Good Practice in Traditional Chinese Medicine Research in the Post-genomic Era

GP-TCM

223154

D3.9

Review papers published in scientific journals

Document description	
Name of document	Review papers published in scientific journals
Abstract	The present report presents the papers that were published in J. Ethnopharmacology, the reviews considered for preparation as well as the talks given by WP3 members along which the activities of WP3 were presented.
Document identifier	D3.9
Document class	Deliverable
Version	1
Author(s)	Prof. Pierre Duez, Prof. Liu Xinmin and other WP3 members
Date of creation	10th April 2012
Date of last modification	28th April 2012
Status	Final
Destination	European Commission
WP number	WP3

TABLE OF CONTENTS

1 OBJECTIVES OF REPORT D3.9

The present report presents the papers that were published in J. Ethnopharmacology as well as the talks given by WP3 members along which the activities of WP3 were presented.

2 PUBLISHED REVIEWS

Three reviews were organized and published.

a) Journal of Ethnopharmacology, http://dx.doi.org/10.1016/j.jep.2012.01.059**.**

Contents lists available at SciVerse ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Review of current and "omics" methods for assessing the toxicity (genotoxicity, teratogenicity and nephrotoxicity) of herbal medicines and mushrooms

Moustapha Ouedraogo[a,b], Thomas Baudoux[c], Caroline Stévigny[b], Joëlle Nortier[c], Jean-Marie Colet[d], Thomas Efferth[e], Fan Qu[f], Jue Zhou[g], Kelvin Chan[h,i], Debbie Shaw[j], Olavi Pelkonen[k], Pierre Duez[b,*]

[a] Laboratory of Pharmacology and Toxicology, Health Sciences Faculty, University of Ouagadougou, 03 BP 7021 Ouagadougou 03, Burkina Faso
[b] Laboratory of Pharmacognosy, Bromatology and Human Nutrition, Université Libre de Bruxelles (ULB), CP 205-9, B-1050 Brussels, Belgium
[c] Experimental Nephrology Unit, Faculty of Medicine, Université Libre de Bruxelles (ULB), Belgium
[d] Service de Biologie humaine et Toxicologie, Université de Mons (UMONS), "Le Pentagone" Aile 2A, 6 Avenue du champ Mars, 7000 Mons, Belgium
[e] Department of Pharmaceutical Biology, Johannes Gutenberg University, Staudinger Weg 5, 55128 Mainz, Germany
[f] Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, 310006, Zhejiang, China
[g] College of Food Science and Biotechnology, Zhejiang Gongshang University, Hangzhou, 310012, Zhejiang, China
[h] Centre for Complementary Medicine Research, University of Western Sydney, Sydney, NSW 2560, Australia
[i] Faculty of Pharmacy, the University of Sydney, Sydney, NSW 2006, Australia
[j] Guy's and St Thomas NHS Trust London SE1 9RT, UK
[k] Department of Pharmacology and Toxicology, University of Oulu, 90014 Oulu, Finland

The increasing use of traditional herbal medicines around the world requires more scientific evidence for their putative harmlessness. To this end, a plethora of methods exist, more or less satisfying. In this post-genome era, recent reviews are however scarce, not only on the use of new "omics" methods (transcriptomics, proteomics, metabonomics) for genotoxicity, teratogenicity, and nephrotoxicity assessment, but also on conventional ones. The present work aims *(i)* to review conventional methods used to assess genotoxicity, teratogenicity and nephrotoxicity of medicinal plants and mushrooms; *(ii)* to report recent progress in the use of "omics" technologies in this field; *(iii)* to underline advantages and limitations of promising methods; and lastly *(iv)* to suggest ways whereby the genotoxicity, teratogenicity, and nephrotoxicity assessment of traditional herbal medicines could be more predictive.

Literature and safety reports show that structural alerts, in silico and classical in vitro and in vivo predictive methods are often used. The current trend to develop "omics" technologies to assess genotoxicity, teratogenicity and nephrotoxicity is promising but most often relies on methods that are still not standardized and validated. Hence, it is critical that toxicologists in industry, regulatory agencies and academic institutions develop a consensus, based on rigorous methods, about the reliability and interpretation of endpoints. It will also be important to regulate the integration of conventional methods for toxicity assessments with new "omics" technologies.

b) Journal of Ethnopharmacology, http://dx.doi.org/10.1016/j.jep.2012.01.051**.**

Contents lists available at SciVerse ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Pharmacovigilance of herbal medicine

Shaw Debbie[a,*], Ladds Graeme[b], Duez Pierre[c], Williamson Elizabeth[d], Chan Kelvin[e,f]

[a] Chinese Medicine Advisory Service, Medical Toxicology Information Services, Guy's & St Thomas NHS Foundation Trust, Guy's Hospital, London SE1 9RT, UK
[b] Pharsafer 29 Frederick Sanger Road, Guildford, Surrey GU2 7YD, UK
[c] Université Libre de Bruxelles CP 205/9, Bd du Triomphe, 1050 Bruxelles, Belgium
[d] The School of Pharmacy, University of Reading, Whiteknights, Reading RG6 6AJ, Berkshire, UK
[e] Centre for Complementary Medicine Research, University of Western Sydney, NSW 2560, Australia
[f] Faculty of Pharmacy, The University of Sydney, NSW 2006, Australia

Pharmacovigilance is essential for developing reliable information on the safety of herbal medicines as used in Europe and the US. The existing systems were developed for synthetic medicines and require some modification to address the specific differences of medicinal herbs. Traditional medicine from many different cultures is used in Europe and the US which adds to the complexities and difficulties of even basic questions such as herb naming systems and chemical variability. Allied to this also is the perception that a 'natural' or herbal product must be safe simply because it is not synthetic which means that the safety element of monitoring for such medicines can be overlooked because of the tag associated with such products. Cooperation between orthodox physicians and traditional practitioners is needed to bring together the full case details. Independent scientific assistance on toxicological investigation, botanical verification can be invaluable for full evaluation of any case report. Systematic pharmacovigilance is essential to build up reliable information on the safety of herbal medicines for the development of appropriate guidelines for safe effective use.

c) **Journal of Ethnopharmacology,** http://dx.doi.org/10.1016/j.jep.2012.01.058**.**

Contents lists available at SciVerse ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Pharmacovigilance practice and risk control of Traditional Chinese Medicine drugs in China: Current status and future perspective

Li Zhang[a], Jingbo Yan[b], Xinmin Liu[c], Zuguang Ye[d,*], Xiaohui Yang[b], Ronald Meyboom[e], Kelvin Chan[f,g], Debbie Shaw[h], Pierre Duez[i,**]

[a] Center for Drug Reevaluation, SFDA, Beijing 100045, China
[b] Dongfang Hospital, Beijing University of Chinese Medicine, Beijing 100078, China
[c] Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences, Beijing 100193, China
[d] China Academy of Chinese Medical Sciences, Beijing 100700, China
[e] Department of Pharmacoepidemiology and Clinical Pharmacology, University of Utrecht, The Netherlands
[f] Centre for Complementary Medicine Research, University of Western Sydney, NSW 2560, Australia
[g] Faculty of Pharmacy, The University of Sydney, NSW 2006, Australia
[h] Guy's and St Thomas NHS Trust, London SE1 9RT, UK
[i] Laboratory of Pharmacognosy, Bromatology and Human Nutrition, Université Libre de Bruxelles (ULB), CP 205-9, B-1050 Brussels, Belgium

Traditional Chinese Medicine (TCM), including Traditional Chinese Medicine drugs (TCM drugs), has been playing a very important role in health protection and disease control for thousands of years in China. Relying on natural products, mainly of herbal origin, used either as raw materials for decoction, as prepared herbal medicines or as formulated traditional medicines, TCM is still widely accepted by Chinese people, especially for chronic diseases treatment. This extensive use warrants safety measures and so TCM drug safety monitoring and risk management are becoming increasingly important tasks for the Chinese State Food and Drug Administration (SFDA).

The Adverse Drug Reaction (ADR) monitoring system in China was established both for western and TCM drugs in 1989 as a voluntary reporting system with a National Center collecting and compiling reports. About 10% - 15% of the ADR reports received by the National Center are related to TCM drugs and mainly pertaining to the formulated products.

Serious or multi-case reports on individual TCM drug or formulated products are detailed in the Chinese ADR Information Bulletin to inform the public and Drug Administrative authorities for risk management. In certain cases, the suspension of a particular TCM preparation is decided by SFDA China.

The model of safety monitoring and risk management of TCM drugs is still under exploration. Indeed, the characteristics and risk factors associated with these drugs require both proper understanding and control of the risk by strengthening standardization of clinical applications, basic science research, quality control in manufacturing, exploration of the actives monitoring methodology and enhancement of international communication and cooperation.

3 FURTHER REVIEWS CONSIDERED

The following reviews are being considered by WP3 members; if enough material can be collected, the group will work towards publication of these items.

a) Review of current and "omics" methods for assessing the toxicity (hepatotoxicity, and neurotoxicity) of herbal medicines and mushrooms

b) Potential genotoxicity of traditional Chinese medicinal plants and phytochemicals: an overview

c) Detoxification by processing and/or by mixing different hebs: scientific basis?

d) Review of neurotoxicity of Chinese herbal medicines

e) Review of Classifications of toxicity important to Chinese herbal medicines.

4 TALKS IN WHICH WP3 ACTIVITIES WERE PRESENTED

- A joint workshop was organized with WP1, WP3, and WP7 members and experts of the EDQM European Pharmacopoeia TCM workgroup (Strasbourg, France, 29 September 2011). P. Duez presented a short talk: *"GP-TCM – Introduction & brief progress of WP3"*.
- Prof. Liu Xinmin organized mini-workshop in IMPLAD, Beijing in Sept. 2011 for discussing review manuscripts on pharmacovigilance.
- X. Liu and Z. Ye presented GP-TCM activities at the *"International Symposium of Drug Discovery from Chinese Materia Medica and its Sustainable Use"*, Beijing, 12/2011 (organized by Specialty Committee of Chinese Materia Medica, World Federation of Chinese Medicine Societies, jointly with IMPLAD ,Chinese Academy of Medical Sciences.
- Prof. Liu Xinmin, Dr. Andre presented GP-TCM activities at the *"International Symposium of Drug Delivery system of Chinese Materia Medica and it's application"* in Wuhan city, Hubei Province, China, 11/2011 (organized by Specialty Committee of *Drug Delivery system of Chinese Materia Medica*, World Federation of Chinese Medicine Societies.
- One workshop was organized (09/2011) by Prof. Liu XInmin in Louzhou Medical College, Sichuan Province, China, for discussing review manuscripts on neuro-toxicity of CHMs. Prof. Williamson from Reading University, UK gave crucial comments by email, one joint manuscript titled "Classifications of toxicity of CHMs" is under preparation.
- P. Duez organized a 3-months writing session for WP3 reviews, jointly with M. Ouédraogo, C. Stévigny, J. Nortier and T. Baudoux.
- J. Nortier was invited in Taipei, Taiwan by the Taiwan Urological Association (01/2012) for a Symposium *"Aristolochia-related nephropathy and urothelial carcinoma"* to present a lecture about her clinical and experimental experience in aristolochic acid nephropathy.
- P. Duez was invited for conferences that allowed to introduce WP3 activities at
    - The Guangzhou Institute of Drug Control ("Authentication and quality assessment of TCM", Guangzhou, China (09/2009)
    - The University for Traditional Chinese Medicines ("Chinese - European Exchange forum on TCM"), Chengdu, China (09/2009),
    - The Institut des Hautes Etudes de Belgique (10/2010),
    - The Université Al Hawache, Homs, Tal-Kalack, Syrie (12/2010)
    - The University of Lubumbashi, RD Congo (01/2011),

- The Seminar on THMP registration in the EU, Beijing, China (10/2011),
- The Workshop on herbal exports to US & EU markets, Chengdu, China (10/2011),
- The Agronomic University of Hanoi, Vietnam (03/2012).