



HERB-DRUG INTERACTION:AN REVIEW

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ABSTRACT

Herb-drug interactions represent a significant concern in modern healthcare due to the increasing use of herbal supplements alongside conventional medications. Herbal products can influence the pharmacokinetics and pharmacodynamics of drugs, potentially leading to altered therapeutic outcomes or adverse effects. Key mechanisms of interaction include modulation of drug-metabolizing enzymes (such as cytochrome P450) and transport proteins (like P-glycoprotein), which can result in either increased toxicity or reduced efficacy of the co-administered drugs. Commonly used herbs such as St. John's Wort, Ginkgo biloba, Ginseng, and Garlic have been reported to interact with a wide range of drugs, including anticoagulants, immunosuppressants, and antidepressants. Clinical outcomes of these interactions can range from mild to severe, emphasizing the need for healthcare professionals to recognize and manage potential herb-drug interactions effectively. Despite the growing body of evidence, challenges in studying herb-drug interactions include variability in herbal product composition, lack of standardization, and limited clinical data. This review aims to provide an overview of the mechanisms, common examples, and clinical implications of herb-drug interactions. Increased awareness and understanding among healthcare providers and patients are crucial for minimizing risks and ensuring the safe use of herbal and conventional medicines concurrently.

INTRODUCTION

People combine prescription and over-the-counter drugs with herbal remedies. A drug interaction occurs when two or more drugs interact with food, drink, supplements, or other substances inside the body. Of the 1,500 therapeutic plants recognized by the Indian medical system, 500 are regularly utilized. Over 7800 medical medicine production facilities are thought to exist in India, and these facilities are thought to use about 2000 tons of herbs a year.(1) The World Health Organization (WHO) recently estimated that 70–80% of the world's population, particularly in underdeveloped nations, depends on traditional medicine, primarily plant-based medications, for their basic medical needs.(2,3)

One fundamental issue is the frequent occurrence of the term "herb-drug interaction" in the media, which lacks a clear definition and presumes that everyone is aware of its meaning. Drug-drug interactions are likewise lacking in information. Published clinical studies are mostly case reports; there are few controlled trials because it is unethical to randomly assign patients to studies looking at unintended effects.(4)

The pharmacological or toxicological effects of any component may be increased or decreased by interactions between medical herbs and pharmaceutical medications. Many medicinal herbs and drugs are poisonous at one dose and therapeutic at another. Synergistic therapeutic effects, such as those of herbs commonly used to lower blood glucose levels in diabetics, may make it more difficult to take long-term drugs as prescribed.(5)

In a study of a thousand senior patients admitted from the emergency room to a hospital, it was shown that 538 patients had 1087 drug-drug interactions, and 30 patients had negative side effects as a result of these interactions.(5)

Note of Advice Regarding Parthenium Management

Parthenium hysterophorus L. is an annual herbaceous plant of the "Asteraceae" (Compositae) family that is also referred to as congress grass, carrot weed, and white top in India. The reason for its common name, "gajar ghas LIC rbs," is that it resembles a carrot plant. *Parthenium* is thought to have originated in Argentina, Mexico, and the island of Trinidad. *Parthenium* was first discovered in Pune, Maharashtra, in 1956. Following notable events in America, CT scans spread throughout India like wildfire. *Parthenium* was once an issue with trash and undeveloped land, but it is now a troublesome weed in crops as well. *Parthenium* has grown to be a significant issue in grasslands within forests, especially



Fig no: 1

How does parthenium propagate?

Its seeds are mostly how it spreads. a single plant can yield between 15,000 and 25,000 seeds, with the potential to generate as many as 154,000 seeds/m². Because the seeds are so light, they can be carried or transported by the wind, water, The weed's es arc allows it to withstand a variety of human actions from its damaged or clipped portions. Due to its allelopathic properties and the fact that partheniums may regrow in the absence of natural enemies like insects and diseases, W. has spread quickly throughout India.

Why is parthenium a harmful plant?

Parthenium is generally toxic, harmful, troublesome, allergic, and violent. plant that is extremely dangerous to people and their animals In Australia and India, this Weed is thought to be one of the main causes of dermatitis, asthma, nasal-dermal disorders of the nose and

bronchi In addition to its negative impacts, it also results in a number of additional issues, such as blocking public walkways and diminishing the aesthetic value of parks, gardens, and residential areas.

Methods for Managing Parthenium

The success of parthenium management depends on the combination of all available strategies and their use over the years indicated below:

- Uprooting of parthenium
- Mechanical Management
- Cultural Management
- Legal Management
- By use of chemicals

Mechanism of herbal-drug interactions:

Pharmacokinetic or pharmacodynamic mechanisms may be at play when there are interactions between herbals and medications.

Pharmacokinetic interactions:

These occur when a herb affects a drug's metabolism, excretion, protein binding, absorption, distribution, or excretion, changing the drug's or its metabolites' levels. The majority of the available data on pharmacokinetic drug interactions relates to drug transporters and metabolizing enzymes. The majority of herbal medication interactions are associated with oxidative metabolism via the cytochrome P-450 system (CYP) or with the impact of a herbal on the efflux drug transporter, even though drug interactions can also involve enzymes like glutathione S-transferases and uridine diphosphoglucuronyl transfereases (UGTs). P-glycoprotein.

Interference with Absorption:

When drugs are taken with soluble or insoluble fibers, such as psyllium (*Plantago psyllium*) or tannins like those in tea (*Camellia sinensis*), pomegranates (*Punica granatum*), cinnamon (*Cinnamomum* spp.), and rhubarb (*Rheum* spp.) (7,8) their oral bioavailability may be reduced. This was shown in a clinical research where individuals receiving lovastatin together with pectin or oat bran had an increase in low-density lipoprotein (LDL) levels. Once fiber supplementation was stopped (9) the LDL levels recovered to normal. The most plausible reason for this interaction was that lovastatin was bound to pectins or bran fibers in the intestinal lumen (10) which reduced lovastatin absorption. (15)

Drug Metabolism:

Pharmacokinetic interactions and drug metabolism occur in the liver, intestines, kidneys, and lungs (11,12) Of them, the intestines have a secondary but possibly significant function in drug metabolism, with the liver being the primary location. (10) Phase I and Phase II drug metabolic

pathways have historically been distinguished from one another.(13) The majority of phase I metabolites move via phase II as these two phases operate sequentially. The superfamily of hemoproteins known as cytochrome P450s (CYP) include phase I enzymes. They make comparatively non-polar molecules more polar by oxidizing them, which enables the urine to eliminate them. CYP isoforms 1A2, 2D6, 2C9, 2C19, and 3A4 are the primary types.(16)

Modified Metabolism:

It is commonly recognized that the bioactive chemicals found in herbs can influence the expression and activity of CYP and Pgp both in vitro and in vivo 2. 5'-methoxyhydnocarpin (5'-MHC), a substance that was isolated from *Berberis* (*Mahonia*) spp., inhibits bacterial efflux pumps in vitro and may be useful in treating antibiotic-resistant bacterial strains. Given that 5'-MHC can also block cancer cell Pgp, it may possibly be useful in cancer treatment. Additionally, clinically significant CYP genetic polymorphisms 17 have been found by recent research. An estimated 55 CYP isoforms exist in humans, and sexual dimorphisms for the CYP1A2 and 3A4 isozymes have recently been found. In two clinical investigations, SJW stimulated CYP1A2 in females but not in males. Alelic variants modify the kinetics of CYP isozymes and account for variations in drug metabolism rates.8 Theophylline in serum.(17)

Pharmacodynamic Interactions:

These interactions can have an impact on OT enzymes, receptor sites, and rgan systems. They are associated with the pharmacological activity of the interacting drugs. When antiplatelet herbals are combined with antiplatelet/anticoagulant medications, a pharmacodynamic interaction may arise, increasing the risk of bleeding. Additional instances include the combination of herbals that may lower blood sugar and medications that depress the central nervous system (CNS), such as kava, or both. An illustration of an antagonistic interaction occurs when a sedative-hypnotic drug is combined with a herbal supplement that contains a lot of caffeine, like guarana. Furthermore, when medications with comparable toxicity are used with herbals that have the potential to be toxic to the organs, there may be an increased risk of toxicity.

Adulteration, contamination, and misidentification:

The composition of herbal products may not always be adequately labeled, and negative interactions or incidents that are linked to particular herbs may really be the result of mislabeled plants, prescription medications, or heavy metals.(18) An study of a Siberian ginseng (*Eleutherococcus senticosus*) product linked to a case of newborn androgenization (19) revealed that it was actually Chinese silk vine (*Periploca sepium*)(20) an unrelated species. Guang-fang-ji (*Aristolochia fangchn*) was the true cause of more than 48 cases of renal toxicity linked to fang-ji (*Stephania tetrandra*) in a weight-loss supplement: One well-known nephrotoxin is aristolochic acid.(21)

Many Chinese patent medications sold outside of Asia contain benzodiazepines and non-steroidal anti-inflammatory drugs; they include Shuch and Chuifong Toukuwan.(22) The latter preparation is well-known; since 1974, aminopyrine, phenylbutazone, indomethacin,

hydrochlorothiazide, chlordiazepoxide, diazepam, corticosteroids, diclofenac, mefenamic acid, and dexamethasone have all been used in the formulation at various times. 61 It is not unusual for Asian herbal products to include heavy metal contamination. Out of the 251 Asian patent medications that were gathered from herbal stores in T and distributed throughout California, USA, 24 of them had lead (at least 1 ppm); 36 goods had arsenic, and 35 had mercury."(23)



Fig -2 ginkgo biloba

patient counseling regarding herb-drug interactions

Use of dietary supplements and herbal products is very common. In a US survey of adults who take prescription medications on a regular basis, 18:4% of respondents said they also use at least one high-dose vitamin or herbal product concurrently (and 61:5% of those who used unconventional therapies did not disclose such use to their physicians).(24)

Because they are afraid of being criticized, patients might not disclose the use of herbal medicine even if it has serious side effects. Ginseng Panax It is imperative for clinicians to inquire about patients' herb use from them in a nonjudgmental and informal manner. Offering disapproval will only encourage a patient to conceal their use of herbs. Any laxative or bulk-forming substance can hasten intestinal transit and can impede the absorption of nearly all drugs absorbed through the intestines.(25)

It is advised not to use ginkgo, danshen, dong quai, papaya, or garlic at the same time if a patient has clotting issues, is undergoing surgery, or is on anticoagulant medication. Patients who insist on using these herbs in addition to anticoagulants should have their bleeding times monitored, even though it is discouraged because most of these herbs interfere with platelet function rather than the coagulation cascade and do not affect prothrombin time or partial

thromboplastin international normalized ratio [INR] or time. A week after beginning any herbal treatment, people taking warfarin should have their INR measured because many other herbs also contain anticoagulant compounds.

Garlic:

The *Allium sativum* plant bulb, which is a member of the Amaryllidaceae family, is the biological source of garlic. Allin, ajoene, diallyl polysulfides, vinyl dithiols, S-allylcysteine, and enzymes, saponins, flavonoids, and Maillard reaction products are sulfur-containing chemicals that can be obtained from fresh or crushed garlic. Garlic's taste and aroma are mostly attributed to its abundance of sulfur compounds (30). It has been discovered that the main ingredient giving raw garlic its "hot" feeling is allicin. It is used to treat a number of illnesses, including lowering blood sugar, lowering cholesterol, lowering menstruation discomfort, and lowering blood pressure. Its primary usage is as a flavoring agent. Garlic is mostly consumed orally. The following side effects may occur: skin blistering when applied, bleeding, bad breath, heartburn, and redness. (26)

Drug interactions:

a) That have been shown to decrease efficacy The distribution of garlic is reliant on the efflux transporter mechanism. International Journal of Medicinal and Life Sciences

b) Has also been shown to affect blood clotting; hence, it should be avoided in individuals who are using blood-thinning medications such as warfarin and aspirin. Supplementing with garlic has lowered blood levels of

c) HIV protease when combined

d) It is advised to stay away from the following medications when using garlic: The drug acetaminophen Pills for birth control Cyclosporin C with Chlorzoxazone Theophyllin Warfarin NSAIDs Ephedra, a medication for HIV/AIDS

Ginseng:

Also known as Korean ginseng, South China ginseng (*P. notoginseng*), and American ginseng (*P. quinquefolius*), it is derived from the root of the herb *Panax ginseng* (27) which is a member of the Araliaceae family. Ginsenosides and gintonin are two of its common characteristics. It is applied to strengthen the body's defences against stress, strengthen the immunological system, and enhance vitality and endurance. Small amounts of ginseng can be found in herbal teas and energy drinks, or it can be purchased as a nutritional supplement. (28) Usually taken orally to enhance cognition, focus, memory, muscular Alzheimer's disease, work efficiency, and to guard against exercise-related damage. It is also used to treat multiple sclerosis, anxiety, sadness, and overall exhaustion as well as to strengthen the immune system. Among the earliest documented works discussing the application of In 1596, Li Shizhen wrote in his *Compendium of Materia Medica* herbs that ginseng was a "superior tonic". But the herb was employed as a tonic for people with chronic ailments and those convalescing, rather than as

a "cure-all" medication(29) In the sixteenth century, disputes arose about who owned the ginseng fields in China and Korea. (30)

Adverse effects:

The most frequent adverse effect is insomnia, or difficulty falling asleep. Menstrual issues, breast pain, elevated heart rate, blood pressure, headache, rash, itching, mood swings, vaginal bleeding, etc. are some more.

Relationships :

- a) When taken with warfarin, it lessens the blood thinner's activity. and raise the possibility of blood clotting. Therefore, taking it with anticoagulants should be avoided.
- b) It is also alter the activity of anti diabetic medications, Ginseng lower blood sugar levels, raising danger of Hypoglycemia. Hence it should be avoided in such instances. It has also been noted that ginseng reduces the effectiveness of antihypertensive medications, which leads to d) elevated blood pressure. Ginseng may intensify the effects of caffeine, which could result in jitters, perspiration, sleeplessness, or erratic heartbeats. Angiotensin converting enzyme (ACE) inhibitors such as captopril, benazepril, enalapril, and others may interact with ginseng. Asian ginseng causes prescription heart drugs, such as calcium channel blockers, to function differently than intended. Among these medications are Nifedipine and diltazem. Ginseng might combine with medications used to treat autoimmune diseases or following organ transplantation. Thus, in these circumstances, it ought to be avoided. Some medicines used to treat Deficit Hyperactivity Disorder may become more stimulating when ginseng is consumed. When ginseng and morphine are taken together, the latter's ability to relieve pain is diminished. Thus, in these situations, it ought to be volace. j) Ginseng may raise the risk of manic episodes when taken with monoamine oxidase inhibitors (MAOIs). It functions as an antidepressant.

CONCLUSION:

Herb-drug interactions are a growing concern due to the widespread use of herbal supplements alongside pharmaceutical drugs. Herbs such as *ginseng, **ephedra, **St. John's Wort, **garlic, and **gingko biloba* are commonly used for their health benefits but may interfere with drug metabolism, particularly through the *cytochrome P450* (CYP450) enzyme system and *P-glycoprotein* pathways. These interactions can lead to reduced drug efficacy or increased toxicity.

For example, *St. John's Wort* can reduce the effectiveness of medications like antidepressants and oral contraceptives, while *garlic* and *gingko biloba* can increase the risk of bleeding when taken with anticoagulants. *Ephedra* poses cardiovascular risks when combined with stimulants or drugs affecting blood pressure.

Review articles stress the importance of awareness, as many patients and healthcare providers may not fully consider the risks of herb-drug interactions. As herbal use rises, it is vital for healthcare professionals to inquire about supplement use and educate patients on potential interactions. Further research and clinical studies are necessary to better understand these interactions and to establish clear guidelines for the safe use of herbal products alongside conventional medications.

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