ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 6, Issue – 4, July – 2021 , Page No. : 102 - 111

Possible interactions between Dietary Herbs/Food and conventional drugs: A review

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Citation this Article: Pradnya Deolekar, Kavitha Dongerkery, Pramila Yadav, Swati Sonawane, "Possible interactions between Dietary Herbs/Food and conventional drugs: A review", IJMSIR- July - 2021, Vol – 6, Issue - 4, P. No. 102 – 111.
Type of Publication: Review Article
Conflicts of Interest: Nil

Abstract

Dietary Herbs/Food & drug interactions result from medicines, reacting with food or beverages in the diet. Food-drug interactions can lead to a loss of therapeutic efficacy or toxic effects of drug therapy. Drug -food interactions may result in reduced, delayed, or increased systemic drug availability. Generally, the effect of food on drugs results in a reduction in the drug's bioavailability, however, food can also alter drug clearance.This review article will stipulate information about such interactions and will help physicians to prescribe drugs cautiously with only suitable food supplement to get maximum benefit for the patient.

Keywords: Food-drug interaction, Bioavailability, adverse effect.

Introduction

The effect of drug on a person may be different than expected because that drug interacts with another drug the person is taking (drug-drug interaction), food, beverages, dietary supplements the person is consuming (drug-nutrient/food interaction) or another disease the person has (drug-disease interaction). The definition of drug-nutrient interaction is that it is an interaction resulting from a physical, chemical, physiologic, or pathophysiologic relationship between a drug and a nutrient, multiple nutrients, food in general, or nutritional status.[1]

These interactions may occur out of accidental misuse or due to lack of knowledge about the active ingredients involved in the relevant substances. Regarding food-drug interactions physicians recognize that some foods and drugs, when taken simultaneously, can alter the body's ability to utilize a particular food or drug, or cause serious side effects.[2] Food-drug interactions may lead to loss of therapeutic efficacy, toxicity or therapeutic failure. In some events, the interaction may have a helpful effect by increasing the drug effectiveness or reducing possible side effects. Major side-effects of some diet (food) on drugs include alteration in absorption by fatty, high protein and fiber diets. Bioavailability is an important pharmacokinetic

parameter which is correlated with the clinical effect of most drugs.[3 4]

Food–drug interactions can result in 2 main clinical effects: the decreased bioavailability of a drug, which predisposes to treatment failure, or an increased bioavailability, which increases the risk of adverse events and may even precipitate toxicities. [5,6,7]

An interaction is considered significant from a clinical perspective if it alters the therapeutic response. With some drugs, it's important to avoid taking food and medicines together because the food can make the drug less effective. For other drugs, it may be good to take the drug with food to prevent stomach irritation. Some drugs interfere with the absorption of a nutrient and may lead to a nutrient deficiency.[8,9,10] The literature survey was conducted by extracting data from different review and original articles on general or specific drug interactions with food. This review gives information about various interactions between different dietary herbs/foods and drugs and will help physicians and pharmacists prescribe drugs cautiously with only suitable food supplement to get maximum benefit for the patient.

Pharmacokinetic interactions

Pharmacokinetic interaction comprises changes in the way dietary herbs/ Food and drug arrive into the body and can modify the amount, or level of a drugs in the body. If it increases the levels of a drug in body it would lead to side effects and/ or toxicity. And if it decrease the levels of a drug due to the interaction, the drug may be less effective and a possibility to treatment failure/ or drug resistance. Following are the drug-food interactions of clinical significance-

Anti-hyperlipidemic agent Lovastatin should be taken with food to enhance gastrointestinal absorption and bioavailability, while Rosuvastatin should be administered on an empty stomach.[11] Most drugs are better absorbed on empty stomach e.g. For rapid relief, acetaminophen should be taken in an empty stomach because food may slow the absorption of acetaminophen.[12] often cause stomach irritation. Analgesics, like aspirin, are administered with food decreases gastric irritation. [13] Long-term use of Anti-inflammatory drugs for arthritis may lead to gastritis and hence preferably these medications should be taken with food.[14]

Isoniazid should be taken on an empty stomach because it requires an acid medium in order to be absorbed. Foods, particularly carbohydrates, can decrease the absorption of the drug by 57% and the plasma concentration of the drug by 30%.[15] Rifampin should be taken on an empty stomach. Foods decrease the absorption of the drug by as much as 26%.[16] Drugs like penicillin and erythromycin are most effective when taken on an empty stomach. This is because they may be partially destroyed by stomach acid when taken with food.[17] Acid resistant Penicillins were synthesized and erythromycin esters were made to counter the destruction by the acid. Azithromycin absorption is decreased when it is taken with food, resulting in a 43% reduction in bioavailability.[18,] Eating charbroiled food may decrease warfarin activity, while eating cooked onions may increase warfarin activity.[19]

Theophylline products when taken with high-fat foods may cause a sudden release (dose dumping) of theophylline, resulting in increased theophylline concentrations and possible toxicity.[20, 21] The serum concentration of Cycloserine, an anti-tubercular drug is decreased when consumed with high fatty meals and results in incomplete eradication of bacteria.[22]

Licorice may increase the absorption of digoxin thereby aggravating the risk for digoxin toxicity.[23] Licorice

extract, contains glycyrrhizin and glycyrrhetinic acid. It is a potent inhibitor of 11- beta- hydroxyl steroid dehydrogenase, it increases excess of cortisol to mineralocorticoid receptors causing sodium retention and potassium depletion, so it may interfere with antihypertensive and antiarrhythmic agents. [24,25]

Clinically significant interactions between Levothyroxine and papaya can alter the safety and efficacy of the treatment. The interaction between L-T4 and papaya is due to its active principle papain, which reduces the secretion of gastric acid (up to 48 h) and increased gastric pH is associated with lower L-T4 absorption. [26]

Propranolol is a beta blocker. Garlic homogenate with propranolol which can cause increase in the bioavailability and half-life along with decrease clearance and elimination rate constant of propranolol, is found to be most effective in reducing systolic blood pressure.[27,28]

When fibre rich foods (Wheat bran, Oat bran, Rolled oats, Sunflower seeds, Coconut shreds, Raisins, green peas, beans) reacts with Digoxin, Amoxicillin, Levothyroxine, TCAs the fibre binds to the drug in the gut delaying the absorption of drug. This interaction could result in decreased serum concentrations of drugs and therapeutic effectiveness.[32]

Mercaptopurine is a purine analog, gets inactivated by Xanthine oxidase (XO), concurrent intake of substances containing XO may potentially reduce bioavailability of Mercaptopurine. Cow's milk is known to contain a high level of XO. This interaction may be clinically significant. Therefore most patients should try to separate the timing of taking mercaptopurine and drinking milk.[33]

If isoniazid is taken with garlic it decreases absorption of isoniazid, so an effect of a drug may decrease. Garlic slightly increases glucuronidation of a therapeutic dose of paracetamol; after a long period of time the effect of the drug may be altered.[34]

Thiazides are first line antihypertensives and also used as an diuretic in cardiac failure. Garlic increases the oral bioavailability and half-life of hydrochlorothiazide along with a decrease in the clearance and elimination rate constant.[35] Anti-tubercular drugs like isoniazid have been associated with tyramine interactions.[36] Inhibition of monoamine oxidase by isoniazid can cause significant drug food interactions. Drug should not be taken concomitantly with foods rich in tyramine, such as certain types of cheese (Swiss and Cheshire), fish (tuna and herring), and alcohol, especially red wine.[37] This is also seen with concomitant administration of MAO inhibitors with tyramine rich foods.

Cilostazol is antiplatelet agent used for preventing intermittent claudication without rest pain in cases of PVD. Similarly Statins like Lovastatin and Simvastatin are used for the treatment dyslipidaemia, undergoes extensive metabolism by CYP3A4 enzyme. Grapefruit juice, in large quantities, can inhibit the CYP3A4 enzyme and increase blood levels of these drugs metabolized by this pathway. This interaction with Statins and can lead to elevated risk of rhabdomyolysis. [38] A case was reported by Taniguchi in 2007 in 79 years old man on concomitant ingestion of cilostazol and grapefruit juice developed purpura.[39]

There is increased risk of torsade de pointe with Erythromycin and Terfenadine when consumed along with grape fruit juice. Fruit juice causes prolongation of QT interval of heart beat by inhibiting the metabolism of these drugs.[40]

CYP2C19 and CYP3A4 participate in the bioactivation of clopidogrel whereas grapefruit juice constituents

potently inactivate intestinal CYP3A4 and also inhibit CYP2C19, markedly decreasing the platelet-inhibiting effect of clopidogrel.[41] Based on increased oral bioavailability of estrogens with grapefruit juice, 2 large epidemiologic studies reported the risk of breast cancer. [42]

Ginkgo Biloba can increase the risk of bleeding in surgical patients on anticoagulants due to several flavonol aglycones (e.g., amentoflavone) found in Ginkgo which are potent inhibitors of human CYP2C9.[43]

Mango contains high concentrations of retinol, a known inhibitor of CYP2C19. Increases in PT-INR resulting from consuming even small amounts of mango while receiving warfarin therapy can be clinically relevant.[44]

When fluoroquinolons or tetracyclines or bisphosponates taken with dairy products like cheese, yoghurt, milk containing multivalent cations (calcium), leads to the formation of insoluble chelates, reduces the absorption of the drug and reduces the therapeutic efficacy of the drug.[45]

Milk thistle that contains potent CYP3A4, and P-gp inhibitor (silibins and silymarin) and would increase the oral bioavailability and decrease the clearance of co administered drugs. According to Wu and Tsai, silibinin had altered the hepatobiliary elimination of pyrazinamide an anti-tuberculous drug.[46] Rajnarayana et al., showed that another component, silymarin caused an increased clearance of metronidazole and its metabolite hydroxymetronidazole, thereby decreasing the half life of this antiprotozoal agent.[47] Garlic preparations decrease the plasma concentrations of saquinavir.[48]

Pharmacodynamics interactions

Pharmacodynamics interactions are those dietary herbs / food drug interactions that cause change in pharmacological responses; changes in the physiological effect and mechanism of action of the drug on the body. Pharmacodynamics interactions may result in augmentation or inhibition of the pharmacological activity of a co-administered drug. Herb-drug pharmacodynamics interactions would, therefore, involve changes in the pharmacological effects of the drug through additive, synergistic or antagonistic actions.[49]

Warfarin inhibits the enzyme vitamin K epoxide reductase (VKOR) causes decarboxylation of clotting factors II, VII, IX and X and and endogenous anticoagulant proteins C & S. Garlic has been interrupting thromboxane synthesis, and may interfere with vasoconstriction process. Thereby it inhibiting platelet function and may increase bleeding risk.[50]

Large amounts of foods rich in vitamin K (liver, and green vegetables such as broccoli, spinach and other leafy greens) when adminster along with warfarin may decrease the effect of warfarin.[51]

Cyclosporine is an immunosuppressant taken after an organ transplantation. Allicin, an active component of Garlic may interact with cyclosporine and may decrease its eficacy.[52]

Atorvastatin inhibits HMG-CoA reductase enzyme, the rate limiting enzyme for cholesterol synthesis. From the findings of the study renal damage could be attributed to the increased lipid peroxidation due to Atorvastatin inhibiting the metabolizing enzyme and P- glycoprotein by garlic. According to the study done by Reddy DG et al. Kidney injury was observed when Atorvastatin taken alone or in combination with the higher concentration of garlic and Nephrotoxicity was observed while taking a low dose of atorvastatin in combination with the high concentration of garlic.[53]

Ginkgolides, the major chemical components of Ginkgo biloba, have anti-inflammatory and anti-platelet properties. Ginkgo should be avoided in patients receiving anticoagulants or antiplatelet agents as bleeding may occur because ginkgo itself possesses antiplatelet action. In a patient with chronically stable PT-INR values on warfarin, intracranial hemorrhage was reported after 2 months of concomitant use of Ginkgo biloba.[54] The clinical interaction of Risperidone and Ginkgo biloba results in Priapism. Postulated mechanism could be that both ginkgo and risperidone have vessel-dilating properties. Priapism, lasting for 4 h, was reported in a 26-year-old man.[55] Alcoholic beverages may increase the central nervous system depressant effects of medications such as benzodiazepines, antihistamines, antidepressants, antipsychotics, muscle relaxants, narcotics or any drug with sedative actions.[56]

Caffeine has additive effects on Theophylline. It has been reported that caffeine increases serum theophylline levels by 20%–30%. A lower dosage of theophylline may be necessary for those patients who consume excessive quantities of coffee (more than 6 cups daily).[57] Pseudoephedrine is an symapathomimetic causing CNS stimulation which along with caffeine administration may increase feelings of anxiety and nervousness.[58]

Concomitant use of Salty foods with Oral contraceptives and steroids may increase fluid retention.[44]

Naturally occurring goitrogens found in legumes, plants, cabbage, cauliflower, broccoli, turnip, forms of root cassava. Soy or soy enriched foods can also aggravate thyroid problems reducing T4 absorption and interfering with thyroid hormone action and are reported to increase auto-immune thyroid disease.[59]

Oral Contraceptives ("the pill") may be affected by the enzyme induction of St John's Wort. Some episodes of breakthrough bleeding reported overseas have been attributed to the interaction. Unintended pregnancy has not been reported but, given the mechanism involved, there are grounds for concern that the interaction might reduce the contraceptive efficacy of some oestrogen-containing Oral Contraceptives.[60]

St John's Wort may reduce the efficacy of warfarin,,digoxin, theophylline, other HIV protease inhibitors, HIV non-nucleoside reverse transcriptase inhibitors and anticonvulsants .[61]

MAO inhibitors shouldn't be consumed with excessive amounts of chocolate. The caffeine in chocolate interact with stimulant drugs such as Ritalin (methylphenidate), increasing their effect, or by decreasing the effect of sedative-hypnotics such as Ambien (zolpidem).[62] Licorice may also reduce the effects of blood pressure drugs or diuretic (urine-producing) drugs, including hydrochlorothiazide and Spironolactone.[63]

There is greater chance for potentiation of hepatotoxicity when hepatotoxic herbs like chapparal, echinacea are co administered with hepatotoxic drugs such as non-steroidal anti - inflammatory drugs (NSAIDs), ketoconazole and methotrexate.[48]

Herbs have been shown to mitigate or prevent adverse effects associated with drugs. For example, aromatic herbs such as ginger can be used to prevent drug-induced nausea; milk thistle can be used to prevent the liver toxicity associated with drugs.[64] In addition, the scientific studies have proven that capsaicin reduces gastric mucosal damage induced by aspirin.[65]

There are several reports where ginseng induced mania when used concomitantly with phenelzine[66] and ginkgo raised blood pressure when combined with a thiazide

diuretic and caused coma when combined with Trazodone, an atypical antidepressant.[67]

Kava (Piper methysticum) caused a semicomatose state when given concomitantly with alprazolam.[68] A patient with Parkinson's disease taking levodopa in combination with kava had increased duration and number of "off" periods.[69] This may be due to the dopamine antagonistic activity of kava.

Several epidemiological studies suggest an antihypertensive effect of garlic and of many of its bio active components. there are studies that indicate that the blood pressure-lowering action could be due to the inhibition of angiotensin and nitric oxide expression. Thus simultaneous use of garlic and ACE inhibitors could exert supradditive interaction with respect to a fall in blood pressure and ACE inhibition, indicating that hypotension could be a potential adverse reaction.[70]

Aloe.vera is mainly employed for inflammatory conditions, diabetes and hyperlipidaemia. Blood loss during surgery as a result of a possible interaction between A. vera and the anaesthetic sevoflurane has been reported.[71] An additive effect on platelet function has been hypothesized since both sevoflurane and A. vera ingredients may inhibit platelet aggregation.

Garlic and Glibenclamide is a synergistic combination as it increases hypoglycaemic effect of a drug.[72]

Conclusions

We conclude that Food-drug interactions can produce negative effects in safety and efficacy of drug therapy, as well in the nutritional status of the patient. Therefore, efforts to elucidate potential risks resulting from food-drug interactions should be intensified in order to prevent undesired and harmful clinical consequences. In cases where certain foods or beverages are known to impact therapy, both patients and clinicians should be educated on the clinical significance of Food / dietary herbs drug interactions.

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