directly used for UV measurement and there is no need to remove residual water.

Linearity, reproducibility, repeatability and recovery

As shown in Fig. 3, the calibration curve of peimisine exhibited a good linear regression ($R^2 = 0.9992$): $y = 0.0263x + 0.0964$. The results of reproducibility, repeatability, and recovery tests of the optimized method are displayed in Table 3, which shows that the developed colorimetric method for the determination of total alkaloids are reproducible with good repeatability and recovery.

Application to *Fritillaria* spp.

The optimized protocol was applied to *Fritillaria* samples. The total alkaloid content of *Fritillaria ussurienses* bulb is presented in Table 1. The total alkaloid among *Fritillaria* samples is between 0.2246-0.2840 (%w/w).

DISCUSSION

So far, few approaches have been developed for the determination of total alkaloids in plant materials, such as gravimetric method, titrimetric method, and colorimetric method.⁽⁸⁻¹³⁾ When compared to the colorimetric method, gravimetric and titrimetric approaches show weaker sensitivity. In most gravimetric methods, impurities were found to be present in the residue as more than one spot is displayed by TLC.⁽¹³⁾ The titrimetric assays may not be able to reflect the reality as the endpoint could be obscured by the color of the extract. Thus, a colorimetric method adapted in this study is more sensitive and reliable for the determination of total

alkaloids. Based on the initial acid-dye colorimetric method mentioned above, a series of experimental conditions were further optimized and satisfactory results were obtained.

Sonicated solution containing a surfactant as extracting agent was used by Djilani *et al.* (2006) in the extraction of alkaloids from natural products such as *Hyoscyamus muticus*, *Datura stramonium* and *Ruta graveolens*.⁽¹⁴⁾ The extracting reagent used was chloroform and precipitated with Mayer's reagent dissolved in a basic solution.⁽¹⁴⁾ In Fig. 1C, it is clear that using 120-min reflux as the extracting method gave the highest extraction efficiency of total alkaloids as compared to sonication.

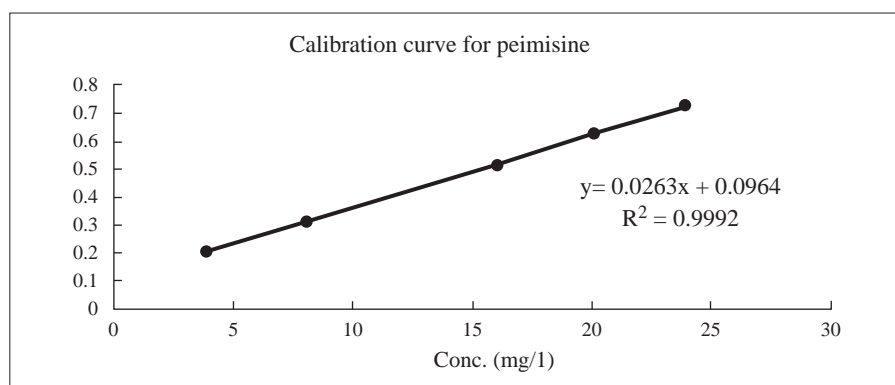


Figure 3. Calibration curve for peimisine determined by acid-dye colorimetric method.

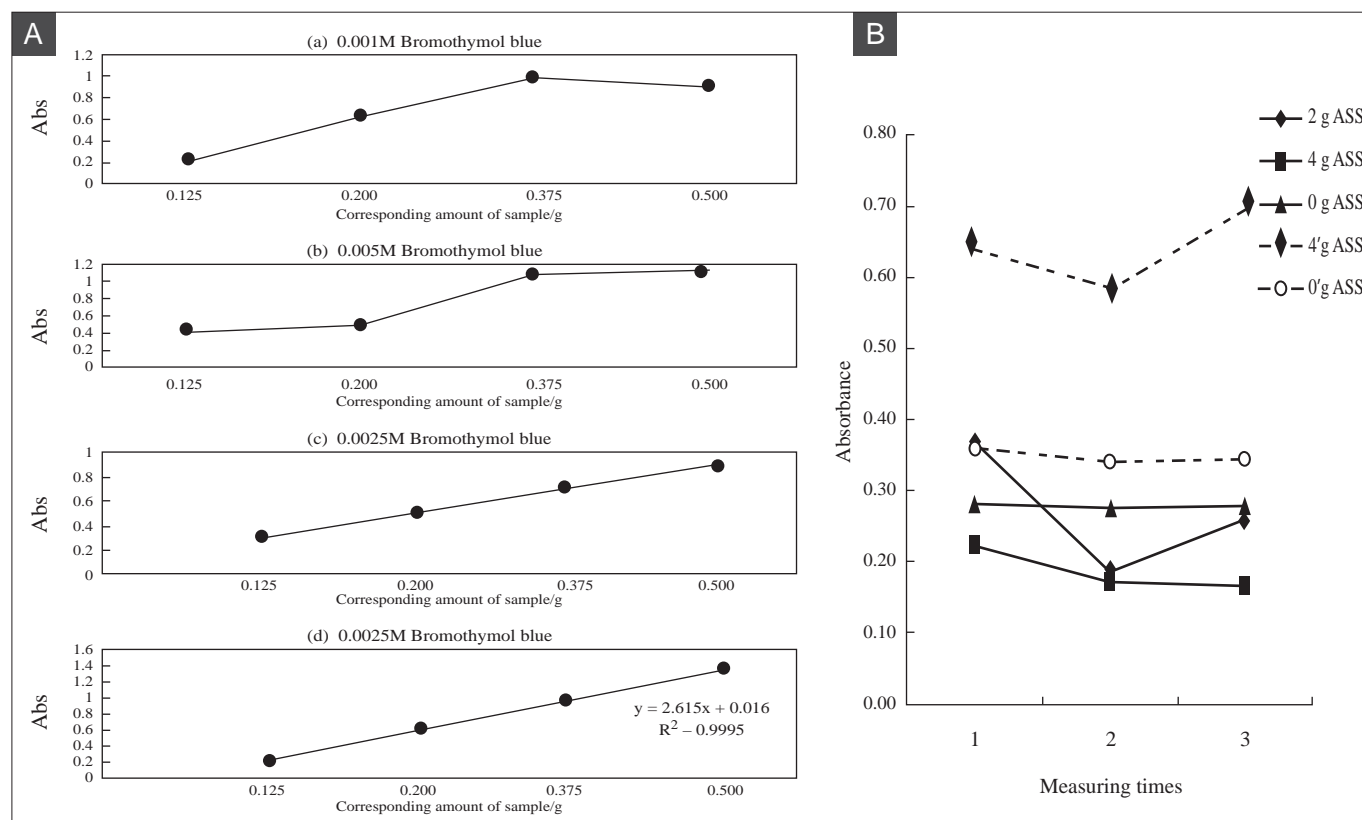


Figure 2. Absorbance of the sample-dye solutions. **A** = Sample prepared with different amounts of acid dye using 0.001 M (a), 0.005 M (b) and 0.0025 M (c) bromothymol blue, and the corresponding amount of total alkaloids (d) in the colorimetric method. **B** = Absorbance of the mixture of blank dichloromethane solution and 0 / 2 / 4 g of anhydrous sodium sulfate (solid lines), and the mixture of sample-dye solution and 0 / 4 g of anhydrous sodium sulfate (dashed lines).

Table 3. Results of reproducibility, repeatability, and recovery tests in the determination of total alkaloid contents in *Fritillaria* samples using acid-dye colorimetric method

Test		Mean (n=5)	SD ^a	RSD ^b
Reproducibility	Absorbance (16 mg/L peimisine)	0.45	0.01	2.62
Repeatability	Amount (mg/Kg) (0.2 g of FUB sample)	2616.54	91.25	3.49
Recovery	Recovery (%) (0.2 g of FUB sample spiked with 0.7 mg of peimisine)	96.33	3.71	3.85

^a Standard deviation; ^b Relative standard deviation

Thus, 120 min reflux was selected as the extraction method instead of sonication. Shams *et al.* (2009) utilized different methods of preparation of total alkaloids using different solvents like benzene, methanol, ethyl acetate, chloroform, and methylene chloride.⁽¹⁾ It was found that vincristine and vinblastine alkaloids in *Catharanthus roseus* L. Don are as low as 0.001 and 0.002% respectively.⁽¹⁾ Among wild morning-glory species (*Ipomoea* spp.), the range of the total ergot alkaloids is between 0.0029% to 0.0059%.⁽²⁾ The scopolamine alkaloids in *Atropa belladonna* were determined as low as 0.00168 (% dry wt) using chloroform-methanol-ammonia extraction.⁽³⁾ Various solvents including diethyl ether, chloroform, and methanol were used to extract alkaloids from *Fritillaria* with the quantity of the analyte varied markedly.⁽¹⁵⁻¹⁸⁾ In the present study, it was shown that dichloromethane:methanol (4:1) is the most efficient extraction solvent coupled with 120 min reflux. It yielded 0.2246-0.2840% total alkaloids. This simply shows that this extraction method has higher efficiency compared to others. Table 2 shows the result of marker selection assay in the determination of alkaloids in FUB. In this case, it can be inferred that HPLC is not the method of choice. Although the mean peimisine was slightly higher than 0.01%, the variation of the content is very large as reflected by large RSD values. It has been depicted by various results that the alkaloid contents of different herbs varied remarkably and that the amount may be so low that it can hardly be assayed individually even with HPLC. Therefore, determination of the total alkaloids is still necessary in this scenario.

CONCLUSION

In this study, a colorimetric method for the determination of total alkaloids has been optimized and has been successfully applied to quantify the total alkaloids in some samples of herbal medicine (i.e., *Fritillaria* bulb). The method gave satisfactory reproducibility. Therefore, this method with minor modifications

can be a suitable quality control tool for medicinal plants especially those containing a variety of small amounts of active alkaloids.

ACKNOWLEDGMENT

This study arose from partial work on the projects (CityU Project No. 9210026 and No. 9211007) of Hong Kong Chinese Materia Medica Standards (HKCMMS) funded by the Department of Health, Hong Kong SAR Government. The funding support is highly appreciated.

Author's background

Dr. CHEUNG Hon-Yeung, who is an associate professor of Pharmaceutics at the City University of Hong Kong, is a manufacturing pharmacist and biotechnologist. He has more than 30 years of working experiences in industries, academic and consultancy jobs. He was an expert witness in court and a member of the Biotechnology Committee for Hong Kong and Shenzhen Government. Dr. Cheung has published more than 200 papers and articles in many prestigious international journals. He is frequently interviewed by the mass media. He can be contacted through his email address: bhonyun@cityu.edu.hk

Prof. Joewel Tarra Baibado is a doctor of Public Health Medical Microbiology student at the University of the Philippines. He obtained his Master of Science in Biology (Microbiology), BS in Biology, and Professional Education from the same university. He is an assistant professor of medical microbiology, parasitology and human biology at Iloilo Doctors' College, College of Sciences and Nursing in Philippines. His research interests include screening of antimicrobial properties of bioactive compounds of Philippine mangroves and indigenous Philippine herbs. Recently, he is a research associate at the City University of Hongkong doing histologic sectioning and imaging microscopy of Traditional Chinese Medicines. Correspondence to: Joewel20022002@yahoo.com; jbaibado2@cityu.edu.hk

CHAN, Gallant GL obtained his BSc and MPhil degrees from CityU and worked as Research Assistant when this work was pursued. He is currently doing his PhD project in the HKUST.

Dr. Zhi-feng Zhang is an associate professor of Pharmacognosy and Pharmaceutical Botany at the Ethnic Pharmaceutical Institute of Southwest University for Nationalities, Chengdu, Sichuan, China. His research interest is on microscopic studies and isolation and purification of bioactive compounds in Traditional Chinese Medicines. He is currently, a post doctoral fellow at the City University of Hongkong. He can be contacted at Zhangzhf99@gmail.com.

References

- Shams KA, Nazif NM, Azim NSA, Shafeek KAA, El-Missiry MM, Ismail SI, Nasr MMSE (2009). Isolation and Characterization of Antineoplastic Alkaloids from *Catharanthus Roseus* L. Don. Cultivated in Egypt. *Afr J Tradit Complement Altern Med*. 2009; 6(2):118-122.
- Wilkinson RE, Hardcastle WS, McCormick CS (1988). Psychotomimetic ergot alkaloid contents of seed from *Calonyction muricatum*, *Jacquemontia tamnifolia*, *Quamoclit lobata*, and *Quamoclit sloteri*. *Bot. Gaz*. 149(1):107-109
- Fateme A, Fateme S (2011). Tropane alkaloids of *Atropa belladonna* L. and *Atropa acuminata* Royle ex Miern Plants. *J Med Plant Res* 5(29):6515-6522
- Yu, H, Jiang, Y, Li, P, Li, SP, & Wang, YT (2005). Study on analytical method for alkaloids in Bulbus *Fritillariae cirrhosae*. *China journal of Chinese Materia Medica* 30:572-575.
- Ding, K, Lin, G, Ho, YP, Cheng, TY, & Li, P (1996). Prederivatization and high-performance liquid chromatographic analysis of alkaloids of bulbs of *Fritillaria*. *Journal of Pharmaceutical Sciences* 85:1174-1179.
- Hong Kong Chinese Materia Medica Standards* (2008) Hong Kong: Department of Health, Hong Kong Government SAR. 4:195-205
- Liu, J, & Xie, Jintao (1995). Determination of total alkaloids and trace elements in *Fritillaria*. *Guangdong Trace Elements Science* 2:63-66.
- Kumar, R, & Hemalatha, S (2010). Pharmacognostical standardization of leaves of *Alangium lamarckii* Thwaites. *Pharmacognosy Journal* 2:19-26.
- Wu, H, Tang, Z, Qiu, L, & Ye, D (1999). The comparison of component contents and pharmacological actions between two kinds of processed products of *Pinellia rhizoma* prepared by ginger juice and alum. *China journal of Chinese Materia Medica* 24:25-28, 63.
- Davidson, AG & Hassan, SM (1984). The simultaneous assay of emetine and cephaeline in Ipecacuanha and its preparations by spectrofluorimetry. *Journal of Pharmaceutical and Biomedical Analysis* 2:441-448.
- Derya, C, Nehir, US, & Gulen, IK (2010). Quality control and anticholinesterase activity determinations on *Stembergia sicula*. *Marmara Pharmaceutical Journal* 14:121-124.
- Saleh, MR, El-Masry, S, & El-Shaer, N (1979). Colorimetric and spectrophotometric determination of total and non-phenolic alkaloids in ipeca and its formulations. *Journal Association of Official Analytical Chemists* 62:1113-1115.
- Shamsa, F, Monsef, H, Rouhollah, R, & Verdian-rizi, M (2008). Spectrophotometric determination of total alkaloids in some Iranian medicinal plants. *Thai Journal of Pharmaceutical Sciences* 32:17-20.
- Djilani A, Legseir B, Soulimani R, Dicko A, Younos C (2006). New Extraction Techniques for Alkaloids. *J. Braz. Chem. Soc*. 17:3
- Li SL, Chan SW, Li P, Lin G, Zhou G, Ren YG, Chiu FCK (1999). Precolumn derivatization and gas chromatographic determination of alkaloids in bulbs of *Fritillaria*. *J Chromatogr A* 859:183-192
- Li SL, Li P, Lin G, Chan SW, Ho YP 2000. Simultaneous determination of seven major isosteroidal alkaloids in bulbs of *Fritillaria* by gas chromatography. *J Chromatogr A* 873:221-228
- Li SL, Lin G, Chan SW, Li P (2001). Determination of the major isosteroidal alkaloids in bulbs of *Fritillaria* by high performance liquid chromatography coupled with evaporative light scattering detector. *J Chromatogr A* 909:207-214
- Xu DM, Huang EX, Wang SQ, Wen XG, Wu XY (1990). Studies on the alkaloids of *Fritillaria pallidiflora*. *Acta Bot Sin* 32:789-793

Turtle Shell Extract as a Functional Food and Its Component-based Comparison among Different Species

LI, Lin-Qiu; CHEUNG, Hon-Yeung*

Research Group for Bioactive Products, Department of Biology & Chemistry, City University of Hong Kong, 83 Tat Chee Avenue, Kowloon, Hong Kong SAR, China.

(*Correspondence author) Tel.: +852 3442 7746; Fax: +852 3442 0522

Email address: bhhonyun@cityu.edu.hk

Scientific Names: *Chinemys reevesii* (Gray); *Cuora trifasciata*; *Cuora aurocapitata*; *Cuora galbinifrons*, *Trachemys scripta*; *Hardella thurjii*

Family: Emydidae (includes *Chinemys* spp., *Cuora* spp., *Trachemys* spp.);

Common Names: Chinese Pond Turtles (*Chinemys reevesii* (Gray)); Asian Box Turtles (*Cuora trifasciata*; *C. aurocapitata*; *C. galbinifrons*); Crowned River Turtle (*Hardella thurjii*); Slider Turtles (*Trachemys scripta*)

Chinese Names: 烏龜; 閉殼龜; 金頭閉殼龜; 黃額閉殼龜 巴西龜; 冠背龜

Part Usually Used: Plastron

Common Uses: sthenic yang suppression, bone invigoration, menstruation regulation, metrorrhagia relief, anti-aging

Plastron has been prescribed to nourish *yin* and suppress the sthenic yang. It benefits kidney, invigorates the bone, relieves metrorrhagia and can regulate menstruation. In recent decades, many studies have been done to ensure that diverse species

of turtle could be used as material medica. In this review article, sources, identification and chemical composition of some turtle shells, as well as their biological effects and medical uses are reviewed. Its addition to a few popular functional foods by the Chinese herbalist are also described.

Keywords: turtle shell, plastron, functional food, guling gao, gui lu erxian jiao, cell proliferation



Contraindications

Turtle shell could excite the uterus. Therefore, it should not be used by pregnant women. In addition, for those people with cold stomach and *yin* deficiency it may not be good because it is extremely *yin*.^(1,2)

Undesirable Effects

Nil, but parasites may be present.

Interaction with Conventional Drugs

At the time of publication, no interaction with conventional drugs has been reported.

ABSTRACT

Turtle shell is a traditional Chinese medicine, which has been used for thousands of years by the Chinese.

INTRODUCTION

Animals of the Order Testudines are classed as reptiles, whose common names may be different from country to country.⁽³⁾ According to **Animals: A visual encyclopedia, Hand Book of Turtles and Turtles of The World**, testudinates that live on dry land and have round, stumpy legs are called tortoise, while turtles spend most of their time in water and have flipper-like limbs. Freshwater turtles are often called terrapins.⁽⁴⁻⁶⁾ For the sake of easy description, "turtle shell" is used in this review as a general name that means all types of shells of testudine animals.

The turtle shell is a highly complicated shield for the ventral and dorsal parts of the turtle, completely enclosing all the vital organs of the turtle and in some cases even the head. It is constructed of modified bony elements such as the ribs, parts of the pelvis and other bones found in most reptiles. The bone of the shell consists of both skeletal and dermal bone, showing that the complete enclosure of the shell probably evolved by including dermal armor into the rib cage.



Figure 1. Pictures of Turtles. A1 = *Chinemys reevesii* (Gray) (烏龜), A2 = plastron; B1-3 = *Cuora trifasciata* (三線閉殼龜, 金錢龜), B4 = plastron; C1 = *Cuora aurocapitata* (金頭閉殼龜), C2 = plastron view; D = *Trachemys scripta* (巴西龜); E = *Hardella thurjii* (冠背龜, 草龜)

It is widely accepted that turtle shells have broad functional effects. It has been used by Chinese people as a medicine for thousands of years, and the shell of *Chinemys reevesii* (Gray) (Fig. 1-A1 & -A2) was first recorded as Guijia in ***Shen Nong Ben Cao Jing***.⁽⁷⁾ Turtle shell is mostly utilized in *Rehmannia*-based formulae that nourishes *yin* and suppresses the sthenic *yang*. Meanwhile, herbalists believe that it can benefit kidneys, invigorate bone, and regulate menstruation and relieve metrorrhagia.⁽⁷⁻⁹⁾ Until now most shells used as medicine and functional food belong to *Chinemys reevesii* (Gray); which is recorded in the Chinese Pharmacopoeia (2010) as the only recommended source of turtle shell. Thus, demand for this species is growing, resulting in a dramatic drop in the number of wild *Chinemys reevesii* (Gray). In other cases, such as Guiling Gao (sometimes referred to as Turtle Jelly) and Gui Lu Erxian Jiao, turtle shell is an important component.

What is Guiling Gao?

Guiling Gao (or “Kwei Ling Ko” in Cantonese) is a glue-like food produced by long-term boiling of turtle shells along with some other herbal ingredients. It originated during the Ham Fung Era of the Ching Dynasty in China between 16-19th Century, AD. It is an extravagant food originally prepared for the nobles and the Emperor. No one knows who invented the prescription of Guiling Gao. What people know is that the recipe was passed to farmers by a doctor of the emperor after his retirement and it subsequently became a popular herbal functional food amongst Chinese people. It is claimed to have wide application to different diseases. It has a diuretic effect that may dissipate wetness, and remove toxic wastes from the body. It nourishes vital essences and cures spots or blemishes on the skin.

Guiling Gao contains some twenty to thirty herbal drugs without a definite formula except that plastron and Poria are the main components. Other common ingredients include *Lobelia chinensis*, *Akebia trifoliata*, *Dictamnus dasycarpus* and *Hedyotis diffusase* etc. According to the 1998 edition of the Chinese-English manual of commonly used traditional Chinese Medicines, plastron is described to (1) nourish *yin* and suppress the sthenic *yang*; (2) benefit kidney and invigorate bone and (3) regulate menstruation and relieve

metrorrhagia. There is a legend that plastron of *Cuora trifasciata*, as shown in Fig. 1, plates B1-4, has a higher nutritive value and is believed effective to heal certain tumours. If it is added to Guiling Gao, the best medical treatment can be achieved. However, *Cuora trifasciata* is classified as a “critically endangered” species, and trading this species is totally prohibited.

What is Gui Lu Erxian Jiao?

Gui Lu Erxian Jiao (龜鹿二仙膠) is a semifluid extract of turtle plastron and deer-antler. It is a tonic decoction usually mixed with some other herbal ingredients such as ginseng and Lycium berries (Goji). Gui Lu Erxian Jiao tonifies qi and blood, supplements kidney *yin* and *yang*, and replenishes *jing* (essence). The imbalance between the *yin* and *yang* can lead to fatigue, lack of energy, dizziness, sweating, easy to catch a flu and feeling cold. The Gui Lu Erxian Jiao has been claimed capable to improve overall health, ensuring vitality at all times. It can enhance a significant improvement in gynecological condition including menstrual pain, breast pain, excessive secretion, feeble conditions, etc. Clinical applications include weight loss, seminal emissions, impotence, dizziness, and soreness and weakness of the lower back and knees. It is regarded as a warm tonic.

Due to burgeoning demand in the market, more than half of freshwater turtle and tortoise species from Southeast and East Asia have been severely threatened by over exploitation for food and traditional medicines. Therefore, in recent decades, many studies have been carried out aiming to find substitutes for these turtles in danger of extinction with the same biological functions. Literature surveys reveal that the results of most published works were conducted in China. In this review, the component based comparison of different turtle shells and the progress of recent study will be described.

SPECIES AND SOURCES OF TURTLE SHELL

The turtle shells used in Chinese medicine are obtained from aquatic or land-based tortoise. Unlike sea turtles or some desert species, they are not included in the endangered species list.⁽¹⁰⁾ However, due to the modernization of

China along with the environmental disruption, even these land tortoises will become endangered in the future. Increasing efforts, therefore, are being made to raise the tortoise by farming in China.

As mentioned above, the official listed shell recorded in the ***Chinese Pharmacopoeia (2010)*** comes from *Chinemys reevesii* (Gray). This is a land tortoise, found in rivers, lakes, and marshes, which is known in the west as the Reeve's tortoise. Two substitute species obtained from Anhui Province, *Cuora amboinensis* and *Cuora flavomarginata*, have been raised and sold on the market, but they are not officially-recognized as substitutes.⁽¹¹⁻¹²⁾ The latter species is thought to be the one denoted as *shuigui* in Li Shizhen's ***Ben Cao Gang Mu***.⁽¹³⁾ Other substitutes include *Mauremys mutica* and *Testudo elongata*.⁽¹⁴⁾ Another tortoise, *Eretmochelys imbricata*, is used as a separately listed item in the ***Chinese Materia Medica***, known as daimao.⁽¹⁰⁾

Although the Reeve's tortoises and some of the substitute species are raised in China for their shells,⁽¹⁵⁾ there is still a huge natural supply and the majority of the shells are obtained from wild resources. They can be collected all year round, but are preferably obtained in autumn and winter. Tortoise collection, like that of fish in the same region, is mainly accomplished by use of nets.⁽¹⁶⁾

MEDICAL USE OF THE DORSAL AND THE VENTRAL SHELL

Turtle shell has two sections: the dorsal shell is known as the carapace, and the ventral shield is called the plastron.⁽¹⁷⁻¹⁸⁾ From the very first time they were introduced for use as medicinal medica in ***Shen Nong Ben Cao Jing*** in the Han Dynasty,⁽⁷⁾ both carapace and plastron were recommended. However, after Zhu Dan Xi (a medical scientist of the Yuan dynasty) proposed a theory of nourishing *yin*,⁽¹⁹⁾ folk began to use plastron only. Hence, for a very long time people believed that only plastron was suitable for medicinal uses and for functional purposes, resulting in a huge waste of carapace. But some recent research indicated that the carapace and plastron gave similar results in terms of nourishing *yin*.^(20,21) It was only after 1990 that the dorsal and ventral shells were employed as a whole again when the ***Chinese Pharmacopoeia (1990)*** was published.⁽²²⁻²³⁾

AUTHENTICATION OF TURTLE SHELLS

In recent years, many adulterants have appeared in the turtle shell trading market. Hence, various techniques are required to identify the real ones from their adulterants. Mostly, people employ the appearance-feature based methods for identification: the color, the shape, odour, hardness,^(24,25) and formula methods such as the ratio diagrammatic method,⁽²⁶⁾ the similarity factor of standard mode,⁽²⁷⁾ and the clustering method etc.⁽²⁸⁾

In order to identify the shells more precisely, on top of morphological examination (Fig. 1), biological and chemical methods have also been applied. A PCR technique was introduced to detect DNA of *Colla Carapax et plastrum testudinis* (shell of *Chinemys reevesii* <Gray>) glue from six commercial tortoise shell glue products.⁽²⁹⁾ UV spectrum was also used for the identification while Guo *et al.* employed UV-cluster analysis methods for the identification of six types of turtle shell, namely shells of *Chinemys reevesii* (Gray), *Cuora spp.*, *Geoemyda grandis*, *Trxudo elongata* (Blyth), *Clemmy smutica* (Can tor) and *Platysternon megacephalum*.⁽³⁰⁾

CHEMICAL COMPOSITION OF TURTLE SHELL

It is widely known that turtle shell is rich in various kinds of amino acids.^(31,32) Fan *et al* compared 9 types of turtle shells and found 18 essential amino acids with total content of 30.7%-39.6%.⁽³³⁾ Cheung & Cheung were able to identify and analyse sixteen amino acids in the plastrons and found that the content of glycine and glutamic acid was extra-ordinarily high followed by proline, asparagine and arginine.⁽³⁴⁾ This was subsequently confirmed by Gu after analysing the shells of *Chinemys reevesii* (Gray), *Cuora amboinensis* (Guenther), *Tesrudo elongate* (Blyth), *Ocadia sinensis* (Gray), and *Trachemys scripta elegans* and reporting that all these shells contained amino acids ranging from 25.7% - 31.24% with a higher content of glycine, proline, glutamic acid, alanine, arginine and aspartic acid [Table 1].⁽³⁵⁾

Both macroelements and trace elements were found in turtle shells, such as P, K, Ca, Mg, Fe, Cu, Mn, Mo,

Co, Ni, V, Si and Se etc.[Table 2],⁽³³⁻³⁶⁾ in which Se is an anticancer element.⁽³⁷⁻³⁸⁾ Although some toxic heavy metals were found in some turtle shells, the amount was very low and they were within acceptable ranges.⁽³⁴⁾

In addition, some organics also were found in turtle shells. Cholesterol, eicosenoic acid cholesterol ester and

cholester-4-ene-3-one were claimed to exist in shells of *Mauremys mutica*.⁽³⁹⁾ Fatty acid compounds of shells of *Chinemys reevesii* (Gray) and *Mauremys smutica* were determined by using GC-MS, and 32 kinds (with content of 49% of unsaturated fatty acid) of these acids were found in the previous one while 28 (with content of 66% of unsaturated fatty acid) were found in the latter species.⁽⁴⁰⁾

Table 1. Contents of amino acids in different species of turtle shell (%)⁽³⁵⁾

Amino Acids	Different Species of Turtle Shell				
	<i>Chinemys reevesii</i>	<i>Testudo elongata</i>	<i>Testudo elongata</i>	<i>Ocadia sinensis</i>	<i>Ocadia sinensis</i>
Asp	1.91	1.87	1.69	1.92	1.95
Thr	0.80	0.68	0.55	0.81	0.82
Ser	1.34	1.30	1.03	1.41	1.38
Glu	3.31	3.30	3.02	3.35	3.40
Gly	6.41	6.42	6.10	6.73	6.60
Ala	2.52	2.53	2.40	2.41	2.52
Cys	0.38	0.33	0.21	0.33	0.33
Val	0.99	0.99	0.78	1.24	1.06
Met	0.22	0.18	0.17	0.22	0.22
Ile	0.63	0.61	0.50	0.68	0.64
Leu	1.31	1.25	1.05	1.68	1.50
Tyr	1.09	1.04	0.77	1.84	1.33
Phe	0.5	0.77	0.72	0.96	0.91
Lys	1.03	1.05	0.88	0.87	0.96
Amide	0.35	0.35	0.34	0.37	0.36
His	0.50	0.48	0.39	0.66	0.56
Arg	2.41	2.41	2.06	2.40	2.47
Pro	3.59	3.64	3.38	3.73	3.68
trp	/	/	/	/	/
Total	29.29	28.58	25.70	31.24	30.33

Table 2. Parts per million (ppm) contents of trace elements in three species of turtle shell⁽³⁶⁾

Elements	Species		
	<i>Chinemys reevesii</i> (1)	<i>Chinemys reevesii</i> (2)	<i>Cuora amboirenaia</i>
Si	6440	5133	4946
Ca	133300	123200	149000
Fe	1056	770	2593
Al	1660	1419	1220
Mg	1056	1008	116
K	340	340	174
Na	6464	6167	4057
Ti	36110	13910	49710
Mn	5.60	1210	28101
Cr	61.80	35.00	70.40
Sr	1773	4928	6090
Rb	3.80	3.60	9.10
Ni	14.00	14.50	14.00
Co	20.50	23.20	23.50
Zn	473	251	342
Pb	95.60	58.20	44.50
Cu	834	150	144
Zr	0.50	0.36	0.16
Y	19.40	2.10	0.17
Cl	364010	676000	319000
Cs	5.80	6.20	5.11
V	57.80	24.20	79.80
Ce	61.10	36.90	69.80
Ba	56110	19010	86100
As	77.40	43.20	37.60
Ga	9.00	6.10	6.73
Hf	14.50	162.00	169.00
La	32.30	4.60	6.97
Mo	5.30	5.70	4.83
Nb	7.90	2.70	0.36
P	424000	425000	449000
S	188000	282000	221000
Sc	9.60	11.10	9.67
Th	8.90	6.60	4.10
Se	0.150	0.030	0.066
B	0.36	0.35	0.21
Hg	0.012	0.015	0.160
Cd	0.016	0.043	0.280
Be	0.45	----	----

Lei *et al.* applied TLC scanning for studying of cholesta-4, 6-dine-3-ol in shell of *Chinemys reevesii* (Gray), and different species were found to differ in content.⁽⁴¹⁾ Proteome and peptide in *Colla Carapax et plastrum testudinis* were studied by using SELDI-TOF-MS (surface enhanced laser desorption/ionization time-of-flight mass spectrometry). There was one peak for each interval of 1500-3000, 8000-8600, 10000-13000, and three peaks for interval 4800-5400 with different relative Mol Wt of 410.8 and 151.7.⁽⁴²⁾ Our group studied the protein extracts of plastron by using SDS gel. As shown in Fig.2, all sorts of plastron contain various proteins and peptides with their size continuously ranging from small to large.

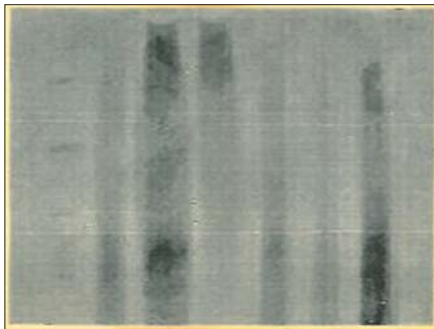


Figure 2. SDS electrophoretogram of protein extracts of plastron from different species.

BIOLOGICAL FUNCTION AND PHARMACOLOGICAL EFFECTS

Recent research showed that turtle shell has the effect of tonifying the blood, enhancing immunity, reducing the speed of aging, promoting development of the body, protecting the nerves, being an anti-cancer agent and regulating and controlling energy metabolism rate, and so on.

Chen *et al.* identified proliferation of mesenchymal stem cells (MSCs) after the culture was treated with plastrum testudinis extracts (PTE). They pointed out that the mechanism of PTE action may be associated with the up-regulation of MBP4.⁽⁴³⁾ Besides, this group also conducted some work on injured neural stem cell of focal cerebral ischemia and injured spinal cord. According to their study, the turtle shell decoction could ease the neurologic deficit and promote the expression of protein (Nestin).^(44,45) As one of the major components of turtle jelly (Gui Ling Gao, 龜苓膏), turtle shell was found to be good for cell growth. We compared the effect of different ingredients of turtle jelly on NBT-II cells and found that significantly beautiful

growth in culture whenever plastron was supplemented [Fig. 3] The control culture did not show such a response.

Turtle extract can improve the condition of the immune system. Recovery of the cell and hormonal immunity has been reported after *yin*

deficient rats were given a turtle shell decoction. Besides, cell numbers of the peritoneal macrophages increased, the atrophic thymus gland recovered, the conversion rates of lymphocytes increased and the aging of normal cells was slowed down.⁽⁴⁶⁾

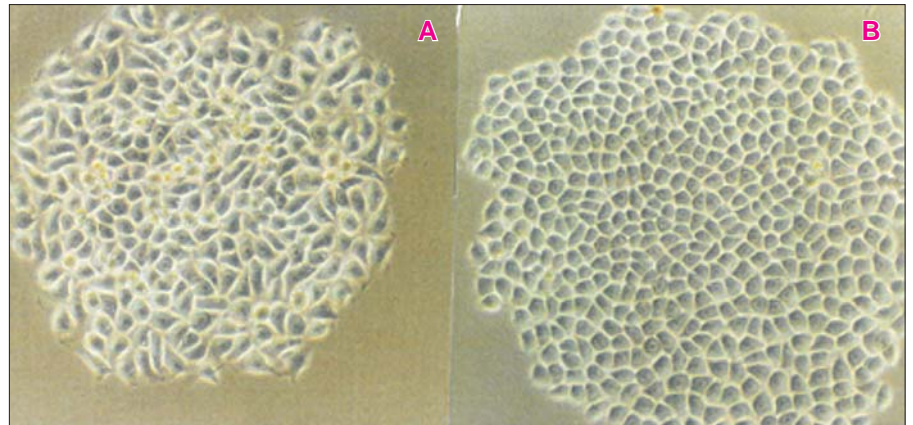


Figure 3. Effect of plastron extract on the growth of NBT-II cells. Plate A: control culture; Plate B: in the presence of plastron extract.

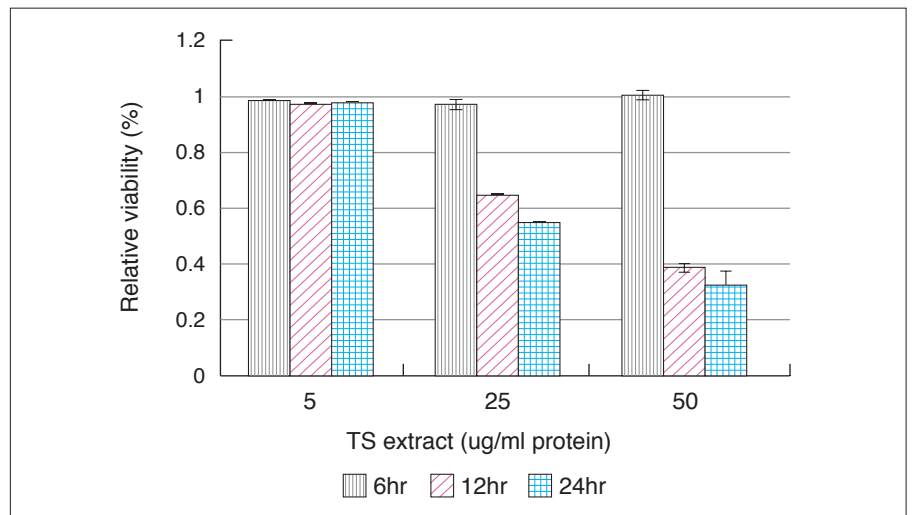


Figure 4. Effect of TS plastron extracts on the viability of HL-60 cells with various protein concentrations; i.e. 5, 25 and 50 μ g/ml of protein for 6, 12 or 24 hr.

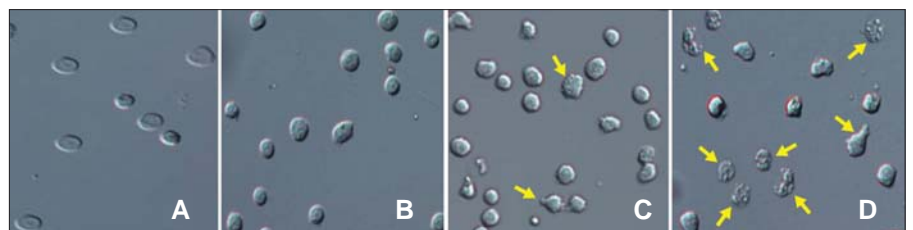


Figure 5. Morphology alternation of HL-60 after treatment with TS extract with (A) control, (B) 5, (C) 25 and (D) 50 μ g/ml of protein. Yellow arrows indicate collapse of cell.

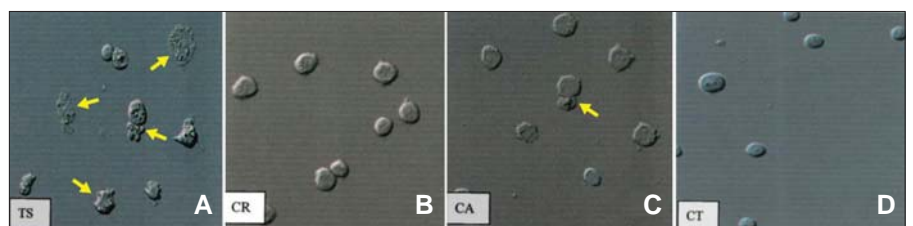


Figure 6. Morphology of HL-60 after 24 h treatment with 50 μ g/ml protein of turtle shells extracts. (A) *Trachemys scripta*, (B) *Chinemys reevesi*, (C) *Cuora auroreolata*, and (D) *Cuora trifasciata*. Yellow arrows indicate collapse of cells.

The anticancer effects of turtle shells had also been explored by Bayazit *et al.* Female rabbits (*Lepus capensis*) were injected with one mL dimethylbenzanthracene/kg/day between 36 and 42 days in order to obtain tumor cells. Then the tumor was removed and tumor cells were incubated in RPMI-1640 medium. Results of the survival time and cell count indicated that the ethanolic extract of turtle shell possessed significant anticancer activities.⁽⁴⁷⁾ We investigated the effect of aqueous extracts from plastron of four turtle species (*Chinemys Reevesii* <CR>, *Cuora aurocapitata* <CA>, *Cuora trifasciata* <CT>, *Trachemys scripta* <TS>) on the viability of HL-60 and human HepG2 cell line. In both cases, cells treated with the plastron extract of *Trachemys scripta* were less viable in a concentration-dependent manner [Fig. 4 & 5]. Our experimental results revealed that all the studied plastron extracts except *Cuora trifasciata* had significant cytotoxic effect towards HL-60 cells [Fig. 6], while plastron extract of *Trachemys scripta* exerted the greatest toxic effects on HepG2 cells [data not shown]. Besides, more cell lyses were found in HL-60 than that in HepG2 culture.

Some fine differences in pharmacological effects were found among different species of turtle shells. Gu *et al.* compared the biological responses of five types of turtle shells; namely *Testudo elongate* (Blyth), *Ocadia sinensis* (Gray), *Cuora amboinensis* (Guenther), *Trachemys scripta elegans*, *Chinemys reevesii* (Gray). They found that all these shells except *Ocadia sinensis* improved the weight loss of rats that were *yin* deficient. The anoxia tolerance of rats was also enhanced by turtle extract except that from *Testudo elongate* (Blyth).⁽⁴⁸⁾

CONCLUSION

The turtle shell is an interesting area to be studied. It is not merely because of its usefulness in taxonomic identification and evolutionary relationship, but also of its usefulness in understanding its importance as a source of functional food and medicine.

Author's background

Li, Lin-Qiu is a full-time PhD student at the City University of Hong Kong. She received her Master of Science in Analytical Chemistry and Bachelor of Science in Chemistry at Guangxi University. Her research interests are mainly focused on biochemical characterization and evidence-based study of traditional herbs. **Dr. CHEUNG Hon-Yeung**, who is an Associate Professor of Pharmaceutical Microbiology & Biotechnology at the City University of Hong Kong, is a manufacturing pharmacist and biotechnologist. He has more than 35 years of work experience in industry, academic and consultancy jobs. He has been an expert witness in court and a member of the Biotechnology Committee for Hong Kong and Shenzhen Government. Dr. Cheung has published more than 200 papers and articles in many prestigious international journals. His email address: bhonyun@cityu.edu.hk

References

- 王福席, 蘇玲, 劉荔, 徐磊. 臨證本草. 中國古籍出版社, 2006, p674-677.
- 代賈所學 (明代). 藥品化義, 學苑出版社, 2011.
- 黃紅 (1999). 漢、拉、英、中國龜鱉目動物名稱. 鐵道師範學院學報, 16 (1):55-78.
- Animals: a visual encyclopedia*. New York: Dorling Kindersley Publishing, 2008, Dorling Kindersley Limited.
- Archie Carr. *Handbook of Turtles: The Turtles of the United States, Canada, and Baja California (Comstock Classic Handbooks)*. Cornell University Press: New York, 1995.
- Carl HE, Roger WB. *Turtles of the World*. Smithsonian Institution Scholarly Press: Washington, 1989.
- 顧觀光 (清, 原著), 楊鵬舉 (校注). 神農本草經, 學苑出版社, 2007, p124.
- 王福席. 臨證本草: 劉啟庭醫學經驗續編. 中醫古籍出版社, 2006, p674.
- 中國藥典. 中國醫藥科技出版社, 2010, p168.
- Dharmananda S. *Tortoise shell: with brief reports on Treating Aplastic Anemia and Parkinson's Disease*. Accessed on 30 March, 2012. Available from: <http://www.itmonline.org/arts/tortois2.htm> [accessed on March 30, 2012]
- Zhang NR (1985). Identification and criticism of two kinds of tortoise close-shell. *Bulletin of Chinese Medicinal Herbs* (10):253.
- Chen BH, Li BH (1979). Ecological material from *Cuora flavomarginata*. *Journal of Zoology* 1:22-24.
- Li SZ. *Ben Cao Gang Mu*. People's Medical Publishing House: Beijing, 1982.
- Zhang E. *English-Chinese Rare Chinese Materia Medica*, Publishing House of Shanghai College of Traditional Chinese Medicine: Shanghai, 1990.
- Li J *et al.* (1986). Report on the survey of the cultivation of tortoise. *Bulletin of Chinese Medicinal Herbs*, 11: 583.
- 石青, 方前波 (2001). 各種龜板的鑒別. *Primary Journal of Chinese Materia Medica*, 15(5):34.
- Zangerl R. The turtle shell. In: Gans, C., Bellairs, D.d'A. and Parsons, T.A. (Eds). *Biology of the Reptilia*, Vol 1, Morphology A Academic Press: London. 1969, p311-340.
- Alderton D. *Turtles & Tortoises of the World*. Facts on File, New York, 1988.
- 朱震亨 (元). 本草衍義補遺, 丹溪心法附錄本. 墨潤堂印, 卷首: 11, 1920.
- Yang MX, Yang Y (1988). Pathological impact of carapace and plastron on the thyroid, thymus, adrenals, and spleen of thyroid-induced hyperthyroidism *yin*-deficiency model of rats. *Bulletin of Chinese Materia Medica*, 13(3):41-43.

- Miao YL, Yang MX, Liu E, Yang Y (1988). Impact of carapace and plastron on the weight, amount of water intake, amount of urine, and blood viscosity of thyroid-induced hyperthyroidism *yin*-deficiency model of rats. *Bulletin of Chinese Materia Medica*, 13(3):42-44.
- Chen QJ, Yu DF, Feng DK (2009). A research overview on turtle shell. *Strait Pharmaceutical Journal*, 21(6):105-1106.
- 鄭金生 (1982). “龜甲、敗龜、龜板”考辨—論龜甲當用上、下甲. *中醫雜誌*, 3:56-58.
- 陸敏儀, 鐘麗新 (1986). 四種龜板的鑒別和化學成份含量測定的比較. *中藥通報*, 11(11):15-19.
- 李志林, 朱志峰 (2010). 龜板及其混偽品性狀鑒別. *傳統醫藥*, 19(14):74-75.
- 李水福, 胡清宇, 吳慧清 (1995). 比值圖示法鑒別龜板及其混偽品. *中藥材*, 18(9):449-451.
- 李水福, 胡清宇, 呂麗清, 王或麗 *et al.* (1996). 標準模式相似係數法鑒別龜板的研究. *中草藥*, 27(9):562-564.
- 胡清宇 (2003). 聚類分析法在龜板鑒別中的應用. *藥學實踐雜誌*, 21(6):364-367.
- Pin LV, Zhou XS, You JH, Qin YF *et al.* (2010). Tortoise DNA Detection from Highly Processed Tortoise Shell Using SINE Element. *Journal of Food and Drug Analysis*, 18(2):113-119.
- 郭文信, 李水福, 胡清宇, 王或麗 (1996). 龜板及其混偽品的紫外光譜聚類分析. *時珍國藥研究*, 7(4):224-225.
- 方達任, 張克蘭, 劉焱文 (1989). 龜板、鱉甲的化學成分研究. *中國藥學雜誌*, 24(1): 26-28.
- 苗明三, 王智民 (2002). *對藥的化學, 藥理與臨床*. 軍事科技出版社, 2002, p937.
- 範亞剛, 王建雲 (1997). 13種龜甲的無機元素和氨基酸含量比較. *廣東微量元素科學*, 4(10):48-52.
- 張漢揚, 張翠珊 (1998). 龜板抽取物的營養價值及對癌細胞增生影響. *Hong kong Pharmaceutical Journal*. 7(4):104-107.
- 顧迎寒 (2007). 龜甲的生藥學研究. 成都醫藥大學碩士學位論文.
- 崔健, 薑大成, 孫麗霞, 宿麗梅 *et al.* (1997). 三種龜板中無機元素的測定. *吉林中醫藥* 3:37.
- Thiry C, Ruttens A, Temmerman LD, Schneider YJ *et al.* (2012). Current knowledge in species-related bioavailability of selenium in food. *Food Chemistry*, 130:767-784. .
- Combes GF, Gray WP (1998). Chemopreventive agents: Selenium. *Pharmacology and Therapeutics*. 79:179-192.
- 孫蘇亞, 李發美 (2000). 黃喉擬水龜板中三種出體化合物的分離和鑒定. *中國中藥誌*, 25(3):165-166.
- 孫蘇亞, 李發美 (1999). 龜板中脂肪酸的GC-MS分析. *藥物分析雜誌*, 19(6):406-409.
- 雷鈞濤, 蔡柏玲 (2005). 薄層掃描法測定龜甲中膽甾醇, 4,6-二烯-3-醇的含量. *醫藥導報*, 24(11):1051.
- 李春梅, 王若光, 王陸穎, 劉小麗 *et al.* (2007). 基於鐳射解析離子化飛行時間質譜技術的中藥龜甲膠蛋白質組分析. *湖南中醫藥大學學報*, 27(6):21-29.
- Chen DF, Zeng HP, Du SH, Li H *et al.* (2007). Extracts from plastrum testudinis promote proliferation of rat bone-marrow-derived mesenchymal stem cells. *Cell Proliferation*, 40:196-212.
- 陳東風, 杜少輝, 李伊為 (2001). 龜板對局灶性腦缺血後神經幹細胞的作用. *廣州中醫藥大學學報*, 18(4):328-332.
- 李伊為, 崔曉軍, 陳東風 (2003). 龜板對脊髓損傷大鼠神經幹細胞的作用. *解剖學雜誌*, 19(3): 321-324.
- 李長泉 (2003). 龜甲藥理作用及臨床應用的現代研究. *長春中醫學院學報*, 19(4):55.
- Bayazit V, Khan KM (2005). Anticarcinogenic activities of biological and chemical agents on lung carcinoma, breast adenocarcinoma and leukemia in rabbits. *Journal of the Chemical Society of Pakistan*, 27(4):413-422.
- 顧迎寒, 盧先明, 蔣桂華 (2007). 不同品種龜甲滋陰作用對比研究. *時珍國醫藥*, 18(16):1417.

Hong Kong Pharmacy Conference 2012

Reporter: Gloria Hung, Programme Coordinator, Hong Kong Pharmacy Conference 2012

“Pharmacist: your Healthcare Partner 藥劑師 — 健康之侶” was the theme of the 24th Hong Kong Pharmacy Conference 2012 which took place at the Hong Kong Convention and Exhibition Centre on 4th to 5th February, 2012. It was organized by The Pharmaceutical Society of Hong Kong, The Practising Pharmacists Association of Hong Kong, The Society of Hospital Pharmacists of Hong Kong, School of Pharmacy of the Chinese University, Department of Health and Hospital Authority. The Organizing Committee of the Conference was led by Mr. SO Yiu Wah, the chairperson and Ms. Ritchie KWOK, the vice-chairperson. We were glad to have Mr. Richard Yuen Ming-fai, Permanent Secretary for Food and Health (Health) to be our officiating guest.

The Conference attracted over 400 participants from Hospital, Community, Industry, Government and Education sectors. We saw a technology breakthrough this year. An on-line registration system was set up. It was highly popular with almost half of the registrants registered on-line.

The Day 1 theme speeches covered a wide scope of topics, including needs, skills and value based pharmacist education, environmental toxins, enhancement of compliance to chronic

medications and medication safety in hospital pharmacies in China. The Day 2 program encompassed information technology, elderly care, community and hospital practices. Ms. Linda Woo and Mr. Lot Chan, Chief Pharmacist and Senior Pharmacist respectively, from the Drug Office were invited to speak in the plenary session on the regulation of pharmaceutical products post-75-recommendations by the review committee in 2009. Representatives from the three pharmacist societies/ association, Hong Kong Pharmaceutical

Manufacturers Association, Pharmaceutical Distributors Association of Hong Kong and Hong Kong Association of Pharmaceutical Industry contributed in a Q&A session facilitated by Mr. Michael Ling.

The Conference dinner on 4th February was definitely a highlight. Talents from our young pharmacists and students were uncovered in the drama performance and games, and the site organization of the event. All the participants and guests thoroughly enjoyed the occasion.”



Plate-2: Opening ceremony of the HK Pharmacy Conference 2012. From left to right: Mr. William CHUI, Vice-President, Society of Hospital Pharmacists of Hong Kong; Ms. Mary CHENG, President, Pharmaceutical Society of Hong Kong; Ms. Iris CHANG, President, Practising Pharmacists Association of Hong Kong; Mr. Richard YUEN, Permanent Secretary for Food and Health (Health); Mr. Y W SO, Chairperson of the Hong Kong Pharmacy Conference 2012; Ms. Anna LEE, Chief Pharmacist, Chief Pharmacist's Office, Hospital Authority, Hong Kong; Dr. Heston KWONG, Drug Office, Department of Health, Hong Kong; Prof. Joan ZUO, Associate Director (Research and Graduate Affairs), School of Pharmacy, The Chinese University of Hong Kong.



Plate-1: The organizing committee with the student helpers at the conference dinner

Road Traffic (Amendment) Ordinance 2011: Briefing Seminars for Transport Trades in March 2012

Reporters: CHAN Henry; CHAN Shirley; CHEUNG Peggy; LAM Daisy

Representatives, namely from the Pharmaceutical Society of Hong Kong (PSHK), the Practising Pharmacists Association of Hong Kong (PPAHK) and the Society of Hospital Pharmacists of Hong Kong (SHPHK) joined as medicines advisers of the captioned event on 1st March 2012 and 10th March 2012, organized by the Transport Department.

The purposes of these seminars are to introduce the enforcement procedures against drug driving under the Road Traffic (Amendment) Ordinance 2011 and to brief effects of common medicinal drugs on driving ability.

The chairman of SHPHK, Mr. SO Yiu Wah (Plate-3) was responsible to conduct a speech on "Common medicinal drugs that may have side effects on driving ability". Other representatives

were responsible to answer inquiries related to drug treatment and side effects encountered by drivers.



Plate-3: Mr Yiu-Wah So is giving the speech on drugs may affect driving ability

Plate-4 shows leaflets containing information about legal advice and side effects of selected medicines that may pose a risk to driving were distributed to all attendants. The 3 pharmacist organizations provided drug related

information to the authority to support the development of these leaflets.



Plate-4: Leaflet distributed to the attendees



Plate-5: Fellow pharmacists who helped to organize the seminar

The Pharmaceutical Society of Hong Kong Pharmacy Legislation Lectures 2012 Registration Form

Surname _____ First Name _____

Contact No. _____

Name of Place of Work (If any) _____

Membership

Member/ Non-member

PSHK 2011/2012 Membership No _____

Membership Type

Voting/ Pre-reg/ Associate/ Student

Lectures Attending

L1 L2 L3 L4 L5 All

Payment Method

Online Cheque Cash (on site only)

Total Amount: HK\$ _____

Cheque No _____ Bank Name: _____

Payment Methods:

- (1) Online Payment <http://www.pshk.hk/>
- (2) Make cheque payable to "The Pharmaceutical Society of Hong Kong" and send by mail to Kowloon Post Office, P.O. Box 73552, Yaumatei, Kln.
- (3) Deposit the appropriate fee into our account HSBC 0022-163-166 and send bank-in receipt by mail to Kowloon Post Office, P.O. Box 73552, Yaumatei, Kln.

PSHK Forensic Lectures

Dear Members / Fellow Pharmacists,

PSHK Forensic Lectures on Pharmacy Legislation 2012

Drug Office, The Department of Health, and The Pharmaceutical Society of Hong Kong will co-organise a series of five lectures on Pharmacy Legislation of Hong Kong. This will be a good learning opportunity for anyone who is interested in gaining knowledge and latest updates in this aspect and for the candidates who will be sitting in the Hong Kong Pharmacist Registration Examination on Pharmacy Legislation.

Venue: PSHK Headquarters, 1303 Rightful Centre, 12 Tak Hing Street, Jordan, Kln.

Time: 6:30 pm – 8:30 pm, please arrive at 6:00 pm for registration

Date	Topic	Lecturer
20.4.2012 (Friday)	Wholesale & Retail Sale of Poisons Undesirable Medical Advertisements Labelling of Poisons and Pharmaceutical Products	Kevin LO Arkie LO
27.4.2012 (Friday)	Control of Antibiotics Classification of Poisons	Charlotta CHAK Karena Lee
4.5.2012 (Friday)	Registration of Pharmaceutical Products Manufacture of Pharmaceutical Products	Iris LEE Agnes TSE
11.5.2012 (Friday)	Licensing of Authorised Sellers of Poisons and Listed Sellers of Poisons Import/Export Control of Pharmaceutical Products and Dangerous Drugs	Tony CHAN Brenda LAM
18.5.2012 (Friday)	Classification and Sale of Dangerous Drugs Questions and Answers	Mandy Ho

All members and non-members are welcome to attend the lectures.

Each individual lecture is offered at **HK\$200 for non-members**.

Members will enjoy a special privileged deal of HK\$150 for all the 5 lectures, only to online payment or by cheque in advance. On-site cash payment would be \$200.

Registration Methods:

- (1) Registration on Line: Members & Non members joining the lectures can register and pay on line. You will receive a registration confirmation and receipt after payment has been made. (Please refer to our website: www.pshk.hk)
- (2) Registration by Mail: Members & Non-Members joining the lectures can also register by filling in the registration form and write a cheque payable to "The Pharmaceutical Society of Hong Kong" and send by mail to Kowloon Post Office, P.O. Box 73552, Yaumatei, Kln.
- (3) Registration on site: Members & Non members joining the lectures can register on-site by completing the registration Form & payment by cash or cheque.

Joining as PSHK Member:

All non-members who would like to join us as **new voting & pre-reg members** have to pay non-member fee HKD\$1,000 at first & you will receive the reimbursement [**\$250 for new voting members & \$450 for new pre-reg members**] with the membership card after successfully joining our membership.

For non-members who wanted to join our society, please be reminded to bring along the following:

- (1) Pharmacy Legislation Lectures 2012 Registration Form & **PSHK Membership Application Form** which can be downloaded from the "downloads" section of our web site: <http://www.pshk.hk/>
- (2) One recent passport-size photograph
- (3) Photocopy of certificate of academic qualification
- (4) Photocopy of certificate of overseas professional qualification if available
- (5) Photocopy of Hong Kong Certificate of Pharmacist Registration (to join the voting membership)
- (6) Payment :

Normal Membership Fee:

Entrance Fee: HK\$200 (for all membership except CUHK & HKU student chapter membership)

Annual Fee: HK\$200 (for pre-registration membership)

HK\$400 (for voting membership)

HK\$600 (for associate membership)

HK\$20 (for CUHK & HKU student chapter membership)

Lecture Fee:

Member: HK\$150 for 5 lectures

Non Member: HK\$200 per lecture

For payment by cheque, please make cheque payable to "The Pharmaceutical Society of Hong Kong".

Please refer to the following table for fees calculation.

Fees Calculation Member Status	Member Type	Entrance Fee	Membership Fee 2012	Fee per Lecture	Total Fee for 5 Lectures	Refund
Old Member	All	Paid Up	Paid Up	\$150	\$150	N/A
New Member	Voting	\$200	\$400	\$150	\$750	\$250
New Member	Pre-Reg	\$200	\$200	\$150	\$550	\$450
New Member	Associate	\$200	\$600	\$150	\$950	\$50
New Member	CUHK/ HKU	N/A	\$20	\$150	\$170	\$830
Non Member	N/A	N/A	N/A	\$200	\$1,000	N/A



THE 12TH ASIAN CONFERENCE ON CLINICAL PHARMACY

7 – 9 July 2012, Hong Kong SAR, China

www.accp2012.org



“Citius, Altius, Fortius” appraising clinical excellence, nurturing eminent practice

Important Dates

Abstract submission deadline: **31 January 2012** | Early bird registration deadline: **31 March 2012**

Topics

Keynote Lecture

- ▶ Development of Clinical Pharmacy - East Meets West

Plenary Lectures

- ▶ Nurturing Eminent Practice - Strategies to Success
- ▶ Appraising Clinical Excellence - What Have We Achieved and How Do We Measure It?

Symposia

- ▶ Ambulatory Care
- ▶ Cardiology
- ▶ Geriatrics and Patient Education
- ▶ Medication Reconciliation
- ▶ Oncology
- ▶ Paediatrics
- ▶ Pharmaceutics
- ▶ Psychiatry
- ▶ Renal



Hosts:



Enquiry:

UBM Medica Pacific Ltd.
Tel: (852) 2155 8557 or 3153 4374
Fax: (852) 2559 6910
Email: info@accp2012.org

NEW PRODUCTS

Avonex™

(Biogen Idec (Hong Kong) Limited)

Product Name

Avonex Solution For Injection
30mcg / 0.5ml

Presentation

Injection each 0.5ml containing
30mcg of Interferon β -1a

Pharmacology

Interferons are a family of naturally occurring proteins that are produced by eukaryotic cells in response to viral infection and other biological inducers. Interferons are cytokines that mediate antiviral, anti-proliferative, and immunomodulatory activities. Three major forms of interferons have been distinguished: α , β , and γ . Interferons- α and β are classified as type I interferons, and interferon- γ is a type II interferon. These interferons have overlapping but clearly distinguishable biological activities. They can also differ with respect to their cellular sites of synthesis. Interferon- β is produced by various cell types including fibroblasts and macrophages. Natural interferon- β and Avonex (interferon β -1a) are glycosylated and have a single N-linked complex carbohydrate moiety. Glycosylation of other proteins is known to affect their stability, activity, biodistribution and half-life in blood. However, the effects of interferon- β that are dependent on glycosylation are not fully defined.

Avonex exerts its biological effects by binding to specific receptors on the surface of human cells. This binding initiates a complex cascade of intracellular events that leads to the expression of numerous interferon-induced gene products and markers. These include MHC class I, Mx protein, 2'5'-oligoadenylate synthetase, β_2 -microglobulin and neopterin.

Indications

Treatment of patients diagnosed with relapsing multiple sclerosis. In clinical trials, this was characterized by ≥ 2 acute exacerbations (relapses) in the previous 3-years without evidence of continuous progression between relapses. Avonex slows the progression of disability and decreases the frequency of relapses.

It can be used among patients with single demyelinating event with an active inflammatory process, those who severely warrant treatment, those whose alternative diagnosis have been excluded, and those who are determined to be at high risk of developing clinically definite MS (see Pharmacology under Actions). Avonex should be discontinued in patients who develop progressive MS.

Dosage and Administration

Adults: The recommended dosage for the treatment of relapsing MS is 30 mcg (0.5 mL), administered by IM injection once a week. At the initiation of the treatment, patients may either be started on a full dose of 30 mcg (0.5 mL) or on approximately half the dose once a week to help them to adjust to treatment and thereafter increased to the full dose of 30 mcg (0.5 mL). In order to obtain adequate efficacy, a dose of 30 mcg (0.5 mL) once a week should be reached and maintained after the initial titration period. A manual titration device to enable delivery of approximately half the dose is available for patients initiating Avonex treatment.

No additional benefit has been shown by administering a higher dose (60 mcg) once a week.

Children: The safety and efficacy of Avonex in adolescents 12-16 years have not yet been established. Currently available data are described in Pharmacology under Actions and Adverse Reactions but no recommendation on dosage

can be made. The safety and efficacy of Avonex in children <12 years have not yet been established. No data are available.

Elderly: Clinical studies did not include a sufficient number of patients ≥ 65 to determine whether they respond differently than younger patients. However, based on the mode of clearance of interferon β -1a, there are no theoretical reasons for any requirement for dose adjustments in the elderly.

The IM injection site should be varied each week (see Toxicology under Actions). Doctors may prescribe a 25 mm, 25 gauge needle to patients for whom such a needle is appropriate to administer an IM injection.

Prior to injection and for an additional 24 hrs after each injection, an antipyretic analgesic is advised to decrease flu-like symptoms associated with Avonex administration. These symptoms are usually present during the first few months of treatment.

At the present time, it is not known for how long patients should be treated. Patients should be clinically evaluated after 2 years of treatment and longer-term treatment should be decided on an individual basis by the physician. Treatment should be discontinued if the patient develops chronic progressive MS.

Contraindications

Initiation of treatment in pregnancy.

Patients with a history of hypersensitivity to natural or recombinant interferon- β or to any of the excipients of Avonex.

Patients with current severe depression and/or suicidal ideation (see Precautions and Adverse Reactions).

Warnings

Avonex should be administered with caution to patients with previous or current depressive disorders, in particular to those with antecedents

of suicidal ideation (see Contraindications). Depression and suicidal ideation are known to occur in increased frequency in the MS population and in association with interferon use. Patients should be advised to immediately report any symptoms of depression and/or suicidal ideation to their physician.

Patients exhibiting depression should be monitored closely during therapy and treated appropriately. Cessation of therapy with Avonex should be considered (see Contraindications and Adverse Reactions).

Avonex should be administered with caution to patients with a history of seizures, to those receiving treatment with antiepileptics, particularly if their epilepsy is not adequately controlled with antiepileptics (see Interactions and Adverse Reactions).

Caution should be used and close monitoring considered when administering Avonex to patients with severe renal and hepatic failure and to patients with severe myelosuppression.

Hepatic injury including elevated serum hepatic enzyme levels, hepatitis, autoimmune hepatitis and hepatic failure has been reported with interferon- β in post-marketing (see Adverse Reactions). In some cases, these reactions have occurred in the presence of other medicinal products that have been associated with hepatic injury. The potential of additive effects from multiple medicinal products or other hepatotoxic agents (eg, alcohol) has not been determined. Patients should be monitored for signs of hepatic injury and caution exercised when interferons are used concomitantly with other medicinal products associated with hepatic injury.

Patients with cardiac disease, such as angina, congestive heart failure or arrhythmia, should be closely monitored for worsening of their clinical condition during treatment with Avonex. Flu-like symptoms associated with Avonex therapy may prove stressful

to patients with underlying cardiac conditions.

Laboratory abnormalities are associated with the use of interferons. Therefore, in addition to those laboratory tests normally required for monitoring patients with MS, complete and differential white blood cell counts, platelet counts, and blood chemistry, including liver function tests, are recommended during Avonex therapy. Patients with myelosuppression may require more intensive monitoring of complete blood cell counts, with differential and platelet counts.

Patients may develop antibodies to Avonex. The antibodies of some of those patients reduce the activity of interferon β -1a *in vitro* (neutralizing antibodies). Neutralizing antibodies are associated with a reduction in the *in vivo* biological effects of Avonex and may potentially be associated with a reduction of clinical efficacy. It is estimated that the plateau for the incidence of neutralizing antibody formation is reached after 12 months of treatment. Recent clinical studies with patients treated up to 3 years with Avonex suggest that approximately 5-8% develop neutralizing antibodies.

The use of various assays to detect serum antibodies to interferons limits the ability to compare antigenicity among different products.

Interaction

No formal interaction studies have been performed in humans.

The interaction of Avonex with corticosteroids or adrenocorticotrophic hormone (ACTH) has not been studied systematically. The clinical studies indicate that MS patients can receive Avonex and corticosteroids or ACTH during relapses.

Interferons have been reported to reduce the activity of hepatic cytochrome P450-dependent enzymes in humans and animals. The effect of high-dose AVONEX administration on P450-dependent metabolism in monkeys was evaluated and no changes in liver metabolising

capabilities were observed. Caution should be exercised when Avonex is administered in combination with medicinal products that have a narrow therapeutic index and are largely dependent on the hepatic cytochrome P450 system for clearance such as antiepileptics and some classes of antidepressants.

Pregnancy and lactation

Use in pregnancy: There is limited information on the use of Avonex in pregnancy. Available data indicates that there may be an increased risk of spontaneous abortion. Initiation of treatment is contraindicated during pregnancy.

Women of Childbearing Potential: Women of childbearing potential have to take appropriate contraceptive measures. If the patient becomes pregnant or plans to become pregnant while taking Avonex, she should be informed of the potential hazards and discontinuation of therapy should be considered (see Toxicology under Actions). In patients with a high relapse rate before treatment started, the risk of a severe relapse following discontinuation of Avonex in the event of pregnancy should be weighed against a possible increased risk of spontaneous abortion.

Use in lactation: It is not known whether Avonex is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made either to discontinue breastfeeding or Avonex therapy.

Side effects

The highest incidence of adverse reactions associated with Avonex therapy is related to flu-like symptoms. The most commonly reported flu-like symptoms are myalgia, fever, chills, sweating, asthenia, headache and nausea. Flu-like symptoms tend to be most prominent at the initiation of therapy and decrease in frequency with continued treatment.

Transient neurological

symptoms that may mimic MS exacerbations may occur following injections. Transient episodes of hypertonia and/or severe muscular weakness that prevent voluntary movements may occur at any time during treatment. These episodes are of limited duration, temporally related to the injections and may recur after subsequent injections.

The frequencies of adverse reactions are expressed in patient-years, according to the following categories: Very common ($\geq 1/10$ patient-years); common ($\geq 1/100$ to $< 1/10$ patient-years); uncommon ($\geq 1/1000$ to $< 1/100$ patient-years); rare ($\geq 1/10,000$ to $< 1/1000$ patient-years); very rare $< 1/10,000$ patient-years).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Investigations: Common: Decreased lymphocyte count, decreased white blood cell count, decreased neutrophil count, decreased hematocrit; increased blood potassium, increased blood urea nitrogen. Uncommon: Decreased platelet count. Not Known: Decreased weight, increased weight, abnormal liver function tests.

Cardiac Disorders: Not Known: Cardiomyopathy, congestive heart failure (see Precautions), palpitations, arrhythmia, tachycardia.

Blood and Lymphatic System Disorders: Not Known: Pancytopenia, thrombocytopenia. **Nervous System Disorders:** Very Common: Headache². Common: Muscle spasticity, hypoesthesia. Not Known: Neurological symptoms, syncope, hypertonia, dizziness, paraesthesia, seizures, migraine. **Respiratory, Thoracic and Mediastinal Disorders:** Common: Rhinorrhoea. Rare: Dyspnoea.

Gastrointestinal Disorders: Common: Vomiting, diarrhoea, nausea.

Skin and Subcutaneous Tissue

Disorders: Common: Rash, increased sweating, contusion. Uncommon: Alopecia. Not Known: Angioneurotic oedema, pruritus, vesicular rash, urticaria, aggravation of psoriasis.

Musculoskeletal and Connective Tissue Disorders: Common: Muscle cramp, neck pain, myalgia², arthralgia, pain in extremity, back pain, muscle stiffness, musculoskeletal stiffness. Not Known: Systemic lupus erythematosus, muscle weakness, arthritis.

Endocrine Disorders: Not Known: Hypothyroidism, hyperthyroidism.

Metabolism and Nutrition Disorders: Common: Anorexia.

Infections and Infestations: Not Known: Injection site abscess.

Vascular Disorders: Common: Flushing. Not Known: Vasodilation.

General Disorders and Administration Site Conditions:

Very Common: Flu-like symptoms, pyrexia, chills, sweating. Common: Injection site pain, injection site erythema, injection site bruising; asthenia², pain, fatigue², malaise, night sweats. Uncommon: Injection site burning. Not Known: Injection site reaction, injection site inflammation, injection site cellulitis¹, injection site necrosis, injection site bleeding; chest pain.

Immune System Disorders: Not Known: Anaphylactic reaction, anaphylactic shock, hypersensitivity reactions (angioedema, dyspnoea, urticaria, rash, pruritic rash).

Hepatobiliary Disorders: Not Known: Hepatic failure (see Precautions), hepatitis, autoimmune hepatitis.

Reproductive System and Breast Disorders: Uncommon: Metrorrhagia, menorrhagia.

Psychiatric Disorders: Common: Depression (see Precautions), insomnia. Not Known: Suicide, psychosis, anxiety, confusion, emotional lability.

Forensic Classification:

P1S1S3

Prolia® Injection
(GlaxoSmithKline)

Active Ingredient:

Denosumab

Presentation:

1 mL of a 60 mg/mL solution in a single-use prefilled syringe.

Pharmacological Properties:

Prolia (denosumab) is a human IgG2 monoclonal antibody with affinity and specificity for human RANKL (receptor activator of nuclear factor kappa-B ligand). Prolia binds to RANKL, a transmembrane or soluble protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption.

It prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts and their precursors. Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in both cortical and trabecular bone.

Indications:

Prolia is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Dosage and Administration:

The recommended dose is 60 mg administered as a single subcutaneous injection once every 6 months. Administer via subcutaneous injection in the upper arm, the upper

thigh, or the abdomen. All patients should receive calcium 1000 mg daily and at least 400 IU vitamin D. Prolia should be administered by a healthcare professional. If a dose is missed, administer the injection as soon as the patient is available and every 6 months from the date of the last injection.

Prolia should be clear, colorless to pale yellow solution that may contain trace amounts of translucent to white proteinaceous particles. Do not use if the solution is discolored or cloudy or if the solution contains many particles or foreign particulate matter. Prior to administration, Prolia may be removed from the refrigerator and brought to room temperature (up to 25°C/77°F) by standing in the original container. This generally takes 15 to 30 minutes. Do not warm Prolia in any other way.

Contraindications:

Pre-existing hypocalcemia must be corrected prior to initiating therapy with Prolia

Precautions:

Hypocalcemia, serious infections, concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections, Osteonecrosis of the Jaw and Suppression of Bone Turnover.

Drug Interactions:

No drug-drug interaction studies have been conducted with Prolia

Side Effects:

Abdomen, urinary tract, ear infections, endocarditis, cellulitis, dermatitis, eczema, rashes and pancreatitis

NEW INDICATION

PRADAXA®
(Boehringer Ingelheim)

Active ingredient:

Dabigatran etexilate

Presentation:

Capsules of 75 mg, 110 mg and 150 mg

Pharmacological Properties:

Dabigatran etexilate is a prodrug which does not exhibit anticoagulant activity itself. Following oral administration, dabigatran etexilate is rapidly absorbed and converted to dabigatran by esterase-catalysed hydrolysis in plasma and in the liver.

Dabigatran is a competitive, reversible direct thrombin inhibitor, and is the main active principle in plasma. Since thrombin (serine protease) enables the conversion of fibrinogen into fibrin during the coagulation cascade, its inhibition prevents the development of thrombus. Dabigatran also inhibits free thrombin, fibrin-bound thrombin and thrombin-induced platelet aggregation. *In-vivo* and *ex-vivo* animal studies have demonstrated antithrombotic efficacy and anticoagulant activity of dabigatran after intravenous administration and of dabigatran etexilate following oral administration in various animal models of thrombosis.

Indications:

Prevention of venous thromboembolic events (VTE) in patients who have undergone elective total hip replacement or total knee replacement surgery. Prevention of stroke and systemic embolism in patients with atrial fibrillation, in whom anticoagulation is appropriate.

Dosage and Administration:

PRADAXA may be taken with food, or on an empty stomach with water. The capsule should be swallowed intact.

VTE prevention following elective knee replacement surgery: The recommended dose of PRADAXA is 220 mg daily, taken orally as two (2) capsules of 110 mg once a day in patients with intact renal function. Treatment should normally be initiated within 1-4 hours of completed surgery once hemostasis is secured. Start with a single capsule of 110 mg, and continue with two (2) capsules once daily thereafter for a total of **10 days**. If hemostasis is not secured, initiation of treatment should be delayed. If treatment is not started on the day of surgery for whatever reason, then treatment should be initiated with 2 capsules at once.

VTE prevention following elective hip replacement surgery: The recommended dose of PRADAXA is 220 mg daily, taken orally as two (2) capsules of 110 mg once a day in patients with intact renal function. Treatment should normally be initiated within 1-4 hours of completed surgery once hemostasis is secured. Start with a single capsule of 110 mg, and continue with 2 capsules once daily thereafter for a total of **28-35 days**. If hemostasis is not secured, initiation of treatment should be delayed. If treatment is not started on the day of surgery for whatever reason, then treatment should be initiated with 2 capsules at once.

Prevention of stroke and systemic embolism in patients with atrial fibrillation: The recommended dose of PRADAXA is 300 mg daily, taken orally as one 150 mg capsule twice a day.

Forensic Classification:

P1S1S3

Hong Kong Pharmaceutical Journal: For Detailed Instructions for Authors

INTRODUCTION

Hong Kong Pharmaceutical Journal (HKPJ) is the official publication of the Pharmaceutical Society of Hong Kong, the Practising Pharmacists Association of Hong Kong and the Society of Hospital Pharmacists of Hong Kong. It is a journal of the pharmacists, for the pharmacists and by the pharmacists. The Journal is currently divided into several sections: **Editorial Comment; News & Short Communications; Pharmacy Practice; Over-the-Counter & Health; Drugs & Therapeutics; Herbal Medicines & Nutraceuticals; Pharmaceutical Technology** and **New Products**. It publishes review articles or original papers relevant to these different fields of pharmacy. In addition to the regular four issues of the Journal per year, there are issues dedicated solely to reports on special function of the society. The Aims and Scope of the Journal are published on the inside back cover of each issue.

Submission of Manuscript

Submission of a paper implies that it has not been published previously, that it is not under consideration for publication elsewhere, and that if accepted it will not be published elsewhere in the same form, in English or in any other language, without the written consent of the publisher. Authors are specifically discouraged from submitting papers as fragmented studies of a particular topic. A manuscript must be indicated which section it is belonged. Upon received, it will be screened by a **Sectional Editor** of HKPJ for initial consideration before it is sent out for further review or comment.

For online submission:

Authors are encouraged to submit manuscripts using the online submission system. Access to the system, and full instructions on its use, can be found on the HKPS website at: <http://www.HKPS.org/HKPJ/Guidelines>. In creating the electronic version of their manuscript, authors are requested to follow the guidelines for submitting files. The paper should be submitted as a single file, prepared with a standard word-processor such as Microsoft Word, with embedded tables and graphics. Please note that any embedded graphics must also be submitted as separate, original files. The preferred formats for graphics files are tiff or postscript. All correspondence between Editor and author is performed by email. Authors are reminded that the copyright of their article or paper is automatically transferred to HKPJ once it is accepted for publication in the journal.

For hardcopy submission:

Three copies of the manuscript are required on either 8.5"x11" or A4 paper (two copies are used for review purposes and the original is kept on file at the Section Editor). Copies must be produced on a high-quality printer, and originals and copies of all Figures and Schemes must be fully legible. Initially only send hard copies of the paper; when it has been refereed, revised if necessary, and accepted, you will be requested to send a disk containing the final version with the final hard copy to the appropriate Editor. Make sure that the disk and the hard copy match exactly. The revised manuscript must be returned to the Editors within one month, otherwise it may be deemed to be new and subject to further review. When submitting the final version with a disk please label all disks with "HKPJ", your name, software (e.g. word 2000), hardware used (e.g. PC or Macintosh) and file names with the correct extension (e.g. Fig 1.cdx, Table 1-6.xls). Save text on a separate disk from the graphics, include the text and tables in one file, and provide graphics and structures in separate numbered files. Please remember to keep a backup copy of both the electronic files and original manuscript for reference and safety since we cannot accept responsibility for damage or loss of papers. Original manuscripts are discarded three months after publication unless the Publisher is asked to return original material after use.

Suggested Referees

Please submit, with your manuscript, the names and addresses of 2 potential referees. You may also mention persons who you would prefer not to review your paper.

Editorial Authority

The Editors of HKPJ reserve the right to make alterations to manuscripts submitted for publication. Such alterations will be made if manuscripts do not conform with accepted scientific standards or if they contain matter which in the opinion of the Editors is unnecessarily verbose or unclear. Alterations may be queried, but this will inevitably delay publication.

Preparation of manuscript

The manuscript is required to be written in English, with numbered pages, single-spaced, using Arial 9 point font, and in a suitable word-processing format. Each page should have adequate margins (4 cm) and liberal spaces at top and bottom of the manuscript. All textual elements should begin flush left, with the second paragraphs onwards indent, and should use the wrap-around end-of-line feature, i.e. no returns at the end of each line. Place two returns after every element such as title, headings,

paragraphs, figure and table call-outs. Most formatting codes will be removed or replaced on processing your article. Please do not use options such as automatic word breaking, justified layout, double columns or automatic paragraph numbering (especially for numbered references). However do use bold face, italic, subscripts, superscripts etc. The Editors reserve the right to adjust style to certain standards of uniformity. If authors are unfamiliar with HKPJ, they should consult a recent copy (or the free online sample copy available from www.HKPS.com/HKPJ) to see the conventions currently followed for guidance in preparing submissions.

The content of manuscripts must be arranged as follows: (1) a Title Page with authors name(s) and address(es); (2) an Abstract, in which contents are briefly stated; (3) a 4 to 6 Key Word Index, (4) Introduction, and (5) the Results and Discussion (preferably combined). Although each section may be separated by headings, they should form one continuous narrative and only include details essential to the arguments presented. If a discussion is separately provided, it should not include a repetition of the results, but only indicate conclusions reached on the basis of them, and those from other referred works; (6) Conclusions or Concluding Remarks; (7) the Experimental should include brief details of the methods used such that a competent researcher in the field may be able to repeat the work; (8) Acknowledgments; (9) References; (10) Legends, Formulae, Tables and Figures.

Title Page and Author Names: Titles must be as brief as possible, consistent with clarity, and should not exceed 10 words in length. Uninformative phrases such as "Chemical examination of", "Studies on", "Survey of", "New", "Novel" etc. will be deleted. If a paper is part of a series, this must not be given in the heading, but referred to in a footnote in the form: *Part 9 in the series "The Role of Pharmacists in Medical Care of Patients" followed by a numbered reference to the previous part. Author names should be typed right underneath the article title. Each author should identify himself or herself with Surname in capital letters, followed by the first name. All names are separated by a semicolon (;). An asterisk should be placed following the name of the author to whom correspondence inquiries should be made. Full postal addresses must be given for all co-authors. Superscript letters; a, b, c should be used to identify authors located at different addresses.

An **Author's background box** at the end of each article is mandatory to include the author's job title and the affiliated institute or organization. Full details of telephone, fax numbers and e-mail

address should also be indicated for the corresponding authors. No academic or professional membership title is allowed.

ABSTRACT: The abstract should be on a separate page and briefly describe the results obtained and conclusions reached, not the methods used, or speculations on any other matter. They are not expected to be a complete summary but only an outline of the main findings. The abstract should be contained within 250 words and should be readable without reference to the rest of the paper.

Key Words: Authors must give four to six "key words" or phrases, which identify the most important subjects covered by the paper.

INTRODUCTION should give the minimum historical data needed to give appropriate context to the author's investigation and its relationship to other similar research previously or currently being conducted. Only information essential to the arguments should be presented. Much data can be taken for granted or quoted in abbreviated form. Specific term (genus, species, authority) of all experimental works must be given at first mention and preferably be in the form adopted by the International Scientific Community.

RESULTS AND DISCUSSION: These sections should be carefully prepared with discussions of the results being compared with existing and/or previous knowledge within the field. Authors are, however, encouraged to combine the Results and Discussion sections wherever possible.

EXPERIMENTAL: Subsections on the Experimental Procedures should be italicized and inserted as part of the first line of the text to which they apply. HKPJ encourages an extensive use of abbreviations (these are listed at the back of the Instructions to Authors, or the reader is referred to other sources). The Experimental should begin with a subsection entitled General Experimental Procedures. This subsection will typically contain brief details of instruments used, and identification of sources of specialized chemicals, biochemicals and molecular biology kits. The next subsection describes the source(s) and documentation of biological materials used, whether in reference to whole plants or parts there from, crude drugs, or any other plant material from which identifiable chemical substances are obtained for the first time. Documentation must also include a reference to voucher specimen(s) and voucher number(s) of the compounds, plants or other material examined. If available, authors should quote the name and address of the authority who identified each sample investigated. Specimens should preferentially be deposited in a major regional herbarium where the collection is maintained by state or private institution and which permits loan of such materials. With other microorganisms, the culture collection from which they were either accessed and/or deposited should be included, together with identification of the strain designation

code. The Experimental Procedures employed should be concise but sufficiently detailed that a qualified researcher will be able to repeat the studies undertaken, and these should emphasize either truly new procedures or essential modifications of existing procedures. Experimental details normally omitted include: (1) method of preparation of common chemical and biochemical derivatives, (2) excessive details of separation of compounds, proteins and enzymes, e.g. preparation of columns, TLC plates, column and fraction size. Compound Characterization: Physical and spectroscopic data for new compounds must be comprehensive, and follow the order shown below: compound name (and assigned number in text); physical state of compound (e.g. oil, crystal, liquid, etc.), melting and/or boiling point; optical rotation and/or circular dichroism measurements, if optically active; UV; IR, ¹H NMR; ¹³C NMR; MS. For all new compounds, either high-resolution mass spectral or elemental analysis data is required. See later section for method of data presentation.

Nomenclature: Chemical nomenclature, abbreviations and symbols must follow IUPAC rules. Whenever possible, avoid coining new trivial names; every effort should be made to modify an existing name. For example, when a new compound is described, it should be given a full systematic name according to IUPAC nomenclature and this should be cited in the Abstract or in the Experimental section.

ACKNOWLEDGMENTS: This section is used to provide brief credit for scientific and technical assistance, and in recognition of sponsorship through financial support and any other appropriate form of recognition.

References: All publications cited in the text should be presented in a list of references following the text of the manuscript. In the text refer to the author's name (without initials) and year of publication (e.g. "Since Peterson (1993) has shown that ..." or "This is in agreement with results obtained later by Kramer.⁽⁴⁾" For two authors both authors are to be listed, with "and" separating the two authors. For more than two authors, use the first author's surname followed by et al. The list of references should be arranged according to the order of their appearance in the text with no more than three authors listed. If number of authors of a reference exceeds three, "et al" is used followed by year of publication in bracket after the first author. Journal titles should be completely shown followed by the volume, issue number in bracket if included, colon and start – final page number. The manuscript should be carefully checked to ensure that the spelling of authors' names and dates are exactly the same in the text as in the reference list. Some examples of references are shown below:

- (1) Cabello-Hurtado F, Durst F, Jorin JV, Werck-Reichhart D. et al. (1998). Coumarins in *Helianthus tuberosus*: characterization, induced accumulation and biosynthesis. *Biochemistry*, 49(1):1029-1036.

- (2) Mabry T, Markham KR, Thomas MB. (1970). *The Systematic Identification of Flavonoids*. 2nd Ed, pp. 79-105. Springer Verlag, New York.
- (3) Harborne JB. (1999). Plant chemical ecology. In: Barton D, Nakanishi K, Meth-Cohn O, (Eds.), *Comprehensive Natural Products Chemistry*, Vol. 8. pp. 137-196. Pergamon, Oxford.

Preparation of Illustrations: All illustrations should be provided in camera-ready form, suitable for reproduction (which may include reduction) without retouching. Illustrations (figures, tables, etc.) should be prepared for either single or double column format. For online submission illustrations should be included in the manuscript and also be submitted separately as high resolution files. For hardcopy submission illustrations should be submitted on separate pages in camera-ready format with legends on separate pages. Hardcopy illustrations supplied by authors are digitally scanned into the appropriate page and must therefore be of the highest quality. Where possible the original electronic files are used, figures produced by computer must therefore be prepared at a minimum resolution of 300 dpi. Refer to all photographs, charts and diagrams as "Figure(s)" and number them consecutively in the order to which they are referred. They should accompany the manuscript, but should not be included within the text. All illustrations should be clearly marked with the figure number and the author's name (either on the back if submitting on paper or with a clear file name if submitting online). All figures are to have a caption, which should be supplied on a separate page. Note: Illustrations of the following type generally will not be accepted for publication: (1) diagrams or photographs of chromatograms (PC and TLC), electrophoretic separations, or recorder traces of GC and HPLC data which are given merely to prove identification; (2) straight-line graphs; (3) generalized pH and temperature-denaturation curves of enzymes; (4) illustrations of IR, UV, NMR or MS (values can be quoted in the text or Experimental); (5) flow sheets illustrating isolation of compounds; (6) expectable MS fragmentation patterns; (7) formulae of well-known compounds or reaction schemes; (8) tables giving either single values for each parameter which could be easily quoted in the text, or repeating data shown elsewhere.

Illustrations should be drawn on separate pages and prepared with good contrast (black on a white background). Lettering in tables, figures, etc: lettering in formulae, figure axes etc. must be large enough to be legible after reduction. Lettering should be drawn in 6-7pt Helvetica (Arial) font to ensure optimum visibility. Chemical formulae must be made absolutely clear; printers are not chemists and much delay is caused by poor drawing. Aromatic rings must be drawn with alternate double bonds and conformation of single bonds shown by thickened or dashed (III) lines according to convention. Formulae should be numbered consecutively in Arabic numerals. If graphics are created using ChemDraw or ISISDraw the preferred settings are: font 10 pt Helvetica (Arial), chain angle 120°

bond spacing 18% of length, fixed (bond length 14.4 pt (0.508 cm), bold width (bond thickness) 2.0 pt (0.071 cm), line width 0.6 pt (0.021 cm), margin width 1.6 pt (0.056 cm), and hash spacing 2.5 pt (0.088 cm). The overall size should be not more than 95mm (single column) or 194mm (double column) by 285 mm.

Tables must be typed on separate pages, numbered consecutively, given a suitable caption and arranged to be viewed vertically. They must be so constructed as to be intelligible without reference to the text. Every table must have an Arabic number and a title, and each column must be provided with an explanatory heading. No vertical rules should be used. Tables should not duplicate results presented elsewhere in the manuscript (e.g. in graphs). Footnotes may be used to expand column headings, etc. and should be referenced by superscript lowercase letters a,b,c rather than symbols. Results should be cited only to the degree of accuracy justified on the basis of the errors of the method and usually only to three significant figures. Units must always be clearly indicated and chosen so as to avoid excessively high (>100) or low (<0.01) values. The figure zero should precede the decimal point for all numbers below one (e.g. 0.1).

Half-tone photographs must have good contrast and not be more than 25 cm wide and not more than 30 cm high. Original photographs (or high resolution graphic files of at least 500 dpi) must be supplied as they are to be reproduced (e.g. black and white or colour). If necessary, a scale should be marked on the photograph. Please note that photocopies of photographs are not acceptable.

Colour charges

Authors are encouraged to submit their works in colour. There is no charge for colour print.

Supplementary data

HKPJ now accepts electronic supplementary material to support and enhance your scientific research. Supplementary files offer the author additional possibilities to publish supporting applications, movies, animation sequences, high-resolution images, background datasets, sound clips and more. Supplementary files supplied will, subject to peer review, be published online alongside the electronic version of your article in HKPS website. The presence of these files will be signified by a footnote to the article title, and by a description included in a 'Supplementary Data' section at the end of the paper. In order to ensure that your submitted material is directly usable, please ensure that data is provided in one of our recommended file formats and supply a concise and descriptive caption for each file. Please also clearly indicate whether data files are either i) for publication online or ii) only to be used as an aid for the refereeing of the paper. For more detailed instructions please visit our Author Gateway at <http://authors.hkpj.org>

Errata and Corrigenda to publish articles will be included, at the discretion of the Section Editors and the publisher.

Abbreviations

About, approximately: ca.
Anhydrous: dry (not anhyd.)
Aqueous: aq.
Circular dichroism: CD
Concentrated (or mineral acids): conc.
Concentrations: ppm (or ppb), μ M, mM, M, %, mol
Dry weight: dry wt; fresh weight: fr. wt
Electricity: V, mA, eV
Force due to gravity (centrifugation): g; rpm (revolutions min⁻¹)
Gas chromatography: GC
Gas chromatography-mass spectrometry: GC-MS
Trimethylsilyl derivative: TMSi (TMS cannot be used as this refers to the internal standard tetramethylsilane used in ¹H NMR)
High performance liquid chromatography: HPLC
Infrared spectrophotometry: IR
Length: nm, μ m, mm, cm, m
Literature: lit.
Mass spectrometry: m/z [M]⁺ (molecular ion, parent ion)
Melting points: uncorr. (uncorrected)
Molecular mass: Da (daltons), kDa
Molecular weight: M,
Nuclear magnetic resonance: ¹H NMR, ¹³C NMR, Hz, δ
Numbers: e.g. 1, 10, 100, 1000, 10000; per or ⁻¹
Optical rotatory dispersion: ORD
Paper chromatography: PC
Precipitate: ppt.
Preparative thin-layer chromatography: prep. TLC
Radioactivity: dpm (disintegrations per min), Ci (Curie), sp. act (specific activity), Bq (1 becquerel = 1 nuclear transformation sec⁻¹)
Repetitive manipulations: once, twice, x3, x4, etc.
RR_t (relative retention time), R₁ (Kovat's retention index), ECL (equivalent chain length- term frequently used in fatty acid work)
Saturated: satd.
Solution: soln.
Solvent mixtures including chromatographic solvents: abbreviate as follows n-BuOH-HOAc-H₂O (4:1:5)
Statistics: LSD (least significant difference), s.d. (standard deviation), s.e. (standard error)
Temperature: (with centigrade), mp, mps, mmp, bp
Temperature: temp.
Thin-layer chromatography: TLC, R_f
Time: s, min, h, day, week, month, year
Ultraviolet spectrophotometry: UV, A (absorbance, not aD-optical density)
Volume: l, (litre), μ l, ml
Weight: wt, pg, ng, μ g, mg, g, kg

Inorganics, e.g. AlCl₃ (aluminum chloride), BF₃ (boron trifluoride), Cl₂, CO₃, H₂, HCl, HClO₄ (perchloric acid), HNO₃, H₂O, H₂O₂, H₂SO₄, H₃BO₃ (boric acid), He, KHCO₃ (potassium bicarbonate), KMnO₄ (potassium permanganate), KOH, K-Pi buffer (potassium phosphate buffer), LiAlH₄ (lithium aluminium hydride), Mg²⁺, MgCl₂, N₂, NH₃, (NH₄)₂SO₄, Na⁺, NaBH₄

(sodium borohydride), NaCl, NaIO₄ (sodium periodate), NaOH, Na₂SO₃ (sodium sulphite), Na₂SO₄ (sodium sulphate), Na₂S₂O₃ (sodium thiosulphate), O₃, PPI (inorganic phosphate), SO₄²⁻, Tris (buffer).

Organics, e.g. Ac₂O (acetic anhydride), n-BuOH (butanol), C₆H₆ (benzene), CCl₄ (carbon tetrachloride), CH₂Cl₂ (methylene chloride), CHCl₃ (chloroform), CH₂N₂ (diazomethane), CM (carboxymethyl), DEAE (diethylaminoethyl), DMF (dimethylformamide), DMSO (dimethyl sulphoxide), EDTA (ethylene-diaminetetraacetic acid), Et₂O (diethyl ether), EtOAc (ethyl acetate), EtOH (ethanol), HCO₂H (formic acid), HOAc (acetic acid), iso-PrOH (iso-propanol), Me₂CO (acetone), MeCOEt (methyl ethyl ketone), MeOH (methanol), NaOAc (sodium acetate), NaOMe (sodium methoxide), petrol (not light-petroleum or petroleum ether), PhOH (phenol), PrOH (propanol), PVP (polyvinylpyrrolidone), TCA (trichloroacetic acid), TFA (trifluoroacetic acid), THF (tetrahydrofuran).
¹H NMR solvents and standards: CDCl₃ (deutero-chloroform), D₂O, DMSO-d₆ [deuterodimethylsulphoxide not (CD₃)₂S], pyridine-d₅ (deuteropyridine), TMS (tetramethylsilane).

For further terms used in biochemistry and molecular biology the authors should see the websites of the nomenclature committees (www.chem.qmul.ac.uk/iubmb/).

Page charges.

There is no page charges for HKPJ.

Proofs and Articles in Press

Proofs will be despatched via e-mail to the corresponding author, by the Publisher and should be returned with corrections as quickly as possible, normally within 48 hours of receipt. Proofreading is solely the author's responsibility. Authors should ensure that corrections are returned in one communication and are complete, as subsequent corrections will not be possible. Any amendments will be incorporated and the final article will then be published online as an Article in Press.

Offprints

Two copies containing the offprints will be supplied free of charge. Additional offprints and copies of the issue can be ordered at a specially reduced rate using the order form sent to the corresponding author after the manuscript has been accepted. Late orders for reprints will incur a 50% surcharge.

Copyright

Upon acceptance of an article, Authors will be assumed to transfer copyright unconditionally to HKPJ. This transfer will ensure the widest possible dissemination of information. If excerpts from other copyrighted works are included, the Author(s) must obtain written permission from the copyright owners and credit the source(s) in the article.

Author enquiries

For enquiries relating to the submission of articles (including electronic submission) please send your query by email to editor@hkpj.org

Saving Lives with Anti-infective Innovation



Antibiotics

INVANZ[®]
(ertapenem, MSD) IV/IM

(imipenem/cilastatin sodium, MSD)
TIENAM[®]

Antifungal

Cancidas[®] IV
caspofungin

NOXAFIL[®]
posaconazole

Antiviral

ISENTRESS[®]
raltegravir, MSD

STOCRIN[®]
(efavirenz)

PegIntron[®]
Peginterferon alfa-2b

Before prescribing, please consult full prescribing information.



MSD
Merck Sharp & Dohme (Asia) Ltd.

Copyright © 2010 Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, N.J., USA. All rights reserved.