



An Overview on Drug-Food Interactions

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ABSTRACT

Drug-Food interactions refers to modifications in the pharmacokinetics or pharmacodynamics of a drug or nutritional component, as well as a reduction in nutritional status as a result of the addition of a drug. Food-drug interactions should be avoided since they may have a detrimental impact on the patient's nutritional state as well as the safety and effectiveness of pharmacological therapy. This review provides information regarding the numerous interactions between various foods and medications, which will assist doctors and pharmacists in wisely prescribing medications with only appropriate food supplements to provide patients with the greatest benefit attainable.

Keywords: Drug-Food interactions, nutritional status, food supplements.

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INTRODUCTION

Nowadays, the term "drug-food interactions" refers to modifications in the pharmacokinetics or pharmacodynamics of a drug or nutritional component, as well as a reduction in nutritional status as a result of the addition of a drug.¹ In other words, the rate of drug absorption and metabolism can be influenced by the presence or absence of certain nutrients in the gastrointestinal tract and/or in the body's physiological systems, such as the blood. Both prescription and over-the-counter medications, such as antacids, vitamins, and iron supplements, can have undesirable drug-food interactions.²

A frequent and unrecognised issue in clinical practise is the interaction between food and drugs, which can result in prolonged hospital stays or readmissions, prescription cascades, and deterioration of the patient's health.³ This review provides information regarding the numerous interactions between various foods and medications, which will assist doctors and pharmacists in wisely prescribing medications with only appropriate food supplements to provide patients with the greatest benefit attainable.

Mechanisms of Food Drug Interactions

Pharmacokinetic interaction

Interaction involving Absorption

Food consumption and drug administration can have a big influence on how well drugs dissolve and are absorbed. Food offers components for drug and nutrient chelation and adsorption, modifies gut pH, and affects gastric motility. Without affecting the drug's total bioavailability, a slower absorption rate allows for more nutritional interactions and potential delays in therapeutic effectiveness. When eaten right after a meal, water-insoluble medications (such as the prescription medications spironolactone and griseofulvin) are more readily absorbed. Many medications take longer to be absorbed after a meal heavy in carbohydrates, and supplements for vitamins A, E, D, and K are more readily absorbed after a meal high in fat. Chelation is the process by which certain dietary elements, particularly divalent or trivalent cations (such as Ca, Mg, Al, Fe, and Zn), and specific medications form a complex.⁴

Interaction involving metabolism

By inducing or inhibiting the mixed-function oxidase system, dietary components of food may change how certain medicines are metabolised in the liver. Diets high in protein and low in carbohydrates stimulate the mixed-function oxidase system and speed up the metabolism of medicines that act as its substrates. Indoles, which are present in cruciferous vegetables like cabbage and Brussels sprouts, also dramatically increase the chemical oxidation of pharmaceuticals. Drug hepatic metabolism may be inhibited by bioflavonoids and other naturally occurring compounds in fruits and vegetables. The parent drug's blood levels are often increased, the therapeutic impact is extended, and the frequency of side effects is generally



enhanced when the mixed-function oxidase system is inhibited.⁴

Interaction involving excretion

Some medications' renal excretion may be affected by food and nutrition. Changes in urine pH can have a major impact on the half-lives of several drugs. Meats, fish, cheese, and eggs can acidify the urine, whereas milk, vegetables, and citrus fruits can alkalize it. Antihistamines, ascorbic acid, and nicotine are examples of drugs that are eliminated in acidic urine but reabsorbed in alkaline urine.⁴

Pharmacodynamic interactions

High vitamin K content foods such as green leafy vegetables (e.g., spinach, broccoli, turnips, etc.) compete with the anticoagulant medication warfarin. Contrarily, coffee in the diet significantly increases the bioavailability and blood levels of theophylline. Alcoholic beverages boost the sedative effects of benzodiazepines, antihistamines, antipsychotics, narcotics, and other drugs that depress the central nervous system.²

In this overview, interactions between a few of the most widely used drugs are described.

Fruit juices

Grape juice has the highest level of medication interaction out of all the fruit juices. The juice alters the cytochrome oxidase system functioning, which changes how the body metabolises the medicine. The grapefruit isoenzymes 1A2 and 3A4 are thought to be inhibited by grapefruit juice and whole grapefruit. Large doses of grapefruit juice (32 ounces or more per day) can block the CYP3A4 enzyme and raise blood levels of medications metabolised by this route, such as certain statin medications. According to *in vitro* research, substances in grapefruit juice may be able to suppress P-gp activity, changing how medications like talinolol that are P-gp substrates are disposed of. Patients are also advised not to consume grape juice within 1-2 hours of taking these anticonvulsants.^{5,6} The active bioflavonoids and furanocoumarins in GFJ are OATP inhibitors as well, and when taken together, they can lessen the oral bioavailability of the OATP substrate, fexofenadine.⁷ When using anticoagulants, stay away from cranberry products like juice since they can alter warfarin's effects.⁸

Food

Food in the digestive system might hinder a drug's ability to be absorbed. Frequently, one hour before or two hours after ingesting the medicine will prevent such interactions. High-fiber diets may affect a person's ability to absorb the medication. Acetaminophen absorption is slowed down by soluble fibres like pectin. Digoxin, a medication used to treat heart failure, is affected similarly by bran and other insoluble fibres. Therefore, it is advisable to take digoxin at least two hours before or after eating fiber-rich meals or snacks. Levothyroxine, a medication used to treat an underactive thyroid gland, may be less effective when

taken with soybean flour, walnuts, and other high-fiber foods. The anticoagulant warfarin and foods containing vitamin K, such as broccoli, cabbage, spinach, seaweed, and other leafy greens, are among the most well-known food-drug interactions. A significant quantity of K is also present in several vegetable oils. These foods can work against the effects of heparin, warfarin, and other clotting-prevention medications by promoting the development of blood clots.^{2,9} Garlic, ginger, glucosamine, ginseng, and ginkgo must be avoided since they might make bleeding more likely.⁸

Antihypertensive drugs

Antihypertensive drug bioavailability may be impacted by food. Therefore, in some situations, this should be carefully evaluated. The food with the highest potential for interactions and harm when taken with several antihypertensive and antiarrhythmic medications is grapefruit juice.¹²⁴ The bioavailability of felodipine is increased by GFJ (a Ca² channel blocker). It also should be noted that the bitter Sevilla orange juice interacts with felodipine in a manner similar to grapefruit juice. When administering antihypertensive medications, it is important to consider other juices, such as orange juice. Celiprolol's (beta-blocker) absorption is slowed down by the hesperidin found in orange juice.^{8,10}

Hypertension (HT) and hypercholesterolemia have been proven to be improved by moderate salt restriction diets. However, felodipine, a calcium channel blocker with natriuretic effects, continues to have its antihypertensive effect even when salt intake is substantial, at least when taken at the maximum antihypertensive dose. Nisoldipine coat-core should be administered 30 minutes before the consumption of food in order to prevent a rise in plasma concentration when combined with high-fat, high-calorie foods. Propranolol serum levels may rise if taken with a high-protein meal. Changing from a high-carbohydrate, low-protein diet to one that is low-carb, high-protein may result in enhanced oral clearance.^{11,12,13,14}

ACE inhibitors such as captopril and moexipril are advised to be taken at least an hour before meals. When ACE inhibitors or diuretics (Triamterene) are combined with potassium-rich meals, the serum potassium concentration rises dramatically, and an excess of potassium frequently causes cardiac palpitation. As a result, patients should avoid eating potassium-rich foods such as bananas, oranges, and green leafy vegetables.¹¹

Antibiotics

In the entire world, prescriptions for antibiotics are among the most popular. Similar to other medications, antibiotics also have food-drug interactions. Mineral supplements, such as those containing magnesium, calcium, zinc, iron, selenium, and iodine, should be taken at least two hours before or after taking antibiotics since they can bind to the medication and lessen its absorption.¹⁵ Due to the chelation of milk's casein and calcium, ciprofloxacin absorption is reduced. Tetracyclines shouldn't be used



with milk since it binds calcium and iron, altering the drug's bioavailability. It should be given an hour before or two hours after meals. The bioavailability of azithromycin is reduced by 43% when taken with food.¹⁶ In order to avoid therapeutic failures, it is highly advised to take many frequently used antibiotics like erythromycin and penicillin on an empty stomach because they are destroyed by stomach secretions when taken with food. Caffeine metabolism is inhibited by ciprofloxacin, which enhances the effects of caffeine. Fortunately, concurrent caffeine use has no effect on the activity of other fluoroquinolones, making them the first choice for patients who are dependent on or frequently drink caffeine throughout the day.¹⁵

MAOIs

Antidepressant medications known as monoamine oxidase inhibitors suppress the activity of monoamine oxidase enzymes. The most common MAOI toxicity results from interaction with tyramine-rich foods, an amino acid that has the potential to result in hypertensive crisis, cardiac arrhythmias, hyperthermia, cerebral hemorrhage, and eventually stroke. Tyramine-rich foods include aged cheeses, fermented meats, aged meats and poultry, red wine, some draught beers, soy products, and extremely ripe bananas. Despite their effectiveness in treating depressive disorders, MAOIs should be taken with extreme caution due to their interactions with foods that contain tyramine and their propensity to trigger hypertensive crisis in MAOI-treated individuals.^{9,17}

Antihistamines

Antihistamines are used to treat or relieve symptoms of colds and allergies, such as sneezing, a runny nose, stuffy nose, and itchy eyes. They inhibit the histamine your body releases in response to an allergen that triggers allergic symptoms.⁸ Fexofenadine, loratadine, rupatadine, cimetidine, and cetirizine are some of the antihistamines available. It is preferable to take antihistamines on an empty stomach to maximise their effectiveness. Rupatadine is frequently used in the treatment of allergic inflammatory disorders. According to a study, rupatadine's bioavailability is significantly increased when food is consumed concurrently with a single oral administration of 20 mg of the medication. To aid in the maintenance of a therapeutic blood concentration, cimetidine is administered with food. When taken with food, some cimetidine is partially absorbed, leaving the remaining medication to dissolve when the gut has cleared. As a result, therapeutic levels are maintained throughout the dosing interval.^{18,19}

Antimycobacterials

Antimycobacterials are drugs used to treat infections caused by mycobacteria, a class of bacterium that causes TB and other kinds of infections. Ethambutol, isoniazid, rifampin, rifampin + isoniazid, rifampin + isoniazid + pyrazinamide are some of the examples. Ethambutol may be administered with or without food. Take the remaining

medications one hour before or two hours after meals, with a full glass of water. If you take isoniazid alone or in combination with other antimycobacterials, avoid foods and beverages containing tyramine or histamine. High tyramine levels (from foods that are spoiled or not refrigerated, handled, or stored properly, and aged, pickled, fermented, or smoked foods) can cause an unexpected and dangerous rise in blood pressure. Histamine-containing foods such as tuna, tropical fish, Caffeine can cause headaches, sweating, palpitations (rapid heartbeats), flushing, and hypotension (low blood pressure).⁸ In contrast, oleanolic acid, a triterpenoid found in numerous foods, herbs, and other plants, exhibits antimycobacterial activity against Mycobacterium TB and exerts a synergistic effect when combined with isoniazid.²⁰ High-fat meals significantly lower the serum concentration of cycloserine, a bacteriostatic anti-tubercular medication, which leads to incomplete eradication of bacteria.²¹

Antidiabetics

Glimepiride is an antidiabetic that should be taken with breakfast or the first main meal of the day. As a result of its complete bioavailability and the lack of food interactions, it shows extremely reproducible pharmacokinetics. Glipizide is available in the form of immediate and extended-release tablets. The immediate-release tablet is usually taken 30 minutes before food, whereas the extended-release tablets should be taken with breakfast. Alpha-glucosidase inhibitors, such as acarbose, delay the absorption of carbohydrates by inhibiting the enzyme alpha-glucosidase. Hence, the medication is most effective when given just at the beginning of each meal rather than 30 minutes before or after the meal. Bitter melon consumption in diabetic patients who are on hypoglycemic medications (primarily Phenformin and chlorpropamide) or insulin should be avoided or used with caution as it may increase the drugs' effectiveness and increase the risk of severe hypoglycemia.^{22,23} When garlic is combined with chlorpropamide, it causes hypoglycemia.²⁴

Bronchodilators

Bronchodilators are used to treat and prevent breathing problems from bronchial asthma, chronic bronchitis, emphysema, and chronic obstructive pulmonary disease (COPD). Theophylline, albuterol, and epinephrine are examples of bronchodilators that have various effects when taken with food. Food can have varying effects on various forms of theophylline (some forms are regular release, sustained release, and sprinkles). Food's effect on theophylline can vary depending on its nutritional content. The bioavailability of theophylline is increased by a high-fat diet (food), whereas it is decreased by a high-carbohydrate diet. Avoid drinking alcohol while taking theophylline because it increases the risk of side effects such as nausea, vomiting, headaches, and irritability. The bioavailability of theophylline is increased by a high-fat diet (food), whereas it is decreased by a high-carbohydrate diet. Avoid drinking alcohol while taking theophylline



because it increases the risk of side effects such as nausea, vomiting, headaches, and irritability. Patients may be advised not to drink GFJ while taking theophylline because it enhances the bioavailability, and monitoring plasma theophylline levels in GFJ-consuming patients may aid in better patient care management. When bronchodilators are combined with caffeine-containing foods and beverages (e.g., coffee, tea, chocolate), it increases the risk of side effects such as excitability, nervousness, and rapid heartbeat.^{8,25}

Antitumour drugs

When dietary supplements and cancer medications are used together, there is always a chance that the supplement will affect the pharmacokinetics or

pharmacodynamics of the medication. A purine analogue known as mercaptopurine is used to treat chronic myelogenous leukaemia and acute lymphoblastic leukaemia. Concurrent consumption of substances containing xanthine oxidase (XO) may potentially lower the bioavailability of mercaptopurine since it is inactivated by XO. Therefore, the majority of patients should attempt to space out when they take mercaptopurine and consume cow's milk (which contains a high level of XO).²⁶ Tamoxifen is an antitumour drug when taken with sesame seeds, it negatively affects the ability of tamoxifen to induce regression of established MCF-7 tumour growth.²⁷ Here, Table 1 shows some of the other food interactions with antitumour drugs.

Table 1: Food interactions with antitumour drugs²⁸

Dietary Supplement	Anticancer Therapy	Effect
Green tea	Sunitinib	Decreased drug absorption and bioavailability of sunitinib , Decreased anticancer effect, worsened symptoms
Green tea	Palbociclib	Decreased oral bioavailability of palbociclib
Green tea extract	Erlotinib	Decreased AUC and oral bioavailability of erlotinib
Green tea extract	Lapatinib	Decreased AUC and oral bioavailability of lapatinib
EGCG	Tamoxifen	Increased bioavailability of tamoxifen
EGCG	Irinotecan	Increased plasma concentration of irinotecan and decreased hepatobiliary excretion of drug and its metabolite SN-38
Green tea and EGCG	Fluorouracil	Increased AUC and C _{max} of fluorouracil
Grapefruit	Imatinib	May increase plasma levels of imatinib by inhibiting CYP3A4
Grapefruit	Etoposide	Decreased AUC and bioavailability of etoposide
Grapefruit	Sunitinib	Increased bioavailability of sunitinib
Grapefruit	Nilotinib	Increased AUC and C _{max} of nilotinib
Vitamin A	Imatinib	Increased bioavailability of imatinib
Vitamin E	Imatinib	Increased bioavailability of imatinib
Vitamin D3	Imatinib	Increased bioavailability of imatinib
Vitamin C	Imatinib	Decreased bioavailability of imatinib

CONCLUSION

Every year, a significant number of new medications are released. Food-drug interactions can have a detrimental impact on the patient's nutritional state as well as the safety and effectiveness of pharmacological therapy. Drug interactions should generally be avoided since they might have negative or unexpected effects. Certain diets have a significant impact on medication therapy and can cause harmful side effects, toxicity, or therapeutic failure. By

improving therapeutic efficacy or reducing potential negative effects, the interaction may occasionally have a positive impact. Without a doubt, the combination might have catastrophic, potentially fatal effects. Consequently, pharmacists must educate patients about foods and drinks to avoid while taking specific drugs and monitor for any possible drug-food interactions.



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