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INTRODUCTION

TCM Trends

Traditional Chinese Medicines (TCM) has been widely practiced for thousands of years in China and Eastern Asia.It is now an integrated part of the health care system in this part of the world; and currently in China,a strong push to modernize TCM through both scientific research and industrial development is under-way. As part of a global trend favoring healthcare with natural products, we are also witnessing in the past decades an increasing interest in Europe,US and other parts of the world on the use of natural herbs to formulate drug, dietary supplement or functional food products. In Germany, herbal medicines are categorized as medical products, and the estimate is that they account for about 10% of the market for prescription drugs, and nearly 30% of those of the OTC market.In the US, it is estimated that a quarter of the prescription drugs include at least one component which is derived from botanical plant extract or chemicals; and the market growth of herbal products such as St John's Wort,Ginkgo, Echinacea,Garlic, etc. has been phenomenon since the nineties.

HERBS AND HERBAL EXTRACT

In traditional TCM practices, the main forms of application for herbal drug are dried herb plants in the forms of slices, granules or powders. These are commonly called crude drugs, i.e., herbal plants which have had preliminary treatments according to tradi-tional procedures such as cleaning, simple heating,baking or specialized cooking. The TCM drugs in real practice usually consist of a mixture of crude drugs in a complex herbal formulation or concoction. The concoction prescribed by the doctor is extracted and taken by the patient through oral administration. Another popular form of crude drugs is “Jingao”, or “extract”, which is the concentrated syrup form of the extract. In the 1999 New Drug regulations promulgated by Chinese SFDA, an active component(s) extracted from either a single herb or a concoction is classified as Class I new drug; whereas a group of active compounds in the whole extract or its chemical fractions is classified as Class II new drugs.

In the 2005 Chinese Pharmacopoeia, 13 different kinds of“jingao” each prepared from a single herb have been recorded. A list of these extracts along with their major therapeutic functions and marker compounds are given in Table 1. In Europe and the US, extract is the main form of herbal products, and accounts for 95% of the TCM applications.

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Over the last decades, a number of lead compounds and new natural products derived from medicinal herb have been successfully isolated and identified, and great efforts have been made on the chemical and pharmacological studies of Chinese herbs. However, up to now,the scientific basis of majority of the Chinese medicinal material remains poorly understood both chemically and pharmacologically. Compositional analysis of the herbal extracts is the key to unlock the secret of their effectiveness, and the typical way in such studies involves the preparation of herbal extracts, testing their pharmacological activity, isolating the individual components of the extracts, followed by instrumental analysis to identify and quantify the target active compounds of interest. Depending on the objective of the study, this multistep process could lead to the preparation of three distinct types of intermediate extracts. The first is a“marker compound extract”, in which a specified amount of a marker compound or a class of compounds with similar properties is included in the finished product. The marker compound is usually bioactive, although such activity may or may not represent the beneficial or therapeutic function of the entire extract. Examples of marker extracts include ginseng extract with ginsenosides as the markers, or licorice with flavornoids or glycyrrhizinic acids as the markers. The second type of extract is “active constituents extract” in which a specific component(s) with confirmed bioactivity has been enriched to a higher level than those present in the herbal plant itself. Examples of active constituents extracts include Gingko with enriched levels of glycosides or grape seed with enriched concentration of polyphenols.Table 2 lists some of the better known extracts of the above two types sold commercially as dietary supple-ments. The third type of extract is normally called an“active fraction”, and is a term gaining increasing popularity in the TCM community in recent years. In these extracts, a broad base of compounds rather than a specific species or class of compounds are believed to be responsible for the bioactivity of the material. Many of the TCM extracts fall in this category, and will be the focus of our discussion in the text follows.

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As a reference standard, the entire process for the preparation of extracts needs to be standardized in order to produce extracts with compositional uniformality,batch to batch consistency and consistent quality and property.Standardization requires the control of all variables which could potential affect the final quality of the extracts. These factors include the plant species,the plant part, the primary processing step, post plant harvest, the extraction procedure and the manufacturing process leading to the products. A standardized extract should provide as detailed information as possible about the raw material as well as process conditions. Because of the complexity of the material, it is often difficult, and perhaps unnecessary, to establish an all-embracing chemical extract. Instead, several extracts from the same herb, each with its own composition and properties, can be produced to meet different objectives. Some common examples include the preparation of separate lipid soluble and water soluble extracts, or the separation of extracts based on compound types such as flavonoids, terpenoids,alkaloids, glucosides etc.

SIGNIFICANCE OF STANDARDIZED EXTRACT

The extraction method should be selected and optimized based on two considerations: (1) it should contain at least the major and preferably all the active components in the original herb, and (2) it should reflect the efficacy of the original herb. The two objectives are met respectively by chemical analysis and bioassay in order to establish the chemical identity and to quantify the bioactivity of the active component. To better reflect the multi-components and multi-target nature of herb medicines, fingerprinting analysis coupled with computerized whole spectrum analysis has been developed recently to better represent the biochemical properties and compositional features of the material. As will be exemplified in later discussions, fingerprinting analysis of the extract provides a convenient means to establish the authenticity and assess the quality of the extract.

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CThe focus of our discussion is the development of standardized extract for the quality assessment of herbal drugs. To evaluate the quality of a drug means to establish the authenticity of the herbal species, and to determine the purity, consistency and potency of the material.The authenticity of a Chinese herb is usually established by reference to its descriptions given in the Chinese Pharmacopoeia, in which the sensory, macroscopical and microscopical characteristics of the herb is prescribed.Potency study refers to the determination of the intrinsic quality of the herb, i.e., the amounts and purity of the medicinal principles or active constituents present. Standardized extract plays a key role in both areas.

In TCM, it is a known fact that one herb may originate from more than one source and sometimes different plants are used under one common name. Even for the same species, the qualities of individual herbs vary greatly because of variation in geographical origin, cultivation practice, harvest time, and storage or processing conditions (1,14,30) . There are 540 different kinds of TCM listed in Chinese Pharmacopoeia (2005). Microscopic identification and chemical analysis are the two main techniques to distinguish different TCM species. To distinguish TCM through their apparent feature even under microscopy is often difficult. The technique is time consuming and strong expertise of the analyst is necessary for interpretation. Until recently, authentication by chemical analysis usually relies on comparative analysis using a single chemical compound as the marker or indicator species, e.g., the identification of American ginseng (Panax quinquefolium. L) using ginsenoside Rb1, Re and Rg1 as the marker compounds (15) . The method, however, has low specificity because these ginsenoside species are present in more than one herbal species besides American ginseng. Similar situation exists between Ligusticum chuanxiong and Radix Angelica Sinensis which share common ingredients of ligustilide and phthalide compounds (16) . The use of standard extract coupled with fingerprinting analysis (see sections follow) provides higher specificity and is more reliable.

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Definable quality and quantifiable dose/bioactivity relationship are two major technical issues in the development of drugs or health products derived from natural herbs. It is now well documented that the pharmaceutical actions of herbal products often cannot be attributed to a particular compound, but owe rather to the synergy of a complex compound mixture. Currently, a common practice in natural product research is to select one or more compounds as either active or “markers” for quality assessment, similar to the situation described above in authentication exercise. Again, the application of bioactive extracts accompanied by reproducible fingerprints provide a more effective quality assessment system to truly represent its therapeutic effects.