packing which required to be further looked into;

- EWG for traditional processing suggested that it is crucial that the standard processing for frequently processing materials should be established, with the example Rehmaniae Radix given.
- Case study of the content of Benzo(a)pyrene in Rehmanniae radix was done, and result showed that processing with hot steaming of raw roots reduced the Benzo(a)pyrene content from 26ppb to 20ppb;
- As for area on information sharing, the website www.fhhm.net was constructed. The maintenance cost of the website is US$2000 - $3000 per year and this cost is currently sponsored by KFDA;
- It was concluded that Subcommittee II will continue the establishment of guidelines for standard processing methods and upgrading of website.

Brief notes of Subcommittee III report

Dr. Chen Yixin from China

- Brief history regarding the setting up of Subcommittee III, which was originally an EWG under Subcommittee II;
- There was an operation document formulated and chaired by the Prof. Jin Shaohong of China;
- Types of information for exchange were identified and consolidated;
- Some issues and information among members on herbal safety, evenly safety information on other medical products were communicated and discussed;
- All information from member parties were compiled and delivered;
- Content of ADR information Bulletin to public in China was described in details;
- Definition of ADR, factors resulting in ADR, safety of TCM were mentioned under the topic of Analysis on the Safety in TCMs;
- Holding a seminar on safety of herbal medicine to discuss on what kinds of factors will result in ADR or ADE related to Herbal medicines was proposed.

Comments and questions:

Mr. Victor Wong asked Dr. Chen Yixin whether ADRs arising from herbal medicines adulterated with Western drugs should be included in the ADR reporting, and Dr. Chen Yixin clarified that they should not be considered because the definition of ADR is adverse effects arising from the intrinsic properties/toxicities of the herbal ingredients. Prof. David Briggs concurred with Dr. Chen Yixin. Mr. Smith and Dr. Vu commented that adulterated herbal products are a major problem and should be taken seriously. To safeguard public health, herbal products found adulterated with Western drugs must be recalled from the market and enforcement action should be taken.

Plaque of Appreciation

After the Subcommittee reports, Dr SY Chang presented the Plaque of Appreciation to Dr SH Choi and Dr. Chen Ken on behalf of FHH Standing Committee members to thank his long support to FHH as the former representative of WHO WPRO. Dr SH Choi then gave a short speech acknowledging the efforts and achievements of FHH through the years. Dr. SY Chang said that he will send Dr. Chen Ken the Plaque of Appreciation by parcel post because he couldn't attend this meeting.

Presentation by Prof. Kiichiro Tsutani

The meeting is then followed by a presentation of ADR reporting and classification/coding of herbal medicines by Prof. Kiichiro Tsutani from Japan. The brief notes of presentation are as follows:

- Brief history on establishment of Uppsala Monitoring Centre (WHO collaborating centre);
- Number of ADR reports from Asian Countries in Vigibase;
- There were significant difference in number of ADRs reported among different countries and it was due to the difference in joining date of country, country size and also the underreporting of cases which might be caused by translation and coding problems (e.g. Saikokeishitou);
- Situation of exchange of ADR information in WHO Western Pacific Region was shared and the coming challenges were also projected for consideration;
- Suggestions on how and where to establish database of ADR were put forth for consideration;
- The coding system for reporting ADR used (e.g. DDD) was explained.

Comments and questions:

Prof. IM Chang from Korea asked about the message Prof Tsutani would like to convey in this presentation and Prof Tsutani responded that he would like to highlight the difficulties among countries on ADR underreporting due to various factors such as the classification of products.

In response to Prof Tsutani's question in this presentation about the establishment of FHH ADR database, Dr. Chen Yixin commented that it is very difficult for FHH to establish a new ADR database and she suggested FHH consider some easier channels. Prof Tsutani pointed out there might be issues regarding the maintenance of database and problems on data collation.

Discussion on Future of the Subcommittees

Mr. Yee acknowledged the great efforts of all subcommittees and he asked for views on whether the subcommittees should continue their current work.

Dr. Goda suggested that the work of subcommittee I should be continued. He proposed that the next task to look into could be the naming of herbs (English/Latin) since there are differences among different pharmacopoeias. He said that information on naming rule of herbs could be gathered from member countries so that the naming of herbs might be gradually harmonized.

Prof. Briggs agreed on the continuing work of subcommittee. Regarding the funding issue, he proposed that FHH might explore possibility of support from industry as one of the aims of FHH is to facilitate trade. He also suggested that funding might be sought from institutions.

Prof. Lin commented that Subcomittee I should continue its work as in the past 6 years work done showed good results. As for funding, Prof Lin suggested establishing a foundation to seek different contributions, and he also asked for support from WHO.

Dr. Lee from WHO responded that she could not give FHH a certain reply on behalf of WHO at the moment.

Mr. Yee then concluded that Subcommittee I should continue its work and Dr Goda would continue to head Subcomittee I.

Prof. IM Chang commented that Subcommittee II should continue to put effort on finding the issues and problems related to processing of herbal medicines, as well as to upgrade the FHH website. He agreed to continue to lead Subcommittee II and Dr. SY Chang of KFDA has kindly agreed to continue supporting the FHH website expenses.

Dr. Chen Yixin commented that China would continue the work of Subcommittee III with the support of FHH member parties.

Prof. David Briggs suggested that Subcommittee II and III could review the issues highlighted by the presentation by Prof. Tsutani and then reported back to the FHH Standing Committee for further consideration. As adulteration of herbal medicines is a major safety issue in many countries, Prof. Briggs suggested that an EWG for reviewing the situation of adulteration, contamination, substitution of herbal

medicines could be formed under Subcommittee III. Prof IM Chang agreed with Prof. Briggs' idea and suggested that Hong Kong to lead this EWG.

In view of past experience of reporting adulterations of herbal medicines to FHH, Mr. Robert Law agreed that Hong Kong would lead the above EWG. Mr. Law suggested that Singapore also participate in this EWG since the situations in Hong Kong and Singapore are similar. Mr. Yee agreed that Singapore could participate.

Discussion on FHH Funding Issue

On the issue of FHH funding, Mr Yee suggested that FHH may consider looking for support from WHO. Dr. Smith concurred with the idea and he also suggested that member countries could seek support from other government departments besides health regulatory agencies.

Dr. Goda stated that if industry is providing direct financial support, it could be difficult for Japan to attend due to the government policy in Japan. He proposed that trade sponsorship could be channeled to WHO as a neutral third party to reimburse FHH.

Prof. IM Chang explored the possibility of contribution from member countries of FHH. There was feedback from FHH members on the difficulties of obtaining funds from their respective government agencies.

Mr Yee proposed that sufficient time be allocated in the next FHH Standing Committee meeting to further discuss the funding issue which can be very complicated. The meeting agreed that the coordinating member party could continue to work within their means and source appropriate fundings. Following this, the morning session was closed.

-End of Morning Session-

Afternoon Session

Country Report by FHH Members and Canada

Prof David Briggs from Australia

- Brief introduction of regulatory framework.
- Regulatory Framework: 2-tiered risk based system of registered complementary medicines and listed complementary medicines.
- Regulatory Update: changes in quality, manufacturing, labeling and packaging standards of homeopathic medicines.
- Quality update:
  - TGA will incorporate EP and USP as alternate standards other than BP.
  - Other pharmacopoeial monographs or standards may be considered on a case-by-case basis as well.
  - Development of Australia monographs.
- Homoeopathic medicine regulation will be tightened e.g. manufacture according to GMP requirements, follow pharmacopoeial standards for quality
- National Institute of Complementary Medicine (NICM) was established to support and direct research of complementary medicines, with one of the main projects being studies in TCM.

Comments and questions:

Mr. Frank Chan from Hong Kong asked more about the monographs development under TGA. Prof. David Briggs mentioned that the information is available on TGA website.

Prof. IM Chang asked if TGA would travel to another country to conduct audit. Prof. Briggs replied that TGA current recognizes GMP audits conducted by PICs countries and for GMP standards that are not recognized by TGA, overseas audit will be conducted.

Dr Goda asked about regulation of herbal medicines and fish oil in Australia. Prof. Briggs replied that herbal medicines are regulated as complementary medicines in Australia, and culinary herbs for cooking are regulated as food. Fish oils in pharmaceutical presentation and with therapeutic claims are regulated as complementary medicines.

Prof. IM Chang asked about the progress of the proposed joint Australian and New Zealand regulatory system and Dr Briggs commented that this project has been

postponed due to political concerns from New Zealand.

Dr Zhang Wei from China

- Brief introduction of the law and regulation of herbal medicines in China.
- Legislations of drug registration.
- Technical requirements for TCM and Natural Medicinal Products (NMP) – dossier requirements, technical guidelines for TCM and NMP registration.
- Highlight of concerns on review and approval.
- Supplementary rules for TCM registration to encourage research and development of TCM, highlighting the importance of clinical treatment experience of TCM while ensuring the safety of TCM.
- Standard of TCM – national drug standards, provincial standards.
- Introduction of Chinese Pharmacopoeia.
- Drug Standards Improvement Action (2006-2010) on TCM.
- Administration of ADR of TCM.

Comments and questions:

Prof. IM Chang asked about the difference between TCM and NMP. Prof Lin explained that TCM are used according to TCM theories while NMP are products containing herbal ingredients such as Western herbs.

Dr Yukihiro Goda from Japan

- Update on JP15 – supplement published Oct 2007, schedule on JP15 supplement 2 and its topics related to herbal medicines, e.g. new monographs on crude drugs, dry extracts, and new QC methods.
- Identification methods and markers of some Kampo dry extract.
- Schedule of JP 16 on 8 Kampo extracts.
- Some contents of JP15 supplement 2:
  - New HPLC component quantification e.g. apricot kernel, turmeric, Perilla herb.
  - New TLC identification and purity tests in bear bile.
  - Additional upper limit of heavy metals and arsenic – 5ppm adopted for some herbal medicines.
  - Regulation on heavy metal in crude drugs in the near future.
  - Change of scientific name of Evodia rutaecarpa to Euodia ruticarpa.

Comments and questions:

Prof. Lin asked about the definition of herbal extracts, and Dr. Goda explained that extracts are considered intermediate products and not finished products. JP does not include finished products.

Mr. Nguyen queried the reason of using porcine bile and bovine bile in the identification of bear bile, and Dr Goda explained that porcine bile and bovine bile are used because they are the usual adulterants of bear bile.

Prof. IM Chang sought clarification from Dr. Goda on the difference between pharmacopoeia, supplement and monograph.

Mr Frank Chan from Hong Kong

- Brief introduction of current legislation on Chinese Medicine i.e. Chinese herbal medicines and proprietary Chinese medicines (pCM).
- Statutory structure of Chinese Medicine Council.
- Registration of pCM: products have to fulfill safety, quality and efficacy requirements.
- Definition of pCM.

Comments and questions:

Prof. IM Chang asked about import and export control as well as whether products imported from China into Hong Kong are bound by the same regulations. Mr Chan replied that as Hong Kong adopted the "One country, two system" policy, therefore imported products from China also have to comply with the pCM regulations of Hong Kong. Prof. IM Chang also asked about the difference of GMP requirements in China and Hong Kong, and Mr. Chan explained that the current optional GMP requirement in Hong Kong is to allow sufficient transitional period for local manufacturers to improve their standards and obtain GMP.

Dr Park Juyong from Korea

- Updates on the revision of KP 9th Edition and KHP.
- Published guidelines for herbal materials.
- Currently preparing the English edition of KP.
- Regulation of hazardous substances: heavy metals, pesticides, sulfur dioxide, aflatoxins and benzo(a)pyrene.
- Integrated KFDA regulations for drug permission and review and publication of guidelines.

Comments and questions:

Dr. Vu asked whether the limit of benzo(a)pyrene was set at 5ppb due to detection limit, and Dr Park replied that the detection limit is 0.9ppb. Dr. Vu commented that the limit of benzo(a)pyrene should be as low as possible since it is a carcinogen.

Prof. Lin asked about the difference between KP and KHP, and Dr Park explained KP and KHP both have the same legal status. While KP includes commonly used herbal medicines, KHP might include some less commonly used herbal medicines.

Dr. Goda commented the use of dichloromethane and toluene as solvent in the identification of a herb. He said that even though dichloromethane and toluene is less toxic than benzene, it is still harmful. Dr Park responded that KFDA will continue to improve.

Mr Yee Shen Kuan from Singapore

- Update on regulation of Complementary Health Products (CHP).
- Current regulatory framework and brief introduction of the Chinese Proprietary Medicines (CPM) listing system.
- Review of CHP regulatory framework – background, progress, and proposed new regulatory approach.
- ASEAN TMHS PWG – updates on 8th and 9th meetings.
- Adulteration of Herbal Medicines – illegal "Power 1 Walnut" adulterated with sildenafil and high dose of glibenclamide. Other adulterated herbal products were also found to contain similar adulterants. These resulted in 10 deaths and many serious adverse effects.

Comments and questions:

Dr. Goda asked if the level of glibenclamide was consistently high in all adulterated products mentioned, and Mr. Yee replied that though the amount of glibenclamide varied in these adulterated products, the levels of glibenclamide found in many samples were very high, (some were six times higher than the therapeutic dose). This resulted several comatose cases and 10 deaths to-date.

Dr Vu asked if the adulterated products were eventually removed from the local market, and Mr Yee responded the products were removed. Enforcement and prosecution actions were also taken by HSA. Mr Yee commented that Singapore takes such adulterations very seriously due to major safety concerns, and this has

become a major global problem.

Dr Michael J Smith from Canada

- Brief introduction on regulation of Natural Health Products (NHP) and the definition of NHP.
- Regulatory framework in Canada: Food, NHPs, OTC drugs, prescription drugs.
- Currently there are 110 monographs developed.
- Licensing of NHP: Product and Site Licences.
- Future direction: evidence proportional to risk, role of pre-cleared information and enhanced generalized claims, more use of electronic and online tools and solutions, strengthened international partnerships.
- International collaborations: strengthened collaborations with western pacific including China and Hong Kong, IRCH.

Dr Duc Vu from Canada

- Introduction of progressive licensing framework – a framework originally for pharmaceutical and biologics products which may also be applicable to the safety surveillance of NHP.
- Cycle of Vigilance Activities and Vigilance Toolkit.
- Challenges related to Surveillance activities of NHP – lack of clinical trials and registries, GMP issues, language barrier etc.
- International Regulatory Cooperation: relations with China, Singapore, Australia, IRCH, FHH, etc.

Election of Next FHH Coordinating Party

After some discussions, the meeting agreed that Hong Kong be the next FHH coordinating party.

Discussion on New FHH Membership

Prof. IM Chang raised the issue of whether Canada could be considered as a future FHH Member party. Dr Goda commented that the formation of FHH was mainly due to the similarities of oriental herbal medicines used among FHH members residing in the Western Pacific region and this has resulted in close collaborations and understanding among FHH members throughout the years.

Prof. Briggs commented that consideration should be given to the fact that Health Canada is currently having close working relationship with some of the FHH members such as Australia, China, Hong Kong and Singapore, though Canada is not

part of the Western Pacific region.

Mr Yee agreed with Prof. Brigg's view. He also asked the meeting to consider if FHH is sufficiently matured and ready to accept new members and also if Canada had expressed its interest to join FHH as an ordinary member. In addition, FHH would need to consider other countries which have expressed interest to join FHH.

Prof. Briggs agreed with Mr Yee that the maturity and readiness of FHH at this point of time is an important consideration, and Prof. Briggs felt that FHH is currently not ready to open to other countries yet. He suggested that considering Canada's close relationship with a number of FHH members and attendance of Health Canada in the last few FHH Standing Committee meetings as an observer, Canada could be granted a special observer status in FHH, with the right to participate in the discussions but with no voting right.

After some discussions, the FHH Standing Committee agreed to offer Canada the above special observer status. Future requests from other countries can be considered based on the above principles.

FHH Secretariat

Mr. Frank Chan sought clarification from the FHH Standing Committee on the next FHH Secretariat. It was agreed that the FHH Secretariat would be appointed by the next FHH Coordinating Party (Hong Kong).

-End of afternoon session and meeting-

PROGRAM

FHH 2008 International Symposium on Regulatory Affairs of Herbal Medicines -Quality, Safety, and Efficacy-

Venue: Samsung Convention Center, Seoul National University
Date: November 5 (Wed), 2008

Registration

08:30 ~ 09:30 am

Opening and Photo

09:30 ~ 10:00 : Opening Address: Dr. S.Y. Chang, Chairman, Standing Committee 3
Welcome Address: Dr. Y. P. Yun, Commissioner, KFDA 4

Morning Session:

10:00 ~ 10:40 : CDER, U.S. FDA (Dr. Dou, Jinhui) 5
Quality, Safety, and Efficacy of Herbal Medicines: A Regulatory Perspective on Botanical Drugs and Dietary Supplements

10:40 ~ 11:20 : TGA, Australia (Dr. David Briggs) 26
The Regulation of Complementary Medicines in Australia and International Harmonization

11:20 ~ 12:00 : Res.Center Medicinal Plants Resources, Nat'l Inst. Biomed. Innov. (Dr. Fumiyuki Kiuchi) 44
Recent Topics in the Japanese Pharmacopoeia (JP) Regulation

12:00 ~ 12:30 : Department of Health, Singapore (Mr. YEE, Shen Kuan) 58
Regulation of Complementary Health Products in Singapore

Lunch (Crystal Room, HoAm Faculty House)

12:30 ~13:40 pm

Afternoon Session 1

13:40 ~ 14:20 : SFDA, China (Dr. Zhang, Wei) 80

Overview on Registration Administration of Traditional Chinese Medicine (TCM) in China

14:20 ~ 14:40 : Health Canada, Canada (Dr. Duc Vu and Dr. M. Smith) 97

Life-Cycle Approach in the Safety Surveillance of Health Products in Canada: Challenges and Opportunities with Natural Health Products

14:40: 15:00 : Health Canada (Dr. M. Smith) 105

Canada's Regulatory Framework in Natural Health Products

Intermission: Coffee Break

15:00 ~ 15:20

Afternoon Session 2

15:20 ~ 15:50 : National Inst. Drug Quality Control, Vietnam (Dr. Nguyen Duc Toan) 113

Affairs on Quality, Efficacy and Safety of Herbal Medicines in Vietnam

15:50 ~ 16:20 : Department of Health, Hong Kong (Mr. Robert Law) 136

The Development of Hong Kong Chinese Materia Medica (HKCMM) Standards

16:20 ~ 16:50 : KFDA, Korea (Dr. Soo jung Sohn) 165

Current Aspects of Regulations for approval of Herbal Medicinal products in Korea

16:50 ~ 17:20 : Closing Ceremony (Announcing the Next Chair Country)

厚生労働科学研究費補助金（医薬品・医療機器レギュラトリーサイエンス総合研究事業）
分担研究報告書

分担研究課題
生薬及び漢方処方の国際調和に関する研究

分担研究者　川原　信夫　国立医薬品食品衛生研究所生薬部室長

西太平洋地区４カ国（日本、中国、韓国、ベトナム）の薬局方収載生薬の各種試験法並びに規格値の比較に関する研究
—クリーンアナリシスと国際調和を指向したTLC条件の比較—

クリーンアナリシスを指向した国際調和の観点から，日本，中国，韓国，ベトナム４カ国の薬局方に収載される共通生薬について，TLCを用いた確認試験法で使用される各種有害試薬の比較表を作成し，比較試験を行った．この結果，15種の生薬のうち，同一の指標成分を有する12生薬において，すべて有害試薬を使用しない方法においても指標成分が確認可能であることが示された．特にサイコでは，現行の日本薬局方（JP）において展開溶媒にクロロホルムを用いているが，中華人民共和国薬典及びベトナム薬局方の有害試薬を用いない試験条件でも指標成分が検出可能であることが確認された．今後はJPの確認試験における試験条件の変更を視野に入れた対応が必要であると考えられた．

A．研究目的

近年，代替医療として漢方薬あるいは生薬への関心が高まる中で，名称の類似，同名異物等の問題が表面化してきている．生薬の安全性を確保し，有効利用を考える上で，生薬の正しい認識と理解が必須であり，各国で使用されている生薬に関する情報を収集，整理し，共通認識を得ることは生薬，薬用植物の国際調和の観点からも非常に重要と考えられる．このような背景から2002年３月に北京において「生薬・薬用植物に関する国際調和のための西太平洋地区討論会」（FHH : Western Pacific Region Forum for the Harmonization of Herbal Medicines）設立のための国際会議が開催された．本フォーラムでは，西太平洋地区の６カ国７地域（日本，中国，韓国，ベトナム，シンガポール，オーストラリア，香港）の生薬・薬用植物の規制に関する関係者が一堂に会し，生薬・薬用植物の安全性，有効性及び品質に関する技術的な記録とコンセンサスを提供することが目的に掲げられた．日本はその下部組織であるNomenclature and Standardization に関するSub-Committee 会議を主催することを受諾し，2002年５月，FHH 東京会議が開催された．本会議において以下の５つの専門部会（Expert working group, EWG）が設立された．

1) Nomenclature
2) Testing Method in Monographs
3) List of Chemical Reference Standards (CRS) and Reference of Medicinal Plant Materials (RMPM)
4) List of Analytically Validated Method
5) Information on General Test

これらの専門部会では，将来的な国際調和を踏まえ，各国の薬局方収載生薬について共通点と相違点を認識すること目的として，それぞれの分野に

おける各国薬局方の比較表を作成することが課題事項として議決された．EWG2 (Testing Method in Monographs) の責任者となった分担研究者は，試験法及び規格値に関する比較表の作成について担当し，昨年度までの本研究において，日本，中国，韓国，ベトナム 4 カ国の薬局方に収載された生薬の試験法，特に確認試験法における TLC 条件並びに定量法（成分含量測定法）における分析条件の詳細について比較表を作成し，比較検討を行った[1-3]．

一方，近年，環境汚染防止並びに実験者の健康保護を目的として，各種試験における有害試薬の使用を極力排除する“クリーンアナリシス”が世界的に浸透しつつある．日本においても 2002 年に公示された第十五改正日本薬局方原案作成要領，第一部，第十五改正日本薬局方原案の作成に関する細則において，有害な試薬の扱いと題して，人及び環境への影響を配慮した試験方法となるよう努めるとの記載がなされている[4]．本項目には，ベンゼン，四塩化炭素，水銀化合物等の試薬は原則使用せず，またクロロホルム，ジクロロメタン（塩化メチレン）等のハロゲン化合物は使用について慎重に検討すると記載されている．有害試薬の扱いについては，2007 年に公示された第十六改正日本薬局方原案作成要領においても継承され，特にクロロホルム等のハロゲン化合物は代替溶媒がない場合についてのみその使用を認めると記載され，より厳密な表記に変更されている[5]．

このような背景の下，2006 年の FHH 会議において，クリーンアナリシスを指向した国際調和の観点から，TLC の展開溶媒として有害試薬を使用している国は，他国の有害試薬を使用しない試験法を参考にして自国の試験法を変更する努力を行うことが重要であるとの提案がなされ，自国内で流通する生薬を用い，有害試薬を使用しない他局の試験法について検討することが承認された．本報では，FHH 諸国の局方に収載された共通生薬の TLC を用いた確認試験法について，各種試験条件の詳細な検討を行い，比較実験を行ったので報告する．

B．研究方法

本研究では FHH 参加国及び地域のうち，独自の薬局方を保有している日本，中国，韓国，ベトナムの 4 カ国の生薬に関して検討を行っている．対象となる生薬は著者の一人で EWG1 (Nomenclature) の責任者でもある酒井が作成した共通生薬リストに収載された 106 種である[2]．これらの生薬をもとに TLC を用いた確認試験における有害試薬の使用実態を調査し，比較表を作成した．次いで，日本薬局方 (JP) に記載された試料調製法により検液を調製し，TLC の比較検討を行った．本比較表の作成に使用した各国薬局方を Table 1 に示す．尚，本研究において動物由来試料を用いた実験は行わず，倫理面で大きな支障となる問題は無いと考えられる．

Table 1 Pharmacopoeias Used in Preparation of Comparative Table

日本薬局方（JP） 第 15 改正日本語版，英語版 日本薬局方外生薬規格1989年日本語版
中華人民共和国薬典　（CP） 2005 年版中国語版，英語版
大韓民国薬局方　（KP） 2002 年第 8 版韓国語版，英語版
ベトナム薬局方　（VP） 2005 年第 3 版英語版

C．研究結果

作成した比較表を Table 2 に示す．この結果，サイコ，ケイヒ，サンシュユ，ウコン，マオウ，カンゾウ，コウボク，シャクヤク，キョウニン，オウゴン，キクカ，ジャショウシ，リュウタン，カッコン及びカイカの 15 生薬において，いずれかの薬局方の確認試験に有害試薬が使用されて

いることが明らかとなった．そこでこれら 15 種の生薬について，各国局方の試験条件により TLC 検討を行った．結果を Fig. 1 に示す．15 種の生薬のうち，サンシュユ (Fig. 1-3) では JP 及び大韓民国薬局方 (KP) は，loganin を指標としているのに対し，中華人民共和国薬典 (CP) 及びベトナム薬局方 (VP) では ursolic acid を指標としていた．また，コウボク (Fig. 1-7) では JP 及び KP は magnocurarine 等のアルカロイド成分を指標としているのに対し，CP 及び VP は magnolol 及び honokiol を指標としていた．さらにキクカ (Fig. 1-11) では CP は buddeleoside を指標にしているのに対し，JP 及び VP は luteolin を指標としていた．従ってこれら 3 生薬では対象とする指標成分が異なるため，直接比較は不可能であった．

一方，サイコ (Fig. 1-1)，ケイヒ (Fig. 1-2)，ウコン (Fig. 1-4)，マオウ (Fig. 1-5)，カンゾウ (Fig. 1-6)，シャクヤク (Fig. 1-8)，キョウニン (Fig. 1-9)，オウゴン (Fig. 1-10)，ジャショウシ (Fig. 1-12)，リュウタン (Fig. 1-13)，カッコン (Fig. 1-14) 及びカイカ (Fig. 1-15) の 12 生薬では，すべて有害試薬を使用しない方法でも同一の指標成分が確認可能であることが示された。特にサイコでは，JP 及び KP でクロロホルムを使用しているのに対し，CP 及び VP では有害溶媒を使用しておらず，CP 及び VP 法を用いても国内流通生薬の確認が可能であることが明らかとなった．

D．考察

今回の比較表作成並びに比較試験により，東アジア地区 4 カ国の薬局方に収載された生薬の確認試験法で使用される有害試薬の設定状況が明らかとなった．特に CP 及び VP については有害溶媒の使用頻度が高かった．重要生薬であるサイコに関しては，有害試薬を用いないこと並びに明瞭な検出の二点において CP 及び VP 法が優れていることが明らかとなり，JP 法を変更する必要性があると考えられた．一方，ケイヒ，ウコン，マオウ，カンゾウ，シャクヤク，キョウニン，オウゴン，ジャショウシ，リュウタン及びカッコンの 10 生薬における確認試験では，クリーンアナリシスであることのみならず指標成分の *Rf* 値，スポットの形状等，様々な面において JP 法が最も適していると考えられた．

E．結論

クリーンアナリシスを指向した国際調和の観点から，日本，中国，韓国，ベトナム 4 カ国の薬局方に収載される共通生薬について，TLCを用いた確認試験法で使用される各種有害試薬の比較表を作成し，比較試験を行った．この結果，15種の生薬のうち，同一の指標成分を有する12生薬において，すべて有害試薬を使用しない方法においても指標成分が確認可能であることが示された．特にサイコでは，現行の日本薬局方において展開溶媒にクロロホルムを用いているが，CP及びVPの有害試薬を用いない試験条件でも指標成分が検出可能であることが確認された．今後はJPの確認試験における試験条件の変更を視野に入れた対応が必要であると考えられた．

F．参考文献

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G．健康危険情報

本研究において健康に危険を及ぼすような情報はない。

H．研究発表

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2．学会発表

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I．知的所有権の取得状況

特になし

Table 2 Comparative Table on TLC Solvent of Identification for Crude Drugs in CP, JP, KP and VP

No.	Latin name	TLC condition (developing solvent)
1	***Bupleurum falcatum* Linné（サイコ）**	
	CP RADIX BUPLEURI	ethyl acetate / ethanol / water (8 : 2 : 1)
	JP BUPLEURI RADIX	***chloroform*** / methanol / water (30 : 10 : 1)
	KP BUPLEURI RADIX	***chloroform*** / methanol / water (30 : 10 : 1)
	VP RADIX BUPLEURI	ethyl acetate / ethanol / water (8 : 2 : 1)
2	***Cinnamomum cassia* Blume（ケイヒ）**	
	CP CORTEX CINNAMOMI	petroleum ether / ethyl acetate (17 : 3)
	JP CINNAMOMI CORTEX	hexane / ethyl acetate (2 : 1)
	KP CINNAMOMI CORTEX	hexane / ethyl acetate (2 : 1)
	VP CORTEX CINNAMOMI	n-hexane / ***chloroform*** / ethyl acetate (4 : 1 : 1)
3	***Cornus officinalis* Siebold et Zuccarini（サンシュユ）**	
	CP FRUCTUS CORNI	toluene / ethyl acetate / formic acid (20 : 4 : 0.5)
	JP CORNI FRUCTUS	ethyl acetate / water / formic acid (6 : 1 : 1)
	KP CORNI FRUCTUS	ethyl acetate / water / formic acid (6 : 1 : 1)
	VP FRUCTUS CORNI OFFICINALIS	cyclohexane / ***chloroform*** / ethyl acetate (20 : 5 : 8)
4	***Curcuma longa* Linné（ウコン）**	
	CP RHIZOMA CURUCUMAE LONGAE	***chloroform*** / methanol / formic acid (96 : 4 : 0.7)
	JP CURCUMAE RHIZOMA	ethyl acetate / hexane / acetic acid (100) (70 : 30 : 1)
	KP CURCUMAE LONGAE RHIZOMA	***chloroform*** / methanol / formic acid (96 : 4 : 0.7)
	VP RHIZOMA CURUCUMAE LONGAE	***chloroform*** / acetic acid (9 : 1)
5	***Ephedra sinica* Stapf（マオウ）**	
	CP HERBA EPHEDRAE	***chloroform*** / methanol / concentrated ammonia (20 : 5 : 0.5)
	JP EPHEDRAE HERBA	1-butanol / water / acetic acid (100) (7 : 2 : 1)
	KP EPHEDRAE HERBA	n-butanol / water / acetic acid (7 : 2 : 1)
	VP HERBA EPHEDRAE	***chloroform*** / methanol / ammonia (20 : 5 : 0.5)
6	***Glycyrrhiza uralensis* Fischer, *G. glabra* Linné（カンゾウ）**	
	CP RADIX ET RHIZOMA GLYCYRRHIZAE	ethyl acetate / formic acid / glacial acetic acid / water (15 : 1 : 1 : 2)
	JP GLYCYRRHIZAE RADIX	1-butanol / water / acetic acid (100) (7 : 2 : 1)
	KP GLYCYRRHIZAE RADIX	n-butanol / water / acetic acid (7 : 2 : 1)
	VP RADIX GLYCYRRHIZAE	petroleum ether / ***benzene*** / ethyl acetate / glacial acetic acid (10 : 20 : 7 : 0.5)
7	***Magnolia officinalis* Rehder et Wilson var. *biloba* Rehder et Wilson（コウボク）**	
	CP CORTEX MAGNOLIAE OFFICINALIS	***benzene*** / methanol (27 : 1)
	JP MAGNOLIAE CORTEX	1-butanol / water / acetic acid (100) (4 : 2 : 1)
	KP MAGNOLIAE CORTEX	n-butanol / water / acetic acid (4 : 2 : 1)
	VP CORTEX MAGNOLIAE OFFICINALIS	***benzene*** / methanol (27 : 1)
8	***Paeonia lactiflora* Pallas（シャクヤク）**	
	CP RADIX PAEONIAE ALBA	***chloroform*** / ethyl acetate / methanol / formic acid (40 : 5 : 10 : 0.2)
	JP PAEONIAE RADIX	acetone / ethyl acetate / acetic acid (100) (10 : 10 : 1)
	KP PAEONIAE RADIX	acetone / ethyl acetate / glacial acetic acid (26 : 14 : 5)
	VP RADIX PAEONIAE	***chloroform*** / ethyl acetate / methanol / formic acid (40 : 5 : 10 : 0.2)
9	***Prunus armeniaca* Linné, *P. armeniaca* Linné var. *ansu* Maximowicz（キョウニン）**	
	CP SEMEN ARMENIACAE AMARUM	***chloroform*** / ethyl acetate / methanol / water (15 : 40 : 22 : 10)
	JP ARMENIACAE SEMEN	ethyl acetate / methanol / water (7 : 3 : 1)
	KP ARMENIACAE SEMEN	ethyl acetate / methanol / water (7 : 3 : 1)
	VP SEMEN ARMENIACAE AMARUM	***chloroform*** / ethyl acetate / methanol / water (15 : 40 : 22 : 10)
10	***Scutellaria baicalensis* Georgi（オウゴン）**	
	CP RADIX SCUTELLARIAE	toluene / ethyl acetate / methanol / formic acid (10 : 3 : 1 : 2)
	JP SCUTELLARIAE RADIX	1-butanol / water / acetic acid (4 : 2 : 1)
	KP SCUTELLARIAE RADIX	***chloroform*** / methanol / glacial acetic acid (20 : 10 : 3)
11	***Chrysanthemum indicum* Linné（キクカ）**	
	CP FLOS CHRYSANTHEMI INDICI	ethyl acetate / butanone / ***chloroform*** / formic acid / water (15 : 15 : 6 : 4 : 1)
	JP CHRYSANTHEMI FLOS	ethyl acetate / 2-butanone / water / formic acid (25 : 3 : 1 : 1)
	VP FLOS CHRYSANTHEMI INDICI	ethyl acetate / formic acid / water (8 : 1 : 1)
12	***Cnidium monnieri* Cusson（ジャショウシ）**	
	CP FRUCTUS CNIDII	toluene / ethyl acetate / n-hexane (3 : 3 : 2)
	JP CNIDII MONNIERIS FRUCTUS	hexane / ethyl acetate (2 : 1)
	VP FRUCTUS CNIDII	***benzene*** / ethyl acetate (30 : 1)
13	***Gentiana scabra* Bunge（リュウタン）**	
	CP RADIX ET RHIZOMA GENTIANAE	ethyl acetate / methanol / water (20 : 2 : 1)
	JP GENTIANAE SCABRAE RADIX	ethyl acetate / ethanol (99.5)/ water (8 : 2 :1)
	KP GENTIANAE SCABRAE RADIX	***chloroform*** / methanol / water (30 : 10 : 1)
14	***Pueraria lobata* Ohwi（カッコン）**	
	CP RADIX PUERARIAE LOBATAE	***chloroform*** / methanol / water (7 : 2.5 : 0.25)
	JP PUERARIAE RADIX	ethyl acetate / methanol / water (12 : 2 : 1)
	KP PUERARIAE RADIX	***chloroform*** / methanol / water (6 : 4 : 1)
15	***Sophora japonica* Linné（カイカ、局外）**	
	CP FLOS SOPHORAE	ethyl acetate / formic acid / water (8 : 1 : 1)
	JP SOPHORAE FLOS	***chloroform*** / methanol / water (6 : 4 : 1)
	KP SOPHORAE FLOS	ethyl acetate / formic acid / water (8 : 1 : 1)

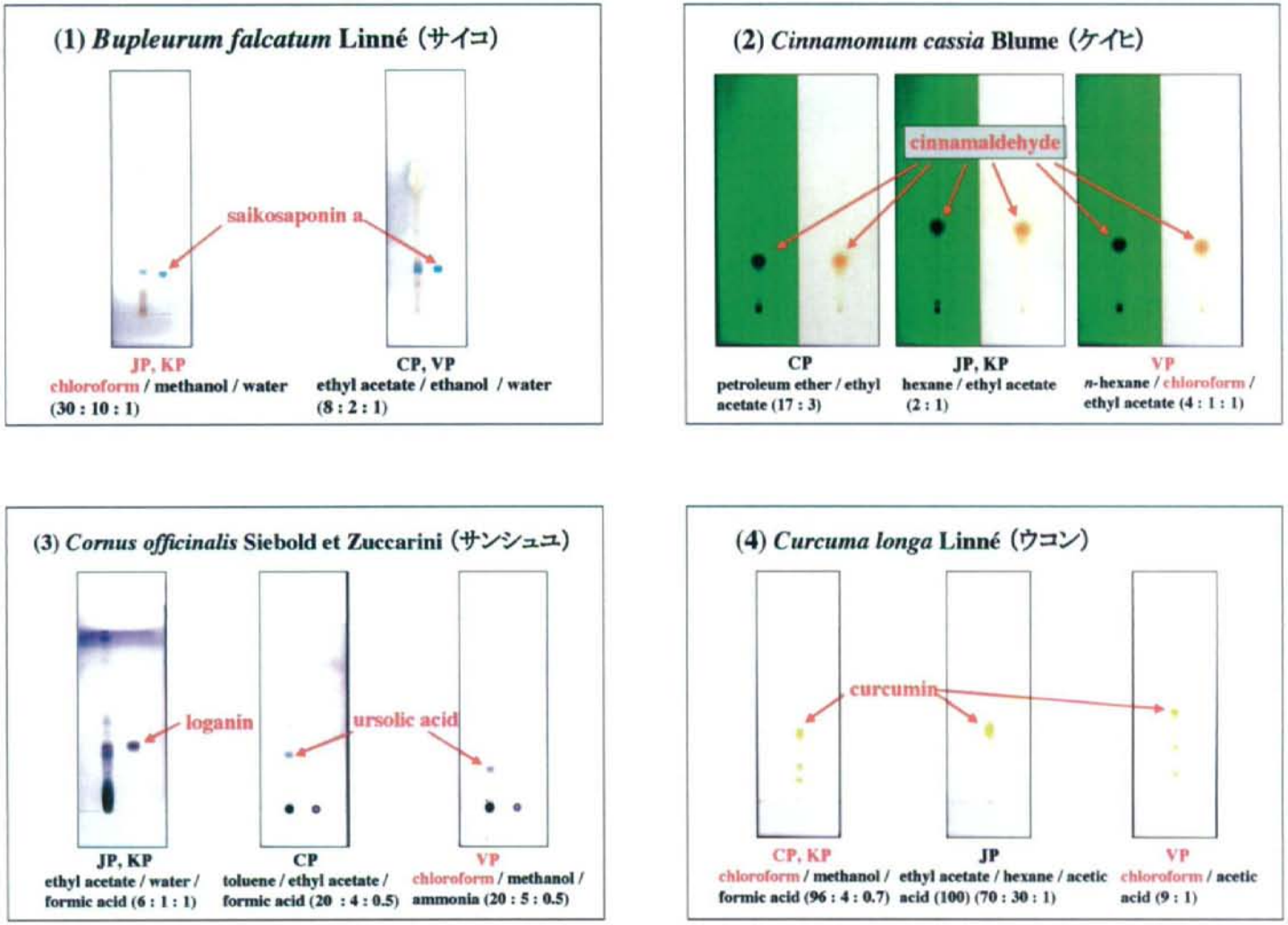
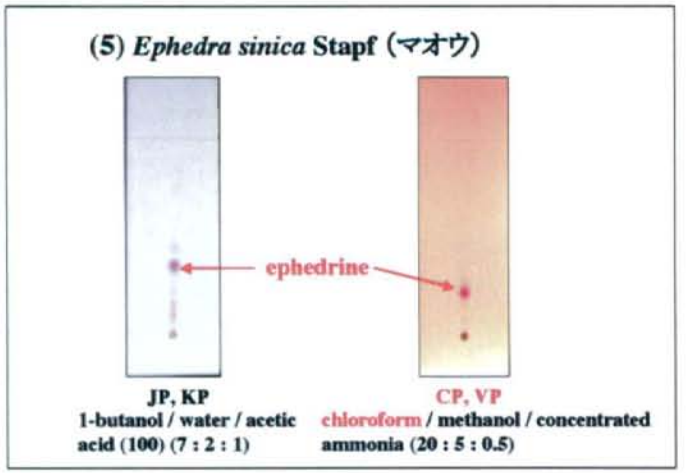
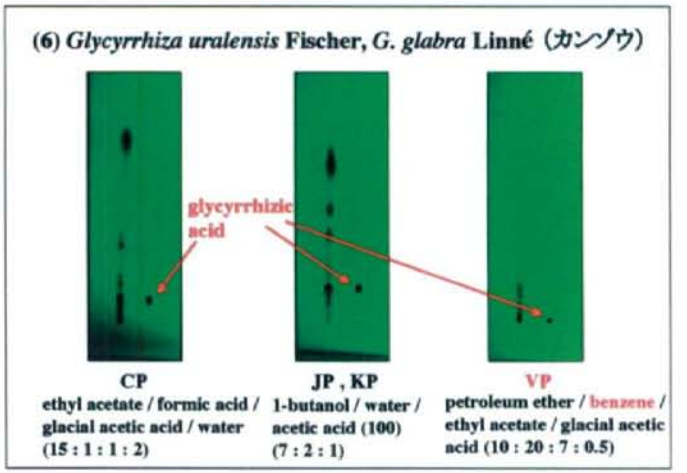
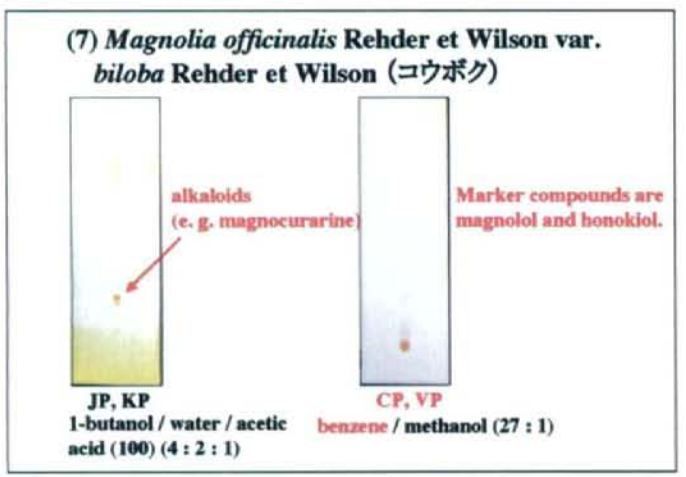
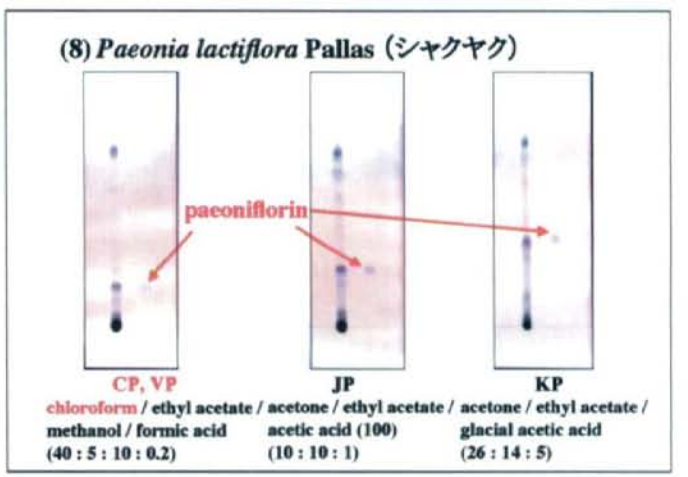


Fig. 1 Comparative Study on TLC Identification for Crude Drugs in CP, JP, KP and VP









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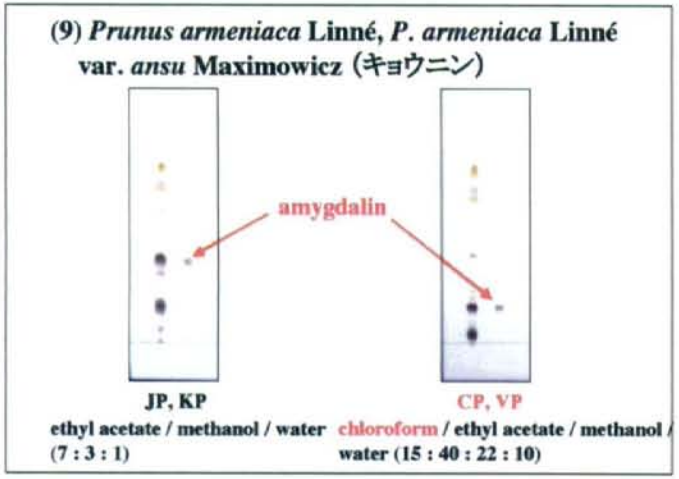

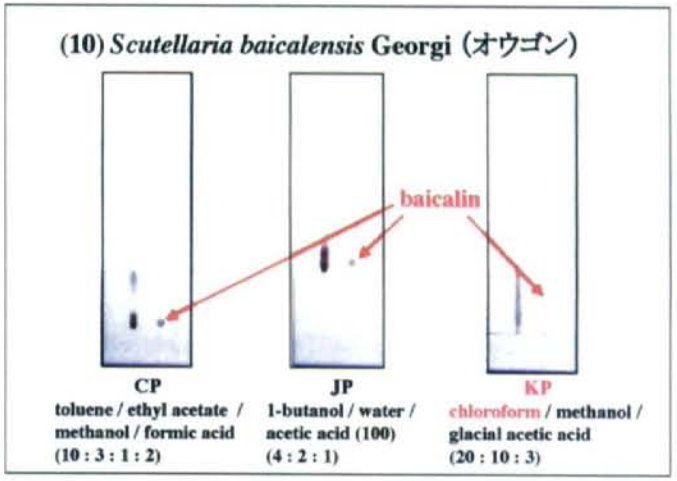

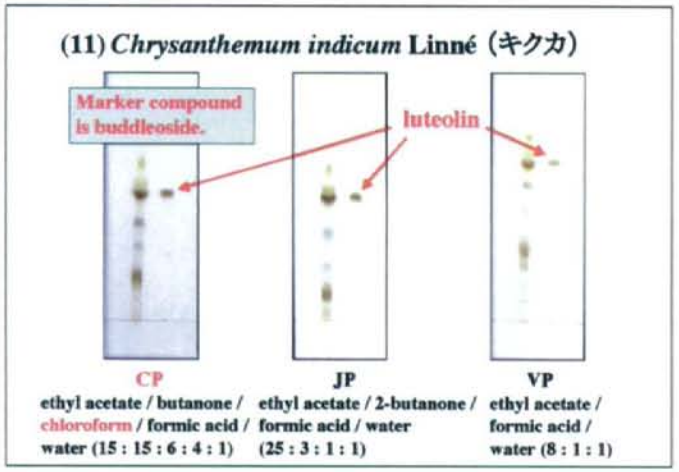

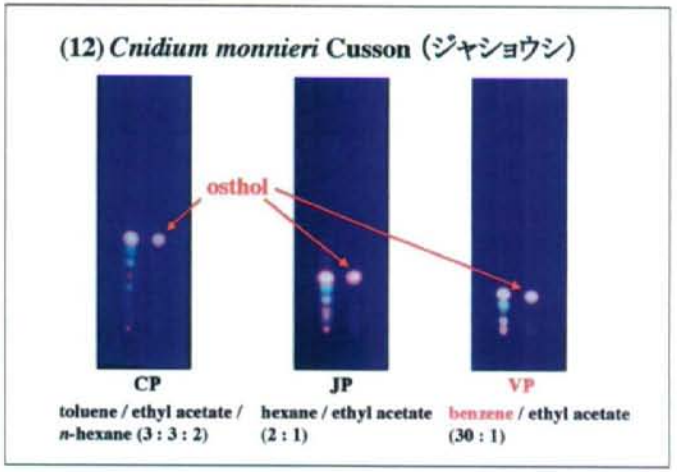

Fig. 1 Comparative Study on TLC Identification for Crude Drugs in CP, JP, KP and VP