

Significance of herb-drug interactions in clinical practice: A narrative review

K J Malagi¹, Kamath Madhusudhana²

1) Professor, Department of Ayurveda, Kasturba Medical College, Manipal

2) Assistant Professor, Department of Ayurveda, Kasturba Medical College, Manipal

Abstract

Background: There has been a drastic increase in herb-drug interactions day-by-day as a result of an increase in the population using herb and its supplements along with the contemporary medicines. **Objectives:** To discuss the safety of usage of herbal medicines along with contemporary medicines in the management of lifestyle disorders. **Method:** This is a systemic review with narrative analysis. A study was carried out to understand the mode of herb-drug interaction in lifestyle disorders. Literature search was conducted with various titles and reports on medical indexed journals, focusing on herb-drug interaction on selected lifestyle disorders. **Conclusion:** The issue like herb-drug interaction can successfully be combated by bringing change in the curriculum, active participation of regulatory agencies, reforms in statutory bodies and by creating a golden triangle of traditional and modern medicine, and science.

Keywords: Herb drug interactions, Lifestyle disorders.

INTRODUCTION

Use of Complementary and Alternative medicine (CAM) is increasing in both developed and developing countries (Eisenberg et al., 1998) for the last two decades. Though hundreds of complementary and alternative therapies exist, the herbal medicine's popularity in the form of medicine, dietics and nutraceuticals is increasing due to its over the counter sale and cost effectiveness which leads to enhanced purchasing power and due to the general perception that they are safe. It is reported that approximately 10 million deaths occur annually in developed countries like United States of America (Lazarou, 1998) due to use of herbal supplements with the conventional treatment in lifestyle disorders like diabetes, hypertension, stress and arthropathies etc. This may be attributed to the adverse drug interactions in the form of herb-drug, food-drug, drug-drug, and disease-drug. Due to the reasons mentioned earlier, the nature of drug interactions should be given more importance by healthcare professionals and accreditation agencies. The herb-drug interactions occur frequently because they are unnoticed or underrated. Special patient groups like children, elderly or immunocompromised are more

vulnerable to adverse interaction like herb-drug interaction. When a herb enters into human body, it produces a complex mixture of bioactive entities, measurement of which is extremely difficult. There is no particular method to evaluate the mode of herb-drug interactions,

Causes for the herb-drug interactions

1. General human perceptions that products of, herbal origin, herbal drugs and their supplements are usually safe.
2. Pharmacokinetics and pharmacodynamics, potentiality and incidences of adverse reactions like herb-drug interactions are unknown or have little information.
3. Herbs contain multiple ingredients, some of which are natural buffers while herbal extracts contains active, unstable chemical constituents, which may have a high chance of adverse reactions.
4. Lack of evidence pertaining to the studies, dose and route of administration of herbs, herbal formulations and herbal drugs.
5. Lack of standardization, and issues like difficulty in authentication of species, substitutes, adulteration and presence of contaminants.

K J Malagi

Professor, Department of Ayurveda, Kasturba Medical College, Manipal. E-mail: kjmalagi@gmail.com

6. Family physician may not be aware of the use of herbal supplement by patients and also knowledge about the herb-drug interaction may differ from place to place.

Types of herb-drug interactions

1. Synergistic and antagonist
2. Positive and negative

OBJECTIVE

To discuss the safety of intake of herbal medicines along with contemporary medicines in management of lifestyle disorders

METHODS

This is a systemic review in which most common herb-drug interactions in lifestyle disorders were taken and studied. A thorough literature search was conducted using various titles and reports on peer-reviewed medical indexed journals., The search was carried out using various databases like DHARA, MEDLINE, Wiley online, Scopus, Ovid SP, CINAHL, Researchgate. In the review of this article, 150 search items were considered. The literature relevant to the herb-drug interactions and lifestyle disorders were included.

RESULTS

One hundred and fifty peer-reviewed medical index journals comprising of review articles, editorials, clinical and experimental trials were screened for the study after thorough evaluation and analysis of herb-drug interaction.

Assessment of herb-drug interactions in Diabetes

Diabetes Mellitus is both a lifestyle disorder and a metabolic disease. There are approximately four hundred plants documented for their hypoglycaemic action (Bever and Zahnd, 1979). The most common herbs as well as herbal supplements useful in treating diabetes are bitter gourd, ivy gourd, jamun, fenugreek, gymnema.

Fenugreek (*Trigonella foenumgraecum*)

It is popularly known as methi. It stimulates pancreas and possesses many medicinal properties such a lowering of blood sugar level and

hypcholesterolemic action in diabetic patients. (Kassaian, 2009; Madar, 1988)

Ivy gourd (*Coccinia indica*)

It is used as both a vegetable and a medicine. A detailed description of its usage in diabetes is available in the Indian traditional system of medicine like Ayurveda. It is a fruit and its leaf juice possesses hypoglycaemic action (Platel and Srinivasan, 2004).

Bitter melon (*Momordica charantia*)

It is more commonly used as a vegetable in Indian subcontinent. It can be used in the form of fresh juice, in curry, as a supplement and as an extract in management of diabetes. It contains plant insulin, a polypeptide that possesses antidiabetic activity. (Singh, 2011; Welihinda and Karunanayake 1986). It also helps in preventing complications of diabetes like enteropathy, nephropathy, cataract and neuropathy.

Jamun (*Eugenia jambolana*)

It is an evergreen tree and its fruits are edible with astringent taste, used both by rural and urban community. The useful part of jamun in managing diabetes is its seeds (Debjit Bhowmik et al., 2013).

Assessment of herb-drug interactions in Psychosis

Globalization is bringing out a sudden change in socio- economic life and behavioural pattern of human population, resulting in psychological conditions like stress, depression, anxiety and other psychological disorders. It is observed that the consumption of antipsychotic drugs, especially antidepressants, increases significantly during situations of stress and crises. According to a survey report, the geriatric population in India will reach 113 million by 2016 (Chaubey and Aarti, 1999). Some percentage of these people may require antipsychotropic drugs for various psychological manifestations. In psychological diseases like depression, anxiety, convulsions people are using both Indian and Traditional Chinese herbal medicines like Ashvagandha and Ginseng respectively, in their crude and extract forms. They are being used because of their memory enhancing and mood stabilizing qualities.

St. John's wort (*Hypericum perforatum*)

It is a popular "natural" antidepressant. When it is used with other antidepressant agents, it exhibits symptoms of serotonin excess like gastrointestinal disturbance, mood changes, tremor and motor restlessness (Lantz, 1999). According to data available, herbal supplements containing St. John's wort should be discontinued at least two weeks earlier, if someone is undergoing surgery. When administered along with cyclosporines, a decrease in plasma concentration level of cyclosporines was observed.

Ginseng (*Panax ginseng* and *P. quinquefolium*)

It might act together with tricyclic antidepressants, and result in decreased seizure threshold and increased risk of seizures (Miller, 1998). Along with antidiabetic drugs, it may cause hypoglycemia and has potential to interact with warfarin (Jiang et al., 2004)

Winter Cherry (*Withania somnifera*)

It is popularly known as "Indian Ginseng" and is known as 'Ashvagandha' in the Ayurvedic literature. It is commonly used as an aphrodisiac, nervine tonic, immunomodulator, adaptogen and antioxidant. It induces hypoglycaemic and hypocholesterolemic effects in the system. It can be used as a preventive, curative and rejuvenator agent in various conditions. The research reveals that Ashvagandha possesses stress-reducing property and it acts synergistically when administered along with anxiolytics and anti-stressors (Archana and Namasivayam, 1998).

Assessment of herb-drug interactions in Arthropathies

According to the World Health Organization report, there are more than one hundred and fifty diseases grouped under musculoskeletal as well as arthropathies. Prolonged usage of non-steroidal anti-inflammatory agents (NSAIDs) like aspirin, paracetamol may cause severe gastrointestinal damage, nephrotoxicity and hepatotoxicity. The most commonly used herbs in arthritis are garlic, guggulu and boswellia

Garlic (*Allium sativum*)

It is one of the most commonly used spices throughout the world. The local application of its paste is used in treatment of headache and musculoskeletal pain. It may cause skin burns. It is an antioxidant, hypoglycaemic and hypocholesterolemic agent. A significant fall in blood glucose level has been observed in patients taking garlic while on chlorpropamide medication. As a blood-thinning agent, it elevates bleeding tendency when used with NSAIDs, anticoagulants like aspirin, warfarin (Burnham, 1995).

Guggulu (*Commiphora mukul*)

It is one of the most common and most popular drugs of Ayurveda. There is a separate dosage modality in Ayurvedic formulary known as Guggulu preparations. The resin of the tree *Commiphora mukul* is used in Ayurvedic formulations since 500 BC, to treat a variety of ailments like arthritis, rheumatoid disorders, obesity and atherosclerosis. Guggulusterone and oleoresins decrease the thickness of the joint and edema. When administered simultaneously guggulipids reduces (Uzizar and Moore, 2003) the actions of propranolol (Banerjee, 2012).

Sallaki (*Boswellia serrata*)

It acts by directly blocking the conversion of 5-lipo-oxygenase into leucotrienes, thus reducing inflammation. Till now, no contraindications have been reported. (Etzel, 1996; Kulkarni et al., 1991; Kulkarni et al., 1992)

Ginger (*Zingiber officinale*)

Since the early days of human civilization, ginger is used in the treatment of common ailments like cold, migraine and digestive disorders. It can be used as an analgesic, anti-inflammatory (Grzanna, 2005) and antioxidant agent. It produces positive or synergetic action with nifedipine in platelet aggregation, which is commonly seen in cerebrovascular complications (Young et al., 2006).

Assessment of herb-drug interactions in cardiovascular diseases

Cardiovascular disease is the principal cause of morbidity and mortality in the world. Each year, 9.4

million or 16.5% of all deaths can be attributed to high blood pressure. (Alwan, 2011) Cardiovascular diseases may be of coronary, cerebrovascular or rheumatic type. The frequent use of herbs and its supplements is recorded in various clinical conditions like hypertension, obesity and in management of hypercholesterolemia. It can be used as a cardio tonic, peripheral vasodilator, circulatory stimulant or diuretic agent. In general, herb-drug interactions frequently occur when anticoagulants and antiplatelet agents are used with herb or herbal supplements (Holbrook *et al.*, 2005) (P. Dunn and E. Macaulay, 2011).

Liquorice (*Glycyrrhiza glabra*)

Liquorice is a constituent in many of home remedies for cough and sore throat. The active constituent glycyrrhizin causes hypokalaemia and sodium retention (Walker and Edwards, 1994) and may result in hypertension, pulmonary edema and cardiomyopathy (Walker and Edwards, 1994; Hasegawa *et al.*, 1998). Prolonged use may cause irregular heartbeats and muscle weakness. Prolonged use of liquorice along with cardiac glycosides may cause cardiotoxicity (Cheng, 2000).

Onion (*Allium cepa*)

It is used as a dietary supplement in the form of vegetable. It possesses anticoagulant activity as well as antioxidant properties (Slimestad, 2007; Morimitsu, 1992; McLellan and Jurd, 1992; Reddy, 1993).

DISCUSSION

The term 'herbal medicine' has always been used in a broad sense and it is often said to include folklore medicine,, traditional systems of medicine like Ayurveda, Siddha, Unani along with the recently introduced phytomedicine, dietary supplements and nutraceuticals. The term "traditional systems" refer to those systems, which possess their own principles like; constituted lifestyle, body constituents and spiritual teachings (Hoffer, 2003). Recent researches have supported the established concept mentioned in Ayurvedic texts such as Prakrti (body constituent) types with the aid of advanced concepts like premolecular genomics (Bhushan, 2005) and their metaphysical theories. However, folklore medicines

are said to be not in the possession of these ideologies. Phytomedicine is purely based on the concepts like the extraction of the principle constituents from herb source. It is, therefore, important to clearly demarcate these issues during the study of herb-drug interactions. People are now resorting to the use of herbal medicines along with other contemporary medicines in the treatment of various chronic ailments. The expertise of the physician and detailed analysis of the constitutional type, various dosage modalities when dealt with before and the prescription of the medicine, can however nullify the problems of herb-drug interaction. Proper and complete understanding of patient/ medicine history plays a pivotal role in the reducing herb-drug interactions. Documentation of concomitant medications gives an opportunity for the healthcare provider to avoid such incidences. More norms are required to bring changes in the entire scenario. Medical, allied health and basic science scholars must come together to find a solution to address the problems mentioned. This may be achieved by organizing Continuing Medical Education (CME) programs or by conducting workshops and undertaking systemic and scientific research. Policy makers must encourage restructuring of curriculum by introducing the concepts of herb-drug interactions in the entire healthcare education setup. The regulatory authorities must introduce more reforms by giving more power to the statutory bodies for better implementation of standards of healthcare professionals and also educate the key stakeholders i.e. the patients.

CONCLUSION

The use of herbal drugs along with prescribed contemporary medicines is escalating in both developed and developing countries, with or without the knowledge of herbal remedies resulting in potential herb-drug interactions. This can be avoided by bringing effective changes in healthcare curriculum, positive response from the accreditation agencies, by proper implementation of the acts like Drugs and Cosmetics Act, Consumer Protection Act, with necessary amendments. A separate cell to conduct research in various fields of herbal medicines without changing their original philosophy can be

created. As Hippocrates rightly said "Life is short and the art long; the occasion fleeting; experience fallacious; and judgment difficult". Health care professionals must work in this area to accustom herbal and contemporary medicines, for the effective launch of Integrative Medicine, which may provide the best possible medicine/healthcare to patients. Efforts should be made to bring herbal and contemporary medicines under the umbrella of scientific as well as evidence based medicine. As Dr Ramashekhara rightly said, 'What is urgently required is the change in attitude of scientists, traditional practitioners and industry on one hand and the special policy initiatives by the government on the other. Then only we can create the golden triangle of traditional medicine, modern medicine and modern science'.

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