

•Editorial•

Deciphering the metabolic fates of herbal constituents and the interactions of herbs with human metabolic system

GE Guang-Bo *

Institute of Interdisciplinary Integrative Medicine Research, Shanghai University of Traditional Chinese Medicine, Shanghai 200000, China

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Herbal medicines play a crucial role in the healthcare system in China and other East Asian countries, and also have been used as alternative medicines in most Western countries [1-3]. However, in most cases, the metabolic fates of herbal constituents and their effects on drug metabolism or endogenous metabolism in the human body have not been well-investigated [4-5]. Notably, the concomitant use of herbal medicines may lead to clinically relevant herb-drug interactions or adverse reactions or even metabolic disorders, when some herbs are co-administrated with those drugs with narrow therapeutic indices (e.g. warfarin, digoxin, thyroid hormones and some anticancer agents) [6-8].

Unlike Western therapeutics, herbal medicines are complex mixtures, and these complex mixtures (as well as their *in vivo* metabolites) may interact with a wide range of proteins in various metabolic organs (such as the intestine, liver and kidney) in extremely complex ways. The lack of this key information has aroused great concerns on the risks of herb-drug interactions (HDI) or herb-endobiotic interactions (HEI), by both the consumers and the clinical pharmacologists [9-10]. Improvements in the knowledge of the metabolic fates of herbal constituents, as well as the interactions of herbal products with Western therapeutics, will be very helpful for the rational use of herbal products in clinical settings, especially to avoid the occurrences of clinically relevant HDI or HEI. Thus, it is necessary to systematically decipher the metabolic fates of herbal constituents and to carefully characterize the interactions of herbal products with the key enzymes in human metabolic system.

In this issue of *Chinese Journal of Natural Medicines (CJNM)*, we are pleased to publish four timely research articles and two comprehensive review articles regarding the metabolic fates of herbal constituents and the interactions of herbs with the metabolic system. In the first paper, WANG Shu-Fang *et al.* [11] have systematically identified the constituents in a herbal prescription (Gui-Zhi-Jia-Ge-Gen-Tang)

and carefully decipher the prototype components and the detectable metabolites in rat plasma following oral administration of this herbal medicine, using two state-of-the-art analytical techniques including liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-Q-TOF-MS) and liquid chromatography-ion trap mass spectrometry (LC-IT-MS). They have detected a total of 141 constituents in GZJGGT, and 77 compounds have been tentatively identified. Meanwhile, 45 prototype compounds and 48 metabolites were tentatively identified in rat plasma after oral administration of GZJGGT, while their metabolic network was also described for the first time. In the second paper, YANG Xiu-Wei *et al.* [12] present a good example to systematically profile the metabolites of a given herbal constituent. The authors use a high-resolution mass spectrometry based metabolomics strategy to carefully study the metabolic profiles of Angelol B in rats, following oral administration of this bioactive herbal constituent to rats. A total of thirty-one metabolites of Angelol B are detected in rat plasma, feces and urine, including 20 phase I metabolites and 11 phase II metabolites. CAI Shao-Qing *et al.* [13] report the *in vitro* phase I metabolism of a pure pterocarpan (astrapteropan, a bioactive constituent of *Astragali Radix*) in rat hepatic S9 incubation system for the first time. Totally, 40 new metabolites and 1 new degradation product of AP are identified with the aid of NMR and HPLC-DAD-ESI-IT-TOF-MSⁿ techniques.

ZHOU Ji-Chao and ZHANG Xiao-Wei [14] discuss the interactions between natural products and intestinal bacteria. They have summarized the relationships between *A. muciniphila* (a new mucolytic bacterium that produces more than 60 enzymes) and host health or diseases, especially focusing on the metabolic diseases and related molecular mechanisms, as well as the natural compounds and drug-derived substrates affecting its colonization in the host, expecting to provide evidence and clues for the development

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[*Corresponding author] E-mail: geguangbo@shutcm.edu.cn

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of drugs targeting *A. muciniphila*. ZHOU Qi-Hang *et al.* [16] systematically summarize the metabolic interactions between Buguzhi constituents and human drug-metabolizing enzymes (DMEs), an important class of enzymes participating in drug disposition and endogenous metabolism. In this review article, the metabolic pathways of the major constituents from the Chinese herb Buguzhi, along with their chemical structures, involved enzymes and pharmacokinetic parameters have been well-summarized, which will be very helpful for the pharmacologists to gain deeper understanding of the metabolic fates of Buguzhi constituents in both human and experimental animals.

TANG Yu-Ping *et al.* [16] provide one of the best examples for a comparative study on pharmacodynamic, pharmacokinetic and tissue exposure of bioactive constituents in Dahuang-Gancao decoction in normal and experimental constipation mice. An UPLC-MS/MS based method has been constructed for the quantitative analysis of the key ingredients in DGD (rhein, emdin, aloe-emodin, rhein-8-*O*- β -D-glucoside, sennoside A, glycyrrhizic acid, and liquiritin) and such method has been applied to determine the comparative pharmacokinetic and tissue exposure of these key ingredients in mice. The authors found that compared with normal mice, Dahuang-Gancao decoction treatment in constipation mice exhibit stronger purgative effect by the increased fecal excretion and reduced first defecation time, which can be attributed to the higher exposure of the anthraquinones in plasma, liver and colon in the constipation mice.

The use of herbal products as dietary supplements or as herbal therapeutics is increasing worldwide. As did in the past and the current issue [10-18], the information on the metabolic fates of herbal constituents in the human body and the interactions of the herbal constituents with human metabolic system are very useful for avoiding the occurrence of adverse drug events. In the future, more information or sufficient knowledge should be provided to deeply understand the metabolic fates of commonly used herbal medicines and the interactions of these herbal medicines with Western drugs, which would be very helpful for regulation and globalization of herbal medicines [19-20].

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Dr. Ge has been working in Shanghai University of Traditional Chinese Medicine as a full professor and the vice dean of Institute of Interdisciplinary Medicine since 2017. His current researches are focused on drug metabolism and herb-drug interactions. His representative achievements have been published in many top journals, such as *J. Am. Chem. Soc.*, *Angew. Chem. Int. Ed.*, *Chem. Sci.*, *Biosens. Bioelectron.*, *ACS Applied Materials & Interfaces*, *J. Med. Chem.*, *Anal. Chem.*, *Chem. Commun.*, *et al.* Now he is the editorial board member of more than 10 scientific journals, such as *Acta Pharmaceutica Sinica B*, *Journal of Ethnopharmacology*, *Chinese Chemical Letters*, *Chinese Journal of Natural Medicines* and *Current Drug Delivery*.