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A REVIEW ON INTERACTION OF HERBALS WITH ALLOPATHIC MEDICINES

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ABSTRACT

The use of herbal remedies is more prevalent in patients with chronic diseases such as cancer, diabetes, asthma and renal diseases. Multiple factors such as gender, age, ethnicity, education and social class are also shown to have association with use of herbal remedies in treatment of diseases. It is quite common for a patient to seek herbal treatment while taking several prescription medications. The aim of this article is to highlight the clinical interactions between herbal remedies and prescribed drugs which are generally not in knowledge of doctors in recent time.

KEYWORDS: herbal, diseases, interactions, prescribed drug.

INTRODUCTION

During the last decade, an explosion in the consumption of herbal remedies has been witnessed. The vast majorities of these products are unlicensed and are not required to demonstrate efficacy, safety or quality.[1] Recent examinations have indicated that as many as 16% of prescription drug users consume herbal supplements. Moreover, fewer than 40% of patients disclose their herbal supplement usage to health care providers and many physicians are unaware of the potential for herb–drug interactions.[2]

Several challenges that preclude identification and reporting of adverse reactions to Ayurvedic drugs can be identified related to detection, assessment and prevention of adverse reactions.[3,4]

A drug interaction can be defined as an interaction between a drug and another substance that prevents the drug from performing as expected. This include interactions of drugs with other drugs (drug-drug interactions), as well as drugs with food (drug-food interactions) and other substances. Certain foods and specific nutrients in foods, if ingested concurrently with some drugs, may affect the overall bioavailability, pharmacokinetics, pharmacodynamics and therapeutic efficacy of the medications.[5]

The aim of this article is to highlight the clinical interactions between herbal remedies and prescribed drugs. One drug alters the rate or extent of absorption, distribution, metabolism or excretion of another drug. A change in the blood concentration causes a change in the drug's effect. Most of the possible interactions may be classified in two major categories:

Pharmacokinetic and Pharmacodynamic interactions.[6]

Pharmacokinetic interactions are those that can affect the processes by which the drug increases or decreases ADME interactions i.e.

1. The Absorption of a drug into the body.
2. Distribution of the drug within the body.
3. Alterations made to the drug by the body (Metabolism).
4. Elimination of the drug from the body.

Absorption

Depends on surface area of absorption (less in stomach and more in intestines).

Alteration in stomach HCL e.g. avoids antacids with antibiotics which reduces the activity of antibiotic.[7,8]

Capsicum annum increases gut motility there by decreases absorption of aspirin Blood flow to the site (blood flow α absorption) e.g. *Capsicum annum* increases blood flow to GIT absorption site.[9,10]

Distribution

Distribution refers to the process in which herbs or drugs are carried and released to different parts of the body to exert their effect. Interactions occur during the distribution phase if the drug has a narrow range of safety index and is highly protein-bound. For example, Warfarin

is an anticoagulant medication that is very highly bound to protein and has a very narrow range of safety index.[8]

Some known examples that interact with Warfarin include *Medicago sativa* (alfalfa), Aspirin, Ibuprofen, Vitamin K and some types of tea, green leafy vegetables.[8] These items interact with Warfarin by either enhancing its effectiveness or thus leading to prolonged bleeding, or by decreasing its effectiveness and thus increasing the risk of blood clots in the vessels, both of which may be quite dangerous to the patient. This is why patients who are taking Warfarin need to be exceedingly cautious when taking herbs concurrently.[9,11]

Blood clotting times have been reported to double in patients taking Warfarin and garlic (*Allium sativum*) supplements (WHO1999). WHO states that ginger may affect bleeding times and immunological parameters owing to its ability to inhibit thromboxane synthase and to act as a prostacyclin agonist.[12]

Metabolism

Many drug interactions are due to alterations in drug metabolism. Most herbs and drugs are metabolized by the liver to inactive derivatives. The rate at which the liver metabolizes these herbs and drugs determines the length of time these herbs or drugs stay active in the body. If the liver were induced to speed up its metabolism, herbs and drugs would be inactivated at a faster pace and the overall effectiveness of ingested substances would be lower and vice versa.[7,8]

Although all the mechanism is undoubtedly relevant to interaction with herbal medicines, the main focus will be on the cytochrome p450 and drug transporter proteins. Drug metabolism goes in the serum, the kidneys, the skin and the intestines but the greatest portion is carried out by enzymes that are found in the liver mainly cytochrome p 450.[13,14]

Excretion

Drugs are eliminated from the body as an unchanged drug or changed by a process of excretion or converted to metabolite. Renal excretion the major route of elimination; affected by renal function and urinary pH, some drugs are eliminated in bile and other by body Fluids.[7,8]

Loop diuretics (furosemide, bumetanide) increase excretion of potassium, magnesium, sodium, chloride, calcium and corticosteroids (prednisolone) decrease sodium excretion,

resulting in sodium and water retention; increases excretion of potassium and calcium so that electrolyte imbalance should be monitored.[8]

Pharmacodynamic interaction

Pharmacodynamic interactions are those where the effects of one drug are changed by the presence of another drug at its site of action. Pharmacodynamic refers to the study of how drugs actually behave inside the human body.[5] One drug causes a change in patient response to another drug without altering that drug's pharmacokinetics.[9]

E.g. Shankapushpi (*Convolvulus pluricaulis*) may decrease phenytoin levels as well as diminishes drug Efficacy.[15]

Pharmacodynamic interactions refer to the fluctuation in bioavailability of ingested substances as a result of synergistic or antagonistic interactions between herb/drug molecules. Pharmacodynamic interactions are generally more difficult to predict and prevent than pharmacokinetic interactions.[8,9]

Garlic (*Allium sativum*) and ginseng (*Panux ginseng*) should be discontinued at least seven days before surgery because both herbs have been reported to aggressive bleeding.[9,13]

Factors Which Increase the Chance of Herbal Interactions with Allopathic Drugs[16]

- Information related to adverse effects is scattered in Ayurvedic literature and not in electronic form, hence making it is difficult to access. Many publications are not in peer-reviewed journals and the quality of available publications is questionable.
- Most Ayurvedic formulations are multi-ingredient-fixed dose formulations rarely prescribed alone.
- In additional, there is the confounding factor that the patient is often receiving allopathic medicines at the same time.
- Dose-related responses are rarely measured and reported.
- One of the most challenging aspects is the lack of expertise in performing causality analysis with Ayurvedic medicines. A person trained in pharmacovigilance rarely understands Ayurveda while an expert in Ayurveda is not trained in the science of Pharmacovigilance.

TABLE I: Drug Interaction Between Herbals And Allopathic Components: [1, 9, 10, 13, 16, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29]

Common name	Latin name	Potential interactions with different class of drugs			
		Beneficial Interaction		Harmful Interaction	
		Category of drug	Effect	Category of drug	Effect
Garlic	*Allium sativum*	**Anticoagulant (with low dose)**	Synergistic Effect Decrease the platelet aggregation	**Warfarin (with normal or high dose)**	Postoperative bleeding and spontaneous spinal epidural hematoma
				Chlorpropamid	Hypoglycaemia
				Saquinavir	Reduces the plasma level concentration
Ginkgo	*Ginkgo biloba*	**Anticoagulant Like Warfarin (with low dose)**	Synergistic Effect Decrease the platelet aggregation	**Ibuprofen, Aspirin, Acetaminophen**	Chances of bleeding & Subarachnoid hemorrhage
				Anticonvulsant	Increases seizures
				Anticoagulant (with normal or high dose)	Interfere with platelet function & increase the risk of bleeding
				Alprazolam	Might decrease effect of alprazolam and increase awakeness
Yashti madhu	*Glycyrrhiza glabra*	**Prednisolone**	Increases plasma concentration	**Loop diuretics**	Increase potassium loss and Sodium -fluid retention
Guggulu	*Commiphora mukul*	**Hypolipidamic**	Synergistic effect	**Warfarin**	Increase the clotting time.
		NSAIDS	Reduce the dose of NSAIDS	**Diltiazem, Propanolol**	Decreases the bioavailability of these drugs.
Ashwgandha	*Withania somnifera*	**Barbiturates & Sedatives**	May potentiate the effects	-	-
Ginger	*Zingiber officinalis*	-	-	**Anticoagulants like Warfarin**	Increase bleeding tendencies
Pippali	*Piper longum*	**Phenytoin, Propranolol, Theophylline,**	Increases the plasma concentration	-	-

		Rifampicin			
Bitter melon (karela) & Fenugreek	*Momordica charantia & Trigonella foenum-graecum*	**Anti-diabetic Drugs (with low dose)**	Synergistic effect, improve glucose tolerance without increasing insulin levels	**Antidiabetic drug like Glipizide, Tolbutamine (with normal or high dose)**	Hypoglycemia due to excessive lowering of blood sugar level
Psyllium seed	*Plantago ovata*	-	-	**Coumarin derivates**	Retards absorption of drug
Ephedra	*Ephedra sinica*	-	-	**Antiarrhythmic drug like Amiodarone, Sotalol, Quinidine**	Chances of heart attack
Aloe vera	*Aloe barbadensis*	-	-	**Digoxin , Thiazide**	Increase cardiac toxicity and decrease the absorption of drug
Grape fruit	*Vitis vinifera*	**Calcium channel blockers**	Increase oral bioavailability	-	-
Capsicum	*Capsicum annum*	**Theophylline**	Increase absorption	**Hypoglycemic drugs**	Affect blood glucose level
Feverfew	*Tanacetum parthenium*	**Aspirin**	Additive effect	**Drugs like Amitriptyline, Ondansetron, Propranolol, Theophylline**	Modify the liver metabolism of drugs
Alcohol	*in Asava & Arista*	-	-	**Aspirin & NSAIDS**	Increased risk of gastric mucosal damage and gastric bleeding.
				Metronidazole, Tinidazole, Tolbutamide	"Disulfiram effect"
Castor oil	*Ricinus communis*	-	-	**Antiarrhythmic drugs, Diuretics, Fat soluble Vitamins & Antihistamines**	Reduces the efficacy
Kapikachu	*Mucuna pruriens*	**Anti-Parkinson's medicine**	Potentiate the action as it contains L-dopa	-	-
Bhanga	*Cannabis*	**Barbiturates**	Additive effects	-	-

	sativa				
Jatamansi	*Nardostachys jatamansi*	**Sedative medicine, Anti-hypertensive medicine**	Additive effect	-	-
Horse chestnut	*Aesculus hippocastanum*	**Anticoagulant (Synergistic Effect)**	Decrease the platelet aggregation	**Lithium**	Increase the blood concentration of lithium
Kava	*Piper methysticum Forster*	**Drugs acting on CNS**	Increase drowsiness	**Sedative medication**	Combination with sedative medication might cause too much sleepiness
St john's wort	*Hypericum perforatum*	**All drugs metabolized by cytochrome p450 enzyme system**	Increase effect	**Cyclosporine**	Reduces the plasma concentration of cyclosporine
Betel nut	*Areca catechu*	-	-	**Neuroleptic drugs**	Exacerbation of extrapyramidal effects

Ways to Prevent Drug Interactions[1,5,17,18]

- Encourage pharmacovigilance concepts into the curriculum of Ayurveda at the under graduate and post-graduate level.
- Encourage studies on drug safety.
- Necessary to close monitoring of patient itself.
- When therapeutic goals are not met, clinicians should ask questions about how and when drugs are being taken in relation to foods and nutritional supplements.
- Give health care practitioners a complete list of all of the drugs that you are using or have used within the last few weeks.
- Inform health care practitioners when medications are added or discontinued.
- Inform health care practitioners about changes in lifestyle (for example, exercise, diet, alcohol intake).
- Ask your health care practitioners about the most serious or frequent drug interactions with the medications that you are taking since the frequency of drug interactions increases with the number of drugs used, Work with your health care practitioners to eliminate unnecessary medications.

CONCLUSION

The increasing popularity of Ayurveda has led to the concurrent use of the medicines in the system with allopathic medicines. The free availability of even single drug churna as over the counter medicine and its irrational use at any time concurrently with any medicine has increased the chance of drug interactions. A detailed study on the possible candidates of Ayurvedic and allopathic drugs which may interact with each other is needed and it should be established by experimental studies.

Also the beneficial combinations can be found out and used for removing the side effects of or decreasing the dose of important drugs. There are very few Herb-drug interaction reported up till now but they can't be ignored as patients who are not aware about the adverse effects that can possibly occur due to concurrent administration of herbal and OTC drugs, would have to face disastrous consequence.

To conclude what becomes important is creating a detailed database about clinically relevant interactions of Ayurvedic and Allopathic drugs and making awareness about these types of interactions so that the patient's life will never be at risk.

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