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Comprehensive review on: Interaction between herbal drugs & allopathic drugs

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Abstract
Interaction between foods and drugs can have profound influence on the success of drug Treatment and on the side effect profiles of many drugs. The use of herbal medicine to treat a wide range of conditions is rising rapidly, leading to increased intake of phytochemicals. Recent studies reveal potential fatal interactions between herbal medicines and drugs. Herbal medicine is amongst the 16 alternative systems of medicine, which is used to treat existing illness and also for preventive and health conditions. Herbs have been used for medicinal purposes since long. Majority of our people have a feeling that herbs are harmless plants although many of our drugs (including digitalis, morphine, atropine, and several chemotherapeutic agents) were developed from plants. Hence, herbs can be potent products. Herbal medicines are generally not held to the same rigorous standards as allopathic medicines. There is usually a lack of industry regulation and manufacturing standards and guidelines, resulting in inferior (or unsafe) medicines being sold to consumers. Similarly, there is a lack of understanding amongst many medical practitioners of both traditional and allopathic medicine systems of how drugs from the two systems can be safely used together. It is imperative for Pharmacists to keep up-to-date on potential drug-food interactions of medications, especially today's new drugs, so that they may counsel properly to the patients.

Keywords: Herb-drug interaction, Allopathic, World Health organization, over the counter

Introduction

When two or more drugs are given to apatient simultaneously a drug interaction occurs i.e. the effects are increased or they produce a new effect that neither produces on its own. The effects of the drugs may increase, decrease or a new effect may be produced that neither produces on its own. When we mention about an interaction it is always drug-drug interactions that come toour mind. However, interactions mayalso exist between drugs and foods (drug-food interactions), as well as drugs and herbs (drug-herb interactions). Some herbal medicines are associated with adverse effect which include interactions with prescribed drugs.

Herbal medicines also have different pharmacokinetic and pharmaco-dynamic properties which ultimately lead to produce therapeutic responses, but sometimes cause adverse actions and/or drug-herbal interactions [1].

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 should have to face disastrous consequence. Herbs may be used either in their primary forms or combined into mixtures.

Herbal Medicine can be broadly classified into various basic systems: Traditional Chinese Herbalism, which is part of Traditional Oriental Medicine, Ayurvedic Herbalism, which is derived from Ayurveda, and Western Herbalism, which originally came from Greece and Rome to Europe and then spread to North and South America. Chinese and Ayurvedic Herbalism have developed into highly sophisticated systems of diagnosis and treatment over the centuries. Western Herbalism is today primarily a system of folk medicine. Interest in the United States had been growing in the recent years from the reported success stories from the use of herbs [2, 3]. The total number of plant species and endemics in the region are given in Table

Table 1: Total numbers of plant species and endemics in the region.

S. No.	Region	Endemics	Species
1.	South East Asia	40,000	42-50,000
2.	China and East Asia	18,650	45,000
3.	Indian Subcontinent	12,000	25,000
4.	South West Asia	7,100	23,000

Advantages of Herbal medicines [4]

1. Patient tolerance
2. Renewable source
3. Cultivation and processing- environmental friendly
4. Local availability (in developing countries)
5. Important recent break- through
6. Plant constituents to be a major source of new lead generation

The advantages of herbal medicine are that they can treat the diseases where chemicals and other drugs have failed. Herbal medicines can be used for treating all kinds of problems and diseases with very few exceptions. These include common illnesses, which lead to drowsiness and other side effects when treated through the regular medicines. Hence both cold and cough, which can be treated or healed through the regular methods of herbs and other serious ailments, can be treated through these herbal medicines. There is various method of using these herbal treatments and they are safe, effective and do not lead to any kind of side effect for the person using it.

Another advantage to herbal medicine is cost. Herbs cost much less than prescription medications. Research, testing,

and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.
Yet another advantage of herbal medicines are their availability. Herbs are available without a prescription. You can grow some simple herbs, such as peppermint and chamomile, at home. In some remote parts of the world, herbs may be the only treatment available to the majority of people.
Herbal remedies have the capacity to bring a certain amount of effect in the body and prove to be effective in treating problems of health. These herbal medicines are popular since they cost less and also because they are better than their pharmaceutical counterparts. Usually these herbs grow in very common places, but they do not require complicated preparation procedures and are also easily available. Hence buying the fresh forms of these herbs is not possible all the time, but their dried and refined forms are easily available for treating various kinds of ailments and diseases of the body.

1.2 Disadvantages of Herbal medicines [4]

Any form of herbal medicine takes some time to act. One has to have immense patience while undergoing herbal treatment. Various ingredients go into the preparation of herbal medicine. One has to be sure that none of the ingredients would cause allergic reactions. Many herbal remedies have negative side effects. Most of these side effects take months to appear. Since governments do not regulate the industry of herbal medicine, there is no chance of any quality control during the manufacturing of the herbal supplements. It is absolutely necessary to find a renowned practitioner of herbal medicine. Another disadvantage of herbal medicine is the very real risks of doing yourself harm through self-dosing with herbs. While you can argue that the same thing can happen with medications, such as accidentally overdosing on cold remedies, many herbs do not come with instructions or package inserts. There's a very real risk of overdose. Harvesting herbs in the wild is risky, if not foolhardy, yet some people try to identify and pick wild herbs. They run a very real risk of poisoning themselves if they don't correctly identify the herb, or if they use the wrong part of the plant. Regular medicines are still the best bet during serious or sudden illness or injury. Herbal medicine cannot treat serious injuries like a broken leg. Nor can it heal appendicitis or heart attacks effectively as no diagnostic tests or surgery is involved in it. Often self-dosing of various herbs leads to serious risks among users. Though one can argue that such a thing can occur with regular medicines as well, it should be remembered that those packages have specific instructions regarding dosage. This is entirely absent with herbal medications. Herbs harvested in the wild are risky. Incorrect identification of the required herb can even lead to poisoning [5].

Global market of Herbal medicines

The world market for herbal medicine, including herbal products and raw materials has been estimated to have an annual growth rate between 5 and 15%. Worldwide market of herbal medicines is estimated to be around US $80 billion to US $100 billion and this market is expected to reach US $2500 billion by the year 2010. In the West, the demand for herbal drugs has reached a new high in recent years. Since 1999, the global market for herbal supplements exceeded US $ 15 billion, with a US $ 7 billion market in Europe, US $ 2.4 billion in Japan, US $ 2.7 in the rest of Asia and US $ billion in North America. The results of a nationwide survey indicated a marked increase in the number of individuals using alternative therapies between 1990 and 1997 estimating total out-of-pocket expenditures for alternative therapies at $27 billion. In India the value of botanicals related trade is about US $10 billion per annum with annual export of US $1.1 billion, while Chinas annual herbal drug production is worth US $48 billion with export of US $3.6 billion. Presently, the United States is the largest market for Indian botanical products accounting for about 50% of the total exports. Japan, Hong Kong, Korea and Singapore are the major importer of herbal medicine taking 66% share of Chinas botanical drugs export [6].
The utilization of herbal drugs is on the flow and the market is growing step by step. The annual turnover of the Indian herbal medicinal industry is about Rs. 2,300 crore as against the pharmaceutical industry's turnover of Rs. 14,500 crores with a growth rate of 15 percent. The export of medicinal plants and herbs from India has been quite substantial in the last few years. India is the second largest producer of castor seeds in the world, producing about 1, 25,000tonnes per annum. The major pharmaceuticals exported from India in the recent years are isabgol, opium alkaloids, senna derivatives, vinca extract, cinchona alkaloids, ipecac root alkaloids, solasodine, Diosgenine/16DPA, Menthol, gudmar herb, mehndi leaves, papian, rauwolfia guar gum, Jasmine oil, agar wood oil, sandal wood oil, etc. The turnover of herbal medicines in India as over-the-counter products, ethical and classical formulations and home remedies of traditional systems of medicine is about $ 1 billion and export of herbal crude extract is about $ 80 million [7].

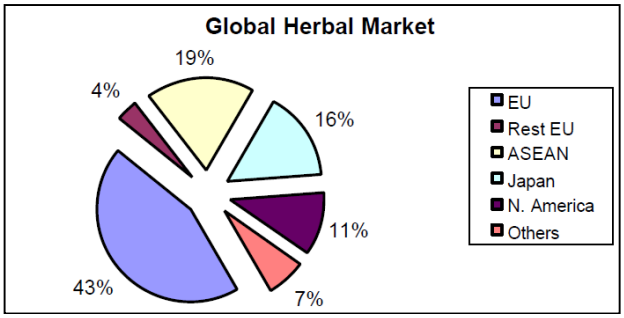

Fig 2: Global Herbal Market.

The market for Ayurvedic medicines is estimated to be expanding at 20% annually. Sales of medicinal plants have grown by nearly 25% in India in past ten years (1987-96), the highest rate of growth in the world. But the per capita expenditure in India on medicines per annum is amongst the lowest in the world. In other developing countries too, plants are the main source of medicine. Two of the largest users of medicinal plants are China and India. Traditional Chinese Medicine uses over 5000 plant species; India uses about 7000. According to Export Import Bank, the international market for medicinal plant related trade having a growth rate of 7% per annum. China's share in world herbal market is US$ 6 billion while India's share is only US$1 billion. The annual export of medicinal plants from India is valued at Rs. 1200 million. All the major herbal-based pharmaceutical companies are showing a constant growth of about 15 per

cent. Traditional medicine has served as a source of alternative medicine, new pharmaceuticals, and healthcare products. Medicinal plants are important for pharmacological research and drug development, not only when plant constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds.

Interaction/Adverse Effects

"A drug-herb interaction can be defined as pharmacologic or clinical response to the co-administration of a traditional drug or pharmaceutical preparation and an herbal product" [9].

one of the major factors contributing to the increasing popularity of herbs in developed countries and the sustained use in developing countries is the perception that herbal remedies are efficacious, and in some cases more so than physician-prescribed allopathic medicines. This favorable level of perceived efficacy would support continued use, and in a significant number of patients, concomitant use with conventional allopathic medicines [8, 9].

This scenario, of concomitant herb-drug use, raises the growing public health concern of potentially harmful interactions. It is known still that the indiscriminate use of medicinal plants and herbs is due to the lack of knowledge on their adverse effects. Almost one third of current users of herbal medicines do not know about the risk of herb-drug interactions [10, 11].

According to a study in the Journal of the American Medical Association (JAMA), roughly 15 million adults are at risk of possible adverse interactions between prescription medicines and herbs or high dose vitamins [7].

Used correctly, multicomponent herbal preparations can help treat a variety of conditions and in some cases may have fewer side effects than some conventional medications. But because they are unregulated, they are often mislabeled and may contain additives and contaminants that are not listed on the label. Some herb components may cause allergic reactions or interact with conventional drugs, and some are toxic if used improperly or at high doses. Some herbal supplements may contain high levels of heavy metals, including lead, mercury, and cadmium which may be injurious to health [12].

Plants have chemical defense mechanisms against predators that can have adverse or lethal effects on humans. Although not frequent, adverse reactions have been reported for herbs in widespread use. A case of major potassium depletion has been attributed to chronic licorice ingestion. Some herbs may amplify the effects of anticoagulants; certain herbs as well as common fruit interfere with cytochrome P450, an enzyme critical to much drug metabolism.

The idea that herbal medicines have no adverse effects is erroneous and ignores the obvious fact that certain herbs may change the distribution and effect of certain allopathic medicines, affect their metabolism and eliminate the good effects of the formulations. Moreover, it is clear that there is an increased risk of adverse interactions between herbal and allopathic medicines than between herbal medicines and synthetic drugs, which is due to the diversity of pharmacologically active chemical constituents in the medicinal herbs. On the other hand, synthetic drugs have unique chemical identities.

General Considerations or Mechanism of Herb-to-Drug Interactions

Co-use of herbs and drugs might alter the drug's pharmacokinetics and/or pharmacodynamics, hence causing unexpected adverse effects of the drug.

Herb-to-drug interactions are based on the same pharmacokinetic (changes of plasma drug concentration) and pharmaco-dynamic (drugs interacting at receptors on target organs) principles as drug-to-drug interactions. The pharmacokinetic interactions that have been identified so far all point towards the fact that a number of herbs, most notably St. John's wort, can affect the blood concentration of different conventional medicines that are metabolized by cytochrome P450 (CYP, the most important phase I drug-metabolizing enzyme system) and/or are transported by P-glycoprotein (a glycoprotein which influences drug absorption and elimination by limiting the cellular transport from the intestinal lumen into epithelial cells and by enhancing the excretion of drugs from hepatocytes and renal tubules into the adjacent luminal space). Polymorphisms in the genes for CYP enzymes and P-glycoprotein may influence the interactions mediated through these pathways. Probe drugs used in pharmacokinetic trials include midazolam, alprazolam, nifedipine (CYP3A4), chlorzoxazone (CYP2E1), debrisoquine, dextromethorphan (CYP2D6), tolbutamide, diclofenacand flurbiprofen (CYP2C9), caffeine, tizanidine (CYP1A2) and omeprazole (CYP2C19). Fexofenadine, digoxin and talinolol have been extensively used in pharmacokinetic trials as P-glycoprotein substrates. Pharmaco-dynamic interactions have been less studied but may be additive (or synergetic), i.e. the herbal medicines potentiate the pharmacological/toxicological action of synthetic drugs, or antagonistic, i.e. the herbal medicines reduce the efficacy of synthetic drugs. Warfarin interactions are a classical example of pharmaco-dynamic interactions. Theoretically, increased anticoagulant effects could be expected when warfarin is combined with coumarin-containing herbs (some plant coumarinsexert anticoagulant effects) or with antiplatelet herbs. Conversely, vitamin K-containing herbs can antagonize the effect of warfarin (the action of warfarin is due to its ability to antagonize the cofactor function of vitamin K). Drug-herb interactions are based on the same pharmacokinetic and pharmaco-dynamic principles as drug-drug interactions.

Recent Developments in Herbal

Due to growing concern over the reliance and safety of drugs and surgery and failure of modern medicine in treating most common health conditions, interest has increased in herbal drug research in India. This inclination is also due to the following reasons –

1. Many natural medicines are being shown to produce better results than drugs or surgery without the side effects [13].
2. They have a strong traditional or conceptual base and the potential to be useful as drugs in terms of safety and effectiveness whereas modern medicines have a very strong experimental basis for their use but are potentially toxic [14].

3. They can deliver mixtures of multi-functional molecules with potentiating and synergistic effects.
4. They are well suited for long-term disease prevention in an era of genetic testing and increased life expectancy [15].
5. They also provide additional vehicles for delivering health and wellness.

How to determine the Herbal Drug Interaction [13-15]

The incidence of clinically considerable interaction between herbals & conventional drugs is un-identified. A feature that may account for the lack of data on the true prevalence of herbal drug interaction is that information needed to determine whether an interaction has occurred is often unavailable owing to the following:

1. Multiple Ingredients.
2. A lack of information concerning the "Concept of the herbal products".
3. Incomplete or inaccurate product information.
4. Poly-pharmacy.

Additionally patient may not inform health care providers of health care interactions, or they do not attribute the reaction to the natural product. Controlled clinical studies are needed to clarify & determine the clinical importance of the herb-drug interactions. Considering lack of understanding of the herb-drug interactions, proper reporting of such cases, careful vigilance, and evidence based appraisal & constantly updated reviews of such information are very important to promote understanding in this area.

Recommendation or Prevention of Herbal drug Interaction [14-15]

Now a days, use of herbal dietary supplements is extremely prevalent. Patient may not be approaching about use of herbal drugs even if it causes severe side effects because, they fear scorn.

1. There is a need for an adequate regulatory framework for herbal products to effectively protect consumers and patients.
2. Patients with cancer should avoid HM that may complicate their cancer care.
3. During the preoperative evaluation, physicians should be familiar with the potential preoperative effects of the commonly used herbal medications, in order to prevent, recognize, and treat potentially serious problems associated with their use.
4. The clinical importance of herb–drug interactions depends on many factors associated with the particular herb, drug, and patient. HM should be appropriately labeled to alert consumers to potential interactions when concomitantly used with drugs.
5. The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) requires that a patient's medication profile include potential drug-food interactions, that the pharmacist call the prescriber whenever the potential for a medication-food interaction exists and document the communication and follow-up action on the prescription or order form, and that patients be given instructions and counseling regarding the potential for drug-food interactions before their hospital discharge.
6. Elderly patients may be at a greater risk for drug-food interactions because they typically consume more medications for their chronic medical conditions.

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