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

GP-TCM

D2.11

Workshop reviewing the correlation of methodology used in the analysis of priority list with best practice standards recommended in this study

Document description	
Name of document	Workshop reviewing the correlation of methodology used in the analysis of priority list with best practice standards recommended in this study.
Abstract	A brief report about the coordination action taken to agree on the recommendations given in D2.12.
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1 REPORT ON COORDINATION ACTION

1.1 Purpose of D2.11

According to WP2's 3-year plan a personal meeting was scheduled to take place in fall 2011 in order to discuss the correlation of the data acquired for D2.10 with best practice standards and to address particular aspects for either giving best practice recommendations or addressing particular topics for a future research agenda. As WP1 was involved with the work on D2.10, a joint meeting of WP1 and WP2 was desired.

1.2 Reasons for superseding a face-to-face meeting

A face-to-face meeting as originally scheduled did not take place for the following reasons:

- Delayed progress. According to WP2's 3-year plan, D2.15 (Review papers) was meant to base on the total results obtained by WP2 after month 36. However, the deadline for WP2's contribution to the special issue of Journal of Ethnopharmacology fell into month 30. In order to deal with this distortion of the WP2's time plan, we focused our activities in summer and fall 2011 on compiling this review while delaying the actual month 30 deliverables. Consequently, the timeframe for organising a personal meeting became tight and we could not find a meeting date which *(i)* would allow the participation of a significant number of WP1/WP2 members and *(ii)* would not delay the progress any further.
- The finances of WP2 would probably only suffice for organizing one further meeting. Many WP2 participants appreciated to have this meeting after finalisation of any deliverables.
- The coordinated work towards D2.10 and the aforementioned JEP-review already anticipated a lot of the discussions planned for D2.11.
- The remaining issues to agree on were quite clearly arranged and well suited to be dealt with remotely by telecommunication.

1.3 Action taken to replace a face to face meeting

- The topics to be discussed were already preformed by the results of D2.10. These topics were internally published in the Forum of the GP-TCM website to be perceived by the whole consortium and open for discussion.
- A teleconference was organised by Helen Sheridan on 15.12.2011, where the aforementioned topics were discussed with the contributors for D2.12, which would contain the outcome of the coordination actions described here (see 2 for further details).
- Further coordination took place bilaterally by E-Mail or telephone. Due to the abundant preparatory work that had originated from D2.10 and D2.15, no further teleconference was necessary but the final document of D2.12 was approved by the participants.

2 PROTOCOL OF TELECONFERENCE

Draft Minutes of WP1/WP2 Teleconference 15.12.2011

14:00 -15:00 UK time (15:00 – 16:00 German/Austrian/Netherland time)

Attendees

Host: Helen Sheridan (HS)

Chair: Jandirk Sendker (JS)

Attendees (in alphabetical order): Svetlana Ignatova; Jandirk Sendker; Helen Sheridan; Ian Sutherland; Rob Verpoorte.

Apologies: Dr. Werner Knöss

Minute taking: Helen Sheridan

1. JS gave a brief Introduction to month 30 deliverables:

The deliverable D2.11 is a proposed workshop reviewing the correlation of methodology used in the analysis of priority list (D2.10) with best practice standards recommended in this study. However, it has been too difficult to coordinate participants to attend this workshop and it has been decided to replace the workshop with a (series of) teleconference(s).

The second deliverable, D2.12 is a report on the teleconference(s) (workshop D2.11) and recommendations highlighting the status of the information and identifying non-standard areas. D2.12 WAS DUE TO BE SUBMITTED October 31st 2011. It has now been decided to extend this submission deadline to Jan 31st 2012.

2. JS addressed the results of the species survey (D2.10) which were posted on the WP2 GP-TCM forum for discussion and for recommendations.

JS led the discussion on these topics and feedback was received from conference participants. Discussion was centred on the forum topics. JS explained that within the data mined for the D 2.10 species survey over 400 papers were reviewed and data was extracted into EXCEL and analysed. Data subsets were filtered.

Characterisation of botanical origin: There was agreement that important detail was omitted from a high portion of the research papers. In many cases botanical origin of species was missing from the Materials and Methods section although it may have been located within the text of the paper. Many examples were lacking species authority; pinyin name; identification information/voucher specimen; plant part; link of drug name to appropriate Pharmacopoeia. **For consideration for D2.12 Recommendations:** That gold standard publication criteria, should include full descriptors of species

authority, voucher specimens or validation using Pharmacopoeial monograph, pinyin name, method of treatment or preparation etc.

Source of the herbal specimen: The reviewed publications were also lacking in detail relating to the place of harvesting (for single or multiple non blended species location using geographical coordinates - Google maps or GPS could be used) , season of harvesting (should be documented and possibly notations on location, climate (drought etc), plant age. Lot numbers for commercial products were also lacking as was detail on blended samples. RV thought these was an overlap in this area with a WP1 report and will source this report and pass to attendees for consideration. Recommendations will be determined in the light of RV WP1 report findings. **For consideration for D2.12 Recommendations: The report that has been circulated by RV (16th Dec 2011)**

Traditional or non-traditional use: From the 400 papers reviewed it proved difficult to ascertain which were related to traditional application. The data in the papers was not clearly linkable. It was agreed that there is an overall need for pharmacologists to standardise the Chinese medical terminology with western medical terminology. The WHO has a new initiative to improve classification. **Action:** Monitor this WHO initiative

Post harvest treatment and *paozhi* processing: In the reviewed papers it is currently unclear, in most cases, if herbal the specimen has been *paozhi* processed. It is also unclear in 90% of papers what postharvest treatment (drying, wet-cutting etc.) has been employed. Such processing may be linked to the Pinjin name, but this is unclear. There was a discussion on the importance and effects of processing on enzymatic processes and hence on the metabolome. **For consideration for D2.12 Recommendations:** Sample histories should be linked. It was agreed that when publishing, it is essential to clarify whether it is the dry drug that is under investigation. If it is not there are QC implications. The Materials and Methods section should detail any post harvest treatment including drying, wet cutting, (pesticides), storage. Information on whether samples are remoistened after drying should also be included. Publications should also mention pharmacopoeia directions re the grade of processing and quality.

Extraction: In most cases of reviewed literature comparative reports about modern extraction technology are scarce and never linked to activity; 50% of biologically tested extracts are traditional water extracts: specific problem of cold water soaking. In the Materials and Methods section approximately half of the papers including traditional studies use aqueous extraction. Others use solvent extraction. There was a discussion on the significant differences that arise in the extraction of metabolites, and hence in the metabolomic profile of the extracts that arise depending on the sequence of extraction e.g. if you add to boiling water to the sample or boil in water. There appear to be significant issues in connection with water extraction, which initially looks like a simple process. Materials and Methods section vary and there appears to be little clarity. Whatever the protocols, it is important to clarify in the experimental section. There was a detailed discussion on the common practice to soak some TCM's beforehand. It was agreed that very different activity profiles can arise depending on method used. **For consideration for D2.12 Recommendations:** It is important to emphasise that extraction is not as simple as it is made out to be. It is essential for best practice to detail the sequence of events e.g. do you add honey before or after extraction?

Granules: There is a growing trend in GMP manufacture of the formation of granules to increase stability of TCM products. In the literature reviewed there is poor distinction Extract between the use of granules and traditional preparations. A major question arises as to whether granules be considered to be (equivalent to) traditional preparations? There was some discussion on this topic. In many instances the water ext of a TCM is precipitated with ETOH to remove polar constituents to help properties of the TCM product and make it suitable for granule formation. Excipients (up to 60%) can be added. **For consideration for D2.12 Recommendations:** There is a need to emphasise that these preparations are not the same as a decoction; that there are differences between a traditional (aqueous) formulation of a TCM product and a granulated product. Comparative, metabolomic studies, safety and efficacy data is needed. {Comment (HS) - There is likely to be an issue on the registration of such granulated preparations in the EU as they will not fall under the established use category]

Fingerprinting and quantitative analysis: From the data analysed, it was apparent that there was significant variation in the standard of reporting of chemical fingerprinting. Many of the studies assessing biological activity included no chemical characterisation (53%); others included no quantification of known markers (22%); fingerprint without discussion (9%), and only a small percentage included fingerprint with discussion (6%). The method of extraction of a sample – prior to measuring the fingerprint was discussed. It was agreed that significant variation can occur (fingerprint MeOH 1:1 and MeOH 4:1 totally different). **For consideration for D2.12 Recommendations**. The importance of characterising the fingerprint of the TCM preparation that the patient actually receives was emphasised. RV underlined that HPLC is not always the best method due to column variations and availability. The use of TLC and microscopy as presented in the Pharmacopoeia is still very important for TCM.

Validation: In the literature analysed the majority of quantifications were without validation data. **For consideration for D2.12 Recommendations:** referencing needs to be included. Pharmacopoeia needs to be references.

Analytical methods used: vast majority HPLC-based (UV/DAD and MS detection). **For consideration for D2.12 Recommendations** HPLC based with UV or MS detection methods are not problematic. there is also room for inclusion of NMR methods. SI mentioned the advantage of NMR in detecting the presence of isomers.

Actions: SI to find out more about French NMR project

1. **Items to be addressed for research agenda** :

- Influence of *paozhi* processing. **Research Question:** Does *paozhi* processing influence the mettabolome?
- Influence of cold-water-soaking during cutting and extraction. **Research Question:** Does *extraction / soaking process* influence the mettabolome?
- Co-extraction and synergism of CHM (e.g. extract A alone 10%, co-extraction with B yields higher content). **Research Question** : Does the presence of additional herbal material influences extraction?
- Co-ordinated assessment of fingerprints and activity data of multiple related products for a metabolomics approach.

4. Actions to be taken by the attendees (all).

It was agreed that participants should read the documentation to be sent by RV. In the light of these documents and the minutes of this meeting, participants (Jandirk) will adopt (assign) topic(s) which will then be merged to form a draft document for deliverable D2.12.

Each contribution (should have similar format and max 1 A4 page??) will describe concern and make recommendations.