Readers' Tribune

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Re-examination of the General Monographs on Herbal Drugs and Herbal Drug Preparations with Reference to Monographs on Traditional Chinese Herbal Ingredients

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The European Pharmacopoeia (Ph. Eur.) Traditional Chinese Medicine (TCM) Working Party is now in its 4th year of elaborating monographs on traditional Chinese herbal ingredients. A number of these monographs have been adopted by the European Pharmacopoeia Commission and published in the Ph. Eur. Work continues on many more such monographs for individual TCM ingredients which will, in due course, enter the pharmacopoeia.

A text on the *Preparation of drugs for traditional Chinese medicines (5.18)* was published for National Authority comment in Pharmeuropa 22.2 [1]. This text was very similar to that published in the Chinese Pharmacopoeia (2005) and detailed the methods of processing which may be applied to herbal drugs to render them suitable for their intended purpose when used in TCM therapy. The processing methods listed vary from simple physical processes, such as cleaning and cutting of the herbal drug, to various 'cooking' procedures with or without the addition of other ingredients. The products resulting from some of this more sophisticated processing would no longer fall within the Ph. Eur. definition of a herbal drug, nor would they be encompassed within the current Ph. Eur. definition of a herbal drug preparation as this requires such products to be homogeneous which many TCM processed herbal drugs are not, retaining the same integrity of the individual pieces of herbal drug after processing as prior to processing. As a result, there exists an unsatisfactory situation where TCM herbal drugs which are treated, after harvesting, in the same or a similar way to the more familiar herbal drugs subject to a monograph in the Ph. Eur. would fall within the Ph. Eur. definition of herbal drugs but those subjected to more sophisticated processing would fall outside the scope of any current Ph. Eur. definition for herbal ingredients. This paper proposes how this situation might be resolved.

Current Ph. Eur. definitions for herbal drugs and herbal drug preparations

Herbal Drugs

The intention of the definition for an herbal drug is to describe one or more plant parts (or certain exudates) which are harvested and, in the majority of cases, dried with a minimum of additional processing. Such processing would include peeling (removal of the outer layers of plant part e.g. ginger or liquorice) and/or size reduction, for example, to aid drying or for ease of packaging. An herbal drug should comply with its monograph including its macroscopical description necessitating in most cases that an herbal drug will be in a physical state consisting of distinct, recognizable non-homogeneous pieces (root, leaves, flowers, barks, etc.). The cutting of a drug for extraction purposes is not intended to render the herbal drug homogeneous but to ensure that the production process is efficient and reproducible. However, when a herbal drug is cut or powdered for a specific purpose (e.g. as a component of a herbal tea or for the manufacture of tablets or capsules) resulting in an homogeneous herbal drug it is deemed to have been processed to an extent where it is no longer considered an herbal drug but an herbal drug preparation.

Herbal Drug Preparations

In the Ph. Eur. there are 4 herbal drug preparations where the principle component is a finely divided herbal drug, these are: *Belladonna, prepared (0222)* [2], *Ipecacuanha, prepared (0093)* [3], *Opium, prepared (1840)* [4] and *Stramonium, prepared (0247)* [5], which may contain excipients, where necessary, to adjust the assay value to within the limits stated in the monograph.

Those herbal drug preparations resulting from herbal drugs which have been processed by, for example, expression, distillation, fractionation, extraction, concentration, purification, fermentation, etc. bear no physical resemblance to the parent herbal drug and are homogeneous products composed of a selected range of constituents from the herbal drug from which they are derived. A further characteristic of some herbal drug preparations obtained by these processing methods, particularly extracts, is that they usually contain other components not derived from the herbal drug. Thus, a dry extract will contain excipients (processing aids) to ensure that a stable product is achieved; liquid extracts and tinctures will contain ethanol. Other processing aids/excipients/ingredients may also be present depending upon individual product requirements.

The following may be regarded as *key characteristics* of herbal drugs and herbal drug preparations:

- Herbal Drugs, other than being dried are subjected to minimal additional processing;
- Herbal drugs are usually of a size and appearance as defined by their macroscopic description (Ph. Eur. or other monograph);

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- Herbal drugs do not usually have excipients added;
- Herbal drug preparations are homogeneous;
- Herbal drug preparations, particularly extracts, usually contain processing aids/excipients/other ingredients;
- Herbal drug preparations may be obtained from herbal drugs as result of processing involving heat with or without the addition of other substances.

These characteristics give a benchmark by which to assess the impact of traditional Chinese processing methods on the current Ph. Eur. definitions for herbal drugs and herbal drug preparations.

Categorisation of traditional Chinese processing methods for herbal drugs

The methods of processing given in the Chinese Pharmacopoeia (2005) and in general chapter 5.18 published in *Pharmeuropa* (cited previously) are categorised into 3 sections as follows:

Cleaning

The majority of the procedures listed under Cleaning would be considered as either normal processes applied to freshly harvested or harvested and dried material (depending upon the process) or minimal additional processing. Therefore, the product resulting from the cleaning and drying or drying and cleaning process would normally be considered to an *herbal drug*.

Cutting

A feature of the presentation of herbal drugs for use in TCM is their characteristic sizes and shapes. The herbal drugs may be cut in this way whilst fresh, prior to drying or, more commonly, by partial re-hydration after being previously dried, followed by re-drying. Provided that the process of re-hydration, cutting (sometimes with reshaping) and re-drying does not significantly affect the content of constituents in or cause contamination to the herbal drug, these processes would normally be considered as minimal additional processing. Therefore, the product resulting from this processing should be considered to be an *herbal drug*.

[*Note*: if, for a particular herbal drug, the processing requires significant re-hydration (e.g. prolonged soaking in large quantities of water because of the hardness of the herbal drug) leading to excessive leaching of constituents the resultant product should no longer be considered as an herbal drug as it would be significantly different in one or more constituents from the dried herbal drug from which it was derived.]

Roasting and Broiling

These are methods of processing by the application of heat with or without added ingredients and include the following processes: stir-baking, scalding, calcining*, carbonising, steaming, boiling, stewing, defatting*, levigating* and roasting. All of these processes have the potential to significantly alter the physical and/or chemical characteristics of an herbal drug.

For those methods of processing marked '*' the resulting products should be powders which are homogeneous and such products would normally be considered to be *herbal drug preparations*.

[*Note*: the process of levigating may only involve heat at the final stage of processing].

In all of the types of processing listed, except for those marked '*', the integrity of the shape and size of the pre-processed herbal drug is retained to a greater or lesser extent. Therefore, the resulting product cannot be homogeneous and is thus precluded from the current definition of an herbal drug preparation as it fails one of the key characteristics of such a preparation. The other 2 key characteristics of an herbal drug preparation are, however, satisfied by these products.

Proposal for the inclusion of non-homogeneous processed herbal drugs in the Ph. Eur. definition for *herbal drug preparations*

It is proposed to define 2 types of herbal drug preparations. The text of the current general monograph *Herbal drug preparations (1434)* [6] would therefore be:

HERBAL DRUG PREPARATIONS

Plantae medicinales praeparatae

DEFINITION

Type 1 herbal drug preparations are **homogeneous** products obtained by subjecting herbal drugs to treatments such as, but not restricted to: expression, distillation, fractionation, extraction, concentration, purification and fermentation. This type of herbal drug preparation includes, for example, essential oils, extracts, expressed juices and processed exudates. It also includes herbal drugs and Type 2 herbal drug preparations that have been subjected to size reduction for specific applications for example, cut for teas or powdered for encapsulation.

Type 2 herbal drug preparations are **non-homogenous** products obtained by subjecting herbal drugs to treatments such as those described in *5.18. Preparation of drugs for traditional Chinese medicines*, Section 2-3. *Roasting and Broiling* where the herbal drug, after processing, still retains, to a greater or lesser extent, its pre-processed shape and size or Section 2-2. *Cutting*, where leaching from a herbal drug occurs during the re-hydration process to such an extent that it leads to a significant decrease in the content of one or more constituents from the herbal drug.

Where a ***Type 2*** herbal drug preparation is either the subject of or included in a Ph. Eur. monograph, this will be clearly indicated in the relevant monograph.

Note: the term *comminuted* used in European Community legislation on herbal medicinal products describes an herbal drug that has been either cut or powdered. The term *herbal drug preparation* is synonymous with the term *herbal preparation* used in European Community legislation on herbal medicinal products.

Examples of TCM monographs published in *Pharmeuropa 22.4* will serve to illustrate how this would work in practice.

The draft monograph for *Fleeceflower root (2433)* [7] fulfils the definition of an herbal drug. Therefore, there would be no alternation to the *Definition* in this monograph.

The draft monograph for *Fleeceflower root, Processed (2480)* [8] fulfils the proposed definition for a Type 2 herbal drug preparation and the text under Definition in this draft monograph would be altered from:

DEFINITION

Processed *Fleeceflower root (2433)*.

to:

DEFINITION

Fleeceflower root (2433) processed as described under Production is a *Type 2* herbal drug preparation, according to the general monograph *Herbal drug preparations (1434)*.

The draft monograph for *Drynaria rhizome (2563)* [9] appears to describe only the herbal drug under *Definition*. However, under Identification A is stated that: 'After roasting, the brown colour turns darker.' indicating that two separate materials are described in the one monograph with the change in colour being the only reference to distinguishing between them. The herbal drug after roasting would fulfil the proposed criteria for a *Type 2* herbal drug preparation. Therefore, the Definition section in this monograph would be altered from:

DEFINITION:

Dried rhizome of *Drynaria fortunei* (Kunze) J. Sm. It is collected all year round and the ramenta removed.

to:

Dried rhizome of *Drynaria fortunei* (Kunze) J. Sm. It is collected all year round and the ramenta removed.

Drynaria rhizome processed by roasting (*5.18*) is a *Type 2* herbal drug preparation, according to the general monograph *Herbal drug preparations (1434)*.

Likewise, the Definition section in the Ph. Eur. monograph for Ginseng (1523) [10] would alter from:

DEFINITION

Whole or cut dried root, designated white ginseng; treated with steam and then dried, designated red ginseng, of *Panax ginseng* C.A. Meyer.

to:

DEFINITION

Whole or cut dried root of *Panax ginseng* C. A. Meyer, known as 'white ginseng'.

When the whole or cut fresh root of *Panax ginseng* C. A. Meyer is treated with steam and then dried, it is known as 'red ginseng'. Red ginseng is a *Type 2* herbal drug preparation, according to the general monograph *Herbal drug preparations (1434)*.

This differentiation between the herbal drug and its processed counterpart (to be defined as a *Type 2* herbal drug preparation) is important in order that all stakeholders understand that, from a good manufacturing practice perspective, the 2 materials are distinct entities and are not equivalent or interchangeable and that, as for all herbal drug preparations, data should be available on the herbal drug from which the herbal drug preparation was derived.

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