

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

GP-TCM

223154

D6.6

Agreed conclusions of literature review reported

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D6.6 - Report on agreed conclusions of the review of literature:

1. DEFINING THE SCOPE OF THIS REVIEW:

There is a tremendous body of literature, both in China and increasingly in the West, on the evaluations of the clinical effectiveness of traditional Chinese medicine (TCM) for virtually all diseases known to man.

As such it was impossible for the work-package members to attempt any other than a selective review. Following discussions at the kick-off meeting the 3 factors were used to focus a literature review and to use such chosen conditions to provide a wider overview of research in Chinese herbal medicine (CHM)..

1.1. The group will restrict their focus to a limited number of conditions that: (i) Are an important public health condition; (ii) Do not have an effective Western medicine; (iii) A member within the work package had particular interest and expertise in; (iv) Other conditions in which there is recent evidence of promise.

On this basis the following conditions were identified and are considered further in D6.5:

1.1.1. Endometriosis.

1.1.2. Polycystic ovary disease.

1.1.3. Prostate diseases including benign, pre-malignant and malignant.

1.1.4. Breast cancer, including early disease and treatment of side effects in western therapy.

1.1.5. Selected skin diseases - in particular, eczema/psoriasis.

1.1.6. Irritable bowel disease.

1.1.7. Impaired glucose tolerance.

1.1.8. Other conditions in which there have been recent studies into TCM clinical use, these included :

- *primary dysmenorrhea*
- *schizophrenia*
- *nephritic syndrome*
- *angina*
- *type II diabetes mellitus*
- *severe acute respiratory syndrome (SARS)*
- *acute pancreatitis*
- *hepatitis B*
- *common cold*
- *viral myocarditis*
- *Alzheimer's disease*
- *ischemic stroke*
- *heart failure.*

1.2. For the above conditions, the literature review focuses on Cochrane reviews, as these have the highest standard of credibility, and the purpose of the review was to identify further “early wins” for the development of future clinical trial suggestions.

1.3. Special attention is paid to reviews from the very recent period, as these reviews will themselves have covered the earlier works.

The following report therefore summarises the positive evidence supporting CHM meeting the above conditions. The work was undertaken by Dr Andrew Flower and led by Professor George Lewith, and subsequently edited by Prof Ken Muir and other WP6 members.

It is not intended as a full systematic review of all published literature. It does not include systematic reviews that were inconclusive. It also excludes several hundred randomised controlled trials (RCT's) reported in journals of Chinese medicine but such additional data are commented on later. Instead it focuses on systematic reviews published in the Cochrane library. These provide more robust evidence than can be obtained from most individual clinical trials. It is of note that one exception to this is: an interesting and methodologically rigorous RCT comparing CHM and a conventional drug in the treatment of rheumatoid arthritis that is, published in a prestigious journal in English. Finally, it provides details of the innovative CHM Database Project and comments on the future use of systems biology and other “omics” approaches to further evaluate Chinese medicine.

Recent research studies, in keeping with the majority of previous work, do not provide conclusive evidence of the effectiveness of CHM according to the highest standards of rigorous Western “evidenced based” medicine”. However, they continue to provide preliminary evidence for plausibility and the potential therapeutic benefit of CHM in the treatment of a wide range of medical conditions. Additional more rigorous research is required to verify these findings but, despite these limitations, recent studies have made an important contribution establishing an evidence base to support the developing role of CHM in the provision of healthcare in the wider world.

2. COCHRANE REVIEWS AND BEYOND

Cochrane reviews require the use of explicit and transparent methods, are peer-reviewed at both the protocol and complete review stage, and are regularly updated. For these reasons, they have been found to be of comparable to, or better quality than, reviews published in even the leading print journals.

Manheimer et al (2009) systematically reviewed all Cochrane reviews relating to Chinese medicine. In total, at the time of writing, there were 36 reviews. 56% of these reviews provided evidence that CHM could have a useful therapeutic role in the management of the following medical conditions:

- *atopic eczema*
- *primary dysmenorrhea*
- *schizophrenia*
- *nephritic syndrome*
- *angina*
- *type II diabetes mellitus*
- *severe acute respiratory syndrome (SARS)*
- *acute pancreatitis*
- *hepatitis B*
- *common cold*
- *side effects of chemotherapy in breast cancer*
- *irritable bowel syndrome*
- *viral myocarditis*
- *Alzheimer's disease*
- *ischemic stroke*
- *heart failure.*

The evidence within these Cochrane reviews is not conclusive. The numbers involved were frequently too small, the methodological quality of the trials was generally poor, and the studies were highly heterogeneous. However these reviews do provide preliminary evidence supporting the use of CHM in the treatment of these conditions. These findings need to be verified by future research. In addition to Manheimer's review there were two other important Cochrane reviews published in 2009 and which are directly relevant to conditions selected by WP6.

- CHM for endometriosis. In a review of 110 clinical trials using CHM to treat this common and disabling gynaecological condition, only 2 studies involving 158 women could be included and

these trials indicated that post surgical administration of CHM may have comparable benefit to the conventional treatment of endometriosis, but with fewer side effects.

- CHM for people with impaired glucose tolerance or impaired fasting blood sugar (Grant et al (2009) examined 16 trials involving 1391 participants and provided some evidence to support the role of CHM in normalising blood sugar levels and preventing the progression to diabetes over time. As with most Cochrane reviews, more and better quality trials are required to substantiate these early findings.

3. DISCUSSION:

3.1. Wider observations on research into CHM medicines and TCM generally

The conclusions of the above review are in keeping with a number of other reviews that often conclude that, by the standards of Western based assessment of evidence, the majority of Chinese medicines lack the rigour of full evidence from well designed full scale clinical trial evaluations. This is due to a number of reasons and wider considerations that need to be placed in context as discussed further below:

- CHM is a key component of the system of TCM that has been practised, developed and recorded for more than two thousand years within China and other East Asian countries. The process of transmission of TCM to the West started gradually around 400 years ago (Unschuld 1998) but in recent years it has gathered momentum and TCM is now rapidly becoming a major contributor to healthcare in all the major industrialised countries.
- CHM has its own unique understanding of the aetiology, pathophysiology, diagnosis and treatment of disease that has developed over two thousand years as a result of recorded observation and experimentation. This summary of knowledge includes the accumulated insights of experienced individual practitioners and in recent years has been bolstered by data derived from observational studies, RCT's and systematic reviews.
- Unsurprisingly TCM has developed over hundreds of years into a medical system that contains diverse and sometimes contradictory accounts of disease. It has been convincingly described as a form of medical pluralism (Scheid 2002). Unlike Western medicine where technological progress encourages rapid, comprehensive and continuous revision, TCM essentially uses the same methods of diagnosis and treatment that were prevalent in the pre-industrial era. As a result historical records of hundreds of years of empirical experience are profoundly relevant to contemporary TCM practice. However, there is very little research comparing the diverse strands to emerge from this long history and there is no single tradition that can be considered to provide an uncontested basis for best practice.
- Best practice of CHM is usually considered to require the use of individualised herbal formulations that are adapted to address the particular needs and the changing clinical presentations of each patient (Bensky et al 1986). This makes CHM a dynamic and highly responsive system of medicine that resonates strongly with the increasing emphasis within bio-medicine for the use of both combination therapies to achieve optimum benefits and individualised treatments to take into account genetically variable responses to modern drugs.
- CHM has also been responsible for a number of adverse reactions – particularly in the kidney and liver – which have raised concerns in the West.
- There is then a clear need to investigate both the effectiveness and the potential adverse effects of CHM so that it can be assessed in a rational and consistent manner (Colquhoun 2009).

It has been estimated that there are over 17,000 clinical trials on CHM that have been reported in East Asian medical journals (Tang et al 1999, Wang et al 2007) although the reliability of many of these studies has become questionable owing to a lack of methodological rigour and apparent publication bias (Tang et al 1999). In the West recent peer reviewed research has demonstrated the effectiveness of an individual herb Lei Gong Teng (*Radix Tripterygii Wilfordii*) in the treatment of rheumatoid arthritis (Goldbach-Mansky et al 2009) and herbal combinations in the treatment of irritable bowel syndrome (Bensoussan et al 1998), atopic eczema (Sheehan et al 1992) and as an adjunctive treatment in leukaemia (Wang et al 2008).

- There have been over 42 Cochrane Reviews on CHM (Manheimer 2009). Manheimer's review concluded that 19 of these Cochrane reviews provided preliminary evidence of the possible benefits of CHM in the treatment of a number of conditions. However the poor methodological quality of CHM clinical trials leads to the majority of trials being excluded from a Cochrane review.

CHM uses herbal products that contain highly active compounds that have been extensively researched and developed into pharmaceutical drugs, such as ephedrine from Chinese herb Ma Huang (*Radix Ephedra chinensis*), artemesinin from Qing Hao (*Herba Artemisiae Apiaceae*) and tamiflu from Ba Jiaoanise (*Illicium verum*) which are just a few examples of how some of these active compounds have been refined into conventional medicines.

3.2. Whole systems research

CHM is a complex intervention that draws its therapeutic potential from more than just the specific effects of herbal medicines. The practice of CHM frequently involves providing dietary advice, discussing lifestyle choices, and recommending exercise, massage, and relaxation techniques. CHM encourages the cultivation of the therapeutic relationship between practitioner and patient and provides a philosophical and linguistic framework that allows a patient to understand and contextualise their illness. These non-specific factors have been shown to provide important therapeutic benefits.

3.3. Future work on CHM medicines and the contribution that “omics” approaches may offer

The newly emerging approaches of systems biology, genetic fingerprinting and gene profiling offer great potential to better understand the effects of Chinese and other herbal medicines. Such greater understanding of the effects and mechanisms will greatly enhance the ability to better plan for improvements to be made to the evidence base for CHM medicine for the future. Such work is central to the wider development of the GP-TCM initiative as a whole and to the future planning of large scale clinical trials in TCM as greater understanding of the mechanisms by which both the effectiveness and side effects are manifested will underpin a rationalisation and wider acceptance of TCM around the world.

4. FEATURED REFERENCES

[1] Manheimer E, Wieland S, Kimbrough E, Cheng K, Berman BM. (2009) Evidence from the Cochrane Collaboration for Traditional Chinese Medicine therapies. *J Altern Complement Med.* 15(9):1001-14.

[2] Wu T, Li Y, Bian Z, Liu G, Moher D. (2009) Randomized trials published in some Chinese journals: how many are randomized? *Trials.* 2;10:46.