IASR J. Med. Pharm. Sci.
ISSN: 2582-9343
Website: https://ijmps.com/
Open Access Journal
Country: India

IASR Journal of
Medical and Pharmaceutical
Science

ORIGINAL ARTICLE OPEN ACCESS

Commonly prescribed medications experience altered pharmacokinetics due to food-drug interactions

Supriya Gupta[1*], Vishal Rai[2], Shekhar Singh[3]

[1,2,3]Suyash Institute of Pharmacy, Hakkabad, Gorakhpur, Uttar Pradesh, India

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Corresponding Author
Supriya Gupta
Suyash Institute of Pharmacy, Hakkabad, Gorakhpur, Uttar Pradesh, India.

Received: 15-09-2024
Accepted: 24-10-2024
Available online: 25-11-2024

ABSTRACT

The pharmacokinetic process namely absorption, distribution, metabolism, and excretion of the drug may be affected due to the food-drug interaction. It's important to study because at smaller or wider levels the lack of knowledge of food-drug interaction affects the pharmacokinetics and pharmacodynamics which gives rise to potential adverse effects or altered therapeutic outcomes. To avoid this type of complication healthcare professionals need to provide basic food-drug interaction knowledge about prescribed drugs to the patient to minimize the risk and improve the drug effects for faster recovery. To increase patient safety it's necessary to highlight the commonly prescribed drugs (such as Amoxicillin, Omeprazole, Cephalexin, Atorvastatin, Vitamin D) and food-drug interaction. This review provides information about various commonly prescribed food-drug interactions and it will help healthcare professionals in prescribing drugs cautiously with an appropriate diet to avoid complications.

Key Words: *Food-drug interaction, pharmacokinetic, safety , complications.*

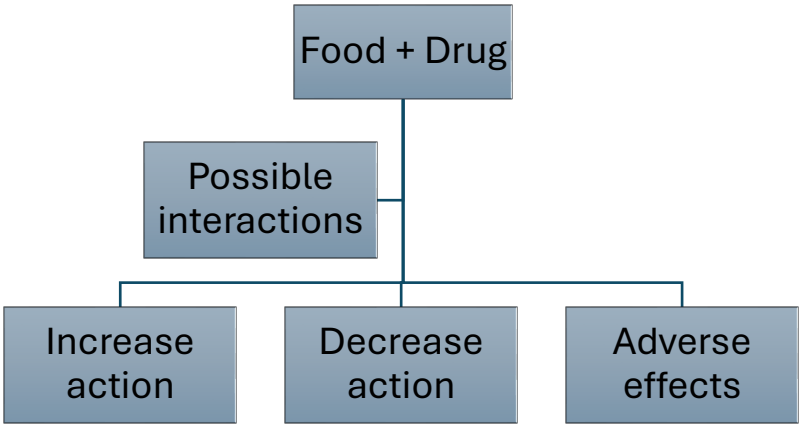
Introduction

For the body to maintain its physiological processes, it needs a constant supply of various foods containing essential vitamins, minerals, proteins, fats, and sugars. However, people undergoing therapy, especially those on chronic polytherapy, may experience changes in their situation. Several studies have confirmed that the interaction between medication and food can pose a potential risk for therapy failure. Medications can interact with different mechanisms present in certain foods. A substance affects the activity of a drug, causing a drug interaction resulting in increased, decreased, or new effects that neither substance produces on its own. Individuals may accidentally interact with these substances due to misuse or a lack of knowledge about their active ingredients.(1)

Patients often ask healthcare providers whether they should take medication with food, fluids, juices, or milk after a doctor prescribes medication or they are considering over-the-counter drugs, herbal products, dietary supplements, etc. Answering these questions can be challenging due to a lack of available information about food-drug interactions. A growing number of pharmacists, physicians, and other researchers in the medical field now recognize the impact of the food a patient consumes on the speed and degree to which a drug is absorbed into the body.(2)

Studying food-drug interactions helps us understand how certain foods can affect the effectiveness and toxicity of drug., and :

- Reviewing the scientific data related to the interaction of drugs with certain foods
- Evaluating the clinical significance and consequences that patients may face if they experience drug-food interaction
- Raising awareness among medical staff to provide advice to patients regarding these issues
- Properly educating patients about therapy usage and encouraging them to follow the advice of doctors and pharmacists
- Improving drug safety and promoting individualized drug therapy through these actions (3)



Food drug interaction

Food-drug interactions (FDIs) can alter the way drugs are absorbed as well as their overall effectiveness in the body. Some interactions may decrease the effectiveness of the medication, while others can lead to the potentially harmful concentrations of medications in the body. (4)

Food-drug interactions can lead to two primary clinical effects: they can decrease drug absorption, leading to treatment failure, or increase drug absorption, raising the risk of adverse events and potentially causing toxic effects. (5)

Types of food

Certain foods can have major side effects on drugs by causing changes in absorption. This can occur with fatty, high protein, and high fiber diets (6). Fruits (especially grapefruit), dairy, vitamin K, tyramine-containing foods, and alcohol are commonly involved in food-drug interactions. (7)

High fat

A high-fat, high-calorie meal is recommended as the test meal in food effect studies by the US Food and Drug Administration (8). This recommendation is made because it is believed to have the largest effects on GI physiology and may have the greatest impact on drug absorption and disposition. The total caloric content of high-fat and high-calorie meals is approximately 50%. Generally, gastric emptying can be significantly slowed down by high-fat food compared to a low-fat diet. (9).

A lipophilic environment that increases the solubilization of fat-soluble drugs is provided by high-fat food. For example, gefitinib, an anti-cancer agent with a high log partition coefficient (LogP) of around 4, benefits from the lipophilic environment provided by high-fat food.(10)

Carbohydrate Rich Food

Categories of dietary carbohydrates include monosaccharides, disaccharides, oligosaccharides, and polysaccharides. These components consist of sugars, starches, and fiber. Pancreatic enzymes or colon fermentation digest them rapidly, slowly, or not at all, depending on specific components and their physical size (11). High-carbohydrate foods have a uncertain effect on drug absorption correlated to other foods due to their complex nature. (12)

High protein

High-protein meals can change the absorption of certain medications. It can increases the blood flow to the intestines, which can increase the drug absorption (13). However, protein rich food is also breakdown into smaller units peptides and amino acids, which go head to head with certain drugs for absorption through transporters in the intestine. As a result, the consumption of a protein rich diet may inhibit the uptake of some drugs that depend on similar transport mechanisms (14). Some drugs may show decreased absorption when taken with high protein foods like levodopa, beta-lactam antibiotics, etc(15).

Fiber rich

Dietary fibre is mainly derived from fruits, vegetables, and grain products. These sources contain non-starch polysaccharide substances such as cellulose, hemicellulose, and gums, which have specific chemical structures and physical properties including large volume, viscosity, water-holding capacity, adsorption, and fermentation. (16). Food that is rich in high fiber can affect drug absorption even if the enzymes are resistant to the human digestive system. (17)

Coffee

Caffeine is majorly found in beverages and foods which can interact with various medications in different ways. Such as, consuming caffeine-containing beverages or food may decrease the effectiveness of medications. This is the case with hypnotics, drugs for treating urinary incontinence (like anticholinergics and topical estrogens), and lithium. On the other hand, the effects of some drugs can also be enhanced by caffeine, potentially leading to the onset of side effects. For example, the effects of oral warfarin can be increased by caffeine, raising the risk of bleeding. Moreover, the stimulation of the sympathetic nervous system by MAO inhibitors can be increased by caffeine, possibly leading to diseases like cardiac arrhythmias or hypertension. Furthermore, caffeine can worsen the stomach-damaging effects of NSAIDs (18).

Alcohol

The liver metabolizes alcohol through Cytochrome P450 enzymes where majority of drug metabolism due to which alcohol drug interactions were seen(19). This type of interaction can result in high risk of damage to the CNS due to increased concentrations of alcohol and/or drugs in the bloodstream. This risk is relevant when the drugs are from classes like antidepressants, anxiolytics, antiepileptics, and hypnotics. Specifically, sedative effects of some drugs may be intensified by alcohol consumption, resulting in mood changes, reduced alertness and judgment, and decreased muscle tone. This could potentially lead to a coma, which is life-threatening. (20).

Milk

Milk can intervene with certain antibiotics, decreasing their absorption like tetracyclines and fluoroquinolones when taken orally. These medications react with the calcium which was majorly found in milk and dairy products leading to a decrease in drug absorption. (21)

Fruits(grapefruit juice)

Fruit juices like apple and citrus juices, have been found to decrease the absorption of certain medications in the intestines. This includes drugs like fexofenadine, montelukast, ciprofloxacin, aliskiren, atenolol, celiprolol, and talinolol.

Alongside the widely recognized interaction between grapefruit juice and cytochrome P450 3A4 substrates, it should be noted that grapefruit juice is a strong inhibitor of certain isoforms of the cytochrome that are active in the intestine, particularly the cytochrome P450 3A4 isoform. The CYP3A4 isoform is responsible for metabolizing around half of the total drugs taken. The inhibitory activity is attributed to substances like grapefruit and its juice, such as naringin (a phenolic compound with anti-inflammatory and antioxidant properties) and bergamottin (a furanocoumarin). Due to its inhibitory effects, grapefruit juice is generally not recommended for patients taking psychoactive medications, and it is advised to properly inform patients about this.(25)

Vegetable rich in vitamin – K

Warfarin, a well-known medication, interacts with foods rich in vitamin K. This is because a crucial role in the synthesis of coagulation factors that affect the therapeutic effect of the drug is played by vitamin K. Foods rich in vitamin K, including Brassica vegetables (such as broccoli and cabbage), lettuce, spinach, and parsley, as well as other items like asparagus, peas, lentils, soy, egg yolk, and liver. Other than this interaction, patients taking warfarin can still consume these vegetables. The only precaution that must be taken is to record and examine the quantity consumed, maintain consistency in daily intake, and adjust the warfarin dose accordingly. Research shows that restricting vitamin K intake may not be an effective strategy for improving warfarin efficacy. (26)

Metal rich food

Dairy products contain bivalent cations like calcium, magnesium, and ferrous ion that can interact with certain medications, leading to the formation of complexes. These complexes can either become insoluble precipitates or soluble complexes, preventing their absorption (27). Tetracycline antibiotics, including tetracycline hydrochloride and minocycline hydrochloride, are examples of drugs that can be affected by these interactions. (28)

Purine rich food

The notorious reputation of organ meats, lentils, spinach, mushrooms, and especially seafood is due to their high purine content, which can contribute to health issues such as gout. (29). The intestinal concentrative nucleoside transporter 2 (CNT2) actively uptakes dietary purine nucleosides for absorption. (30). For instance, ribavirin is one such example (31).

Pharmacokinetics

Pharmacokinetics is a study of how a drug works in the body, and it is affected by the ADME (absorption, distribution, metabolism, and excretion) processes. Traditional pharmacokinetic evaluation involves, the levels of the drug and/or its metabolites in the bloodstream and are measured at different time laps. Phase 1 of pharmacokinetics involves the activation of a drug to make it functional in the body, while phase 2 involves the inactivation of the drug or making it more water-soluble for excretion. (32)

Absorption

Remember that food in the stomach can affect how some commonly used drugs are absorbed.It happens as a result of the food's ability to change the movement, acidity, and secretion of the stomach, as well as the duration of food passage through the gastrointestinal tract (GIT). As example, taking azithromycin with food may reduce its absorption, which will significantly reduce its efficacy. Also, some components of food, like calcium or iron, can bind to the drug, making it difficult for the body to absorb it. It can occur with drugs like tetracycline, sodium fluoride, and ciprofloxacin. On the other side, few drugs are absorbed more properly when taken with food. Such as, an acidic environment in the stomach is needed for ketoconazole to be absorbed, and fat in the food can influence the absorption of griseofulvin. (33)

Distribution

Distribution after a drug is entered into the body is played a critical role. The reversible transfer of a drug between different compartments or tissues is involved in distribution, primarily influenced by plasma protein binding. The primary drug-binding proteins in plasma include albumin, a1-acid glycoprotein, and lipoproteins. Long-chain fatty acids and acidic drugs such as warfarin, phenylbutazone, diazepam, and ibuprofen are bound by albumin.(34)

Metabolism

Certain foods can interact with the metabolism of many drugs, especially in the liver. For example, when you take concentrated grapefruit juice with antihypertensive drugs like felodipine and nifedipine, it can raise the level of these drugs that reach the bloodstream. This is because the compounds in grapefruit juice can interfere with the breakdown of these drugs in the body. In conclusion, this interaction can enhance both the effectiveness and potential side effects of these

drugs. Likewise, citrus fruit and its juice are common ingredients in breakfast, which can have significant clinical implications. Patients should be aware of this potential interaction.(35,36)

Excretion

Certain food ingredients can affect the pH of urine, which in turn can impact the rate at which drugs are metabolized in the body. Foods like meats, fish, cheese, and eggs can cause acidic urine, leading to a longer half-life for acidic drugs as they remain in their non-ionized form. On the other hand, foods like milk, vegetables, and citrus fruits can result in alkaline urine, causing a shorter half-life for acidic drugs as they are in their ionized form. Additionally, in the kidney, lithium and sodium compete for reabsorption. A high-salt diet increases the excretion of lithium, while a low-salt diet decreases the renal excretion of lithium, resulting in higher levels of lithium in the blood.(37)

Pharmacokinetic Process	**Mechanism of Food Interaction**	**Effect on Drug**
Absorption	Chemical-physical interaction (bond formation)	Decreased drug absorption
	Physiological changes (gastric acidity, emptying time, bile secretion, gut motility)	Altered absorption rate
	pH changes (gastric)	Affects drug solubility and absorption
	Binding to food molecules or transport proteins	Reduced drug absorption
	Gastric emptying time	Delays or speeds up absorption
Distribution	Body composition (fat mass, water content)	Affects drug distribution volume
	Plasma protein binding	Influences drug distribution
Metabolism	Enzyme inhibition (CYP450)	Increased or decreased drug levels
Elimination	Urine pH changes (acidifying or alkalizing)	Affects drug reabsorption and excretion

Mechanisms of food drug interactions

Gastric emptying time

When a person takes drugs orally, the stomach initially stores them. While the stomach absorbs some drugs (38), most of them need to be pushed out of the gastric cavity and absorbed in the intestine. Observed data indicate that the stomach undergoes three distinct phases of movement(39) and that eating solid food can delay the emptying of the stomach (40) until the food (and drug particles) are broken down into smaller particles (41).

In conclusion, for majority drugs, taking them with food can prolong their absorption due to the delayed emptying of the stomach and postponed absorption in the intestine. Such as, taking capecitabine with food caused a 1.5-hour delay in the time it took for the drug to reach its peak concentration in the blood(42). Likewise, taking ketoprofen with food increased its Tmax from 2.8 to 7.1 hours (43). Although, in many cases, while food delayed Tmax, it did not significantly change the overall amount of the drug in the body (AUC) when compared to taking the drug on an empty stomach. This was observed with drugs like reboxetine(44) and Amoxicillin (45). Only a few drugs, such as erythromycin stearate and midazolam, are affected by stomach acidity. The absorption of erythromycin stearate can be decreased by extended retention in the gastric cavity, as it degrades in acidic environments (46). Additionally, the absorption of drugs like chlorothiazide, which are absorbed in the upper intestine through active and saturable transport, can be increased by delayed stomach emptying.(47)

Impact on drug transporter and drug metabolizing enzymes

In certain situations, when medications are taken with fruit juice instead of water, the uptake transporters and enzymes responsible for drug metabolism can be interfered with by the components of the juice. For example, the absorption of atenolol, a drug processed by organic anion-transporting polypeptide 1A2 (OATP1A2), is significantly reduced by apple juice.(48). Similarly, grapefruit juice inhibits OATP2B1 (49) and the intestinal enzyme cytochrome monooxygenase 3A4 (CYP3A4) (50).

Effect on change in pH of gastrointestinal tract

When the stomach is empty, the average pH is 1.7, but after eating, it increases to around 5.0. However, the pH in the duodenum changes only slightly, from 6.1 to 6.3 (51). Overall, food intake tends to raise the pH in the gastrointestinal tract (GIT) (52). The absorption of drugs is most effective when they are in a un-ionized form and can pass through easily. Therefore, changes in the GI tract's pH can affect how ionizable drugs, whether acidic, basic, or zwitterionic, are absorbed. For example, food can increase the dissolution rate and absorption of weakly acidic drugs like griseofulvin by raising the gastric pH (53). On the other hand, for weakly basic drugs like chloroquine, higher post-meal pH levels can increase the percentage of drugs in a form that can easily pass through the intestinal membranes, aiding their absorption (54).

Example of clinical significant food-drug interactions

Anticoagulants

Warfarin

Warfarin is commonly used for treating or preventing thromboembolic events (54). Patients taking warfarin face a heightened risk of interactions with dietary supplements (55). Certain vegetables such as broccoli, Brussels sprouts, kale, parsley, and spinach contain high levels of vitamin K. Eating large quantities of these vegetables or suddenly changing the amounts eaten can interfere with the effectiveness and safety of warfarin therapy. (56).

Antibiotics

Tetracyclines

Taking tetracycline with food reduces its bioavailability by 46 to 57%, and when taken with dairy products, the reduction is 50 to 65% . Additionally, when tetracycline is taken with iron supplements, its bioavailability can be reduced by up to 81% due to chelation (57,58). This interaction could lead to treatment failure, especially when dealing with pathogens that have moderate resistance to tetracycline (59). A 49% reduction in tetracycline bioavailability can be caused by adding even a small amount of milk to tea or coffee. (60).

Penicillin

When ampicillin is taken with food, its effectiveness can be reduced by 22 to 50%. This occurs because ampicillin does not stay in the body for a longer duration to fight against bacteria effectively due to which treatment failures were seen. Whereas, taking ampicillin in the form of suspension with milk or formula does not alter its absorption(61). The effectiveness of amoxicillin is not alter by regular diet or milk/formula intake(62). Whereas, a high-fiber diet in smaller extent may decrease the effectiveness of amoxicillin(63).

Cephalosporin

In adolescents and adults, a regular diet does not affect the bioavailability of cephalexin (64). Whereas, in young children, taking cephalexin with milk reduces its bioavailability by 40%. Nevertheless, the clinical significance of this interaction is limited as most young children do not reach sufficient antibacterial drug concentrations of cephalexin regardless of their feeding status (65).

When individuals take cefuroxime axetil with food, the bioavailability of the medication increases by 28 to 70% (66) and when taken with milk, cefuroxime absorption increases by 25 to 97%. However, at the recommended dosages, individuals generally achieve sufficient antibacterial concentrations of cefuroxime regardless of feeding status, rendering this interaction of minor clinical significance. (67).

Quinolones

Ciprofloxacin remains equally effective when taken with food (68), but dairy products reduce its effectiveness by 30 to 36% due to chelation. This interaction can potentially cause treatment failure as standard ciprofloxacin dosages are only slightly higher than the minimum inhibitory concentration (MIC) for moderately susceptible pathogens (69). Norfloxacin effectiveness is reduced by 38 to 52% when consumed with milk and milk products (70). However, consuming food or dairy products does not impact the effectiveness of ofloxacin (71). Certain cations present in specific enteral feeds, such as iron, magnesium, and zinc, can also lead to chelation with quinolones. (72)

Antimycobacterials

Food intake can reduce the effectiveness of isoniazid by 12 to 43%, potentially leading to treatment failure (73). Additionally, since isoniazid acts as a monoamine oxidase inhibitor (MAOI), it's important to be cautious with tyramine-rich foods (74).

When rifampicin is taken with food, its bioavailability can decrease by up to 26%. However, the duration of bactericidal drug concentrations remains unchanged, limiting the risk of treatment failure (75). Nonetheless, there have been eight reported cases where rifampicin treatment failure was suspected due to coadministration with a meal, although drug concentration measurements were not performed to confirm these observations (76).

Ethambutol can be taken regardless of meals (77).

The bioavailability of the anti-leprosy agent clofazimine can be increased by 62% with food intake, potentially reducing the required treatment time to achieve therapeutic drug concentrations. (78).

Analgesic and antipyretics

These medications are used to manage slight to medium pain and reduce fever. Acetaminophen, when taken on an empty stomach, will show faster action, while when taken with food, its absorption in our bodies can be slowed. The administration of acetaminophen with pectin will delay both absorption and onset of action. (79).

Stomach irritation can be caused by NSAIDs like ibuprofen, naproxen, ketoprofen, and others, and they should be taken with food or milk. It is advised to avoid or limit the use of alcohol because the risk of liver damage or stomach bleeding can be increased by chronic alcohol consumption. (80)

Respiratory system

Bronchodilators

Different effects may be experienced when bronchodilators like theophylline, albuterol, and epinephrine are taken with food. Theophylline medications can be affected by the presence of food, with high-fat meals potentially increasing the concentration of theophylline in the body, while high-carbohydrate meals may have the opposite effect.

When theophylline medications are administered, it is recommended to avoid alcohol, as it can heighten the likelihood of experiencing side effects such as nausea, vomiting, headache, and irritability. Furthermore, it is advised to avoid consuming excessive amounts of caffeine-containing foods and beverages, such as chocolate, coffee, and tea, as they contain xanthine

compounds that are similar to theophylline. Consumption of high quantities of these substances while taking theophylline may raise the risk of drug toxicity.(80)

Anti histaminic

Antihistaminic drugs like Fexofenadine, loratadine, rupatadine, cimetidine, cetirizine etc. To increase the effectiveness of prescription antihistamines it is recommended to consume without having eaten. (81).

Allergic inflammatory conditions are commonly managed by the drug Rupatadine. A study shows that to increase the bioavailability of a single 20mg oral dose of Rupatadine is done by taking it with food. (82)

To maintain a therapeutic blood concentration it is recommended to take Cimetidine with food. It is beneficial as when taking food as small amount of Cimetidine is absorbed which enables the remaining portion of the drug to dissolve once the gastrointestinal tract is empty. This helps in maintaining therapeutic levels throughout the dosing interval. (83,84)

Antitubercular

The medication isoniazid, which is used to treat tuberculosis, can interact with certain substances found in food such as tyramine and histamine (85). Isoniazid obstructs monoamine oxidase and histaminase activity, leading to potential interactions between the drug and food. Moreover, taking isoniazid with food significantly decreases its bioavailability (86). On the other hand, oleanolic acid, a triterpenoid present in several foods, medicinal herbs, and plants, exhibits antimycobacterial activity against Mycobacterium tuberculosis. When given with isoniazid, oleanolic acid produces a synergistic effect.(87)

Nervous system

Anti epileptic

When carbamazepine tablets are taken with food, a 22% increase in bioavailability is exhibited. Adverse fluctuations in drug concentration may result from not maintaining a consistent relationship to meals while taking carbamazepine due to significant individual variations. (88). However, latest prolonged-release (89) and time-release formulations of carbamazepine are not influenced by food intake (90). The bioavailability of carbamazepine is enhanced by 41% with grapefruit juice by preventing first-pass metabolism through Cytochrome P450 3A4, which could potentially give rise to adverse outcomes. (91). In contrast, the ingestion of milk does not affect the bioavailability of phenytoin (92).

Anti dementia

Tacrine's effectiveness is decreased when taken with a meal, with a 26% decrease in bioavailability, and even when taken 2 hours after a meal, with a 21% reduction. However, taking tacrine on an empty stomach is often not well-accepted by patients due to negative gastrointestinal impact (93).

Cardiovascular system

Cardiac glycoside and Antiarrhythmics

The absorption of digoxin is not affected by a regular meal, but digoxin bioavailability can be decreased by 16 to 32% with a high intake of dietary fiber, commonly found in fiber preparations (94). The bioavailability of sustained-release quinidine gluconate is either unaffected (95) or slightly increased (by 10 to 12%) when taken with food, although there is significant variation between individuals (96). While the bioavailability of quinidine sulfate is not altered by food intake, the absorption rate is slowed down.(97,98)

Antihypertensive

A moderate sodium-restricted diet is recommended for patients who are prescribed anti-hypertensive drugs. (99) It should be noted that the consumption of rich protein food may lead to an increase in the levels of propranolol in the bloodstream. Changing the diet from high in carbohydrates and low in protein to one that is low in carbohydrates and high in protein may result in increased oral clearance. The levels of propranolol in the blood can be decreased by smoking, as it speeds up its metabolism. (100)

When administering celiprolol (a beta-blocker), be alert that its absorption in the intestines may be obstructed if it is consumed with orange juice due to the presence of hesperidin in the juice. Absorption of celiprolol is reduce due to presence if hesperidin. (101) On the other side, when you take ACE inhibitors on an empty stomach, they increase absorption. Additionally, grapefruit juice increases the bioavailability of the calcium channel blocker, felodipine. (102)

Diuretics

Taking furosemide (frusemide) with food decreases the absorption by 16 to 45%. (103) In one study, this decreased absorption was linked to a decrease in diuretic action(104), while another study showed almost zero impact on diuretic action. (105) Overall, the interaction between food and medication (furosemide) is not thought to be significantly clinically important, but it may to some extent show why some individuals seemingly resistant to furosemide may respond to bumetanide drugs. Significantly clinically important no drug-food interaction has been observed with bumetanide drug. (106)

Consuming high amounts of potassium-rich foods like bananas and spinach may cause hyperkalemia, when taken with potassium-sparing diuretics like Amiloride, Spironolactone, etc.(107) In some cases, severe hyperkalemia and serious cardiac arrhythmias like disease, which can be life-threatening to some extent, have been resulted from excessive use of potassium-containing salt substitutes in patients taking spironolactone. (108)

Antidiabetics

Glimepiride, a new generation sulfonylurea derivative and antidiabetic medication, should be taken with breakfast or the first main meal of the day to ensure its maximum effectiveness. This medication has absolute bioavailability and does not interact with food, maintaining highly reproducible pharmacokinetics.(109) Immediate-release glipizide should be taken 30 minutes before meals, while extended-release tablets should be taken with breakfast. (110)

Acarbose, an alpha-glucosidase inhibitor, achieves maximum effectiveness when taken immediately at the start of each meal. This is because acarbose inhibits the enzyme alpha-glucosidase, causing a delay in the absorption of carbohydrates.(111)

Influence of nutritional status and diet on drug pharmacokinetics

Drugs and nutrition interact in a large number of ways. Drugs and nutrients often share the same sites for absorption and undergo metabolism and excretion through the same organs in various conditions. Poor nutritional status can potentially slow down drug metabolism.

Individuals who are at a higher risk for drug-nutrient interactions include those who:

• People with liver failure, gastrointestinal or renal function.
• People who are nutritionally conceded due to long-term illness.
• People with recent dehydration or slimming.
• People who are on prolonged medications and polytherapy.
• People in middle or older age experience changes in lean body mass, overall body fluids, and plasma protein levels.

Drug treatment can affect nutritional status in a defined manner, with drugs that often have nutritional implications being those that:

• Drugs with a limited therapeutic range.
• Patients must take them for a extended duration.
• Irregular food timing can have implications.
• Necessary restrictions or regulations on dietary.
• Side effects may influence appetite and gastrointestinal function.
• They immediately compete with nutrients. (112)

Drug-nutrient interactions

Most drugs recommend defined food intake to maximize absorption. This type of recommendation can change normal eating patterns and decrease overall food intake when meals are skipped, which is common in the elderly.

Medication with specific dosing instructions includes examples.:

• 30 minutes before food or on an empty stomach, you should take Phenoxymethylpenicillin and itraconazole.
• Avoid taking ketoconazole with indigestion medication.
• Do not take ofloxacin, levofloxacin, doxycycline, or penicillamine with antacid preparations or metals like iron, zinc, etc.
• Do not combine milk, iron, zinc, or antacid preparations with ciprofloxacin, norfloxacin, or tetracycline. (112)

Certain drugs may cause nutrient absorption in the gut to be enhanced, inhibited, or prevented. Additionally, the metabolism of some nutrients can be accelerated by these drugs, resulting in higher dietary requirements for that specific nutrient. Furthermore, the urinary excretion of nutrients may be enhanced or inhibited by drugs.(113)

Nutrients-drug interaction or drug-nutrient interaction are:

Effects	**Drugs**	**Nutrients**
Absorption Decrease	1. Laxative 2. Anticonvulsants 3. Norfloxacin 4. Ofloxacin	1. Vitamins and minerals 2. Folate 3. Iron 4. Zinc
Increase Metabolism	Anticonvulsants	Folate, Vitamin D & Vitamin K
Prolong clotting time	Anticoagulants	High dose Vitamin K
Increase fecal elimination	Metformin	Iodine

Table *114

Clinical implications of food drug interactions

Clinically important food-drug interactions are common and multiple classes of drugs have reported them. However, researchers have conducted only a minimum number of studies on this topic.

This lack of research has led to limited understanding of the full scope and potential impact of these interactions on patient health and medication management. Further investigation is needed to identify and address potential risks and improve patient outcomes.

Some of the clinical implications of food drug interactions are as below :

Food	**Medication**	**Interaction Type**	**Therapeutic impact**
Dairy products	Fluoroquinolones antibiotics like levofloxacin, ciprofloxacin	Reduced drug absorption	Take 2 hours before or after consuming dairy
Carbohydrate rich meals	Bronchodilators, mucolytic, anticholinergics and other medicines use in respiratory diseases	Side effects (headache, nausea, emesis)	Avoid or take 2 hours after the medication
Fat rich meals	Bronchodilators (theophylline)	Decreased drug uptake	Avoid or suspend feeding 1 hours before administering medications

Fiber rich and cholesterol rich foods	Statins or HMG-CoA reductase inhibitors	Decreased drug uptake	Take 1 hour after the medication or with low-fiber foods
Grapefruit and grapefruit juice	Beta-adrenergic receptor blockers, Amiodarone	Increased drug absorption, increased toxicity	Escape or take 1 hour after the medication
High fiber products	Cardiac glycosides	Decreased drug absorption	Administer 1 hour prio or 4 hours later
Fruits (bananas, oranges), legumes, meats	Diuretics, potassium-sparing	Increased potassium levels	Limit potassium-rich foods and salt substitutes

Table *115

Conclusion

Food-drug interaction can have a influence on the pharmacokinetics of commonly prescribed medications which results in altered effectiveness and safety levels of the medications. Certain foods can increase, decrease or inhibit the absorption, change the drug metabolism by activating certain enzymes like liver enzymes, or can change drug distribution and excretion patterns. These interactions show the importance of taking drugs/medications correctly and tell with which type of food or without food(empty stomach) medication should be taken to get the desired effect.

Unknown food and drug interactions can lead to a various undesirable effects which can be a life-threatening. So, to avoid undesirable effects, healthcare professionals should be alert of potential food-drug interactions and advice patients on food and medicine scheduling, possible interactions, and dietary restrictions. Alertness of potential food and drug interactions can promote to gain the maximum therapeutic action and reduce side effects which help to cure at faster rate. Overall, a thorough understanding of food-drug interactions is important for separate and effective medication treatment.

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