

Understanding the relevance of herb–drug interaction studies with special focus on interplays: a prerequisite for integrative medicine

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Abstract

Integrative medicine refers to the blending of conventional and evidence-based complementary medicines and therapies with the aim of using the most appropriate of either or both modalities for ultimate patient benefits. One of the major hurdles for the same is the chances of potential herb–drug interactions (HDIs). These HDIs could be beneficial or harmful, or even fatal; therefore, a thorough understanding of the eventualities of HDIs is essential so that a successful integration of the modern and complementary alternative systems of medicine could be achieved. Here, we summarize all the important points related to HDIs, including types, tools/methods for study, and prediction of the HDIs, along with a special focus on interplays between drug metabolizing enzymes and transporters. In addition, this article covers future perspective, with a focus on background endogenous players of interplays and approaches to predict the drug–disease–herb interactions so as to fetch the desired effects of these interactions.

Keywords: Ayurveda, drug metabolizing enzymes–transporter interplays, herb–drug–disease interactions, integrative medicine

Introduction

Modern system of medicine has emerged as the primary choice for the treatment of nearly all types of health-related issues, although, it is mainly based on the nonholistic/bug killing/target-based approach, which ultimately leads to future side effects (notable in case of chronic disorders such as cancer, diabetes, arthritis, etc.).^{1–3} However, patients with such chronic illnesses directly/indirectly undergo combinational/multimodal therapy with or without the knowledge of physicians, leading to potential herb–drug interactions (HDIs).¹ The MD Anderson Cancer Centre, in USA, reported that 52% of their cancer patients had used at least one form of complementary and alternative medicine (CAM), and 77% of those were using herbs.⁴ While, according to the World Health Organization (WHO) and other reviews >80% world's population uses CAM for their health care needs and particularly in western countries CAM has become increasingly popular over the last few decades.^{1–5} However,

concomitant usage of herbs and conventional medicines globally could be much higher as healthcare professionals often do not ask about herbal remedies when prescribing and patients do not volunteer that they are taking them.^{1,7–11} Indeed, such a scenario of concomitant usage of herbs/CAM and conventional medicines brings with it the potential problem of HDIs and this issue has emerged as a major hurdle/problem in our journey toward integrative medicine (IM).^{1,2,12} IM refers to the blending of conventional and evidence-based complementary medicines and therapies with the aim of using the most appropriate of either or both modalities for efficient patient care.¹⁴ In short, IM uses all appropriate, evidence-based therapies to achieve health.¹⁵ For example, *Withania somnifera*, have been widely accepted as a novel complementary therapy for integrative oncology care.¹⁶ *W. somnifera* not only helps in controlling the tumor growth but also exerts antioxidant, anti-inflammatory, immunomodulating, and antistress properties that help in combating the cancer and associated complications. It has also been found that, *W. somnifera* enhances the effectiveness of radiation therapy and chemotherapy while potentially mitigating their undesirable side effects.^{16–18} Similar experiences were also observed by Patil et al and Borse et al for *Asparagus racemosus* and/or *Timospora cordifolia* accepted as novel complementary therapy for integrative oncology care.^{19–22} IM/care practices are getting increased day by day throughout the world. For instance, IM is being practiced at BSDT's Ayurvedic Hospital & Research Centre, India, The Osler Center for Integrative Medicine, Arizona Center for Integrative Medicine, and many other places in the world.^{23–26} However, integrative management of the disease is far bigger challenge in spite of high scientific efforts proceeding globally mainly because of the potential risk associated with HDIs.^{27–33} Hence, the focus needs to be shifted on potential interactions between herbs and pharmaceuticals because of the growing popularity of herbal medicines/CAM. Here, it must be highlighted that the probability of HDIs can be much higher than drug–drug interactions, since most herbal medicines (even single-herb products) contain mixtures of pharmacologically active

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