#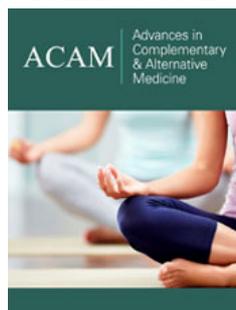 Importance of Pharmacokinetic Profiling & Drug-Drug Interaction Evaluations in the Development of Complementary and Alternative Medicines

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Introduction

Complementary and alternative medicines (CAM)

These are the therapeutic approaches other than the conventional medicine practices that are used to ameliorate, mitigate and/or treat a patient. These approaches including Acupuncture, Aromatherapy, Homeopathy and Herbal medicines etc. are practiced in various parts of globe for thousands of years. CAM are widely used alone or in combination with conventional medicines across the globe. It has been reported that approximately 80% of global population use herbs and other CAM based treatments as their primary medications [1-2].

Discussion

Herbs as CAM

Herbal medicines are widely practiced across the globe form very ancient time. The traditional medicine system including Ayurvedic medicine system predominantly in South-East Asia, Kampo in Japan, Traditional Chinese Herbal Medicine (TCM) in China are best example of herbal medicinal practices. In the recent years, the phytotherapies have gained a substantial attention and are becoming increasing popularity in the Western world [3-4]. Herbal medicines as multicomponent complementary interventions against number of medical conditions like metabolic disorders, liver injury, diabetes, neurodegenerative disorders, and chronic diseases like cancer are getting more attention compared to single drug therapy. Since, herbal medicines contain an array of biologically active components, multiple components interact in vivo with multiple targets to achieve an optimal therapeutic effect [5].

CAM Pharmacokinetics

Being a nature derived medicine, patients believe that taking CAM for treating a medical condition is safe and has no adverse effects is not always true. In fact, the efficacy

of herbal medication depends on multiple constituents and respective pharmacokinetics (PK). Many factors like vast number of constituents, wide range of chemical structures, various concentrations, complex intra-interactions etc. makes PK profiling of multiple constituents difficult and erroneous. Furthermore, the complexity of biological matrices poses additional inevitable challenges to bio-analytical approaches for quantitative measurements. Due to these hurdles, the poly-pharmacokinetics (poly-PK) has been determined for very few cases [6].

CAM co-administration

With the advancements and increasing knowledge in this field, researchers understand that the PK profile explaining the tissue distribution and metabolism of individual constituents are critical contributor to the pharmacological efficacy and safety of herbal medicines. There are documented evidence showing that the PK of a single compound could be significantly different as compared to PK of same compound in a multiple constituent treatment due to interactions at various levels including absorption, distribution, metabolism, and excretion (ADME). Moreover, different physiological and disease status including sex differences, age, genetic polymorphism etc. profoundly affects the absorption and hence the oral bioavailability, tissue distribution, herbal medicine plasma concentration and related PK parameters [7-10]. Such undesirable alterations in the intrinsic PK profile could significantly variate the observed therapeutic efficacy of herbal medications. It has been seen that the most prevalently, herbal medicines are used as "Herbal formula" that often includes combination of two or more herbs in various proportions as clinical application. PK compatibility of more than two herbs further complicates PK and herb interaction potential. If herbal medicines and/or formula are practiced in combination with the conventional drugs, enhanced risks of potential herb-herb and herb-drug interactions are imperative. All these aspects raise concerns about the safety and efficacy of herbal CAM due to lack of evidence-based PK profiling [8-11].

Other factors influencing the PK and interaction potential of herb CAM

There are several factors that influences the PK and interaction potential of herbal medicines. One among these factors is the post-harvest processing of crude herbal material. Post-harvest processing is a crucial and routine step that is performed on raw herbal materials before clinical application. The aim targets to obtain a modified herbal material that offers enhanced therapeutic effects and reduced toxicity. This is accomplished either by concentrating or reducing or removing some ingredients in herb or herb formula after processing. Changing the physiochemical characteristics often influences the PK of individual constituents. This overall help to achieve the desired pharmacological response. In various traditional post-harvest processing, use of animal derived adjuvants like bile, animal fat etc. could also affect the PK profile of herbal constituents [12-14].

Differential expression of a variety of gastro-intestinal, hepatic, nervous and renal transporters along with differential CYP expression, percent body fat composition, body weight, different blood flow between sexes, body fluid volumes are few more factors that attributes to the differences in PK and various levels of interaction potential of herbal constituents [15].

Conclusion

To mitigate the gaps between clinical use of herbal medicine and traditional practices, evidence-based labeling of herbal medicines in terms of PK profiling and generating safety and efficacy data is essential. Further understanding of the metabolic fate of individual constituents of herbal medicines to flag them as pharmacologically active or toxic components is desirable. The bioavailability estimation of various components in different compositions of herbal formula is essential to obtain optimized pharmacological response. More emphasis should be given to explore the Pharmacokinetic profiling of major active components and their interaction potential in various herb formula. Besides this, drug-herb interactions, herb-herb interactions, pretreatment, and processing techniques influencing the efficacy, age and gender of patients, pathological status are few factors that are to be addressed.

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