



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

**GP-TCM**

**223154**

**D.1.7**

**Report on the knowledge gaps about quality control of the  
priority list of plants**

Document description	
Name of document	Report on the knowledge gaps about quality control of the priority list of plants
Abstract	Very few of the reviewed papers contain enough information about the plant studied to enable a reviewer to be confident that the work had been undertaken on the correct species. If the reviewer then looks at the chemical data provided very few papers provide enough background data about the material and the methods used to link results directly back to the traditional use of the plant. This makes it difficult to be confident in using the data in these papers to enable a review of the scientific content to undertake a gap analysis of data to evaluate the traditional uses of the plants. It is clear from this review there are many gaps in our scientific knowledge about what the chemical criteria (finger print) associated with a good quality plant and what agricultural practices are needed to grow quality material. It is acknowledged that the review was undertaken on papers available in the west and mostly in English. A more in depth review of the Chinese literature might enable many of the gaps to be filled.
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## **1 Knowledge Gaps about the quality control of the priority**

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## **1 Knowledge Gaps about the quality control of the priority list of species (D1.7)**

### **1.1 Introduction**

The overall objectives of WP1 are to:

- Design a standard system for the quality control of Chinese herbal medicines (CHM) in the EU
- Design a system that will provide greater transparency about the complexity of TCM nomenclature, thus clarifying plant identities and improving data gathering on CHM species
- Propose guidelines as a basis for the rational development of research methods to authenticate and monitor the quality of TCM plants entering the trade. Guidelines will aim to avoid duplication of research efforts and maximise the use of modern molecular and chemical techniques, especially a functional genomic approach.

### **1.2 Template for quality control procedures**

Output: Template for quality control procedures.

#### **Scope of information being gathered**

This report builds on WP1 report D1.6 that identified the scope of data that should be collated for developing a best practice template for the information that should be available for the quality control of plants used in Chinese traditional medicine (CHM). The data presented in this report are based on information discussed at the joint workshop between members of WP1 and WP2 held at Braga, Portugal (3/4 Dec 2010), the Annual Meeting at Braga in 2011 as well as email and face-to-face meeting with different colleagues working on the quality control and cultivation of plants used in CHM.

The proposal was to develop a simple Excel based database that could contain appropriate fields that could be filled in when reading through manuscripts. The aim was to use this Excel database to collate data together to enable the members of WP1 and WP2 (and members in other WPs) to not only collate information about what is known about the quality control of each species but also review the quality of papers published on the selected species. The outputs from this exercise would assist WP 1 and WP2 have a better understanding of the scope of the information available about the quality control for each of the key species as well as support the development of best practise methods. The scope (fields) of information to be collated in the database have been discussed and agreed at different meetings. The fields associated with quality control were presented in WP 1 report 1.6 section 1.4. The aim of this report was to identify the gaps in the knowledge about the quality control for the priority list of plants that resulted from undertaking this review. The priority list of “plants” are the five plants and one fungus used in the formula “Liu Wei Di Huang Wan” (Table 2).

The tasks were divided among members of WP1 and WP2. The initial idea was to undertake a literature review using Scopus or Pubmed. However, although members of the team had access to Pubmed, their access to Scopus was limited. The impact of this limitation on the data gathered was not evaluated. However, it was suggested that alternative search engines such as Google Scholar or SciFinder could be used. The scoring system used to evaluate the



botanical information in papers has been developed into a Standard Operating Practice (SOP) by WP8. This method was based on the scoring system for botanical data developed and evaluated by WP4 in collaboration with WP1 and by WP2. The robustness of this system needs further evaluation by a greater range of people using it.

- It involves checking whether the following information is available in the paper:
- Latin binominal name as used by say Chinese Pharmacopeia 2005
- Identifier of the specimen given:

The following identifiers were taken into account and had been provided by WP1 for all species of the priority list:

- CP2005 Latin binominal name
  - Accepted Latin binominal name and authority (e.g. Flora of China)
  - Other Latin binominal names (accepted synonyms) and authorities
  - Latin drug name as used in CP2005
  - Chinese Pin Yin names
- Examined as Individual herb or as part of a formula
  - Name of the formula, if given
  - Plant part used
  - Source of the specimen, if given
  - Processing method, if applicable
  - Processing additive, if applicable

The presence or absence of this information in papers can then be used to score publication and also evaluate whether authors have taken care to provide basic information to support the quality control of their plant material.



**Table 1: Scoring system for documentation of herbal quality**

	Score	
Sources of herbs and herbal entities indicated? (specification of location of harvesting or specification of a commercial source)		
<u>Herbs harvested:</u> Botanical identification: details on authenticator and reference number? Herbarium voucher specimens deposited? Voucher number? Herbarium voucher specimen verified by named botanist DNA barcoding? Post-harvest treatment specified? Perceived quality and reproducibility of treatment?		
<u>Herbs bought from commercial suppliers:</u> Shop or company name and location? Voucher specimens (e.g. dried plant part, extract) deposited? Voucher number? DNA bar-coding? Post-harvest treatment (drying, washing, etc.)? Perceived quality and reproducibility of treatment?		
Absence of processing clearly indicated or deduced?		
Perceived quality and reproducibility of process?		

**Table 2. The following 6 species are those used in the TCM formula: "Liu Wei Di Huang Wan"**

Latin scientific name(s) as stated in the Pharmacopoeia of the PRC (English eds.) <sup>1,2</sup>	Accepted* Latin scientific name <sup>3,4,5</sup>	plant part used in TCM <sup>1,2</sup>	Latin pharmaceutical/pharmacopoeia name(s) <sup>1,2</sup>	Chinese and Pin Yin names <sup>1,2</sup>
<i>Alisma orientale</i> (Sam.) Juzep. <sup>1,2</sup> (note different and incorrect spelling in the 2005 ed. of the Chinese Pharmacopoeia ' <i>Alisma orientalis</i> (Sam.) Juzep.')	<i>Alisma orientale</i> (Samuelsson) Juzepczuk <sup>3</sup>	tuber/rhizome	Rhizoma Alismatis <sup>1</sup> ; Alismatis Rhizoma <sup>2</sup>	泽泻 'Ze Xie' or 'Zexie'
<i>Cornus officinalis</i> Sieb. et Zucc. <sup>1,2</sup>	<i>Cornus officinalis</i> Siebold & Zuccarin <sup>3</sup>	ripe fruit (processed with yellow rice wine) b	Fructus Corni <sup>1</sup> ; Corni Fructus (processed with wine)	山茱萸 'Shan Zhu Yu' or 'Shanzhuyu'
<i>Dioscorea opposita</i> Thunb. <sup>1,2</sup>	<i>Dioscorea polystachya</i> Turczaninow <sup>3</sup> ; (note c)	tuber/rhizome	Rhizoma Dioscoreae <sup>1</sup> ; Dioscoreae Rhizoma <sup>2</sup>	山药 'Shan Yao' or 'Shanyao'
<i>Paeonia suffruticosa</i> Andr. <sup>1,2</sup>	<i>Paeonia ostii</i> T. Hong & J. X. Zhang <sup>3</sup> ; (note d)	Rootbark	Cortex Moutan <sup>1</sup> ; Moutan Cortex <sup>2</sup>	牡丹皮 'Mu Dan Pi' or 'Mudanpi'
<i>Poria cocos</i> (Schw.) Wolf. <sup>1,2</sup>	<i>Wolfiporia extensa</i> (Peck) Ginns <sup>5</sup>	sclerotium (storage organ and non-reproductive part)	Poria <sup>1,2</sup>	茯苓 'Fu Ling' or 'Fuling'
<i>Rehmannia glutinosa</i> Libosch. <sup>1,2</sup>	<i>Rehmannia glutinosa</i> (Gaertner) Liboschitz ex Fischer & C. A. Meyer <sup>3</sup>	processed tuber/rhizome <sup>(note e)</sup>	Radix Rehmanniae Praeparata <sup>1</sup> ; Rehmanniae Radix Praeparata <sup>2</sup>	熟地黄 'Shu Di Huang' or 'Shudihuang'

### References

1. State Pharmacopoeia Commission of the P.R. China (2005, English ed.) *Pharmacopoeia of the People's Republic of China*, vol,1, 791 pp.
2. State Pharmacopoeia Commission of the P.R. China (2010, English ed.) *Pharmacopoeia of the People's Republic of China*, vol,1,1584 pp.
3. *Flora of China* (<http://flora.huh.harvard.edu/china>)
4. *World Checklist of Selected Plant Families* (<http://apps.kew.org/wcsp>).
5. *Index Fungorum* (<http://www.indexfungorum.org/Names/Names.asp>).

### Notes

- \*: an 'accepted' Latin scientific name is a taxonomically preferred name (i.e. it should be used in preference to any other Latin scientific name used for the same species).
- b: the Chinese Pharmacopoeia 2010 definition of the formula 'Liuwei Dihuang Wan' states Fructus Corni is 'processed with wine' (i.e. steamed or stewed in yellow rice wine).

c: the name '*Dioscorea opposita* Thunb.' is considered taxonomically 'illegitimate' and therefore should not be used in a scientific context even as a scientific synonym. Owing to its continued common use in TCM, however, it is a useful name for literature searching. Little has yet been published under the 'accepted' Latin scientific name of *Dioscorea polystachya* Turczaninow

d: a recent and authoritative taxonomic revision (Hong De-Yuan Hong and Pan Kai-Yu, 1999, *Nord. J. Bot.*, 19(3): 289-300) concludes that the name '*Paeonia suffruticosa* Andr.' has been misapplied for many years as the source of the TCM herb 'Cortex Moutan' or 'Moutan'; instead, the correct identity of this TCM herb is '*Paeonia ostii* T. Hong & J. X. Zhang'. *P. suffruticosa* Andr. is considered to be a separate species (not a synonym) and includes a huge array of popular cultivars grown for ornamental purposes only. Owing to the widespread use of the name *P. suffruticosa* in TCM, however, it continues to be a useful name for literature searching.

e: 'processed' is defined here means 'stewing'<sup>2</sup> (i.e. steaming or stewing with yellow rice wine (20-30kg wine/100 kg of clean crude dried rhizomes/tubers/roots) until wine is totally absorbed.)

### 1.3 Overview of findings

The number of references about each species varies greatly depending on the search engine used and the terms used to search the literature. What is clear is that there is very little scientific information about what the quality of the six plants as used in Liu Wei Di Huang Wan. For some plants there is a wealth of scientific information about the chemistry of the plants and their proposed medicinal properties. However, very few of these publications link directly back to the traditional use of the plant as used in Liu Wei Di Huang Wan, the formula that is widely used in China. Data about the nomenclatural issues and the chemistry of some of the target plants assessed from reviewing 400 publications has been presented by WP 2 in D2.10.

For each of the priority species the literature was searched for the following as indicated above:

#### Information about the species

Species name

Latin binomial + authority and family

Name used in the Chinese Pharmacopoeia (English version 2005 was used in this review)

Vernacular Chinese names

Pin Yin name

Part of the plant used

**Findings:** The information about the species studied was poor in over 50% of the papers. This information varied among the journals and could reflect the emphasis placed on the importance of this information by the journal editors or reviewers. In about 23% of cases it was unclear as to the exact species studied or the part of the plant used.

#### Complex drug (does the paper relate to the species being used singly or as part of a formula)

Is the species part of a complex mixture with other plants (if yes then what proportion of the specific species is in the "drug")

What is the name of the drug.

**Findings:** The majority of papers provided information about a species, when the studies were on formula then there was very little information about the quantity of each species in the mixture and whether this had been evaluated.

#### Collection and processing (Any information about the plant material studied)

Collection time

Collection method

Processing method after collection

Drying method





## Primary processing

**Findings:** There are only a few papers on the processing of the selected species. There is also very little information in the literature as to the influence of the processing on the chemistry, quality and thus biological activity of the species.

## Geographical distribution and major production areas

Geographical distribution

Major production areas

**Findings:** Very few studies provided information about the original source of the material. The scope of information varied. There were a few papers on the variability of chemistry or on genetic variability within a species and these papers provided information about the sources of the plant material.

## Plant material

When is the material harvested

Is the plant wild harvested or cultivated

If wild harvested – what procedures are in place to avoid over-harvesting

If cultivated - what are the good agricultural practises in place

Has the material been tested for pesticides, heavy metals, and bacteria

What are the levels of heavy metals in the sample (what are the accepted levels)

**Findings:** Unless the paper was about the specific cultivation of the species this information was lacking and very few papers indicated whether the supply of material was wild harvested or cultivated.

## Medicinal uses

What is the plant used for and what scientific data are available to support this use

(More data from other WPs)

Does the data relate to traditional uses or modern uses of the plant

How much of the plant is used (dose)

Are adverse responses associated with the plant

Are herb-drug interaction reported.

**Findings:** Most papers have a reference about the traditional uses of the plant but the focus of papers did not always relate to the traditional use. Thus a high proportion of papers do not provide scientific evidence to support their traditional use. This part of the evaluation needs further work by other WPs.

## Chemistry

How are extracts made

Do extracts tested relate to those used in traditional methods

What is known about the chemistry of the plant

Does the chemistry link to known medicinal activity of plant

Is there information available about compounds that can be used as markers for identification (chemosystematic markers) or activity (quality markers)

What is known about the toxicity of the plant; which compounds

**Findings:** Many of the publications that involve chemistry either report background information about the chemistry of the plant or report the results of activity-guided isolation studies. However, very few of these relate back to the original use of the plant.

## DNA-bar-code

Is there information known about DNA sequences of the plant

Is there a DNA bar code and which sequence is used.



**Findings:** There is information about the DNA for most species. However, there were no studies that related genetic variability with the chemistry/quality of the selected species and DNA was not used as a method to verify the identification of the species

#### **Good Agricultural Practice**

Life Cycle and environmental requirements  
Optimal growth conditions  
Cultivation and Planting methods  
Field management  
Pest and disease control

**Findings:** Very few publications report on how the plants were grown

#### **Quality control requirements**

National quality specification and requirements of medicinal materials (China and Europe)  
Trade specification  
Determination of Residual heavy metals and organochlorine pesticides

**Findings:** Very few publications report on whether the material being used in the study meets the national quality control standards. However, some papers on formula indicated that the products they tested did meet these standards.

### **1.4 Conclusion**

The results of this initial survey show that there are many gaps in the literature that need to be filled to provide the scientific evidence needed to support the traditional uses of the plants. There is a need to co-ordinate studies that focus on these activities and the challenge here is to integrate the uses as described in traditional Chinese medicine with those used in western medicine.

The review of the literature available on search engines such as PubMed and Scopus provide information from papers published in academic journals on the six species of plants used in Liu Wei Di Huang Wan and their substitutes. In contrast, Google Scholar provided the greatest diversity of publications on the Chinese formula Liu Wei Di Huang Wan. However, none of these search engines provided an overview of the material available in books, especially pharmacopoeia. It is clear that if a comprehensive review of the literature on the quality control of the selected plants is to be completed a greater emphasis needs to be placed on reviewing the information in books. This poses a problem for many researchers who have limited access to these books.

However, the results of the survey support the use of a template that can be used when evaluating publications on the traditional uses of plants to access whether authors have evaluated the plant material they study and whether they research relates to traditional uses.

- Information about the plant studied:
- Voucher sample of the plant (or sample of drug/material studied)
- Part of plant studied and information as to whether it has been processed and how.
- Chemical profile of plant (to assist evaluate quality)
- Information about traditional use and how does proposed extraction method link to traditional use and how do proposed bioassays relate to traditional use.

If publication relates to quality control then some information about:

- Source of the material should
- Methods used to evaluate the chemistry
- Methods used to evaluate the biological/pharmaceutical activity of the material



If publications relate to the proposed clinical use of a plant then more information should be provided

- Source of the material,
- Supply chain and
- Whether material covered by Good Agricultural Practice.

**Those members and collaborators of WP1 and WP2 that have been involved in this review**

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