

HONG KONG PHARMACEUTICAL *JOURNAL*

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A Multi-Dimensional Perspective Functions of Adverse Event Reporting System in Pharmaceutical Companies

Implementational Experience of Medical Reconciliation in Queen Mary Hospital

Overview on the International and Local Situation of Smoking Cessation (2 CE Units)

Accurate Measurement of Liquid Medication

"Absence of Specified Microorganisms" versus "Absence of Objectionable Microorganisms" of the Microbial Limits Tests for Non-Sterile Pharmaceuticals

The Pharmaceutical Society of Hong Kong 60th Anniversary Lecture & Dinner

Extract of Herba Scutellariae Barbatae Has Anti-inflammatory, Antipyretic and Cancer Chemopreventive Effects

Hong Kong Pharmacy Conference 2010 - Good news vs Bad news

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1. Pradaxa® (dabigatran etexilate) Product Insert. 2. Stangier J *et al. Clin Pharmacokinet* 2008; **47**:47-59. 3. Stangier J. *Clin Pharmacokinet* 2008; **47**: 285-295. 4. Stangier J *et al. Br J Clin Pharmacol* 2007; **64**:292-303. 5. Stangier J *et al. J Clin Pharmacol* 2005; **45**:555-563. 6. Blech S *et al. Drug Metab Dispos* 2008; **36**:386-399.

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Be a Competent and Responsible Professional to Safeguard People's Life



The Oxford Dictionary defines "professional" as "a person who does a job that needs special training and a high level of education."⁽¹⁾ According to this definition, all pharmacy practices carried

out by registered pharmacists can be considered to be professional because the jobs require several years of intensive training before a person is allowed to handle drugs under the regulation of law. However, people expect more than just training and education from professionals. Today, professional practices should incorporate at least five important elements; i.e. (a) having a sense of responsibility to one's practice; (b) being in accordance with ethical standards; (c) to be commensurate with appropriate technical facilities and resources; (d) regular supervision or monitoring to ensure high standard of practices and (e) maintaining proper documentation and records for tracing.⁽²⁾ Bearing these requirements in mind, missing any element described above is already unprofessional.

This issue covers a number of articles addressing different aspects of safe use of drugs based on professional practice and continuous monitor by pharmacists. A couple of them are related to adverse drug events and the others are about proper practice when executing a job.

Adverse drug reaction (ADR) occurring after patients are given a medicine has been a great concern for all healthcare professionals. Although some information about how ADR should be handled as advised by the Hong Kong government was given in the second issue of volume 15 (2008) of this journal,⁽³⁾ the advice given is still a passive approach. It is encouraging to see that besides our government, some drug manufacturers have, indeed, implemented the ADR reporting system to ensure the safe use of drugs. Efforts voluntarily initiated by drug manufacturers, if not more important, are at least equally important. Alan Choi shares his observations about the reporting system setup in a number of multi-national companies (page 48-49). The author indicates that this reporting system is dynamic and requires regular updates to cope with the latest understanding of activities of a drug.

A more successful healthcare system requires close co-operation amongst drug companies, regulatory authority, the general public, as well as patients. The necessity of joint effort to avoid the occurrence of ADR is exemplified in another article written by Kwok et al about the implementation of a medication reconciliation protocol in Queen Mary Hospital (page 50-52). Medication reconciliation is a formal process of identifying the most complete and accurate list of medications a patient has been taking and using that list to provide correct medications for the patient anywhere within the health care system. The authors point out that it will not work without the co-operation of patient.

Besides a good monitoring and documentation system, ADR may occasionally result from improper practices. For example, excess dosage due to improper use of spoons for measuring liquid medication as Tong wrote in page 62-63. The majority of the public are not well informed of the proper use of spoons in liquid measurement. Hence, it is pharmacist's responsibility to educate them so that undesirable effects could be avoided when high potent drugs are prescribed.

Of course, ADR can be avoided if comprehensive and extensive investigations are done for medicinal products. Herbal medicines are no exception; comprehensive studies on activity, assay method and quality control are absolutely required before they are dispensed to patients as a therapeutic material. In recent years, a herb, called *Scutellariae barbata* or *Banzhilian* in Chinese, has drawn lots of interest from medical professionals because of its reported effectiveness against infectious diseases and cancers.⁽⁴⁾ Through extensive researches and investigations, this herb has passed phase II investigations of clinical trials designed by the FDA. If everything goes well, it may be the first successful herb that receives official approval through a series of clinical trials with proven therapeutic effects. For a detailed description of this herb, please refer to page 66 – 69.

Adverse effects sometimes may originate from other things. The recent fatal death of some cancer patients after given a pill contaminated with fungal spores is an example.⁽⁵⁾ The fatal accidents have alerted most pharmacists in Hong Kong about the safety problem

of therapeutic beyond the drug per se. Although many pharmacists have already taken a one-day-intensive microbiology training workshop organized by both the Hong Kong Institute of Biotechnology and the Hong Kong Pharmaceutical Manufacturer's Association, to become a competent professional capable to handle microbial problems it is necessary to be further educated on other relevant subjects. Although this editor doesn't know how many pharmacists really understand the differences between two microbial control terms, i.e. "absence of specified microorganisms" and "absence of objectionable microorganisms" described in USP and in title 21 of the CFR regulation of USA, an article written by O'Toole and Cheung in page 64-65 is certainly good for those still confused. A practicing pharmacist who misunderstands these two terms could put himself/herself at risk when a job is carried out. Therefore, whoever doesn't know these two terms yet, you are urged to go through the content to make yourself familiar with these terms.

A lot of people claim that natural products are safe and good. Such statements are actually unscientific. Indeed, many reported cases about adverse drug events were related to herbs partly because of some unprofessional practices using the herbs. All of them, whether it was fatal or causing partial damage to a body, were either due to misunderstanding or malpractice. Amongst some latest examples spotted recently, a few cases are reported in this current issue. This editorial believes that the only effective way to stop such accidents from happening is by means of regulatory control. Public education and support of further research will also definitely help.

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Cheung Hon-Young
Editor-in-Chief
20th July, 2009

People Killed after Drinking Excess Amount of Alkaloids in Home Made Chinese Medicinal Wines

Date: February 5, 2009

A case of massive poisoning was reported in Mei Zhou Shi, Guangdong. After consuming the self made anti-rheumatism Chinese medicinal wine for lunch, four people developed symptoms of poisoning such as nausea, vomiting, seizures and numbness of the whole body. The victim who drank the most medicinal wine died despite efforts to save his life. Three of

the victims recuperated after 20 hours of life saving measures taken by doctors in the hospital. After investigation by the health authorities, it was found that the self made Chinese medicinal wine contained excessive amount of alkaloids which caused the toxic effects. Alkaloids suppress cardiac muscle cells and after consuming alkaloids in the amount

equivalent to 0.1 per cent of one's body weight, toxic effects will appear. Pang Ming Wai, a registered Chinese medicine practitioner in Hong Kong advised the public to seek the advice of a Chinese medicine practitioner before preparing their own Chinese medicinal wines.

Source: Apple Daily News

Budget for Procurement of Swine Flu Vaccine Endorsed

Date: June 9, 2009

On June 9, the Executive Council endorsed a vaccination program for human swine influenza. The program will involve procuring vaccines for health workers, children aged from six months to six years, seniors aged 65 and above, and people at higher risk of death and complications from swine flu due to pre-existing medical conditions. These four

target groups amount to about 2 million people. Since each person requires 2 doses, 4 million doses are required. The ExCo decided to order an extra 1 million doses for those people who want to pay for the vaccination. 500,000 people could benefit from this measure. This category of individuals will not be subsidized. Dr. York Chow said the 5 million doses are

insurance to safeguard public health in case there is an outbreak in Hong Kong. The total cost is estimated to be about \$700 million.

Source: <http://www.news.gov.hk/en/category/healthandcommunity/090609/html/090609en0500>

Probiotics Must Meet Europe's New Health Claim Laws

Date: April 2, 2009

Aside from gut health and immunity benefits probiotics are best known for being increasingly linked with cardiovascular, brain and nervous system benefits. A French health food consultancy company, Alcimed, estimated that the global market for probiotics in 2008 was worth about €10bn. But the market will soon be shaken up by the implementation of a tougher new European regulations, which only allow

a list of approved claims be used for probiotics by the end of January, 2010. Those rules state that only products that have an overall healthy profile can bear health claims. The company pointed out that the controversial regulation has about 4000 claims to be processed and the European Food Safety Authority (EFSA) has issued opinions on about 60 so far, including the rejection of a handful of probiotic dossiers that

failed to demonstrate causality for gut, immunity and other health benefits. Hence, the European Union nutrition and health claims regulations are presenting challenges for the probiotics industry. With these factors taken account of, Alcimed estimates a growth rate of four per cent per annum until 2013 when the market will be worth €12bn.

Source: Decision News Media SAS

Germany Highlights Contaminated Chinese Weight Loss Herbs

Date: April 10, 2009

Seventeen people have been poisoned by a Traditional Chinese Medicine (TCM) in the German cities of Freiburg and Göttingen since 2005, according to a German report. Writing in the current edition of *Deutsches Ärzteblatt International*, pharmacologist Dieter Mülle, Wolfgang Weinmann and Maren Hermanns-Clausen, said the product, which has been on sale over the internet, contained twice the permitted amount of the controlled substance, sibutramine, in Germany.

Sibutramine is an amphetamine-like

substance that inhibits the re-uptake of serotonin and noradrenaline in the brain. It typically goes by the name, Reductil in Europe, and was recently found to have contaminated a herbal Viagra product that has been recalled by the medicines regulator there.

That product, Jia Yi Jian was marketed as being "100% herbal", yet each tablet contained 68.1 mg of sibutramine and 50.06 mg of tadalafil when respective levels of only 15 mg and 20 mg are permitted in the UK. In the German case, lead author, Müller,

did not name the product in question but noted one adverse effect saw a 14-year old girl who had taken the slimming capsules along with atomoxetine and methylphenidate had to be admitted to hospital for psychiatric treatment for agitation and severe confusion.

Of the 17 people affected in the two German cities between 2005 and 2008, 15 were women. Most cases involved the botanical being used in combination with drugs.

Source: Decision News Media SAS

Biotech Centre Opens at Hong Kong Science Park to Boost the Life Science Industry

Date: April 23, 2009

Hong Kong Science and Technology Parks Corporation (HKSTP) has reinforced its commitment to the biotechnology industry with the opening of a dedicated Biotech Centre. The opening unveiled the 200,000-square-foot centre, incorporating two dedicated life science buildings, which provides some basic equipment and wet laboratory facilities

for shared use, technical engineering support and an SME centre. The latter will be an ideal home for small and medium-sized enterprises. The initiative was accompanied by the launch of a Life Science Acceleration Programme (LAP) jointly with Hong Kong's Innovation and Technology Commission (ITC), and the signing of a Memorandum of

Understanding (MOU) with a leading global pharmaceuticals company. Under the scheme, funds will be awarded under three programmes to incubatees for research assistance and acquisition of laboratory equipment, to help accelerate their growth beyond concept stage to attract venture capital.

Source: Hong Kong Science and Technology Parks Corporation

FDA Safety Changes: Epzicom, Trizivir, Tracleer

Date: April 29, 2009

On March 9, the FDA approved safety labeling revisions for abacavir sulfate and lamivudine tablets and abacavir plus lamivudine and zidovudine tablets (*Epzicom and Trizivir*; GlaxoSmithKline) to warn of the increased risk for potentially fatal hypersensitivity reactions (HSRs) in

patients who carry the human leukocyte antigen allele B*5701 (HLA-B*5701). The revised safety labeling was officially adopted to warn of the increased risk for potentially fatal hypersensitivity reactions in patients who carry the human leukocyte antigen allele B*5701 receiving

abacavir sulfate, the potential increased risk for myocardial infarction in patients receiving combination antiretroviral therapy, and drug interactions between ritonavir-boosted lopinavir and bosentan that preclude their coadministration.

Source: Medscape Medical News

China Clamps Down on Controversial Therapies

Date: May 30, 2009

China has issued a new regulation on clinical applications of medical technologies. The health ministry hopes that the new regulation, which came into effect in May, will put a stop to such unauthorised medical practices as stem-cell interventions and brain ablative surgeries. The new regulation divides medical treatments into three categories.

Type I and type II categories include those that have proved to be safe and effective, with type II therapies carrying higher risks and entailing potential ethical issues. Individual hospitals are responsible for overseeing type I interventions, whereas provincial health bureaus regulate those falling into type II category. More importantly, the new regulation bans

the use of xenotransplantation of stem cells, human somatic-cell cloning, and cross-species gene therapies in clinical application. The ministry will directly regulate so-called type III interventions—procedures that are risky, ethically controversial, and yet to be proven to be safe and effective. These include stem-cell treatments, gene therapies, and

brain ablative surgeries on people with mental health problems.

The ministry is in the process of convening an expert committee, consisting of officials, clinicians, scientists, and ethicists to detail the procedures of regulating type III interventions through a licensing system, says Ma Xudong, an official at the ministry's division of medical-service management. It will

issue technology-specific licences only to hospitals that have the capacity of applying a particular type of technology, such as stem-cell therapies, and will assess the safety and efficacy evidence of interventions on a case-by-case basis.

Within 6 months of the regulation coming into effect, hospitals around the country have to either stop providing unproven therapies or to apply to the ministry for

approval. Under the new regulation, any violations could lead to fines of up to ¥3000 (US\$430) and the suspension of technology and treatment licences. If necessary, hospitals and clinics may lose their permits to practise medicine for serious breaches.

Source: The Lancet, Volume 373(9678):1834 – 1835.
By Jane Qiu

WHO Announce H1N1 Global Pandemic

Date: June 1, 2009

The World Health Organization (WHO) raised the H1N1 global pandemic alert level to phase 6 on June 11. More than 70 countries have now reported cases of human infection. Many of the cases reportedly had links to travel or

were localized outbreaks. The WHO designation of a **phase 6** pandemic alert reflects the fact that there are now ongoing community-level outbreaks in multiple parts of world. It should be noted, however, that the WHO's decision

to raise the pandemic alert level to **phase 6** is a reflection of the spread of the virus and not of the severity of illness caused by the virus.

Source: WHO

Chinese Herbal Tea Found Adulterated with Western Drug Ingredients

Date: June 16, 2009

A spokesman for the Department of Health (DH) of HKSAR government said Chinese herbal teas sold by herbal tea shops were found to have been adulterated with western drug ingredients that may cause serious side effects. The spokesman said DH mounted a special operation to enhance surveillance of herbal tea shops following a case of herbal tea adulterated with western medicine in May.

Laboratory results on the samples taken from three different herbal tea shops in Tai Kok Tsui, Kowloon City and

Tai Wo Hau showed presence of western drug ingredients, either paracetamol or both paracetamol and chlorpheniramine.

Paracetamol is a pain killer which can cause liver damage when taken in high doses. Chlorpheniramine is commonly used for treating runny nose and allergy and is associated with side effects of drowsiness, dry mouth, blurred vision, nausea and constipation.

DH reminded the trade that sale of herbal teas adulterated with western

medication is an offence. Investigations are in progress.

Members of the public should immediately stop consuming the Chinese herbal tea from the Chinese herbal tea shops concerned. The spokesman said: "They should seek medical consultation if they don't feel well after consuming the herbal tea."

Source: Department of Health of HKSAR, China

Letter to the Editor

Date: May 15, 2009

Dear Chief Editor Mr. CHEUNG:
Re. Hong Kong Pharmaceutical Journal, Vol.16 No.1(Supplement) Jan - Mar 2009

I wish to thank you & all the editorial staff with the Journal in publishing the said Supplement attaching to the said Journal.

Date: June 19,2009

Dear Anthony,
Thank you for your encouraging words. It's nice to know that our efforts are appreciated by others. We are really glad that you and other community pharmacists find the consolidated list

Many, many years ago, I had been hoping that someone knowing to use the computer applications would kindly prepare a hand book in the nature as set out in the Supplement. Now it is at our hands. It definitely would give great help to candidates preparing for their Pharmacist's Registration Exam & pharmacists especially in Community

of poisons, antibiotics and dangerous drugs useful.

We have an OTC section in the HKPJ. If you have time, please write an article on OTC drugs and send it to

Service etc.

Again my sincere appreciation to all who had contributed & made this Supplement possibly available.

Regards,
Anthony LAU
Community Pharmacist.

us. We would be happy to publish it. Please pass along the message to other community pharmacists.

Regards,
Mary CHENG
Publication Manager

A Multi-Dimensional Perspective Functions of Adverse Event Reporting System in Pharmaceutical Companies

CHOI, Alan

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ABSTRACT

Adverse Drug Reaction (ADR) reporting is an important tool for collecting the safety information so that the pharmaceutical companies could meet the ethical and legal responsibilities when collecting and analyzing the safety information. It also helps them to understand the product safety profiles and allow communication of accurate information to regulators, prescribing physicians, and consumers. Nowadays, although ADR reporting system is currently used, there are still many drug-safety related incidences. To improve the problem, both pharmaceutical companies and the Health Authority need to contribute and work together so that a win-win situation could be achieved. Furthermore, education of the healthcare professionals and the general public would also be a benefit to everyone; the pharmaceutical companies and the healthcare professionals could both earn the trust from the public and consequently, patients and consumers could use drugs safely.

Keywords: safety; adverse event; adverse drug reaction; ADR reporting system

INTRODUCTION

The guidance notes for adverse drug reaction (ADR) reporting in Hong Kong has recently been updated and this was presented in a previous article of HKPJ (Vol 15, No 2, Jul-Sept 2008, pp49-52).⁽¹⁾ From what has been described, there are several interesting questions which come to mind: why do we need to provide the safety information of the investigational drug to the Department of Health (DoH) when the compound is still under investigation in clinical trials? How could we add more value to the drug safety profile of the marketed medicine if we submit the ADR cases to the regulatory authorities? What is the rationale behind the ADR system?

If we try to take an overview of our current ADR system, there is always a question on whose responsibility it

is to report the adverse events of the medicines - is it the responsibility of the pharmaceutical companies or the Health Authorities? In general, there is no certain answer, but most would undeniably think that pharmaceutical companies should be the one most responsible regarding these kind of matters. Therefore, this thought caused most of the pharmaceutical companies to report all adverse events (AEs) to the health authorities and resulted in it being compulsory for all pharmaceutical companies to report any spontaneous AE case to the regulatory authorities, such as the US FDA.⁽²⁾ This outlines the milestone of the basis of ADR reporting system in the areas of the general public and healthcare professionals.

With the consensus of more than 30 Collaborating Centers of the World Health Organization (WHO) International Drug Monitoring Centre (Uppsala, Sweden), the definition of adverse event has been outlined as followed:⁽³⁾

"Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product."

Therefore, any adverse event noted should be reported to the regulatory authorities, even though the causality of the event may not be fully established; that is whether it is due to the suspected drug or not. The terms adverse event (AE) and adverse drug reaction (ADR) are easily confused. The definition of adverse drug reaction has also been outlined in the above consensus of the Collaborating Center of the WHO International Drug Monitoring Centre:

"In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic

dose(s) may not be established: All noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions (ADR).

Regarding marketed medicinal products, a well-accepted definition of an adverse drug reaction in the post-marketing setting is found in WHO Technical Report 498 [1972] and reads as follows:

A response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function."

Subsequently, the DoH in Hong Kong also requires pharmaceutical companies to report all serious unexpected ADR cases. For the marketed products which meet the category of New Chemical Entity (NCE) and if the approval of the product is granted after March 2005, pharmaceutical companies must report any serious unexpected AE to the DoH, but excluding AE reports from medical devices at the moment.⁽⁴⁾ These kinds of medical device AE reports can be reported to DoH in Hong Kong voluntarily until the registration of the medical device becomes fully compulsory. In addition, any serious unexpected AE cases of the investigational products are submitted to the DoH (local cases only) and the Ethics Committees (both local and overseas) within the timeline as well (7 calendar days for death and life threatening cases and 15 calendar days for other serious unexpected cases).

ADR REPORTING SYSTEM

Besides gaining insight into the development of the ADR reporting system, we also need to know what the benefits are for reporting the AE cases of medicine. There is no doubt that this data could become evidence for the safe use of medicines in humans and also allow pharmaceutical companies to sustain their marketing licenses. This data can also support the safe use of drugs on a

scientific basis, hence earning the trust of the public. As the quality of life has been steadily improving in our society, everyone is also very concerned about the safe use of drugs and medical devices. People are concerned about how the drugs can help them survive deadly diseases, and also they think of ways to use medicine as a supplement to improve and maintain their quality of life.

From the teratogenesis case of newborn babies due to the use of thalidomide in 1961 to the recent death case of Jesse Gelsinger in 1999, health authorities have discovered that there is a lack of an AE reporting system to control and monitor the safety of drugs.^(2,5) As a result, thousands of AE cases may not be reported during the period when the clinical trials are conducted. Therefore, pharmaceutical companies have learnt a lesson from those unfortunate cases and make it their ethical and legal responsibility to report any AE to regulatory officials, even though that information may not contribute to the successful approval of new drug registrations. These efforts might even result in wasting money, time, and resources after many years of research.

Apart from the incidents of clinical trials, post-marketing surveillance is also an important system to obtain safety information after the drug has been launched into the market. This safeguards and prevents any drug launched into the market with approval but with safety issues from being under-reported. Vioxx from Merck Co. was widely used for pain after the license was granted from FDA in 1999.⁽⁶⁾ However, this drug triggered many concerns worldwide since the post-marketing research (VIGOR study) indicated that patients taking this drug with a high dosage and for a long time may suffer from increased risk of heart attack and stroke. Vioxx was, therefore, one of the drugs to be withdrawn from the market globally in 2005 because of the risks of drug safety. Although there is no evidence to show that the pharmaceutical companies mishandled the safety information during clinical trials and post-marketing surveillance, this case has once again made the public feel concerned regarding the safe and ethical use of drugs. This has also led the pharmaceutical industry to re-consider the importance of drug safety and the instigation of a good plan including clinical trials with robust safety systems and databases.

Managing the demand of safety documents is challenging. Therefore, the adverse event reporting system (AERS) is one of the most useful tools for regulatory authorities to manage all sources and information.⁽⁷⁾ AERS is the computerized database to help the FDA

monitor safety issues of marketed drugs and in return differentiate signals and report to the regulatory authorities if there are safety concerns that are related to the marketed drugs worldwide.⁽⁷⁾ This system may also guide both the pharmaceutical companies and the manufacturers to follow rules of certain kinds, such as the ICH guidelines. If there are any concern being identified and noted, the FDA could request the related pharmaceutical companies and manufacturers to initiate the epidemiological studies, or even to recall and withdraw a certain marketed drug if necessary. On the other hand, the EMEA in Europe also monitors the safety of drugs in a rolling five-year window and reviews again five years after the drug has been approved and registered.⁽⁶⁾

DISCUSSIONS

Therefore, the ADR reporting has a paramount function to monitor the safe use of drugs. Pharmaceutical companies and the regulatory authorities can use it as the standard of AE signals. However, this system is not yet the perfect one.

Spontaneous safety reporting could only be initiated when pharmaceutical companies obtained the safety information externally, mainly from health professionals and consumers. What would happen if they never report any AE after taking drugs?⁽⁸⁾ If the public does not know the function of the safety reporting system, no matter how good the system is, it can not function effectively and efficiently. Therefore, the awareness of safety reporting should be increased to the public. The local regulatory authorities should also have a modern reporting system and a standard communication platform regarding drug safety issues; a simplified system to provide any drug safety information is always an advantage to share the information between the regulatory authorities and the public. We also need to improve the culture of health professionals to report certain safety issues and to ensure that they understand why the details they report are highly important to the pharmaceutical companies.⁽⁶⁾ Educating both the health professionals and the public is the best way to resolve the problem. However, in reality, it is not possible due to the labor-intensive process. It may be a good idea to incorporate drug safety into the curriculum of medical or medical-related students in universities so that they can be informed and get experience with it at an earlier stage.

Another weakness of the adverse event system is that it is difficult for anybody to definitely confirm the causality of AE with the marketed drugs. This will result in the health professionals

and the consumers not reporting to the pharmaceutical companies.⁽⁸⁾ On the other hand, information that is provided from the reporters may not be detailed enough to evaluate the AE. Therefore, many scientists are working on a better system to report AE cases. A user-friendly system is always an advantage to obtain more safety information from the public and they could complete any AE reporting by providing essential information to pharmaceutical companies and regulatory authorities.

CONCLUSION

To conclude, safety AE reporting system is one of the ways to ensure the safe use of drugs in the public. Full utilization of this system could enhance the safety reporting overall. Therefore, a win-win situation could be achieved; pharmaceutical companies have fulfilled the safety responsibilities and the public could understand more about drugs. However, we cannot only promise and rely on this current system. To improve the problem, pharmaceutical companies surely need to work hard together with the public. It is not only the responsibility of the industry, but also the health professionals and consumers. Continuous and never-ending improvement is the only way to keep track on our drug safety, not just only in our local area but also worldwide.

Author's background

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Implementational Experience of Medical Reconciliation in Queen Mary Hospital

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ABSTRACT

Medication Reconciliation was initiated in the Queen Mary Hospital in 2008. The ultimate goal of the service was to enhance patient medication safety by compiling the complete and accurate medication list of patients. Drug-related problems would be identified through the process of medication reconciliation and clinical pharmacists' input. Patient medication safety could then be enhanced by addressing and solving these problems. Promulgation of the service was advocated with the expectation of further enhancing patient medication safety. Our preliminary monitoring of the service reveals that medication reconciliation could prevent the occurrence of adverse drug events.

Keywords: *Medication Reconciliation; Clinical Pharmacy; Adverse drug events; Drug-related problems*

INTRODUCTION

In 2007, experts from the Joint Commission International (JCI) of the United States visited hospitals of the Hospital Authority (HA) to review the standard of the hospitals. The Queen Mary Hospital had a trial evaluation of various aspects of its service and some of them were highly rated. Recommendations on medication safety were received from these experts. Implementation of medication reconciliation (MR) was one of these recommendations as a means to enhance patient medication safety. Medication reconciliation is actually one of the National Patient Safety Goals (NPSG) of the JCI on enhancing medication safety.^(1,2) After careful evaluation of the service, medication reconciliation was introduced in March 2008, with Queen Mary Hospital being the first hospital in Hong Kong to introduce the practice. A busy medical admission ward was selected as the initial place to start MR work. It was thought that the very high turnover of patients in such a unit would be a major catalyst for medication incidents, and hence would be an ideal place to initiate MR.

What is medication reconciliation?

Medication Reconciliation (MR) refers to a proactive process by the healthcare team, with an aim to obtain a complete, accurate and up-to-date list of medications at each transition point of care. This practice is being endorsed by an increasing number of countries as an important strategy to improve medication safety. For a typical episode of hospitalized care, these transitions would occur at admission, intra-hospital and inter-hospital transfer and the eventual discharge of patient to convalescent or home care. It involves the taking of a thorough medication history and then comparison with the admission medication orders. Discrepancies identified during these processes are followed up with the prescribing doctors and appropriate actions are undertaken to resolve or clarify the discrepancies.⁽¹⁻³⁾ Reports have shown that patients are generally more vulnerable to medication errors during the transitions of care and even reports of fatality have been associated with medication reconciliation failure.⁽⁴⁾ Medication reconciliation is therefore a critical process in reducing medication errors and adverse drug events to enhance patient safety.⁽⁵⁾ From early experience of other countries, implementation of medication reconciliation together with a series of interventions could reduce the rate of medication errors by 70% and reduce adverse drug events by 15%.⁽⁶⁾

WHY MEDICATION RECORDS ARE INACCURATE?

Although the computer system in HA could actually provide a fairly comprehensive medication history for all patients under HA; many local issues, however, could undermine the usefulness of the HA medication record. For example, doctor-shopping is a common habit in HK, as they are often keen for a speedy 'cure' or are impatient when their therapies bring about a less than timely 'resolution' of their symptoms. Medications may be adjusted or even changed by private doctors which are never captured by the HA computer system. Moreover, despite

a good working relationship between the public and private doctors in Hong Kong, where the sharing of information is never impeded on request, a complete free-flowing of information or the full sharing of information on a common platform is still non-existent at present. Even if patients may be attending several clinics only within HA, duplications and even omissions are still conceivable as thorough review of medications from the corporate drug history for every patient is impossible in these busy clinics.

People in Hong Kong are increasingly taking ownership of their own health, with an ever greater tendency to self-medicate with over-the-counter (OTC) products. Whether or not some of these self-medicated OTCs clashing with the prescribed regimens is unknown to the HA system. Consistent with these behaviours that could lead to medication discrepancies/incidents would be patients' own, often erroneous, health beliefs. They may self-adjust or even discontinue their prescribed therapies, for different reasons. All the contributory factors described, though may not be unique to Hong Kong, do compound the medication management issue and add considerably to the difficulties of its proper management. It could also explain why the HA medication record is not completely accurate, despite possibly being the most comprehensive patient medication record available in the territory.

THE IMPLEMENTATION OF MEDICATION RECONCILIATION

Although as previous described, the HA computer record may not be complete, it does serve as a backbone on which a complete, accurate and up-to-date record should be built. The clinical pharmacist would review the computer record first to compile an initial medication list, as shown in Figure 1, before proceeding to interview the patients or their care-givers (Figure 2). If the patient is an old age home resident, the clinical pharmacist would contact the old age home staff to clarify the drug list. When discrepancies

are found, attempts would be made first to clarify if they are intentional or unintentional. This is because they could be unintentional discrepancies caused by misleading computer record, or they could be intentional changes of medications not documented properly on previous consultations. Normally, clinical pharmacist will review the complete

medical record of the patients and then compare the initial medication list with the first MAR prescription.

If any discrepancy is found, the clinical pharmacist will first look at the medical record to see if the difference is intentionally made by the prescriber due to changes in current clinical conditions.

The second possible source in retrieving information to explain the difference would be the laboratory and other related test results. These data could also cause the prescriber to make changes on the medications. Indeed, the prescriber may have other reasons to change the medications. In that case, close working relationship with doctors and nurses is very important in helping to identify the causes of changes.

During the hospital stay, the clinical pharmacist is expected to continuously monitor the medication changes, commonly by participation in ward rounds, such that any changes on the medication regimen are known and managed. Eventually at the point of discharge, a final reconciled medication list should be passed on to the next point of care. In the current HA computer system, a function to generate and document a reconciled medication list has not been built in. The clinical pharmacist currently has to self-prepare a printed final reconciled medication list and have it filed in the medical file. To supplement this, the patient's care-givers, e.g., old age home staff, will be contacted by phone to notify them of an updated and reconciled medication list. When possible, patients or their family would be interviewed with a detailed discharge medication counselling given.

THE ROLE OF PHARMACIST IN MEDICATION RECONCILIATION

MR process is generally initiated by one of the members in the health care team and facilitated by other members of the team. Different members of the health care team could contribute their expertise. With broad drug knowledge and skills in consolidating drug history from different sources, clinical pharmacists are ideally equipped to reconcile the medications of a patient. Nursing colleagues could provide precious information about patient care issue, for example, the best care-givers to obtain information from. Doctors also play a critical role in the process as they represent the point of reference for any changes in the patient medication regimen. With the cooperation of different disciplines, effective MR could be achieved even if the medication history was chaotic to start with.

Considering that MR largely involves preventable medication problems, the Department of Pharmacy at Queen Mary Hospital took the initiative of starting the MR project. The benefit of MR initiation by pharmacy may be two folds. First, the clinical pharmacist is generally recognized as the drug expert within the

The form is titled 'Allied Health Discharge Note' and is from Queen Mary Hospital. It contains the following information:

- Hospital Authority:** Queen Mary Hospital
- Case No.:** [Redacted]
- HKID:** [Redacted]
- Name:** [Redacted]
- DOB:** 05/02/1919
- Sex:** F
- Age:** 90y
- Ward:** B2
- Spec:** MED
- Admission Date:** 10-02-2009 19:19
- Admission Source:** A&E
- Transfer From:** GMH
- Discharge Date:** 13-02-2009 17:21
- Discharge Type:** CONV.
- Discharge To:** GH

Allied Health Discharge Note:
MEDICATION RECONCILIATION RECORD (PILOT RUN)

Change of medications:

1. Step up - Imdur from 30mg daily to 60mg daily
2. Add - PO Augmentin 750mg tds since 11.2.09 11a.
3. Off - Slow K 800mg BD

Current Medication List:

1. PO Lasix 20mg daily
2. CalCO3 1g daily
3. Digoxin 62.5mcg daily
4. Carlia 100mg daily
5. TNG SL tab pm
6. Plavix 75mg daily
7. Pariet 20mg daily
8. Imdur 60mg daily
9. PO Augmentin 375mg tds
10. Dologelic 1tab QID pm
11. Spironolactone 12.5mg daily

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Figure 1. A typical form adopted by Queen Mary Hospital for the purposes of medication reconciliation.



Figure 2. Medication reconciliation in practice. A patient was being interviewed by a clinical pharmacist for her medication history.

multidisciplinary health care team, a role of medication reconciliation that is part of good medication management is most suitable and certainly more efficiently taken up by the clinical pharmacists. Second, there is an additional benefit if a clinical pharmacist is to take care of MR. This is for reason that while carrying out MR, a clinical pharmacist can exercise his/her considerable clinical pharmacy expertise in providing full pharmaceutical care to the patients concurrently. It involves pharmaceutical input across the entire medication use process. This in brief encompasses advice on therapeutic choices; monitoring of therapy for appropriate response, emergence of adverse effects, drug interactions; appropriate administration in terms of dose, route, rate, compatibility and stability; and counselling of patients to enhance their understanding of therapies and regimen compliance. These are all additional benefits to be realized if the clinical pharmacists within the health care team were responsible for MR.

CASE EXAMPLE OF MEDICATION RECONCILIATION

Although HA provides medical care for more than 80% of population in HK, patients always have their rights to choose where to receive their medical care. A 72 years old lady was admitted to the medical admission ward presenting with problem of coffee ground vomiting. An oesophagogastroduodenoscopy (OGD) was arranged. After the doctor had examined the OGD result, the patient was diagnosed to have upper gastrointestinal bleeding and an oral proton-pump inhibitor (PPI) was prescribed.

From the computer record, the patient should have no chronic medication. The doctor then planned to discharge the patient with a prescription of PPI. When the clinical pharmacist interviewed the patient, it was found that

the patient was actually taking chronic medications. She had been buying some over-the-counter drugs from community pharmacy and didn't follow up with the prescribing private doctor recently. In such situation, the chronic medications of this patient could not be retrieved from HA medication record or record of her private doctor. There was no dispensing record available in local community of non-prescription medications. The only way to identify her chronic medications was to inspect the actual drugs she was taking, though it cannot always be done. Luckily, her relative brought back her home medications which were identified to be Aspirin and Simvastatin. For this particular event, it's of crucial importance that the clinical pharmacist could identify this drug-related problem, to know that the patient was taking aspirin, to inform her doctor about that, and to educate patient to stop this drug after having an agreement with her doctor.

RESULTS

In the first 12 months of service (from March 2008 to February 2009), 3317 patient records (31%) out of 10,700 records were reviewed. As shown in Figure 3, 435 of these reviewed records (13% of records) contain unintentional discrepancies. Some minor discrepancies, like missing strength of drugs or dosage form, were excluded. Additionally, during this period, 600 clinical pharmacist interventions (18%) were made at the same time when MR was carried out. These interventions were on dosage adjustment based on renal function, alert on possible adverse drug reactions, possible drug interactions and discrepancies on medication profiles. When interventions were made, clinical pharmacists often discuss with the prescribing doctors to decide on the best solution for drug therapies. Since the rapport within the health care team has been good, most

of the suggested interventions were accepted by the prescribing doctors.

DISCUSSION

After the initial implementation of Medication Reconciliation in Queen Mary Hospital for one year, promising results with great acceptance and recognition by other health care professionals were received. Unique pharmaceutical inputs include drug formulation, dosing in patients with renal or hepatic impairment, pharmacokinetic properties of drugs and special effort in maintaining complete medication record could contribute a lot to the health care team. Investigating home medications and drug compliance problems are also very helpful to nurses in preventing and solving drug-related problems. It is also very meaningful to provide detail drug counselling to patients to provide proper drug education.

Early results of the service have attracted funding to support further expansion of the service and enlisted the information technology team to upgrade the computer system. It is hoped that further expansion of the service could benefit more patients, enhance the quality of care and establish a clinical role for clinical pharmacists in patient medication management.

Author's background

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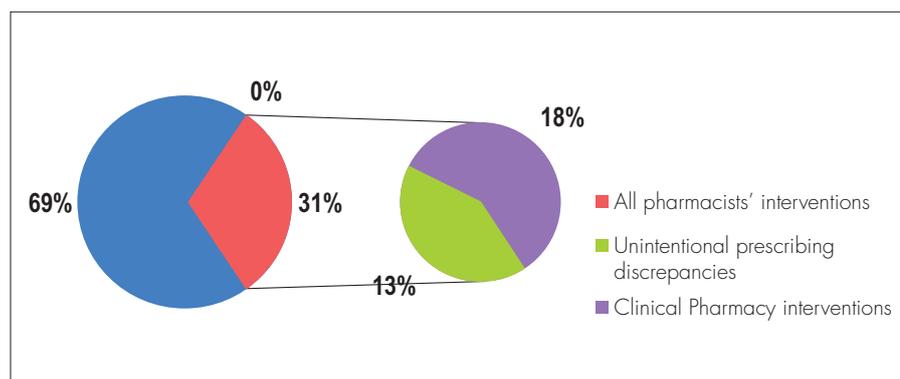


Figure 3. Distribution of all pharmacists' interventions

Transform dis-oriented, loose lipids into a well-structured, integrated and cohesive bilamellary lipid barrier

LIQUID CLEANSER

Supportive Cleansing in Skin Disorders



Revolutionary Concept in Skin Care

- **sebamed** pH5.5 activates the **skin surface hydrolases** (pH-dependent enzymes) to repair & build up own bilamellary lipid barrier and hence restore the healthy acid mantle.
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- **Drug free**
- **Non-comedogenic**

Overview on the International and Local Situation of Smoking Cessation

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ABSTRACT

Smoking is an addiction with potentially lethal consequences. It does not only affect the smokers, but also non-smokers via second-hand smoking. It is estimated that 100 million people died worldwide in the 20th century due to smoking-related illnesses. This includes deaths in smokers due to cancer, cardiovascular and respiratory disease. Smoking also has serious economic consequences e.g. direct (healthcare and fire damage) and indirect (productivity losses due to morbidity and mortality). The global consensus that we must fight the tobacco epidemic has been established by more than 150 parties to the World Health Organization (WHO) Framework Convention on Tobacco Control. The WHO has given countries a roadmap into a global reality through the MPOWER guideline. Prompt action is crucial. As part of the healthcare professional team, pharmacists must contribute to this worldwide effort. Hence, the position of WHO in tobacco control and antismoking initiatives by the Department of Health of Hong Kong SAR government are reviewed. The barriers to smoking cessation, the different smoking cessation interventions and the cost-effectiveness of smoking cessation therapies are addressed

Keywords: Smoking cessation; WHO policies; Department of Health (DoH); Nicotine Replacement Therapy (NRT); Bupropion; Varenicline

INTRODUCTION

Tobacco use is the leading

preventable cause of death in the world.⁽¹⁾ According to the WHO Reports on the Global Tobacco Epidemic in 2008, tobacco epidemic has caused 100 million deaths worldwide in the 20th century. If no urgent actions are to be taken, there will be more than 8 million deaths every year by the year 2030.⁽²⁾

Clinical consequence of tobacco smoking represents a remarkable burden to public health and preventive medicine, as tobacco smoking is associated with the development of cardiovascular disease, lung diseases and cancers.⁽³⁾ The benefits of smoking cessation are unquestionable. Therefore, as a healthcare professional, we must take part in the promotion and education of smoking cessation.

Smoking – a potentially lethal addiction

When tobacco products are inhaled into the lungs, nicotine is delivered to the brain immediately (Figure 1 and 2). Nicotine alters the function of several central nervous system (CNS) neurotransmitters. It binds to and activates the nicotine acetylcholine (nACh) receptors which are widely distributed in the brain, and the primary receptor is the $\alpha\beta 2$ nicotine receptor in the Ventral Tegmental Area (VTA) of the brain (Figure 3). After nicotine binds to the $\alpha\beta 2$ nicotine receptor in the VTA, it results in a release of dopamine in the Nucleus Accumbens (nAcc) which is believed to be linked to the reward system.

This perhaps explains why some tobacco users will want to quit but will be unable to because of their dependence

on nicotine. Tobacco products deliver nicotine to the brain immediately after smokers inhale. But the effect of smoked tobacco last only a few minutes, smokers experience withdrawal symptoms unless they continue to smoke.⁽⁴⁾

Impacts of smoking

Smoking increases the risk of death from

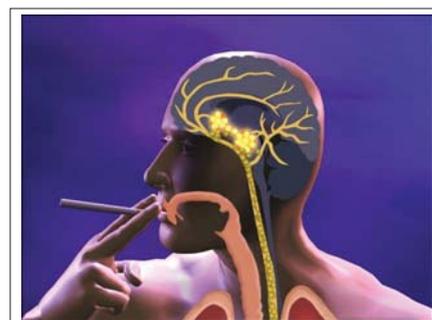


Figure 1. Inhaled tobacco enters the lung

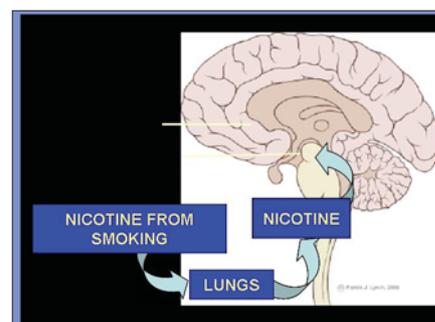


Figure 2. Nicotine is delivered to the brain

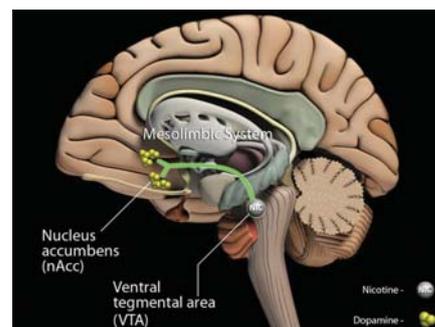


Figure 3. The $\alpha\beta 2$ nicotine receptor in the VTA

cancers of the mouth, esophagus, pharynx, larynx, lung, pancreas and bladder; from chronic obstructive pulmonary disease and other respiratory diseases; from vascular diseases; from peptic ulcer; and from cirrhosis, suicide, poisoning and tuberculosis.^(5,6) Much of the excess mortality associated with smoking can be avoided by quitting smoking.⁽⁷⁾

Six policies of smoking cessation by World Health Organization⁽²⁾

WHO is helping countries fight tobacco use and the tobacco industry's marketing of its deadly product. In May 2003, the WHO World Health Assembly unanimously adopted the WHO Framework Convention on Tobacco Control, one of the United Nations' most widely embraced treaties – and the world's first against tobacco- in order to galvanize actions at the global and country level against the tobacco epidemic. This treaty provides the context for effective policy interventions to reduce the use of tobacco. Leaders around the globe

have begun to recognize that tobacco use is an epidemic that can and must be confronted and stopped. Some countries have started mobilizing to protect their citizens and their economies. WHO has introduced the MPOWER package of six proven policies:

- Monitor tobacco use and prevention policies,
- Protect people from tobacco smoke,
- Offer help to quit tobacco use,
- Warn about the dangers of tobacco,
- Enforce bans on tobacco advertising, promotion and sponsorship, and
- Raise taxes on tobacco.

THE DEPARTMENT OF HEALTH OF THE HONG KONG SAR SMOKING BAN AND GOVERNMENT'S HEALTH PROMOTIONS⁽⁸⁾

The Department of Health (DoH) of the Hong Kong SAR has fully adopted the WHO's MPOWER guideline in its anti-smoking policy and here are the summary of actions taken:

1. Monitor and Protection

The DoH has been monitoring the pattern and prevalence of tobacco use and the table (Table 1) below shows the prevalence of current smokers (aged ≥15).

The Smoking (Public Health) Ordinance (Cap. 371) was first enacted in 1982 in Hong Kong with several amendments subsequently. It is currently the major part of the legal framework on tobacco control in Hong Kong.

With effect from 1 January 2007, statutory no smoking areas have been extended to cover the indoor areas of all restaurant premises, indoor workplaces, public indoor places, and some public outdoor places in accordance with the amended Smoking (Public Health) Ordinance (Cap. 371). No person shall smoke or carry a lighted cigarette, cigar, or pipe in no smoking areas. Additionally, various posters (Figure 4) have been used by the



Figure 4. Implementation posters used by the Department of Health

DoH since the implementation of non-smoking areas.

2. Offer Help on Smoking Cessation

At present, there are a number of smoking cessation clinics run by the DoH, the Hospital Authority and various organizations. Some private doctors and private hospitals also provide smoking cessation services that smokers may join. Smoking cessation hotline (Figure 5) has also been set up to aid smokers who are willing to quit. In addition, the hotline also helps to provide information on smoking cessation and pharmacological treatments.

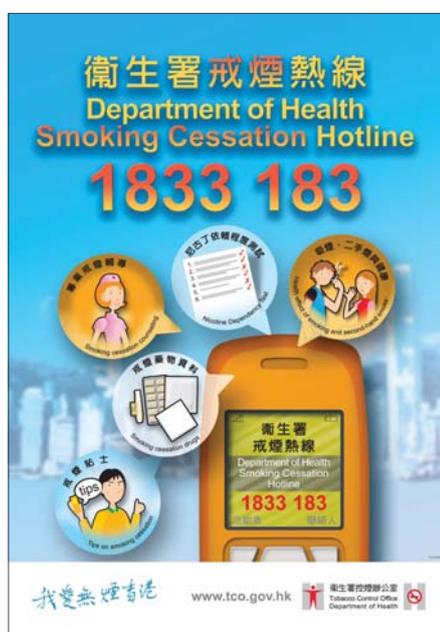


Figure 5. Posters of the Department of Health, Smoking Cessation Hotline

3. Warn About the Danger of Tobacco Through Education and Health Promotions

The Tobacco Control Office of the DoH has been promoting a smoke-free culture to the public through the mass media, in order to raise the public awareness on the hazards of smoking and secondhand smoke. In order to assist control officers of no smoking areas to adopt and implement a smoke-free policy and to promote a smoke-free culture, the following activities have been promoted:

- Seminars and talk are organized by the Tobacco Control Office of the DoH, such as seminar on smoking ordinance, and other smoking cessation health talks and seminars.
- Health education materials include Tobacco Control Bulletin, implementation guidelines, pamphlets, posters, no smoking signs and audio-visual materials. (Figure 6)

4. Enforce Bans on Tobacco Advertising

The Smoking (Public Health) Ordinance (Cap. 371) prohibits the exhibition of tobacco advertisement in printed publications, in public places, by film, or on the Internet. Health Warning on Cigarette Packet and Retail Container with brief description of the specifications of pictorial and graphic contents of the health warning on cigarette packet and retail container has been implemented, such as “Smoking Causes Lung Cancer”, “Smoking Kills”, “Smoking Harms Your Family”, “Smoking Causes Peripheral Vascular Diseases”, “Smoking May Cause Impotence”, “Smoking Can Accelerate Aging of Skin” (Figure 7).

5. Raise Taxes on Tobacco

Recently, the HKSAR Government financial policy has also increased the tobacco tax, with the intention to help smoking cessation. The Dutiable

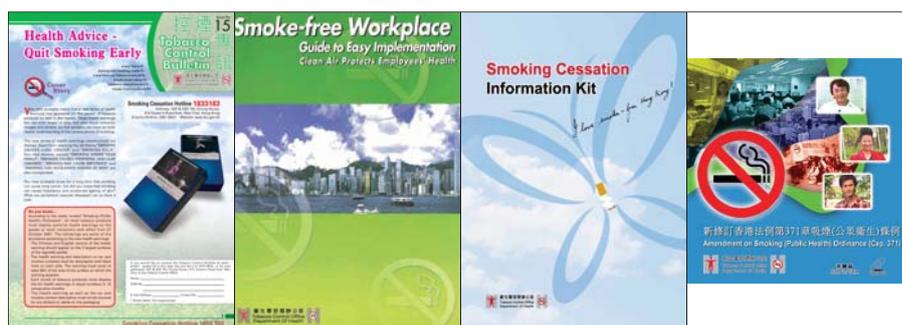


Figure 6. Various health bulletin, Smoke Free Implementation Guideline, Audio-visual materials and information booklet developed by the Tobacco Control Office of the Department of Health, the HKSAR.



Figure 7. Pictorial and graphic contents of health warnings that are mandated to be included on the tobacco product packets

Table 1. Prevalence of current smokers aged 15 and above in Hong Kong, Department of Health, HKSAR

Year	1982	1984	1986	1988	1990	1993	1996	1998	2000	2002/2003	2005	2007/2008
Daily cigarette smokers[1]	23.3	18.7	17.4	16.8	15.7	14.9	14.8	15.0	12.4	14.4	14	11.8
Ex-daily cigarette smokers[2]	#	3.7	3.2	3.2	2.3	2.9	4.8	3.8	3.8	2.7	4.5	5.1

[1] "Daily cigarette smokers" referred to those persons who at the time of enumeration had a daily cigarette smoking habit (although they might not smoke on certain days because of illness or other reasons)

[2] "Ex-daily cigarette smokers" referred to those persons who previously had a daily cigarette smoking habit for a continuous period of six months or more but had given it up at the time of enumeration

Data not available

Commodities Ordinance (Cap.109) also has included taxation and duties of tobacco sales, to help to cut tobacco use.

BARRIERS TO SMOKING CESSATION⁽⁹⁾

Barriers to the provision of cessation services among clinicians serving medically underserved communities include the following themes, which in some aspects were found to be peculiar to providers caring for the underserved:

- Lack of time
- Patient unreadiness to change
- Inadequate patient resources
- Inadequate provider resources
- Inadequate cessation clinical skills

SMOKING CESSATION INTERVENTIONS

Tobacco smoking is a highly addictive behavior: even after an acute myocardial infarction, half of the patients continue to smoke. Current smoking cessation interventions include counseling and behavioral support, as well as pharmacological treatments.

1. Non-pharmacological interventions

a. Counseling and behavioral intentions

The role of the doctor can be critical in the identification, evaluation, follow-up and possible referral, to smoking cessation clinics. Evidence suggested that doctors who intervene with smokers have an impact on their cigarette smoking behavior. Brief advice to quit smoking by doctors resulted in higher cessation rates compared to those who received no such advice.^(10,11) (Table 2 shows some basic patient assessment and counseling tips)^(12,13,14)

b. Tobacco withdrawal

A portion of smokers may quit on their own without any assistance (i.e. "cold turkey") and this is associated with the appearance of withdrawal symptoms. These symptoms begin within hours of the last cigarette and are in the maximal intensity the first week. Most of the affective symptoms then resolve over 3 or 4 weeks, but hunger can persist for several months. Cravings, sometimes intense, can also persist for many months, especially if triggered by situational cues.^(15,16,17)

2. Common pharmacological interventions

Pharmacologic support for smoking cessation has been available for a long time, with an increasing important role. The main purpose of the current drug therapy is to ameliorate the symptoms and signs of acute nicotine withdrawal.⁽¹⁸⁾ Pharmacotherapy is significantly more effective in achieving abstinence than placebo or "cold turkey".

a. Nicotine replacement therapy (NRT)

NRT was the first successful pharmacological interventions for nicotine dependency and is now widely employed. The main mode of action of NRT is thought to be the stimulation of nicotine receptors in the Ventral Tegmental Area (VTA) of the brain and the consequent release of dopamine in the Nucleus Accumbens (nAcc). NRT is supplied in several forms: patch, gum, inhaler, nasal spray and lozenges. Favorable features of these medications are: (a) effectiveness, (b) easy to use, (c) readily available, and (d) inexpensive.⁽¹⁹⁾ (Table 3 below summarizes the types of NRT available and the disadvantages.)

b. Varenicline

Varenicline is the first partial agonist of the $\alpha 4\beta 2$ nicotine acetylcholine receptor to be developed.⁽²¹⁾ The efficacy of varenicline in smoking cessation is a result of its' binding with high affinity and selectively at the $\alpha 4\beta 2$ neuronal nicotinic acetylcholine receptors. Nicotine competes for the same human $\alpha 4\beta 2$ nACh receptor binding site for which varenicline has higher affinity. Therefore, varenicline can effectively block nicotine's ability to fully activate $\alpha 4\beta 2$ receptors

Table 2. Patient assessment and counseling tips	
Patient assessment and Counseling topics	
-	Determine the patient's preparedness to quit.
-	Quantify the patient's degree of nicotine dependence in order to determine appropriate medication and dose.
-	Inform patient of the symptoms of nicotine withdrawal. Have him/her monitor these symptoms and actively report the symptoms.
-	For patient taking concurrent medications that may be affected by smoking cessation, inform him/her of symptoms of medication toxicity.
-	Counsel patient on the correct chewing technique with nicotine gum (jaw pain and hiccups develop, in part, due to poor technique).
-	Counsel patient to reduce caffeine consumption after smoking cessation in order to avoid the effects of excessive caffeine. (Smoking increases caffeine metabolism by approximately 50-60%)
-	Provide continuous support and feedback to the patient throughout the quit attempt.

and the mesolimbic dopamine system, the neuronal mechanism underlying reinforcement and reward experienced upon smoking.⁽²²⁾

c. Other oral smoking cessation (i.e. bupropion)

Bupropion hydrochloride, the atypical antidepressant phenylaminoketone, is the first non-nicotinic containing agent approved by the FDA for smoking cessation in 1997. Bupropion is a selective inhibitor of the neuronal reuptake of catecholamines (noradrenalin and dopamine) with minimal effect on the reuptake of indolamines (serotonin) and no inhibitor effect on monoamine oxidase. Although not proven, its mechanism of action in the treatment of nicotine dependence is likely to be related to reduced re-uptake of dopamine in the mesolimbic system and reduced reuptake of noradrenaline in the locus coeruleus.⁽²³⁾ Bupropion is available in a 150mg tablet for oral administration and the initial recommended dose is 150mg per day everyday, and slowly titrate the dose upward to a maximum of 150mg twice daily (300mg per day). The common adverse events of bupropion are dry mouth, GI disturbances, taste disturbance, headache, and agitation.⁽²⁴⁾

Table 4 below shows the summary of

different pharmacological treatments.

GUIDELINES TO SMOKING CESSATION

International Guidelines – WHO⁽²⁶⁾

According to the WHO policy recommendation published in 2003, pharmacotherapy has focused on the alleviation of tobacco-withdrawal symptoms. In 2003, two categories of medication, nicotine replacement medications and non-nicotine medications, were available for smoking cessation.

Nicotine replacement (NRT) medication is the most direct way to manage the symptoms of nicotine dependence. Different dosage forms are available. In order to improve delivery of nicotine, use of higher-dose patches and combination of NRT medications are preferred as they improve treatment outcomes. Due to the possible risk of nicotine during pregnancy, WHO recommends consultation with doctor before using NRT medication in pregnant women and person with history of heart disease.

Wide range of non-nicotine substances are also used for treating

tobacco dependence. In the policy published in 2003, WHO has also introduced bupropion, clonidine and nortriptyline. Among them, only bupropion was approved as a smoking cessation therapy. It is possible that combination of bupropion and nicotine patch can increase efficacy.

Although there is a wide range of treatment options, there is no single application that should be emphasized to the exclusion of others.

Country guidelines

A comparison between the guidelines of US⁽²⁷⁾, UK⁽²⁸⁾, Australia⁽²⁹⁾ and New Zealand⁽³⁰⁾ is shown in table 5 below.

Application to HK prescription habits

With reference to overseas guidelines, Tobacco Control Office of the Department of Health in Hong Kong also developed an Information Kit on smoking cessation.⁽³¹⁾ Nicotine replacement therapy including the use of nicotine patch, gum, inhaler and lozenges, is recommended for smokers. They are now available in all Authorized Seller of Poisons and Listed Seller of Poisons. Bupropion and varenicline are offered as prescription medicines. Smoking cessation

Table 3. Summaries of the type of Nicotine Replacement Therapies⁽²⁰⁾

Type	Dosage	Dose/day	Comments	Disadvantages
Patch	Initially 15mg patch for 16 hours daily for 8 weeks, then 10mg patch for 16 hours daily for 2 weeks, then 5mg patch for 16 hours daily for 2 weeks.	one	- If abstinence not achieved within 3 months- further courses may be given	- Skin irritations - Slow delivery - Wearing at night
Gum	Individual smoking ≤20 cigarettes/day: initially chew one 2mg gum slowly for approx. 30 mins. when urge to smoke occurs. Individual smoking ≥20 cigarettes/day or need more than 15 pieces of 2mg gum: use the 4mg strength.	Maximum 15 gums/day	- Withdraw gradually after 3 months - Review treatment if abstinence not achieved within 9 months	- No food or drink 15 minutes before use - Jaw pain, mouth soreness
Inhaler	Inhale when urge to smoke occurs. Initially use between 6-12 cartridges daily for up to 8 weeks, then reduce number of cartridges used by half over next 2 weeks and stop altogether at end of further 2 weeks	6-12 cartridges	- If abstinence not achieved within 3 months- further courses may be given	- Mouth and throat irritation - Frequent dosing necessary
Nasal Spray	Spray 1 puff into each nostril as required, max. 2 puffs within an hour for 16 hours daily for 8 weeks, then reduce gradually over next 4 weeks (reduce by half at the end of first 2 weeks, stop altogether at end of next 2 weeks)	Max. 64 puffs daily	- If abstinence not achieved within 3 months- further courses may be given	- Frequent dosing - Nose and eye irritation - Cough
Lozenge	Individual smoking ≤30 cigarettes/day: suck one 1mg lozenge every 1-2 hours, when urge to smoke occurs. Individual smoking ≥30 cigarettes/day: suck one 2mg lozenge. Withdraw gradually after 3 months. Max. period should not exceed 6 months.	Max. 30mg daily	- If abstinence not achieved within 3 months- further courses may be given	- No food or drink 15 minutes before use - Dyspepsia, mouth soreness, flatulence, nausea

pharmacotherapy in Hong Kong is similar to the above guidelines. Nevertheless, recommendation on priority and use of medication combination is not mentioned in the Information Kit. More extensive and thorough research in prescription habit and use of medication will be beneficial to development of an official local guideline for smoking cessation in

Hong Kong.

COST EFFECTIVENESS OF SMOKING CESSATION

Cost and effects of different interventions in smoking cessation could be examined to guide the optimal healthcare resource allocation. Nowadays, the BENESCO-model was used to estimate the long-

term health and economic benefits of smoking cessation of smokers making a one-time quit attempt.⁽³⁰⁾ It is used to simulate the consequences of smoking and the benefits of quitting in terms of smoking-related morbidity, mortality, and associated medical costs. Asthma exacerbation, chronic obstructive pulmonary disease (COPD), lung cancer,

Table 4: Summary of different approved pharmacological smoking cessation therapies⁽²⁵⁾

Name of drug	Dosage & regimen	Special contraindications/ Precautions in use	Special advice in counseling	Additional notes
NRT	<ul style="list-style-type: none"> Different dosage forms are available. Transdermal patch is easiest to use. Nicotine gum has an unpleasant taste and some patients may find the chewing action difficult. 	<u>Contraindication</u> <ul style="list-style-type: none"> Post myocardial infarction Severe arrhythmias Severe or worsening angina pectoris. Pregnancy <u>Use with cautions</u> <ul style="list-style-type: none"> Peripheral vascular disease Endocrine disorder (phaeochromocytoma, hyperthyroidism, and diabetes mellitus) Peptic ulcer disease 	<ul style="list-style-type: none"> Patients should be advised to completely stop smoking when the therapy is initiated. Nicotine gum should be chewed slowly until it tingles and park it between cheek and gum until tingle is gone. Repeat "chewing and parking" for 30 minutes. Nicotine patch should be applied to a different site everyday. 	<ul style="list-style-type: none"> Nicotine gum should be chewed slowly. Nicotine patch should not be cut.
Champix (Varenicline)	Except for the first 3 days of the therapy, varenicline is supplied in a twice-daily regimen.	Patients with neuropsychiatric symptoms, including suicidal thoughts, agitation, depression, or other changes in behavior, should be monitored.	Treatment is started 1-2 weeks before the patient attempts to stop smoking.	Patients should be informed to report any behavioral and/or mood changes to healthcare provider.
Bupropion	Except for the first 3 days of the therapy, bupropion is supplied in a twice-daily regimen.	<u>Contraindication</u> <ul style="list-style-type: none"> Epilepsy Patients undergoing abrupt discontinuation of ethanol or sedatives <u>Use with caution</u> <ul style="list-style-type: none"> Recent myocardial infarction or unstable heart disease Bipolar disorder 	Treatment is started 1-2 weeks before the patient attempts to stop smoking.	NA

Table 5. Comparisons between different countries smoking cessation guidelines

Country	First-Line	Second-line	Notes:
US	<ul style="list-style-type: none"> Bupropion (Rx) Nicotine Gum (OTC) Nicotine Inhaler (Rx) Nicotine Lozenge (OTC) Nicotine Nasal Spray (Rx) Nicotine Patch (OTC) Varenicline (Rx) 	<ul style="list-style-type: none"> Clonidine Nortriptyline (For use on a case-by-case basis after 1 st line treatment has been used without success or is contra-indicated)	Combination of smoking cessation medications not included.
UK	<ul style="list-style-type: none"> NRT (all forms) (OTC) Varenicline (Rx) Bupropion (Rx) 	NA	<ul style="list-style-type: none"> NRT is available to smokers > 18 yrs OR ≤ 18 yrs on recommendation. Combination of NRT may be used with high level of dependence or inadequate control by single form of NRT. Varenicline & Bupropion are only suitable for smokers aged > 18 yrs. NICE also recommends not to offer NRT, Varenicline or bupropion in any combination (as per the instructions of the prescribing information)
Australia	<ul style="list-style-type: none"> NRT - all forms (OTC) Bupropion (Rx) * Varenicline (Rx) * 	<ul style="list-style-type: none"> Nortriptyline (Not indicated for smoking cessation)	* Varenicline and Bupropion are used as a short term adjunctive therapy for nicotine-dependence.
New Zealand	<ul style="list-style-type: none"> NRT – all forms (OTC) Bupropion (Rx) Varenicline (Rx) Nortriptyline (Rx) 	NA	Combination of smoking cessation medications not included.

coronary heart disease (CHD) and stroke are regarded as smoking-related morbidities. It has been suggested that varenicline, NRT and bupropion all prevent excess mortality and morbidity compared with unaided cessation. The direct medical cost related to different smoking cessation interventions, the cost used to prolong QALY (quality adjusted life-year) as well as the costs used to prevent smoking-related diseases are taken into consideration.⁽²⁹⁾

THE ROLES OF PHARMACIST

Pharmacist frequently comes into contact with individuals and can play an important role in assessing patients' smoking status and readiness to stop smoking. For those not prepared to quit, pharmacists can relay reinforcing messages about the hazards of smoking and the benefits of quitting. The more frequently individuals hear such messages, the more likely they are to quit smoking.⁽¹⁹⁾ For individuals who wish to quit smoking, pharmacists can play an important role in partnering with physicians to determine whether the timing is right, educating patients about smoking cessation products, monitoring patients' progress in terms of

nicotine withdrawal symptoms, assisting in the development of coping strategies and educating patients about signs of medication toxicity. Educating physicians about the need for dosage reduction and the possibility of drug interactions, as well as advising about drug levels are also the important roles of the pharmacist.

Author's background

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Questions for Pharmacy Central Continuing Education Committee Program

(Please be informed that this article and answer sheet will be available on PCCC website concurrently. Members may go to PCCC website (www.pcccchk.com) to fill in their answers there.)

Overview on the International and Local situation of smoking cessation

1. Which of the following statements is NOT TRUE?

- Nicotine from the tobacco products was rapidly delivered to the brain after inhalation.
- The primary receptor of nicotine is the $\alpha 4\beta 2$ nicotine receptor in the Ventral Tegmental Area of the brain.
- The 5-HT is released in the Nucleus Accumbens after nicotine binds to the $\alpha 4\beta 2$ nicotine receptor.
- The Nucleus Accumbens is believed to be linked to the reward system.
- Quitting smoking could substantially reduce the number of premature deaths from smoking-related illnesses.

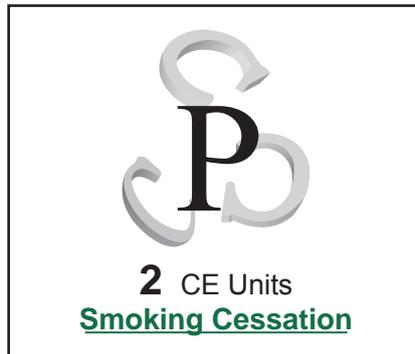
2. Which of the following statements is true regarding the actions taken by the DoH to fight tobacco use?

- In accordance with the amended Smoking (Public Health) Ordinance, there have been no smoking areas of the indoor areas of all restaurant premises and indoor workplaces since January 2008.
- Smoking cessation clinics are only run by the Hospital Authority and private hospitals.
- The tobacco Control Office of the DoH organized seminars on smoking ordinance and other smoking cessation health talks to promote a smoke-free culture.
- The Smoking (Public Health) Ordinance prohibits the exhibition of tobacco advertisement only in printed publications and in public places.
- Health warning on Cigarette Packet with brief description of the specifications of pictorial and graphic contents of the health warning has been implemented, but such warning has not been implemented on Retail Container.

3. Which of the following are the barriers to the provision of cessation services among clinicians?

- Lack of time
 - Patient unreadiness to change
 - Inadequate patient resources
 - Inadequate cessation clinical skills
- i and ii only
 - i and iii only
 - ii and iv only
 - ii, iii and iv only
 - All of the above

4. Which of the following statements is NOT TRUE regarding the smoking cessation guidelines from WHO?



- Combination of NRT medications are preferred to improve treatment outcomes.
- WHO recommends consultation with doctor before using NRT medication in pregnant women.
- It is possible to combine varenicline and nicotine gum to increase efficacy.
- Bupropion is one of the approved non-nicotine substances as a smoking cessation therapy.
- There is no single application that should be emphasized to the exclusion of others.

5. Which combination(s) of smoking cessation products may be used to increase efficacy?

- Varenicline & NRT
 - NRT patch & NRT gum
 - Bupropion & varenicline
 - Bupropion & NRT
 - Bupropion & NRT patch & varenicline
- i, iii and v only
 - ii and iv only
 - iii, iv and v only
 - i, ii, iv and v only
 - ii only

6. Which of the following statements is TRUE regarding the tobacco withdrawal?

- The tobacco withdrawal symptoms are in the maximal intensity in the second week.
- Huger can persist for several weeks.
- Most of the affective symptoms resolve over 2 weeks.
- Craving can be triggered by situational cues.
- Pharmacotherapy cannot ameliorate the nicotine withdrawal symptoms.

7. Which of the following is NOT TRUE regarding the nicotine replacement therapy?

- Further courses may be given to patient if abstinence cannot be achieved within 3 months by nicotine patch and inhaler.

- Patients should not drink or eat 15 minutes before taking nicotine gum.
- Maximum 2 puffs within an hour for 16 hours daily for nicotine nasal spray.
- Patients should completely stop smoking when starting nicotine replacement therapy.
- Nicotine patch can be cut.

8. Which of the following combinations of patient population and the smoking cessation therapy describes an incorrect drug-disease contraindication pair?

- Patients with epilepsy using varenicline
- Post MI patients using NRT
- Patients undergoing abrupt discontinuation of sedatives using bupropion
- Patients with severe angina pectoris using NRT
- Patients with epilepsy using bupropion

9. Which of the following statements is TRUE regarding varenicline?

- It is the only one non-nicotinic smoking cessation aid.
- No dose titration is needed when starting varenicline therapy
- Varenicline starting dose is 1mg twice daily.
- Varenicline has no side effects.
- Varenicline should only be used alone as a smoking cessation aid, because the efficacy and safety of such combination with other smoking cessation has not been confirmed.

10. Which of the following statements is NOT TRUE?

- The more frequently the individuals hear the messages about the hazards of smoking and the benefits of quitting, the more likely they are to quit smoking.
- Recommendation on priority of the smoking cessation products and the use of medication combination is mentioned in the Information Kit developed by the Tobacco Control Office.
- Pharmacists can educate physicians about the need for dosage reduction and the possibility of drug interactions of the smoking cessation therapy.
- Patients should reduce caffeine consumption after smoking cessation.
- Brief advice to quite smoking by doctors resulted in higher cessation rates compared to those who received no such advice.

Answers will be released in the next issue of HKPJ.

Accurate Measurement of Liquid Medication

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ABSTRACT

Consolidated trainings and education for pharmacy students as well as patients on the proper measurement of liquid medication are important for the safe use of drug with accurate dosing. This short review article includes a self-evaluation question, and a brief description about how pharmacy technicians can help people to accurately measure liquid medication.

Keywords: Standardized teaspoon; Oral syringe; Patient education; Liquid medication measurement; Dosing accuracy

INTRODUCTION

Dispensing skill was used to be one of the most important components in the training of students to become a qualified pharmacist. Before the Sixties, students were given chances to practice the skill of drug dispensing for at least two semesters with at least 6 – 8 hours of practices per week in the third year of their study. With the introduction of a variety of modern unit dosage forms, however, the requirement for such training has been reduced in order to spare time for learning other things. Hence, some basic skills may be ignored, for example, the proper dispensing of liquid medication. In this short article, the safe use of liquid medication with accurate dosing is reviewed.

SELF-EVALUATION QUESTION

If you were asked by a parent of a pediatric patient in your hospital about the correct way in measuring 5 ml of a liquid medication with **standardized teaspoon**, how would you response? Which level of measurement in Figure 1 will you recommend to the parent for the proper way of liquid medication measurement? The correct answer of the above question is C.

PATIENTS' CHOICES OF LIQUID MEDICATION DOSING APPARATUS

It has been well known that many parents of pediatric patients do not know how to choose the correct apparatus for liquid medication measurement. Many parents may select kitchen teaspoons instead of a standardized teaspoons or oral syringes.⁽¹⁾ As the volume of kitchen teaspoons can range from 2 ml to 9 ml,⁽²⁾ patients should always be advised to use standardized teaspoons or oral syringes to ensure the accuracy of measurement.

STANDARDIZED TEASPOONS AND ORAL SYRINGES

Patient counseling is needed during the provision of standardized teaspoons or oral syringes to ensure dosing accuracy during liquid medication measurement. 73% of the parents of pediatric patients

were found to measure paracetamol syrup inaccurately and thereby increased the workload of hospital emergency departments.⁽³⁾ In our experience, most parents of pediatric patients dosed poorly in standardized teaspoons and oral syringes. When 14 parents of pediatric patients in a health center in Macao were asked to dose 5 ml of paracetamol solution in standardized teaspoons, the average volume of the liquid medication measured was only 3.11 ± 0.87 ml, which is far below the theoretical value of 5.00 ml.⁽⁴⁾ The average volume of liquid medication retrieved became 4.86 ± 0.44 ml after the parents had received detailed patient counseling conducted by pharmacy technicians (Figure 2).

Generally speaking, the parents of pediatric patients can dose better with oral syringe. When the parents were again asked to dose 5 ml of paracetamol solution in oral syringes,

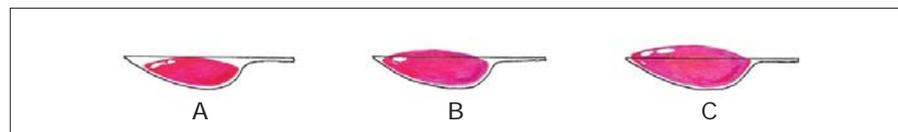


Figure 1. Measuring methods in with a standardized teaspoon

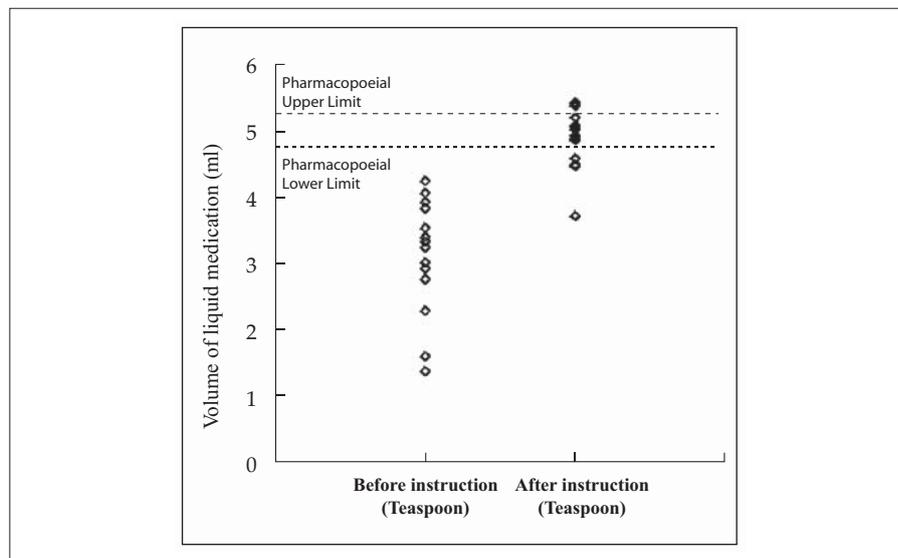


Figure 2. Actual volume of liquid medication measured in standardized teaspoon by the parents of pediatric patients

the average volume of the liquid medication measured was 4.76 ± 1.34 ml. The large standard deviation was due to the inability of some parents to comprehend the markings imprinted on oral syringes.⁽⁴⁾ Upon detailed patient counseling conducted by pharmacy technicians, the average volume of liquid medication measured became 5.14 ± 0.08 ml (Figure 3).

WHAT CAN A PHARMACIST OR PHARMACY TECHNICIAN DO?

Pharmacists and pharmacy technicians have crucial roles in educating parents of pediatric patients on how to select the correct apparatus for liquid medication retrieval, as well as how to measure liquid medication accurately by standardized teaspoons or by oral syringes.

ACKNOWLEDGEMENT

Financial support from the Macao Science and Technology Development Fund (FDCT Fund Project No: 005/2007/A1) is gratefully acknowledged. Special thank is given to Michelle Lei for her help in drawing.

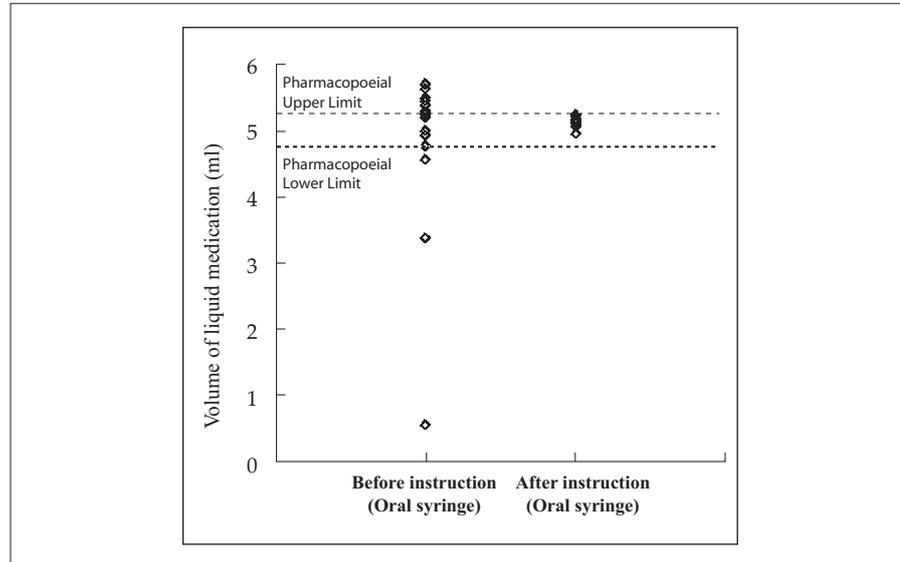


Figure 3. Actual volume of liquid medication measured in oral syringe by the parents of pediatric patients.

Author's background

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- Minimum 1 year's experience in manufacturing / or packaging of pharmaceuticals, cosmetics or toiletries.
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“Absence of Specified Microorganisms” versus “Absence of Objectionable Microorganisms” of the Microbial Limits Tests for Non-Sterile Pharmaceuticals

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ABSTRACT

Different types of Microbial Limits Tests have been introduced and implemented since the outbreaks of microbial diseases in the 70's due to the uses of medications contaminated with unexpected pathogenic organisms. The tests were designed to ensure a product is safe for use. The monographs described in the official compendia, however, are merely the minimal requirements and should not be taken as proof that the product is suitable for sale from a microbiological perspective. In this article, the differences between “Absence of Specified Microorganisms” and “Absence of Objectionable Microorganisms” are highlighted and discussed.

Keywords: *Microbial limits tests; non-sterile products; USP; FDA; CFR; Microbiological contamination*

INTRODUCTION

The executive committee of US Pharmacopeia (USP) and the Food and Drug Administration (FDA) of the USA are both concerned about the same thing with regard to the microbial content of pharmaceutical products but their approach to the problem of microbial contamination stems from different points of view. Neither of their publications is directly concerned with Good Manufacturing Practice (GMP) which is another matter. The former focuses on “the absence of specified microorganisms” while the later emphasizes “the absence of objectionable microorganisms”. Consequently, the USP requires tests for properties such as sterility, antimicrobial efficacy, antibiotic/ vitamin potency, presence of bacterial endotoxin, for microbial limits etc. The tests in the USP are governed by what has been published in the monographs in the National Formulary of the USA, hence the USP-NF. For example, if a monograph calls for a test for antimicrobial efficacy then the reference test is “Antimicrobial Effectiveness Test” which is outlined in Chapter 51 of the USP: This kind of

specifically described text is not covered in the Code of Federal Regulations (CRF), which is the ground for regulatory enforcement by FDA.

As a consequence of the overlapping concerns on the quality control of microorganisms of these two organizations, the question of priority arises. In other words, which should be followed when there are competing situations. For example, when the FDA and the USP requirements are identical, the reference Chapters in the USP, those numbered under 1000 - have priority. However, sometimes the requirements of the FDA are not covered by a USP reference test method. One example of this is with the CFR requirement that non-sterile pharmaceutical products be “free of objectionable microorganisms.” The clause 21 CFR 211.113 under the section “Control of microbiological contamination, (a), states “appropriate written procedures, designed to prevent objectionable microorganisms on drug products not required to be sterile, shall be established and followed.” This is backed up by clause 21 CFR 211.165 which states “testing and release for distribution; (b) there shall be appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms.”

The problem here is that the USP-NF monograph for a product may require “Absence of *Pseudomonas aeruginosa*.” There is a test in the USP Microbial Limits Chapter to demonstrate the absence of *Ps. aeruginosa*. Although this test can demonstrate compliance with the USP-NF monograph, it would not meet the concern of the FDA that any organism in the final product not be “objectionable” to the product or the target population.

THE PERSPECTIVE OF THE USP

As early as 1982 the USP verified that demonstration of the “absence of objectionable microorganisms” is not the intent of the Chapter. The microbiology committee of the time stated (in Stimuli to the Revision Process) the following:

“The tests described in the Microbial Limits Tests 61 were not designed to be all-inclusive, i.e., to detect all potential pathogens. To accomplish this, an extensive text on laboratory detection of microorganisms would be required. The procedures in USP were designed to detect the presence of specific “index” or “indicator” organisms. Nevertheless, the present Chapter does not preclude the detection of *Ps. cepacia* – the organism requires subsequent differentiation. The Chapter does not provide specific methods for this, nor does it provide procedures for detecting thousands of other potentially pathogenic organisms. Individual monographs include requirements for limits on total aerobic counts and/or absence of one or more of the four selected “indicator” organisms. The Chapter on Microbial Limits Tests provides methods to assure that one may test for those microbial requirements in the individual monographs.

THE PERSPECTIVE OF FDA

The FDA enforces the GMP requirements of a product, particularly those requirements specified in a Company's submission to obtain approval. If the submission specifies that a test on the finished product by the Microbial Limits Tests will be done then it must be done. However it may not meet the requirements of the FDA which are that the products contain no “objectionable microorganisms”. The USP testing, although performed according to a submission, may not be sufficient to demonstrate microbial quality as the FDA understands it and demands it. In the 1993 instructional guide for inspections of QC Microbiology Labs ⁽¹⁾ the FDA states: “For a variety of reasons, we have seen a number of problems associated with the microbiological contamination of topical drug products, nasal solutions and inhalation products. The USP Microbiological Attributes Chapter 1111 provides little specific guidance other than: ‘The significance of microorganisms in non-sterile pharmaceutical products should be evaluated in terms of the use of the product, the nature of the

product, and the potential hazard to the user. The USP recommends that certain categories be routinely tested for total counts and specified indicator microbial contaminants. For example natural plant, animal and some mineral products for *Salmonella*, oral liquids for *E. coli*, topical [preparations] for *Ps. aeruginosa* and *Staphylococcus aureus*, and articles intended for rectal, urethral, or vaginal administration for yeasts and molds. A number of specific monographs also include definitive microbial limits."

As a general guide for acceptable levels and types of microbiological contamination in products, Dr. Dunnigan of the Bureau of Medicine of the FDA drew attention to the health hazards. In 1970 he said that topical preparations contaminated with Gram negative organisms are probably a moderate to serious health hazard. Published studies and investigations by Dr Scott Sutton's group have shown that a variety of infections have been traced to contamination of topical preparations with Gram negative bacteria. The classical example of this is contamination of Povidone Iodine products with *Ps. cepacia* as reported by a hospital in Massachusetts, USA.

Therefore, each pharmaceutical company must develop microbial specifications for their nonsterile products, the USP cannot be relied upon. For example, the USP Microbial Limits Chapter 61 covers the testing procedures for selected indicator organisms, but not all "objectionable organisms". To illustrate, high numbers of *Ps. cepacia* are objectionable in a topical preparation or nasal solution; but the USP provides no test methods for the identification of the microorganism.

A practical example of this problem is the recall of Metaproterenol Sulfate Inhalation Solution for which the USP XXII monograph has no microbial testing requirement. The recall was classified as a Class I recall because of contamination with *Ps. gladioli/cepacia*. The health hazard in this case involved the serious risk of pulmonary infection, especially to patients with chronic obstructive airway disease, or cystic fibrosis, and to patients who were immuno-compromised.

Microbiological testing may involve the Total Aerobic Plate Count and enrichment testing, both of which will depend on the product and its intended use. If an oral solid dosage form, like a tablet is tested, isolates may only need to be identified if testing shows high microbial levels. On the other hand, with other products such as topical

preparations, inhalants or nasal solutions where microbiological contamination is a greater concern, isolates from both total aerobic plate counts and enrichment broths should be identified.

To understand why this approach is followed we have to go back to the 1970s. The USP published a test for the "Bacteriological Examination of Gelatin" as early as 1942⁽²⁾ but it was not required to test for most non-sterile medications in the USA for microbiological quality until the introduction of the Microbial Limits Tests in 1970.⁽³⁾ The initiative was influenced by several outbreaks of diseases that were traced back to pathogen contaminated medications that drew attention to the microbial quality of non-sterile drugs.⁽⁴⁾ Later studies in the 1980s described contamination by *Ps. cepacia* (currently *Burkholderia cepacia*)^(5,6) and its survival in disinfectants.⁽⁷⁻¹¹⁾ Consequently further requirements were introduced in the 21 CFR to avoid objectionable organisms in product released to the market. It also became clear that the USP "Absence of *Pseudomonas aeruginosa*" assay was not useful for detecting of *B. cepacia*.

CONCLUSIONS

In conclusion, the Microbial Attributes and Microbial Limit Tests chapters accomplish their intent. If a manufacturer needs particular tests for any specific organisms that are potential problems in a process or a final product, the quality control microbiologist can provide specific detection procedures. Many such procedures are published in several laboratory texts on microbiology."

The objectives of the USP and the FDA with regard to the microbial quality of non-sterile pharmaceuticals are to ensure the product must be safe for use. The NF monograph requirements are minimal and should not be taken as proof that the product is suitable for sale from a microbiological perspective.

The manufacturer is responsible for the quality and safety of the product marketed, and it is clearly expected by the FDA that manufacturers ensure the "absence of objectionable microorganisms" in the product. This position has been publicly stated for decades and should not come as a surprise to anyone. The harmonized microbial limits tests only addresses the "absence of specified microorganisms" and leaves the determination of the "absence of objectionable microorganisms" in the capable hands of each company's

appropriately educated and well-trained microbiology group.

ACKNOWLEDGEMENTS

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Author's background

Dr O'TOOLE, DK is an Australian. He holds a BSc and MSc degrees some forty years ago in food microbiology. He was awarded a PhD degree from Queensland in the 1990's. Coming up through the microbiology laboratory, Dr O'Toole has served many times in court as expert witness in food microbiology and currently is the Honourary Staff of CityU. **Dr CHEUNG, Hon-Yeung** is a pharmacist and had several years of experiences in the manufacturing of sterile products before pursuing his PhD degree in Pharmaceutical Microbiology and subsequently post-doctoral training in Molecular Biology and Biotechnology in NIH. He is currently the Associate Professor of Pharmaceutical Microbiology and Biotechnology. He is also the Director of Pharmaceutical & Chemical Technology Center in the City University of Hong Kong. For further information about this article, contact Dr Cheung via his email: bhonyun@cityu.edu.hk

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Extract of Herba Scutellariae Barbatae Has Anti-inflammatory, Antipyretic and Cancer Chemopreventive Effects

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Official Name: Herba *Scutellariae barbatae*

Chinese Name: 半枝蓮, 溪邊黃芩, 狹葉韓信草, 小韓信草, 並頭草, 紫蓮草, 通經草, 四方草

Chinese Phonetic Name: Banzhilian

Plant Family: Lamiaceae/Labiatae

Botanical Name: *Scutellaria barbata* D. Don; *Scutellaria rivularis* Wall

Pharmacopoeia Name: Herba *Scutellariae barbatae*

Other Names: Barbated skullcup; Banjiryun (Korean)

Part Used: Any part or whole plant

ABSTRACT

The traditional Chinese medicinal herb, Banzhilian, also known as Barbata skullcup, is derived from the dry whole plant of *Scutellaria barbata* D. Don, which is a perennial plant native to Southern China and Korea. It is an important herb for clearing heat that ascends from the liver and drying dampness inside the stomach and intestines. Its' reported biological effects include anti-inflammatory, diuretic, and antitumor activities. It is commonly used for the treatment of tumors, hepatitis, cirrhosis and other diseases. Recent studies have confirmed that the aqueous extract of Banzhilian can significantly enhance the tumor inhibition rate of 5-fluorouracil, reduce the toxic effects, prolong the survival time, and improve immune function in an animal model.

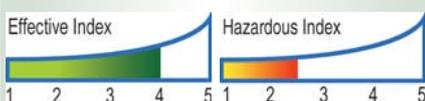
Keywords: Herba *Scutellariae barbatae*; anti-inflammatory; antitumor; antiviral; diuresis; scutellarin

DESCRIPTION AND IDENTIFICATION

The herb, as shown in Figure 2, is prepared from the dried whole plant of *Scutellaria barbata* D. Don. It is native to southern China and Korea. The plant is common in Huabei, Zhongnan, Huadong, Huanan and Xinan but other closely related species could be found elsewhere. The herb is collected, washed to eliminate mud and sand, and then dried under the sun when foliage branch growing luxuriantly in summer and autumn. HSB has been used as a medicine in different forms; such as crude drug, capsule or dissolvable powder. Obvious medicinal properties of this herb are documented in literature although not much high quality studies have been done in human beings. But nowadays, the use of HSB is very different from the past. According to a classic Chinese medicinal book “外科正宗” (The Orthodox Surgery), it was used to treat snakebites rather anti-tumor. The latest version of Chinese Pharmacopoeia indicates that HSB is used for removing tonic heat and causing diuresis.



Figure 1. Photo of *Scutellariae barbatae* D. Don. Insert is the lateral enlarge picture of flowers.



Contraindications

Do not use scutellaria if “cold” diarrhea is present, i.e. diarrhea due to foodborne diseases. Use with caution in pregnancy, nursing or in administration to children.

Undesirable Effects

Adverse effects rarely reported; occasionally produces nausea, diarrhea, headache, flatulence, vomiting and fatigue.

Interaction with Conventional Drugs

No obvious adverse event reported in combination with other drugs.

INTRODUCTION

Herbal *Scutellaria barbata* D. Don (HSB), which is also called Banzhilian in Chinese or Barbata skullcup Herb (Figure 1), is frequently used in traditional Chinese medicine (TCM). It belongs to the plant family Lamiaceae/Labiatae and the genus *Scutellaria*. In this genus, there are more than 300 related species. Amongst them, 100 species are grown throughout China.⁽¹⁾ Although some of these species share similar morphology and chemical components, they have different pharmacological properties. For example, *Scutellaria indica* L (韓信草) and *Salvia plebeian* R. Br. (荔枝草) are similar to HSB in morphology. However, only HSB has the medicinal effects on cancer cells.

Macroscopic appearance of dried herb

The crude drug of HSB is usually coiled due to the desiccation by the sun. The roots are tiny and slender. The branching stems are either hairless or there is little hair, about 15~35 cm in height and dull purple or brown green in color, thin and square in shape. The blade is multi-shrinkages. After wetting with water and expansion, it can be observed that the leaves, 1.5~3 cm long, 0.5~1 cm wide, are mainly triangular ovals and a few lanceolate in shape. Each pair of leaves is grown in opposite and they have a short handle on them. The tips of the leaves are obtuse and the base is wide wedge-shaped. The upper surface is dark blue and the undersurface is grayish-green.



Figure 2. Dried crude drug of herbal *Scutellaria barbata* D. Don (Scale bar = 1 cm)

Flower grows on the upside and calyx is obtuse lobe or round. Corolla is two-labiate in shape, approximately 1.2 cm in length, yellowish brown or light blue purple in color. The fruit is oblate and light brown.

Microscopic features

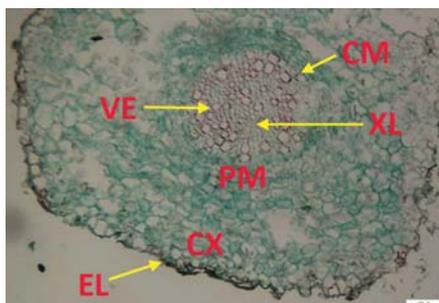


Figure 3. A microscopic picture of transverse section of dried root of *Scutellaria barbata*. EL=Epidermis layer; CX=Cortex; PM=Phloem; CM=Cambium; XL=Xylem; VE=Vessels (scale bar = 100 μ m)

Figure 3 shows the transverse section of the root of *Scutellaria barbata*. The epidermis layer (EL) is consists of only 1 layer of cell while the cortex (CX) is broad, containing 8 to 11 layers of parenchyma cells. Phloem (PM) is relatively broad and cambium (CM) in a ring. The greater part is occupied by xylem (XL), vessels (VE) scattered and accompanied by wood fibers, without pith.

BIOACTIVE CONSTITUENTS

In recent years, Analysis of the chemical compounds in HSB has been carried out continually with the development of analytical separation techniques. The

research of the bioactive constituents of HSB attracts more and more attention.⁽²⁻⁵⁾ Although there is a series of qualification and quantification analysis reported, in particular, using High Performance Liquid Chromatography (HPLC) for establishing fingerprint of the herb.⁽⁶⁾ there is still no approved analysis method to assay the bioactive constituents. As the pharmacological effects of HSB have been confirmed, the demand for quality control of bioactive constituents of HSB is growing. The bioactive compounds in HSB have been investigated by domestic and foreign experts. So far the chemical composition found and isolated from this herb includes the following categories:

Flavonoids

At present, it has been proved that flavonoids are the major kind of ingredient. Twenty six flavonoids compounds have been isolated and identified in HSB, including flavonones, flavonone glucosides and flavanones (Table 1).⁽⁷⁻¹²⁾ Particularly, the content of scutellarin may achieve 1% in the dried herb of HSB.⁽⁶⁾

Diterpenoids and diterpenoids derivatives

Diterpenoids and diterpenoids derivatives are the second major ingredients of HSB. The isolated diterpenoids are scutellones A, B, C, D, E, F, G, H, I⁽¹³⁻¹⁹⁾ and diterpenoids derivatives are scuterivulactones A, B, C₁, C₂⁽²⁰⁾, D⁽²¹⁾.

Alkaloids

Scutebarbatine A⁽¹²⁾ has been isolated from HSB and its empirical formula is C₃₀H₃₆O₇N₂⁽²⁸⁾.

Trace elements

Some trace elements, such as Fe, Mn, Mg, Cu and Zn have been determined in HSB. The contents of Fe and Mn are relatively high.⁽²⁶⁾

Glucosides

The isolated glucosides from HSB are ethyl-7-O-apigenin-glucuronate, apigenin-7-O- β -glucoside, apigenin-7-O-neohesperidoside,⁽¹⁰⁾ viscidulin III-2'-O- β -D-glucoside,⁽¹¹⁾ carthamidin-7-O-glucuronide.⁽⁶⁾

Other constituents

Flavonoids compounds are the main constituents in HSB. According to the assessable literature, steroids,^(25,27) scutellaric acid⁽²¹⁾ and scutellaria barbata polysaccharide,⁽²²⁾ have been isolated and identified.

Quantification analysis

The only approved test for HSB is a qualitative analysis described in the Pharmacopoeia of the People's Republic of China,⁽¹⁾ Total flavonoids was determined according to UV spectrophotometry. The total flavonoids in terms of scutellarin (C₂₁H₁₈O₁₂) is not less than 1.50%, and Scutellarin (C₂₁H₁₈O₁₂) is not less than 0.20% through HPLC determination, calculated by the dry goods.

PHARMACOLOGICAL EFFECTS

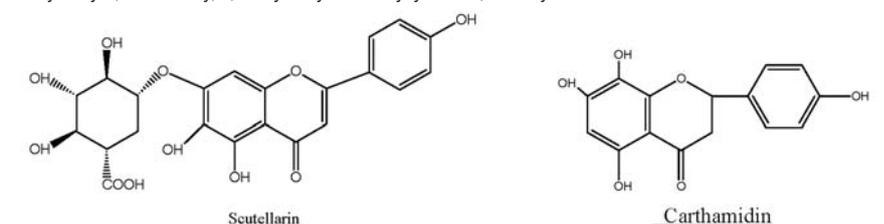
HSB has been used for clearing heat, detoxification, diuresis and removing blood stasis in traditional Chinese medicine. And now it is proved to have several pharmacological effects such as anti-tumor, anti-inflammation, liver protection, anti-bacteria, anti-oxidation and immune system enhancement.

Anti-tumor effect

Anti-tumor treatment activeness test indicated that aqueous extraction and ethanol extraction of HSB have obvious anti-lung cancer, digesting system cancer, liver cancer breast cancer, and fabric membrane epithelioma's activeness.

Table 1. Reported Flavonoids isolated from Herba *Scutellariae barbatae*

scutellarin, scutellarein, baicalein, wogonin, naringenin, apigenin, hispidulin, eriodictyol, luteolin, skullcapflavone, 2',5,6-trihydroxy-7,8-dimethoxyflavone, carthamidin, iso-carthamidin, 7-hydroxy-5,8-dimethoxyflavone, 4'-hydroxywogonin, 5,7,4'-trihydroxy-8-methoxyflavanone, 5,7,4'-trihydroxy-6-methoxyflavanone, 5-hydroxy-7,8-dimethoxy, 5,7-dihydroxy-8-methoxyflavone, eriofictyol and rivularin.



Many researchers have made some tests to confirm its anticancer activity, seeking for its anticancer active constituents and discussing its anticancer mechanism.

Xie L k, *et al.* discovered that the ethanol extract of HSB can inhibit the K_{562} cell multiplication and induced apoptosis obviously, and cause the change of the cell morphology and biochemistry characteristic, which prompts apoptosis protein caspase 3 in cell's expression. The results demonstrated that HSB can simultaneously inhibit K_{562} cell multiplication and induce apoptosis. Wang G studied the treatment effect of sarcoma and liver cancer in mice using transplanting tumor experiments by oral administration the ethanol extract of HSB. It was found that the extract has remarkable inhibitory multiplication to sarcoma S_{180} and liver cancer H_{22} with good dose-dependent relationship.⁽²³⁾

Yin X, *et al.* researched the inhibitory effect of HSB by human lung cancer cell line A_{549} and anticancer treatment mechanism. The results demonstrated that the ethanol extract of HSB may obviously inhibit A_{549} growth by cDNA micro array analysis and the DNA damage, mitotic cycle control, nucleic acid synthesis, protein phosphorylation related 16 genes has had the change. Its anticancer treatment mechanism is mainly promotes cell programming death and cytotoxin function.⁽²⁴⁾

Lee T K, *et al.* discovered that HSB may inhibit the humanity fibroid cell's growth. HSB through increasing the womb myoma levicellulare cell's cAMP density, activates cAMP/PKA indirectly (protein kinase A) the passageway, thus induces original cancer gene c-fos in the fibroid cell expression. But PKA inhibitor H_{89} may inhibit the c-fos gene expression. The original cancer gene c-fos expression mechanism causes womb myoma levicellulare to be different with other myometrium cancer. At present it was not still clear by HSB inducing original cancer gene expression whether to affect the myoma levicellulare cell's degeneration or induce other differentiations.⁽²⁷⁾ It was also reported that the normal myometrium smooth muscle cell and the fibroid smooth muscle cell with aqueous extract of HSB (but also not clear about the two's difference at present) are inhibited. Statistics analysis with the current capacity of blood corpuscle discovered that the mitotic cycle G1 the cell increases. RNA mark analysis demonstrated that aqueous extract of HSB may induce smooth muscle

cell differentiation in these two kind of cells designated object, like a smooth muscle actin (a-SMA), calcium conjugated protein h, with mitotic cycle adjustment protein dependant form activating enzyme inhibitor P_{27} , but in mitotic cycle G1 with mitotic cycle related gene product, like mitotic cycle adjustment protein E and CDK_2 has not been affected. These results showed that HSB inhibits the womb smooth muscle cell's multiplication by inducing a-SMA.⁽²⁷⁾

In 2004, Sonoda, *et al.* reported that 10 flavanones from HSB have cytotoxin function, can inhibit HL-60 cell multiplication, and 4'-hydroxywogonin, apigenin, wogonin, luteolin demonstrated stronger activeness compared to baicalein.⁽²³⁾

Effect on respiratory system

In 1983, Xiang Rende reported that carthamidin from HSB has the function of inhibiting smooth muscle contraction function by antihistamine induced as well as preventing cough and eliminating phlegm.

Liver protection

HSB chemical constituents containing baicalein, wogonin, baicalin have obviously protection effects to the liver damage caused by APAP, carbon tetrachloride and β -D- α -Galactose glucoside.⁽²⁴⁾

Anti-senile function

Through determining HSB polysaccharide to the oxygen negative free radical scavenging action and to the superoxide dismutase 's influence, it has been proved that HSB polysaccharide has anti-senile and anti-lipid peroxidation function.⁽²⁵⁾

Anti-fever, anti-inflammatory, antibacterial and the anti-viral function

Aqueous extract of HSB has an anti-fever effect on the mice that have fever. However, it is not obviously to observe the effect on the normal mice's body temperature. Wogonin and scutellarin from HSB have obvious anti-inflammatory activity and may inhibit carrageenan-induced paw edema of mice. Moreover, apigenin and luteolin have anti-MRSA activity. They also have obvious antibiotic activity and are more sensitive to the gland masculine fungus. *In vitro* experiments, it is indicated that HSB may inhibit hepatitis B virus (HBV) to grow.⁽²⁴⁾

Immune system enhancement

Polysaccharide of HSB may promote the growth of lymphocyte of mouse induced by ConA. The mouse is kept hypodermic injection of 50, 100, 200 mg/kg polysaccharide of HSB. After one week, it can be observed that the percentage of lipoidase masculine in periphery lymphocyte was significantly increased and promoted delayed allergy induced dinitrochlorobenzol (DNCB). The results indicated that this herbal has promotion action to cellular immunity, but large dose injects (200 mg/kg) may inhibit the mouse thymus index, does not have the influence to the spleen index. Therefore, small dosage polysaccharide can strengthen cell immunity. Wang G has also determined that the extract of HSB inhibit the spleen cell proliferation activeness in mice. The results suggested that HSB can finally prompts the mouse spleen cell proliferation, and indicated that HSB has the anticancer activities by strengthening organism immunity.⁽²⁷⁾

POISONOUS SIDE EFFECT

Clinical trial testing suggest that no significant side effect observed even a large dose of HSB decoctum (120 g) was taken based on monitoring the hepatorenal function, routine blood test, immune globulin, protein substitute for plasma. In traditional Chinese medicine, HSB belongs to cool properties; so only patient with stomach empty cold should use cautiously.⁽²⁴⁾

DOSAGE

A daily dose of 5 to 30 g of HSB crude drug for adult has been suggested by the Pharmacopoeia of China: and large dosages can be up to 60 g has been reported safe.

Author's background

Both **TO Ka-Wing** and **NG Chi-Wa** are currently doing their undergraduate final year project on herbal qualitative analysis under the supervision by **Dr. CHEUNG Hon-Yeung** in the City University of Hong Kong. **Dr. ZHANG Zhifeng** is a postdoctoral fellow recently joint **Dr CHEUNG's** research team. He obtained his BSc, MSc and PhD degrees in Pharmacognosy from West China Medical University. **Dr. CHEUNG** is the Associate Professor of Pharmaceutical Microbiology & Biotechnology. His email address: bhonyun@cityu.edu.hk

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Hong Kong Pharmacy Conference 2010 - Good news vs Bad news

Dear Pharmacists,

As you may be aware, the Hong Kong Pharmacy Conference has been held for 21 consecutive years with lots of support and participation from our local and overseas pharmacists and the pharmaceutical industry. While many of us are expecting our conference in year 2009, we regret to inform you that there will be no Hong Kong Pharmacy Conference in year 2009. (What a sad news!)

Wait, don't be disappointed. The good news is, the Hong Kong Pharmacy Conference 2010 (yes, on 23rd January & 24th January 2010) will be held in Hong Kong's most premiere and convenient meeting venue -- the Hong Kong Convention and Exhibition Centre. From previous conference evaluations received, we understand that a convenient conference venue is important. Actually, over the past few years we have been actively searching for venues that are multi-purpose and superbly equipped that could suit our conference needs. We believe the Hong Kong Convention and Exhibition Centre is the ultimate venue that could provide the necessities to meet your expectation of the Hong Kong Pharmacy Conference.

With the theme "Pharmacist in the new decade – Building our healthy land", the 2010 Hong Kong Pharmacy Conference will be held on 23rd and 24th January, 2010. Same as previous years, the conference will be co-organized by the six organizations, namely 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 of Hong Kong; Department of Health and Hospital Authority.

Undoubtedly, the recent drug incidents have created great impact on the pharmaceutical industry as well as the pharmacy profession. Crisis creates opportunities. The government has immediately spent extra efforts to review and optimize the drug regulatory regime to ensure patient safety. Meanwhile, pharmacists have worked hard to educate the public and minimize risks for enhanced medication safety. Quality assurance is the building block we need to work on. To suit our needs, the conference committee has tailor-made a program that targets multiple aspects of quality assurance for building a healthy land. Imminent speakers from different sectors will be invited to share their views and experiences on the fundamentals and necessary skills for ensuring high quality outputs in various sectors of the pharmaceutical industry.

The new supplement to Mainland and Hong Kong Closer Economic Partnership Arrangement (CEPA) signed in May 2009 has allowed Hong Kong licensed pharmacist to sit the Mainland's licensed pharmacist qualification examination and to practice in Mainland thereafter. As you may have noticed, the pharmaceutical care development in Mainland China has grown exponentially in recent years. It will be interesting to have an overview of what is happening in China. In the Conference 2010, several key pharmacists from Mainland will share with us what and how their

pharmaceutical care models are developed.

The importance of Information Technology in health care cannot be undermined. As such, Information Technology will again be another focus of the conference. The government has been actively pursuing an electronic health record system. Pharmacy, being a part of the healthcare system, should get involved and be a participant of the e-healthcare team in the coming future. Want to know what is happening in Hong Kong and what will be the trend? What is the model being practiced in the pharmacies of other countries? Specialists in the field will give you a clearer picture in the conference.

Pharmacists in the new decade, join hands and contribute to making Hong Kong a healthy land. The conference committee members are all working hard to make this conference a success. However, your participation is the most essential! Please come and support the Hong Kong Pharmacy Conference 2010.

The registration booklets will be sent to all pharmacists in the coming months. Please register, together with your friends and colleagues and take advantage of the early bird privilege. Should you have any enquiry about the conference, please feel free to contact our registration officers through email or phone. By the way, remember your "CU next year" coupon? Find it and use it!

Warmest regards,
Pharmacy Conference Organizing Committee

Hong Kong Pharmacy Conference 2010

Pharmacist in the new decade – Building our healthy land

Date: 23rd January 2010 & 24th January 2010

Venue: Hong Kong Convention and Exhibition Centre
1 Expo Drive, Wanchai, Hong Kong

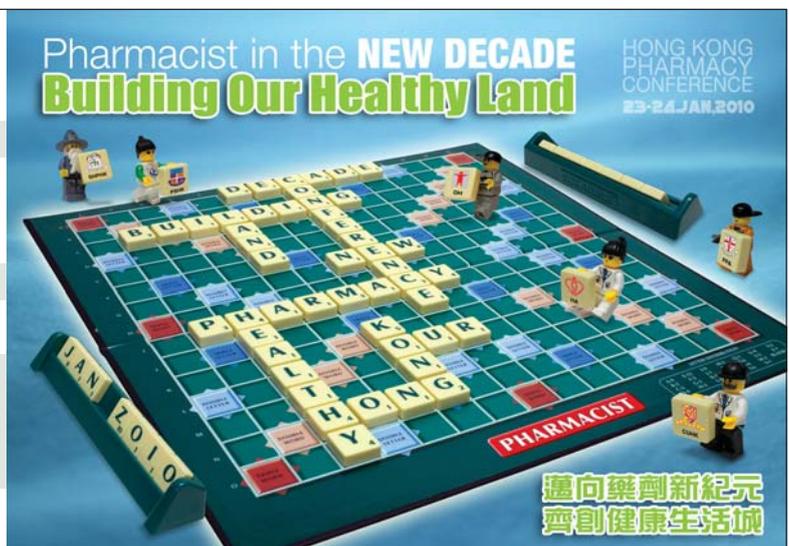
Website: <http://www.pharmacyconference.org>

Email: hkpharmacyconference@gmail.com

Registration Contact: Ms. Judy Kwok (Tel: 9633 4533)

Ms. Heidi Chan (Tel: 6037 7635)

Mr. Ng Man-keung (Tel: 6155 6652)





THE PHARMACEUTICAL
SOCIETY OF HONG KONG
香港藥學會

Lecture: 5:00pm

Venue: The Hong Kong Jockey Club, 5/F, Happy Valley Stand
(Entrance B), Happy Valley Racecourse, Hong Kong.

Cocktail Reception: 6:30pm,

Dinner: 7:30pm

二零零九年十月三十一日(星期六)

Saturday, 31st October 2009

Venue: The Hong Kong Jockey Club, 3/F, Members Stand 1
(Entrance E), Happy Valley Racecourse, Hong Kong.

香港藥學會60週年
紀念講座及晚宴

Anniversary

The Pharmaceutical Society of Hong Kong 60th Anniversary

Lecture & Dinner

60th

From Today Onwards

Dinner Ticket: HK\$400 for members, HK\$800 for non-members.

Registration: Please complete the registration form and enclose cheque payable to
"The Pharmaceutical Society of Hong Kong" and send them to The Pharmaceutical
Society of Hong Kong, Kowloon G.P.O. Box 73552, Yau Ma Tei, Kowloon.

Enquiry: Ms. Peggy Cheung, email address: peggyntp@gmail.com

PSHK members are reminded to send in their latest passport size photograph to the above
address or email their digital photo to: photo@pshk.hk for inclusion in the 60th anniversary
publication book prior to 31st July 2009. The digital photo should be of
size (W)1.5" x (H)2", 300dpi, jpg/bmp file (not more than 200KB).

Web address: <http://pshk.hk>

The Pharmaceutical Society of Hong Kong 60th Anniversary Lecture & Dinner
香港藥學會六十周年紀念講座及晚宴



“From Today Onwards”

Date: Saturday, 31st October 2009

Lecture: 5pm

日期: 2009年10月31日(星期六)

Cocktail reception :6.30pm Dinner: 7.30pm

Lecture Venue: The Hong Kong Jockey Club, 5/F, Happy Valley Stand, Happy Valley Racecourse, Hong Kong

Cocktail & Dinner Venue: The Hong Kong Jockey Club, 3/F, Members Stand 1, Happy Valley Racecourse, Hong Kong

Registration Form/登記表格

- I would like to attend the Pharmaceutical Society of Hong Kong 60th Anniversary Lecture & Dinner on 31 Oct 2009
我有興趣出席 2009年10月31日香港藥學會六十周年紀念講座及晚宴
- I would like to attend the Pharmaceutical Society of Hong Kong 60th Anniversary Dinner on 31 Oct 2009
我有興趣出席 2009年10月31日香港藥學會六十周年紀念晚宴

Personal Details/個人資料

*Please fill in with **BLOCK LETTERS** and tick where appropriate / 請填寫清楚及在適當方格內填上 號*

*Title/銜頭: Prof./ 教授 Dr./ 博士 Mr./ 先生 Mrs./ 女士 Ms./ 小姐

*Surname/姓: _____ *Given name/名: _____

*Correspondence address/通訊地址: _____

*Contact Tel No/聯絡電話: _____ Fax No/傳真: _____

*E-mail address/電郵: _____

Working field/工作界別: Community/社區 Education/教育 Government/政府 Hospital/醫院
 Industry/製藥業 Student/學生 Others/其它

* **Compulsory fields** / 必須填寫

Tickets/入場券費用

Member/會員 HK\$ 400 x _____

Non-member/非會員 HK\$ 800 x _____

Membership No/會員編號: _____

(Each member can purchase 2 tickets at the price of HK\$400 each)

Payment/付款方法

I enclose a Cheque No. _____ of HK\$ _____

Payable to 'The Pharmaceutical Society of Hong Kong'

隨函附上支票號碼 _____ 港幣\$ _____

抬頭為 'The Pharmaceutical Society of Hong Kong'

Please complete the registration form and send it together with your payment to:

'The Pharmaceutical Society of Hong Kong, G.P.O. Box 73552, Yau Ma Tei, Kowloon, Hong Kong.'

請確保已填妥此登記表格並連同支票寄回: 香港九龍油麻地郵政信箱 73552 號香港藥學會

Seating is limited so please reply NOW to ensure your seat for this anniversary event

名額有限, 如閣下有興趣出席敬請儘快登記預留座位

General Committee Members of Society of Hospital Pharmacists of Hong Kong, 2009 - 2010

President:	SO Yiu Wah
Vice President:	CHUI Chun Ming William
Treasurer:	LAI Oi Lun Ellen
Secretary:	NG Long Yee Stephanie

General Committee Members:	CHAN Man Chi, Sarah
	CHUNG Wing Fai Kenneth
	HUI Hoi Yun, Helen
	KWOK Ching Chi, Ritchie
	LAM Nga Pan Athena
	LAM Po Yu Daisy
	LAW Kwok Ming Kenneth
	LEE Wing San, Ken
	LO Cheuk Hang Charles
	PANG Ying Ho, Bobby
	WONG Sze Ho, Johnny

38th Practising Pharmacists Association of Hong Kong (PPAHK) G.C. Member, 2009-2010

President :	Chang Iris Jacqueline
Vice-president :	Kevin Cheung
Vice-president :	Lui Ming Fung Godfrey
Hon. Treasurer :	Vivian Ng
Hon. Secretary :	Yan Chung

Executive Members :	Chan Lok Hang
	Arthur Chan
	Foster Cheung
	James Ho
	Carmen Lai
	Gordon Lee
	Jacky Chan
	Christy Sung
	Bernard Tang
	Ng Hei

How Can I Receive A copy of the Hong Kong Pharmaceutical Journal Regularly?

If you are a member of any one of the following societies, you will be on the HKPJ mailing list:

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

Why not take the dual advantage of becoming a member of these societies, as well as getting the HKPJ free of charge?

Great News

Continuing Education Units (CEUs) for Authors of Articles in the HKPJ. At the most recent meeting of the Pharmacy Central Continuing-education Committee (PCCC), it was decided that CEU would be awarded to authors of articles published in the HKPJ. For each issue, the Editorial Committee, led by the Managing Editor, will choose an article from all the published articles in that issue, for PCCC to use for CE purposes. The author(s) is(are) responsible for setting questions for the approved CE article. Primary authors are entitled to receive 6 CEUs and other co-authors of the same CE article are entitled for 4 CEUs granted by PCCC. For details on how to get CEU, please refer to the article named "PCCC Continuing Education Units (CEU) Accrediting System" [HKPJ 2002;11(2):79-80] or visit the PCCC Website at www.pccchk.com

Great news to boost the professional standard and recognition of the contributions to the HKPJ!

NEW PRODUCTS

Celsentri® (Pfizer)

Active Ingredient:

Maraviroc

Presentation:

150mg and 300mg blue, biconvex, oval film-coated tablets

Pharmacological Properties:

Maraviroc is a member of a therapeutic class called CCR5 antagonists. Maraviroc selectively binds to the human chemokine receptor CCR5, preventing CCR5-tropic HIV-1 from entering cells.

Indications:

CESENTRI, in combination with other antiretroviral medicinal products, is indicated for treatment-experienced adult patients infected with only CCR5-tropic HIV-1 detectable

Dosage and Administration:

Before taking CESENTRI it has to be confirmed that only CCR5-tropic HIV-1 is detectable (i.e. CXCR4 or dual/mixed tropic virus not detected) using an adequately validated and sensitive detection method on a newly drawn blood sample. The Monogram Trofile assay was used in the clinical studies of CESENTRI. Other phenotypic and genotypic assays are currently being evaluated. The viral tropism cannot be safely predicted by treatment history and assessment of stored samples.

Adult: 150mg, 300mg or 600mg twice daily depending on interactions with co-administered antiretroviral therapy and other medicinal products

Children: Not recommended

Elderly (>65yrs): Used with caution

Can be taken with/without food.

Contraindications:

Hypersensitivity to the active substance or to peanut or soya or to any of the excipients

Precautions:

Antiretroviral therapies including CESENTRI have not been shown to prevent the risk of transmission of HIV to others through sexual contact or contamination with blood. They should continue to use appropriate precautions. Patients should also be informed that CESENTRI is not a cure for HIV-1 infection. Caution must be exercised when administering CESENTRI in patients with a history of postural hypotension or on anti-hypertensive medications, severe cardiovascular disease, impaired immunity, immune reconstitution syndrome (any inflammatory symptoms should be evaluated and treated immediately), osteonecrosis (patient must seek medical advice if joint aches and pain, joint stiffness or difficulty in movement is experienced), renal impairment (CrCl<80ml/min who are on potent CYP3A4 inhibitors & clinical response to treatment should be closely monitored) & hepatic impairment (patient with signs/symptoms of acute hepatitis, esp. if drug-related hypersensitivity is suspected or with increased liver transaminase combined with rash or other systemic symptoms of potential hypersensitivity, discontinuation of CESENTRI needs to be considered).

Drug Interactions:

Dose adjustment of CESENTRI

is needed if coadministered with CYP3A4 inducers/inhibitors, as they may reduce/increase maraviroc concentrations and its therapeutic effects; Dose adjustments of CESENTRI is also needed when administering with Protease Inhibitors (e.g. atazanavir, ritonavir, lopinavir, saquinavir, darunavir, nelfinavir), Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) (e.g. efavirenz), Antibiotics (e.g. rifampicin, rifabutin, clarithromycin, telithromycin), Antifungals (e.g. ketoconazole, itraconazole, fluconazole). Concomitant use of CESENTRI and rifampicin + efavirenz & concomitant use with St. John's Wort (*Hypericum Perforatum*) or products containing St. John's Wort, are not recommended.

Side Effects:

Very common: nausea; Common: Investigations – increased level of ALT, AST and GGT levels, total bilirubin, amylase, lipase and/or absolute neutrophil count, and weight decreased; Nervous system disorders – dizziness, paraesthesia, dysgeusia, somnolence; Respiratory, thoracic and mediastinal disorders – cough; Gastrointestinal disorders – vomiting, abdominal pain, abdominal distension, dyspepsia, constipation; Skin and subcutaneous tissue disorders – rash, pruritus; Musculoskeletal and connective tissue disorders – muscle spasms, back pain; General disorders and administration site conditions – asthenia; Psychiatric disorders – insomnia.

Forensic Classification:

P1S1S3

Humira® (Abbott)

Active ingredient:

Adalimumab

Presentation:

Available in prefilled syringe

Indications:**Psoriatic arthritis**

HUMIRA is indicated for the treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying anti-rheumatic drug therapy has been inadequate. HUMIRA has been shown to reduce the rate of progression of peripheral joint damage as measured by X-ray in patients with polyarticular symmetrical subtypes of the disease and to improve physical function.

Psoriasis

HUMIRA is indicated for the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or PUVA.

Dosage and Administration:**Psoriatic arthritis**

The recommended dose of HUMIRA for patients with psoriatic arthritis is 40mg adalimumab administered every other week as a single dose via subcutaneous injection.

Psoriasis

The recommended dose of HUMIRA for adult patients is an initial dose of 80mg administered subcutaneously, followed by 40 mg subcutaneously given every other week starting one week after the initial dose.

Continued therapy beyond 16 weeks should be carefully reconsidered in a patient not responding within this time period.

Forensic Classification:

P1S1S3



Active ingredient:

Dabigatran etexilate (as mesilate)

Presentation:

Available in 75mg and 110mg hard capsules

Pharmacological Properties:

Dabigatran etexilate is a small molecule prodrug which does not exhibit any pharmacological activity. After oral administration, it is rapidly absorbed and converted to dabigatran by esterase catalysed hydrolysis in plasma and liver.

It is a potent, competitive, reversible direct thrombin inhibitor and is the main active principle in plasma. Dabigatran inhibits free thrombin, fibrin-bound thrombin and thrombin induced platelet aggregation.

Indications:

Primary prevention of venous thromboembolic events in patients who have undergone total elective hip replacement surgery or total knee replacement surgery.

Dosage and Administration:

Prevention of VTE in elective knee replacement surgery:

Recommended dose is 220mg once daily taken as 2 capsules

of 110mg. Treatment should be initiated orally within 1-4 hours of completed surgery with a single capsule and continuing with 2 capsules once daily for a total of 10 days.

Prevention of VTE in elective hip replacement surgery:

Treatment should be initiated orally within 1-4 hours of completed surgery with a single capsule and continuing with 2 capsules once daily for a total of 28-35 days.

With both surgeries if haemostasis is not secured, initiation of treatment should be delayed.

Renal Impairment:

Treatment is contraindicated in severe renal impairment (creatinine clearance < 30ml/min)

Moderate renal impairment (creatinine clearance 30-50 mls/min), caution 150mg daily.

Elderly:

There is limited clinical experience, therefore patients should be treated with caution. Recommended dose is 150mg once daily.

Hepatic Impairment:

Elevated liver enzymes of 2 ULN were excluded in clinical trials hence not recommended.

Contraindications:

- Hypersensitivity to the active substance or to any of the excipients
- Patients with severe renal impairment (CrCl < 30ml/min)
- Active clinically significant bleeding
- Organic lesion at risk of bleeding
- Spontaneous of

pharmacological impairment of haemostasis

- Hepatic impairment of liver disease expected to have any impact on survival
- Concomitant treatment with quinidine

Precautions:

Hepatic Impairment :

The use of Pradaxa is not recommended in this population.

Haemorrhagic risk:

Close clinical surveillance (looking out for signs of bleeding) is recommended throughout the treatment period, especially in the following situations that may increase the haemorrhagic risk: diseases associated with an increased risk of bleeding, such as congenital or acquired coagulation disorders, thrombocytopenia or functional platelet defects, active ulcerative gastrointestinal disease, recent biopsy or major trauma, recent intracranial haemorrhage or brain, spinal or ophthalmic surgery, bacterial endocarditis.

Where bleeding occurs treatment should be discontinued and the source of bleeding investigated.

Spinal anaesthesia/epidural anaesthesia/lumbar puncture

Pradaxa is not recommended in patients undergoing anaesthesia with post-operative indwelling epidural catheters.

Interactions:

Anticoagulants and platelet aggregation agents:

The following treatments are not recommended concomitantly with Pradaxa: unfractionated heparins and

heparin derivatives, LMWH, fondaparinux, desirudin, thrombolytics, GPIIb/IIIa receptor antagonist, clopidogrel, ticlopidine, dextran, sulfinpyrazone and Vit K antagonist. Unfractionated heparin can be administered at doses necessary to maintain patient central venous or arterial catheter.

Amiodarone:

Dosing should be reduced to 150mg Pradaxa daily in patients who received concomitantly dabigatran etexilate and amiodarone.

P-glycoprotein inhibitors:

Caution should be exercised with strong P-glycoprotein inhibitors like verapamil, clarithromycin and others. Quinidine is contraindicated.

P-glycoprotein inducers:

Potent inducers like rifampicin or St. John's Wort may reduce the systemic exposure of Pradaxa.

Gastric pH:

Pantoprazole had decreased the dabigatran area under the plasma concentration – time curve of approximately 30% was observed.

Side Effects:

Bleeding, bleeding at wound sites, anaemia, thrombocytopenia, haematoma, epistaxis, gastrointestinal disorders, rectal haemorrhage, abnormal liver function tests, haemarthrosis, haematuria and others.

Forensic Classification:

P1S1S3



戒煙新突破
3個月，感覺
「脫胎換骨」



戒必適[®] CHAMPIX[®] 乃是第1種專門針對戒煙而研發的非尼古丁特效戒煙藥物¹，從兩方面著手幫助煙民解決：

1. 脫癮期間所引發的不適²
2. 吸煙後所帶來的滿足感²

戒必適[®] CHAMPIX[®] 特效戒煙療程為3個月，是決志戒煙人士的新希望。

譽滿全球：

- 戒必適[®] CHAMPIX[®] 於2007年榮獲美國著名Prix Galien 國際最佳藥物大獎(譽為醫學研究界之諾貝爾獎)³
- 澳洲皇家全科醫學院推崇戒必適[®] CHAMPIX[®] 為最有效藥物戒煙療程⁴
- 英國國家臨床卓越研究推薦戒必適[®] CHAMPIX[®] 為有意戒煙人士的藥物選擇⁵



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北角郵政信箱64563號

戒必適[®] CHAMPIX[®] 乃處方藥物，分「初用」及「持續」包裝，基本療程為12星期。有關產品詳情及是否適合閣下，請向你的醫生或藥劑師查詢。

References:
1. CHAMPIX[®] Prescribing Information, Hong Kong March 2008; 2. Gonzales D, et al. Varenicline, an α4β2 Nicotinic Acetylcholine Receptor Partial Agonist, vs Sustained Release Bupropion and Placebo for Smoking Cessation: A Randomized Controlled Trial. 2006 American Medical Association. JAMA, July 5, 2006 - Vol 296, No. 1, 3. <http://www.prix-galien-usa.com/> (Accessed on 19 May 2008); 4. Zwar N, Richmond R, Borland R, et al. Smoking cessation pharmacotherapy: An update for health professionals. Melbourne: Royal Australian College of General Practitioners; 2007; 5. National Institute for Health and Clinical Excellence. Press Release. NICE advice on the best way to quit smoking. Ref: 2007/0114. <http://www.accessdata.fda.gov/scripts/cder/drugattda/index.cfm?useaction=SearchDrugDetails> (Accessed on 21 May 2008); 7. Data on file

美國FDA認可
至今美國超過475萬人使用