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Food-drug interaction: A review

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Abstract
The success of drug therapy to some extent does depend on interaction between food and the drug. A drug-food interaction is a condition in which the food affects the activity of a drug. The change most of the time may results in detrimental effect on the patient. Therefore it is advisable for patients to follow the physician and doctors instructions to obtain maximum benefits and simultaneously to prevent such unfortunate event. This review article will provide information about such interactions and will help physicians and pharmacists prescribe drugs cautiously with only suitable food supplement to get maximum benefit for the patient.

Keywords: Food-drug interaction, Bioavailability, adverse effect, Pharmaceutical, Pharmacokinetic, Pharmacodynamic

Introduction
Medicines (Nutrients) and food are often taken together. Drug-nutrient interaction is defined as an alteration of kinetics or dynamics of a drug or a nutritional element, or a compromise in nutritional status as a result of the addition of a drug [2]. It can prevent a medicine from working the way it should or can cause a side effect from a medicine to get worse or better. Besides, it can cause a new side effect [3]. Apart, the knowledge of food-drug interaction plays a crucial role in the field of Ayurveda and also while the patient is taking both (ayurvedic and allopathic) drugs at the same time. Some of the herbs used can interact adversely with prescription drugs. Two notable examples are mahuang (ephedra) and feverfew. Mahuang is a stimulant that can cause hypertensive crises in patients taking monoamine oxidase inhibitors (MAOIs). Feverfew has anticoagulant properties that can augment the effects of warfarin.

Mechanisms of Food Drug Interactions
Pharmacokinetic interaction
Interaction involving Absorption
Presence of food in the stomach may affect the absorption of many commonly used drugs, due to alteration of gastric pH, gastric secretion, motility and of course transit time of the GIT. For instance, azithromycin absorption is decreased when it is taken with food, resulting in a significant reduction in bioavailability. However, the components of the food, such as calcium or iron, may form complexes with the drug that are less easily absorbed. Examples include tetracycline, sodium fluoride and ciprofloxacin. On the other hand, the bioavailability of some drugs may be enhanced by food. For instance, an acid environment is necessary for the absorption of ketoconazole. The absorption of griseofulvin is increased by fat in the food.

Interaction involving Metabolism
Food sometimes interacts with the metabolism (mostly hepatic) of many drugs. For example, concentrated grape fruit juice when administered with antihypertensive drugs, felodipine and nifedipine, cause an increase in the bioavailability of the both. It is postulated that flavonoid compounds in grapefruit juice concentrate inhibit cytochrome P-450 metabolism of felodipine and nifedipine. This interaction could increase both the efficacy and toxicity of these drugs. Citrus fruit or its juice is a common ingredient of a breakfast so, there is huge clinical significance. Patients should be advised of this possible interaction [4, 5].

Interaction involving excretion
Many ingredients present in food may alter the pH of the urine which eventually cause either Decrease or increase in the half of drug taken by the patient.

Thus, half-life of acidic drugs will be more in acidic urine (caused by foods like Meats, fish, cheese and eggs) because the drug in acidic medium remains in its unionized form and likewise half-life of an acidic drug in alkaline urine (caused by milk, vegetables and citrus fruits) is reduced because the drug is in its ionized form. Also, Lithium and sodium compete for tubular reabsorption in the kidney. A high-salt diet causes more lithium to be excreted, whereas a low-salt diet causes decreased renal excretion of lithium and high serum level of lithium [6].

Pharmacodynamic interactions

Green leafy vegetables (e.g. spinach, broccoli, turnip etc), cauliflower, chick peas, green tea, pork liver and beef liver are rich source of Vitamin K and thus cause antagonism of warfarin, an anticoagulant drug and decreased therapeutic efficacy of the latter. Central nervous system depressant action of benzodiazepines, antihistamines, antipsychotic, narcotic or any drug with sedative action is enhanced by alcoholic beverages [7]. Conversely, the bioavailability and serum concentration of theophylline is markedly increased by caffeine in the diet.

This review describes interaction of some of the commonly used medications with clinical significance.

Monoamnine Oxidases Inhibitors

Perhaps the most feared and the most deadliest food-drug interaction is between monoamine oxidase inhibitors (MAOIs) and the amino acid tyramine, as tyramine is found in a variety of aged, fermented, overripe or pickled foods and beverages and, to a lesser extent, chocolate and yeast-containing foods. Despite the effectiveness of MAOI in the control of depressive disorders, they are to be consumed with full precautions due to their interaction with tyramine-containing food (matured cheese, yogurt, ripped bananas etc.) because of their tendency to produce hypertensive crises in patient taking MAOIs [8]. Older or first generation MAOIs comprises of drugs such as Phenelzine and isocarboxazid which were mostly nonselective inhibitors of both subtypes of MAO (MAO_A and MAO_B). Restriction in the diet while taking these medication was a mandate [9]. Tyramine, an indirectly acting sympathomimetic agent, is a substrate for MAO but when the patient is taking MAOIs, it escapes degradation and reaches the systemic circulation and exhibits its action as hypertensive crisis [10]. When its metabolism is suppressed, as it is by MAOIs, it can cause a significant release of norepinephrine, resulting in markedly increased blood pressure, cardiac arrhythmias, hyperthermia, cerebral hemorrhage and eventually stroke.

Case report (as an example)- History of depressive disorder was encountered in a forty-nine year old patient (male) and was tried with tricyclic antidepressants and selective serotonin reuptake inhibitor (SSRI) but failed to exhibit visible response hence a trial of monoamine oxidase inhibitor (MAOI) was initiated. Strict diet restriction to avoid tyramine containing food was advised. As advised the patient maintained the diet restriction and was showing dramatic response. However, soon the patient was re-admitted to the emeregency department of the hospital with the history of severe headache, after he consumed a large quantity of chocolate (source of tyramine) on one occasion. Careful examination revealed the patient became victim of hypertensive crisis and necessary treatment was started immediately. Unfortunately, the patient died of stroke within 30 minutes of treatment initiation. [11]. This shows the necessity to understand the interactions between the drug and the food we take and the need for awareness amongst the pharmacist from whom the patient receives drug.

Antidiabetics

Alcohol can cause a disulfiram-like reaction when taken in combination with oral sulfonylureas, particularly chlorpropamide. Diabetics not prescribed sulfonylureas are also wise to cease or limit alcohol consumption as it has adverse effects on glycemic control with a tendency towards hypoglycaemia. Pre-existing hypoglycemia can be potentiated. Alcohol consumption genrerally results in loss of glycemic control by as it reduces metabolic clearance of most of the hypoglycaemic drugs [12, 13]. Glimepiride is a sulfonylurea derived antidiabetic that needs to be administered with the first main meal of the day. The bioavailabity of Glimepiride is so good that empty stomach results in variable pharmacokinetics [14]. Diabetic patients taking/receiving hypoglycemic drugs (likely Phenformin and chlorpropamide) or insulin [15] the use of bitter melon should be avoided or taken with caution as it may potentiate the effectiveness of the drugs and may lead to severe hypoglycaemia. Allium sativum (Garlic) results in hypoglycemia when taken with chlorpropamide [16]. Conventional glipizide (immediate release) should be taken 30 mins to 1 hour before meals [17]. Acarbose, an alpha-glucosidase inhibitor is recommended to be taken right at the begining of each meal as the carbohydrate absorption is delayed by acarbose by blocking the enzyme alpha-glucosidase [11]

Bronchodilators

The effect of food on theophylline, a bronchodilator can vary based on the nutrient content of the food. Bioavailability of theophylline is enhanced by high fat diet (food) while it is reduced by high carbohydrate diet. Concurrent taking of alcohol augment the side effects such as nausea, vomiting, headache and irritability. Stuff rich in caffeine (e.g. coffee, tea, chocolate etc.) should be avoided as it produces synergistic affect and may even reach the toxic level in the serum.

Non-Steroidal Anti-inflamatory Drugs (NSAID)

The maximum serum concentration of Ibuprofen is significantly enhanced when consumed with beverage, coca-cola due to better bioavailability of the former in presence of coca-cola. Thus the daily dosage and frequency of ibuprofen must be reduced when administered with beverage, Coca-Cola [19]. Ibuprofen may also interact with marijuana (Cannabis sativa) and alcohol and increases the risk of GI bleeding and chances of liver damage. Fluid retention and edema have been reported in association with the use of nonsteroidal anti-inflammatory drugs. Thus therapy with NSAIDs should be administered cautiously in patients with preexisting fluid retention, hypertension, or a history of heart failure. The effect of NSAID is further enhanced by the use of caffeine. Taking NSAIDs with coffee gives faster relief in patients thus some drug does come in combination of both for example a mixture of aspirin and caffeine is Excedrin (a trademark of Bayer).

Warfarin

Warfarin, a common anticoagulant is used in routine practice for its vital effect on haemapoietic system [20] St. John's wort and possibly some ginseng formulations may have the potential to diminish warfarin anticoagulation, by inducing CYP2C9 activity since Warfarin is metabolized primarily via oxidation in the liver by CYP2C9.Avoid garlic, ginger, glucosamine, ginseng, and ginkgo because they can increase the chance of bleeding. Moreover, avoiding alcohol is an important issue because it can affect the dose of warfarin. NSAID particularly aspirin can augment the efficacy of warfarin due to its blood thinning property.

Antitubercular Drugs

The bioavailability of food is greatly decreases by isoniazid, an important member in the family of antitubercular therapy [21]. On the other hand, Oleanolic acid, a triterpenoid exists widely in food, medicinal herbs and other plants, has antimycobacterial activity against the Mycobacterium tuberculosis, when administered with isoniazid, it exerts synergistic effect [22]. The serum concentration of cycloserine, a bacteriostatic anti-tubercular drug is significantly reduced by high fat meals thus resulting in incomplete eradication of bacteria [23].

Fruit Juices

Among all, Grape fruit juice possesses is a similar name in the context of food-drug interaction high interaction by altering normal functioning of the Cytochrome oxidase system. One of the most well known food–drug interactions is grapefruit juice (GFJ) and the HMG-CoA reductase inhibitors or statins. Grapefruit juice, in large quantities (32 oz. or more per day), can inhibit the cytochrome P450 3A4 (CYP3A4) enzyme and increase blood levels of drugs metabolized by this pathway, such as certain statin drugs [24, 25]. It has been reported in an old man who was maintained on Cilostazol (a quinolinone-derivative) and aspirin for his Peripheral Vascular Disease (PVD). The patient was concomitantly taking grapefruit juice with the medicines prescribed and reported back to clinic with purpura which later on disappeared with cessation of GFJ. The purpura in this case could possibly due to inhibition of cilostazol metabolism by GFJ which eventually lead to dramatic increase in the blood concentration of cilostazol [26]. Many authors have noted interactions of drug with GFJ that occur via inhibition of CYP3A enzymes, a subtype of cytochrome oxidase enzyme system [27]. The compound furanocoumarins (in GFJ) selectively blocks intestinal CYP 3A4 which results in increase in oral bioavailability of drugs which are substrate of CYP 3A4 viz; Felodipine and cyclosporine ultimately causing toxicity [28].

Antibiotics

Undoubtly, the most commonly prescribed drugs around the world is the antibiotics. Like other medicines antibiotics does show food-drug interaction. The bioavailability and serum concentration of ciprofloxacin is reduced to a greater extent when consumed with milk the drug undergoes chelation with calcium and casein of the milk [29]. The oral bioavailability of Azithromycin (commonly prescribed for the treatment of upper respiratory tract infection) is greatly reduced when taken with food [30]. The bivalent element present in food like calcium in case of milk markedly reduces the oral bioavailabiliy of drugs like tetracycline by the mechanism of chelation [31]. Ciprofloxacin inhibits the metabolism of caffeine, the former augments effects of caffeine. Luckily, the activity of other fluoroquinolones is not affected by simultaneous consumption of caffeine therefore they form the first choice for patients addicted or who frequently takes caffeine during the day.Many commonly used antibiotics like Erythromycin and Penicillin are destroyed by stomach secretions when taken with foods hence they are strictly prescribed to be taken in empty stomach to prevent therapeutic failures.Mineral supplements (like magnesium, calcium, zinc, iron, selenium, iodine) need to be taken at least 2 hours before or after antibiotics consumption, as they can bind to the drug and reduce its absorption of the drug [32].

Antihypertensive drugs

Consuming a high protein meal and taking propranolol concurrently can increase the bioavailability of the latter. When propanolol was given with protein-rich foods, a mean increase in bioavailability of 53% was reported[33].The concentration of serum potassium is remarably elevated by and excess of potassium often results in cardiac palpitation. Some foods like bananas, oranges, green leafy vegetables contain large amounts of potassium hence; patients should avoid eating these foods [34].

With regard to the salt, it is known that a high intake of common salt plays a fundamental role in the development and maintenance of HT [34, 35]. Nevertheless, the antihypertensive effect of felodipine (a calcium channel blocker with natriuretic properties) is maintained during high salt intake, at least when given at the maximal antihypertensive dose [36].

Smoking

Smoking while not a food *per se;* is discussed under this review as it does play a crucial role in the drug metabolism which is clinically significant. Cigarette smoking remains highly prevalent in most countries It is associated with interaction with both pharmacokinetic and pharmacodynamic of drugs. Tobacco smokes causes metabolic activation or induction of carcinogen leading to a greater chance of cancer (Procarcinogen to carcinogen). The noxious compound present is tobacco smoke is Polycyclic aromatic hydrocarbons (PAH) while is blamed to be responsible for the induction of cytochrome P450 (CYP) 1A1, CYP IA2 and possibly CYP2E1. There are genetic polymorphisms in the inducibility of CYP 1A1, with some evidence that high inducibility is more common in patients with lung cancer. The mechanism involved in most interactions between cigarette smoking and drugs involves the induction of Drug metabolism. Drug with clinical significance include theophylline, caffeine, tacrine, imipramine, haloperidol, pentazocine, propranolol, flecainide and estradiol. Also, cigarette smoking results in faster clearance of heparin, possibly related to smoking-related activation of thrombosis with enhanced heparin binding to antithrombin III. Delay absorption of insulin when given by subcutaneous route due to cuteneous vasoconstriction is a common phenomena associated with smokers. The effect of cigarette smoking has been found to lower the efficacy of beta blockers in controlling of blood pressure and heart rate, the sedation from benzodiazepines and also less analgesia from opoids. These could possibly due to stimulant action of nicotine in the CNS [37].

Conclusion

Food and drugs, both are necessary to maintain the health status of an individual. However it is to be kept in mind that

they sometimes also bring side effects and risks when used at same time. Thus, the interactions between food and drug need to be well known and identified. The effect of food on drugs results in a reduction in the drug's bioavailability and alteration in drug clearance. On the other hand, Drugs can influence food intake, digestion, absorption and excretions. The interaction undoubtly may result in serious life threatening consequences hence pharmacists should be well aware of the necessity of monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications.

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