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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

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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
- Drugs & Therapeutics
- OTC & Health
- Pharmaceutical Techniques & 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:

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

Witnessing Primary Healthcare Development in Hong Kong

The Steering Committee on Primary Healthcare Development has been established with Prof. Sophia Chan Siu-chee leading as Chair-person. Non-official members include Mr Philip Chiu Kwok-leung (pharmacist and immediate past president of PSHK), Mr Chua Hoi-wai (CE, HK Council of Social Service), Dr Lam Ching-choi (Chairman of Elderly Commission), Professor Cindy Lam Lo-kuen (Prof. and Head, Dept. of Family Medicine and Primary Care, HKU), Professor Gabriel Matthew Leung (Dean of the Li Ka Shing Faculty of Medicine of the University of Hong Kong, Dr Donald Li Kwok-tung (Specialist in Family Medicine), Mr Shum Ho-kit (Yuen Long District Council member, solicitor), Professor Hector Tsang Wing-hong (Head of Dept. of Rehabilitation Sciences, HK Polytechnic University), Professor Frances Wong Kam-yuet (President, The HK Academy of Nursing), Professor Samuel Wong Yeung-shan (Head, Division of Family Medicine & Primary Heathcare, CUHK) and Dr Zhu En (Chinese Medicine Practitioner).

The terms of reference is to develop a blueprint for the sustainable development of primary healthcare services for Hong Kong. The Steering Committee would deliberate on the following – *Manpower and infrastructure planning* - review the software and hardware provision for the delivery of primary healthcare, with a view to achieving better efficiency and effectiveness, and identifying scope for enhancement; *Collaboration model* - develop primary healthcare service models which can enhance medical-social collaboration and public-private partnership and facilitate interfacing with other levels in the healthcare system; *Community engagement* - develop strategies and incentives to raise the health awareness of the community, and promote health management and patient empowerment; Planning and evaluation framework - exploit the use of big data to plan and devise strategies that best fit the needs of the community. *Develop the framework for monitoring and evaluating initiatives or pilot projects*, including the development of performance indicators and clinical and health outcomes, such as the reduction in avoidable use of accident and emergency and inpatient services in the public system; and *Strategy formulation* – having regard to Tasks 1–4 above, formulate strategies for enhancing primary, secondary and tertiary prevention in the community.

Food and Health Bureau has held a consultation with non-governmental organisations (NGOs) and allied health professionals on 18 April, 2018 on the District Health Centre (DHC) project. The key points to note for the DHC model: The first DHC will be launched in Kwai Tsing district in third quarter 2019, and will be rolled out to all 18 districts. The centre will be funded by the Government with copayment by service users. District-based NGOs will be responsible for running the model and direct service provision. The DHC will focus on chronic disease prevention and management with respect to the specific needs of the district. The priority disease and health problems to target in Kwai Tsing are preliminarily set as: Hypertension; Diabetes Mellitus; Musculoskeletal Disorders (E.g. Preventing bone fracture), Coronary Heart Disease; Stroke; Common risk factors (e.g. Obesity and overweight, smoking). Multidisciplinary services will be provided, include health assessment, case management as well as medication counselling.

With the sufficient supply of pharmacists in recent years, the way forward is to expand the role of pharmacists in primary care to counsel patients on drugs, conduct medication review for the patients (in particular upon discharge from hospital), provide consultation to patients by assessing their overall disease and medication profile, including prescribed medications, over-the-counter drugs, health supplements and proprietary Chinese medicine; perform disease screening to enhance early diagnosis and early prevention; and to educate public on disease prevention and management.

In the article on **page 11**, Chan Yi Ming and Chan Chung Ho provides a brief overview on the classification of adverse drug reactions, with examples illustrating their features and characteristics, and highlights the differences between drug allergy and non-allergic reactions. Adverse drug reactions refer to any unintended, noxious response to a drug that is used in normal dose. They can be of “predictable” or “unpredictable” nature. Drug allergy is a subtype of unpredictable ADR which is immune-mediated. Reactions are usually unexpected from the pharmacological properties of the drug, dose-independent, reproducible upon re-exposure, and may be elicited by structurally-related compounds, thereby closely associated with the risk of cross-sensitivity. Differentiation and accurate documentation of different types of ADR is essential to assist future clinical assessment of the risks and potential therapeutic benefits of prescribing a drug when there is a history of ADR.

Enteral feeding is a common means of delivering nutrition and medications to patients with dysphagia, which may arise from conditions such as stroke and dementia. In the article on **page 8**, Jennifer Ng and Phoebe Chan wrote about the risks and evidence associated with enteral feeding. Studies and evidence-based recommendations suggest that the use of tube-feeding in advanced dementia may be associated with unfavorable health outcomes including agitation, greater use of physical and chemical restraints. Practice points for pharmacists are also discussed.

In the article on **page 16**, Cheung Hon Yeung, Wang Fang and Terrence Lau wrote that some raw foods and medicinal herbal substances are unsuitable for drying at high temperature range whenever there is high content of water and mucilage substances. If they were air dried above 80ºC, they could be discolored as well as coagulated into masses. This change in physical property affects their flowability and subsequent handling. After systematic investigations, they show that a suitable drying condition could be established for successful pulverizing them. For example, Asparagi Radix could be dried at an ambient air temperature not more than 50ºC, while Lycii Fructus coud be freeze dried for sufficient time prior to crushing in order to produce native and non-cohesive fine powder by centrifugal-impact pulverizer. This is very important in the further manufacturing of the powders to finished products.

I hope you will take your time to read this issue and I look forward to the submission of manuscripts and reviewed articles for publication in the journal.

Cheng Mary Catherine
Managing Editor
19 April 2018

Prepared by Tommy Lee and Bryan Kan

New Therapy for Cystic Fibrosis

Date: January 30, 2018

Tezacaftor and ivacaftor, a new combination of cystic fibrosis transmembrane conductance regulator (CFTR) modulators, shown to be an effective and safe treatment for patients 12 years or older with *CFTR* gene mutations, according to the trial published in the *New England Journal of Medicine*. Tezacaftor increases CFTR cell surface expression and the ivacaftor enhances CFTR channel function.

In a randomized double-blinded trial, patients homozygous for the most common CFTR mutation that impairs CFTR cell surface expression, Phe508del, were randomly assigned to receive the combination therapy (tezacaftor and ivacaftor) or placebo. The primary outcome was measured by the absolute change from the baseline in forced expiratory volume in 1 second (FEV_1). Over the 24 weeks, the patients taking the combination therapy (tezacaftor and ivacaftor) showed a significant improvement in the primary outcome measure of lung function (+3.4 percentage point) than the placebo group (-0.6 percentage point).

The tezacaftor-ivacaftor group also showed a 35% lower incidence of pulmonary exacerbation than the placebo group. Besides, the tezacaftor-ivacaftor group showed a lower rate of severe adverse events (12.4%) than placebo group (18.2%). The trial concluded that the tezacaftor-ivacaftor therapy could offer an alternative for the treatment of cystic fibrosis.

Source: www.jamanetwork.com

US FDA Limits Packaging of Loperamide to Encourage Safe Use

Date: January 31, 2018

The US Food and Drug Administration (FDA) is adopting limitations on the packaging of loperamide amid surge in the number of reports about intentional misuse despite previous measures. New measures include working with manufacturers to use blister packs or other single dose packaging and to limit the number of doses in a package.

Loperamide acts on opioid receptors in the gut to slow the movement in the intestines and bowel. It is FDA-approved to help control symptoms of diarrhoea, including travellers' diarrhoea. The maximum approved daily dose for adults is 8 mg per day for OTC use and 16 mg per day for prescription use. It is safe at approved doses. However, it is suspected that people attempted to manage opioid addiction or to get euphoria via consumption of loperamide at dose much higher than recommended. This can lead to serious problems, including severe heart rhythm problems and death.

In Hong Kong, there are 63 registered pharmaceutical products containing loperamide. So far, the Department of Health (DH) has not received any case of adverse drug reaction related to loperamide. Loperamide users should seek medical attention immediately if they experience symptoms like fainting, rapid heartbeat or irregular heart rhythm.

Source: www.drugoffice.gov.hk

FDA: Updated Black Box Warning for Ocaliva About Incorrect Dosing

Date: February 01, 2018

Ocaliva (active ingredient: obeticholic acid) works by increasing bile flow from the liver, suppressing bile acid production in the liver and reducing the exposure of the liver to toxic levels of bile acids. Progressive primary biliary cholangitis (PBC) can lead to liver failure or death. Treatment of PBC with Ocaliva may delay or prevent progression of the disease.

FDA warned that the medication Ocaliva has been improperly dosed daily rather than weekly in patients with moderate to severe PBC, which increases the risk of serious liver injury. To ensure correct dosing and reduce the risk of liver damage, FDA clarified the current recommendations for dosing and managing PBC patients with moderate to severe liver disease taking Ocaliva. FDA added a new Boxed Warning to highlight this information in the prescribing information of the drug label and required a Medication Guide for patients to inform about this issue.

Health care professionals should follow the dosing regimen in the drug label, which is based on Child-Pugh score in PBC patients with suspected liver cirrhosis before treatment to determine their specific classification and starting dosage. Close monitoring is recommended for patients at an increased risk of liver decompensation.

Source: www.fda.gov

Extra-fine Inhaled Triple Therapy Superior to Dual Therapy in COPD

Date: February 08, 2018

Chronic obstructive pulmonary disease (COPD) is highly prevalent and prevention of exacerbations is a key therapeutic goal. Currently, the pharmacological treatment is based on the use of inhaled long-acting bronchodilators (long-acting antimuscarinic agents, long-acting β2 agonists or both as dual therapy), with or without inhaled corticosteroids. However, research is lacking regarding the effect of adding inhaled corticosteroids onto dual therapy.

TRIBUTE was a randomised, parallel-group, double-blind, double-dummy, controlled, multicentre trial conducted from 2015 to 2017. It aimed to compare the efficacy to prevent COPD exacerbations between single-inhaler triple combination of beclometasone dipropionate, formoterol fumarate, and glycopyrronium (BDP/FF/G) versus a single-inhaler dual bronchodilator combination of indacaterol plus glycopyrronium (IND/GLY). 1532 patients were randomly assigned with 52-week treatment of two inhalation of extra-fine BDP/FF/G (87μg/5μg/9μg twice daily) or one inhalation of IND/GLY (85μg/43μg once daily) in approximately 1:1 ratio. The primary outcome was the rate of moderate-to-severe COPD exacerbations over 52 weeks of treatment.

BDP/FF/G had significantly lower rate of moderate-to-severe exacerbation (0.50 per patient-year) than IND/GLY (0.59 per patient-year) (rate ratio: 0.848; 95% CI: 0.723-0.995; p=0.043). Meanwhile, there were no significant difference in the occurrence of reported adverse events and corticosteroid-related pneumonia between the two treatments.

In patients with symptomatic COPD, severe or very severe airflow limitation, and an exacerbation history despite maintenance therapy, extra-fine BDP/FF/G significantly reduced the rate of moderate-to-severe exacerbations compared with IND/GLY, without increasing the risk of pneumonia.

Source: www.thelancet.com

New Treatment for Non-metastatic Castration-resistant Prostate Cancer

Date: February 14, 2018

FDA approved Erleada (apalutamide) for the treatment of patients with prostate cancer that has not spread (non-metastatic) but continues to grow despite treatment with hormone therapy (castration-resistant). This is the first FDA-approved treatment for non-metastatic and castration-resistant prostate cancer.

Erleada works by blocking the effect of androgen such as testosterone, which can promote tumor growth, on the tumor. The safety and efficacy of Erleada was based on a randomized clinical trial of 1,207 patients with non-metastatic, castration-resistant prostate cancer. Patients in the trial either received Erleada or a placebo. All patients were also treated with hormone therapy, either with gonadotropin-releasing hormone (GnRH) analog therapy or with surgery to lower the amount of testosterone in their body (surgical castration). The median metastasis-free survival for patients taking Erleada was 40.5 months compared to 16.2 months for patients taking a placebo.

Common side effects of Erleada include fatigue, hypertension, rash, diarrhea, nausea, weight loss, arthralgia, hot flush, decreased appetite and peripheral edema. Severe side effects are fractures and seizures.

Source: www.fda.gov

FDA Warns of Heart Problem Risk by Clarithromycin

Date: February 22, 2018

FDA advises caution before prescribing clarithromycin (Biaxin) to patients with heart disease because of a potential increased risk of heart problems that can occur years later. FDA's recommendation is based on a review of a 10-year follow-up study of patients with coronary heart disease from a large clinical trial that first observed this safety issue.

The large clinical trial, called the CLARICOR trial, observed an unexpected increase in deaths among patients with coronary heart disease who received a two-week course of clarithromycin that became apparent after patients had been followed for one year or longer. After all, it is still unclear why the risk of death is greater for patients with heart disease. Therefore, FDA added a new warning about this increased risk of death in patients with heart disease and advised prescribers to consider using other antibiotics in such patients.

It is recommended that health care professionals should be alert to these risks and weigh the benefits and risks of clarithromycin before prescribing it to patients, particularly those with heart disease. Counsel the patients on signs and symptoms of cardiovascular problems, regardless of the medical condition that clarithromycin is indicated for.

Source: www.fda.gov

CHP: Vaccination Highly Recommended for Local Influenza

Date: February 28, 2018

Influenza can cause severe illness even in healthy persons. As of February 28, 458 severe influenza cases have been reported, including 284 deaths. Elderly population with age 65 or above was the most vulnerable group.

The Centre for Health Protection highly recommends vaccination as safe and effective mean of protection besides adopting personal, hand and environmental hygiene practices against respiratory illnesses.

Both trivalent (IIV3) and quadrivalent (IIV4) inactivated influenza vaccines are recommended for use in Hong Kong. Recommended trivalent vaccines to be used comprise A/Michigan/45/2015 (H1N1) pdm09-like virus, A/Hong Kong/4801/2014 (H3N2)-like virus and B/Brisbane/60/2008-like virus. Quadrivalent influenza vaccine shall contain the above three viruses and a B/Phuket/3073/2013-like virus. Based on local laboratory data, trivalent influenza vaccine may potentially prevent majority of influenza burden in Hong Kong, while quadrivalent influenza vaccine may potentially offer additional protection against influenza B.

All persons aged 6 months or above except those with known contraindications are recommended to receive influenza vaccine to protect themselves against seasonal influenza and its complications, hospitalizations and deaths. The Vaccination Subsidy Scheme continues to provide subsidized vaccination to various vulnerable groups.

Source: www.chp.gov.hk

Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

Date: March 01, 2018

Septic shock is a persisting hypotension requiring vasopressors to maintain a mean arterial pressure of 65 mmHg or more and having a serum lactate level of greater than 2 mmol/l despite adequate volume resuscitation. Glucocorticoid is believed to be effective and is widely used as an adjunct for maintaining hemodynamic stability.

The ADRENAL trial was conducted to investigate the effectiveness of hydrocortisone in reducing mortality of patients with septic shock who were undergoing mechanical ventilation. Conducted from 2013 to 2017, ADRENAL is a double-blind, parallel-group, randomized, controlled trial with 3658 patients enrolled. Patients were randomly assigned with hydrocortisone (200mg IV daily) or placebo in approximately 1:1 ratio. Primary outcome included death from any causes at 90 days while secondary outcomes included assessment on other aspects like new-onset infection in blood and ICU stay.

Hydrocortisone treatment had no significant difference in mortality at 90 days when compared with placebo (27.9% vs 28.8%; odds ratio: 0.95; 95% CI, 0.82-1.10; p = 0.50). Except with faster resolution of shock (hazard ratio: 1.32; 95% CI, 1.23-1.41; p < 0.001), hydrocortisone had no significant difference with respect to other secondary outcomes when compared with placebo.

Among patients with septic shock undergoing mechanical ventilation, continuous infusion of hydrocortisone is not effective in lowering 90-day mortality.

Source: www.nejm.org

Opioid Non-superior to Non-opioid therapy for Chronic Back Pain or Hip or Knee Osteoarthritis Pain

Date: March 06, 2018

Opioids have long been recommended by guidelines for management of moderate to severe pain while nonopioids have been suggested for management of mild to moderate pain. However, the practice is not well-supported by evidence and patients are prone to misuse and severe side effects.

The SPACE trial was conducted to compare the effectiveness of opioids with non-opioid medications on moderate to severe chronic back pain or hip or knee osteoarthritis pain despite analgesic use. It was a pragmatic, 12-month, randomized trial with masked outcome assessment. 240 primary care patients were randomly assigned with opioid or nonopioid prescribing strategies at 1:1 ratio. The primary outcome was pain-related function, assessed with the 7-item Brief Pain Inventory interference scale. Secondary outcomes included pain intensity, follow-up rate, patients' preference, adverse events, potential misuse and others.

For the primary outcome, opioid treatment did not result in significantly better pain-related function over 12 months than nonopioid counterpart (overall P=0.58). Nonopioid treatment was associated with significantly better pain intensity (overall P=0.03) and less medication-related adverse symptoms (overall P=0.03).

Opioid therapy was not superior to nonopioid therapy for improving pain-related function over 12 months. Results did not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.

Source: jamanetwork.com

Steering Committee on Primary Healthcare Development

Date: March 06, 2018

The Steering Committee on Primary Healthcare Development is formed with Prof. Sophia Chan Siu-chee as Chair-person, non-official members include Mr Philip Chiu Kwok-leung, Mr Chua Hoi-wai, Dr Lam Ching-choi, Professor Cindy Lam Lo-kuen, Professor Gabriel Matthew Leung, Dr Donald Li Kwok-tung, Mr Shum Ho-kit, Professor Hector Tsang Wing-hong, Professor Frances Wong Kam-yuet, Professor Samuel Wong Yeung-shan, Dr Zhu En. Ex-officio members include Permanent Secretary for Food and Health (Health), Permanent Secretary for Labour and Welfare (or representative), Director of Health (or representative) Director of Home Affairs (or representative), Head, Primary Care Office, Department of Health (or representative), Chief Executive, Hospital Authority (or representative), Chief Manager (Nursing), Hospital Authority (or representative).

Terms of reference is to develop a blueprint for the sustainable development of primary healthcare services for Hong Kong.

Source:https://www.fhb.gov.hk/en/committees/scphd.htm

Nutrition and Feeding in the Elderly—To feed or not to feed?

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ABSTRACT

Enteral feeding is a common means of delivering nutrition and medications to patients with dysphagia, which may arise from conditions such as stroke and dementia. As the right to adequate food and nutrition is considered a basic human right, the risks associated with enteral feeding may often be overlooked. Studies and evidence-based recommendations suggest that the use of tube-feeding in advanced dementia may be associated with unfavorable health outcomes including agitation, greater use of physical and chemical restraints, healthcare use due to tuberelated complications, and development of new pressure ulcers. Healthcare professionals should be mindful that the use of tube-feeding may not always be the optimal solution for older adults with dysphagia.

EATING AND NORMAL AGING

Swallowing is a complex series of coordinated neuromuscular events in which disruption would lead to dysphagia. With advancing age, the general population will experience a subtle prolongation of the swallowing process as a result of cerebral atrophy, deterioration in nerve function, as well as reduced muscle mass and connective tissue elasticity.[1] This may be accompanied by voluntary alterations in dietary intake owing to decrements in oral moisture, taste, and smell acuity.[2]

EATING AND FEEDING ISSUES IN OLDER ADULTS WITH DEMENTIA

Clinically significant dysphagia however cannot be attributed to normal aging per se. Rather, such changes predispose older adults to dysphagia in conjunction with a variety of age-related diseases that impair oropharyngeal or esophageal function.[1,2] Among these conditions is advanced dementia, where eating problems including oropharyngeal dysphagia, inability to perform the task of eating, disinterest in food or refusal to eat may ensue from cognitive impairment, motor deficits such as apraxia, delusions and/or depression.[2-4] In fact, the presence of eating difficulties has been identified in as many as 85.8% of 323 nursing home residents with advanced dementia in an 18-month prospective cohort study.[5] A local prevalence study reported an estimated number of 103,433 patients with dementia among those aged 60 and over in Hong Kong in 2009, and the number was projected to increase to 332,688 by 2039.[6] Given these figures, it is anticipated that dysphagia in patients with advanced dementia would become increasingly prevalent.

At the onset of eating problems, acute conditions, for instance stroke or dental problems, should be considered, with reversible causes being addressed.[3] Multiple professions including nurses, physicians, speech and language pathologists, occupational therapists, and dieticians are involved in the process of screening, diagnosis, treatment, and monitoring of dysphagia. Conservative approaches such as texture modification of diet or postural adjustments may be adopted to encourage oral intake.[7] Eventually, as eating difficulties become persistent in the final stages of dementia, family members or other surrogate decision makers will often be asked to make wrenching decisions concerning the initiation of artificial nutrition and hydration (ANH) in their loved ones.

DECISIONS ABOUT ARTIFICIAL NUTRITION AND HYDRATION

The quandary arises primarily because patients with dementia lack the mental capacity to make decisions regarding their own care or treatment. This may potentially be circumvented by engaging in advance care planning or choosing a healthcare proxy.[8] The intent of advance care planning is to ensure that treatment decisions for patients align with their goals, values, and beliefs. Advance care planning may include the completion of an advance directive, a formal tool completed by the individual while still in the possession of decisional capacity about how treatment decisions should be made on his or her behalf under circumstances where he or she has lost the capacity to make such decisions.[9] Without a valid advance directive, the decision to withhold or withdraw tube feeding when death is not imminent is made by consensus of the healthcare team and family members based on the best interests of the mentally incompetent patient, taking into account any prior wish or treatment preference.[10]

RATIONALE FOR THE USE OF FEEDING TUBES

There can be myriad reasons why family members or the healthcare team may advocate the use of feeding tubes, which may involve medical, economic, legal, ethical, cultural, social, religious and psychological factors.[11] Underlying the arguments, however, are two predominant assumptions: that the ANH prolongs survival and promotes comfort. As food and

fluid are basic physiological needs fundamental to life, some view tube feeding as basic sustenance care.[12,13] Forgoing tube feeding is therefore considered tantamount to abuse as the patient is being deprived of a basic human right.[14] Family members and caregivers often feel compelled to initiate artificial hydration and nutrition when a terminally ill patient becomes unable to take nourishment orally, in the belief that starvation and dehydration would contribute to suffering and hasten death.[15] From this perspective, withholding or withdrawing tube feeding is deemed comparable to passive euthanasia, and is against the primary obligation of healthcare professionals to preserve life.[16] Due to this and other reasons including the fear of aspiration pneumonia, tube feeding is often initiated in older patients with dysphagia, not to mention practical issues such as manpower shortage and crowded environment, which would discourage quality feeding.[17]

TUBE FEEDING IN ADVANCED DEMENTIA: THE EVIDENCE

The preponderance of evidence however suggests otherwise. In the landmark case *Cruzan v. Director of Missouri Department of Health*, the United States Supreme Court adopted the consensus opinion that treats ANH as a medical treatment instead of basic care.[13] As such, the risks and benefits of feeding tube placement should be considered as for any other medical procedure. As part of the Choosing Wisely® campaign, the American Geriatrics Society (AGS) declared their stance with respect to the use of tube feeding in advanced dementia. Specifically, the society recommends against the use of tube feeding to avoid eating difficulties in older adults with advanced dementia, based on expert opinion and highly consistent empirical work using observational data adjusted for potential confounders and selection bias.[18,19] It was concluded that there was insufficient evidence to support the benefits of tube feeding in patients with advanced dementia in terms of survival, quality of life, nutrition, functional status, the prevention of aspiration, or the prevention and healing of pressure ulcers. On the contrary, tube feeding is associated with substantial burden including recurrent and newly onset aspiration, tubeassociated and aspirationrelated infection, oral secretions that are difficult to manage, discomfort, tube malfunction, use of physical and chemical restraints, and pressure ulcers. Studies also reported frequent transfers of nursing home residents with advanced dementia to the emergency department to address tube-related complications such as blockage and dislodgement. In the meantime, careful hand feeding was found to be as good as tube feeding in terms of the outcomes of death, aspiration pneumonia, functional status, and comfort, and thus should be offered.

In response to whether dehydration contributes to suffering and hastens death, it has been pointed out that dehydration is part of the natural dying process.[20] As body systems begin to shut down to prepare for death, metabolic needs decrease and the usual amount of food and fluid may not be needed or helpful. Inferring data from patients dying with other terminal illnesses, it is revealed that patients with a terminal illness can experience comfort despite minimal intake of food and fluids.[21] One study reported being able to alleviate thirst and hunger in 84% of 32 patients dying of cancer and stroke by providing them with small amounts of food, mouth swabs, sips of water, ice chips, and lubrication of the lips.[22] In fact, there have been case-based reports, retrospective series, and testimony from hospice professionals that indicate an amelioration of symptoms such as relief from choking and drowning sensations, less coughing and chest congestion, decreased urine output with less need for catheterization and bedwetting, decreased gastrointestinal fluid with less vomiting, bloating, and diarrhea, less peripheral edema, as well as less pain in dehydrated terminally ill patients.[21-29] Furthermore, some proposed that patients without ANH would lapse into coma and therefore be unaware of hunger, thirst, or any physical discomfort.[24,30] Conversely, feeding tubes have the potential to preserve a patient's level of consciousness, thereby prolonging the agony of the dying process without affecting the outcome. Attempting to reverse a natural trend may lead to discomfort, with possible presentation or aggravation of the aforementioned symptoms due to excess fluid accumulation.[20]

PRACTICE POINTS FOR PHARMACISTS

Nevertheless, it should be noted that randomized controlled trials comparing the benefits and burdens of tube feeding with those of hand feeding in persons with advanced dementia are lacking, in part due to the vulnerability of the population and hence concerns surrounding ethically appropriate study design and methodology.[18] It has also been argued that current guidelines are oversimplified in that a blanket recommendation is made for a highly heterogeneous group of patients.[31] Being preliminary and provocative, the studies do raise interesting questions about the benefits of tube feeding but should not be cited to patients as definitive proof of the hypothesis that tube feeding does not prolong survival. Pharmacists should keep abreast of the current best evidence in this regard as enteral tube may appear to be the only alternative when dysphagia arises and administration of oral medications cannot be achieved in these patients. Appropriate recommendations can be made on the use of a different dosage form to facilitate administration. Needless to say, the decision to initiate tube feeding may be appropriate under certain circumstances. For example, there is evidence that ANH prolongs life, decreases aspiration, and prevents hunger, thirst, and dryness in patients with amyotrophic lateral sclerosis.[32] Other potential candidates for tube feeding are patients with dysphagia, with a high likelihood of maintaining or recovering swallowing function as in acute stroke, those with intact mental function, and patients with surgically correctable obstruction of the oropharynx due to malignancy.[20,31,33] Under these conditions, pharmacists may be involved in the matter of recommending an appropriate dosage form for administration through a feeding tube, drug-nutrient interactions, liquid medications dilution, and so on.[34] It is worth mentioning that the Choosing Wisely® campaign is an initiative put forth by the American Board of Internal Medicine Foundation (ABIM) to foster conversations between clinicians and patients about choosing medical care that is supported by evidence, not duplicative of other tests or procedures already received, free from harm, and truly necessary.[35] To date, the effort has garnered participation from over 70 medical specialties societies, resulting in the publication of more than 400 recommendations of overused tests and treatments, which includes the AGS recommendation herein. By being aware of these recommendations, we should be able to identify treatments of questionable benefit about which discussions should be initiated.

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Understanding Adverse Drug Reactions and Drug Allergies: a Brief Overview

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ABSTRACT

An adverse drug reaction (ADR) is any unwanted, undesirable effect of a drug beyond its anticipated therapeutic effects which occur during clinical use. It occurs frequently, complicating 5-15% of medical therapies, and may necessitate intervention. However, misclassification of adverse reactions as hypersensitivity reactions may mislead healthcare providers and result in unnecessary avoidance of valuable treatment options. Differentiation and accurate documentation of different types of ADR is essential to assist future clinical assessment of the risks and potential therapeutic benefits of prescribing a drug when there is a history of ADR. This article provides a brief overview on the classification of adverse drug reactions, with examples illustrating their features and characteristics, and highlights the differences between drug allergy and non-allergic reactions.

Keywords: *Adverse drug reactions; drug allergy; drug hypersensitivity*

INTRODUCTION

Medications in modern medicine have therapeutic effects as well as the potential to cause harm. Adverse drug reactions (ADR) are a common, often preventable, cause of morbidity and mortality in daily clinical practice. Different studies have shown that ADR-related admissions comprise up to 10% of the total number of hospital admissions.[1,2] It is the most common iatrogenic illness complicating 5-15% of drug therapies.[3,4] Unwanted clinical responses in an ill patient incurs extra burdens for both the patient and the managing physician. Early recognition and management of ADR is thereby an important aspect in medication management to ensure the quality and safety in patient care. To aid clinical judgment on whether to continue, withdraw or re-challenge the drug in question, it is crucial to understand the nature of ADR and allergic reactions. This article briefly discusses the different types of ADR and highlights the differences between drug allergy and non-allergic ADR.

DEFINITION AND CLASSIFICATION OF ADVERSE DRUG REACTIONS

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, of which the World Health Organization and the US Food and Drug Administration are observer and member, respectively, defines an adverse drug reaction as "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function".[5] This definition differentiates ADR from side effects that can be desirable or beneficial, and excludes harm due to accidental or deliberate overdose.[6]

In early pharmacological classification, ADR is broadly categorized on the basis of dose-related and non-dose-related reactions, referred to as type A (Augmented) and type B (Bizarre) reactions, respectively. The majority of ADR, up to approximately 80%, result from predictable pharmacological actions of the drugs. The dose-dependent nature makes type A reactions relatively more controllable, which usually resolve when the dose is reduced or when the drug is withdrawn.[3,7] Examples include dry mouth and drowsiness caused by antihistamines, constipation associated with opioid use, and muscle tremors from salbutamol. On the other hand, bizarre reactions are generally unpredictable, and are unrelated to the drug's pharmacological effects and independent of the dose. They may or may not be immune-mediated. Although some reactions resolve when the offending agent is stopped, some continue to progress and may lead to significant morbidity and mortality.[3]

Since 1980s, more adverse reaction categories have been recognized, taking into account the time-related factor. ADR of chronic type is dose- and time-related, which are associated with the cumulative dose and long-term exposure. Corticosteroid-induced suppression of the hypothalamic-pituitary-adrenal axis is one of the typical examples of chronic adverse reactions. Time-related ADR can present with delayed effect or occurrence upon end-of-treatment. ADR of delayed type appears some time after drug exposure, such as teratogenicity from thalidomide and the development of cervical and vaginal adenocarcinoma induced by prenatal exposure

to diethylstilbestrol.[3,7] End-of-treatment ADR, also known as withdrawal, occurs with little or no delay after withdrawal of the drug. Classical examples are opioid withdrawal syndrome, sedative-hypnotic withdrawal and beta-blocker withdrawal, of which abrupt treatment discontinuation should be avoided with gradual dose tapering. More recently, an ADR category of failure type has been proposed to characterize the unexpected failure of therapy possibly due to drug-drug interactions or resistance. Bacterial resistance to certain antibiotics, mutant tumor cells insensitive to certain targeted therapies or ineffectiveness of oral contraceptives due to concurrent therapy with CYP enzyme inducers belong to so-called type F ADR.[3,7]

For mnemonic purposes, ADR can be classified into (but not limited to) six categories: **A**ugmented (dose-related), **B**izarre (non-dose-related), **C**hronic (dose-related and time-related), **D**elayed (time-related), **E**nd of treatment (withdrawal) and **F**ailure (unexpected failure of therapy).[3,7] Their common features, pharmacological bases and examples of drug reactions are summarized in **Table 1**. It is noteworthy that classifying an ADR into one of these categories is not always possible. The classification is expected to evolve when precise mechanisms of specific adverse drug reactions are known to enable the categorization of currently unclassifiable reactions.[7]

DRUG ALLERGY – A SUBTYPE OF BIZARRE REACTIONS

Of the type B category, many reactions are not mediated by immune mechanisms; namely, pseudoallergy, idiosyncratic reactions and drug intolerance. Pseudoallergic reactions are anaphylactoid reactions produced by direct release or activation of inflammatory mediators of histamine, prostaglandins, kinins from cells such as mast cells and basophils. Common causative agents include vancomycin (causing the classical "red man syndrome"), opiates and iodinated radiocontrast media. Pseudoallergy are often clinically indistinguishable from true immunologically mediated allergies, but they do not involve drug-specific antibodies. Idiosyncratic reactions are aberrant reactions that are unexplained and occur only in small proportion of the population, such as drug-induced hemolytic anaemia in selected persons with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Drug intolerance refers to the lowered threshold to undesirable pharmacological effect of a drug, e.g. tinnitus after a single, normal dose of aspirin.[4,8] Collectively, these reactions are unpredictable from known pharmacology and non-immunological in nature. The remainder of type B reactions, accounting for 5-10% of all ADR, has an immunological basis which is the requirement for true drug allergy. Therefore, drug allergy is only a subset of the unpredictable and dose-independent type B (Bizarre) ADR. **(Figure)**[3,4,7]

Drug allergy is also referred to as hypersensitivities. Based on the predominant immune mechanisms involved, it is sub-divided into four types of hypersensitivity reactions: Type I (IgE-mediated), Type II (cytotoxic), Type III (immune complex) and Type IV (delayed, cell-mediated) reactions. Due to the diversity of immunological pathways, drug allergy can provoke a wide spectrum of clinical manifestations - from a mild T cell-mediated skin rash to an immediate and fatal IgE-mediated anaphylaxis.[4,8] The immune basis, clinical presentation and expected timing of allergic reactions, with examples of culprit drugs, are summarized in **Table 2**.

The most important drug-related risk factor that influences the likelihood of allergic reactions is the chemical properties and structural complexity of the drug. Drugs that contain non-

Table 1. Classification of Adverse Drug Reactions[3,4,6,7]

Type of Reaction	Main Features of Reaction		Examples
A. Augmented pharmacologic effects	– Common (constitute ~80% of the overall ADR) – Predictable – Low mortality – Related to drug's pharmacological action	– Toxic effects – Side effects	– Dysrhythmia caused by digoxin – Constipation caused by opioids – Dry mouth with tricyclic antidepressants – Bronchospasm due to β-blocker in a hypertensive patient
B. Bizarre Immune (allergic) and non-immune	– Relatively uncommon – Unpredictable – High mortality – Unrelated to drug's pharmacological action	**Immune** – Allergy	– Anaphylaxis to penicillin – Anticonvulsant hypersensitivity reaction
		Non-immune – Idiosyncratic reactions – Pseudoallergy – Intolerance	– Hemolytic anemia in a G6PD-deficient patient after primaquine therapy (Idiosyncratic reaction) – "Red man syndrome" from vancomycin; anaphylactoid reaction after injection of iodinated radiocontrast agents (Pseudoallergy) – Tinnitus after a single, small dose of aspirin (Intolerance)
C. Chronic (continuous) effects	– Uncommon – Related to cumulative dose and long-term exposure	– Chronic toxicity – Chronic side effects	– Corticosteroid-induced suppression of the hypothalamic-pituitary-adrenal axis – Osteonecrosis of the jaw with bisphosphonates
D. Delayed effects	– Uncommon – Time-related. Apparent sometime after drug exposure; seen after exposure at a critical time	– Teratogenesis – Carcinogenesis – Tardive dyskinesia	– Thalidomide-induced teratogenicity – Cervical and vaginal adenocarcinoma with exposure to diethylstilbestrol – Tardive dyskinesia with typical antipsychotics
E. End-of-treatment effects (withdrawal effects)	– Uncommon – Occurs with little or no delay after withdrawal of drug	– Withdrawal syndromes	– Opiate withdrawal syndrome – β-blocker withdrawal
F. Failure of therapy	– Common – May be caused by drug interaction	– Resistance to drug action	– Resistant bacteria to antibiotic or tumor to chemotherapy – Inadequate dosage of an oral contraceptive, particularly when used with specific enzyme inducers

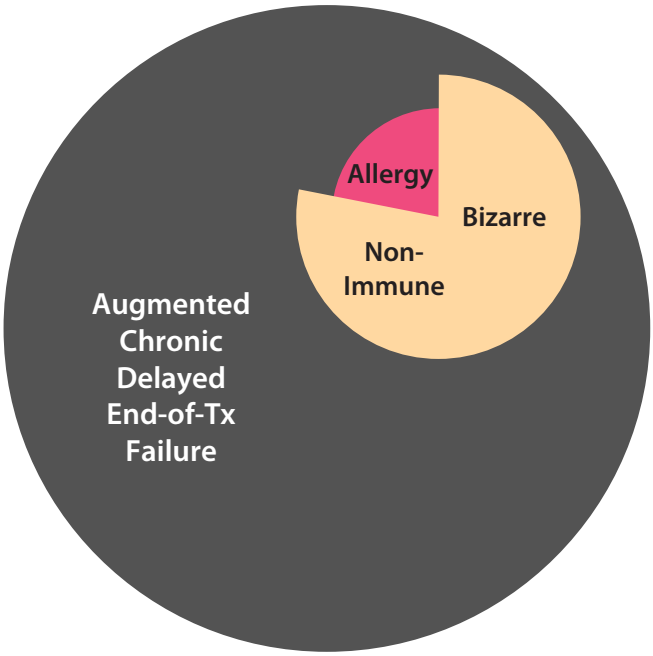

Figure. Rough schematic diagram of ADR
*Allergy is a subtype of **B**izarre ADR. Other Bizarre ADR, including intolerance, idiosyncratic reactions and pseudoallergy, are non-immune mediated. The majority of ADR belongs to **A**ugmented, **C**hronic, **D**elayed, **E**nd of treatment, or **F**ailure type of reactions.*

human protein structure (e.g. chimeric monoclonal antibodies, streptokinase) or haptenate to form antigenic determinants with carrier proteins (e.g. penicillin) are more likely to elicit allergic response.[4,8,9] In principle, drug allergy can occur with any dose of a drug, nevertheless frequent or continuous dosing is more likely to sensitize a patient than a large single dose.[8,9] The route of administration also affects the occurrence and severity of allergic reactions. Topical route is more likely to cause hypersensitivities than the oral route, which is explained by the efficient antigen presentation in the skin; whereas the parenteral route is associated with more severe reactions due to the high concentration of antigen that is rapidly achieved with intravenous administration.[4,8,9] Apart from patient specific factors such as age, female gender and certain concomitant viral infections, pharmacogenomics is playing an increasingly important role in identifying individuals at risk for certain allergic reactions. For instance, severe immune-mediated cutaneous reactions to allopurinol and carbamazepine, including Stevens–Johnson syndrome and toxic epidermal necrolysis, have been associated with the presence of HLA-B*5801 and HLA-B*1502 allele, respectively, in Han Chinese.[8,9]

CLINICAL PRESENTATION

Depending on the immunological basis, the onset time and clinical features of drug allergy may vary. Skin is often the most prominently affected organ with the manifestations of generalized exanthema, urticaria, angioedema, or more severe form of bullous or blistering disorder with epidermal detachment.[4,8] Other organ systems, such as hematologic, hepatic and renal systems, may also be involved in anaphylaxis, drug rash with eosinophilia and systemic symptoms (DRESS) or other multi-organ reactions.[8,9] Generally, presentation in the form of itchy rash, urticaria, laryngeal or upper airway edema, difficulty in breathing and hypotension is suggestive of an immediate, generalized, IgE-mediated (Type I) reaction and would require immediate medical attention. Presence of fever, vasculitis, blistering lesions with mucous membrane involvement, hematological abnormalities or organ dysfunction may also indicate drug allergy but may implicate the other subtypes.

As described in epidemiology studies, the majority of ADR encountered in clinical practice are related to predictable pharmacological actions of drugs, such as dry mouth from tricyclic antidepressants, diarrhea from antibiotics, constipation from opioids, and dry cough from angiotensin converting enzyme inhibitors. It should be made clear that “drug allergy” refers to immunologic hypersensitivity only; thus, the term should not be overused to describe all adverse systemic and local effects of a drug.

RISK OF RE-CHALLENGE

Immune-mediated drug hypersensitivities typically pose a reproducible, but more serious risk upon re-exposure to the causative agent.[4,10] Once a patient has been sensitized, the

Table 2. Classification of allergic drug reactions[3,4,8,9]

Type of hypersensitivity	Typical Onset	Characteristics	Clinical manifestations	Examples
I (IgE-mediated)	Minutes to hours after drug exposure, typically within 30 min to <2 hrs	Allergen binds to IgE on basophils or mast cells, with release of histamine and inflammatory mediators.	– Anaphylaxis – Urticaria – Angioedema – Bronchospasm	– Penicillins – Cephalosporins – Neuromuscular blocking drugs
II (Cytotoxic)	Variable, typically >72 hrs to weeks	Cell destruction occurs due to IgG or IgM initiated cytolysis. Most often involves blood elements.	– Anemia – Cytopenia – thrombocytopenia	– Cephalosporins – Penicillins – Quinine
III (Immune complex)	1 to 3 weeks after drug exposure	Antigen–antibody complexes deposit on blood vessel walls and activate complement.	– Serum sickness – Vasculitis, rash – Fever – Arthralgia	– Penicillins – Cephalosporins – Sulfonamides – Tetracycline
IV (Delayed, cell-mediated)	2 to 7 days after drug exposure	Antigens cause activation of T lymphocytes, which release cytokines and recruit effector cells (e.g. eosinophils and neutrophils).	– Contact sensitivity – Skin rashes – Organ-tissue damage	– NSAIDS – Anti-microbials – Anticonvulsants (carbamazepine) – Local anesthetics

severity of an allergic reaction is often determined by the dose and the duration of exposure.[9] On the other hand, non-immune drug reactions vary in severity, but tend to be less severe and often with reproducibility predictable from known pharmacology. In general, drugs that elicit allergic reactions should not be rechallenged as re-exposure may result in rapidly fatal anaphylaxis or other severe non-IgE reactions. Drug discontinuation and avoidance are the cornerstones in the effective management of this type of drug allergy. When possible, alternative medications with unrelated chemical structures should be substituted.[4,8] Whereas for majority of predictable and dose-related ADR, it may not be necessary to permanently withdraw the offending drugs since these ADR could potentially be mitigated or prevented by dose reduction, slow titration or confined duration of use.[4]

CROSS REACTIVITY

Drugs with similar chemical structures have the potential to cause cross-sensitivity via immunological mechanisms. It is usually explained by the presence of common antigenic determinants in the cross-reacting drugs, such as β-lactam antibiotics (e.g. penicillin and cephalosporin) and non-steroidal anti-inflammatory drugs (NSAID) of the same chemical class (e.g. diclofenac and ketorolac from acetic acid derivatives). In the case of compounds provoking non-allergic ADR, cross-reactivity is explained by a common pharmacological characteristic, such as the cyclooxygenase-1 inhibiting effect of NSAID causing bronchospasm, or histamine release mediated by radiocontrast media.[11] Therefore, cross-reactivity among drugs should be taken into consideration when selecting an alternative agent.[8]

CONCLUSION

Adverse drug reactions refer to any unintended, noxious response to a drug that is used in normal dose. They can be of "predictable" or "unpredictable" nature. Drug allergy is a subtype of unpredictable ADR which is immune-mediated. Reactions are usually unexpected from the pharmacological properties of the drug, dose-independent, reproducible upon re-exposure, and may be elicited by structurally-related compounds, thereby closely associated with the risk of cross-sensitivity. Clinical manifestations of drug allergy range from mild skin rashes to immediately life threatening anaphylaxis. It should be distinguished from the other ADR as it can potentially lead to fatal outcomes. The majority of non-allergic ADR are of predictable nature and caused by dose-related pharmacological effects. Manifestation varies from mild and tolerable aliments to severe conditions requiring prompt medical intervention. Nevertheless, indiscriminate classification of an ADR as drug allergy may unnecessarily preclude valuable treatment options. A general understanding of the clinical characteristics of ADR and drug allergy and their differences is therefore vitally important.

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Questions for Pharmacy Central Continuing Education Committee Program

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

2 CE Units

Understanding Adverse Drug Reactions and Drug Allergies: a Brief Overview

1. ***Which of the following statements best describes ADR according to the WHO definition?***
   - A. An unintended response to a drug which can be desirable or undesirable
   - B. An anticipated response to a drug which is noxious and unwanted
   - C. An unintended, noxious response to a drug which occurs at overdoses
   - D. An unintended, noxious response to a drug which occurs at normal doses

2. ***Which of the following types of ADR is the most prevalent in clinical practice?***
   - A. Augmented pharmacological effects
   - B. Allergic reactions
   - C. End of treatment effects
   - D. Idiosyncratic reactions

3 ***Which of the following statements regarding pseudoallergy is incorrect?***
   - A. Pseudoallergic reactions are produced by direct release or activation of inflammatory mediators of histamine, prostaglandins, kinins from mast cells and basophils.
   - B. Drug-specific antibodies are involved.
   - C. Vancomycin-induced red man syndrome is a classical example.
   - D. Anaphylactoid reactions of pseudoallergy can be clinically indistinguishable from true drug allergies.

4. ***Which of the following ADR has an immunological basis?***
   - A. Idosyncratic reaction
   - B. Intolerance
   - C. Pseudoallergy
   - D. None of the above

5. ***Which of the followings is/are feature(s) of type A ADR?***
   - (i) dose-dependent
   - (ii) predictable from pharmacological properties
   - (iii) mediated by immune mechanisms
     - A. (i) and (ii)
     - B. (ii) only
     - C. (iii) only
     - D. All of the above

6. ***Which of following reactions is unlikely an allergic reaction?***
   - A. Angioedema with penicillin
   - B. Bronchospasm with beta-blocker
   - C. Carbamazepine-induced Steven-Johnson syndrome
   - D. Urticaria with cephalosporin

7. ***Which of the following reactions is classified as a type B ADR?***
   - A. Dry mouth from amitriptyline
   - B. Opioid withdrawal syndrome
   - C. Primaquine-induced hemolytic anaemia in a G6PD-deficient patient
   - D. Teratogenicity from thalidomide therapy

8. ***Which of the followings is/are factor(s) that may increase the likelihood of allergic reactions?***
   - A. Presence of non-human protein structure in the drug molecule
   - B. Topical route of administration
   - C. Frequent and continuous dosing
   - D. All of the above

9. ***Which of the following presentations is suggestive of an IgE-mediated Type I hypersensitivity reaction?***
   - A. Blistering skin lesions with epidermal detachment
   - B. Urticarial rash with difficulty in breathing
   - C. Hemolytic anaemia
   - D. Hepatitis

10. ***Which of the followings is/are appropriate approach(es) to manage drug allergies?***
    - (i) Discontinue the offending agent
    - (ii) Reduce the dose of the culprit drug
    - (iii) Limit the duration of drug exposure
    - (iv) Substitute therapy with an alternative of unrelated chemical structure
      - A. (iv) only
      - B. (ii) only
      - C. (ii) and (iii)
      - D. (i) and (iv)

Answers will be released in the next issue of HKPJ.

CE Questions Answer for 244(D&T)

Update on the Safety of Paracetamol

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

Asparagi Radix Dried at Ambient Air Temperature while Lycii Fructus at Freezing Temperature Favours the Production of Its Native and Non-cohesive Fine Powder by Centrifugal-Impact Pulverizer

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ABSTRACT

Some raw foods and medicinal herbal substances are unsuitable for drying at conventional high temperature range whenever there is high content of water and mucilage substances. If they were air dried above 80ºC, they could be discolored as well as coagulated into masses. This change in physical property affects their flowability and subsequent handling. After systematic investigations, we show that a suitable drying condition could be established for successful pulverizing them. Asparagi Radix could be dried at an ambient air temperature not more than 50ºC, while Lycii Fructus coud be freeze dried for sufficient time prior to crushing in order to produce native and non-cohesive fine powder by centrifugal-impact pulverizer.

Keywords: *milling technology, high-sugar-containing food and herb, coking, drying conditions, stickiness, flowability, baking temperature, Asparagi Radix, Lycii Fructus*

INTRODUCTION

Foods, such as vegetables, fruits and meat are daily necessities for maintenance of life of a human being; they serve as food to provide source of energy, building materials and catalysts for a healthy life.(1) In order to get the maximal benefit out of them, such as having the best quality and be flexible for their use and storage, people may cut, grind and pretreat them into fine powder after harvest but prior to other processing or manufacturing into a desirable product for consumption. Similarly, Chinese herbal substances, because of their pharmacological activities, are frequently required for preservation, authentication and quality control in order to assure their safety and achieve maximal therapeutic efficacy. Dry powders of a herb are found in almost every situation in our daily live, both at home or in industry. In pharmaceutical industry, nutraceuticals, herbal medicines and other ingredients, when they occur in the solid state in the course of being processed into a dosage form, usually are in a more or less finely divided condition. Frequently, this is a powder whose state of subdivision is critical in determining its behavior both during processing and in the finished dosage form. Apart from their use in the manufacture of tablets, capsules, suspensions, pills, etc, powder is also a pharmaceutical dosage form.(2)

In order to have satisfactory grinding of foods or herbal substances from large block into fine powder, it is necessary to carry out removal of their moisture, as well as subsequently preventing reabsorption of water due to the hygroscopic and deliquenscent properties of the material. Food and herbal substances, in general, contain a fairly high content of water and are required to have their water removed prior to be pulverized or subjected to any other manufacturing process. **Table 1** shows that the water content of some representative foods and herbs that are much higher than the other; e.g. pasturized milk, mango fruit, Asparagus Radix and Lycii Fructus. The moisture decreases flowability by forming stronger interparticle liquid bridges and increases flowability by acting as a lubricant during manufacturing. The dynamic density of the celluloses decrease linearly with increasing moisture content as the particles swelled with water. The starches also swell and decrease in dynamic density, but only after a moisture content corresponding to monolayer coverage of water around the particles is reached.(3) Hence, to ensure consistent production of high-quality powder, the moisture content of the powders should be controlled as flowability and dynamic density of powder change with moisture content.

Because the water content of various Chinese medicinal materials or fruits is vary, to establishing a standardized drying protocal may not be feasible. Furthermore, small laboratories or processing plants may not have all the advanced facilities. When people purchase herbs from a local drugstore, they might encounter difficulties to blend the herb. They may be refused by the supplier to crush them because of lacking a proper facility or because of technical difficulty. Substances, such as Asparagi Radix, Ophiopogonis, Lycii Fructus and so on, are not so easy to be crushed due to their high water content. Therefore, it is necessary to find out some principles or guidelines for people to pulverize these substances with a simple and achievable protocal. Through a series of experimental works and systematical study, we report here drying temperature for those high water content foods and herbs should not be higher than 50ºC before they are pulverized. It was also found that fine native powder could be obtained by freezing foods or herbs before they are crushed.

Table 1. Ratio of nutrient components (% w/w) in various fresh foods

Food	Water Content	Protein	Fat	Coarse Fiber	Carbohydrate Total	Ash	References
Beef Carcass	57.26	17.32	24.05	0	0	0.8	(4)
Pork Carcass	49.8	11.2	47.0	ND	ND	0.6	(4)
Chinese ham	23.3	16.4	51.4	0	0	8.9	(5)
Milk (pasteurized)	87.6 ND	3.2 3.33	3.5 2.08	0 0	11.67 5.0	0.38 0.17	(6,7)
Chicken	75.0	22.8	0.9	ND	ND	1.2	(6)
Mango Fruit (unripe)	23.4	6.0	12.8	ND	11	2.0	(8)
Mango Fruit (ripe)	82.9	0.6	17.2	ND	14.8-16	1.2	(9)
Citrus Fruit juice	79.5	1.7	0.8	0.3	16.8	0.7	(10)
Lycii Fructus	77.4 (9.3)	2.5 (10.2)	1.1 (4.4)	2.9 (11.4)	15.3 (61.3)	0.84 (3.4)	(11)
Soya bean	13	38.5	19.3	4.6	21.5-25.3	2.9	(5)
Milk power	3.8	8.58-27.5	27.9	0	34.2-35.5	4.3-5.9	(5,12)
Asparagi Radix	18.3-30	ND	ND	ND	37	ND	(13)
Sword bean	14.7	30.4	2.1	3.4	38.7-58.8	10.8	(5)
Green bean	12.7	21	1.8	3.4	57	3.9	(5)
Rice (Fujian)	10.6	7.6	6.0	2.1	72.8-77	1.3	(5)
Wheat	10.5-13.4	9.5-17.6	1.3-2.0	0.8-2.9	75-77.8	0.6-2.5	(5)
Honey	18.9	1.1	0	0	79.5	0.3	(5)

ND = not described; Figure in parenthesis was derived on dried food basis.

EXPERIMENTAL MATERIALS AND METHODS

Experimental materials

Fresh fruits, including Crataegi Fructus, mango, Balsam pear and Chaenomelis Fructus were used unless it is indicated elsewhere. They were purchased from a supermarket in Shenzhen and are listed in **Table 1**. Baked sweet potatoes were bought from a roadside peddler. In this study some herbal drugs, such as aspartame, ophiopogon root, medlar and Schisandrae Chinensis Fructus, containing more viscous sugar, were purchased from Bozhou Wholesale market of Chinese medicines. Besides, xylem or hard shell raw materials such as Notogiseng et Rhizoma, Smilacis Glabrae Rhizoma, Polygonati Odorati Rhizoma, Gastrodiae Rhizoma, Ginseng Radix et Rhizoma rubra and kelp were obtained from a nearby medicinal materials market.

Experimental equipment

A centrifugal-Impact pulverizing machine (500 gm of swing type, model QEYS-500, powder not sieving 30-300, voltage 2000 W 21000 V/min 22*22*39) equipped with a high speed universal motor was used. Electrothermal constant temperature dryness box (PHG-9053A type) purchased from Shanghai Jinghong Experimental Equipment Co., Ltd., and also a Haier cryogenic refrigerator were used for baking the foods or herbs. A cold freeze drying apparatus (Lyolab-3000), was used whenever freeze drying was nesccessary while standardized sorting sieve No.1 – 6 were applied to monitoring particle size of powder.

Drying Experimental Works

(1) Treatment of foods and medicinal materials with high content of polysaccharides

Asparagi Radix: Dry Asparagi Radix was put into the pulverizing machine for 1 min and transferred to oven at 50ºC for baking. After 2 hr, it was taken out and mixed for 1 min and put back to the oven for another 15-31 hr before the baked material was pulverized to form powder followed by passing through a 80-mesh screen.

Ophiopogonis Radix : Dry Ophiopogonis Radix was put into the pulverized machine directly for 1 min. The sticky object was taken out and put in a tray for 4 hr at 50ºC followed by crushing in a pulverizer to form powder.

Schisandrae Chinensis Fructus was baked at 15ºC for 48 hr. It was directly used to prepare homogeneous powder. It was noted that 99% of the crushed material passed through 50 mesh sieve.

Dry Lycii Fructus was bought from the market. It was processed clean and comminuted after baking at 50ºC for 48 hr. As the crushed material was soft, sticky and coaggulated, it didn't form powdery particles. The coagulated mass of *Lycium barbarum* fruit was then put into a freeze dry apparatus at -20ºC for 48 hr. After it was solidified, the lump was crushed to form granules.

The baked sweet potato was used and put into an oven at 50ºC for 3 hr and then at 60ºC for another 17 hr. As there were water droplets observed on the surface of the sweet potato, it was kept at 45ºC for another 14 hr to make sure that no moisture condensed on its surfacre before it was crushed to form coarse powder, which was subsequently transferred into pallet and baked at 45ºC for another 4 hr. The pallets were used for preparation of fine powder.

(2) Treatment of fresh fruits

All fresh fruits, including Crataegi Fructus (Hawthorn), mango, balsam pear and Chaenomelis Fructus, were washed throughoutly and cut into pieces or slices before they were put in an oven to dry at a specific temperature as indicated for 19 - 27 hr. Dried blocks of the fruit was crushed to form powder at room temperature and subsequently baked for another 2 hr to obtain fine powder.

(3) Treatment of lignified or hard foods

Hard medicinal materials such as Notoginseng radix et Rhizoma, Polygonati Odorati Rhizoma, Kelp, Gastrodiae Rhizoma, Smiliacis Glabrae Rhizhoma and Ginseng Radix et Rhizoma, were firstly smashed with a hammer, or cut into smaller pieces with scissors or hay cutter. The broken pieces were put into a small grinding machine to be pulverized for 2 min before they were put in an oven for drying at 50ºC for 10 hr or other drying temperature as indicated elsewhere, followed by another milling for 2 min to ensure that uniform powder was obtained.

Measurement of moisture content

Water content was measured in food using the gravimetric method described in AOAC with some modifications.[14] This involves drying a known quantity of a food sample in an oven at various temperature for different time. Evaporation of moisture

during the drying was determined by measuring the matter content remaining and the water content was determined.

Analysis of particle size

Particle size of the powders were measured using a set of standardized mesh screens (No. 2 – 6 or mesh 200, 400 & 800). Distribution of a particular size of the powder was based on the quantity of powder retained on the screen and ratio was determined.

RESULTS

Formation of powder of various foods and herbs by centrifugal-impact pulverizer

Foods containing verious water content were picked for determining how good they could be grinded into fine powder by means of pulverization. Overall speaking, substances containing water less than 15% (w/w) moisture were no problem to form fine powder by grinding **(Table 2)**. But once moisture exceed this level, such as Asparagi Radix, Lycii Fructus, honey and Chinese ham, they were difficult to form fine powder. Althogh some of these foods or herbs were crushable to become smaller pieces, they stuck together and formed a sticky mass **(Figure 1C)**. Flowability of these powders or masses **(Figure 1B & C)** was also extremely poor except those formed fine powders **(Figure 1A)**.

Table 2. Physical appearance of various grinded foods at room temperature

Fresh Food	Water	Total Carbohydrate	Physical appearance of material after grinded
Milk powder (sugar free)	3.8	34.2	Come as separating fine powder (as reference)
Northeastern rice	10.6	72.8	Fine separating powder
Wheat	10.5-13.4	75	Fine separating powder
Green bean	12.7	57	Fine separating powder
Large soybean	13	21.5	Fine separating powder
Sword bean	14.7	38.7	Fine separating powder
Asparagi Radix	15-18.3	37	Crushable but stickly and wet, bond together
Lycii Fructus	77.3 (9.3)*	15.3 (61.3)*	Crushable but stickly and wet, bond together
Honey	18.9	79.5	Couldn't be crushed; thick and viscuss fluid
Chinese ham	23.3	0	broken into smaller pieces but stuck together.

•Figures in parenthesis are data obtained at dried status

Effect of dehydration on size, shape and appearance of crushed food

The grinding problem of ham, Asparagi Radix, Lycii Fructus and honey, which all have a higher water content, could probably be overcome by dehydration at higher temperature. To achieve this, they were baked in an airated hot oven at a temperature indicated for different time before they were grinded. **Table 3** shows that except Chinese ham, all other three substances were unsccessful to form fine powder by grinding unless baking temperature exceeded 38ºC or higher **(Figure 1B &C)**. Although baking at a temperature higher than 50ºC could shorten the dehydration time for a food, there was a trade off on physical property and probable chemical structure of the crushed materials.

Table 3. Crushability of various foods and herbs after dehydration

Food	Baking Temperature (ºC)					
	20º for 4.5 day	38º for 56 hr	50º for 48 hr	60º for 18 hr	80º for 12 hr	105º for 1 hr
Asparagi Radix	not effective	sticky crushable mass	+	++	+++	+++
Lycii Fructus	not effective	coarse & sticky	coarse & sticky	coarse & sticky	++	+++
Honey	not effective	not effective	not effective	not effective	not effective	not effective
Chinese ham	not effective	not effective	not effective	+	++	+++

Remarks: + = native and grindable; ++ = grindable but slightly coking; +++ = grindable but brittle & coking

Figure 1. Appearance of some pulverized materials followed by baking at 38ºC for a day. *Plate* ***A:*** *ripe mango fruit;* ***B:*** *crushed Asparagi Radix;* ***C:*** *crushed Lycii Fructus*

Physcial appearance of Asparagi Radix after baked

Figure 2A – 2C show that whenever Asparagi Radix was baked, its color could be changed to dark brown. The higher the baking temperature, the more intensive it was. Physical properties of the baked radix were also changed; radix baked at 80ºC was hard and brittle than those baked at lower termperature. The pulverized powders of the radix also confirmed that the materials had been turned brown or dark bown colour after baked at 80ºC for two days **(Figure 2F – 2G)**, indicating coking was taken place. It was found that an ideal baking temperature should not exceed 50ºC if native and non-cohesive fine powders of Asparagi Radix were wanted **(Figure 2J – 2L)**.

Physical appearance of Lycii Fructus after baked

When the same conditions were applied to Lycii Fructus, the physical appearance of this herbs were not exactly the same. It was noted that Lycii Fructus was more resistant to higher baking termperature **(Figure 3A – 3C)**. Although the fruits were gradually hardened, they were still soft inside when compressed. Their colour was also remained little change in comparison to that of Asparagi Radix.

Contrary to Asparagi Radix, Lycii Fructus required a higher baking temperature in order to crush the fruit. Baking at 38ºC for whatever time had no effect on its crushability. The crushed fruit simply stuck together to form a soft mass **(Figure 3D)**. The fruit would only form Hard granules or pieces of the fruit would only be observed when it was baked at temperature above 50ºC for enough time **(Figure 3E & 3F)**. After baked at 80ºC for a two days, the fruit was grindable to form fine, hard and brittle powders of various sizes **(Figure 3F – 3I)**. At a baking temperature lower than 80ºC, although native and fine powders of Lycii Fructus could be formed in the pulverizer, crumping and sticky masses immediately took place. After two days's storage at room environment, most powders bound together to form soft mass **(Figure 3K – 3L)** and the original physical properties of the powders disappeared.

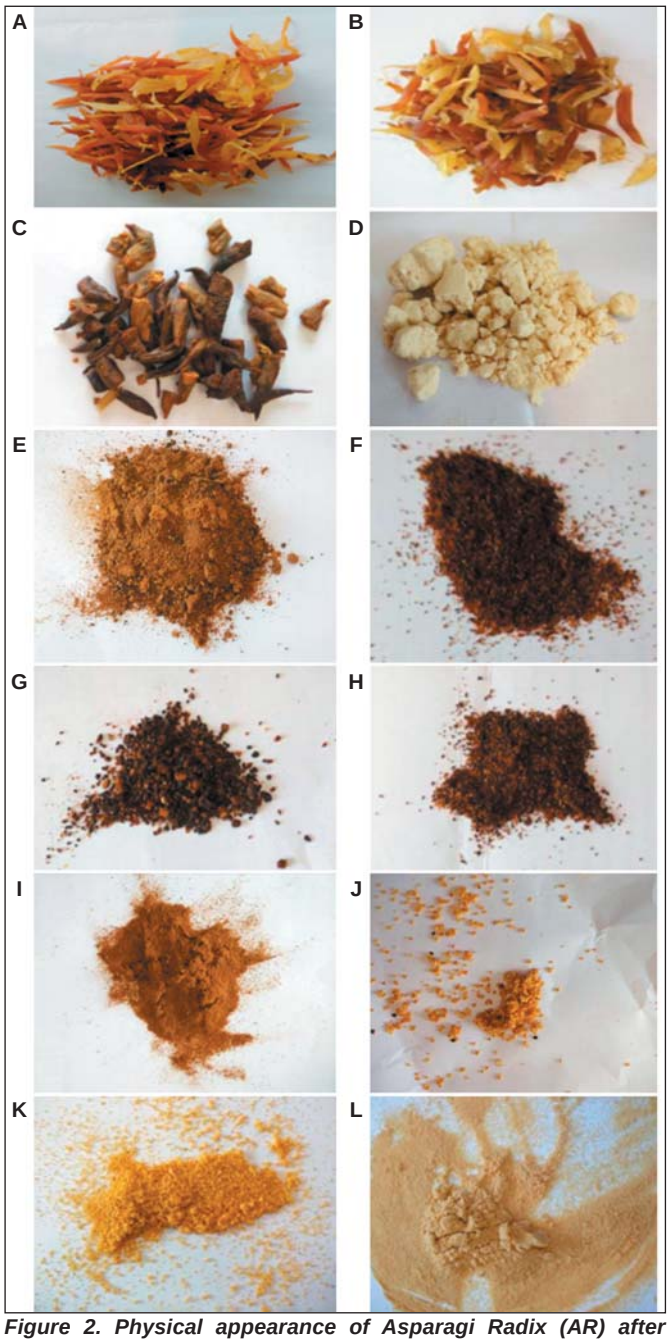

Figure 2. Physical appearance of Asparagi Radix (AR) after baked at various temperature and time. *Plate* ***A:*** *commercially available herb of Asparagi Radix (reference);* ***B:*** *after baked at 38ºC for 48 hr;* ***C:*** *after baked at 80ºC for 48 hr;* ***D:*** *intact AR baked at 38ºC for 24 hr followed by crushing;* ***E:*** *baked at 50ºC for 48 hr followed by crush;* ***F:*** *baked at 80ºC for 48 hr followed by crushing;* ***G:*** *large size particles retained on mesh #20 after C was pulverized;* ***H:*** *medium size particles retained on mesh #50 after C was pulverized;* ***I:*** *fine particles passed through mesh #80 after C was pulverized;* ***J:*** *large size particles retained on mesh #20 after B was crushed and baked at 50ºC for another 48 hr;* ***K:*** *medium size particles retained on mesh #80 after B was crushed and baked at 50ºC for another 48 hr;* ***L:*** *fine powder passed through mesh #80 after B was crushed and baked at 50ºC for another 48 hr.*

Moisture evaporation of herbs during baking

The differences of physical appearance of Asparagi Radix (AR) and Lycii Fructus (LF) might be a reflection of differences in moisture lost during baking. Hence, a series of quantitative measurement on moisture content was carried out as described earlier to determine moisture evaporation during baking. **Figure 4** shows that the patern of moisture lost of these two herbs was indeed different. Generally speaking, AR was more sensitive and quicker response to baking temperature; its moisture evaporated fast while LF was not. The later retained most of its moisture even after a day of baking at 80ºC. Lost of water only accelerated after two days of baking at higher temperature while at lower baking temperature, i.e. less than 50ºC had almost no effect on LF.

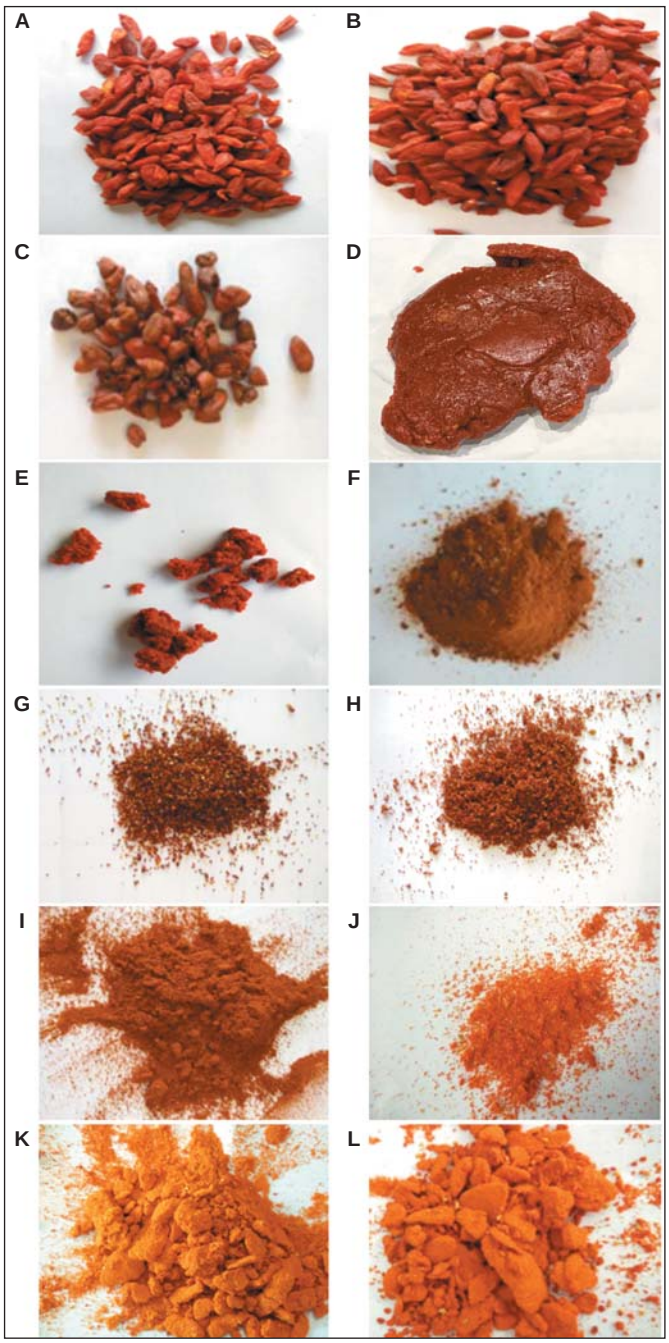

Figure 3. Physical appearance of Lycii Fructus (LF) after baked at various temperature and time. *Plate* ***A:*** *commercially available herb of Lycii Fructus (reference);* ***B:*** *after baked at 38ºC for 48 hr;* ***C:*** *after baked at 80ºC for 48 hr;* ***D:*** *intact LF baked at 38ºC for 24 hr followed by crushing;* ***E:*** *baked at 50ºC for 48 hr followed by crush;* ***F:*** *baked at 80ºC for 48 hr followed by crushing;* ***G:*** *large size particles retained on mesh #20 after C was pulverized;* ***H:*** *medium size particles retained on mesh #50 after C was pulverized;* ***I:*** *fine particles passed through mesh #80 after C was pulverized;* ***J:*** *large size particles retained on mesh #20 after B was crushed and baked at 50ºC for another 48 hr;* ***K:*** *medium size particles of LF retained on mesh #80 right after LF was crushed and baked at 50ºC for another 48 hr;* ***L:*** *crumped powder on mesh #80 an hour later of K.*

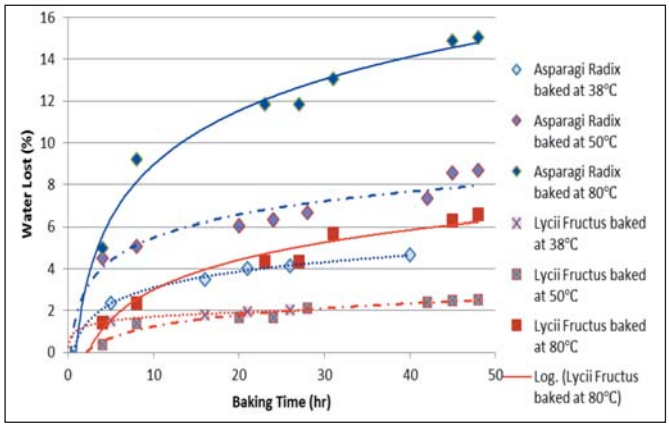

Figure 4. Effect of baking on moisture lost from Asparagi Radix and Lycii Fructus.

Effect of freezing on the grindability of Lycii Fructus

Because at ambient temperature LF could not give separating fine powder **(Figure 5A)** while at temperature above 80ºC it produced brittle and hard granules **(Figure 3F)**, the method of freezing and comminution was applied. When the fruit of *Lycium barbarum* was kept at -20ºC degree for 48 hours prior to grinding **(Figure 5B)**, fine pulverized powder were produced **(Figure 5C)** similar to that for mango or Asparagi Radix prepared at the conventional drying methods. Nevertheless, these native and fine powders of LR still had tendency to bind together unless they were kept at frozen temperature.

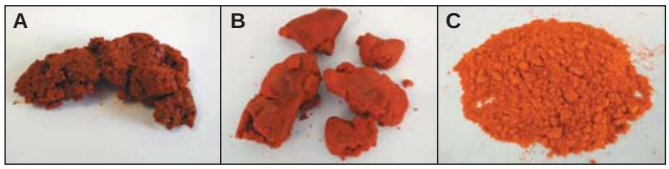

Figure 5. Physical appearance of Crushed Lycii Fructus prepared by freezed drying. A: *crushed Lycii Fructus at room temperature;* ***B:*** *crushed fructus freezed at -20ºC for 48 hr;* ***C:*** *prulverized powder of B.*

Particle size of the powders prepared at different baking temperature

When powders of these two herbs prepared from different baking temperature were subjected to particle size analysis, it was found that uniformly fine powders less than 180 µm in diameter were dominant in Asparagi Radix at all range of baking temperature while Lycii Fructus were not. The later could only be produced at 80ºC. Indead, baking temperature below 50ºC was more favourable for preparation of fine powder for the former **(Figure 6)**. Although the powder of Lycii Fructus prepared from freeze drying was not analysed but it gave an impression that it was a fine powder not larger than 250 µm subjected to that they were kept properly at frozen temperature or deployed of any moisture.

Causes of stickiness in Lycii Fructus and Asparagi Radix

In order to find out the cause of stickiness in the crushed LF and AR at room temperature, some searches in literatures on their carbohydrate components were conducted. **Table 4** lists some of the reported saccharide found in the fruit of LF and AR in comparison to a few other representative foods. Although charring may be related to the presence of sucrose, the sticky property of both LF and AR does not seem to do with any saccharide except that presence of wax or glutinous materials in these two herbs might be the cause on top of their high moisture content.

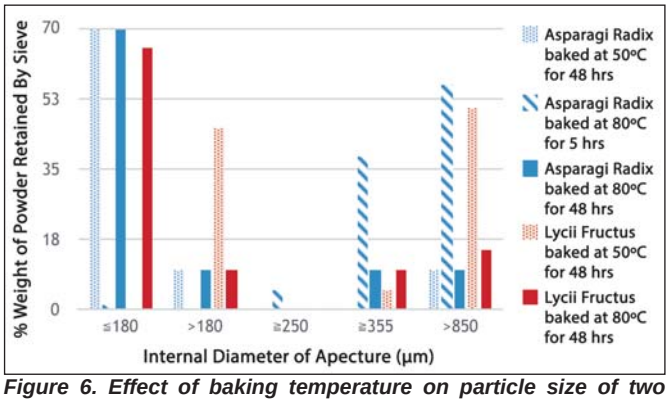

Figure 6. Effect of baking temperature on particle size of two pulverized herbal substances. *Herbal materials, i.e. Asparagi Radix (blue color) or Lycii Fructus (red color) was baked at a particular temperature as indicated for a specific time before it was crushed by a pulverizer. The particules produced were passed through a series of sieve to determine percentage of quantitiy of the particles retained on the screen.*

DISCUSSION

Powder properties and behavior are critical to efficient and successful quality control and manufacturing. Physical reduction of a substance to a desirable size as well as controlling the water or moisture content of the material are important keys to this process. Many raw materials because of the presence of water, sugar or other sticky ingredients, have been reported to cause problems during crushing step of quality control or manufacturing. The amount of water present may profoundly influence properties of the raw materials, granuules or powder subsequently prepared at downsteam processing, and even quality control of the final products.[15-18] Hence, removal of excess water and reducing the size of a material is necessary. Although the Chinese Pharmacopoeia recommends that drying methods for herbal drug or food could be achieved by drying the substnaces in the sun or in the shade,[13] it is unsuitable in industrial manusfactureing. Drying at a higher temperature in an oven is more preferrable as it could be environmentally controlled to avoid contamination and the drying process as well as duration are controllable.

Table 4. Type of carbohydrates present in food or herb

Name of food or herb	Documented report on presence or content (w/w) of saccharide											Wax or Glutinous
	Total CHO	Ara	Fru	Gal	Glc	Lac	Man	Rha	Suc	Starch	Xyl	
Mango (ripe)	14.8	-	+	+	3	-	-	-	14-16	-	-	-
Lycii Fructus	18.3 (3.4)	+	-	+	+	-	-	+	19	-	+	++
Asparagi Radix	37	-	-	+	+	-	+	+	-	+	+	+
Ophiopogonis Radix	ND	-	-	+	+	-	-	-	-	+	-	-
Polygonati Odorati Rhizoma	ND	-	-	-	-	-	-	-	-	25-30	-	+
Honey	80.95	-	-	-	+	-	-	-	76-76	-	-	-

CHO: carbohydrate; **Ara:** arabinose; **Fru:** fructose; **Gal:** galactose; **Glc:** glucose; **Lac:** lactose; **Man:** mannose; **Rha:** rhamnose; **Suc:** sucrose; **Xyl:** xylose; **+:** presence; **- :** absence; **ND:** not described

Oven drying of a herb or food should be carried out carefully as sugar present in the raw materials may be charred at high temperature range. Hence, effect and duration of drying temperature for each medicinal substance have to be determined and optimized.[19-22] As shown in our study, even the water content was almost the same for two different substances, it didn't mean that the same condition of drying could be applied. If a condition were designed merely based on one parameter, effective drying of a substance may not be achieved. On the other hand, if a higher baking temperature were used, some native properties of the raw materials would be destroyed. For foods or medicinal materials that contain high carbohydrate or heat sensitive ingredients such as mucilages, wax, sucrose etc, drying at high temperature should be discouraged; otherwise, the drying treatment would not only promote coking of the material, but also lock the water moisture inside, resulting in difficulty for comminution at subsequent production stage. An ideal condition could only be established for each material after througoutly and systematically explored. We discovered that fine particles could be prepared from wet materials at high temperature (80ºC) only when its moisture content comes down to less than 15% (W/W). This observation confirms Crouter & Briens' study on the flowability of pharmaceutical excipients.[23]

CONCLUSION

In summary, we have demonstrated that high water content of some foods or herbs although plays a very important factor on crushing, it is not the prime cause of difficulty during pulverizing a substance. Presence of other substantces, such as wax or mucilage materials could block the removal of moisture from foods or herbs and therefore, they also play a determining factor to some extend in crushing as revealed in the case of LF and AR. Although both AR and Polygonati Odorati Rhizoma contain glutinous matters, the later in general is dried, probably less than 15% of water content when it is purchased from market while the former doesn't. The water content of commercially available AR, in general is quite vary.[24] This explain some difficulties people may encounter when they pulverize the former but not the later.

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HKUSPACE
香港大學專業進修學院
HKU School of Professional and Continuing Education

Pharmaceutical Studies

MSc Clinical Pharmacy*

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

Programme Features:

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

Entry Requirements:

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

University of Sunderland

Application Code: 1650-HS073A

Application Deadline: 30 June 2018

Enquiries

3762 0096

sheri.ip@hkuspace.hku.hk

BSc (Hons) Pharmaceutical Science*

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

Programme Features:

- a 24-month part-time undergraduate programme
- it covers the area of pharmaceutical science including pharmacology, pharmaceutical design and manufacture, biopharmaceutical, methods of analysis, quality assurance and delivery of pharmaceutical substances

Entry Requirements:

Applicants should hold either:

- Associate of Health Science (Biomedical Sciences)/ Advanced Diploma in Pharmaceutical Science (HKU SPACE); or
- Higher Diploma in Medical and Health Products Management (HPSHCC); or
- Higher Diploma in Pharmaceutical Technology (Western Medicine)/ Dispensing Studies/ Pharmaceutical Science/ Hospital Dispensing Studies (HKIVE); or
- Higher Diploma in Pharmaceutical Dispensing (CBCC)

UNIVERSITY OF WOLVERHAMPTON

Application Code: 1650-HS072A

Application Deadline: 30 June 2018

Enquiries

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sheri.ip@hkuspace.hku.hk

Certificate in Drug Safety and Pharmacovigilance

The programme provides students with a foundation in drug safety and pharmacovigilance principles so as to enable them to be competent in the field. Staff who are working in pharmaceutical production, import/export of pharmaceuticals, retailing and wholesaling of pharmaceuticals, procurement and supply of pharmaceutical products, pharmaceutical regulatory affairs department, risk communication for the drug safety and/or pharmaceutical education can apply.

Entry Requirements:

Applicants shall have attained an Ordinary Certificate in a related discipline; HKDSE Level 2 or above in five subjects including English Language and one of the following science subjects: Biology, Chemistry, Physics, Combined Science, or Integrated Science; HKCEE Level 2 / Grade E or above in English Language and FOUR passes in other subjects including one of the following science subjects: Biology, Chemistry, Physics, or Science and Technology; equivalent qualifications. Applicants who hold other qualifications but are aged 21 or above and have relevant work experience will be considered on an individual basis.

資歷架構 Qualifications Framework

Level 3
Registration Number:16/000894/L3
Valid From:14/09/2016-on-going

Application Code: 1670-HS143A
Course Code: HS143A

Application Deadline: 11 January 2019 (Friday)

Enquiries:

3762 0097

danny.mak@hkuspace.hku.hk

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

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SHPHK – Kicking off 2018

Reported by **Vienna Leung**
Pharmacist of The Society of Hospital Pharmacists of Hong Kong

Welcome to the Year of the Dog!
It is time to start planning your professional development for the year. The Society of Hospital Pharmacists of Hong Kong (SHPHK) will continue to provide different learning opportunities to our members in 2018!

Haematology and Oncology Symposium

To kick-start the 2018 SHPHK educational course series, a symposium on Haematology and Oncology was organised on 26th January 2018 by the Society. Over 80 pharmacists of different sectors attended the symposium, and there were lots of fruitful discussions between the speakers and the audience.

Guest speakers of the Haematology and Oncology Symposium and the President of SHPHK. From left: Dr. Sze Chun-kin Henry, Ms. Ma Yat-man Vivian, Dr. Liu Sung-yu Herman and Mr. Chui Chun-ming William.

There are more continuing professional development programmes coming soon! If you would like to receive our news and join all the upcoming seminars and activities organised by the Society for free, it is still not too late to join us as member now!

Health promotion and public education

SHPHK not only focuses on the development of hospital pharmacy practice, but also actively advocates health promotion via the delivery of reliable health and drug information to the general public through different platforms. For example, in February, in view of the severe outbreak of influenza this winter, and the spread of misleading rumours regarding the efficacy and manufacturing process of flu vaccines throughout the community, the Society had published an educational poster in the Headline Daily and Sky Post to ease public concern over the safety of flu vaccination. The poster also gives answers to some of the common questions about the flu vaccines.

An educational advertorial for flu vaccination published in the Headline Daily and Sky Post on 14th February 2018.

Mark your calendar: The 31st SHPHK Annual General Meeting

This year, the Annual General Meeting (AGM) of the Society will be held on 6th April 2018 (Friday) at The Cityview, Yau Ma Tei. AGM is one of the most important events of the year. During the AGM, general committee members for 2018 will be elected. Members are strongly encouraged to attend the AGM to show support for the nominees of the committee. Furthermore, to celebrate the 31st anniversary of SHPHK, there will be a seminar on pain management prior to the start of the AGM, with a special focus on the breakthrough pain in cancer patients.

We look forward to sharing with you the achievements of the Society in the past year at the AGM!

See you all at the SHPHK AGM 2018!

You are most welcome to follow the Society's Facebook page (@SHPHK) to know more about the Society's development and activities. You may also visit the Drug Education Resources (DERC) Website: www.derc.org.hk to learn more about the latest development of drugs in Hong Kong. To join us as member or to renew your membership, please visit the Society's website: www.shphk.org.hk.

2018 First Quarter Updates of PSHK

Reported by **Ms. Scarlett Pong, BBS, JP**
President, The Pharmaceutical Society of Hong Kong

Happy New Year of the Dog! We are delighted to be the new PSHK cabinet working for our members this year. Thank you to all members for supporting us, voting us in and giving us a chance to work for you.

First GC Meeting in January

Our visions

We have two main visions for the development of the pharmacy sector: to upgrade local pharmaceutical practice to the international standard; and to maintain the quality and professional autonomy of our pharmacists. To achieve these visions, we aim to expand the roles of pharmacists by various initiatives and collaborations, as well as dealing with the current manpower surplus issue. We need to take substantial steps forward and make up for the lost ground, and we have already started the process these couple of months.

Pharmacists are ideally positioned to serve the Hong Kong public on healthcare. We are the missing jigsaw and possibly the solution to the manpower shortage of nurses and doctors. Pharmacists have the knowledge and skills to provide different levels of healthcare, yet there is insufficient recognition by the public, other health professionals and the Government. We hope to rectify the situation and by actively promoting the pharmacy profession to the public; by collaborating with different health professionals; and by continuously advocating our policy proposals. Not only do we do our job on all these, but we should also make constant exposure through various media platforms, so that the great work of pharmacists is noticed and recognized.

Our targets

With the feedback from our members and working partners, we realized different concerns that our sector is facing. There are some areas we will actively and continuously fight for in this year, we must:

- strive for the implementation of **Public Private Partnership** (PPP) for pharmacy services;
- strive for the inclusion of Pharmacists as service providers in the **Health Care Voucher** (HCV) scheme;
- strive for the access to the **Electronic Health Record Sharing System** (eHRSS) by community pharmacists;
- engage pharmacists in the **District Health Centre** service model as part of the **primary healthcare** development of the Government;
- engage community pharmacists in the medication management for **residential care services** and **home care services**;
- engage pharmacists in more **public education** and **disease prevention** programmes;
- address the **manpower surplus** issue by advocating the adjustment of university intake and overseas registration;
- address the **misuse of "藥", "葯", "drug", "medicine"** as titles at retail setting.

There is great potential for the pharmacy profession to be fully utilized. Regarding the above matters, we have met with various parties in the past few months. You can follow on our updates by visiting our website (www.pshk.hk) or Facebook page (@pshongkong).

Meeting with Professor Sophia Chan, Secretary for Food and Health

We will continue to explore opportunities for pharmaceutical development and seize new opportunities for young pharmacists and enhance the recognition of our profession in all sectors. After all, we must work together to build a brighter future for Pharmacy in all sectors. We should bear in mind that the pharmacy profession is only as strong as our weakest link. So, let's put aside our disagreements and unite to make the pharmacy profession more impactful in all sectors, and more invaluable to the Hong Kong public. With concerted efforts and collaboration, we can all make a change for the better.

NEW INDICATION

Giotrif®
(Boehringer Ingelheim)

Prepared and edited by Ivy Chan

Active Ingredient:
Afatinib (as dimaleate).

Presentation:
One film-coated tablet contains 20 mg afatinib (as dimaleate).

Pharmacological Properties:
Afatinib is a potent and selective, irreversible ErbB Family Blocker. Afatinib covalently binds to and irreversibly blocks signalling from all homo- and heterodimers formed by the ErbB family members EGFR (ErbB1), HER2 (ErbB2), ErbB3 and ErbB4.

Indications:
• Epidermal Growth Factor Receptor (EGFR) TKI-naïve adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutation(s);
• locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum-based chemotherapy.

Dosage & Administration:
EGFR mutation status should be established prior to initiation of therapy.

The recommended dose is 40 mg once daily.
This medicinal product should be taken without food. Food should not be consumed for at least 3 hours before and at least 1 hour after taking this medicinal product.
Treatment should be continued until disease progression or until no longer tolerated by the patient (**see Table 1**).
Dose escalation
A dose escalation to a maximum of 50 mg/day may be considered in patients who tolerate a 40 mg/day starting dose (i.e. absence of diarrhoea, skin rash, stomatitis, and other adverse reactions with CTCAE Grade>1) in the first cycle of treatment (21days for EGFR mutation positive NSCLC and 28days for squamous NSCLC).The dose should not be escalated in any patients with a prior dose reduction. The maximum daily dose is 50mg.
Dose adjustment for adverse reactions
Symptomatic adverse reactions (e.g. severe/persistent diarrhoea or skin related adverse reactions) may be successfully managed by treatment interruption and dose reductions or treatment discontinuation as outlined in **Table1**.

Table 1: Dose adjustment information for adverse reactions

CTCAE Adverse reactions	Recommended dosing	
Grade1 or Grade2	No interruption	No dose adjustment
Grade2 (prolonged or intolerable) or Grade>3	Interrupt until Grade0/1	Resume with dose reduction reduction by 10mg decrements

Forensic Classification:
P1S1S3

Hong Kong Pharmaceutical Journal: For Detailed Instructions for Authors

INTRODUCTION

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

Submission of Manuscript

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

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

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

Suggested Referees

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

Editorial Authority

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

Preparation of manuscript

The manuscript is required to be written in English, with numbered pages, single-spaced, using Arial 9 point font, and in a suitable word-processing format. Each page should have adequate margins (4 cm) and liberal spaces at top and bottom of the manuscript. All textual elements should begin flush left, with the second paragraphs onwards indent, and should use the wrap-around end-of-line feature, i.e. no returns at the end of each line. Place two returns after every element such as title, headings, paragraphs, figure and table call-outs. Most formatting codes will be removed or replaced on processing your article. Please do not use options such as automatic word breaking, justified layout, double columns or automatic paragraph numbering (especially for numbered references). However do use bold face, italic, subscripts, superscripts etc. The Editors reserve the right to adjust style to certain standards of uniformity. If authors are unfamiliar with HKPJ, they should consult a recent copy (or the free online sample copy available from www.HKPS.com/HKPJ) to see the conventions currently followed for guidance in preparing submissions.

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

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

An **Author's background box** at the end of each article is mandatory to include the author's job title and the affiliated institutle or organization. Full details of telephone, fax numbers and e-mail address should also be indicated for the corresponding authors. No academic or professional membership title is allowed.

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

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

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

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

EXPERIMENTAL: Subsections on the Experimental Procedures should be italicized and inserted as part of the first line of the text to which they apply. HKPJ encourages an extensive use of abbreviations (these are listed at the back of the Instructions to Authors, or the reader is referred to other sources). The Experimental should begin with a subsection entitled General Experimental Procedures. This subsection will typically contain brief details of instruments used, and identification of sources of specialized chemicals, biochemicals and molecular biology kits. The next subsection describes the source(s) and documentation of biological materials used, whether in reference to whole plants or parts there from, crude drugs, or any other plant material from which identifiable chemical substances are obtained for the first time. Documentation must also include a reference to voucher specimen(s) and voucher number(s) of the compounds, plants or other material examined. If available, authors should quote the name and address of the authority who identified each sample investigated. Specimens should preferentially be deposited in a major regional herbarium where the collection is maintained by state or private institution and which permits loan of such materials. With other microorganisms, the culture collection from which they were either accessed and/or deposited should be included, together with identification of the strain designation code. The Experimental Procedures employed should be concise but sufficiently detailed that a qualified researcher will be able to repeat the studies undertaken, and these should emphasize either truly new procedures or essential modifications of existing procedures. Experimental details normally omitted include: (I) method of preparation of common chemical and biochemical derivatives, (2) excessive details of separation of compounds, proteins and enzymes, e.g. preparation of columns, TLC plates, column and fraction size. Compound Characterization: Physical and spectroscopic data for new compounds must be comprehensive, and follow the order shown below: compound name (and assigned number in text); physical state of compound (e.g. oil, crystal, liquid, etc.), melting and/or boiling point; optical rotation and/or circular dichroism measurements, if optically active; UV; JR, lH NMR; 13C NMR; MS. For all new compounds, either high-resolution mass spectral or elemental analysis data is required. See later section for method of data presentation.

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

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

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

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

(2) Mabry T, Markham KR, Thomas MB. (1970). *The Systematic Identification of Flavonoids.* 2nd Ed, pp. 79-105. Springer Verlag, New York.

(3) Harborne JB. (1999). Plant chemical ecology. In: Barton D, Nakanishi K, Meth-Cohn 0, (Eds.), *Comprehensive Natural Products Chemistry,* Vol. 8. pp. 137-196. Pergamon, Oxford.

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

Illustrations should be drawn on separate pages and prepared with good contrast (black on a white background). Lettering in tables, figures, etc: lettering in formulae, figure axes etc. must be large enough to be legible after reduction. Lettering should be drawn in 6-7pt Helvetica (Arial) font to ensure optimum visibility. Chemical formulae must be made absolutely clear; printers are not chemists and much delay is caused by poor drawing. Aromatic rings must be drawn with alternate double bonds and conformation of single bonds shown by thickened or dashed (III) lines according to convention. Formulae should be numbered consecutively in Arabic numerals. If graphics are created using ChemDraw or ISISDraw the preferred settings are: font 10 pt Helvetica (Arial), chain angle 120° bond spacing 18% of length, fixed (bond) length 14.4 pt (0.508 cm), bold width (bond thickness) 2.0 pt (0.071 cm), line width 0.6 pt (0.021 cm), margin width 1.6 pt (0.056 cm), and hash spacing 2.5 pt (0.088 cm). The overall size should be not more than 95mm (single column) or 194mm (double column) by 285 mm.

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

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

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

Abbreviations
About, approximately: ca.
Anhydrous: dry (not anhyd.)
Aqueous: aq.
Circular dichroism: CD
Concentrated (or mineral acids): conc.
Concentrations: ppm (or ppb), μM, mM, M, %, mol
Dry weight: dry wt; fresh weight: fr. wt
Electricity: V, mA, eV
Force due to gravity (centrifugation): g; rpm (revolutions min^{-1})
Gas chromatography: GC
Gas chromatography-mass spectrometry: GC-MS Trimethylsilyl derivative: TMSi (TMS cannot be used as this refers to the internal standard tetramethylsilane used in ^{1}H NMR)
High performance liquid chromatography: HPLC
Infrared spectrophotometry: IR
Length: nm, μm, mm, cm, m
Literature: lit.
Mass spectrometry: m/z $[M]^{+}$ (molecular ion, parent ion)
Melting points: uncorr. (uncorrected)
Molecular mass: Da (daltons), kDa
Molecular weight: M_r
Nuclear magnetic resonance: ^{1}H NMR, ^{13}C NMR, Hz, δ
Numbers: e.g. 1, 10, 100, 1000, 10000; per or $^{-1}$
Optical rotatory dispersion: ORD
Paper chromatography: PC
Precipitate: ppt.
Preparative thin-layer chromatography: prep. TLC
Radioactivity: dpm (disintegrations per min), Ci (Curie), sp. act (specific activity), Bq (1 becquerel = 1 nuclear transformation sec^{-1})
Repetitive manipulations: once, twice, x3, x4, etc.
RR_t (relative retention time), R_1 (Kovat's retention index), ECL (equivalent chain length- term frequently used in fatty acid work)
Saturated: satd.
Solution: soln.
Solvent mixtures including chromatographic solvents: abbreviate as follows n-BuOH-HOAc-H_2O (4:1:5)
Statistics: LSD (least significant difference), s.d. (standard deviation), s.e. (standard error)
Temperature: (with centigrade), mp, mps, mmp, bp
Temperature: temp.
Thin-layer chromatography: TLC, R_f
Time: s, min, h, day, week, month, year
Ultraviolet spectrophotometry: UV, A (absorbance, not aD-optical density)
Volume: 1, (litre), μ1, ml
Weight: wt, pg, ng, μg, mg, g, kg

Inorganics, e.g. $AlCl_3$ (aluminum chloride), BF_3 (boron trifluoride), Cl., CO_3, H_2, HCl, $HClO_4$ (perchloric acid), HNO_3. H_2O, H_2O_2, H_2SO_4, H_3B0_3 (boric acid), He, $KHCO_3$ (potassium bicarbonate), $KMn0_4$ (potassium permanganate;), KOH, K-Pi buffer (potassium phosphate buffer), $LiAlH_4$ (lithium aluminium hydride), Mg^{2+}, $MgCl_2$, N_2, NH_3, $(NH_4)_2S0_4$, Na^{+}, $NaBH_4$ (sodium borohydride), NaCl, $NaI0_4$ (sodium periodate), NaOH, Na_2S0_3 (sodium sulphite), Na_2S0_4 (sodium sulphate), $Na_2S_20_3$ (sodium thiosulphate), 0_3, PPi (inorganic phosphate), SO_4^{2-}., Tris (buffer).

Organics, e.g. Ac_20 (acetic anhydride), n-BuOH (butanol), C_6H_6 (benzene), CCl_4 (carbon tetrachloride), CH_2Cl_2 (methylene chloride), $CHCl_3$ (chloroform), CH_2N_2 (diazo-methane), CM (carboxymethyl), DEAE (diethylaminoethyl), DMF (dimethylformamide), DMSO (dimethyl sulphoxide), EDTA (ethylene-diaminetetra-acetic acid), Et_20 (diethyl ether), EtOAc (ethyl acetate), EtOH (ethanol), $HC0_2H$ (formic acid), HOAc (acetic acid), iso-PrOH (iso-propanol), Me_2CO (acetone), MeCOEt (methyl ethyl ketone), MeOH (methanol), NaOAc (sodium acetate), NaOMe (sodium methoxide), petrol (not light-petroleum or petroleum ether), PhOH (phenol), PrOH (propanol), PVP (polyvinylpyrrolidone), TCA (trichloroacetic acid), TFA (trifluoroacetic acid), THF (tetrahydrofuran). ^{1}H NMR solvents and standards: $CDCl_3$ (deutero-chloroform), D_2O, DMSO-d_6 [deuterodimethylsulphoxide not $(CD_3)_2S0$], pyridine-d_5 (deuteropyridine), TMS (tetramethylsilane).

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

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