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Mini Review

Drug Interactions Caused by Herbal Products and Food Supplements

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Abstract

The use of herbal products and food supplements have gradually increased among adults and elders to be healthier and to prevent or treat some chronic and malignant diseases. Consumers usually think that these natural products are safe and harmless. However, the fact may be different. Combinations of these products with drugs are usually targeted to increase the pharmacological activity of drugs or reduce their toxicities. But this kind of combination may lead to the increased health risks because of the bioactive contents of these products. The pharmacodynamic and/or pharmacokinetic (absorption, distribution, biotransformation and elimination of the drugs) interactions may occur. Sometimes life-threatening adverse reactions may be appeared due to these interactions. Each of an herbal product can contain dozens of chemicals including alkaloids, flavonoids, glycosides, fatty acids and others. In this manner these interactions may be very complex. The complex results of these interactions can be better evaluated and prevented by understanding molecular mechanisms of bioactive compounds. This short review gives information about interactions of food supplements and prescribed drugs and will help health care professionals and consumer population to aware of interactions.

KeyWords: Drug; Food supplements; Herbal product; Interaction

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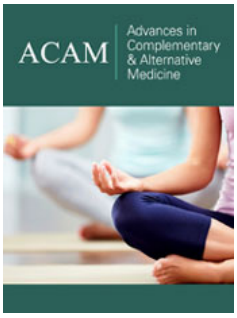

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Introduction

Chronic diseases (such as cardiovascular, neurodegenerative, metabolic diseases and cancers) are increasing as life-span gets longer. The view that these diseases are related to food habits becomes widespread. Therefore, many health organizations suggest consuming more frequently herbal foods to prevent and delay this kind of diseases. Phytochemicals which are ingredients obtained from plants have very large activity spectrum. Their most popular activities depend on antioxidant characteristics. Crude herbal products (such as roots, seeds, flowers, leaves and teas) are more frequently used in developing countries. They can be formulated in different forms such as a mixture (Asian herbal medicine and Indian ayurvedic medicine) [1] or they can be prepared as pharmaceutical products (as tablets or capsules) and named as "nutraceutical" by hybridizing "nutrient" and "pharmaceutic" terms [2]. This kind of commercial herbal products are usually used in developed countries [1]. Sometimes they contain harmful contaminants. The drugs which are targeted their essential effect may also be added secretly to herbal products and their all constituents cannot be known. Because this kind of additives are not remarked on their labels. There are differences in contents and the concentrations of chemical ingredients from batch to batch and producers. These differences can affect their pharmacokinetics and pharmacological activities.

Herbal food supplements are preferred by consumers who want to be healthier and by patients with chronic diseases and especially cancer. There is a popular belief that the natural products are "safe and harmless". However serious problems were reported when these products are used with drugs [1, 3]. There are some regulations to ensure safety and quality standards for the production of these herbal products and dietary supplements in EU and USA but not in developing countries [3].

The most important interactions between herbal products and drugs were reported with St John's Wort, *Ginkgo biloba*, *Echinacea*, *Panax ginseng*, Kava kava (*Piper methysticum*), Licorice roots, glucosamine-chondroitine, melatonine, *Valeriana*, fish oil, resveratrol, curcuminoids, *Sylibum marianum*, *Hydrastis canadensis*. Herbal hepatotoxicity is the most serious adverse effect resulted especially from the use of weight losing products.

St John's Wort is typically used as antidepressant and added to antidepressant therapy. However, it induces CYP3A4 enzymes and P-glycoprotein pump [4, 5]. Therefore, it is expected to interacted with a lot of drugs metabolized by this enzyme and pump systems. These interactions can lead to reduce the activity oral contraceptives, verapamil, nifedipine, cyclosporine, alprazolam, klozapin, metronidazol and imatinib [6-8], and increase the activity of ACEI, the toxicity of paracetamol [9], and interact with digoxin [5, 7], SSRIs and MAOIs [6, 7, 10]. It was reported that *Ginkgo biloba* and *Ginseng* (*Panax spp*) inhibited CYP1A2, CYP2C9, CYP2C19, CYP2D6 ve CYP3A enzymes [5,6]. They can increase the risk of bleeding when used with varfarin, klopidogrel, tiklopidin, dipiridamol, naproksen, diklofenak, ibuprofen and aspirin [5, 7, 8] and change the activity of antihypertensive drugs. *Ginkgo biloba* can interact with carbamazepine and lamotrigine both pharmacodynamically and pharmacokinetically.

Licorice is known to inhibit CYP2A1, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4 enzymes [5]. Its active constituents as glycyrrhizin and glycyrhetic acid inhibit the metabolism of steroids so it can lead to sodium retention and potassium depletion by increasing the levels of cortisol and mineralocorticoids. Therefore, it can be interacting with antihypertensive and antiarrhythmic drugs [11]. Furthermore, it can increase bleeding risk by interacting with varfarine [7] and induce abortus in pregnants [8]. *Glukozamin-kondroitin* can increase bleeding by interacting with coumarines [7] and lead to hyperglycemia when used with antidiabetics [6]. *Echinecea* [8, 12], Kava kava (*Piper methysticum*) [5], *Valeriana* [5], *Sylibum marianum* [13], *Hydrastis canadensis* [5], *Resveratrol and curcuminoids* [14] can inhibit CYP3A4 enzymes and interact with lots of drugs. Fish oil can potentiate the activity of lithium, increase bleeding risk when used with warfarin, nonsteroidal anti-inflammatory drugs [12] and suppress the activity of enalapryl [6].

Conclusion

Consumers and health professionals should be aware of these adverse and harmful effects of herbal products and food supplements to be used for being healthier and supporting the treatments of chronic diseases. These products are used because of their antioxidant activities. However, the antioxidant constituents can be pro-oxidant [15] due to their long-term use and overdose.

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