Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfda-online.com

Preface

It is my great pleasure to make some introductory remarks for this special issue with contributions from top authors across different continents in the realm of drug interactions with herbs, foods and dietary supplements. To all the readers of *JFDA*, I am confident that the collective insights of these papers would definitely extend the frontier of drug interaction studies.

Drug interaction is among the important factors affecting the pharmacokinetics/pharmacodynamics (PK/PD) of medicines and, in some cases, leads to lethal adverse effects. Therefore, it is indispensable to take into account the drug interactions in new drug development, clinical practice and regulatory evaluation. However, measuring drug interaction is not feasible during the clinical trial stage of new drug, therefore, understanding the mechanisms of interaction has huge implications for clinical practice. Since the ground-breaking discovery of grapefruit juice – felodipine interaction was reported in 1991, followed by frequent discussions of St. John's wort – drug interactions near 2000, the botanical – drug interactions and relevant mechanisms have drawn increasing interests of clinicians and pharmaceutical scientists during the past two decades.

In regard to the mechanisms underlying drug – drug interactions, modulations of cytochromes P-450 (CYPs) are the most well known. A number of drugs have been withdrawn from the market around the end of last century as the result of fatal adverse effect due to the inhibition on CYP 3A4 by other drugs. Besides, in recent years, drug transporters, such as P-glycoprotein (P-gp), multidrug resistance-associated proteins (MRPs), breast cancer resistance protein (BCRP), organic anion – transporting polypeptides (OATPs), organic anion transporters (OATs) and organic cation transporters (OCTs) have been recognized to play pivotal roles in pharmacokinetics and drug interactions. Therefore, further studies of transporter – mediated drug interactions with herbs, foods, dietary supplements are becoming essential.

Interestingly, although both grapefruit juice and St. John's wort altered the PK/PD of numerous drugs through modulations on CYP 3A4 and/or P-gp, they exhibited opposite modulations. From the mechanism – based interaction studies of these two botanicals, we could assume that herbs, foods and dietary supplement are potential perpetrators modulating CYPs and drug transporters, which is the core theme of this special issue. In regard to mechanism elucidation, *in vitro* models are usually used; nevertheless, the *in vitro/in vivo* (IVIV) correlations have mostly not been verified. Among the probable reasons, the major one should stem from the fact that a variety of natural compounds, such as glycosides, polyphenolics and esters, were rapidly and extensively metabolized *in vivo*, and exclusively presented in the systemic circulation as their metabolites instead of the parent forms, that is an obvious discrepancy with most synthetic drugs.

Till now, the studies of transporter – mediated botanical – drug interactions focused mostly on the absorption site involving P-gp, BCRP, MRPs and OATPs. As to the excretion site, little has been revealed due to the lack of understanding of the pharmacokinetic properties of natural molecules. Furthermore, owing to the unavailability of authentic metabolites, relevant mechanisms of botanical metabolite – drug interactions have rarely been clarified. In the future, novel approaches are required to bridge the academic gap in exposing the mechanism of botanical – drug interactions at the excretion site.

Nowadays, with more case reports of drug interactions with herbs, foods and dietary supplement published, it is the right time to call for more mechanism – based studies on botanical – drug interactions to ensure the safety and efficacy of pharmacotherapy. The topics in this issue ranged from preclinical to clinical advances and to regulatory viewpoint as well. Herbs, foods, dietary supplements and adjuvants were on the list of perpetrators, while cardiovascular drugs, immunosuppressants and chemotherapeutics were on the victim side. The relevant mechanisms discussed have

covered various modulations mediated by PXR, P-gp, OATPs, OATs, OCTs and CYPs. Hopefully, this special issue provides valuable updated information for researchers, clinicians and regulatory professionals alike.

Finally, I would like to express my gratitude to all the authors and reviewers for their kind and valuable contributions to this special issue. Ms. Lily Chiu, the executive editors of JFDA, is also greatly appreciated for her efforts and cooperation.

Pei-Dawn Lee Chao, Ph.D., Guest editor, Honorary professor
School of Pharmacy, China Medical University, Taichung, Taiwan
E-mail address: pdlee@mail.cmu.edu.tw

Available online 21 March 2018

https://doi.org/10.1016/j.jfda.2018.03.001