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

GP-TCM

223154

D5.12

Future research priority areas in animal studies of CHM

Document description	
Name of document	Future research priority areas in animal studies of CHM.
Abstract	The published studies in CHM and animal models have been analysed and several recommendations are proposed.
Document identifier	D5.12
Document class	Deliverable
Version	1
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Date of creation	4th November 2011
Date of last modification	25th November 2011
Status	Final
Destination	European Commission
WP number	WP5

FUTURE PRIORITY AREAS ARE RECOMMENDED IN ANIMAL STUDIES OF CHM

We have stated the need of animal studies to give evidence-based proof of the efficacy of the CHM formulations. This need led us to identify the more usual problems of the animal studies of CHM in order to give recommendations for further studies. We chose cancer as a sample of the whole field of animal studies of CHM and the experimental design of papers in English written between 2000 and 2009 was analyzed. Most of the papers surveyed did not use randomization (72%) or blinding (98%) to reduce bias in animal selection and outcome assessment. Only 50% of studies used group sizes >5, 40-50% had appropriate statistical analyses and included a relevant control. There was general evidence of efficacy of the test CHMs in most reported papers-the level of which did vary but the CHMs reported were generally shown to be highly efficacious. However, variation in tumour size within experiments was not shown in 41% of studies but where shown was >10% in 34% studies. In addition there was very few cases where biomarkers of response linked to the mechanism of action of the test CHM were used. The clinical relevance of these studies was difficult to dissect out and compare to Western medicines since i) the majority of studies were performed with treatment starting early in the study (39%), whereas only 19% of studies allowed tumours to become established before clinically-relevant treatment of established lesions was initiated. Furthermore, in a large portion of studies it was unclear when treatment was started (42%). ii) only 20% studies compared test CHM effects with conventional medicine standard of care agents and iii) there was little report of toxicity (where defined, it was associated to weight loss). In addition only 14% studies stated adherence to animal welfare guidelines and ethical committee compliance.

As stated in the Handbook on Good Practice in the reporting of CHM experimental work (Buriani & Hylands, 2011), crude herbal drugs and particularly Chinese formulae are natural products and their chemical composition varies depending on several factors, such as the geographic source of the plant material, the climate in which the plant was grown, and time of harvest. Commercially available herbal medicinal products also vary in their composition, both quantitatively and qualitatively, from batch to batch. Even when herbal products are standardized for content of known active or marker compounds there is variation in the concentrations of other constituents that can result in differences in pharmacological activity. Also, preparation methods vary significantly (including the means of extraction, if any; whether the material is heated for a prolonged period, etc) which could also contribute to variability in chemical composition and hence pharmacological activity. In particular, it is a very frequent practice to use herbs of unknown origin, which are subjected to a variety of extraction procedures to render extracts whose composition is unknown.

RECOMMENDATIONS:

Taking into account the IUPAC protocols (Mosihuzzaman & Choudhary, 2008), the GP-TCM Handbook on Good Practice in the Reporting of CHM Experimental Work (Buriani & Hylands, 2011), and the most important problems found in the sample of publications on CHM studies in animals, we have written a short list of minimal quality criteria. These criteria should be taken into account to assure a consistent and acceptable quality herbal product which will be used in animal models of disease and are summarized as follows:

To assure a consistent and acceptable quality herbal product

General records

stage of collection, parts of the plant collected, regional status, details of any voucher specimen

Authentication of the herbal raw material

taxonomic, macroscopic & microscopic

Standardization (to provide quantitative and semiquantitative information about the main active constituents or marker compounds present in the crude drug or herbal products)

Chromatographic and sophisticated modern techniques: spectroscopic evaluationUV–vis spectrophotometry, TLC, HPTLC , HPLC-mass spectrometry, NMR, etc

Physical parameters: organoleptic evaluation, viscosity, moisture content, pH, disintegration time, friability, hardness, flowability, sedimentation and ash value.

Microbiological contamination

Pesticide residue

Heavy metal analysis

Extraction

Solvent used and ratio, time, temperature, yield

When reporting the results of a study, it is necessary to indicate all the details related with the aspects described above. In addition, in the case of processed plant and/or mixtures of plants or of a proprietary product, the batch number of the herbal product should be clearly indicated.

NETWORKING AND ACHIEVEMENTS:

Successful contribution of WP5 and WP4 members to this deliverable took place. Experts in animal models, in vitro models as well as cancer have revised bibliography regarding TCM in animal models and delivered reflexions in documents that have been considered as valuable material to build this deliverable and most importantly, the review “Animal studies of Chinese Herbal Medicine from the perspective of conventional medicine” already submitted to J Ethnopharmacology. On the other hand, several issues addressed in the preparation of this draft have been shared with WP4 and contribute to the review “Omics techniques in systems

biology approaches to Traditional Chinese Medicine research: present and future" recently submitted to J Ethnopharmacology.

Deliverable 5.11 was originally planned in order to suggest Future Priority areas in animals models in CHM. Through the extensive literature review made by WP5, diabetes, cancer as well as neurological diseases are appropriated fields for animal studies in CHM, since CHM exhibited herb preparation, appropriated animal models for diseases as well as appropriated parameters to be analyzed in the models are the critical issues to be improved in those studies, as it was detailed in the review "Animal studies of Chinese Herbal Medicine from the perspective of conventional medicine" already submitted to J Ethnopharmacology.

REFERENCES

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