

GP-TCM Monthly Newsletter September 2009

Consortium News

Appointment of GP-TCM Advisors:

1. Welcome Prof Xinsheng Yao, Academician of Chinese Academy of Engineering, to join GP-TCM as an Advisory Board Member. Xinsheng was Past President of Shenyang Pharmaceutical University and is currently Honorary Dean of College of Pharmacy and Director of the Institute of TCM & Natural Products, Jinan University (Guangzhou, China). Xinsheng holds honorary professorship in many leading universities and is an active organizer in national and international meetings/events. He is Convener of the Pharmaceutical Review Group of Academic Degree Committee of the State Council, Director of the Chinese Medicine Evaluation Group of National Natural Science Foundation and a Vice President of Chinese Pharmaceutical Association. He is also a member of Chinese Pharmacopoeia Commission and the councillor of Japanese Revitalization Foundation for Chinese Medicine. With over 50 years of track record in research and teaching of the chemistry of natural products, Xinsheng has presided over many national key research projects and trained 50 PhD students. He edited 3 textbooks and sits in the editorial board of a number of journals. Since 1986, more than 300 peer-reviewed papers have been published from his laboratory, among which 170 are cited by SCI. His group has filed around 70 patents and his labs have developed 4 new drugs that received official approval by State Food and Drug Administration (SFDA). **While advising the whole consortium, Xinsheng will especially advise Work Package 7 (on R&D of Chinese herbal medicines), of which Dr Tai-Ping Fan and Prof Kelvin Chan are lead scientists.**

http://www.biomedexperts.com/Profile.bme/1580775/Xinsheng_Yao
<http://jd.jnu.edu.cn/yxsx/editor/pro.asp?id=23180>

2. Welcome Prof Boli Zhang, Academician of Chinese Academy of Engineering, to join GP-TCM as an Advisory Board Member. Boli is President of Tianjin University of TCM and Director of the Ministry of Education Key Laboratory for Prescription. In addition, he is Chairman of the World Federation of Medical Education Steering Committee, Vice Chairman of Chinese Association of the Integration of Traditional and Western Medicines, Vice Chairman of the Medical Branch of the Traditional Chinese Medical Association, as well as Vice Chairman of the Medicine Branch of China's Higher Education Committee. Boli is the Principal investigator of many national key projects and has won many national awards. He serves the editorial boards of more than 20 national journals, has published more than 120 papers, filed 16 patents and trained more

than 100 postgraduate students. Boli has wide research interests and achievements and is especially applauded for his research on optimising constituent compatibility in Chinese medicines. **While advising the whole consortium, Boli will especially advise Work Package 6 (on clinical studies of Chinese herbal medicines), of which Prof. Kenneth Muir is the lead scientist.**

<http://news07.tjutcm.edu.cn/bencandy.php?fid=18&aid=244>
<http://news07.tjutcm.edu.cn/bencandy.php?fid=37&id=489>

Consortium Events and New Appointments:

1. GP-TCM Work Package (WP) Kick-off meetings are summarised as follow:

WP no	Kick-off meeting status	Date and location	Attendee number
WP1	Held	13-14 September 2009 (Kew, UK)	15+
WP2	Held	13-14 September 2009 (Kew, UK)	15+
WP3	In progress	24-25 October 2009 (Brussels)	Expected to have ~20
WP4	In Progress	17-18 October 2009 (to be confirmed)	Expected to have ~20
WP5	Held	June 2009 (Madrid, Spain)	N/A
WP6	In progress	8-9 October 2009 (Ascot, UK)	Expected to have ~20
WP7	Held (Phase I)	30 August-1 September 2009 (London, UK)	9
WP8	No info	No info	No info
WP9	N/A	No kick-off meeting	No kick-off meeting
WP10	Held	11-13 January 2009 (Beijing, China)	94

2. GP-TCM 5th Coordination Office (CO) teleconference:

The 5th Coordination Office (CO) teleconference of the GP-TCM project took place on 21st August 2009 as a Skype meeting. The meeting was attended by 8 CO members and 1 Literature Review Standard Operating Procedure (SOP) Co-Chair. Attendees discussed the following issues during the 1.5 hr meeting: FP7 reporting, project website, project management update, etc. Mr Martin Christy of Micrograde (UK) joined the teleconference and updated the CO about the current progress of the project website. The next CO teleconference will be held on the 28th September and it will be featured by updates of each Work Package by its Coordinator or his/her representative.

3. News from WP7 (on R&D):

3.1. WP7 kick-off meeting Phase I was held on 30 August-1 September 2009 at **Brunel University West London**. It was attended by Kelvin Chan, Tai-Ping Fan, Derek Fisher, Svetlana Ignatova, Daryl Rees, Ian Sutherland, Janne Üksti, Yitao Wang, Qihe Xu and Shouming Zhong.

The main conclusion from the meeting was that there was an urgent need for a universal regulatory framework for complex herbal mixtures. Without such a framework in place, major research proposals involving both academia and industry cannot be put forward as their commercial impact would be undermined. WP7 members agreed that their priority should be to support the development of harmonised guidelines for the regulation of botanicals.

The US guidelines for botanicals have been in place for some time. The Canadians supposedly have a better one and the Australian ones a better one still. The EMEA have been working on a regulatory framework of their own and there were differences of opinion on how far these had progressed. It was agreed that WP7 should set up a small sub-group to bring together an easy-to-follow statement on the various regulatory frameworks, emphasising the synergies and highlighting the differences with the aim of helping to establish a universal harmonised regulatory framework for botanicals. In addition to our local expert, Daryl Rees (Salupont Consulting), Dr Shaw Chen of the FDA and Professor Gerhard Franz (University Regensburg, Germany; Chairman of the European Working Party of TCM of the European Pharmacopoeia Commission in Strasbourg (France)) have confirmed their willingness to advise us.

Because a significant number of WP7 members was unable to attend, a Kick-off Phase 2 meeting will be held in Cambridge in late November/early December, 2009.

3.2. Welcome Prof Ian Sutherland Prof Derek Fisher to join WP7: Ian and Derek were local hosts of the WP7 Kick-off meeting. Ian is an existing member of WP1 and WP10 and Derek is an existing member of WP2.

3.3. Congratulations to Dr Tai-Ping Fan for being appointed WP7 Coordinator: As Prof Kelvin Chan is to take up a new post in Sydney, Australia in Dec 2009, his deputy Tai-Ping has succeeded him as the Coordinator of WP7. Kelvin will remain as Co-Coordinator of WP7 and a Co-Chair of the SOP Panel.

3.4. Congratulations to Dr Svetlana Ignatova (Brunel University, UK) for being appointed as Local Assistant of Dr Tai-Ping Fan and Secretary of Sub-group to bring together an easy-to-follow statement on the various regulatory frameworks. Svetlana specialises in separation and concentration techniques, particularly those involving liquid-liquid extraction and

chromatography. After she graduated from Moscow State University (Russia) in 1993, she started her research career by specialising in Counter-Current Chromatography (CCC). After earning her PhD project at Russian Academy of Sciences, Svetlana worked in an international (Russia, France and UK) project until 2003, when she joined Brunel University, playing an important role in development of CCC technology from “home-made” to “industrial competitive”. Her current research interests focus on new applications of novel liquid-liquid extraction technology in herbal extract separations, etc. She is also performing research on novel processing techniques, which become possible when both mobile and stationary phases are liquid. Svetlana is currently involved in a number of collaborative exchange programmes with China, the most active being with Tsinghua University (Beijing) and Sichuan University (Chengdu).

http://www.biomedexperts.com/Profile.bme/606731/Svetlana_Ignatova

4. News from the GP-TCM Italian Interest Group: Appointment of Dr. Mario Dell'Agli (University of Milan, Italy) as Local Assistant to Prof. Enrica Bosisio (University of Milan, Italy). Dr Enzo Tramontano joins GP-TCM as a newsletter recipient and a candidate member of the GP-TCM Italian Interest Group.

5. Welcome Prof Zhongzhen Zhao (Hong Kong Baptist University, Hong Kong, China) to join WP1 of GP-TCM, of which Prof Monique Simmonds is the lead scientist. Zhongzhen graduated from Beijing University of TCM and China Academy of Traditional Chinese Medicine in 1980s. In 1990, he obtained his PhD degree in Pharmacy in Tokyo University of Pharmacy and Life Science in Japan. As an expert in authentication and quality control of Chinese medicine, he is Director of the BPharm programme at School of Chinese Medicine, Hong Kong Baptist University. Zhongzhen serves as a member of the Chinese Medicine's Board of the Chinese Medicine Council of Hong Kong, a member of the HKSAR Department of Health Scientific Committee, a member of the International Advisory Board on Hong Kong Chinese Materia Medica Standards, and an advisor of traditional medicines of WHO and a member of the Steering Committee for Complementary and Alternative Medicine programme at Harvard Medical School. Zhongzhen has published 14 books in either Chinese or English and has published 72 peer-reviewed papers on the authentication and quality assurance of Chinese herbal medicines in Chinese, Japanese and English in the past 5 years.

http://www.hkbu.edu.hk/~scm/aboutus/eng/expert_profzhongzhenzhao.html

6. Welcome Dr Ren-wang Jiang (Jinnan University, Guangzhou, China) to join WP2 of GP-TCM, of which Prof Peter Proksch is the lead scientist. Ren-wang earned his PhD in Department of Chemistry, the Chinese University of Hong Kong in August 2002. His PhD thesis entitled *Antiviral Components against*

Respiratory Viruses from Medicinal Plants was selected to be one of the 3 winners of the Young Scholar Dissertation Awards 2002. After graduation, he continued to work in The Chinese University of Hong Kong as a postdoc. In 2006, he moved to Georgia Institute of Technology and Harvard Medical School for postdoc research. In March 2008, he was appointed a professor in Jinan University. Ren-wang's specialty is natural product chemistry. His work focuses on bioassay-guided isolation and characterisation of bioactive components from medicinal plants. He is proficient in all spectroscopic methods (UV, IR, 1D and 2D-NMR and MS) and X-ray crystallography and is experienced in both analytical and preparative HPLC, which enable him to purify many minor but interesting new compounds. He has undertaken a number of projects mainly involving the phytochemical and biological investigations of medicinal plants, and has isolated more than 300 compounds. Some of them have been tested for their bioactivities, e.g. antiviral and anticancer properties. Ren-wang has published more than 40 papers in international Journals.

http://www.biomedexperts.com/Profile.bme/642287/Ren-Wang_Jiang

7. Welcome Dr Hongcai Shang (Tianjin University of TCM, Tianjin, China) to join WP6 of GP-TCM, of which Prof Kenneth Muir is the lead scientist.

Hongcai is an Associate Professor and Vice Director at the Academy of TCM, Tianjin University of TCM, in charge of research and development. He has been a fellow of the Cochrane Collaboration "Patient Reported Outcome Method Group" and the secretary of CONSORT (Consolidated Standards of Reporting Clinical Trials) for TCM and CONSORT-STRICTA (Standards for Reporting Interventions in Controlled Trials of Acupuncture) since May 2008. He has successfully chaired and participated in more than 10 national projects and has established some new clinical research assessment methods. For example, he has led a large-scale, multi-centre, randomised controlled trial *Qishen Yiqi Dropping Pills for the Secondary Prevention of Myocardial Infarction* since 2004 and won a prize of the National Development of Science and Technology in 2004. Hongcai has published more than 60 papers and has trained more than 10 master students during the past decade.

<http://qualemedicina2000.bologna.it/it/getfile/020%20Hongcai%20Shang-%20CV%20WITH%20PICTUIRE%20.pdf>

Chinese proverb of the month

温故知新 (wen-gu-zhi-xin) – Study the past to gain new knowledge and experience.

温 (wen): study, revise, ponder

故 (gu) : past; former; old; late

知 (zhi) : know; knowledge

新 (xin) : new; up-to-date

Literature re-visited

Computational methods for Traditional Chinese Medicine: A survey. Lukman S, He Y, Hui SC. (2007) *Comput Methods Programs Biomed.* 88(3):283-94. Traditional Chinese Medicine (TCM) has been actively researched through various approaches, including computational techniques. A review on basic elements of TCM is provided to illuminate various challenges and progresses in its study using computational methods. Information on various TCM formulations, in particular resources on databases of TCM formulations and their integration to Western medicine, are analyzed in several facets, such as TCM classifications, types of databases, and mining tools. Aspects of computational TCM diagnosis, namely inspection, auscultation, pulse analysis as well as TCM expert systems are reviewed in term of their benefits and drawbacks. Various approaches on exploring relationships among TCM components and finding genes/proteins relating to TCM symptom complex are also studied. This survey provides a summary on the advance of computational approaches for TCM and will be useful for future knowledge discovery in this area.

New therapies from old medicines. Chen ST, Dou J, Temple R, Agarwal R, Wu KM, Walker S. (2008) *Nat Biotechnol.* 26(10):1077-83. Although new botanical drugs pose many challenges for both industry and the FDA, approval of the first botanical prescription drug shows they can be successfully met.

Recent papers in focus

Application of metabonomic analytical techniques in the modernization and toxicology research of traditional Chinese medicine. Lao YM, Jiang JG, Yan L. (2009). *Br J Pharmacol.* 157(7):1128-41. In the recent years, a wide range of metabonomic analytical techniques are widely used in the modern research of traditional Chinese medicine (TCM). At the same time, the international community has attached increasing importance to TCM toxicity problems. Thus, many studies have been implemented to investigate the toxicity mechanisms of TCM. Among these studies, many metabonomic-based methods have been implemented to facilitate TCM toxicity investigation. At present, the most prevailing methods for TCM toxicity research are mainly single analysis techniques using only one analytical means. These techniques include nuclear magnetic resonance (NMR), gas chromatography-mass spectrometry (GC-MS), and liquid chromatography-mass spectrometry (LC-MS), etc.; with these techniques, some favourable outcomes have been gained in the toxic reaction studies of TCM, such as the action target organs assay, the establishment of action pattern, the elucidation of action mechanism and the exploration of action material foundation. However, every analytical technique has its advantages and drawbacks, no existing analytical technique can be versatile.

Multi-analysed techniques can partially overcome the shortcomings of single-analysed techniques. Combination of GC-MS and LC-MS metabolic profiling approaches has unraveled the pathological outcomes of aristolochic acid-induced nephrotoxicity, which cannot be achieved by single-analysed techniques. It is believed that with the further development of metabonomic analytical techniques, especially multi-analysed techniques, metabonomics will greatly promote TCM toxicity research and be beneficial to the modernization of TCM in terms of extending the application of modern means in the TCM safety assessment, assisting the formulation of TCM safety norms and establishing the international standards indicators.

Aconitum in Traditional Chinese Medicine - A valuable drug or an unpredictable risk? Singhuber J, Ming Zhu M, Sonja Prinz S, Kopp B (2009). *J Ethnopharmacology*. *Aconitum* species have been used in China as an essential drug in Traditional Chinese Medicine (TCM) for 2000 years. Reviewing the clinical application of *Aconitum*, their pharmacological effects, toxicity and detoxifying measures, herb-herb interactions, clinical taboos, famous herbal formulas, traditional and current herbal processing methods based upon a wide range of literature investigations serve as a case study to explore the multidisciplinary implications of botanicals used in TCM. The toxicological risk of improper usage of *Aconitum* remains very high, especially in countries like China, India and Japan. The toxicity of *Aconitum* mainly derives from the diester diterpene alkaloids (DDAs) including aconitine (AC), mesaconitine (MA) and hypaconitine (HA). They can be decomposed into less or non-toxic derivatives through Chinese traditional processing methods (Paozhi), which play an essential role in detoxification. Using Paozhi, the three main forms of processed aconite – Yanfuzi, Heishunpian and Baifupian – can be obtained (CPCCommission, 2005). Moreover, some new processing techniques have been developed in China such as pressure-steaming. The current development of fingerprint assays, in particular HPLC, has set a good basis to conduct an appropriate quality control for TCM crude herbs and their ready-made products. Therefore, a stipulation for a maximum level of DDA content of *Aconitum* is highly desirable in order to guarantee the clinical safety and its low toxicity in decoctions. Newly developed HPLC methods have made the accurate and simultaneous determination and quantification of DDA content interesting. doi:10.1016/j.jep.2009.07.031

雷公藤



Chinese herb Lei Gong Teng (Thunder God's Vine; *Tripterygium wilfordii*) is better than Sulfasalazine in controlling active rheumatoid arthritis

A phase 2b clinical trial results of an extract of the Chinese herb Lei Gong Teng, the root of *Tripterygium wilfordii* Hook F (TwHF), in patients with active rheumatoid arthritis were published in the latest issue of the *Annals of Internal Medicine*.

This randomized, double-blind, active-controlled study was conducted at 11 sites in the U.S., under the auspices of the US National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Patients received the TwHF extract 180 mg/day, divided TID (n=60) or Sulfasalazine (SSZ) 2 g once daily (n=61) for 24 weeks. The primary endpoint of the study was a 20% improvement in disease activity by American College of Rheumatology (ACR) criteria (ACR20).

At six months, 67.6% of TwHF -treated patients vs. 36.0% of SSZ-treated patients achieved at least a 20% improvement in disease activity (p=0.02). In the TwHF group, ACR 50 and ACR 70 responses were observed in 54.1% and 37.8% of patients. In the SSZ group, both ACR50 and ACR70 responses were 4.0% (p<0.001 for all comparisons). Significant improvement was seen with all endpoints as early as 2 weeks, including physical function as measured by the HAQ (Health Assessment Questionnaire) disability score. Patients receiving TwHF had no progression of mean joint space narrowing and erosion scores.

The most common adverse events in both treatment arms were gastrointestinal tract disturbances. Serious adverse events occurred in 3 patients on TwHF and 7 patients on SSZ. Discontinuations for adverse events occurred in 8 (13%) TwHF patients and 17 (28%) SSZ patients.

A proprietary extract of TwHF is being developed by Phytomedics as an oral, disease modifying anti-rheumatic drug in the US. TwHF exerts its potent anti-inflammatory and immunosuppressant activities through unique modes of action. Phytomedics is in talk with FDA for the next phase of this drug candidate. The phase III trial is said to have been convened.

In China, TwHF is has been used for decades for rheumatoid arthritis and other auto-immune disorders. Clinical experience in China showed that alternate use of TwHF and steroid anti-inflammatories is the best treatment regimen for rheumatoid arthritis with optimal clinical benefits and safety profiles.

Meeting reports

8th Annual Meeting of Consortium for Globalization of Chinese Medicine (CGCM) was held 26-28 August in Nottingham University. Qihe Xu represented GP-TCM and spoke on international collaborations. He made good contacts with Head of National Center for Complementary & Alternative Medicine (NCCAM) of the NIH, Dr Josephine Briggs, CGCM Chairman Prof Yung-Chi Cheng and Vice President of European Federation of Biotechnology, Prof Brian Clark.

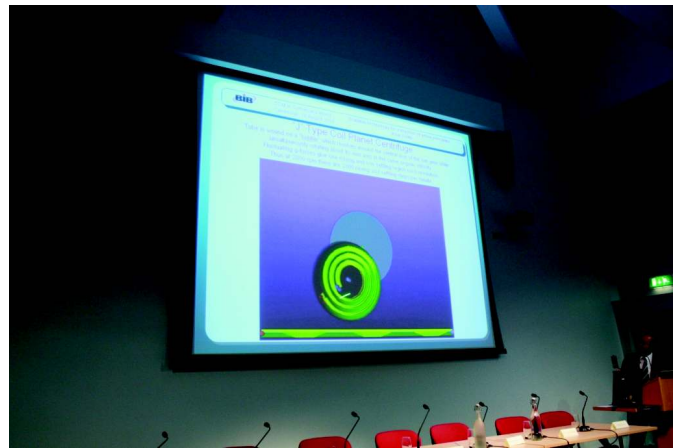
The First Cambridge TCM Forum (in collaboration with CGCM) - *Traditional Chinese Medicine in Tomorrow's World*, 28 August 2009. Presided by Dr Kate Pretty, Pro-Vice-Chancellor (International Strategy) of the University of Cambridge, this highly successful forum attracted ~200 CGCM members, UK scientists, clinicians, IP lawyers, investment bankers and drug developers. Guests of honour included 12 Fellows of the Royal Society and Lord Mark Marlesford, representing All Party Parliamentary China Group. During the Gala Dinner in King's College, all 4 regions of China were represented on the top-table, symbolising closer collaborations. The subsequent tour to **Brunei Institute for Bioengineering and Royal Botanic Gardens Kew** completed an enjoyable and productive trip for overseas and UK delegates alike.



Prof Yung-Chi Cheng (Yale) giving Plenary Lecture 1: *Studies of PHY906, a Chinese medicinal formula, as adjuvant therapy for cancer patients under chemotherapy*



Prof Monique Simmonds (Kew Gardens) giving Hot Topic 1: *Authentication and Conservation of species used in TCM*



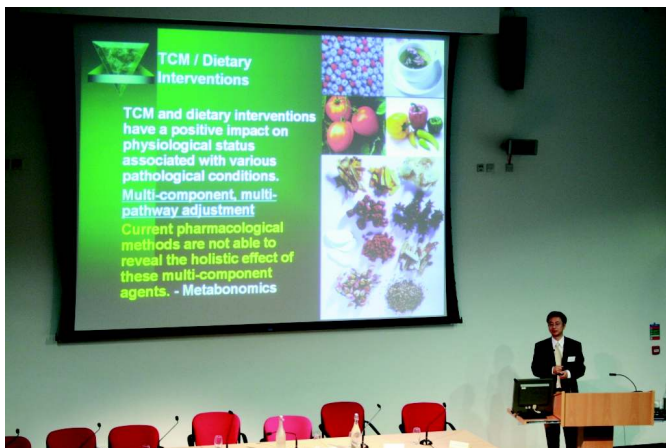
Prof Derek Fisher (Brunel) giving Hot Topic 2: *Scalable technology for the extraction of active principles from Chinese herbal medicines*



Panelists: Prof Brian Clark (Aarhus), Prof Steve Ley (Cambridge), Prof Nancy Ip (Hong Kong U. Science & Technology), Prof Ning-Sun Yang (Academia Sinica), Prof Athene Donald (Cambridge), Dr Songxuan Ke (Middlesex)



Prof Peter Hylands (King's College London) giving Plenary Lecture 2: *Chemometric, metabolomic and chemoinformatic studies on TCM*



Prof Wei Jia (North Carolina, Greensboro) giving Hot Topic 3: *Deciphering traditional Chinese medicine using holistic metabolic signatures*



Panelists: Prof Nicky Robinson (Thames Valley), Dr Jidong Wu (Middlesex), Prof Alan Barrell (Cambridge), Dr Vivian Wong (Hong Kong Hospital Authority), Prof Michael Waring (Cambridge), Prof Michael Heinrich (London School of Pharmacy) and Dr Tai-Ping Fan (Cambridge).



Dr Yita Lee (Sinphar Group) answering questions on Hot Topic 4: *Challenges in botanical product development - Sinphar's perspective*



Dr Daryl Rees (Salupont) giving Hot Topic 5: *From TCM to commercialised products in the West*

Events and meetings

2009 Shanghai International Conference on Traditional Chinese Medicine and Natural Medicines (S-TCM 2009) 17-18 October 2009.
Contact Prof De-an Guo daguo@mail.shcnc.ac.cn

Conference Theme:

Globalization and Regulation Issues of Traditional Chinese Medicine and Natural Medicine

Scientific Topics:

1. Drug discovery from natural sources
2. Bioactive natural products
3. Quality and safety of traditional Chinese medicines
4. Systems biology of traditional Chinese medicine
5. Phytochemical analysis of herbal medicines
6. Modern approaches to traditional Chinese medicine

WorldPharma2010 (16th World Congress on Basic and Clinical Pharmacology), 17-23 July 2010, Copenhagen, Denmark. This congress will include a 3-day focused conference (21-23 July, 2010) on *Natural Products: Past and Future?* For further information, please visit www.worldpharma2010.org or email: WorldPharma2010@ics.dk.

In the next issue:

(i) Welcome Prof Brian Clark and Prof Rudi Bauer *et al.* to join GP-TCM as Advisors, non-beneficiary members/experts; (ii) Report of the 6th CO teleconference; (iii) Report of WP1 and WP2 Joint Kick-off Meeting...

Thanks to Prof **Xinsheng Yao** (China), Prof **Boli Zhang** (China), Prof **Ren-wang Jiang** (China), Dr **Hongcai Shang** (China), Prof **Zhongzhen Zhao** (China), Dr **Svetlana Ignatova** (UK), Dr **Daryl Rees** (UK), Dr **You-Ping Zhu** (the Netherlands), Prof **Brigitte Kopp** (Austria), Dr **Stephanie Mak** (UK) and Dr **Halil Uzuner** (UK) for their contributions.