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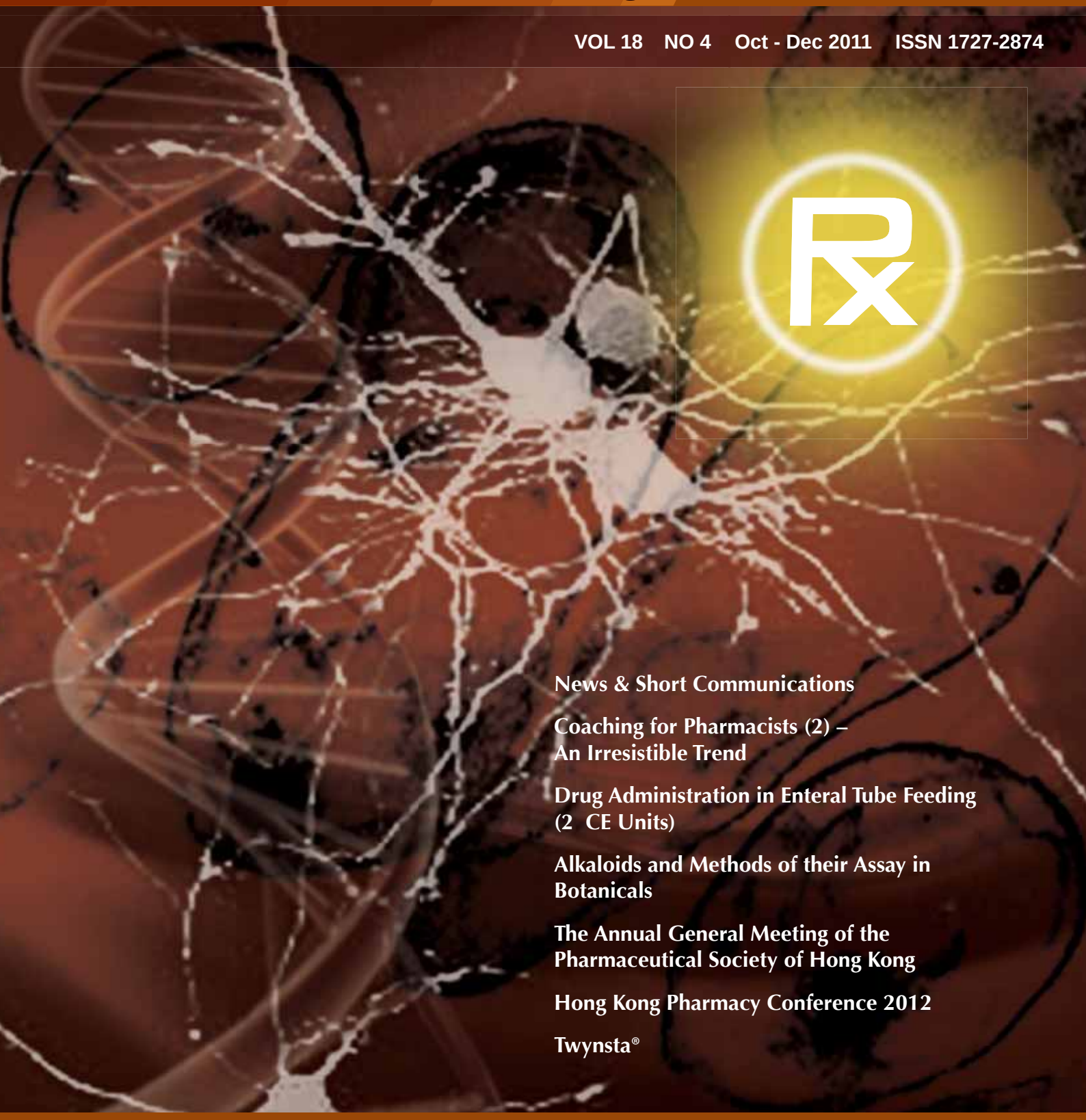

The Pharmaceutical Society of Hong Kong
The Practising Pharmacists Association of Hong Kong
The Society of Hospital Pharmacists of Hong Kong

Bloom to Groan or Groan to Bloom

There were lots of things happened in 2011 around the world. Like what the Chinese say, nighty percent of the news was not good. Upon the arrival of another new year, it is time to recapture a few benchmark events affecting everyone's daily life and don't let bygones simply be bygones; as they may remind or guide us what to do and what not to do in the coming days.

Politically wise, massive demonstrations and demands for political reforms have turned some governments upside down in many countries in Middle East. Since the beginning of 2011, a chain of overthrown power was triggered by the Jasmine Revolution, in which President Ben Ali of Tunisia was ousted last January after a couple of months of protest by his countrymen. The fire of protest and demand for political reforms immediately spread to the nearby countries. Eventually many requests were replaced by violent and the political leaders of Egypt, Libya and other Middle East countries and were ousted or in trouble subsequently. There is no sign that the demand or the social turmoil will come to an end for at least a few more months or even years.

The global economy continues to go downhill or slowdown in the whole year; first in the States followed by European community due to fiscal imbalances in these developed countries. Japanese leaders continue to work through the economic aftereffects of the earthquake and tsunami taken place last March. Although political leaders in the States and Europe have tried their best to resolve some of the near term fiscal problems, the financial markets are not convinced that they are able to address more complex longer term fiscal issues. Despite improved earnings and capital increases, the largest banks in these countries continue to be vulnerable to deteriorating mortgage portfolios, sovereign credit exposure and the approaching deadline to pay huge debts by some governments, adding another source of turmoil to the global financial system.

In the social aspect, the gap of wealth distribution amongst the rich and the poor has widened. The problem has gradually surged to the surface and the poor in many big cities has stood up to ask for their right. Occupy Wall Street (OWS) is a protest movement which began September 17, 2011 in Zuccotti Park, located in New York City's Wall Street financial district, initiated by the Canadian activist group Adbusters. The movement is "in protest against exploitation and oppression by capital, shaking all fabrics of society. It is against social and economic inequality, high unemployment, greed, as well as corruption, and the undue influence of corporations—particularly from the financial services sector—on government. The protesters' slogan "We are the 99%" refers to the growing income and wealth inequality in the U.S. between the wealthiest 1% and the rest of the population. The protests in New York City have sparked similar occupy protests and movements around the world, such as St. Paul's Cathedral Square in London and HSBC headquarter at Central district in Hong Kong.

In Hong Kong, we are quite fortunate as most people can still enjoy their peaceful lives even though there are similar requests for some minor issues but the voice is still small. Be it universal suffrage, the education reform, the district council election, the debate of minimum wage for workers, complaints of medical errors due to human handlings or even the right for foreign domestic helpers to apply for permanent residency, are examples of some hotly debate issues in recent months amongst Hong Kongers. The majority of the local people are not interested in these social or politic issues but more interested in making money instead.

But whether we could continually enjoy our happy lives here and be exempted from all the troubles that this world has is still too early to say. **Are we heading from bloom to groan or from groan to bloom?** We will definitely know after waiting for another few months.

Whatever happened, the journal of HKPS has been published regularly in the last twelve months. Thanks to those who have made some contributions to this journal. Throughout the year, the editorial board of HKPJ has also held regular meetings to discuss which articles should be included in each issue. There were at least four to five members who consistently turned up. Without their participations, the publication of this journal would not be so smooth. Therefore, I would also take this opportunity to thank their devotions and efforts. On top of these, HKPJ have published more articles and pages than ever before. We aim to do it even better with your contributions in the future.

Perhaps, one of the biggest joyful events in last year might be a series of event taken place in different cities to celebrate the achievements of chemistry and its contributions to the well-being of humankind. By unanimous consent, the U.S. Senate even passed a resolution on September 26, 2011, designating 2011 as the International Year of Chemistry (IYC 2011), which under the unifying theme "Chemistry—our life, our future", chemists had been celebrating for whole year with a range of interactive, entertaining, and educational activities for all ages. The IYC activities were originally initiated by International Union of Pure and Applied Chemistry (IUPAC) and UNESCO a couple years ago. After almost a year-long celebration in different parts of the world, it culminated with a unique closing event in Brussels, Belgium on December 1. IYC marks the 100th anniversary of the Nobel Prize Award to Marie Curie and the 100th anniversary of the most significant scientific meetings of all times, i.e. the Solvay Conferences. Because of this meeting, the creation of International Association of Chemical Society (IACS) which subsequently developed into IUPAC was born. In order to celebrate this big event, two chemist scholars representing two universities had independently written a poem. They are printed in this issue for your entertainment during the holiday break.

There are also lots of other important news and articles relevant to pharmacy practices. Because running out of space to brief them individually, I leave it to you to discover and to enjoy. If you have any feedbacks, comments or suggestions, please do not hesitate to let us know.

Before putting a stop to my editorial commentary, I wish all readers a Happy Chinese Lunar New Year of the Dragon!

Cheung Hon-Yeung
Editor-in-Chief
12th January, 2012

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INSTRUCTIONS FOR AUTHORS

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

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

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

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

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

e-mail: ***editor@hkpj.org***

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

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

In advanced RCC:

When a VEGF-Targeted therapy fails

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to a proven 2nd-line therapy

Powered by Phase III evidence, AFINITOR, a new oral mTOR inhibitor, is proven to more than double median progression-free survival vs placebo.[1-3]

The Afinitor pivotal trial is the first phase III prospective, randomised, placebo-controlled trial to demonstrate a therapeutic benefit for patients after either sunitinib or sorafenib failure.

AFINITOR® Important note: Before prescribing, consult full prescribing information. **Presentation:** tablets containing 5 mg or 10 mg of everolimus **Indications:** adult patients with advanced renal cell carcinoma (RCC). **Dosage:** ***Adults:*** one 10 mg dose once daily at the same time every day, with or without food. Dose adjustment may be required due to side-effects or when used with moderate CYP3A4 or PgP inhibitors or strong CYP3A4 inducers •***Children:*** AFINITOR is not recommended for use in children or adolescents •***Patients with hepatic impairment:*** dose should be reduced to 5 mg daily in patients with moderate hepatic impairment (Child-Pugh class B); not recommended in patients with severe hepatic impairment (Child-Pugh class C). **Contraindications:** Hypersensitivity to the active substance, to other rapamycin derivatives or to any of the excipients. **Warnings/Precautions:** •***Non-infectious pneumonitis:*** Cases have been described in patients taking AFINITOR, some of these have been severe and on rare occasions, a fatal outcome was observed. In case of shortness of breath, pleural effusion, cough or dyspnoea not due to infection or malignancy, radiologic assessment for pneumonitis is indicated. In some cases, management of pneumonitis may require dose adjustment and/or interruption, or discontinuation of AFINITOR and/or addition of corticosteroid therapy •***Infections:*** AFINITOR is immunosuppressive. Localised and systemic bacterial, fungal or viral infections (e.g. pneumonia, aspergillosis or candidiasis, hepatitis B reactivation) have been described in patients taking AFINITOR, some of these have been severe and occasionally fatal. Preexisting infections should be treated prior to starting treatment with AFINITOR. Be vigilant for symptoms or signs of a potential bacterial, viral or invasive fungal infection while on AFINITOR. In case of emergent infections, institute appropriate treatment promptly and consider interruption or discontinuation of AFINITOR. If a diagnosis of invasive systemic fungal infection is made, discontinue AFINITOR and treat with appropriate antifungal therapy •***Hypersensitivity reactions*** have been observed with everolimus and other rapamycin derivatives •***Oral ulceration:*** Mouth ulcers, stomatitis and oral mucositis have been seen in patients treated with AFINITOR, topical treatments are recommended, but alcohol- or peroxide- containing mouthwashes should be avoided •***Laboratory tests and monitoring:*** Renal function, blood glucose, and complete blood counts are recommended prior to initiation and periodically during treatment •***Hepatic Impairment:*** Not recommended in patients with severe hepatic impairment (Child-Pugh class C) •***Vaccination:*** Avoid use of live vaccines •***Pregnancy:*** should not be given to pregnant women unless the potential benefit outweighs the potential risk to the foetus •***Women of childbearing potential:*** Use effective contraception methods while receiving AFINITOR, and for up to 8 weeks after ending treatment •***Breast-feeding:*** Women taking AFINITOR should not breast feed •***Fertility:*** Male fertility may be compromised by treatment with AFINITOR. **Interactions:** •avoid concurrent treatment with strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, ritonavir, clarithromycin, telithromycin) and strong PgP inhibitors •caution with moderate inhibitors of CYP3A4 and/or PgP (e.g. erythromycin, verapamil, diltiazem, fluconazole, ciclosporin, amprenavir, fosamprenavir, aprepitant) •avoid concurrent treatment with strong inducers of CYP3A4 or PgP (e.g. rifampicin, rifabutin) St. John's Wort (*Hypericum perforatum*), carbamazepine, phenobarbital, phenytoin, efavirenz, nevirapine, dexamethasone, prednisone, prednisolone •avoid grapefruit juice, grapefruit and other foods affecting CYP3A4 or PgP. **Adverse reactions:** •Very common (≥10%): Stomatitis, rash, fatigue, asthenia, diarrhoea, anorexia, nausea, mucosal inflammation, vomiting, cough, infections, peripheral oedema, dry skin, epistaxis, pneumonitis, pruritus, dyspnoea, dysgeusia •Common (≥1 to <10%): Headache, dry mouth, pyrexia, weight decreased, hand-foot syndrome, abdominal pain, erythema, insomnia, dyspepsia, dysphagia, hypertension, increased daytime urination, dehydration, chest pain, haemoptysis, exacerbation of diabetes mellitus •Uncommon (<1%): Ageusia, congestive cardiac failure, new onset diabetes mellitus, impaired wound healing, grade 1 haemorrhages. Cases of Hepatitis B reactivation have been observed.

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Further information is available on request.

References: 1. Motzer RJ, Escudier B, Oudard S, et al; for the RECORD-1 Study Group. Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomised, placebo-controlled phase III trial. *Lancet.* 2008;372:449-456. **2.** Escudier B, Ravaud A, Oudard S, et al; for the RECORD-1 Study Group. Phase-3 randomized trial of everolimus (RAD001) vs placebo in metastatic renal cell carcinoma. 33rd ESMO Congress. September 12-16, 2008. Stockholm, Sweden. [Slide presentation] Abstract 720. **3.** Kay A, Motzer R, Figlin R, et al. Updated data from a Phase 3 randomized trial of everolimus (RAD001) vs PBO in metastatic renal cell carcinoma. 2009 Genitourinary Cancers Symposium. February 26-28, 2009. Orlando, FL. In press.

HKC-AFI-A027-0110

African Mango Used as Weight Loss Supplement

Date: October 8, 2011

Interest in the use of African Mango extract (irvingia gabonensis) as a safe, effective and inexpensive weight loss alternative surged after Dr. Mehmet Oz called it a "breakthrough supplement" and a "miracle in your medicine cabinet" on his Emmy Award – winning The Dr. Oz Show, which aired on September 13, 2010.

According to a recent study published in the scientific journal *Lipids in Health and Disease*, men and women supplementing with African Mango extract for just 28 days lost an astonishing 3,990% more weight than those taking a placebo (8.9 lbs vs. 0.22 lbs). Beyond the weight loss, the volunteers taking African Mango extract 30 minutes before meals lost a stunning average of 2.4 inches from their waistlines as well as 1.8 inches from their hips — and their bad LDL cholesterol, triglyceride, and glucose levels all plummeted.

African Mango has actually been used as a diet aid for centuries in Cameroon, Africa. The brightly-colored tropical fruit is native to Cameroon's west-coastal rainforests. African Mango, or Bush Mango, differs from other mango fruits in that it produces a peculiar seed, which natives of Cameroon refer to as *Dikka nuts*. For hundreds of years, an extract from the seeds called *irvingia gabonensis* has been used among Cameroon villagers for its wide-ranging medicinal benefits, which range from reducing and preventing obesity to lowering cholestrol to regulating blood sugar to treating infections.

Source: http://healthdiscoveriestoday.com/Supplements.html

Vitamin Supplements Linked to Increased Risk for Death

Date: October 10, 2011

In women aged 55 to 69 years, several widely used dietary vitamin and mineral supplements, especially supplemental iron, may be associated with increased risk for death, according to new findings from the Iowa Women's Health Study. Although many vitamin supplements did not appear to be associated with a higher risk for total mortality, several were, including multivitamins, vitamins B6, and folic acid, as well as the minerals iron, magnesium, zinc, and copper. The findings were reported in the October 10 issue of the Archives of Internal Medicine.

Source: Archives of Internal Medicine

'Bath Salt' Street Drugs Temporarily Banned

Date: October 21, 2011

The US Drug Enforcement Administration (DEA) in October temporarily banned 3 synthetic stimulants marketed as "bath salts" and "plant food" that mimic cocaine, LSD, MDMA, and/or methamphetamine when ingested. The move followed a September 8 letter to the editor in the New England Journal of Medicine reporting that people who overdose on the bath salts are showing up in emergency departments with increasing frequency.

Source: US Drug Enforcement Administration

European Union: Xigris (drotrecogin alfa activated) to be Withdrawn due to Lack of Efficacy

Date: October 26, 2011

The European Medicines Agency has been informed of Eli Lilly's decision to withdraw Xigris from the market worldwide further to the 28-day mortality results from the PROWESS-SHOCK study. The results of the PROWESS-SHOCK study have now become available and they fail to meet the primary endpoint of a statistically significant reduction in 28-day all-cause mortality in patients treated with Xigris compared with placebo. The study also fails its secondary endpoint of a reduction of mortality in the population of patients with severe protein C deficiency. The small difference in the 28-day mortality of the overall population (26.4% in the Xigris arm versus 24.2% in the placebo arm; n=1680 patients) is not statistically significant. The risk of severe bleeding events, which is the main risk with this product, was 1.2% in the Xigris arm and 1.0% in the placebo arm, suggesting there was no increased harm. These results call into question the overall benefit-risk balance of Xigris for the indicated patient population (severe sepsis). Eli Lilly has thus decided to withdraw the product from the market worldwide and also decided to discontinue all other ongoing clinical trials. In Hong Kong, Xigris for Inj. 5mg (HK-51126) and Xigris for Inj. 20mg (HK-51125) have been registered by Eli Lilly Asia Inc. since year 2003. They are prescription medications and are indicated for treatment of adult patient with sepsis with multiple organ failure. The company has written to DH to cancel the registration of the product.

Source: www.psdh.gov.hk

Europe Okays Pneumonia Vaccine for Adults 50 Years and Older

Date: October 28, 2011

The European Commission has extended approval of Pfizer's 13-valent pneumococcal conjugate vaccine Prevenar 13 to adults aged 50 years and older. The 13 pneumococcal serotypes in Prevenar 13 (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) are responsible for causing a significant proportion of invasive pneumococcal disease in older adults, including disease caused by antibiotic-resistant serotypes, the company notes. It was approved based on a review of clinical safety and immunogenicity data in more than 6000 old adults. The vaccine is already approved for children in more than 100 countries.

Source: Medscape Medical News

Australia: Citalopram and Heart Problems - Changes to Recommended Doses

Date: November 4, 2011

The TGA advised that citalopram should no longer be used at doses greater than 40 mg per day. For some patients, the maximum recommended dose is now only 20 mg per day. In addition, it is now advised that people who have been diagnosed with a heart condition known as "congenital long QT syndrome" should not take citalopram. This is due to a recent study by the Forest Research Institute in the USA has shown that higher doses of citalopram can cause abnormal changes in the electrical activity of the heart. In rare cases these changes can result in serious heart problems.

Source: http://www.tga.gov.au/safety/alerts-medicine-citalopram-111104.htm

Chinese Medicine Practitioner Arrested

Date: November 12, 2011

A renowned Chinese medicine practitioner, Mr. Sin Lai Sang was arrested by police for prescribing western medicine without a license and possession of part 1 poisons. The police took action after receiving the complaint from a Mrs. Wong who took her 3 year old daughter to Mr. Sin for treatment of eczema. Mr. Sin prescribed a cream in a white plastic jar with no labeled ingredients. After applying the cream, her daughter's eczema cleared up within hours. However the eczema reccurred very fast. She had asked Mr. Sin whether the cream contained any corticosteroids and was told that there was none. Mrs. Wong 's daughter was also treated by a western medicine practitioner who prescribed corticosteroids cream but advised her to stop the application after 10 days to prevent the side effects of steroids. During the off days, she would used the cream provided by Mr. Sin. Her daughter's skin became hypopigmented with hair growth. However, she was worried about overdosing of steroids and hence lodged in the complaint to Department of Health for investigation. Upon analysis it was found that the cream from Mr. Sin contained corticosteroids. The case is under investigation by police.

Source: Ming Pao Daily News (2011.11.12)

Misoprostol Wrongly Administered to Pregnant Women

Date: November 12, 2011

A 2 months pregnant woman, Ms. Cheng was encountering slight bleeding problem and checked into the hospital in Chiu Chow Shantou for treatment. She was given 3 sugar coated tablets by a nurse. After taking the medication, she experienced hot flushes in the palm and soles of the feet. At the same time, the nurses rushed in, asked if she has taken the medication and then left without saying any thing. She looked at the external label and found that it was labeled "Misoprostal". She checked on the internet and was horrified to find out that Misoprostal was used for abortion. Upon enquiry, the doctor and nurses admitted that she was given the wrong medicine. Ms. Cheng was then given treatment for over ten days. After 20 days, the Ultrasound showed that the foetus was still alive but she was worried whether the medicine has harmed the baby. The head of the of the Shantou O & G Hospital said that Misoprostal would not accumulate in the body and was not teratogenic nor carcinogenic. If the baby is born with defect confirmed by specialist to be caused by the wrongly administered drug, the hospital will take up all related responsibilities. The nurse that administered the wrong drug was a trainee, she was reprimanded and dismissed from the hospital.

Source: Ming Pao Daily News (2011.11.12)

Testing and Certification

Date: November 13, 2011

Testing and certification is one of the six economic areas in which Hong Kong enjoys clear advantages and has potential for further development. The Hong Kong Council for testing and certification (HKCTC) was established on September 17, 2009, to advise the Government on the overall strategy to grow the industry. It comprises members from the industry, the business sector and professional organizations as well as the relevant public bodies and government departments. Last year, the HKCTC formulated a three-year market-oriented development plan for the industry, and the Government has accepted all the recommendations made in the Report of the HKCTC. The Government is now working closely with the HKCTC to strengthen the industry and develop new business opportunities in testing and certification services in four selected trades, i.e. Chinese medicine, construction materials, food and jewellery.

Accreditation is open and voluntary in Hong Kong. It is currently provided by Hong Kong Accreditation Service (HKAS) under Innovation and Technology Commission in Hong Kong. HKAS operates three accreditation schemes: the Hong Kong Laboratory Accreditation Scheme (HOKLAS), the Hong Kong Certification Body Accreditation Scheme (HKCAS), and the Hong Kong Inspection Body Accreditation Scheme (HKIAS). Accredited laboratories, inspection bodies and certification bodies need to undergo rigorous on-site assessments before they are recognised to be competent in performing the conformity assessment activities listed in their respective scopes of accreditation. Users of conformity assessment services may identify and select the services provided by accredited bodies to support their business. To find the list of accredited establishments under HOKLAS, HKCAS and HKIAS, please click http://www.itc.gov.hk/en/quality/hkas/accrorg.htm

The Product Standards Information Bureau (PSIB) provides a comprehensive range of standards-related services to promote general awareness of standards and in particular to local enterprises, provide them with the latest information on local and overseas standards and technical regulations, and assist them to comply with these requirements in their manufacturing, exports and provision of services and to enhance quality and competitiveness. PSIB offers sales services for standards and free technical enquiring service. Members of the public may purchase original copies of standards, guides, publications or handbooks issued by different standards bodies through the PSIB.

The Standards and Calibration Laboratory (SCL) of the Innovation and Technology Commission is responsible for maintaining the reference standards of physical measurements for Hong Kong. These standards are metrologically traceable to the International System of Units (SI). SCL also provides calibration services to users of measurement standards and measuring instruments to ensure measurement accuracy and proper metrological traceability.

Source: www.itc.gov.hk

National Institutes for Food and Drug Control to Participate in Hong Kong's Materia Medica Standards Project

Date: November 22, 2011

The National Institutes for Food and Drug Control (NIFDC) under the State Food and Drug Administration, People's Republic of China, will participate in Hong Kong's Materia Medica Standards project under an agreement signed today with the Department of Health (DH). The contract was signed between Dr PY Lam, Director of Health, who is Chairman of the International Advisory Board (IAB) on the Hong Kong Materia Medica Standards (HKCMMS) project, and Mr. Li Yunlong, Director-General of NIFDC in Beijing .

The work to be undertaken by NIFDC will be funded by the HKCMMS Project and will focus on the development of reference standards for 24 Chinese herbs. The HKCMMS project was launched in 2002 to develop the reference standards for 60 commonly used Chinese herbs. An International Advisory Board, comprising a panel of internationally renowned experts in herbal medicines, pharmacognosy, toxicology, biochemistry and so forth, was set up to give advice on the principles, methodologies, parameters and analytical methods for the development of HKCMM standards. The IAB also helped to decide the contents of the HKCMMS Standards, selected the research institutions to take up the research and laboratory work, and determined the target herbs.

The Government Laboratory, as well as the research teams of the six local universities and Taiwan's China Medical University is also involved in the project. DH has recently developed and released an iPhone Apps for the first eight monographs of HKCMMS, and would continue to work for remaining monographs with a view to promulgate safety and quality standards for use of Chinese medicines.

Source: http://www.dh.gov.hk/english/press

Oral, Topical 5-ASA Combo Most Effective for Ulcerative Colitis

Date: November 22, 2011

Treatment with combined oral and topical 5-aminosalicylates (5-ASAs) is more likely than oral therapy alone to achieve remission of ulcerative colitis (UC). That's one finding from a meta-analysis reported in the American Journal of Gastroenterology online November 22. There was also some evidence to suggest that intermittent topical therapy was superior to oral 5-ASAs for preventing relapse of quiescent UC. Dr. Alexander C. Ford, with Leeds General Infirmary in the UK, and colleagues point out that 5-ASAs are the mainstay of treatment for many patients with ulcerative colitis, but the relative efficacies of oral, topical or combined oral and topical 5-ASA therapy "remain relatively unknown."

They therefore systematically reviewed the literature and found 12 randomized trials examining the effects of different routes of 5-ASA administration in adults with active or quiescent ulcerative colitis. In the case of active disease, the pooled data indicated failure to induce remission was significantly less likely with combined oral and topical 5-ASAs than with oral therapy alone (relative risk, 0.65). The number needed to treat (NNT) with combined 5-ASA therapy to prevent one patient failing to achieve remission was five. the relative risk of failure to achieve remission with topical versus oral 5-ASAs was 0.82, but this was not statistically significant, the report indicates.

For maintenance therapy of quiescent ulcerative colitis, the risk of relapse was significantly less with intermittent topical therapy than with daily oral therapy, the analysis showed. The relative risk was 0.64, and four patients would need to be treated with intermittent topical therapy to prevent one relapse. While the relative risk of relapse with combined therapy versus oral therapy was 0.48, this was not statistically significant as the result was based on a total of just 96 patients, according to the report.

In fact, Dr. Ford and colleagues caution that the total amount of data in their analysis was limited. They conclude: "Further trials of higher quality, which study the relative efficacy of oral vs. topical 5-ASA therapy, and oral vs. combined oral and topical 5-ASAs, for both the induction of remission and prevention of relapse of UC, as well as examining patient preferences on routes of administration for 5-ASAs in these two situations, are required."

Source: www.medscape.com/viewarticle/755194_print

Canada: Yasmin and Yaz (drospirenone) - Updated Information on Increased Risk of Blood Clots

Date: December 9, 2011

Health Canada informed healthcare professionals a safety review of drospirenone-containing oral contraceptives (marketed under the brand names Yasmin and Yaz) with respect to the risk of blood clots (venous thromboembolism, or VTE) has been completed. The review determined that drospirenone-containing birth control pills may be associated with a risk of blood clots that is 1.5 to 3 times higher than other birth control pills. Blood clots are a rare but well known side effect associated with all birth control pills. The risks of blood clots are higher with pregnancy and childbirth than with oral contraceptives. As part of its review, Health Canada considered several recent observational studies evaluating the risk of blood clots with drospirenone-containing oral contraceptives versus other oral contraceptives. Overall, the body of current evidence suggests that the risk of blood clots is 1.5 to 3 times higher with oral contraceptives that contain drospirenone relative to those that contain levonorgestrel, a different hormone. Overall the risk of blood clots with any oral contraceptive (including Yasmin and Yaz) is very small. The drug labels for Yasmin and Yaz have been updated to include information on the studies and the recommendation that, when prescribing an oral contraceptive, health professionals consider the risks and benefits of drospirenone-containing oral contraceptives for a specific patient in light of her risk for developing blood clots, and relative to the risks and benefits of other birth control pills on the market.

Source:http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2011/2011_164-eng.php

CDC Recommends New Regimen for Latent Mycobacterium tuberculosis

Date: December 10, 2011

The US Centers for Disease Control and Prevention (CDC) recommends a new isoniazid-rifapentine (INH-RPT) regimen with direct observation to treat latent Mycobacterium tuberculosis infection (LTBI), according to a report published in the December 9 issue of the Morbidity and Mortality Weekly Report. This new treatment regimen should considerably shorten and simplify treatment. Until now, the standard regimen for treatment of LTBI in the United States has been 9 months of INH daily without directly observed therapy (DOT). However, a new combination regimen of INH-RPT given weekly for 12 weeks as DOT is as effective as other regimens for TB prevention and is more likely to be completed, according to findings from 3 randomized controlled trials and expert opinion.

Source: Morbidity and Mortality Weekly Report

Ranitidine-Associated Risk for Death in Premature Newborns

Date: December 12, 2011

Very-low-birth-weight newborns given ranitidine for stress ulcers and gastroesophageal reflux disease (GERD), are about 6 times more likely to die than similar newborns not given the drug. Researchers said that gastric acid kills pathogens, and by inhibiting its secretion, ranitidine increases the risk for infections. Researchers from 9 centers in Italy, led by Gianluca Terrin, MD, PhD, from the Department of Women's Health and Territorial Medicine, University La Sapienza, Rome, Italy concluded that ranitidine should be administered with care in preterm infants because of the risk of severe infectious disease, necrotizing enterocolitis, and fatal outcome.

The study was the first multicenter prospective study on morbidity and mortality associated with ranitidine in very-low-birth-weight newborns. To test the safety of this application, the researchers enrolled 274 consecutively observed newborns with birth weights ranging between 401 and 1500 g, or a gestational age between 24 and 32 weeks, in 4 Italian neonatal intensive care units. Forty-two of these infants received ranitidine to prevent stress-induced peptic disease. Another 49 received the drug because of suspected GERD. The remaining 183 newborns did not receive ranitidine.

Thirty-four infants who received ranitidine developed infections (37.4%), whereas 28 of those not exposed to ranitidine did (9.8%), which was a significant difference ($P < .001$). Sepsis was the most common infection, affecting 25.3% of the infants who received ranitidine compared with 8.7% of the infants who did not receive the drug. Pneumonia (4.4% vs 0.5%) and urinary tract infections (7.7% vs 0.5%) made up the remainder of the infections, although those differences did not reach statistical significance. The duration of ranitidine treatment did not affect the risk for infection.

The infants who received ranitidine suffered necrotizing enterocolitis at a rate of 9.8% vs 1.6% among the infants who did not receive the drug ($P = .003$). Infants who received ranitidine spent a median of 52 days in the hospital compared with 36 days for the infants who did not ($P = .001$). Finally, 9.9% of the infants receiving ranitidine died vs 1.6% of those who did not receive the drug ($P = .003$). Additional studies are warranted to investigate the reasons for the increased risks associated with ranitidine. The researchers speculated that the drug changes the gastric environment in a way that favors pathogens, such as *Escherichia coli* and *Klebsiella pneumoniae,* both of which were documented in this study, it may also suppress immune defenses, including the production of inflammatory cytokines, and disrupt the Th1-Th2 balance.

Source: Medscape Medical News © 2011 WebMD, LLC

Seafood Revealed as Biggest Source of Dangerous Toxins

Date: December 14, 2011

According to a major food study conducted by the Centre for Food Safety, seafood is the largest source of potentially harmful dioxin-based toxins in the diet of Hongkongers. Researchers tested 142 food samples over the past year, focusing on 2 power classes of toxins - dioxin and dioxin-like polychlorinated biphenyls. The samples were drawn from 71 types of food purchased from markets and prepared as they would be served on the table. The safety standard for both toxins is 70 picograms of toxicity equivalents (pgTEQ) per kilogram of body weight per month set in 2001 by the Food and Agriculture Organisation and the WHO. The test results showed that mandarin fish, oysters and pomfret contained 1.056, 0.926 and 0.885 pgTEQ per gram respectively. However, the toxins are not consumed at dangerous levels based on Hongkongers' normal eating habits. "People should not stop eating fish, because fish contains many essential nutrients", Dr. Xiao Ying, a food safety officer at the Centre said. Dr. Ho Yuk-yin, a consultant in community medicine at the Center, recommended fish three times a week. To lessen the intake of dioxins, the Centre advised Hongkongers to trim the fat from meat and opt for low fat dairy products, since dioxins are fat soluble and accumulate in the fatty tissues of meat and seafood. It recommended a balanced diet with a rich variety of fruits and vegetables.

Source: South China Morning Post (2011.12.14)

Adverse Events Related to Poly Implant Prothese Breast Implants

Date: December 22, 2011

On December 21, the Department of Health was informed by the AFSSAPS of their updated figures on serious adverse events related to Poly Implant Prothese (PIP) breast implants. This included a fatal case of anaplastic large cell lymphoma (ALCL), a rare form of cancer of the immune system, which was earlier reported in November. However, it was not possible for them to conclude whether PIP implant was an additional risk.

DH noted that to date, the French authority has not made any decision on the need to remove the PIP implants, and that an expert meeting is expected to provide further recommendations on the management and follow-up of patients with such implants. In Hong Kong, DH has so far not received any report of adverse events associated with PIP breast implants. Meanwhile, the department will closely follow up with the recommendations issued by AFSSAPS and other medical device regulatory authorities. In March 2010, the AFSSAPS has made a decision to recall and suspend the marketing, distribution, export and the use of the silicone gel breast implants manufactured by PIP, as there were increased reports of ruptures of the implants due to quality defects. A press release was also made by DH on March 31, 2010 in response to AFSSAPS' announcement.

Source: http://www.dh.gov.hk/english/press/2011/111222.html

FDA Safety Changes: Dronedarone Linked With Cardiovascular Events

Date: December 22, 2011

Dronedarone is an antiarrhythmic agent intended to reduce the risk for hospitalization for atrial fibrillation (AF) in patients currently in sinus rhythm but who have a history of paroxysmal or persistent AF. Because dronedarone has been linked to serious cardiovascular events, including death, in patients with permanent AF, the FDA is requiring new safety label warnings that it should be prescribed only to patients who can be converted into normal sinus rhythm, and that it should be discontinued in patients in AF. Patients taking dronedarone should have an ECG at least once every 3 months. The boxed warning also states that dronedarone is contraindicated in patients with recently decompensated heart failure requiring hospitalization or in patients with class IV heart failure. Other contraindications include second- or third-degree AV block or sick sinus syndrome in patients not using a functioning pacemaker, bradycardia, concurrent use of drugs that prolong the QT interval, liver toxicity caused by previous use of amiodarone, severe hepatic impairment, QTc Bazett interval of 500 milliseconds or longer, pregnancy, and breast-feeding. Antithrombotic therapy is indicated before and throughout use of dronedarone, because the risk for stroke is increased, particularly in the first 2 weeks of treatment. Dronedarone should be discontinued if heart failure develops or worsens and requires hospitalization, if hepatocellular liver injury is suspected, or if the QTc Bazett interval is 500 milliseconds or longer. Serum creatinine levels should be monitored periodically.

Source: http://www.medscape.org/viewarticle/755944?src=cmemp

Combination Therapy Useful for Advanced Hepatoma

Date: December 29, 2011

Hepatocellular carcinoma (HCC) is the third leading cause of cancer death worldwide, causing around half a million deaths annually. Japanese researchers reported that patients with HCC that's invaded the portal vein might have better outcomes if they receive intra-arterial 5-fluorouracil plus systemic pegylated interferon alpha-2b.

Source: New York Reuters Health Information

Benefit of Rituximab-EPOCH for HIV-Related Lymphoma Confirmed

Date: December 29, 2011

A pooled analysis of two trials indicates that HIV patients with aggressive B-cell non-Hodgkin lymphoma (NHL) fare better when rituximab is combined with EPOCH chemotherapy instead of CHOP chemotherapy.

Source: New York Reuters Health, also http://bit.ly/sseXAi

FDA Drug Warnings in Year 2011

Date: December 29, 2011

A variety of drug warnings made news in 2011: The FDA recommended in June that physicians should refrain from using the 80-mg dose of simvastatin unless the patient has already been taking the drug for 12 months and there is no evidence of myopathy. Also in June the FDA warned of an increased risk of being diagnosed with a high-grade prostate cancer while taking 5-alpha reductase inhibitors. In July the FDA warned that clinicians generally should avoid prescribing either methylene blue or linezolid in combination with serotonergic agents to avoid a potential drug interaction causing serotonin syndrome. And in August, the FDA said the antidepressant citalopram should not be used in doses higher than 40 mg per day because of concerns that it can cause potentially fatal changes in heart rhythm.

Source: http://www.medscape.com/features/slideshow/year-in-medicine/2011

兩首有關化學的詩詞 (Two Poems about Chemistry)

近日一段由北京大學校長暨著名高分子化學家周其風教授作詞，北京大學中樂學社唱出的《化學是你、化學是我》歌曲在網絡上爆紅。主編聽後感觸良多，遂將歌詞抄錄並與香港城市大學生物及化學系黃寧表教授所作的『化學便是吾心』一詩并列，供同寅共賞。兩首作品文體雖不同，表達內容卻有異曲同工之妙。(主編註)

《化學是你 化學是我》歌詞

– 北京大學校長周其風教授

(抒情空靈)
化學究竟是什麼 化學就是你
化學究竟是什麼 化學就是我

化學究竟為什麼 化學為了你
化學究竟為什麼 化學為了我

化學究竟為什麼 化學為了你
化學究竟為什麼 化學為了我

(跳躍輕快)
1) 父母生下 生下的你我
lalala是化學 過程的結果

你我你我 的消化系統
lalala是化學過 程 的場所

記憶和思維活動 要借化學過程來描摹
要借化學過程來描摹 描摹描摹

即便你我的喜怒哀樂 也是化學神出鬼沒
也是化學物質的 神出鬼沒

(**副 歌** 寬廣)
化學 你原來如此神奇(給力)
哦 化學 難怪你不能不火
哦 四海兄弟 我們攜手努力
哦 為人類的航船 奮力揚波
(結尾：奮力揚波)

2) 你我你我 要溫暖漂亮
lalala化學提供 衣裝婀娜

你我你我 要吃足喝好
lalala化學提供 營養多多

你我要飛天探地 化學提供動力幾何
化學提供動力幾何 動力幾何

即便你我的身心健康 也是化學密碼解鎖
也是化學為生命 密碼解鎖

(**副 歌** 寬廣)
化學 你原來如此神奇(給力)
哦 化學 難怪你不能不火
哦 四海兄弟 我們攜手努力
哦 為人類的航船 奮力揚波
(結尾：奮力揚波)

《化學便是吾心 My heart is all chemistry》

– 香港城市大學生物及化學系黃寧表教授

學海浩瀚　Of the many domains of knowledge
分門別類　In the boundless sea of learning
寄身化學　I set my heart on chemistry –
畢生追隨　A voyage to my lifelong yearning

青銅時代多巧手　In Bronze age times, skillful hands, weapons made
煉鑄寶劍論火候　Controlling heat, forged swords with keen edged blades
取材選料又講究　Material selection was critical
化學之始有源頭　Perhaps the start of science chemical?

長生之道似幻化　In an illusive search wanting to live forever
術士深山煉丹砂　Alchemists thought the synthesis of cinnabar clever
偶爾製成黑火藥　Black powder was an accidental creation
一聲轟鳴震天下　The first explosions shocked the all nations

人類文明幾千載　Over millennia we have advanced
自然產物有取代　We now can substitute what we once got from plants
合成纖維人人愛　Synthetic fibers are useful with them much is done
納米科技拓未來　Nanoscience and nanotech are a future to come

石油年代快告終　The Petroleum age will be ending soon
能源危機勢洶洶　An energy crisis lingers with menace and gloom
幸有陽光量無窮　Nature gives us abundant light from the Sun
化學人才有待用　So it's high time Chemists; there's work to be done

化學之道　The Dao of chemistry is in our lives
生生不息　With endless creativity we all strive
物換相移　For material conversion and phase transformations
多形多式　Giving us variety, complexity and more innovation
持之以道　With proper handling, respect and care
舉世得益　The whole world benefits from our wares
造福萬民　People embrace with happy heart and soul
豐衣足食　Materials, medicine and food our goal
潔淨山河　Mountains and rivers are once more green
天藍水碧　The skies are blue and the waters clean
我等互勉　As we support each other in these tasks
共創奇蹟　We work together so miracles we grasp

辛卯年 (2011) 仲春 寫於香江

Coaching for Pharmacists (2) – An Irresistible Trend

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ABSTRACT

Coaching is a growing trend of leadership style. Due to the positive effect of coaching that brings sustainable benefit to the organizations, it has raised concern in the health-care services as well. Coaching benefits in pushing personal growth and development, assists in relationship building with both internal and external colleagues. Coaching does not only bring benefits to any organization, but also provide better health-care for patients in the community. To facilitate successful implementation of coaching culture in an organization, all individuals should contribute in the actual practices of coaching.

Keywords: *coaching; trend; culture; positive impacts; pharmacist skills.*

INTRODUCTION

Few people have noticed the growth of coaching in recent years. In 2004, the Chartered Institute of Personnel and Development (CIPD), which is taking a leading position in the development of coaching in United Kingdom, reported that 79% of respondents in a survey were using coaching as part of their learning and development activities. Moreover, 99% agreed that "coaching can deliver tangible benefits both to individual and organizations". These are evidences to show that coaching is an essential and valuable feature of a modern organization's learning and development strategy.

There are multiple factors contributing to the explosive growth of coaching. Different representative bodies, such as CIPD, the International Coach Federation (ICF), European Mentoring and Coaching Council (EMCC) and so on, have taken initiatives in the promotion of coaching and standardization of coaching services. Many other factors may also contribute to the transition of coaching from a marginal activity to a mainstream focus of interest, which will be discussed in the up-coming section. [1, 2]

As discussed in the previous chapter on ***Coaching for Pharmacists (1) – Introduction***, coaching is different from other development interventions. It can positively impact both individuals and the hospitals and clinics where there is pharmacy department. Of course, in drug stores where pharmacists as managers need to lead, and where coaching can be applied. In this article, there will be some discussions specially focused on these impacts. After understanding advantages of coaching, the next step is to take initiative for the actual implementation. The cultural development of coaching is the key step for effective coaching services in an organization, especially in an environment like Hong Kong. Ogilvy Publics Relations has reported that Hong Kong people spend 10,000 minutes per day worrying about Hong Kong's future. Every day we hear of job losses, government deficits, rising competition from the Mainland and suicides. The truth is we have lost our competitive advantage and other Asian cities are overtaking us. Hong Kong people are masters of hard work, persistence and entrepreneurialism. But times have changed and many Hong Kong people are running hard in the wrong direction. In order to maintain our healthy economy and high standard of living we must do something different. The key to competitive success is no longer in hard work but in better work. We must develop new creative solutions to problems, and we must give excellent customer service. We must begin to use not just our time, but our creativity and passion to add value. Working smarter does not mean working more hours. Many employees try to please their bosses by working long hours. They come in early, stay late and never ask for help or appreciation. The pressure they put on themselves make them irritable and rigid. They do not enjoy their work and lose their heart for it. Working smarter means taking better care of yourself. It means doing more of what you love doing, what you are passionate about and what you are naturally good at. A good way to achieve this is to take the time to reflect fully, with the help of a trustworthy and informed colleague or manager coach.

COACHING TRENDS

According to the report published by CIPD, 77% of respondents reported that there was an increase in coaching activities in their companies in the last few years (**Fig. 1**). Although there is different

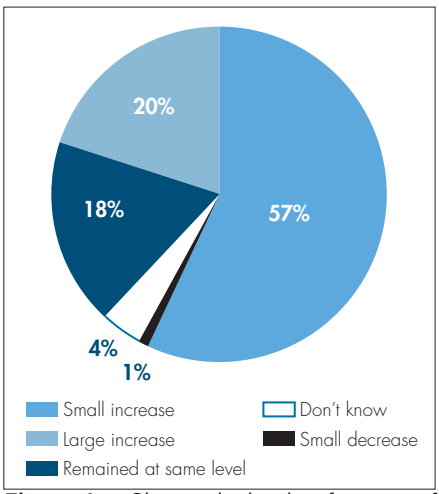

Figure 1. *Change in levels of usage of coaching in the last few years*

degree of increase in various companies, the increasing trend of coaching cultures is catching special attention from most modern organizations.

A number of reasons have contributed in the driving force for increasing popularity of coaching in different organizations. These include:

1. **Rapidly evolving environment:** the fast pace of business requires the ability to learn and adapt quickly. Developing interventions such as coaching can help individuals adjust to these major changes;
2. **Modern organization:** broader management roles and lower job security requires a large step improvement in skills, responsibility and performance. Coaching can support and help in acquiring the respective essential skills;
3. **Lifelong learning:** coaching can support different learning style and changes, so that individualized lifelong learning becomes possible;
4. **Individualized development:** coaching can help individuals identify development needs; it offers a flexible and responsive development approach which cannot be offered by traditional training programmes;
5. **Support for learning progress monitor:** coaching can provide ongoing support and monitoring for personal development plans;
6. **Performance of individuals:** coaching provides proactive approach to identify problems of poor performance and undertake interventions to improve performance;
7. **Improve decision making of senior employees:** senior level employees may have few people to confide in, develop ideas or discuss decisions. A coach can objectively give support.

These characteristics highlighted some of the key reasons that have led to the burgeoning popularity of coaching. There is also little doubt that the increased demand for coaching is partly due to the promotional activities. To become familiar with coaching, there is a need for frequent practicing. In the long run, coaching will be able to evoke excellence and bring benefits to the organization.

EVERYDAY PRACTICE OF COACHING

Nowadays, leaders and managers are expected to be effective coaches to their employees, therefore just having a vague grasp of what coaching really means is insufficient. This gap in coaching proficiency has a big impact on productivity and bottom line managements. Since coaching is the most effective method to enhance performance and development, when coaching is ineffective, or even avoided, opportunities to maximize individual and organizational potential are lost.

Coaching is a tremendous support in work-related learning. Sometimes coaching is an integral part of a larger project, such as process changes, program monitoring and evaluation. However, it is often an intervention by itself to stimulate thinking and make advancements. Individual coaching may involve the reflection on performance, for example, evaluation and feedback for working efficiency, clarification of individual thoughts, behavioral patterns, motivation for works and career development. In team coaching, it may involve working on topics such as creating a shared purpose, making use of all strengths, dealing with diversity and enhancing collaboration. Different approaches of coaching happen in daily works, despite that one may not be able to fully realize the existence of all coaching elements. [3, 4]

Although coaching can be delivered by trained external coaches, specialist internal coaches, line managers, peers, human-resources department or any other sensibly related persons, from the CIPD report on coaching services provision, it was reported that line managers are most likely to deliver coaching and over 40% respondents never use external coaches (**Fig. 2**). Since coaching tends to involve internal managers, all pharmacists and managers should be equipped with the essential skills for coaching. [2]

Since any new skill, attitude, style or belief, adopting a coaching ethos will require much commitment, practice and time before it flows naturally and its effectiveness is optimized consequently. Therefore, it is important to practice coaching in everyday work. Through accumulation of daily experiences, more insights and ideas can be learnt, which can finally evoke excellence in the end.

EVOKING EXCELLENCE

Coaching is a way of improving performance of employees, which involves helping them to build and develop their skills. It was a proven way to cause many positive impacts. A long term excellent performance means that the client meets high objective standards of the discipline in coaching.

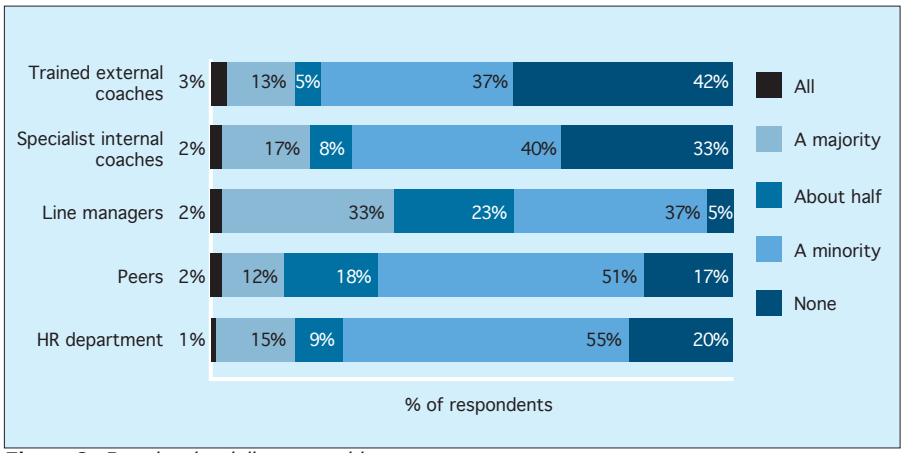

Figure 2. *People who delivers coaching*

These well-coached clients can observe when they are performing well and when they are not. Moreover, a well-coached individual should be able to make necessary adjustments independently of the coach. By keeping this mind, coaches can improve their competence by making continuous advancements and feedbacks. By making use of the dynamic interactions between coachers and coaches, both parties can improve in multiple ways. In the long run, the whole organization will also become more competitive. [5-9]

For coaching executives, benefits include:

- Identification of hidden individual strengths and development needs;
- Leveraging individual strengths;
- Enhanced career planning and development;
- Improved relationships with colleagues;
- Regular ongoing feedbacks and supports through ongoing coaching.

For the organization, benefits include:

- Improved staff engagement and reduced staff turnover rate;
- Enhanced individual and organizational performance;
- Perception of management as being committed to employees and their growth and success;
- Improved employees commitment that can enhance productivity;
- Positively affecting organizational culture and reputation.

As a conclusion, coaching can help individuals develop the capabilities needed to achieve strategic milestones, develop professionals and leaders for tomorrow, enhance productivity, improve relationship, job satisfaction as well as dealing with underperformance. It enables employees to get the most out of every day, also to align their personal values and motivations to daily works and organizational goals. This is a win-win situation for sustainable growth of the organization and stimulating personal growth or development. Therefore it is not exaggerating to say that coaching is becoming an imperative approach for future success of people, organization and healthcare provision.

WHY COACHING HAVE A POSITIVE IMPACT

Coaching is a unique tool to take an individual's personal development further and faster. As discussed in the above paragraphs, coaching is able to bring numerous benefits to both the employees and organization, such as job satisfaction, increased performance, talent retention and dealing with work-related problems including stress. Coaching is able to help personal development due to several reasons: [10-12]

1. **Identify individual blind spots:** every individual have some critical things that he/she cannot see. These blind spots can come across socially, job responsibilities, peer influences, etc. Coaching enables the coachee to understand his/her own limitations;
2. **Choose the best action steps:** there are always multiple ways to deal with a problem. Coaching can help one determine which solution works best for the problem and fits best for the individual;
3. **Stay on track:** coaching gives support to stay on track with personal development. A coach can help to set specific goals, monitor and evaluation the progress constantly.
4. **Effective implementation:** there are enormous differences between understanding an idea conceptually and applying it correctly. Coaching provides an opportunity to study the implementation plan and coacher can guide the coachee in a right direction;
5. **Motivation for action:** coaching gets the coachee motivated and start taking action;
6. **Become more self-reliant:** coachees take greater responsibility and accountability for actions and commitments; this allows the development of self-confidence and job satisfactions;
7. **Work-life balance:** coaching can accommodate and support employees' obligations to their home lives so that they are productive and effective while at work.

Coaching is able to help maintain employees' loyalty and commitments to the organization, to provoke excellence and improvements. The explanations behind these benefits are that coaching can provide chances for improvements, identify the way for improvement, and motivate the coachee to improve. There is a clear idea that coaching can improve the performance of individuals; therefore, managers should develop a coaching leadership style. However, coaching should become a corporate culture before it can actually make a difference.

BUILDING A COACHING CULTURE

Coaching culture is not only about changing the senior managing style, but looking for a way to change existing behavior and attitude between managers and staffs at all levels that impacts bottom-line performance. Coaching culture enables better performance in a more sustainable basis. Therefore, coaching should become the predominant style of management and working behaviors, where a commitment to grow the organization is embedded in a parallel commitment to grow people in the organization. The development of coaching culture benefits in the way that employees become more proactive in seeking for improvements, become passionate and energized and it becomes easier to make collaborative decisions. [5, 13]

Before introducing a coaching culture, one should be able to coach himself/herself around how to implement the coaching programme. As discussed, coaching involves asking questions rather than actual answers, the actual need for implementation can be illustrated using the GROW model:

- **Goal:** what achievements are expected? Why and what changes are expected?
- **Reality:** what is the current situation and practices? How often should the coaching be done? Who else is affected by the coaching programme? What other factors are relevant?
- **Options:** what can be done to change the situation? Any other alternatives? What are the benefits and pitfalls of these options?

- **Way forward:** what are the next steps? When these actions should be taken? Ways to overcome potential challenges? Who should be involved in the coaching sections?

After confirmation of the need for coaching, development of coaching culture can provide the stability and protocol for all interactions between corporate members. It is a powerful strategy to create an adaptive workplace for ongoing process of development and learning. In summary, two factors which support the development of coaching culture in organizations are:

1. A culture of openness, learning and development within the organization;
2. A culture which acknowledges that resources are needed for coaching, these include time, training, development and rewards.

Fundamentally, the development of openness and learning environment requires structural supports and organizational commitment; this ensures all employees understand the organizational goal and the necessary personal contributions. Secondly, the coaching culture requires a behavior-based coaching approach, through actual practices and manager commitments, coaching cultures can be built in a collaborative way. This behavior-based coaching may involve removing certain behaviors, habits or attitude that limits personal or organizational potentials. Also, active promotion of behavior, habits or attitudes for coaching is essential. [14]

The development of coaching culture can engage staffs beyond rational understanding towards an emotional and sustainable behavioral change. It roots coaching excellence into organizational development and ensure sustainable growth. Therefore, the development of coaching should be planned, formalized and structured to promote cultural changes in the organization.

CONCLUSION

To conclude, coaching is a collaborative and interactive process in respond to the real and specific issues of the organization. These complementary activities that can help people take charge of their own development. It allows relationship building that can in turn facilitates insight, learning and change. Through this relationship, individual potential can be identified, possibilities become reality and tangible results are delivered. Coaching and mentoring helps a person to see the present as a springboard to the future and to be strategic about their own development. Since coaching is able to bring paramount benefits to the organizations, it has become a trendy approach for the goodness of both employees and organizations. Although there is no one single right way to coach, through daily practices of coaching, pharmacists will be able to grasp the most suitable skills of coaching in their own working environment. By frequent practices of coaching and contacts with colleagues, pharmacists will be able to build a long term relationship with colleagues and maximize their performance. All efforts eventually benefit the organization and improve patient care.

Working smarter does not mean working more hours. In Hong Kong, many employees try to please their bosses by working long hours. They come in early, stay late and never ask for help or appreciation. The pressure they put on themselves make them irritable and rigid. They do not enjoy their work and lose their heart for it. Working smarter means taking better care of yourself. It means doing more of what you love doing, what you are passionate about and what you are naturally good at. A good way to achieve this is to take the time to reflect fully, with the help of a trustworthy and informed colleague or manager coach.

The development of coaching culture is beneficial for the sustainable development of both people and the organization. It requires long-term, multifaceted and strategic initiatives, supports throughout the organization as well as continuous evaluations and improvements. Therefore, a leader should start planning and modernizing the management styles. The development of coaching culture is vital for successful implementation of coaching in an organization.

Author's background

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Drug Administration in Enteral Tube Feeding

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ABSTRACT

"Can this drug go down the Ryle's tube?" Enteral tube feeding is a common phenomenon encountered in practice settings like hospital and old age home. This article gives an overview of enteral tube feeding and discusses the principles of handling drug administration via feeding tubes. These principles include reviewing the medication list, switching medication or dosage form and prudent consideration before crushing modified release formulations and drugs with enteric coating. Issues associated with specific drugs like phenytoin and proton pump inhibitors are also delineated.

Keywords: *Enteral Tube Feeding, Ryle's tube, medications, dosage forms*

INTRODUCTION

One of the common questions encountered during dispensing is:
"Can this drug go down the Ryle's tube?"

This article is not going to answer this question for every drug but would discuss the principles of handling drug administration via enteral feeding tubes from the perspective of a pharmacist.

ENTERAL TUBE FEEDING

Enteral feeding is the delivery of nutrition to the GI tract, as opposed to parenteral feeding where nutrition is given intravenously. The most common type is Ryle's Tube feeding. Ryle's tube feeding is a form of nasogastric (NG) tube feeding (**Fig. 1**) where nutrition is delivered by a tube entering through the nose into the stomach.

Naso = nose; gastric = stomach

There are other options for tube feedings. The tube may enter through the nostrils (naso-), the mouth (oro-) or through the skin (-stomy); while the tip of the tube may end up in the stomach (gastric) or the small intestine (duodenal, jejunal). (**Fig. 1**) Naso-tubes are more common because they are easier to initiate, less invasive and cheaper. However, for long term access (>4-6months), "-stomy" i.e. entry of the feeding tube through skin into the GI tract, is preferred because of greater patient comfort, less long-term complications and mechanical failure,[1,2] e.g. PEG tube (**Fig. 1**).

WHY ARE PATIENTS PUT ON TUBE FEEDING?

Oral intake may not be adequate or appropriate for some patients, e.g. those with dysphagia (inability to eat) due to stroke, neck and head cancer etc, or the critically ill who are intubated for ventilation.[4]

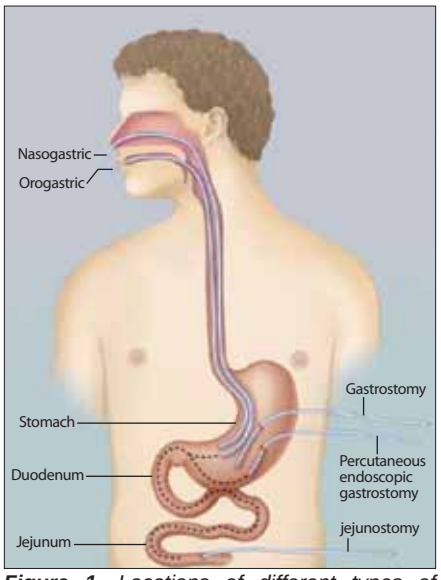

Figure 1. *Locations of different types of feeding tubes. Nasoduodenal, nasojejunal, and percutaneous endoscopic jejunostomy tubes extend (dotted line) to the small intestine instead of ending in the stomach.(Adapted from Reference 1)*

For these patients, an alternative route, enteral or parenteral, is recommended. As long as the gastro-intestinal tract (GIT) is functional, enteral nutrition is always preferred due to lower cost, greater convenience and less infection complications.[1, 5-7] Enteral feeding also stimulates blood flow, secretion and barrier protection of the GIT.[8] This results in enhanced immune function and better preservation of the GIT.[1, 5]

ABOUT FEEDING TUBES

There are 2 important issues relevant to drug administration:

a) Feeding Tube Size

The diameter of the feeding tube is measured in French (Fr) (1 Fr = 0.33 mm). Tubes can range from 5 to >14 Fr. Tubes of smaller Fr are more comfortable but are more likely to be clogged by medications.[1]

b) Placement Site

As mentioned above, the tip of feeding tube may end up in different parts of the GIT, therefore bypassing sites of GIT where drug absorption/ activation/ action take place. This may affect drug properties in the following manners:
1) Action: Stomach is the primary site of action for drugs like antacid, sucralfate and bismuth (which form a protective barrier in the stomach). If the tube is placed in the duodenum, the stomach is bypassed and these drugs lose their values.[1,4]
2) Metabolism: Drugs with extensive first-pass hepatic mechanism e.g. opioids, tricyclic antidepressant, beta blockers and nitrates have increased bioavailability when given into the jejunum.[3,9,10]

3) Absorption: Drugs like ketoconazole require gastric acidity for optimal absorption,[1,3] while drugs like iron are primarily absorbed in the duodenum; decreased bioavailability is observed when these drugs are delivered to sites beyond the stomach and duodenum respectively.[2,11-13]

Drug properties become more unpredictable as the tube ends further down the GIT. Be extra cautious once the placement site goes beyond the stomach. After looking at enteral feeding, let's move on to discuss what we should do with oral medications when tube feeding is initiated.

Let's have a look at the case of Wong MH.

Case Study (Part 1)

Wong MH is a 76 yo lady who was admitted to the hospital because of ischaemic stroke. She was assessed by speech therapist and recommended to be put on Ryle's tube feeding. Her usual medications include:

Alendronate 70 mg PO once weekly
Adalat Retard® (Nifedipine sustained release) 20 mg PO BD
Pantoloc® (Pantoprazole enteric coated) 40 mg PO daily
Imdur® (Isosorbide mononitrate controlled release) 60 mg PO daily
Metoprolol 50 mg PO BD
Cartia® (Aspirin enteric coated) 100 mg PO daily
Epilim Chrono® (Valproate controlled release) 600 mg PO nocte
Lactulose 10 mL PO BD

1. Withholding medications

This is indeed a good chance for drug therapy review. Drugs of no immediate importance or those of no indication should be withheld or discontinued,[1,2] e.g. alendronate for MH. But for drugs deemed to be necessary, the followings might be considered, keeping in mind that these steps may affect the bioavailability or pharmacokinetics. Close monitoring and dose adjustment as appropriate is warranted.[1,9]

2. Giving the drugs via feeding tubes

a) Liquid preparations

Liquid preparations (like lactulose in the case of MH) are favorable because they are easy to handle (does not require grinding) and are less likely to clog tubes.[1] Nevertheless, many commercial liquids have osmolalities 2.5-10 times that of GI secretions. Sometimes, sorbitol* in liquid preparations adds to the osmolality. Hyperosmolar liquid preparations may cause bloating, nausea, cramping and diarrhea. This is normally not a problem because the volume involved is small and the liquid is diluted by gastric juice.[16] However, for patients on tube feeding, hyperosmolar liquid is given directly to the small intestine or a large volume is given rapidly to the stomach, resulting in indirect "dumping" into the intestines.[14,15] Hyperosmolar liquid should thus be diluted with 10-30 ml of water before administration to improve drug delivery.[17,18]

Evaluate the osmotic load and sorbitol content of drugs as a potential cause when a patient experiences GI side effects.[1] Changing to a therapeutic equivalent with no sorbitol/ lower osmolality may help. Alternatively, one may crush tablet/ open capsule.[14,15] Sorbitol is a poorly absorbed polyalcohol sugar, added to improve solution stability/ sweetness or as a vehicle for medicine. Cramping and diarrhea occurs with daily consumption of over 20 g.

b) Switching to a liquid dosage form

In general, switching from solid dosage form should be considered if a liquid counterpart is available. A few points should be noted when performing the switch:

1) Volume

Many of the liquid dosage forms are designed for pediatric use. Giving an adult dose may require a huge volume that may result in GI intolerance.[1,3,9,20,21] For example, co-trimoxazole syrup comes in 240 mg/5ml. 20 ml would be required to give a standard dose of 960 mg.

2) Dosage and frequency adjustment

The liquid counterpart may have a different salt and hence a different bioavailability. Dosage adjustment may be necessary. For instance, due to the differences in absorption, 250 mg of fusidic acid is therapeutically equivalent to only 175 mg of the sodium salt (i.e. bioavailability of suspension= 70% of tab), so doses of fusidic acid suspension appear relatively higher.[22]

Digoxin is another example. The bioavailability for Lanoxin elixir® (digoxin elixir by GSK) and Lanoxin PG® (Digoxin tablet by GSK) is 75% and 63% respectively. Dosage adjustment and monitoring is necessary when switching from one form to another.[2] In addition, when switching a sustained release tablet to a liquid dosage form, dosing frequency may have to increase (with the dose decreased) to make up for the loss of sustained release property.[1] As in this case, MH is taking Epilim Chrono® (Valproate controlled-release) 600 mg tablet Nocte. This should be switched to Epilim syrup® (Valproate solution) 200 mg TID.

c) Solid dosage forms

Simple immediate release products e.g. compressed tablet, sugar-/ film-coated tablets may be crushed with little change.[1] Just as metoprolol in the case of MH.

As for capsules, hard gelatin capsules can be open and the powdered drug may be administered conveniently. But soft gelatin capsules may be more challenging. The shell may be pierced with a needle and the liquid may be squeezed out/ aspirated with a syringe. Another method is to dissolve the capsule in warm water and administer the water without the gelatin shell.[1,2]

Sometimes, tablets/ capsules come in special formulations e.g. sustained release. They are usually denoted by suffixes like: CC, CR, ER, LA, SA, SR, XR, XL[23] Crushing may result in altered pharmacokinetics or compromised action.[12] While some require switching to standard formulation,[3] pellets inside some microencapsulated dosage forms may be poured down the feeding tube e.g. Efexor XR® (Venlafaxine).[23] Product literature should be consulted in case of uncertainty. Care should be taken **not** to crush these pellets/beads. Feeding tubes with larger bore (>14 Fr) may also be required to prevent occlusion.[2,15,23,24] Advantages and disadvantages of administering different dosage forms via feeding tube are summarized in **Table 1**.[1,2,10,12,13,15]

Table 1. Advantages and disadvantages of administration of drugs in different dosage forms via feeding tube

DoDosage Form	Advantages	Disadvantages
Solution	- Even drug distribution - Allows accurate dosing - Ready to use	- Co-solvent may be present in quantities sufficient to cause adverse effect, e.g. sorbitol causing diarrhea - Poor stability and short shelf life - Not easy to carry around - More expensive than tablet
Suspension	- Ready to use	- Risk of clogging for big granules/ high viscosity vehicle - Settling or inadequate shaking may reduce dosing accuracy - Not easy to carry around - More expensive than tablet - Poor stability and short shelf life
Effervescent tablet	- Low osmolarity and won't cause diarrhea - Long shelf life - Convenient to carry around	- May require a large volume to be fully dispersed - Must be fully dispersed before administration to avoid gas production in the feeding tube - Sodium content can be high – harmful to patients with cardiovascular problems e.g. chronic heart failure - Excipients may not dissolve and sediment out
Dispersible/ Orodispersible tablet	- Convenient to carry around - Lower electrolyte content than effervescent tablet	- Particles/ granules may be too large for administration through feeding tubes
Buccal/sublingual tablet	*Not suitable for administration via feeding tube* These are designed for absorption in the oral cavity. Delivery to the stomach/ intestine may result in reduced efficacy	
Compressed tablet	- Readily available	- Not all tablets disintegrate easily, require grinding - Potential risk of clogging
Modified release tablet	*Not suitable for administration via feeding tube*	
Hard gelatin capsule	- Convenient (just open capsule and pour out powder)	- Occupational exposure risk - Small capsules maybe difficult to open
Soft gelatin capsule	Not recommended unless no alternatives: Contents is usually oily and is poorly soluble in water Piercing capsule shell and squeezing out the contents may result in incomplete removal and hence inaccuracy in dosing	
Enteric coated tablet	The enteric coat serves 2 purposes: 1. To protect drug from degradation by gastric acid 2. To reduce local gastric irritation If the enteric coat is for purpose 1, delivery of drug by a nasogastric tube would result in reduced absorption. However, this would not be an issue if the drug is delivered into the intestines directly Another concern is that the crushed enteric coat may block the feeding tube Careful consideration should be made before administering enteric coated drugs through feeding tubes	
Injectable	- The drug is in a soluble form	- Salt or pH may differ from the tablet form - Very costly

3. Seeking alternative route

Alternative routes of administration may be considered. However, these routes may be associated with problems as summarized in **Table 2**.[1,2]

Table 2. Alternative routes and their associated problems

Route	Examples	Problems
Transdermal	Nitrate Ketoprofen	- More costly than tablet - Not many drugs available in this form
Sublingual/ Buccal	Fentanyl *(Not available in Hong Kong)*	- More expensive than tablet - May not be suitable for patients with dry mouth, mouth injuries or decreased mental state - Not many drugs available in this form
Rectal	Bisacodyl Diclofenac	- Unpredictable absorption - Patient discomfort - Not desirable for long term use
Parenteral	Phenytoin Haloperidol (depot)	- Very costly - Not desirable for long term use (except depot) - Pain due to injection - Infection and complications associated with IV line - Require trained personnel for administration

4. Seeking alternative medicine

Switching to a drug within the same therapeutic class is another option. For the case of MH, Pantoloc® (Pantoprazole) (where the enteric coat protects the drug from gastric acid) is not suitable for crushing. It can be switched to lansoprazole or esomeprazole.(Please refer to the section on PPI) A switch from Adalat Retard® (Nifedipine sustained release) to amlodipine might also be considered. Though plain nifedipine is an option, blood pressure control is not as smooth as amlodipine. Besides, amlodipine has a better side effect profile e.g. less peripheral edema,[25] and is given daily, while plain nifedipine is given TDS-QID.

If tube feeding is needed for a prolonged period, therapeutic equivalents with prolonged half life should be considered to minimize the trouble of drug administration, e.g. from captopril (half life <2 hr, given BD-TDS) to lisinopril (half life ~12 hr, given daily-BD).[26]

Case Study (Part 2)

Hemorrhagic stroke was ruled out with CT scan. MH's blood pressure was 110/70. After evaluation, the medications of MH were modified as below:

Withhold:
Alendronate (MH became bed bound

and was not able to maintain an erect posture which is required for 30 min after taking alendronate; the drug was also not of immediate importance)
Adalat Retard® and Metoprolol (withheld to observe blood pressure)
Lactulose (no therapeutic indication, MH was not suffering from constipation and had not been using this drug)

Pantoloc® → Lansoprazole 30 mg PO daily
Imdur® → Elantan® (Isosorbide mononitrate) 20 mg PO BD
Epilim Chrono® → Epilim syrup® (Valproate sodium) 200 mg PO TDS
Cartia® → Aspirin (plain) 80 mg PO daily

OTHER ISSUES

1. Drugs should not be added into enteral formula to prevent incompatibilities.[1,10,16] It is suggested to separate drug administration from feeding 1) for at least 30 min and 2) with flushing (15-30 ml) before and after medication. The tube should also be flushed with 5-10 ml of water between each medication. Flushing maintains tube patency, ensures complete drug delivery and improves bioavailability.[27]

2. Staff, especially pregnant women, should be aware of the risk of occupational exposure when preparing cytotoxic drugs (e.g.capecitabine) and teratogenic drugs (e.g. finasteride) for administration via feeding tube. Necessary precautions e.g. avoidance or handling in a closed system should be taken.[10,24]

3. CAUTION: use **oral** syringes to prevent accidental injection of oral medications.[1,3,12]

CONCERNS WITH SPECIFIC DRUGS

a) Phenytoin

Phenytoin level may be reduced by as much as 70% in patients receiving concomitant enteral feeding.[28-32] This might be the result of binding to the enteral tube or calcium salts/ protein in the feeding formula.[33,34] Solutions include flushing, separating drug administration from feeding, increasing dose and closer serum level monitoring.[1,28] If therapeutic serum level cannot be reached, IV phenytoin may be an alternative.

b) Carbamazepine

Mechanism of interaction which results in reduced absorption is not well understood.[35,36] Closer monitoring is warranted.[10,36]

c) Warfarin

There are reports about warfarin resistance in patients on enteral feeding formula.[37-39] It might be due to the vit K content or binding with protein in enteral formulas. Increasing dose with close monitoring of INR, withholding feeding before and after drug administration or switching to subcutaneous low molecular weight heparin may help to minimize the interaction.[1,3] It is important to step down the dose once patient switches back to oral diet.[9,21,39,41]

d) Fluoroquinolones

Fluoroquinolones bind multivalent cations like calcium, magnesiem, aluminium and iron in enteral formula, thereby resulting in reduced absorption.[41,42] Among the fluoroquinolones, ciprofloxacin shows that greatest degree of interaction (31-82%), followed by levofloxacin and ofloxacin.[43,44] Moxifloxacin is barely affected.[45] Withholding feeding before and after drug administration or increasing the dose of fluoroquinolone may reduce the effect of interaction.[10,46] Jejunal administration should be avoided with ciprofloxacin as bioavailability is reduced with this route, probably because ciprofloxacin is primarily absorbed in the duodenum.[42,47]

e) Proton Pump Inhibitors (PPI)

The administration of PPI is complicated. PPI is acid labile. An enteric coat is needed to protect the drug against gastric acid until it reaches the duodenum, where the coat degrades in an alkaline environment and releases the drug for absorption.[3,9,13] Therefore, **enteric coated tablets** like Pariet® (Rabeprazole) and Pantoloc® (Pantoprazole) is not suitable for administration via feeding tube. Switching to drugs comprising **enteric coated pellets** should be considered e.g. Nexium® (Esomeprazole) and Takepron OD® (Lansoprazole). The pellets should be dispersed in water and administered through tubes of bore large enough to prevent occlusion.[48-49] If clinically indicated, switching to injection may be option.

f) Bulk forming laxatives

Bulk forming laxatives like methycellulose or psyllium (e.g. Metamucil®) should not be given through feeding tubes. They form a semisolid mass and occlude the tube.[23] Occasionally, they may be mixed with 250 ml of liquid and administered successfully. But sometimes, they still clog. Fibre-containing formulas e.g. Jevity® or alternative laxatives should be considered.[9]

g) Sevelamer

Sevelamer is a phosphate binder for renal patient. The tablet is made of a waxy-like polymer that clogs feeding tubes. Alternative medications such as calcium acetate should be considered.[13]

CONCLUSIONS

The following principles should be kept in mind when dealing with drug administered via enteral feeding tubes:

1. Evaluate the importance/ appropriateness of drugs. Seek alternative route/ medicine.

2. Liquid dosage formulations are preferred:
- check sorbitol contents if GI intolerance occurs
- dilute hyperosmolar medications with 10-30 ml of water

3. If liquid preparation is not available, solid dosage form can be crushed (tablet) or opened (capsule):
- avoid crushing modified release formulations
- consider carefully before crushing enteric coating

4. Flushing feeding tubes:
- with 15-30 ml of water before and after drug delivery
- with 5-10 ml of water between each drug

5. Avoid mixing drug with enteral feeding formulas:
- consider holding tube feeding 30 min before and after administering medication, and longer if there is potential for drug-nutrient interactions.

Author's background

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48. Takepron OD® package insert.
49. Nexium® package insert.

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.pccchk.com) to fill in their answers there.)

2 CE Units

Drug Administration in Enteral Tube Feeding

1. ***The most common route for enteral tube feeding is:***

   a. Nasogastric; because it is easy to initiate and less invasive.
   b. Gastrostomy; because it is more comfortable for the patient.
   c. Gastrostomy; because it is associated with less complications and mechanical failure.
   d. Enteral nutrition is avoided as far as possible; it is inferior to nutrition delivery via parenteral route.

2. ***Regarding the feeding tube, which of the following is true:***

   a. A feeding tube with a smaller value of "Fr" has a greater diameter.
   b. Drugs given through Naso-jejunal tube will always have a reduced bioavaiability.
   c. Sucralfate should not be given through a Naso-gastric tube.
   d. Administering ketoconazole through a Naso-jejunal tube might lead to reduced absorption.

3. ***An old lady has been put on Ryle's tube feeding and is currently on the following medications: Herbesser R® (Diltiazem sustained release) 100mg daily for heart rate control; Cartia® (Aspirin enteric coated) 100mg daily and Dipyridamol 75mg tds for stroke prophylaxis; as well as Senna 15mg nocte PRN for constipation. Which of the following is true?***

   a. Herbesser R® should be switched to Amlodipine, which is not a sustained release drug.
   b. Cartia® should not be crushed as grinding will destroy the enteric coating and expose this acid labile drug to gastric acid.
   c. Dipyridamol should be given parenterally.
   d. The patient's need for laxative should be reviewed before administering Senna through the feeding tube.

4. ***Liquid preparation is the preferred formulation for drug administration via feeding tube. However, liquid preparations are commonly associated with which of the followings?***

   a. Diabetes
   b. Diarrhea
   c. Bacterial overgrowth in the gut
   d. Poor absorption of sorbitol

5. ***Which of the following is true?***
   i. Grinding plain tablets should be avoided as far as possible as grinding would result in significant changes in pharmacokinetic properties.
   ii. Special formulations like Extended Release, Modified Release could be ground if the drug is not available as solution.
   iii. Cartia® (Aspirin enteric coated) should be switched to plain Aspirin for administration through feeding tube.

   a. iii b. ii
   c. i d. i and ii

6. ***A physician wrote an order for Sodium Fusidate tablet 500mg TDS. Upon realizing that the patient is on tube feeding, he changed the order to Fusidic acid suspension 500mg TDS. What would be your action?***

   a. Proceed the prescription as ordered.
   b. Contact the physician and tell him that the dose should be lower as suspension has better bioavailability than tablet.
   c. Contact the physician and tell him that the dose should be higher as sodium salt has better bioavailability than the acid form.
   d. Suggest the physician to switch to Fusidic acid cream instead.

7. ***The most inappropriate switch upon Ryle's tube placement is:***

   a. From Captopril to Perindopril
   b. From Imdur® (Isosorbidemononitrate sustained release) to Deponit® (Isosorbidedinitrate) patch when the patient is going to be on tube feeding for a prolonged period of time
   c. From Pantoloc® (Pantoprazole) tablet to Pantoloc® (Pantoprazole) injection when the patient (who has no acute medical problem) is taking Pantoprazole for gastric ulcer prophylaxis
   d. From Metamucil® (Psyllium) to Lactulose for a patient with constipation

8. ***Which of the following procedures of drug administration via feeding tube is the most appropriate?***

   a. Flush feeding tube with 15-30ml of water before and after drug administration.
   b. Do not dilute hyperosmolar medications to minimize dumping effect.
   c. Hold feeding for 4 hours before and after drug administration.
   d. Always try to mix all the drugs and administer them in one go to reduce patient discomfort.

9. ***Which of the followings is not associated with reduced bioavailability when administered through feeding tube?***

   a. Carbamazepine
   b. Warfarin
   c. Lansoprazole
   d. Phenytoin

10. ***When administering Finasteride through feeding tube, which of the following is the most appropriate precaution to take?***

    a. Finasteride should never be given through feeding tube. Inform physician to discontinue it.
    b. The drug should be ground in a closed system to avoid occupational exposure.
    c. Ground Finasteride should be drawn up in syringes for injection.
    d. Pregnant women should best avoid handling Finasteride as it is radioactive.

Answers will be released in the next issue of HKPJ.

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References:
1. Data on file. Stiefel Laboratories, Inc.
2. Physiogel™ Product Package information.

N11SPY456/05092011

Alkaloids and Methods of their Assay in Botanicals

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ABSTRACT

Alkaloids are a group of naturally occurring organic nitrogenous compounds found mostly but not restricted in plants. They are extremely difficult to define as they do not represent a homogeneous group of compounds. They are usually basic properties, bitter and many displays biological or biochemical functions. Therefore, they have been used as therapeutics. Representative examples include atropine, caffeine, colchicines, morphine, nicotine, quinine and strychnine. The term alkaloid also applies to synthetic substances whose structure resembles that of plant alkaloids. This article aims to give a brief review on their chemical classification, biological effects as well as the problem of their quantitative analysis. Because of their diversified structure and low contents in a plant in most instances, a few assay methods reported in literature are not good enough to accurately determine their amount.

Keywords: *alkaloids, classification, biological effects, pharmaceutical applications, determination, assay*

INTRODUCTION

Alkaloids are naturally occurring amines, which are nitrogen-containing basic organic compounds arising from heterocyclic and often complex structures.[1] Their trivial names usually end in – ine. They are found mostly in plants but also present in some animals and are considered the disintegrated products of compounds comprising proteins.[2] The alkaloids appear to have a restricted distribution in plants. Among the angiosperms the Berberidacease, Leguminosae, Papaveraceae, Ranunculaceae, Rubiaceae and Solanaceae are outstanding for plants producing alkaloids. Specific alkaloids of complex structures are ordinarily confined to specific plant families. Alkaloids may occur in various parts of the plant: in seeds (areca, nux vomica), in fruits (black peper, conium), in leaves (belladonna leaf, hyoscyamine), in underground stems (sanguinaria, corydalis), in roots (aconite, belladonna root), in rhizomes and roots (ipecac, hydrastis), and in barks (cinchona, pomegranate). They are found in the fungi (ergot, *Amanita citrine*).

Possibly owing to more electronic density at the nitrogen atom, which can easily react with other molecules in biological systems, many alkaloids are toxic to other organisms.[3] Alkaloids are characterized by powerful physiological effects and many alkaloids exhibit marked pharmacological activity (**Fig. 1**). Hence, they could be used as therapeutic agents or used as a pharmaceutical intermediate.[4]

Figure 1. *Coca beans, a common source of caffeine (left) and fine powder of USP-grade anhydrous (dry) caffeine (right) which has many pharmaceutical applications*

CHEMICAL CLASSIFICATION OF ALKALOIDS

The alkaloids, which are already known, count to more than 2000.[5] They are structurally complex and over 1000 different types of structure have been identified.[3] New varieties are still being discovered, causing difficulty to classify this large group of organic compounds. Nevertheless, people group alkaloids according to a set of rules based on the basic chemical structure of their main nucleus and from which they derive, such as their biological origin, acid-base reaction, solubility, optical activity, volatility, as well as the biogenetic origin wherever known.[6,7] A number of the common categories of alkaloids are described below:

- **Pyrrolidine alkaloids:** The alkaloids derived from the amino acid ornithine, including the tropane, which is a condensation product of pyrroldine and piperidine. Representative alkaloids of this type include atropine, hyoscine (also known as scopolamine), hyoscyamine (**Fig. 2**) and cocaine etc.
- **Pyridine and piperidine alkaloids:** Arecoline, pelletierine, lobeline, coniine and nicotine are derivatives of pyridine and piperidine. These alkaloids consist of a mono carbon hoop which contains one nitrogen atom. This cluster of alkaloids consists of many poisonous plants (**Fig. 3**). The pyrrole alkaloid, stevenine, in marine sponges has also been discovered to elaborate the “oroidin” 5 class of alkaloids.

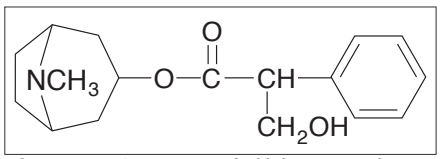

Figure 2. *Structure of (-)-hyoscyamine, a typical tropane alkaloid.*

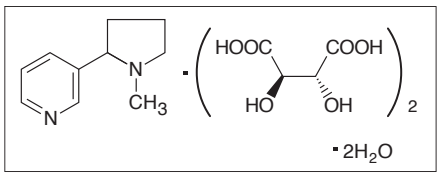

Figure 3. *Structure of nicotine bi-L-(+)-tartrate dihydrate, a typical pyridine alkaloid.*

- **Pyrrolizidine and quinolizidine (Fig. 4) alkaloids:** These two types of alkaloids are known to have lethal features and have raised enormous pharmaceutical concerns to researchers.

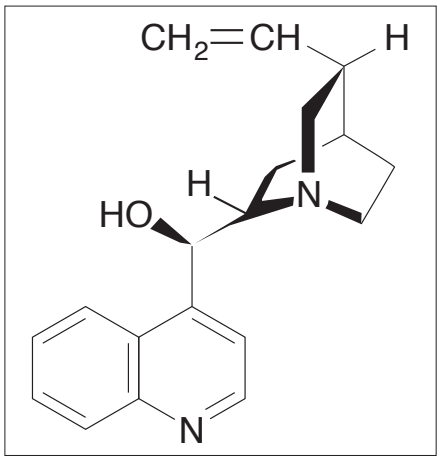

Figure 4. *Structure of cinchonidine, a typical quinolizidine alkaloid*

- **Indole alkaloids:** This type comprises serotonin (known as 5-hydroxyltryptamine), ergonovine, reserpine, strychnine and many others are derived compounds of the indole ring (**Fig.5**).
- **Quinoline alkaloids:** Quinoline alkaloids include twofold carbon rings comprising one nitrogen atom (N) (**Fig. 6**) as the main nucleus. Representative alkaloids are quinine, quinidine, cinchonine and cinchonidine.

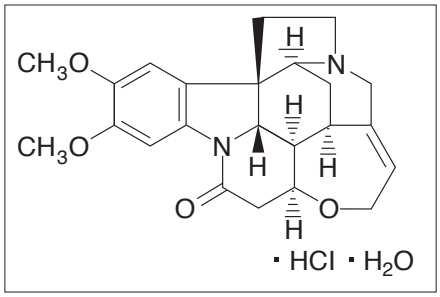

Figure 5. *Structure of brucine hydrochloride, an indole alkaloid*

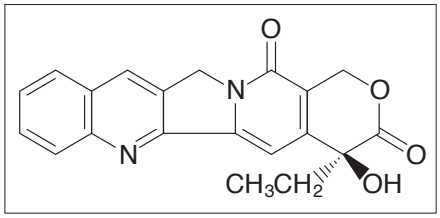

Figure 6. *Structure of (S)-(+)-camptothecin, a quinoline alkaloids*

- **Isoquinoline alkaloids:** Isoquinoline alkaloids always accompany quinoline alkaloids and include simple isoquinolines, benzylisoquinolines, phthalideisoquinolines, protopines, Opium alkaloids, protoberberines, emetine as well as ipecac alkaloids (**Fig. 7**).
- **Purine alkaloids:** Purine alkaloids usually include the alkaloids obtained from cocoa, tea and coffee: caffeine, theophylline, theobromine and aminophylline (**Fig. 8**).
- **Terpenoid alkaloids:** Terpenoid alkaloids are constituted by a group of terpenes like sesquiterpenoids, montoterpenoids, diterpenoids as well as steroids (**Fig. 9**). A number of monoterpenoid indole and oxindoids alkaloids have been isolated from botanical sources and many of them have been found to possess significant pharmacological activities and are ultilized as key lead compounds in new drug research.

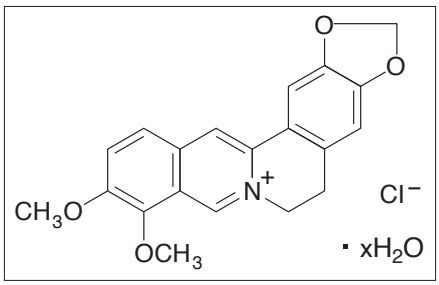

Figure 7. *Structure of berberine chloride hydrate, a typical isoquinoline alkaloid*

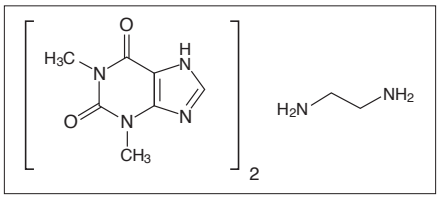

Figure 8. *Structure of aminophyline, a typical purine alkaloid*

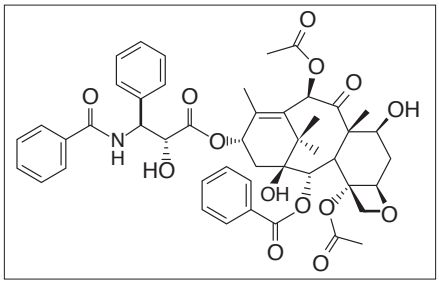

Figure 9. *Structure of paclitaxel, a typical terpenoid alkaloid*

- **Steroidal alkaloids:** Aconitine and protoveratrine, for exemple, contain a steroidal structure.
- **Others:** Besides the common types described above, there are many other basic nitrogenous compounds of plant or animal origins which are physiologically active are presently being explored or studied. For example, the lycopodium alkaloids produced by Lycopodium species are a number of structurally diverse alkaloids, which often possess unusual skeletons, and many of them attract the interest of biogenetic and biological scientists. Epibatidine alkaloids from frog skin are novel non-opoid analgesics. They are the toxins present in the skin of poison-dart frogs of South America.

THE PHARMACOLOGICAL PROPERTIES OF ALKALOIDS

Alkaloids display a wide series of pharmacological activities, partly because these bases act as ligands for a heterogeneous group of molecular targets.[8] For example, veratrum alkaloids exhibit effects such as lowering blood pressure, cardiac, anti-thrombosis, improving cerebral blood circulation and anti-parasitic infections, at the same time exert obvious toxic function on the nervous system, respiratory system, cardiovascular system, digestive system.[9]

On the central nervous system

Caffeine is found in many plant species, including coffee, tea, and cacao with a lesser extent.[10] It is well known as a central nervous system and metabolic stimulant.[11] Research shows that caffeine use relieves fatigue and increase attentiveness.[12] Caffeine acts principally as an antagonist of adenosine receptors in the brain.[13,14] By counteracting with adenosine, which functions as a synaptically released neurotransmitter in some cases, plays a role in the fundamental ATP-related energy metabolism,[15] Caffeine reduces resting cerebral blood flow between 22% and 30%.[16]

Cardiovascular pharmacological effects

Tetrandrine (TET) is a bis-benzylisoquinoline alkaloid purified from Stephanae Tetrandrae Radix, it prevents vascular contraction induced by membrane depolarization with KC1 or α-adrenoceptor activation with phenylephrine (PE).[17] In cardiac muscle cells, TET inhibits both L- and T-type Ca~ (2+) channels. The vivo study of stunned rat revealed that TET treated before ischemia may be involved in the reduction of microvascular permeability in stunned myocardium, which might be associated with its calcium channel blocking effect.[18]

On the respiratory system

Xiong et al reported that the ethanol

extract of Hupeh Fritillary Bulb possessed apparent relaxation effect on a variety of smooth muscle, anti-asthma effect on the guinea pig and can ameliorate tolerance of hypoxia.[19] All the alkaloid monomers from Hupeh Fritillary Bulb have a certain degree of antitussive, expectorant activity, of which ebeinine and hupehenine glycoside showed strong antitussive ability.[20]

Hypotensive effect

Reserpine is an indole alkaloid.[21] It is an antihypertensive drug that has been used to deal with high blood pressure owing to its ability to remove catecholamines from peripheral sympathetic nerve endings.[22] A comparison carried out among reserpine, alseroxylon, deserpidine and rescinnamine demonstrated that 0.5 mg reserpine produced a similar satisfactory response to 4.5 mg alseroxylon fraction and equal amount of deserpidine.[23]

Antibacterial activity

Over 130 biologically active aziridine-containing compounds are confirmed to own pharmacological activity including antitumor, antimicrobial, antibacterial effects,[24] for instance, Arenosclerins A–C and haliclonacyclamine E, new tetracyclic alkylpiperidine alkaloids from the marine sponge *Arenosclera brasiliensis* displayed antibacterial activity,[25] at the concentrations between 1.5 and 7.0 µg/ml, the four compounds present cytotoxic activity against human HL-60 (leukemia), L929 (fibrosarcoma), B16 (melanoma) and U138 (colon) cancer cell lines. The alkaloidal antibiotic, U-47,929 isolated from *Streptomyces ficellus* inhibited the growth of Gram-positive bacteria *in vitro* and is effective to treat experimental *Staphylococcus aureus* infections in mice.[26]

ANALYTICAL DETERMINATION OF ALKALOID

The alkaloids and preparations derived from them constitute a relatively important group of the official substances that employed frequently in modern therapy. As a class of medicinal agents, they are characterized by their high potency. A slight deficiency of alkaloid in a preparation may cause a marked decrease in physiological effect; on the other hand, a slight excess may cause toxic effects when the preparation is administered. It therefore follows that the accurate estimation of the quantity of alkaloids present in a medicinal substance is an important subdivision of pharmaceutical analysis.

The assay of alkaloidal drugs and preparations is generally performed for purposes of standandization, proof of purity, commercial evaluation, or pharmacolegal purposes. Assays of crude drugs may be classified according to the manner in which the percent of extractive is determined. If the percent of extractive represents the total of a class of plant substances, such as alkaloids or glycosides, etc., the assay is referred to as a proximate assay. Therefore, the assay of Ipecae is a typical example of a proximate assay because the total ether-solvent alkaloidal content is determined. If on the other hand, the percent of extractive from a crude drug represents a single chemical species, such as ephedrine or morphine, the assay is referred to as an ultimate assay because a single chemical species is determined.

To fulfill different requirements and expectations of measurements, various methods have been developed and selection of a method depends on the factors parameters:[27]
a) The composition and the structures of the mixture of alkaloids; b) the number, composition and property of the whole samples; c) the volume of sample available; d) the concentration of the analytes and e) the demand for preciseness and sensitivity.

Assay methods of various types have been described for the quantitative estimation of alkaloids. These methods are summarized and discussed below:

- **Potentiometric titration**

In light of their alkaline attributes, alkaloids or alkaloids salts were subjected to the base-acid reaction with satisfactory acids or base in potentiometric titration. As the technique advances, the automatic potentiometric titrator improves the automaticity and accuracy, Wang Chang-Yi et al. described a microdetermination approach of alkaloids in organic solvents by potentiometric titration.[28] The advantages lie in simple operation, treatment of sample and rapid with sharp end-points. But it is confined to small (0.4–4 mg) amounts determination.

- **Capillary electrophoresis**

The principle of capillary electrophoresis is that substances with different velocities (depends on the molecular size, charge and isoelectric point) separate, moved by turns to the photodetector and measured. CE has high selectivity and can provide fast separations.[27] It may be a valuable alternative to chromatographic methods which needs expensive columns and solvents,[28] the disadvantage is in that the LOD value is higher compared with GC and HPLC due to the small sample volumes and the relatively insensitive UV detection for tropane alkaloids.[29]

- **Thin-Layer Chromatography**

TLC is used as a method of initial screening. In case of complex chromatogram the identification by GC–FID or HPLC with UV detection may be erroneous, confirmation by TLC and specific staining is advantageous. It is widely used to analyze alkaloids for semiquantitative evaluation because of the simplicity of sample preparation plus the versatility as the stationary phases and the solvent compositions are nearly unlimited. Manzur-ul-Haque Hashmi et al made an attempt to determine 13 alkaloids from a single drop of solution semiquantitatively,[30] the method was proved to be accurate, rapid, simple and economical. But to explore the quantitative possibility, more equipment and further calibration is needed, e.g., TLC coupled with mass spectrography (MS), TLC-GC-MS or TLC - infrared spectroscopy, ensures higher precision.

- **High-performance liquid chromatography**

The application of HPLC for pharmaceutical preparations of alkaloids can be dated back to about 30 years ago, nowadays, it has been extensively utilized for the quantization of bisbenzylisoquinoline alkaloids, pyrroliziding alkaloids, phenethylamine alkaloids.[31-33] The columns, mobile phases, sample preparation and validation for each individual analyte were investigated in drug use as a result of its widely available instrumentation, high sensitivity and normally simple sample preparation.[34] As for tropane alkaloids, the suitability of UV detector is not good on account of the low absorption. Therefore, other detectors like LC-MS are developed, in combination with microbore columns, a promising future is opened, even regarding measurement of the metabolites and catabolites of tropane ropine which show no UV absorption.[27]

- **Gas chromatography**

Gas chromatography is another routine

chromatographic analysis. Tropane-alkaloids were identified by GC–MS detection (FID).[35-37] The application of capillary columns rendered greater possibility for tropane-alkaloids quantification, since they were more tolerant to high temperature and heightened the separating efficiency to a large extent.[27] GC with various detection methods (FID, NPD, ECD, MS) appeared, with different sensitivities for specialized alkaloids. The limitation lies in the decomposition of compounds not sufficiently volatile,[38] an everlasting trouble for scientists, besides, it often entails elaborate work-up before injection.

- **Acid dye colorimetry**

It is a classic method suitable to detect various alkaloids, especially for the total alkaloid determination. The procedure is based on the principle that certain acidic dyes combine with many alkaloids to form saltlike compounds which are soluble in organic solvents. Thus, they can be separated and the dye component can be estimated colorimetrically.[39] The dye varies depending on the characteristic of the alkaloids, for instance, with the help of bromocresol purple, the method can be applied to atropine and hyoscyamine. It is simple, reproducible and sensitive, even not so compared to the means stated above.

Besides the methods described above, a near-infrared reflectance spectroscopic method has also been developed for the simultaneous prediction of alkaloids and phenolic substances in green tea leaves. However, its application is handicapped by its limited application to the analogues of catechin.

CONCLUSION

To conclude, each individual method is unique for different kinds of alkaloids. However, only the acid dye colorimetry is committed to all types of alkaloids, whereas the chromatographic can only detect limited ones, that is why the acid dye colorimetry is still utilized universally in the Traditional Chinese Medicine analysis. Take the *Fritillaria hupehensis* as an example, the main pharmaceutical substances are steroidal alkaloids,[40] our former researches indicate that acid dye colorimetry show better results in contrast with others, which will be discussed in details in another pieces of articles to be published.

Author's background

ZHO Yuanyuan *was a research assistant in Dr Cheung' Research Group for Bioactive Products when this article was drafted. She is currently doing her MPhil degree in the Chinese University of Hong Kong.* ***Dr CHEUNG Hon-Yeung*** *is the Associate Professor in Pharmaceutical Microbiology & Biotechnology. He is the principal investigator of and scientific committee member of the Hong Kong Chinese Materia Medica Standardization Project for the Department of Health, Hong Kong Government. His email address is: bhhonyun@cityu.edu.hk*

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The Annual General Meeting of the Pharmaceutical Society of Hong Kong

The Annual General Meeting of the Pharmaceutical Society of Hong Kong was held on 17 Dec 2011 at 5:30p.m at the PSHK Club House. The president, Mr. Benjamin Kwong reported on the activities for 2011 and the Treasurer, Ms. Candy Tai reported on the financial standing of PSHK. The GC members election began at 6:15p.m. Last year's President and the three Pharmacy & Poisons Board Representatives naturally become GC members and 11 General Council members were elected by ballots. Nine old GC members stayed on and three new GC members were elected for the coming term. The meeting was followed by dinner at Majesty Seafood Restaurant 〔金御海鮮酒家〕at 7:30p.m.

We look forward to a new year of advancement for the Pharmacy profession.

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Hong Kong Pharmacy Conference 2012

4th – 5th February, 2012

The Hong Kong pharmacy conference this year will be held on February 4-5, 2012 at the Hong Kong Convention and Exhibition Center. This year, our theme is **Pharmacist: Your health care partners!** 藥劑師：你的健康之侶! With no exception from the previous years, we will have a well-structured program addressing the current, popular and interesting issues in our profession. Practical issues on the community pharmacy, hospital pharmacy, manufacturing and even new application of information technology will be discussed in the conference. Frontiers and experts would gather in this special occasion to exchange their ideas and perspectives on these current issues.

If you don't want to miss the great opportunity to be enlightened by this inspiring conference, register now. You can register online through the website http://www.hongkongpharmacyconference.com or you can download the registration form and send it back to us by post. See you in the conference!

Day 1 (4th February, 2012)

Time	Topics
1:30pm	Registration
2:30pm - 2:40pm	Opening ceremony
2:40pm - 2:50pm	Welcome speech by the Chairman of the Conference
2:50pm - 3:00pm	Opening Remarks
3:00pm - 3:40pm	Theme 1: Planting the Seed – Training the Next Generation of HK Pharmacists By Prof. Ian WONG, Professor of Pharmacology & Pharmacy, The University of Hong Kong
3:40pm - 4:00pm	Coffee Break, Poster and Exhibition
4:00pm - 4:40pm	Theme 2: Environmental Toxins – What Pharmacists Should Know By Dr. Sze Hong NG, Associate Consultant, Hong Kong Poison Information Centre
4:40pm - 5:20pm	Theme 3: Enhancing Compliance to Chronic Medications with Antihypertensive Agent as an Example – the Way Forward By Prof. Martin Wong, Associate Professor, School of Public Health and Primary Care, The Chinese University of Hong Kong
5:20pm – 5:50pm	Theme 4: The current status of Medication Safety in hospital pharmacies in China 全國醫院藥劑師用藥安全現狀的實證研究 By Mr. Xiaole ZHANG, Associate Chief Pharmacist, Peking University Third Hospital 北京大學第三醫院張曉樂主任
6:00pm - 6:45pm	Pre-Conference Dinner Symposium: Novel Treatment Target for Osteoporosis By Dr. Annie Wai-chee KUNG, Specialist in Endocrinology, Diabetes & Metabolism
7:00pm - 10:00pm	Conference Dinner

Day 2 (5th February, 2012)

Concurrent Session	I	II	III
Topics	**Information Technology**	**Community Practice**	**Hospital Practice**
8:30am - 9:10am	In-patient Medication Order Entry – What's in it for me? By Mr. Frank CHUNG & Ms. Bonnie LAM, Pharmacists, Chief Pharmacist's Office, Hospital Authority, Hong Kong	Communication in the Community – the Art, the Science and the Balance By Mr. Eric YAU, Pharmacist (Drug information), Watson's The Chemist & Mr. Philip CHIU, Senior Pharmacist, Mannings Health & Beauty Chain Store	Treating Chronic Kidney Disease – Mineral and Bone Disorder – para, plar… are they reaching the par? By Prof. Cheuk-Chun SZETO, Professor, Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong
9:10am - 9:50am	The Journey in Achieving Track and Trace of Pharmaceutical Products in Public Hospitals By Ms. S C CHIANG, Senior Pharmacist, Chief Pharmacist's Office, Hospital Authority, Hong Kong		The Art of ECG Interpretation – How it Saves Lives By Dr. Chi Yeung CHEUNG, Pamela Youde Nethersole Eastern Hospital, Hospital Authority, Hong Kong
9:50am – 10:30am	e-Health Records : Informatics – Pharmacist's Ambition By Mr. Johnny WONG, Pharmacist, Chief Pharmacist's Office, Hospital Authority, Hong Kong		Update on the Treatment for Cardiac Arhythmia in Year 2011 By Dr. Kai Hang YIU, Clinical Assistant Professor, Cardiology Division, Department of Medicine, The University of Hong Kong
10:30am – 11:00am	Coffee Break - Poster & Exhibition		
11:00am - 11:40am	Drug related Problems: Hidden in the Elderly Population By Prof. Vivian LEE Associate Professor, School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong	EBM of Complementary and Alternative Medicines By Prof. Clara LAU, Assistant Director, Institute of Chinese Medicine, The Chinese University of Hong Kong	Basic Skills in Interpreting CXR and CT-Brain By Dr. Miranda LAI, Associate Consultant, Department of Diagnostic Radiology and Organ Imaging, United Christian Hospital
11:40am – 12:20pm	Use of Technology to Improve Medication Safety in Elderly Homes. By Mr. Peter SUEN Pharmacist and CEO, ActiveCare Pharmacy	A Journey to the East – from Western Medicine to Chinese Medicine By Mr. Chi Keung LAW	Therapeutic Hypothermia By Dr. Kevin BOX, Critical Care Pharmacist, University of California San Diego
12:20pm – 1:00pm	Partnering with the Old Age Homes: Lost and Found by the Visiting Pharmacists By Ms. Stella HO, Mr. Alessandro LEUNG & Ms. Grace TANG, Visiting Pharmacist, The Hong Kong Pharmaceutical Care Foundation Dr. Chui Ping LEE Senior Instructor, School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong	The New "3P Patient-Pharmacist Partnership" Model- More Choices for Patients in Primary Healthcare By Ms. Iris CHANG & Mr. Godfrey LUI, The Practising Pharmacists Association of Hong Kong	Managing Dementia & Agitation in Nursing Home: Drugs or No Drugs By Prof. Timothy KWOK, Professor, Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong
1:00pm – 1:40pm	Lunch Symposium: Personalized Treatment in NSCLC By Dr. Siu Kie AU, Consultant, Queen Elizabeth Hospital, Hospital Authority, Hong Kong		
1:40pm - 2:30pm	Lunch - Poster & Exhibition		
2:30pm – 4:00pm	Plenary session: Regulation of Pharmaceutical Products – Now and Future by Drug Office, Department of Health		
4:00pm – 4:15pm	Closing by Ms. Ritchie Kwok, Vice Chairlady		

THE 12TH ASIAN CONFERENCE ON CLINICAL PHARMACY

7 – 9 July 2012, Hong Kong SAR, China

www.accp2012.org

"Citius, Altius, Fortius" appraising clinical excellence, nurturing eminent practice

Important Dates

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

Topics

Keynote Lecture

- Development of Clinical Pharmacy - East Meets West

Plenary Lectures

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

Symposia

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

Hosts:

School of Pharmacy CUHK
Expanding the pharmaceutical universe, Creating opportunities for life

香港中文大學
The Chinese University of Hong Kong

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

Active Ingredients:

1 tablet contains

telmisartan 40 or 80 mg

amlodipine 5 or 10 mg (as amlodipine besilate)

Presentation:

28 tablets of 40/5 mg, 40/10 mg, 80/5 mg and 80/10 mg

Pharmacological Properties:

Twynsta combines two antihypertensive compounds with complementary mechanisms to control blood pressure in patients with essential hypertension

The combination of these substances has an additive antihypertensive effect, reducing blood pressure to a greater degree than either component alone.

Telmisartan: is an orally effective and specific angiotensin II receptor (type AT1) antagonist. Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan does not exhibit any partial agonist activity at the AT1 receptor. Telmisartan selectively binds the AT1 receptor. The binding is long lasting.

Amlodipine: is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle.

Indications:

Treatment of essential hypertension

Dosage & Administration:

Twynsta should be taken once daily.

Twynsta 40 mg/5 mg tablets may be administered in patients whose blood pressure is not adequately controlled with amlodipine 5 mg alone.

Twynsta 40 mg/10 mg may be administered in patients whose blood pressure is not adequately controlled with amlodipine 10 mg.

Twynsta 80 mg/5 mg may be administered in patients whose blood pressure is not adequately controlled with Twynsta 40 mg/5 mg.

Twynsta 80 mg/10 mg may be administered in patients whose blood pressure is not adequately controlled on Twynsta 40 mg/10 mg or Twynsta 80 mg/5 mg.

Patients treated with 10 mg amlodipine who experience any dose limiting adverse reactions such as oedema, may be switched to Twynsta 40/5mg once daily, reducing the dose of amlodipine without reducing the overall expected antihypertensive response.

Contraindications:

- Hypersensitivity to the active substances, to dihydropyridine derivatives, or to any of the excipients
- Second and third trimesters of pregnancy
- Biliary obstructive disorders and severe hepatic impairment
- Shock (including cardiogenic shock)
- Severe hypotension
- Obstruction of the outflow tract of the left ventricle (e.g. high grade aortic stenosis)
- Haemodynamically unstable heart failure after acute myocardial infarction

Precautions:

– Hepatic impairment

– Renovascular hypertension

– Renal impairment and kidney transplant

– Intravascular hypovolaemia

– Dual blockade of the renin-angiotensin-aldosterone system

– Other conditions with stimulation of the renin-angiotensin-aldosterone system

– Primary aldosteronism

– Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy

– Unstable angina pectoris, acute myocardial infarction

– Heart failure

– Hyperkalaemia

Drug Interactions:

– Agents with blood pressure lowering potential e.g. baclofen, amifostine, neuroleptics or antidepressants. Furthermore, orthostatic hypotension may be aggravated by alcohol.

– Corticosteroids (systemic route)

Interactions linked to telmisartan

– frequent monitoring of serum potassium is recommendedcareful monitoring of serum lithium levels is recommended

– Patients receiving NSAIDs and telmisartan should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter.

Interactions linked to amlodipine

– CYP3A4 inhibitors

– CYP3A4 inducers

Side Effects:

Infections and infestations

Cystitis

Psychiatric disorders

Depression, anxiety, insomnia

Nervous system disorders

Syncope, somnolence, dizziness, migraine, headache, peripheral neuropathy, paraesthesia, hypoaesthesia, dysgeusia, tremor

Ear and labyrinth disorders

Vertigo

Cardiac disorders

Bradycardia, palpitations

Vascular disorders

Hypotension, orthostatic hypotension, flushing

Respiratory, thoracic and mediastinal disorders

Cough

Gastrointestinal disorders

Abdominal pain, diarrhoea, vomiting, nausea, gingival hypertrophy, dyspepsia, dry mouth

Skin and subcutaneous tissue disorders

Eczema, erythema, rash, pruritus

Musculoskeletal and connective tissue disorders

Arthralgia, back pain, muscle spasms (cramps in legs), myalgia, pain in extremity (leg pain)

Renal and urinary disorders

Nocturia

Reproductive system and breast disorders

Erectile dysfunction

General disorders

Peripheral oedema, asthenia (weakness), chest pain, fatigue, oedema, malaise

Investigations

Hepatic enzymes increased, blood uric acid increased

Forensic Classification:

P1S1S3

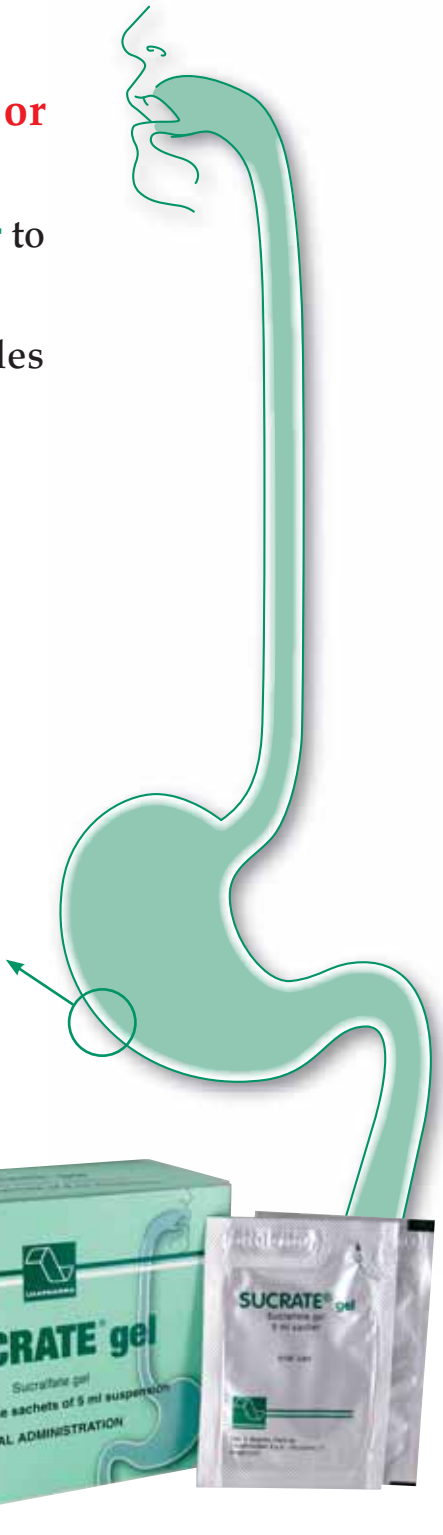
SUCRATE® gel
(Sucralfate 1g/5ml)

Mucosal defense booster

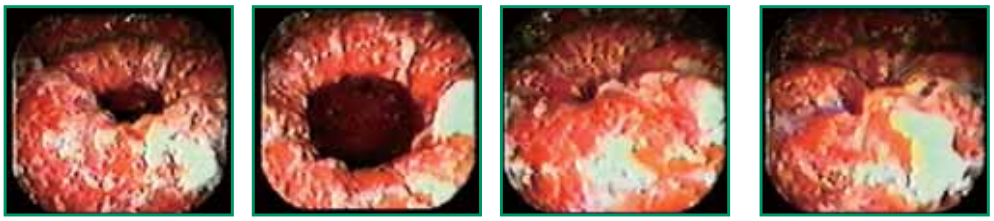
Innovative sucralfate gel form for:

Gastro-intestinal lesions caused by endoscopy or radiation therapy[1, 2, 3]

- **Double bio-adhesion of sucralfate cyto-protective layer** to damaged, inflamed G.I. mucosae[4]
- Better re-construction of mucosal architecture enables **active quality healing**
- Convenient gel form for **easy administration**
- **Excellent safety and tolerability profile**



SUCRATE® gel endoscopic study to show outstanding bio-adhesion power:



Cosentino F. et al., Società Italiana di Endoscopia Digestiva, VII Simp. Naz, Napoli, 1992

Due to a different dispersion technology on sucralfate molecules, **SUCRATE® gel** shows double bio-adhesion ability over normal sucralfate tablet, granule or suspension. The cyto-protective layer guards against attack of gastric acid, pepsin, bile salts; at the same time, it stimulates the production of mucosal defense factors (PGE_2, mucin, bicarbonates) and endogenous growth factors to accelerate active healing.

References

1. C. Mandelli et al.: Sucralfate gel vs sucralfate granules in the treatment of upper gastrointestinal lesions. Current Ther. Res. 1990; 47: 637-643
2. Kochhar et al.: Rectal sucralfate in radiation proctitis. Lancet 1988: 400
3. Kochhar et al.: Radiation-induced proctosigmoiditis. Prospective, randomized, double-blind controlled trial of oral sulphasalazine plus rectal steroids versus rectal sucralfate. Dig Dis Sci 1991 ; 36(1): 103 – 107
4. D. Vaira et al.: Gastric retention of sucralfate gel and suspension in upper gastrointestinal disease. Aliment. Pharmacol. Ther. 1993; 7: 531 – 535.

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