

Herb-drug interaction in diabetes: a bane or a boon

Abstract

Diabetes one among the various life style disorders,¹ has a pandemic existence in today's world. It affects the population, irrespective of the age, sex, religion, etc. A survey work done in Canada recently found that 75% people with diabetes used herbal supplements, vitamins etc.² Overall the research indicates that people suffering from diabetes, are using herbal medicines in the form of a single herb or a polyherbal preparation, besides the prescribed medicine. These herbal formulations are considered to function as a nutritive supplement, nervine tonic or hypolipidemic agent.³ Even though these herbal supplements are claimed to be free from side effects but needs to be approved by FDA.

However, these herbs have their own pharmacological actions with the prescribed antidiabetic drug, which may be synergistic or antagonistic to the same. In the existing system, it is very difficult to control such concomitant usage of medicines of various types, as they are available for over the counter sale. Hence, an earnest attempt has been made here to review and analyze the positive as well as negative role of herbs and its modalities when they are used along with the contemporary medicine.

Keywords: diabetes, herb, herb drug interaction

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Abbreviations: CAM, complementary and alternative medicine; FBS, fasting blood sugar; FDA, food and drug administration

Introduction

The system of Complementary and Alternative Medicine [CAM] is being used by around 80% of the present day global population as a supplement to the conventional medicine.⁴⁻⁷ The rising need and interest for holistic medical approach has contributed to various experimentations and establishments of the esteemed principles of the branch of herbal medicine, which is an integral constituent of the system of Complementary and Alternative Medicine.

As per the forecast made by WHO, the global market for herbal products would be about 5 trillion dollars by the year 2050.⁸ These herbs are either used as a supplement or as an alternative for prescription medicine. Mainly in life style disorders like diabetes. Bever, the author of the book "Medicinal plants in Tropical West Africa" has stated that there are more than 400 traditional plants possessing hypoglycemic action.⁹

Diabetes is one amongst the various lifestyle disorders which acts as a breeding ground for all the other life threatening diseases. It has become the major cause of premature illness in major countries due to cardio vascular disease, blindness and kidney failure etc. It is estimated that there are, presently around 143million Diabetic patients in the world.¹⁰ This may be doubled in 2030.¹¹ The disease puts the immune system of the patients under significant threat, thus, favoring the invasion of the host body by various infectious diseases. It is quite common that people with diabetes use herbal supplements along with contemporary one. Studies have revealed the fact that Thirty five percent of the Americans who are suffering from diabetes use CAM.¹² The patients under multiple systems of medication may have concerns about the possibility of the occurrence of polypharmacosis, thereby resulting in the interaction between drug molecules. The interactions may be apprehended and analyzed to be of drug-drug, herb-drug or food-drug varieties. In case of Drug-Drug Interactions the reaction

mode is either pharmacodynamics or pharmacokinetics.¹³ While the drug-food interactions can affect bioavailability of a drug. For example the hypoglycemic effect of glipizide may be delayed slightly if taken with a meal versus 30–60minutes before a meal, although hemoglobin A1c (A1C) values are unaffected.^{14,15} But the Herb-drug interaction mechanism is still mysterious in the field of medicine. This can be studied similar to the features of modern pharmacological concepts.¹⁶

Out of many such herbs Bitter melon (BN. *Momordica charantia* L) is a popular plant of Asian origin. Different clinical trials, incorporating different kind and forms of the drug, like fresh fruit juice, seed extract and such others have been carried out, with variations in dosage modalities.¹⁷⁻¹⁹ It is used for lowering blood glucose levels in patients with diabetes mellitus.²⁰ Trials reveal that the fruit extract of Bitter melon is effective in treating diabetes.²¹ In addition, experimental researches have demonstrated the positive outcome of bitter melon in complications of diabetes, like neuropathy and enteropathy,²² Cataract²³ and nephropathy.²⁴ While positive effects were seen on various parameters of lipid profile²⁵⁻²⁹ and also, the sap of the plant contains the principle constituent, the 'plant insulin' (a polypeptide) which reduces the blood glucose level in type 1 diabetes mellitus.³⁰

Another most commonly used spice in Indian kitchen is Fenugreek (BN. *Trigonella foenum-graecum* L.). It contains Vitamin A, protein and fiber and is said to possess hypoglycemic and hypocholesterolemic properties.³¹ Food preparations which contain 10% fenugreek seed³² or extract³³ or Fenugreek seed powder³⁴ (~10g/day) is said to be useful in reducing fasting blood sugar [FBS], triglycerides.³⁵ It also stimulates pancreatic action.³⁶

Garlic (BN. *Allium Sativum* L) is one more spice which is routinely used in cooking. It acts as a hypoglycemic, hypocholesterolemic and hypolipidemic agent.³⁷ A significant fall in blood glucose levels have been observed in patients using garlic along with chlorpropamide.³⁸ It reduces blood sugar by producing active nitrogen compounds.³⁹ It can

also be used as an antioxidant and anti-inflammatory agent. But, garlic is known to increase the bleeding tendency, when used with NSAIDs like aspirin. It may also react with vitamin E in high concentrations.⁴⁰ A clinical trial suggests that garlic changes some pharmacokinetic variables of paracetamol.⁴¹ Garlic may act synergistically with anticoagulants like warfarin^{42,43} fluindione⁴⁴ and reduce the efficacy of anti-AIDS drugs like saquinavir.⁴⁵ Animal research shows that garlic preparations may enhance the bioavailability of propranolol.⁴⁶

Onion (BN. *Allium Cepa* L) is more of a vegetable than an herb used in almost all the dietary preparations in India. The animal study reveals the hypoglycemic effect of onion.⁴⁷ Onion, when used as a dietary supplement, is proven to be useful in the management of type 1 and type 2 diabetes mellitus.⁴⁸⁻⁵⁰ The Study conducted by Tاتفeng Y on animals showed significant increase in CD4 count.⁵¹ Experimental studies reveal that it reduces Cadmium induced kidney damage in rats.⁵² The oral administration of onion extract significantly decreases the level of T3, T4 hormones in the experimental animals.⁵³ Onion has been reported to have anticoagulant as well as antioxidant properties.⁵⁴⁻⁵⁷

Likewise, the leaves of *Gymnema* (BN. *Gymnema Sylvestre*, L) are used in Ayurveda, the Indian system of medicine to treat conditions like diabetes, obesity and such others. *Gymnemic acid*, an active principle of the plant has anti-obesity and antidiabetic properties, which helps in weight reduction. It can minimize the insulin dose in both Type 1 and Type 2 Diabetes.⁵⁸⁻⁶⁰ The plant extracts are found to arrest epinephrine-induced hyperglycemia.⁶¹ It also reduces Chromium reduced glycosylated hemoglobin (HbA1c).⁶² It is also observed to be hepato protective in the cases of injury caused as a result of radiation.⁶³

Ginseng (BN. *Panax ginseng* & *P. quinquefolium*) is a Chinese herb which possesses the additive pharmacological action in both insulin dependent and non dependent diabetes mellitus.⁶⁴⁻⁶⁶ The herb, ginseng may either decrease⁶⁷ or increase⁶⁸ the anticoagulant effect of warfarin. It may interact with Tricyclic antidepressants, other drugs that decrease seizure threshold and result in increased risk of seizures.⁶⁹ It also alters the action of Furosemide,⁶⁵ Estrogens, corticosteroids & Digoxin.⁷⁰

The classics of Ayurveda elaborately explained the properties of the drug *Guduchi*- (*Tinospora cordifolia* Wild) as antipyretic and rejuvenating. They have also indicated it to be a remedy for diabetes.⁷¹ Animal experimental studies have proven that, extracts of *Tinospora cordifolia* could change lipid metabolism. It is of immense importance, as hyperlipidemia is one of the complications of the Diabetes.⁷² It also possesses antihepatotoxic⁷³ as well as Immunomodulatory⁷⁴ effects. Till now no such significant adverse event has been observed with the use of *Guduchi* in healthy individuals.⁷⁵

Popularly known as *Ashwagandha* in Ayurveda (BN. *Withania somnifera*) and commonly considered as the Indian ginseng, is having hypoglycemic, diuretic and hypocholesterolemic properties.⁷⁶ The Studies indicate that *Ashwagandha* possesses stress reducing property and it acts synergistically when administered along with anxiolytic and anti-stressors.⁷⁷ It also contains immunomodulatory,^{78,79} antioxidant⁸⁰ properties.

Another herb *Ivy gourd* (BN. *Coccinia indica*) is used in Ayurveda to treat Diabetes. The juice of the ripe fruit is used to treat Hyperglycemia, but the role of pharmacokinetics and Pharmacodynamics in this is unknown.⁸¹⁻⁸³ Potential hypoglycemic action has been observed in administering a single oral dose of the Leaf of *Coccinia*.⁸⁴

Jamun (BN. *Eugenia jambolana*) is an evergreen tree and its fruits are not too tasty, has a sharp sweet and astringent taste. As it has a low glycemic index, the seeds and seed powder of *Jamun* are used in the treatment of diabetes in Ayurveda.^{85,86}

Discussion

According to WHO, the 'herbal medicine' is defined as herbs, herbal materials, herbal preparations and finished herbal products, that contain as active ingredients parts of plants, or other plant materials, or combinations.⁸⁷

WHO elaborately explains the criteria for assessing the safety, efficacy and quality of herbal medicines, utilizing the parameters like acute toxicity, organ targeted toxicity, Mutagenicity, genotoxicity, carcinogenicity as well as herb drug interaction. The main limitations of the herbal medicines are inadequate standardization, lack of quality specifications and lack of scientific data along with insufficient evidence regarding herb drug interactions. Even though no proper data available regarding the herb drug interaction, no attempt has been made to bring the same in the current medical academic curriculum. And also, information regarding the use of these products in the elderly population is almost nonexistent.^{88,89} It is absolutely impossible to differentiate herb-drug interactions from that of adverse drug effects.⁹⁰⁻⁹³ Herb drug interactions may be positive or negative in nature. But, it certainly influences the pharmacological action of a drug molecule in the body. It is difficult to assess the biochemical nature of the all the traditional medicinal plants and its interaction with the pharmaceutical agents of the contemporary medical system. Here the main issue of concern is its inadequate reporting system which makes it difficult to document an herb-drug interaction. Accreditation agencies like the US Food and Drug Administration (FDA) also do not have a clear agenda in this area, to fulfill the knowledge gap.

Conclusion

Today, even though millions of people are using herbal supplements with the assumption that 'natural products' are 'safe' for consumption, there is very little information available on the herb-drug interactions. In this regard, there is a need of public awareness which can be created by proper education and training of both the clinicians and the general public. And also, reliable information can be provided on authenticated websites. The governing agencies must issue proper guidelines for appropriate access and delivery of the reliable herbal medicines. Clinicians are advised to trace and pick up any information regarding usage of any herbal supplement or nutraceuticals along with prescribed medication by their patients. It should be made mandatory to document the adverse events, if any, with all the relevant information. Agencies like FDA, AYUSH and other food and drug regulatory boards must be vigilant about this emerging trend. This documented information can be a guideline for the clinicians, those who are using the anti diabetic drugs with or without the knowledge of the Indian system of medicine. The knowledge and implementation of the complementary and alternative medicine along with that of the antidiabetic drugs is the only way to provide a holistic approach in the treatment of diabetes.

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Conflict of interest

Author declares that there is no conflict of interest.

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