

Review Article

DRUG-FOOD INTERACTIONS AND ROLE OF PHARMACIST

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ABSTRACT

Interaction between foods and drugs can have profound influence on the success of drug treatment and on the side effect profiles of many drugs. The clinical significance of drug-food interactions can be variable. Drug-food interactions can lead to a loss of therapeutic efficacy or toxic effects of drug therapy. Generally, the effect of food on drugs results in a reduction in the drug's bioavailability; however, food can also alter drug clearance. Some foods greatly affect drug therapy, resulting in serious side effects, toxicity, or therapeutic failure. In some instances, the interaction may have a beneficial effect by increasing drug efficacy or diminishing potential side effects. Pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up-to-date on potential drug-food interactions of medications, especially today's new drugs, so that they may counsel properly to the patients.

KEYWORDS Drug-food interactions

INTRODUCTION

Many people have the mistaken notion that being natural, all herbs and foods are safe. This is not so. Very often, herbs and foods may interact with medications normally taken that result in serious side reactions. Experts suggest that natural does not mean it is completely safe. The medication that is taken by mouth travels through the digestive system in the same way as food and herbs taken orally do. When drugs and certain foods are taken at the same time, they can interact in such a way that decrease the effectiveness of the ingested drug or reduce the absorption of food nutrients. Additionally, vitamin and herbal supplements taken with prescribed medication can result in adverse reactions. A drug-food interaction happens when the food affects the ingredients in a medicine which the patient is taking affecting the efficacy of medicine being administered. High-risk patients, such as the elderly patients taking three or more medications for chronic conditions, patients suffering from diabetes, hypertension, depression, high cholesterol or congestive heart failure

should be especially monitored for such drug-food interactions.¹

DRUG-FOOD INTERACTIONS

The relationships and interactions between foods, the nutrients they contain and drugs are gaining recognition in the health care and medical fields. Certain foods and specific nutrients in foods, if ingested concurrently with some drugs, may affect the overall bioavailability, pharmacokinetics, pharmacodynamics and therapeutic efficacy of the medications. Furthermore, the therapeutic efficacy of many drugs depends on the nutritional status of the individual. In other words, the presence or absence of some nutrients in the gastrointestinal tract and/or in the body's physiological system, such as in the blood, can enhance or impair the rate of drug absorption and metabolism. Drug-food interactions can happen with both prescription and over-the-counter medicines, including antacids, vitamins and iron pills. Foods containing active substances that interact against certain medications can produce unexpected or adverse effects. Pharmacist can give the

information of such interactions to the patients.² Nutrients include food, beverages and dietary supplements. Consumption of these substances may alter the effects of drugs the patient takes. For example:

Food: Like food, drugs taken by mouth must be absorbed through the lining of the stomach or the small intestine. Consequently, the presence of food in the digestive tract may reduce absorption of a drug. Often, such interactions can be avoided by taking the drug one hour before or two hours after eating. Dietary fiber also affects drug absorption. Pectin and other soluble fibers slow down the absorption of acetaminophen, a popular painkiller. Bran and other insoluble fibers have a similar effect on digoxin, a major heart medication. Certain vitamins and minerals impact on medications too. Large amounts of broccoli, spinach and other green leafy vegetables high in vitamin K, which promotes the formation of blood clots, can counteract the effects of heparin, warfarin and other drugs given to prevent clotting.³

Dietary Supplements: Dietary supplements, including medicinal herbs are products that contain a vitamin, mineral, herb or amino acid and that are intended as a supplement to the normal diet. Supplements are regulated as foods not as drugs so they are not tested as comprehensively. However, they may interact with prescription or over-the-counter drugs. People who take dietary supplements should inform their doctors and pharmacists so that interactions can be avoided. Some dietary components increase the risk of side effects. Theophylline, a medication administered to treat asthma contains xanthines, which are also found in tea, coffee, chocolate and other sources of caffeine. Consuming large amounts of these substances while taking

theophylline, increases the risk of drug toxicity.²

Alcohol: Alcohol affects body processes and interacts with many drugs. Alcohol is a drug that interacts with almost every medication, especially antidepressants and other drugs that affect the brain and nervous system. For example, taking alcohol with metronidazole can cause flushing, headache, palpitations, nausea and vomiting.⁴ Foods containing active substances that interact against certain medications can produce unexpected or adverse effects. Pharmacist can give the information of such interactions to the patients.²

Factors Affecting the Extent of Interaction between Foods and Drugs

The impact of drug-food interactions depend on a variety of intervening factors like dosage of the drug, person's age, size and state of health. Apart from these, the time foods and the medications are taken also play an important role. Avoidance of drug interactions does not necessarily mean avoiding drugs or foods. In the case of tetracycline and dairy products, these should simply be taken at different times; rather than eliminating one or the other from the diet. Sufficient information about the medications and timing of medications around food intake can help to avoid drug interaction problems.^{2,4}

Effect of Drug-Food Interactions

Not all medicines are affected by food, but many medicines can be affected by the food and it's time. For example, taking some medicines at the same time with food may affect the absorption of the medicine. The food may delay or decrease the absorption of the drug. This is why some medicines should be taken on an empty stomach. On the other hand, some medicines are easier to tolerate when taken with food. It is always advised to ask

the doctor or pharmacist whether it's correct to take the medicine with a snack or a meal or whether it should be taken on an empty stomach.⁵

Table 1: Some examples of drug-food interactions that accelerate the absorption of drugs ^(5, 15-17)

Drug	Mechanism	Counseling
Carbamazepine	Increased bile production, enhanced dissolution and absorption.	
Dicumerol	Increased bile flow, delayed gastric emptying permits dissolution and absorption.	Take with food.
Erythromycin	Unknown.	
Griseofulvin	Drug is lipid soluble, enhanced absorption with high- fat foods.	Take with high- fat foods.
Hydralazine, Labetalol and Metoprolol	Food may reduce first-pass extraction and metabolism.	
Nitrofurantoin, Phenytoin and Propoxyphene	Delayed gastric emptying improves dissolution and absorption.	
Propranolol	Food may reduce first-pass extraction and metabolism.	Take with food
Spirolactone	Delayed gastric emptying permits dissolution and absorption, bile may solubilize the drug.	

MECHANISMS OF DRUG-FOOD INTERACTIONS

Pharmacokinetic Interactions

Drug Absorption Interactions

Food may affect drug absorption in the GI tract by altering gastric pH, secretion, gastrointestinal motility and transit time. This may result in a change in the rate of

absorption or extent of drug absorption or both. For example, azithromycin absorption is decreased when it is taken with food, resulting in a 43% reduction in bioavailability. Sustained-release 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. Children are more prone to this interaction than adults.

Table 2: Some examples of drug-food interactions that delay the absorption of drugs

Drug	Mechanism	Counseling
Acetaminophen	High pectin foods act as adsorbant and protectant.	Take on empty stomach if not contraindicated.
Digoxin	High-fiber, high-pectin foods bind drug.	Take drug same time with relation to food, Avoid taking with high-fiber foods.
Glipizide	Mechanism unknown.	Affects blood glucose; more potent when taken half hour before meals.
Isoniazide	Food raises gastric pH preventing dissolution and absorption.	Take on empty stomach if tolerated.
Levodopa	Drug competes with amino acids for absorption transport.	Avoid taking drug with high-protein foods.
Methyldopa	Competitive absorption.	Avoid taking with high- protein foods.
Nafcillin	Mechanism unknown.	Take on empty stomach.
Penicillamine	May form chelate with calcium or iron.	Avoid taking with dairy products or iron-rich foods or supplements.
Quinidine	Possibly protein binding.	May take with food to prevent gastrointestinal upset
Sulfonamides	Mechanism unknown.	Taking with meals may prolong gastric emptying.
Tetracyclines	Binds with calcium ions or iron salts forming insoluble chelates.	Take one hr before or two hr after meals; do not take with milk.

Table 3: Examples of specific counseling on some drug-food interaction (5, 15-17)

Drugs	Effects and Precautions
Antibiotics	
Cephalosporins, penicillin	Take on an empty stomach to speed absorption of the drugs.
Erythromycin	Don't take with fruit juice or wine, which decrease the drug's effectiveness.
Sulfa drugs	Increase the risk of Vitamin B ₁₂ deficiency
Tetracycline	Dairy products reduce the drug's effectiveness. Lowers Vitamin C absorption
Anticonvulsants	
Dilantin, phenobarbital	Increase the risk of anemia and nerve problems due to deficiency of folate and other B vitamins.
Antidepressants	
Fluoxetine	Reduce appetite and can lead to excessive weight loss
Lithium	A low-salt diet increases the risk of lithium toxicity; excessive salt reduces the drug's efficacy
MAO Inhibitors	Foods high in tyramine (aged cheese, processed meats, legumes, wine and beer among others) can produce a hypertensive crisis.
Tricyclics	Many foods, especially legumes, meat, fish and foods high in Vitamin C, reduce absorption of the drugs.
Antihypertensives, Heart Medications	
ACE inhibitors	Take on an empty stomach to improve the absorption of the drugs.
Alpha blockers	Take with liquid or food to avoid excessive drop in blood pressure.
Antiarrhythmic drugs	Avoid caffeine, which increases the risk of irregular heartbeat.
Beta blockers	Take on an empty stomach; food, especially meat, increases the drug's effects and can cause dizziness and low blood pressure.
Digitalis	Avoid taking with milk and high fiber foods, which reduce absorption, increases potassium loss.
Diuretics	Increase the risk of potassium deficiency.
Potassium sparing diuretics	Unless a doctor advises otherwise, don't take diuretics with potassium supplements or salt substitutes, which can cause potassium overload.
Asthma Drugs	
Pseudoephedrine	Avoid caffeine, which increase feelings of anxiety and nervousness.
Theophylline	High protein diet reduces absorption. Caffeine increases the risk of drug toxicity.
Cholesterol Lowering Drugs	
Cholestyramine	Increases the excretion of folate and fat soluble vitamins.
Gemfibrozil	Avoid fatty foods, which decrease the drug's efficacy in lowering cholesterol.
Heartburn and Ulcer Medications	
Antacids	Interfere with the absorption of many minerals; for maximum benefit, take medication one hour after eating.

Cimetidine, Famotidine, Sucralfate	Avoid high protein foods, caffeine and other items that increase stomach acidity.
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Hormone Preparations

Oral contraceptives	Salty foods increase fluid retention. Drugs reduce the absorption of folate, vitamin B ₆ and other nutrients; increase intake of foods high in these nutrients to avoid deficiencies.
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Steroids	Salty foods increase fluid retention. Increase intake of foods high in calcium, vitamin K, potassium and protein to avoid deficiencies.
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Thyroid drugs	Iodine-rich foods lower the drug's efficacy.
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Laxatives

Mineral Oils	Overuse can cause a deficiency of vitamins A, D, E, and K.
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Painkillers

Aspirin and stronger nonsteroidal anti-inflammatory drugs	Always take with food to lower the risk of gastrointestinal irritation; avoid taking with alcohol, which increases the risk of bleeding. Frequent use of these drugs lowers the absorption of folate and vitamin C.
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Codeine	Increase fiber and water intake to avoid constipation.
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Sleeping Pills, Tranquilizers

Benzodiazepines	Never take with alcohol. Caffeine increases anxiety and reduce drug's effectiveness.
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In other cases, 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. The absorption of alendronate is impaired by food, calcium and almost everything, including orange juice and coffee. It should be taken with plain water and nothing else should be consumed for at least 30 minutes. In many cases, the actual mechanism by which food interferes with absorption is not known. Delayed absorption does not necessarily reduce the total overall exposure to the drug; the area under the curve (AUC) may be equivalent regardless of how the drug is taken. A reduced rate of absorption may sometimes be useful in reducing the side effects of a drug, as in the cases of ibuprofen, without reducing bioavailability. The bioavailability of some drugs may be enhanced by food. For example, an acid environment is necessary for the absorption of ketoconazole. The absorption of griseofulvin is increased by

fat in a meal. Fenofibrate, mebendazole, isotretinoin, tamsulosin, carbamazepine and labetalol are examples of drugs that will be better absorbed when taken with food. Improved absorption of a drug may or may not have a significant effect on the drug's efficacy.⁶ Patients taking digoxin should avoid taking bran fiber, pectin-containing foods such as apples or pears, or fiber-containing, bulk-forming laxatives at the same time, since these agents may bind to the digoxin, decreasing its absorption. This interaction could result in decreased serum concentrations of digoxin and therapeutic effectiveness. It is advisable to take some medications with food to reduce gastrointestinal irritation and possible nausea. Examples of these medications include potassium supplements, ferrous sulfate, nonsteroidal anti-inflammatory drugs, estrogen, prednisone, tacrine, terfenadine and nitrofurantoin. Cholesterol-lowering agent lovastatin should be taken with food to enhance gastrointestinal absorption and bioavailability. Simvastatin, pravastatin

and fluvastatin may be taken without regard to food.^{2, 4} Examples of some drug-food interactions which accelerate and delay the absorption of drugs are shown in table 1 and table 2 respectively with the brief counseling.

Drug Metabolism Interactions

Food may alter the hepatic metabolism of some drugs. It has been reported that when administered with the antihypertensive drug felodipine, concentrated grapefruit juice caused an increase in the bioavailability of felodipine. The mean felodipine bioavailability with grapefruit juice was 284% (range 164%–469%) that of water. This resulted in lower diastolic blood pressures and increased heart rate in the male study volunteers. Adverse effects such as headaches, facial flushing and lightheadedness were more common after ingestion of 250 ml grapefruit juice (125 ml frozen grapefruit concentrate plus 125 ml of water). The bioavailability of nifedipine with grapefruit juice was 134% (range 108%–169%) of that with water. Orange juice did not have these effects. 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 calcium channel blockers. There is potential clinical significance because citrus juices are frequently consumed at breakfast, when many medications are also taken. Patients should be advised of this possible interaction.^{7, 8} First-pass hepatic metabolism of propranolol and metoprolol may be decreased when either medication is taken with food, thereby enhancing bioavailability. Drug levels and therapeutic efficacy may be increased due to this interaction. Monoamine oxidase (MAO) inhibitors are known to interact with foods containing tyramine. Tyramine is normally inactivated by the enzyme monoamine

oxidase and this prevents tyramine from accumulating in the body. Monoamine oxidase inhibitors cause increased levels of tyramine which can lead to a hypertensive crisis. Patients taking monoamine oxidase inhibitors should avoid foods high in tyramine such as aged cheeses, pickled fish, yeast extracts, red wine, some types of beer (including nonalcoholic beer), fava beans and fermented products. High-protein foods that have been aged, fermented, pickled, smoked or bacterially contaminated are unsafe for patients taking MAO inhibitors. Foods considered safe when used fresh and in moderation include sour cream, yogurt, meat extracts, chopped liver, dry sausage and alcoholic beverages.⁹⁻¹²

Drug Excretion Interactions

Foods may alter the urinary pH, which can affect the activity of certain drugs. The half-lives of some medications can be significantly changed by alterations in urinary pH. Therefore, the half-life of acidic drugs will be extended in acidic urine because the drug is in its unionized form. However, the half-life of an acidic drug in alkaline urine is reduced because the drug is in its ionized form. Foods such as milk, vegetables and citrus fruits can alkalinize the urine. Meats, fish, cheese and eggs can acidify the urine. Foods may alter the renal excretion of some medications. 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 an increase in serum lithium levels.⁶

Pharmacodynamic Interactions

Foods may interact with medications by altering their pharmacologic actions. Diets high in vitamin K may cause antagonism of warfarin and decreased therapeutic efficacy of the anticoagulant. Foods rich in vitamin K include green leafy vegetables

(kale, turnip greens, spinach, broccoli and brussels sprouts), cauliflower, chick peas, green tea, pork liver and beef liver. Alcoholic beverages may increase the central nervous system depressant effects of medications such as benzodiazepines, antihistamines, antidepressants, antipsychotic, muscle relaxants, narcotics or any drug with sedative actions.³ An example of a food potentiating the effect of a medication is coffee, as caffeine has additive effects on theophylline. It has been reported that caffeine increased serum theophylline levels by 20%–30% and increased the half-life of theophylline by decreasing clearance. Patients may complain of nervousness, tremor or insomnia. Caffeine has some bronchodilatory effects, which may enhance the effects of theophylline. A lower dosage of theophylline may be necessary for those patients who consume excessive quantities of coffee (more than 6 cups daily).

ROLE OF PHARMACIST IN PREVENTION OF DRUG-FOOD INTERACTIONS

Pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up-to-date on potential drug-food interactions of medications, especially today's new drugs, so that they may counsel properly. In providing drug information to patients, pharmacists often discuss potential side effects and how the medication should be taken. It is important to provide information to patients on when to take their medications in relation to food intake. Consequences of drug-food interactions may include delayed, decreased or enhanced absorption of the drug. Food may also affect the bioavailability, metabolism and excretion of certain medications. The patient may experience

an adverse side effect or toxicity or may not receive the full therapeutic benefit of the medication. The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) requires that a patient's medication profile include potential drug-food interactions, that the pharmacist call the prescriber whenever the potential for a medication-food interaction exists and document the communication and follow-up action on the prescription or order form, and that patients be given instructions and counseling regarding the potential for drug-food interactions before their hospital discharge. Elderly patients may be at a greater risk for drug-food interactions because they typically consume more medications for their chronic medical conditions. A study of drug-nutrient interactions in long-term care facilities found a significant relationship between the number of medications a resident consumed and the number of drug-nutrient interactions for which a resident was at risk.¹³

Counseling and Guidance about Drug-Food Interactions

The following information can be given to the patients while dispensing the medicine.¹³⁻¹⁴

- Read the prescription label on the container. If you do not understand something or think you need more information, ask your physician or pharmacist.
- Read directions, warnings and interaction precautions printed on all medication labels and package inserts. Even over-the-counter medications can cause problems.
- Take medication with a full glass of water.

- Do not stir medication into your food or take capsules apart (unless directed by your physician). This may affect the efficacy of medication.
- Do not take vitamin pills at the same time you take medication. Vitamins and minerals can interact with some drugs.
- Do not mix medication into hot drinks because the heat from the drink may destroy the effectiveness of the drug.
- Never take medication with alcoholic drinks.
- Be sure to tell your physician and pharmacist about all medications you are taking, both prescription and non-prescription.
- Check with the pharmacist on how food can affect specific medications taken with the food.

Examples of specific counseling on some drug-food interaction are summarized in TABLE 3.

Precautions to be taken

- Medications need to be taken at different times relative to meals.
- Consult a physician when health problems persist.
- During pregnancy and nursing always consult a physician or pharmacist before taking any medication. Drugs taken by the mother may affect the infant.
- Check with a doctor or pharmacist for the proper way and time to take medication.

CONCLUSION

Interaction between foods and drugs can have profound influence on the success of drug treatment and on the side effect profiles of many drugs. The clinical significance of drug-food interactions can be variable. Some foods greatly affect drug therapy, resulting in serious side effects, toxicity or therapeutic failure. In some instances, the interaction may have a beneficial effect by increasing drug efficacy or diminishing potential side effects.

The interactions are not always detrimental to therapy, but can in some cases be used to improve drug absorption or to minimize adverse effects. These interactions have received more attention recently, especially drug interactions with grapefruit juice. As new drug approvals occur with ever increasing speed, there is less information available about their adverse effects and interactions when the drugs reach the market. Pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up-to-date on potential drug-food interactions of medications, especially today's new drugs, so that they may counsel properly to the patients.

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