Hospital Authority

Toxicology Reference Laboratory

Annual Report 2006

醫院管理局

HOSPITAL AUTHORITY

7th Floor, Block P, Princess Margaret Hospital,

Kwai Chung, Hong Kong.

Tel: 2990 1941; Fax: 2990 1942;

http://trl.home (via HA intranet only)

HOSPITAL AUTHORITY TOXICOLOGY REFERENCE LABORATORY

醫院管理局 HOSPITAL AUTHORITY

31 December 2006

INSIDE THIS REPORT:

FUNCTION & ESTABLISHMENT

The Hospital Authority (HA) Toxicology Reference Laboratory (TRL) is a centrally established facility, located in the Princess Margaret Hospital. The TRL provides level III toxicology service to all HA hospitals. Level III services include herbal product poisoning, new and uncommon substance of abuse, other clinically important toxins and confirmatory toxicology testing.

Staff of the TRL:

Medical Staff	
Consultant Chemical Pathologist & Director (Honorary)	Dr. Albert Chan
Consultant Chemical Pathologist & Deputy Director	Dr. Tony Mak
Resident Specialist	Dr. WT Poon
Resident Specialist (Honorary)	Dr. Liz Yuen
Resident	Dr. Doris Ching
Resident (Honorary)	Dr. Carol Siu
Scientific Staff	
Scientific Director (Honorary)	Mr. CK Lai
Scientific Officer (Medical)	Ms. Vanessa Lo
Scientific Officer (Medical)	Ms. SW Ng

Princess Margaret Hospital

FUNCTION & ESTABLISHMENT (continue)

The TRL, together with the other HA cluster toxicology laboratories and urgent laboratories, function as a team to provide a full spectrum of toxicology laboratory services.

Level I service includes urgent quantitative analysis of some important toxins (e.g. paracetamol and salicylate). It is offered by the urgent laboratory of each hospital.

Level II service involves broad spectrum toxicology screening service and common drug of abuse service. It is provided by the cluster toxicology laboratory. Cluster toxicology laboratory is located in the largest chemical pathology laboratory within seven clusters, which are Hong Kong West (HKWC), Hong Kong East (HKEC), Kowloon West (KWC), Kowloon East (KEC), Kowloon Central (KCC), New Territories West (NTWC) and New Territories East (NTEC). The laboratories and corresponding representatives are listed below.

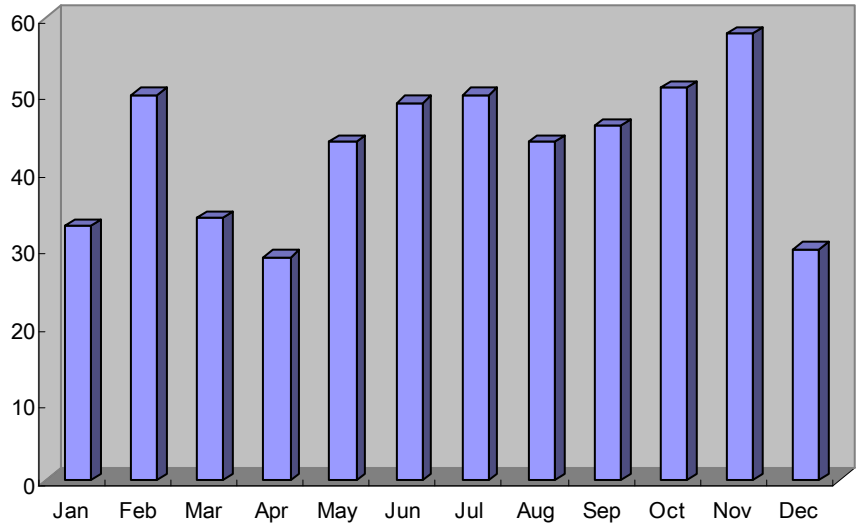
Cluster	Hospital	Representative (s)	
HKWC	QMH	Dr. Sidney Tam	Mr. Simon TS Siu
HKEC	PYNEH	Mr. YC Lo	-
KWC	PMH	Dr. Albert YW Chan	Mr. CK Lai
KEC	UCH	Dr. Ivy SC Luk	-
KCC	QEH	Dr. Anthony CC Shek	Ms. Heidi YP Iu
NTWC	TMH	Ms. Judy PS Lai	-
NTEC	PWH	Dr. Michael HM Chan	Mr. Eric LK Law

SPECTRUM OF REFERRAL

This year, the Laboratory handled 518 referrals and 13 consultations. One referral refers to one case, which might cover one or more than one of the following task(s):

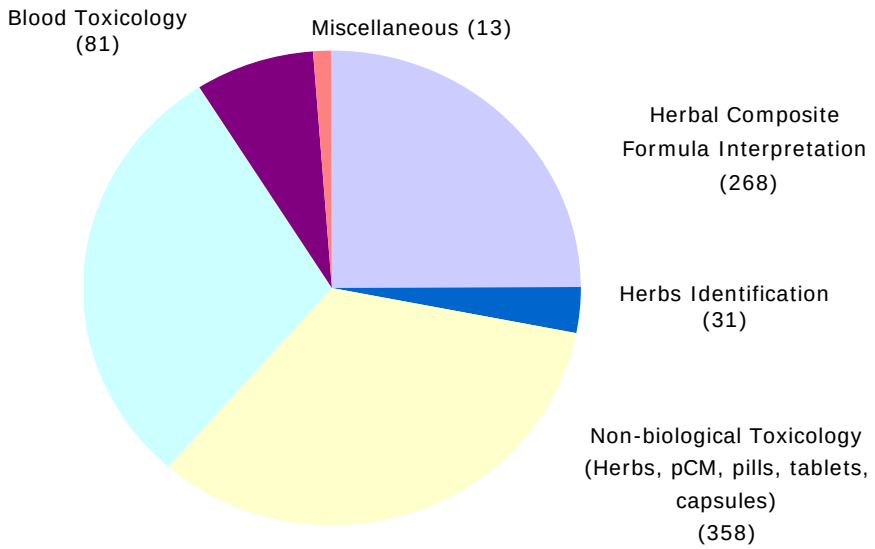
1. Herbal composite formula interpretation
2. Herbs identification
3. Non-biological specimens (including herbs, proprietary Chinese medicine (pCM), pills, tablets and capsules) chemical analysis
4. Urine toxicology chemical analysis
5. Blood toxicology chemical analysis
6. Other biological specimens chemical analysis (such as gastric lavage)
7. Miscellaneous (such as spot test and immunoassay)

Monthly Distribution of Referral (Cases)



Remark: 1 referral = 1 case, 1 case might request for one or more than one of the task(s)

Breakdown of Annual Referral (No. of Analysis)



DEVELOPMENTS

Research plays a crucial role in the TRL's long term development. Summary on progress in four areas:

A spectrum of methodologies for the detection of animal thyroid tissue in slimming products, which includes:

1. Immunoassays for thyroid hormones with or without prior digestion.
2. Detecting thyroid hormones and their precursors using high performance liquid chromatography-diode array detector and/or liquid chromatography tandem mass spectrometry.
3. Microscopic morphological identification.

Liquid Chromatography Tandem Mass Spectrometry

Target screen for warfarin, warfarin metabolite and eleven superwarfarins by liquid chromatography tandem mass spectrometry.

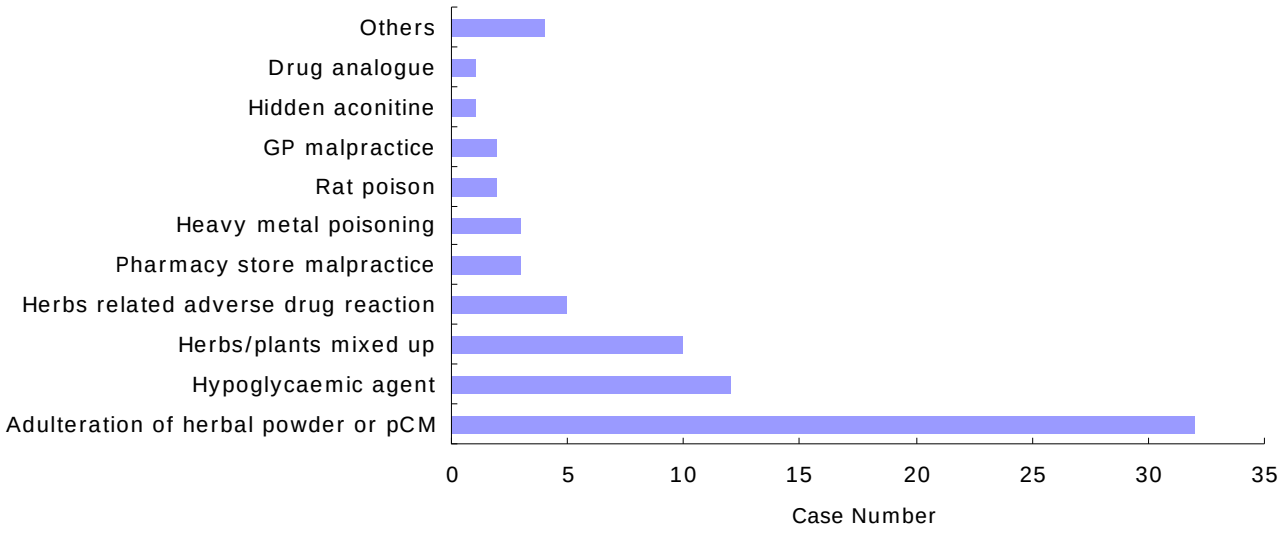
Gas chromatograph mass spectrometry analysis for cyanogenic glycoside (amygdalin) and study their content in two different types of *Prunus species* (南杏 and 北杏).

Target screen for metabolites of benzalkonium chloride in urine by liquid chromatography tandem mass spectrometry.

Gas Chromatography Mass Spectrometry

CASES REPORTED TO THE DEPARTMENT OF HEALTH, SOCIAL WELFARE DEPARTMENT AND/OR CHIEF PHARMACIST OFFICE

Among 518 cases handled, we reported 75 cases with significant public health implication to the Department of Health and Social Welfare Department. The reporting rate was 14.5%. These were the most important output of the Laboratory. The breakdown is as shown:



Adulteration of Herbal Powder or Proprietary Chinese Medicine (pCM)

輕身樂減肥膠囊
(From patient)

Among thirty two cases of adulteration, thirteen related to slimming agents, in which sibutramine, sibutramine derivatives, phenolphthalein, mazindol, fenfluramine and thyroid tissue were detected. Phenolphthalein and fenfluramine are banned drugs in Hong Kong. Another nineteen cases related to adulteration with corticosteroids and various Western medicines. Among the Western medicines identified, banned drugs including phenacetin and aminopyrine were detected in three cases and phenformin was detected in four cases. Three patients acquired the slimming products from the Internet, which is now an important source of illicit drugs.

Hypoglycaemic Agent

Ten out of twelve cases related to hypoglycaemic agent happened in the old age homes and two were of unknown cause.

Herbs / Plants Mix-Up

曼陀羅花
(From patient)

The Laboratory handled a total of nine cases. These included a poisoning case after consuming the flower of *Datura metel* (曼陀羅花) obtained in the countryside, mixing up of the flower of *Campsis radicans L.* (凌霄花) with *Datura metel L.* (洋金花), mixing up the root of *Panax notoginseng* (三七) with *Tupistra species* (開口箭), and contamination of non-poisonous rhizome of *Atractylodes lancea* (蒼朮) with tropane alkaloids.

Herbs Related Adverse Drug Reactions

There were poisoning cases after using *Strychnos nux-vomica* (馬錢子), *Xanthium sibiricum* (蒼耳子), *Dioscorea bulbifera* (黃藥子), *Phytolacca acinosa* (商陸) , as well as proprietary Chinese medicines containing aconitum alkaloids and multiple anthraquinones, strychnine and brucine, and products for vitiligo treatment.

Pharmacy Store Malpractice

Three pharmacy stores sold prescribed drug without prescription.

Heavy Metal Poisoning

There were three heavy metal poisoning cases. Lead was detected in one cream sample, mercury was founded in one skin care product, while the source of another mercury poisoning case was undetermined.

Rat Poison

The Laboratory handled two life-threatening superwarfarin rodenticide poisoning cases involved bromadiolone and brodifacoum.

General Practitioner (GP) Error and Questionable Practice

In one case isopropyl alcohol was erroneously used instead of water to dilute syrup piriton. In another case thyroxine, T3 analogue and phentermine were prescribed for slimming purpose, which is a questionable practice.

Hidden Aconitine Poisoning

The Laboratory encountered the 5th case of hidden aconitine poisoning. I.e., aconitine containing herb was not meant to be prescribed or dispensed but was present in the herbs taken by the patient, resulting in serious, potentially lethal poisoning.

Drug Analogue

A drug analogue of sildenafil (Viagra®) - acetildenafil, was detected in an over-the-counter male erectile dysfunction product, which claimed to contain pure herbal compounds. This was the first of many similar products adulterated by similar analogues detected by the Laboratory.

Others

There was a suspected tetrodotoxin poisoning case related to dried porcupine fish (blowfish) (深海刺猬神魚) and a case of suspected aniline-containing dye in Keroro stamp induced methaemoglobinaemia.

PRESENTATIONS

Event	Author	Topic
Hospital Authority Convention 2006	Dr. WT Poon	When beauty turns to misery
Hospital Authority Convention 2006	Dr. Doris Ching	A summary of drug induced hypoglycaemia cases
Hong Kong Clinical Toxicology Symposium 2006	Dr. Albert Chan	Laboratory diagnosis of poisoning: from clinical to community
The Chinese University of Hong Kong Department of Medicine and Therapeutic Medical Grand Round	Dr. Albert Chan	Toxicological problems related to the use of slimming pills and beauty products
Hong Kong Clinical Toxicology Advanced Course 2006	Dr. Tony Mak	Toxicology puzzles solved by the laboratory
The Hong Kong Society of Community Medicine Academic Meeting 2006	Dr. Albert Chan	The community dimension of poisonings
The Medical Grand Round, PMH, Department of Medicine & Geriatrics	Dr. Tony Mak	Toxicology puzzles solved by the TRL
The 38th NTW Cluster Grand Round	Dr. Tony Mak	Toxicology – one man's drug is another man's poison
Seminar in Clinical Toxicology for Physicians, COC (Medicine) and Hong Kong College of Physicians	Dr. Albert Chan	Toxicology investigation – when and how
2006 North American Congress of Clinical Toxicology	Ms Vanessa Lo	Long acting anticoagulant rodenticide poisoning – bromadiolone pharmacokinetics
Meeting a decade of Challenge, The Scientific Symposium on Emergency Medicine	Dr. Tony Mak	Chinese medicine poisoning– what's new in Hong Kong recently
Meeting the Challenge, there must be a better way, The Hong Kong Pharmacy Conference 2006	Dr. Albert Chan	The community dimension of poisoning
Medical Grand Round, The Chinese University of Hong Kong Department of Medicine and Therapeutics	Dr. WT Poon	Acquired methaemoglobinaemia

PUBLIC EDUCATION VIA MASS MEDIA

Event	Author	Topic
Interviewed by Television Broadcasts Limited	Dr. Tony Mak	新聞透視
Press Release	Dr. WT Poon	Adulteration of Chinese proprietary drug with oral-hypoglycaemic drug
Press Release	Dr. Tony Mak	A poisonous case of consuming flower of *Datura metel L.* (曼陀羅花), which was misidentified by the patient to be non-poisonous flower grown in the country park

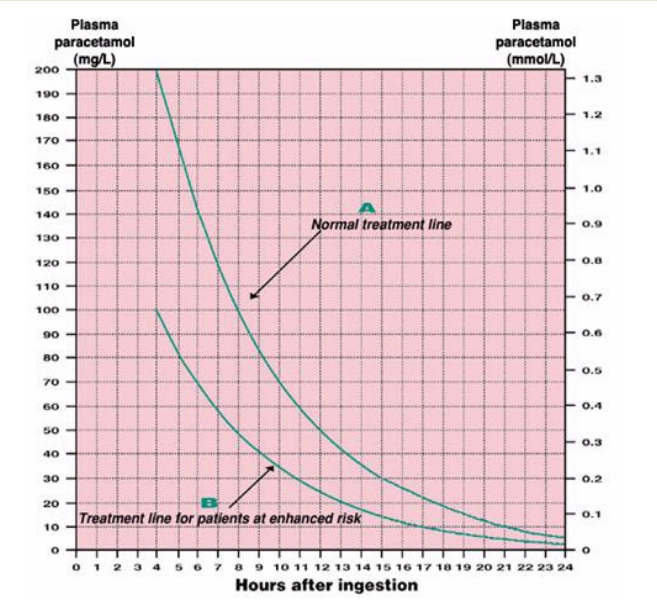
PUBLICATIONS

1. Lam HS, Chow CM, Poon WT, Lai CK, Chan KC, Yeung WL, Hui J, Chan AY, Ng PC. Risk of vitamin A toxicity from candy-like chewable vitamin supplements for children. *Pediatrics*. 2006;118:820-4.
2. Chan W, Hui KM, Poon WT, Lee KC, Cai Z. Differentiation of herbs linked to "Chinese herb nephropathy" by the liquid chromatographic determination of aristolochic acids. *Anal Chim Acta* 2006;576:112–6.
3. Ching CK, Lai CK, Poon WT, Lui MC, Lam YH, Shek CC, Mak TWL, Chan AYW. Drug-induced hypoglycaemia – new insight into an old problem. *Hong Kong Med J*. 2006;12:334–338.
4. Kwan TH, Tong MKH, Leung KT, Lai CK, Poon WT, Chan YW, Lo WH, Au TC. Acute renal failure associated with prolonged intake of slimming pills containing anthraquinones. *Hong Kong Med J*. 2006;12:394–397.
5. MaK Tony WL, Chan Albert YW, Chan Thomas YK, Lau Rick FL. Superwarfarin (Rodenticide) Poisoning. *Poisoning.Comm* Oct 2006; Vol 1 issue 4.
6. Poon WT, Lai CK, Ching CK, Tse KY, So YC, Chan YC, Hau LM, Mak TW, Chan AY. Aconite poisoning in camouflage. *Hong Kong Med J*. 2006;12(6):456-9.
7. Lai CK, Poon WT, Chan YW. Hidden aconite poisoning: identification of yunaconitine and related aconitum alkaloids in urine by liquid chromatography-tandem mass spectrometry. *J Anal Toxicol*. 2006;30:426-33.
8. Lo Vanessa MH, Yuen Liz YP, Lam YH, Mak Tony WL, Chan Albert YW. Long acting anticoagulant rodenticide poisoning – bromadiolone pharmacokinetics. *Clinical Toxicology*. 2006;44 (5):661 (abstract).

LIS ENHANCEMENT

Rolling out of paracetamol normogram printing in the Laboratory Information System

Automatic printing of paracetamol normogram by the Laboratory Information System was first introduced in 2000 by Dr. Tony Mak. TRL helped to update the normogram and roll out the practice to all HA laboratories.



Highlights of Important Issues

"Hidden" Aconite Poisoning

Aconite herbs (烏頭類草藥), like *Radix Aconiti* (川烏) and *Radix Aconiti Kusnezoffii* (草烏), have long been used in Traditional Chinese Medicine. They can, however, cause severe or even fatal poisonings.

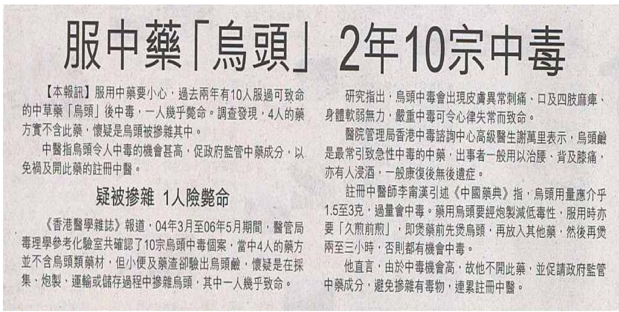
In the first two years of operation, TRL confirmed ten cases of aconite poisonings. Most importantly, in four of these cases, no aconite herb was prescribed but the related toxins were detected. A fifth case was diagnosed recently. In the most severe case, a fit young man nearly died. While the severity of such poisons is important, the most worrying aspect is that these deadly herbs were not intentionally prescribed or dispensed in these cases. Random contamination of the ingested herbs is the most likely explanation. Since random contamination is unpredictable, subjects taking herbal remedies, irrespective of the indications, are theoretically at risk of such life-threatening poisoning.

Our findings illustrate that the quality control system of these dangerous herbs should be reviewed and strengthened.

Related publications:

1. Lai CK, Poon WT, Chan YW. Hidden aconite poisoning: identification of yunaconitine and related aconitum alkaloids in urine by liquid chromatography-tandem mass spectrometry. *J Anal Toxicol*. 2006;30:426-33.
2. Poon WT, Lai CK, Ching CK, Tse KY, So YC, Chan YC, Hau LM, Mak TW, Chan AY. Aconite poisoning in camouflage. *Hong Kong Med J*. 2006;12:456-9.

Hong Kong Economic Times 9.12.2006



服中藥「烏頭」2年10宗中毒

【本報訊】服用中藥要小心，過去兩年有10人服過可致命的中草藥「烏頭」後中毒，一人幾乎斃命。調查發現，4人的藥方實不含此藥，懷疑是烏頭被摻雜其中。

中醫指烏頭令人中毒的機會甚高，促政府監管中藥成分，以免禍及開此藥的註冊中醫。

疑被摻雜 1人險斃命

《香港醫學雜誌》報道，04年3月至06年5月期間，醫管局毒理學參考化驗室共確認了10宗烏頭中毒個案，當中4人的藥方並不含烏頭類藥材，但小便及藥渣卻驗出烏頭鹼，懷疑是在採集、炮製、運輸或儲存過程中摻雜烏頭，其中一人幾乎致命。

研究指出，烏頭中毒會出現皮膚異常刺痛，口及四肢麻痺、身體軟弱無力，嚴重中毒可令心律失常而致命。

醫院管理局香港中毒諮詢中心高級醫生謝萬里表示，烏頭鹼是最常引致急性中毒的中藥，出事者一般用以治腰、背及膝痛，亦有人浸酒，一般康復後無後遺症。

註冊中醫師李甯漢引述《中國藥典》指，烏頭用量應介乎1.5至3克，過量會中毒。藥用烏頭要經炮製減低毒性，服用時亦要「久煎前煎」，即煲藥前先煲烏頭，再放入其他藥，然後再煲兩至三小時，否則都有機會中毒。

他直言，由於中毒機會高，故他不開此藥，並促請政府監管中藥成分，避免摻雜有毒物，連累註冊中醫。

A Case of Syrup Medicine Containing Isopropanol

A six-year-old boy was referred to the TRL for burning sensation in the mouth after taking a transparent syrup medicine labeled "piriton" prescribed by a private medical practitioner on 5 September 2006. Analysis of the syrup medicine revealed isopropanol in addition to chlorpheniramine (piriton). In view of the potential public health implication and that more patients could be exposed to the same medication, the case was reported to the DH immediately. The six-year-old boy was stable and was discharged three days afterwards.

Contact tracing was immediately done by the DH. Five bottles of syrup medicine submitted by other affected patients were found to contain isopropanol by the Government Laboratory. The case was widely reported in the mass media.

【明報專訊】於東涌逸東商場開設診所的西醫幸凌宇，疑開給一名6歲男童的收鼻水及抗敏感藥水含消毒火酒，男童服後口部灼痛難當，昨入院求醫，現時情況穩定。診所職員估計，約有50名病人曾被處方肇事藥水，多數是兒童，診所正聯絡有關病人，而衞生署正調查該醫生是否錯配藥物、是否自行混合藥水，抑或藥水送到診所前已經出問題，並跟進訂藥數量及診所的病人紀錄。

約50病人被處方肇事抗敏藥水

衞生署呼籲，曾被處方該藥水的病人應立即停用及求醫，副署長梁挺雄表示，病人服用含酒精藥水會感到口腔灼痛、作嘔、腹痛，若大量服用會頭痛、頭暈、有睡意，甚至死亡。他補充，若1至2歲的幼兒服用問題藥水，即使分量少仍會出問題。衞生署已設立熱線供查詢：2125 2727。

疑開出問題藥水的醫生幸凌宇，1994年在愛爾蘭貝爾法斯特皇后大學內外全科醫學士畢業，已在港註冊，其診所設於東涌逸東商場。有電視台記者昨晚到其診所採訪時，被診所內一名男子推出門外。

副衞生署長梁挺雄表示，該名6歲男童因感冒及咳嗽於本月4日到幸凌宇的診所求醫，獲處方5種藥物，其中包括一種顏色透明的收鼻水、抗敏感藥水。男童兩日內曾3次服用該藥水，每次5毫升，每次服後都表示口腔灼痛，後來更拒絕再服。男童母親遂帶他再往幸的診所求醫，幸將男童轉介到瑪嘉烈醫院急症室。

男童在瑪嘉烈留院後，院方即化驗幸所處方的5種藥物，驗出上述收鼻水藥水含有消毒火酒，遂通知衞生署。男童現時情況穩定，仍有感冒病徵。

衞署派藥劑師醫生調查

衞生署隨即派藥劑師及醫生到幸的診所調查，該署及醫管局均未透露肇事藥水的火酒含量。據悉，肇事藥水由一本地藥廠生產，衞生署正展開調查。

兒科醫生謝鴻興稱，某些口服藥水，如退燒藥，會含小量酒精成分，讓兒童更易吸收藥效，但這酒精是人類可吸收，絕非濃度高達75%的消毒火酒。他指出，藥廠會預先把藥物混合妥當，毋須醫生自行混藥。

醫學會會長蔡堅表示，一般醫生絕不會將酒精混入藥水；香港醫院藥劑師學會藥物教育資源中心教育總監崔俊明指出，10多年前有醫生以酒精充當防腐劑，但現在已沒有人這樣做。

西醫幸凌宇拒回應

疑處方問題藥水的醫生幸凌宇，診所設於東涌逸東商場。昨晚診所有人在內執拾，但拒絕回答記者問題。（秦偉攝）

Ming Pao 7.9.2006

明報 港聞 2006・09・11 星期一

酒精濃度50% 衞署已報警

火酒咳水醫生或遭控

【明報專訊】東涌西醫幸凌宇「火酒咳藥水」事件，調錯的藥水火酒酒精濃度原來高達逾50%，基本上病童吃藥有如喝火酒。由於衞生署調查發現，幸凌宇配予病人的咳藥水本身亦未有註冊，署方已就事件向警方報案，並正研究控告他違反《藥劑業及毒藥條例》。

咳藥水亦未經註冊

醫學會草擬良好配藥守則

Ming Pao 11.9.2006

Oral Hypoglycaemic Agents Administrative Errors in Elderly Homes

In May 2005, a cluster of patients with hypoglycaemia who were seen by the same general practitioner was referred to the TRL for suspected drug-induced hypoglycaemia. Mixing up of an oral hypoglycaemia drug (gliclazide) and simethicone was confirmed by the Laboratory. The associated publicity triggered a surge of similar requests. The TRL has received a total of 51 referrals for suspected drug-induced hypoglycaemia in patients without a history of current hypoglycaemia agent use from June 2005 to March 2006. In 23 (45%) of these patients, oral hypoglycaemic agents (OHA) and/or their metabolites were detected. The possible sources of OHA deduced on the basis of available clinical information are shown in Table 1.

Table 1. Possible sources of OHA in positive cases

Possible Sources of OHA	No. of Cases (Total = 23)
Elderly home resident, drug administration error confirmed/suspected	9
Took family member's / employer's medication	6
Taking stock medication by mistake	2
Patient reported taking an over-the-counter medication, which was not available for analysis	1
Chinese proprietary medicine adulterated with Western medications	1
Unknown	4

As there was a possible widespread drug administration error in elderly homes, the incidences were reported to the Social Welfare Department and the DH for follow up. The incident was widely reported in the mass media in April 2006. A notification system for future cases was established. Other remedial/preventive actions included circulating a guideline on proper procedure and handling of drug to all elderly homes staff, arranging elderly home-based enhanced training on proper drug administration, and monitoring those homes with unsatisfactory record of drug administration closely.

Related publication:

1. Ching CK, Lai CK, WT Poon, Lui MC, Lam YH, Shek CC, Mak TW, Chan AY. Drug-induced hypoglyacemia—new insight into an old problem. *Hong Kong Med J.* 2006; 12(5):334-8.

安老院派錯糖尿病藥

院友昏迷 社署警告了事

【明報專訊】西醫李世澧配錯藥事件在安老院上演！過去9個月，23名無患糖尿病市民，誤服糖尿病藥，引致血糖過低，年紀最小的只有2歲。23食錯藥者中有9人是在安老院，當中更涉及安老院派錯藥，但社會福利署只向出事院舍發出警告信，未有檢控，還以「事件已處理」為由，拒絕透露出事院舍名稱。

9間院舍 9人誤服

衞生署跟進 員工再培訓

年齡最小2歲 兩長者去世

倡制訂嚴謹派藥程序

Ming Pao 26.4.2006

A13 港聞

屢派錯藥保健員 社署擬除名

【明報專訊】對於「老人院派錯藥事件」，社會福利署長鄧國威承認是「嚴重事故」，指署方已和有關部門制訂院舍派藥指引、提高保健員的入職要求及加強培訓。他表示，由於保健員需要向社署註冊，未來會考慮對屢次派錯藥的保健員採取「除名」措施。

提升入職學歷 培訓時數

長者獲發過期藥致病發

老人院不妥善處理藥物

Ming Pao 1.5.2006

Drug Analogues – an Under-recognised Threat to the Society

Drug analogues are created by modifying the chemical structures of existing drugs. Although drugs with similar structures are presumed to have similar clinical effects and toxicity, unanticipated problems often occur. For example, phenacetin, close in structure to acetaminophen, is associated with carcinogenicity not observed with acetaminophen. Hence, it is prudent to test the safety and efficacy before a drug analogue is licensed as pharmaceutical for human use. The drug testing process is lengthy and costly.

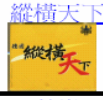
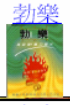
On the other hand, illicit drug analogues are marketed for human consumption without formal evaluation. The potential adverse effects are numerous and unpredictable. Drug analogues of anti-obesity drugs and male erectile dysfunction drugs are some examples.

In Sep 2004, a woman was referred to the TRL for suspected drug-induced fulminant liver failure. The herbal anti-obesity product taken by the woman was found to contain N-nitrosofenfluramine, an analogue of fenfluramine. Use of fenfluramine is associated with heart valve problem while its illicit analogue N-nitrosofenfluramine causes fatal hepatic failure not observed in the parent drug. The incident was widely reported in the mass media in October 2004.

In July 2006, a health product for erectile dysfunction was received for analysis. This product was obtained from a young man admitted to a hospital for unstead gait, suspected to be drug-induced. An illicit drug analogue of sildenafil was identified. As a follow up, a limited local survey of erectile dysfunction health products was conducted and the majority of these products were found to contain concealed illicit drug analogues.

Often disguised as health supplements or herbal products, such illicit drug analogues are readily available to the public. The drug analogues are difficult to detect by ordinary laboratory methods and pose an under-recognized threat to the society. Furthermore, these illicit drug analogues are not regarded as pharmaceuticals in Hong Kong. Their use in health products is therefore not under specific legal regulation. We suggest that new legislation should be introduced to control these products. A surveillance system is also required.

Local survey findings: erectile dysfunction products containing drug analogues

Products	Findings	Source
Power 58 轟天炮 	Acetildenafil	7-Eleven HKD113
Ehanix 來康力 	Acetildenafil	Watsons HKD118
Jolex 壯力仕 	Piperidenafil	Watsons HKD89
Power 58 轟天炮(白金裝) 	Acetildenafil	Watsons HKD484
温養ONYO錠劑 	Acetildenafil Piperidenafil	Mannings HKD90
縱橫天下 	Acetildenafil	7-Eleven HKD119
勃樂 	Hydroxyhomosildenafil	華潤堂 HKD168
皇力 	Hydroxyacetildenafil	Mannings HKD220
天力 	Hydroxyacetildenafil	Watsons HKD128
火龍 	Hydroxyhomosildenafil	信安大藥房有限公司 HKD250
Ehanix 特強來康力 	Piperidenafil	7-Eleven HKD120
Power58 轟天炮金裝特強版 	Piperidenafil	7-Eleven HKD124
Power58 轟天炮白金裝特強版 	Piperidenafil	7-Eleven HKD149

Ming Pao 17.10.2004

Sing Tao 18.11.2006

Slimming Agent Related Poisonings in Hong Kong

Introduction

The slimming agent market is rich in variety, including prescription drugs and proprietary slimming products. While prescription drugs are generally effective, they have their limitations. For proprietary slimming products, there is little evidence for effectiveness but numerous safety concerns. The TRL encounters slimming agent related poisonings frequently. A few significant examples are summarized below to illustrate the problem.

Inappropriate use of prescription drugs

Adverse effects could result from inappropriate use of prescription drugs for weight reduction. For example, the TRL has encountered a number of patients presenting with acute psychosis after taking combinations of multiple appetite suppressants (sibutramine, phentermine and amfepramone (diethylproprion)). In other poisonings, registered drugs not intended as slimming agents were inappropriately used for weight reduction (thyroxine, tiratricol, growth hormone and diuretics). Such “off-label” use is risky and should be discouraged.

Adulteration of proprietary slimming products

Adulterants commonly identified in proprietary slimming products by the TRL include appetite suppressants (sibutramine, desmethylsibutramine, fenfluramine, N-nitroso-fenfluramine), animal thyroid tissue, laxatives (bisacodyl, phenolphthalein) and drugs used to mask the undesirable effects of other adulterants (e.g. propranolol). The adulterants are associated with numerous side effects. For example, use of thyroid hormones as slimming aid carries a risk of hyperthyroidism and related cardiovascular complications. A young man developed factitious thyrotoxicosis and hypokalemic paralysis after taking a proprietary slimming product that contained animal thyroid tissue.

Most importantly, some adulterants are unsafe for human consumption. For example, fenfluramine is a banned appetite suppressant linked to valvular heart disease and pulmonary hypertension. A middle aged woman died of pulmonary hypertension and heart failure after taking a slimming product adulterated with fenfluramine.

Drug interactions

Adverse effects could be caused by drug interactions between slimming product and concurrent medications. Anthraquinones and derivatives are cathartics. They are frequently found in proprietary slimming products. Renal and liver complications resulting from the combined use of non-steroidal anti-inflammatory drugs and anthraquinone-containing slimming agent have been reported in Hong Kong.(1, 2)

Summary

Slimming product is popular in Hong Kong. Consumers may not realize the risk involved. Adverse events are not uncommon and can be life-threatening. This is an important clinical as well as public health problem.

References

1. Li FK, Lai CK, Poon WT, Chan AY, Chan KW, Tse KC, Chan TM, Lai KN. Aggravation of non-steroidal anti-inflammatory drug-induced hepatitis and acute renal failure by slimming drug containing anthraquinones. *Nephrol Dial Transplant* 2004; 19:1916-7.
2. Kwan TH, Tong MK, Leung KT, Lai CK, Poon WT, Chan YW, Lo WH, Au TC. Acute renal failure associated with prolonged intake of slimming pills containing anthraquinones. *Hong Kong Med J.* 2006;12(5):394-7.


曾服藥減肥
女子昏死
含動物甲狀腺 衞署擬全面抽驗

Other Traditional Chinese Medicine Related Poisoning

Herbal poisonings in Hong Kong

In Hong Kong, Chinese medicine coexists with orthodox medicine. As is the case with Western pharmaceuticals, some herbs are toxic and must be used with caution. The TRL encounters herbal poisonings frequently. Recent examples include the aconite herbs (川烏/草烏/附子), aristolochic acid-containing herbs (馬兜鈴藥材), *Flos Daturae* (洋金花), *Rhizoma Dioscoreae Bulbiferae* (黃藥子), *Semen Strychni* (馬錢子) and *Venenum Bufonis* (蟾酥). The mechanisms of poisoning are protean. Some notable examples are summarized below to illustrate the problem.

Erroneous substitution

Adverse effects could result from erroneous substitution of non-toxic herb with toxic one having similar name or appearance. For example, an elderly patient developed progressive renal failure and bladder cancer after taking herbs for six months. The non-toxic *Herba Solani Lyrati* (白英) in his prescription had been mixed up with the aristolochic acid-containing *Herba Aristolochia Mollissemae* (尋骨風). Both herbs share a common name, 白毛藤, that means furry. This incorrect substitution is believed to be a local systemic problem for years. Our findings contributed to the withdrawal and banning of the various aristolochic acid-containing herbs in Hong Kong.

Related publication

1. Wing-Tat Poon, Chi-Kong Lai, Albert Yan-Wo Chan. Aristolochic acid nephropathy: the Hong Kong perspective. *Hong Kong J Neprol*. 2007;9(1):7-14.

On another occasion, a middle-aged woman suffered from life threatening methaemoglobinaemia after taking a herbal prescription that included the Chinese medicine *Natrii Sulfas* (芒硝). Apparently, *Sodium Nitrite* (牙硝) was substituted inadvertently at the wholesale level. While *Natrii Sulfas* is harmless, *Sodium Nitrite* can induce life-threatening methaemoglobinaemia. The erroneously distributed medication was recalled from more than 20 herbal shops, preventing further poisonings.

Related publication

1. Chui JS, Poon WT, Chan KC, Chan AY, Buckley TA. Nitrite-induced methaemoglobinaemia—aetiology, diagnosis and treatment. *Anesthesia*. 2005;60(5):496-500

Inadvertent contamination

Other erroneous substitutions involved the *Tupistra species* (開口箭) and *Flos Daturae* (洋金花) mistaken for other herbs and resulted in cardiac and anticholinergic toxicity respectively.

Herbal poisonings could result from inadvertent contamination of non-toxic herb with toxic substances. The TRL has investigated an outbreak of anti-cholinergic toxicity following the intake of *Rhizoma Atractylodis* (蒼朮). The herb had been contaminated with anticholinergic substances. Another striking example is the "hidden" aconite poisoning which has been discussed separately in this report.

Other Traditional Chinese Medicine Related Poisoning (continue)

Unsafe prescribing practices

Some herbs are toxic and must be used with caution. For example, aconite poisoning (烏頭碱中毒) is the most common severe herbal poisoning and is potentially fatal. Many patients were prescribed an obviously toxic dosage. In some cases, the prescribing Chinese medicine practitioner did not provide proper decoction instruction (prolonged boiling) to reduce the toxicity.

Another example of unsafe prescribing practice is the prolonged prescription of Rhizoma Dioscoreae Bulbiferae (黃藥子) resulting in hepatitis. This herb should be used for a short period of time only.

Sometimes prescription of herbs was illegible and resulted in dispensing error. A patient developed a fatal arrhythmia shortly after taking some herbs and died. One of the items in his formula was "乾蟾皮炭". It was not clear whether the dosage was 0.2 or 2 and no unit was stated. It was suspected that "蟾酥", which is much more potent than 蟾皮, could have been dispensed instead.

Venenum Bufonis (蟾酥)

Picture courtesy: HA Herbal Toxicology Database

Unsupervised herbal consumption

Self-administration of herbals is common. Nonetheless, such unsupervised herbal consumption can be dangerous. For example, several patients had been poisoned after self-administering an excessive dose of Semen Strychni (馬錢子), aconite herbs (川烏/草烏/附子) or other toxic herbs.

Adverse effects could also arise from self-administration of proprietary Chinese medicine products. A number of patients had developed acute hepatitis after intake of various over–the-counter herbal products for treatment of vitiligo (補骨脂注射液, 驅白巴布期片, 促黑素細胞生長劑 and 百草清雪丸). Another case developed skin problems associated with the use of Lei Gong Teng capsule (雷公藤片).

Semen Strychni (馬錢子)

Picture courtesy: HA Herbal Toxicology Database

Summary

Our findings illustrate that there is scope for improvement in the quality control of herb supply, prescription and dispensing. The importance of an effective surveillance system for adverse effects associated with herbal use, similar to the one for Western medicine, cannot be overemphasized.

Adulterations

Adulteration is concealed addition of undeclared drugs, or other substances with therapeutic effects, to a health product. Consumption of such products, and the concealed components unwittingly, is obviously dangerous. The TRL has identified more than 30 such products in 2006. A summary of our findings is shown in the table.

Some adulterants, like corticosteroids and hypoglycemic drugs, are dangerous medications requiring prescription. Multiple adulterants in one product are often seen. Untoward adverse effect or drug interaction could occur. Overdose subsequent to poor standardization of the adulterants is another concern.

Adulterated products, as attempts to evade regulatory control, are often available over-the-counter. They therefore constitute a major health hazard to the general public. Enhanced surveillance and augmented public education are essential to tackle this problem.

#	Product Name	Indication	Listed Ingredients	Related Adverse Effects	Adulterants Identified
1	天星鎮癇膠囊	Epilepsy	Herbal	Withdrawal seizure	Phenobarbitone
2	降糖寧膠囊	Diabetes	Herbal	Hypoglycemia	Rosiglitazone, nateglinide & glimepiride
3	Neovidan	Musculoskeletal pain	Vitamin B1, B6, B12	Hemolytic anemia	Prednisolone, mefenamic acid & famotidine
4	复方消屑靈	Psoriasis	Herbal	Nil	Griseofulvin
5	減肥降脂美	Weight reduction	Herbal	Nil	Sibutramine
6	常青春	Weight reduction	Herbal	Sudden cardiac arrest	Thyroid tissue, N-nitrosofenfluramine, fenfluramine, sibutramine, phenolphthalein, propranolol, riboflavin, nicotinamide, pyridoxine
7	常青春	Weight reduction	Herbal	Hypokalemic paralysis	Thyroid tissue, N-nitrosofenfluramine, fenfluramine, sibutramine, phenolphthalein, propranolol, riboflavin, nicotinamide, pyridoxine
8	健美素	Weight reduction	Herbal	Fulminant liver failure	Thyroid tissue, N-nitroso-fenfluramine, fenfluramine, nicotinamide
9	清酯酶	Weight reduction	Herbal	Postural syncope	Thyroid tissue, fenfluramine, propranolol, and phenolphthalein
10	Anonymous (bought from internet)	Weight reduction	Not available	Severe thyrotoxicosis	Thyroid tissue, sibutramine, N-bis-demethylsibutramine
11	活力33	Weight reduction	Not available	Acute psychosis	N-bis-demethylsibutramine
12	Unknown herbal powder	Gout	Not available	Acute hepatitis	Phenacetin, aminopyrine, ibuprofen, diclofenac, indomethacin
13	姿婷纤維胶囊	Weight reduction	Herbal	Acute psychosis	Thyroid tissue, fenfluramine, metformin
14	Power 58	Erectile dysfunction	Herbal	Ataxia	Acetildenafil
15	天天素	Weight reduction	Herbal	Acute psychosis	Phenolphthalein, sibutramine, mazindol
16	奥美斯	Weight reduction	Herbal	Acute psychosis	Phenolphthalein, hydrochlorothiazide, sibutramine, mazindol
17	藍婷	Weight reduction	Herbal	Acute psychosis	Fenfluramine
18	神效頭痛散	Headache	Herbal	Nil	Phenacetin, aminopyrine, phenobarbitone, caffeine
19	Slim瘦腩の寶	Weight reduction	Herbal	Heart failure	Sibutramine
20	金聖美	Skin whitening	Not available	Nephrotic syndrome	Mercury content (74810 ppm)
21	Unknown herbal pill	Asthma	Not available	Cushingnoid	Dexamethasone acetate

Adulterations (continue)

#	Product Name	Indication	Listed Ingredients	Related Adverse Effects	Adulterants Identified
22	Unknown herbal powder	Cough	Not available	Unsteady gait	Dyphylline, dextromethorphan, phenobarbitone, chlorpheniramine, and betamethasone/dexamethasone
23	Unknown herbal capsule	Unknown	Not available	Nil	Sibutramine
24	Unknown herbal pill	Arthritis	Not available	Cushingnoid	Aminopyrine, caffeine, phenacetin, prednisone acetate, prednisone and cortisone acetate
25	Unknown herbal topical treatment	Arthritis	Not available	Cushingnoid	Prednisone acetate
26	Unknown herbal pill	Arthritis	Not available	Cushingnoid	Dexamethasone, mefenamic acid
27	消可舒平 - 降糖寧膠囊	Diabetes	Herbal	Hypoglycemia	Glibenclamide, phenformin, rosiglitazone
28	Unknown herbal pill	Weight reduction	Not available	Nil	Sibutramine
29	Unknown herbal pill	Diabetes	Not available	Nil	Phenformin, glibenclamide
30	喘咳靈	Asthma	Not available	Cushingnoid	Prednisone acetate, morphine, codeine, chlor-pheniramine, diazepam
31	Unknown herbal pill	Weight reduction	Not available	Factitious thyro-toxicosis	Thyroid tissue, sibutramine, caffeine
32	Unknown herbal pill	Weight reduction	Not available	Factitious thyro-toxicosis	Thyroid tissue, sibutramine, caffeine

Illicit Pharmacy Practice

The TRL encounters from time to time suspected illegal pharmacy practice where prescribed drugs are available over-the-counter without prescription. The most commonly incriminated drug is synthetic corticosteroid. Many patients developed iatrogenic Cushing's syndrome and adrenal insufficiency. In another instance, an elderly went into coma following an overdose of a muscle relaxant (Baclofen). Apparently a pharmacy store hastily dispensed the medication as a substitute for an analgesic (Voltaren).

The illegal sale of prescription drugs is dangerous. More effective surveillance and control are required.

Food Related Poisoning

The TRL encounters food poisoning occasionally. For example, three members of a family developed central nervous system depression following an ioverdose of *Radix Stephaniae* (地不容). The herb, which contains a potent neuro-toxin, is readily available as "health food" from the marketplace.

There have also been several episodes of food poisoning associated with the consumption of raphide-containing plants resembling some common vegetables. On one occasion, a patient developed tingling and burning sensation in the mouth immediately after taking "芋頭" bought from the marketplace. Apparently, the "芋頭" was mixed up with the raphide-containing "姑婆芋".

Other food related poisonings involved toxic mushrooms and puffer fish which resulted in gastrointestinal and neurological toxicity, respectively.

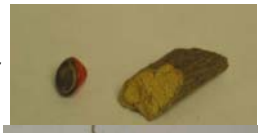
Toxic Plants From Countryside

Introduction

From 2003 to 2006, eight cases of plant intoxication were referred to the TRL. The role of the TRL goes beyond biochemical analysis while facing these cases. We liaise with experts of different professionals, including analytical chemist, biologist, botanist, mycologist, pharmacist, Chinese medical practitioner and herbalist; explore the possibility of various analytical strategies, including morphological identification, genetic/chemical profiling, light/electronic microscopy, chromatography and mass spectrometry; to have the mystery of intoxication solved.

Acute renal failure after taking herbs collected from Lamma island

In August 2003, a 51-year-old woman, who developed acute renal failure after taking herbs collected from Lamma Island for 10 days, was referred to the TRL. From the remaining fresh plant, some ovoid seeds with two well defined red and black areas were identified as *Abrus precatorius L* (相思子) morphologically and further confirmed by analysis on its alkaloid profiles. The toxicity of the major toxin, abrin, is mainly gastrointestinal. It may also have direct toxicity to the kidney and could be lethal. The patient finally required intensive care and haemodialysis.



From patient

Apple Daily 2.11.2004

Oriental Daily 2.11.2004

From countryside

Mixing-up of "血見愁" with "鬼見愁" leading to acute hepatitis

In July 2005, a 51-year-old patient presented with acute hepatitis was refer to the TRL. The patient had taken some wine prepared from a fresh plant named "鬼見愁" one week before admission. The plant was identified to be 山薑香 (*Teucrium viscidum*) commonly known as "血見愁". Chemical analysis supports the findings and the toxins present in *Teucrium* genus are well known to be liver toxic. It was considered that the mixing-up of "血見愁" with "鬼見愁" may account for the hepatic status of the patient. The liver function of the patient returned to normal after two months with conservative treatment.

From patient

Toxic Plants From Countryside

Gastrointestinal symptoms after taking wild mushroom

In August 2006, a 70-year-old man was referred to the TRL for vomiting, diarrhea and oral numbness about one hour after the intake of some wild mushroom taken from the countryside. The mushroom was identified to be *Chlorophyllum molybdites* (綠褶菌) by a mycologist. The mushroom is commonly found in the countryside of Hong Kong and is a very common cause of mushroom poisoning around the world. The consumption of small amount may cause severe gastrointestinal symptoms within one to three hours. The toxin involved is not known but seemed to be heat stable. The symptoms of the patient subsided after a few days.

From patient

Mucosal irritation after taking taro

Two cases of taro poisoning were encountered by the TRL. One of the cases was received in November, 2005 and the taro was collected by the patient in Cheung Chau while the other case, which happened in December, 2006, was bought from a hawker. Both patients experience oral mucosa burning and tingling sensation after taking boiled taro and one of them developed epigastric pain and central chest discomfort. These symptoms subsided after a few days. The toxin in these taro were not known but needle shaped crystals were observed under microscope in both samples which might account for the symptoms.

三人吃湯渣中招 灼傷口腔舌及胃

食野芋中毒 嚴重可致命

Oriental Daily
18.1.2007

From patient

Confusion after taking wild flower broth

A 67-year-old lady was admitted with confusion shortly after drinking a broth prepared with what she believed to be "珠龍花" collected from the countryside. The residual flower was identified as *Datura metel L* (白花曼陀羅, also known as 洋金花). *Datura metel L* is one of the most toxic plants in Hong Kong. The alkaloids hyoscyamine and scopolamine were detected in both the flower and patient's urine. Both alkaloids have anticholingergic effects which account for the symptoms of the patient. Patient was discharged after three days.

From patient

郊外採摘 婦服洋金花中毒

Ming Pao
27.1.2006

From countryside

Rodenticides

The TRL has established a semi-quantitative target screen method for warfarin, warfarin metabolites and 11 superwarfarins in blood, urine, gastric lavage, baits and food etc. by liquid chromatography tandem mass spectrometry. Compounds identified are divided into two categories:

4-hydroxycoumarin (9 Compounds)				
Brodifacoum	Coumachlor	Coumatetralyl	Difethialone	Warfarin
Bromadiolone	Coumafuryl	Difenacoum	Focoumafen	-

Indandione (3 Compounds)		
Chlorophacinone	Diphacinone	Pindone

All registered superwarfarins in Hong Kong, both 4-hydroxycoumarin and indanedione, are covered in the test list.

From April to December 2006, 20 cases (75 laboratory analysis) of suspected rodenticide poisoning were handled. Among which four patients were self poisoned, seven presented with unexplained coagulopathy, and the rest were studied for suspected rodenticide ingestion without abnormal clotting profile. Eleven and three cases were found positive in blood and urine respectively. Three cases were found positive in baits. Compounds identified were brodifacoum, bromadiolone, coumatetralyl, warfarin and warfarin metabolite.

In three patients, apart from abnormal coagulation profile, blood rodenticide levels provided additional information to help vitamin K_1 therapy monitoring.

At times, laboratory analysis provides the only means to confirm or exclude rodenticide poisoning. In addition, serial measurements of blood rodenticide level provide valuable information on the timing of exposure.

Related publications:

1. Superwarfarin (Rodenticides) Poisoning Alert was issued on 1 August 2006 and distributed to all clinicians in the Hospital Authority.
2. Tony WL Mak, Albert YW Chan, Thomas YK Chan, Rick FL Lau. Superwarfarin (Rodenticide) Poisoning. *Poisoning.Comm* Oct 2006; Vol 1 issue 4.
3. Vanessa MH Lo, Liz YP Yuen, YH Lam, Tony WL Mak, Albert YW Chan. Long acting anticoagulant rodenticide poisoning – bromadiolone pharmacokinetics. *Clinical Toxicology*. 2006;44(5):661 (abstract).

Related presentation:

1. Vanessa MH Lo. Long-Acting Anticoagulant Rodenticide Poisoning – Bromadiolone Pharmacokinetics was presented as a poster in the North American Congress of Clinical Toxicology, 7th October 2006.


誤服鼠藥可致流血不止

影響凝血能力 持續吸收積聚體內

超級鼠藥（老鼠毒藥）資料

Apple Daily 11.8.2006