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Review

Revision and Improvement of Criterion on Traditional Chinese Medicines in *Chinese Pharmacopoeia* 2015

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ABSTRACT

Chinese Pharmacopoeia is updated every five years, of which traditional Chinese medicine (TCM) is the most important part. The 2015 version completed by the 10th Pharmacopoeia Commission has come into operation since December 1, 2015. Here we introduced the revision and improvement of quality evaluation and control standards of TCMs in *Chinese Pharmacopoeia* 2015.

Key words

Chinese Pharmacopoeia 2015; quality control; safety control; traditional Chinese medicines

1. Background

The *Chinese Pharmacopoeia* is updated every five years and promulgated by the China Food and Drug Administration. In *Chinese Herbal Medicines* (No. 2, Vol. 2, 2010), we introduced the 2010 version (Qian et al, 2010). Nowadays the 2015 version (Pharmacopoeia Committee of P. R. China, 2015), the 10th Pharmacopoeia in China has come into operation since December 1, 2015. The updated Pharmacopoeia is requested to be improved in Chinese Pharmacopoeia system structure, and the criterion of quality evaluation and safety control, and to largely cover drugs in the *National Essential Drugs List* (2004 edition) *of China*. The updated criterion on chemical drugs and biological products is required to be parallel with or close to the international standards, and the criterion on traditional Chinese medicines (TCMs) is expected to take the leading level around the world. The updated Pharmacopoeia will play more important roles in promoting technical development in pharmaceutical industry and optimizing the structure of pharmaceutical industry in China.

As one of the important features of the *Chinese Pharmacopoeia*, TCM is the most interested part. It is an important issue for TCM modernization that TCM is controllable in quality and safety. Upon TCMs, this version is requested to be improved mainly in the following guidelines: reference drug standards are expected to be established, in order to improve Chinese Pharmacopoeia standard system itself; homogeneous drugs are expected to have a general quality standard because various quality standards of homogeneous drugs are present in the pharmacopoeia; the approach of drug safety control is expected to be improved, especially for "toxic" TCMs, it is dispensable to know safe formulas, use

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dosage, and safe contents. For a long term in the TCM field, it is highly concerned that what are the most suitable quality evaluation and control models or approaches for TCMs, and nowadays diverse models have been or being developed, e.g., quantitative analysis of multi-components by single marker (QASM), chemical fingerprinting and analyte-specific chromatograms, DNA molecular identification, and bioassay.

Being the key techniques in TCM quality evaluation and control system, they are used more widely in 2015 version than before. Since China is the major country in production, consume, and export of TCMs in the world, it is a mission that China should develop a set of the quality criterion of TCMs leading the world in the TCM field. The improvement of TCM quality evaluation, and control systems in the 2015 version are shown in the following aspects.

2. *Chinese Pharmacopoeia* system improvement

2.1 Compiling structures of 2015 version revised

The *Chinese Pharmacopoeia* system basically consists of three parts such as general notices, general rules, and monographs, which are individually covered in a total of three volumes in previous versions. The 2015 version is composed of four volumes, Volume I−III cover traditional Chinese medicines (TCMs), chemical medicines, and biological medicines respectively, which include information on the standards of purity, description, test, dosage, precaution, storage, and the strength for each drug, and Volume IV is a new block specifically responsible for general rules and pharmaceutic adjuvants ever admitted to the appendix of previous Volumes I−III.

2.2 New principles

The 2015 version first covers several principles about the national criterion of reference drug preparation, drug package materials, and glass vessel of drugs. So the individual chains of drug production and circulation can be fully supervised by the official agencies according to the *Chinese Pharmacopoeia*. TCM related principles have been improved in several rules: the general rule on identification and quantitative determination of Chinese medical materials (CMMs) and prepared slices, the general rule on CMM processing, and the general rule on pharmaceutic adjuvants. Several principles are first established in the 2015 version directly related to CMMs: the guidance on DNA barcoding identification in CMMs (9107), the guidance on allowed contents of harmful residuals in CMMs (9302), and the guidance on fungi toxins detection in CMMs (9305). Based on those principles, several parameters are subjected to CMM identification and content allowance in CMMs, e.g., SO_2, heavy metals, harmful elements, pesticide residuals, and afltoxins.

3. More drugs admitted

A total of 5608 drugs are admitted to the 2015 version, of which 1082 are more admitted to and 43 are expunged from the 2015 version due to backward production and poor in quality, safety, and stability. So 90% of drugs in the *National Essential Drugs List of China* (2004 edition) have been covered. Volume I covered a total of 2598 TCMs including CMMs, prepared slices, plant oils and extracts, and Chinese patent medicines (CPMs), of which 440 were more admitted, 517 revised, and seven expunged. In the 2010 version, crud drugs, prepared slices, and CPMs are all greatly increased in variety (Qian et al, 2010), while in the 2015 version, crud drugs are increased by only three, and CPMs greatly increased by 400. CPMs that are ingredient with *Saigae Tataricae Cornu*, *Os Draconis*, apatite, and fossil have been expunged from the 2015 version.

CMMs are also revised or completed in botanical resource, character description, identification, quantitative determination, and atomic absorption to improve the quality control criterion (Tables 1−4). Twenty-three Chinese herbal medicines are revised in character description: *Smilacis Glabrae Rhizoma*, *Lonicerae Flos*, *Chuanxiong Rhizoma*, *Gastrodiae Rhizoma*, *Pseudostellariae Radix*, *Fritillariae Ussuriensis Bulbus*, *Luffae Fructus Retinervus*, *Lilii Bulbus*, *Angelicae Sinensis Radix*, *Saposhnikoviae Radix*, *Ophiopogonis Radix*, *Euryales Semen*, *Citri Sarcodactylis Fructus*, *Alismatis Rhizoma*, *Aurantii Immaturus Fructus*, *Citri Fructus*, *Nelimbinis Semen*, *Platycodonis Radix*, *Codonopsis Radix*, *Chrysanthemi Flos*, *Puerariae Lobatae Radix*, *Propolis*, and *Ziziphi Spinosae*.

4. Drug safety control

The 2015 version showed maximum allowance quantities of harmful and residual substances based on their toxicity, exposure level, residual levels, and transmission in environment. How to control harmful substances in TCMs, both endogenously and exogenously, is thought to be the key issue for developing TCM quality standards. So the quality standards admitted in the 2015 version are therefore believed to be important references for quality control of other similar drugs.

4.1 Chinese medical materials

4.1.1 More parameters admitted

TCM safety control system is updated for TCMs in the following parameters: contents of SO_2 residual, heavy metals, harmful elements, pesticides, fungi toxin, pigments, microorganism, and pathogens (Table 5).

The 2015 version first describes that residual SO_2 is not allowed over 150 mg/kg in CMMs and the corresponding prepared slices except special ones. Since historically multi-pesticides are not allowed in CMMs and the residual contents are controlled as stringent as in foods, more pesticides, in a total of 16, are admitted in the list of prohibition in the 2015 version, seven of which are admitted for the first time. *Ginseng Radix* et *Rhizoma* and *Panacis Quinquefolii Radix* are first requested in the maximum allowed residual contents of pesticides as well as the corresponding prepared slices. In the 2010 version, only *Glycyrrhizae Radix* et *Rhizoma* and *Astragali Radix* were