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Herbal, Drug and Food Interaction

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Introduction

All medicines were derived from natural materials in the ancient time (1). Most of those early medicines are described under the broad heading “herbs,” although that term may prove misleading. Even though people often think of herbs as plants or plant-derived materials, several commonly used items were obtained from animals and minerals. Further, although the term “herbs” suggests something that is beneficial and has little potential for harm, numerous toxic materials were used, such as foxglove, deadly nightshade, and jimson weed (*Datura*). Herbalists sometimes processed the herbs to change them from their original form. As the science developed the researchers attempted and succeeded to isolate some active constituents from herbs, so that the end products were not as nature presented them. For example, aconite was processed extensively in China to reduce its toxicity so that it could more readily be used, and borneol, the active constituent found in a few tropical plants, was isolated centuries ago in relatively pure form, a translucent crystal, for both internal and external use. The use of potent and toxic substances and the intentional alteration of natural substances are characteristics of production of modern drugs. Thus, some issues that arise today about interactions of herbs and drugs may have already been encountered in earlier times when herbs were combined with each other (2).

The ancient Indian system of Ayurveda is practicing in India since 1500 BC, the main aim of this system is to preservation of normal health and curing the diseased one. Ayurveda has focused on patient safety and benefits. In fact it is known that drug safety is a very basic and fundamental concept in medical practice. The current raised issue with respect to Alternative medicine and Ayurveda is increasing reports of Adverse Drug Reaction (ADR) related to herbal medicine (3). This may be due to increase in number of people taking herbal products either as a medicine or as a nutritional supplement. Such reports many a times neglect to identify the cause behind the event which can be pertaining to variety of issues which are already considered in Ayurveda but are neglected many a times either due to ignorance or negligence. There is mis-belief that natural drugs are safe and devoid of toxicity.

But this is not true as Ayurveda states that every material in the universe is medicine and thus exerts one or the other therapeutic effect if utilized properly. But injudicious use may alter the action of drug, the intensity of which may be mild to severe or unpredictable. Also activity could be synergistic, decreased, antagonistic action or increase in the bioavailability.

Type of interactions

The interactions mentioned in Ayurveda can be categorized into herb with herb, herb with food, herb-animal origin drugs and Drug disease interaction.

- 1. Herb-Herb interaction:** Piper betel is contraindicated while taking *Garcinia Morella*, *Basella alba* along with *Sesamum indicum* (4, 5)
- 2. Herb-Food interaction:** Combination of Payasa (milk preparation) and Mantha (gruel) is contraindicated wine with steamed grains, Radish with milk (4,6)
- 3. Herb-animal origin drug interaction:** Kapotamamsa (meat of pigeon) is contraindicated with Sarshapataila (*Brassica alba*). Pork is contraindicated with Narikelataila (oil of *Coccoloba nucifera*), Equal quantity of Madhu (Honey) with Grutha (Ghee) is contraindicated and this has been proved to produce toxic effect by combination (4, 6)
- 5. Disease related interaction:** Haritaki (*Terminalia chebula*) contraindicated in pregnancy, malnourished, anorexia after bloodletting (7).

Common food interactions in Ayurveda

For the most part, the possibility of herb-drug interactions had been largely ignored during this revival of medicinal herb use. Ayurveda has mentioned different type of interaction of herb and its formulation. Harmful effect of interaction should be explained to patients and such type of food should be avoided during the medication. Some examples are as follows.

- Pippali (*Piper longum*) prepared with fish fat, Kakmachi (*Solanum nigrum*) with honey or with roasted meat, Seeds of pushkara (*N. nucifera*) with honey, Bhallataka (*Semecarpus anacardium*) with hot water, Kampillaka (*Mallotus*

Table 1: Some reported interactions causing herb

Herbs	Source	Parts	Interactions
St. John's wort	<i>Hypericum perforatum</i>	Tops	Warfarin (to cause bleeding); serotonin-uptake inhibitors (to cause mild serotonin syndrome); indinavir (decreased bioavailability); digitoxin, theophylline, cyclosporin, phenprocoumon, and oral contraceptives (all with reduced bioavailability)
Ginseng	<i>Panax ginseng</i>	Root	Antidepressants such as phenelzine sulfate (to cause manic episodes, headaches); warfarin (to cause bleeding or to decrease effectiveness); corticosteroids (potentiation); estrogens (potentiation)
Ginkgo	<i>Ginkgo biloba</i>	Leaf	Warfarin (to cause bleeding)
Ginger	<i>Zingiber officinale</i>	Rhizome	Sulfaguanidine (enhance absorption)
Garlic	<i>Allium sativum</i>	Bulb	Warfarin (to cause bleeding)
Licorice	<i>Glycyrrhiza uralensis</i>	Root	Corticosteroids and thiazide diuretics (potentiation); digitalis or other cardiac glycosides (increased sensitivity)
Bupleurum	<i>Bupleurum falcatum</i>	Root	Sedatives (potentiation)
Astragalus	<i>Astragalus membranaceus</i>	Root	Cyclosporine, azathioprine, methotrexate (to impair intended immunosuppressive effects).
Mahuang	<i>Ephedra sinica</i>	Leaf	MAO inhibitors (to cause hypertension); cardiac glycosides or halothane (to produce cardiac arrhythmia); caffeine (to intensify cardiovascular side effects)
Aloe	<i>Aloe ferox</i>	Leaf sap	Cardiac glycosides and antiarrhythmic agents (potentiating by reducing potassium via laxative effect)
Rhubarb	<i>Rheum officinale</i>	Root	Cardiac glycosides and antiarrhythmic agents (potentiating by reducing potassium via laxative effect)

philippinensis) with buttermilk should not be taken; these combinations may lead to various harmful effects, even death.

- Milk should not be taken after intake of radish, garlic and bitter gourd (*Momordica charantia*). Leaves of *Ocimum sanctum* may cause various types of skin diseases. Leaves of asofoetida (*Ferula narthex*) or ripe fruit of lakucha (*Artocarpus lakoocha*) should not be taken with honey and milk; it may cause loss of strength and complexion and may lead to oligospermia, sterility and many other diseases, even death (8).
- Intake of bhallataka seeds with hot water and kampillaka with buttermilk are also unwholesome and may cause various ailments in the body. Shilajatu should not be taken with kakmachi and meat of pigeon. Fruits of lakucha and decoction of masha should not be taken in combination. Paste of sesame seeds with leaf of black cumin (*Nigella rubra* Linn.) may cause diarrhea (9).

Herb drug interaction in modern system of medicine

Green vegetables (especially broccoli, spinach, peas, cabbage, and cucumbers) were found to have a measurable impact on anticoagulant therapy. The main active ingredient in the green vegetables is vitamin K. It has coagulation promoting qualities that overcome the effects of the anticoagulant drug, thus making the therapy less effective (the drug dosage has to be increased). Vitamin K is produced by intestinal bacteria; use of antibiotics that inhibit intestinal bacteria can also change the vitamin K content of the patient's blood.

Teas, pills, and other forms of herbal preparations generally have low levels of vitamin K, due to the relatively small amount of leafy tops (the main source of this vitamin) that are consumed. Still, many herbs are reputed to have anticoagulant properties that were investigated because of the importance of anticoagulation therapy. The concern that arises is whether or not these herbs will further reduce platelet aggregation and, as a result, increase the chance of spontaneous hemorrhage, as can occur when

two anticoagulant drugs are taken. In particular, the most commonly used Chinese herb for treating blood stasis in modern practice is salvia. It has been reported that salvia may enhance the warfarin effects and may cause significant changes in blood properties. Tang-kuei was also mentioned as a possible cause of warfarin potentiation (10, 11).

Examples can be cited of bleeding tendency after intake of Phenprocoumon along with ginger, warfarin with Fenugreek, claw, garlic, mango or papaya (12,); decrease in activity of Lithium when consumed along with herbal diuretics like *Tribulus terrestris*, *Syzygium cuminii* (13). These can be bizarre reactions since interacted herb has no role in the event, as in Phenytoin along with *Convolvulus pluricaulis* (Shankapushpi) leading to loss on seizure control thus difficult to predict (14).

Conclusion

Not all subjects taking interacting drugs or foods experience adverse consequences, but it is advisable to take due precautions to avoid mishaps in all cases where interactions are possible. The food-drug and drug-drug interactions occur by following two basic mechanisms. The predominant mechanism for these interactions is the inhibition of cytochrome P450 3A4 in the small intestine, resulting in a significant reduction of drug presystemic metabolism. Another mechanism is the inhibition of P-glycoprotein, a transporter that carries drug from the enterocyte back to the gut lumen, resulting in a further increase in the fraction of drug absorbed (15). Recent studies on Ayurvedic food-drug interactions reported that the possible mechanism of actions of interactions between foods and drugs mentioned in Ayurveda are formation of chelates or complexes leading to inadequate absorption, and antagonism also plays a vital role (16, 17-19).

Therefore, when drug absorption is considered a critical matter, such as cases where a suboptimal dose of the drug has the potential to significantly influence the outcome of a disease, the drug should not be taken along with meals, nutritional supplements, or herbs. There are some exceptions, such as when small amounts of food are considered protective against irritant actions of the drug, or when there are specific foods are known to improve absorption of the drug (for

example, a small amount of fatty food may enhance absorption of a drug that disperses more easily in fats).

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