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INTERACTIONS BETWEEN DIET AND DRUG

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ABSTRACT:

Interactions between diet–drugs are an important yet often underestimated factor affecting therapeutic outcomes. Although drug-drug interactions are widely recognized, the influence of foods, nutrients, and dietary habits on drug absorption, metabolism, and clinical effectiveness has gained attention more slowly. With the increased use of medications and the growing availability of dietary supplements, the likelihood of interactions continues to rise. Individuals with chronic illnesses, poor nutritional status, or vulnerable physiological conditions are at greater risk. This review outlines how foods and nutrients affect drug transport, metabolism, and systemic distribution, and presents key examples of clinically relevant interactions. A deeper understanding of these mechanisms is essential for improving patient safety, optimizing therapy, and guiding appropriate dietary recommendations.

INTRODUCTION:

Drugs do not always act uniformly across all individuals. Variations in therapeutic response often arise from interactions between medications and other substances, including foods, beverages, and dietary supplements. A drug interaction occurs when any consumed substance alters the expected pharmacological action of a medication by increasing, decreasing, or modifying its effects. While accidental misuse is common, interactions also occur due to a lack of knowledge about the active components in food or medicine.

Foods can significantly alter how a drug is absorbed, distributed, metabolized, or eliminated. In some cases, food may reduce side effects, while in many others, it can lead to inadequate therapeutic effects or increased toxicity. As medication use continues to expand globally, food–drug interactions have become a crucial consideration in clinical practice.

This article reviews the mechanisms underlying drug–nutrient interactions and summarizes common interaction patterns to help clinicians and patients make informed decisions

MECHANISMS OF DRUG NUTRIENT:

Interactions

Food–drug interactions result from complex physiological and biochemical processes that influence how a drug behaves in the body.

- **Pharmaceutical Interactions**

These occur when food components affect the physical or chemical stability of a drug within the gastrointestinal tract. For example, certain minerals bind with medications to form poorly soluble complexes, reducing drug absorption.

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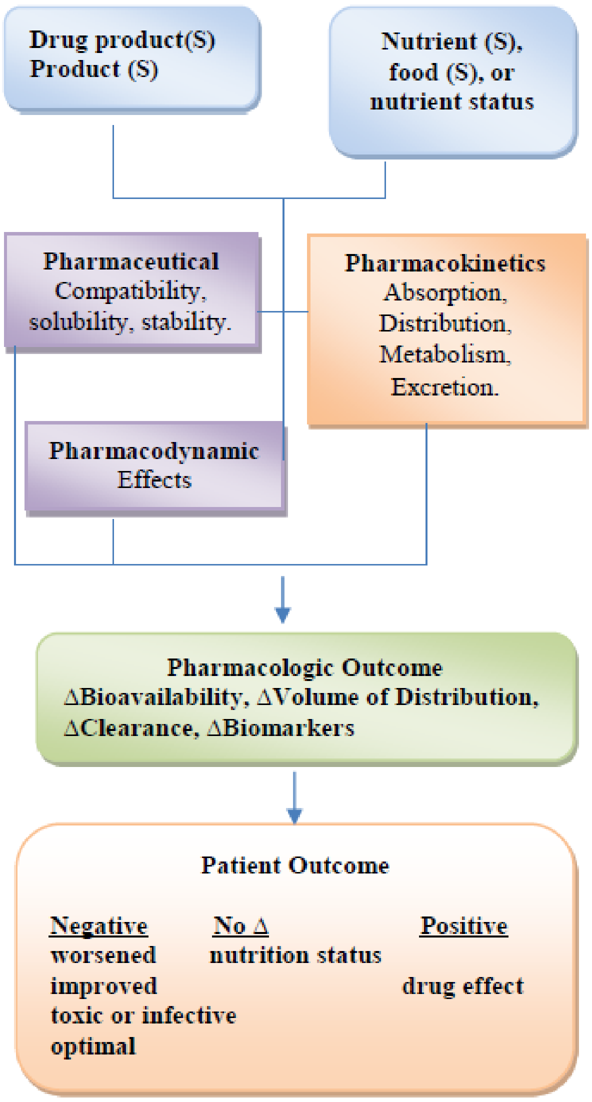

- **Pharmacokinetic Interactions**

These involve changes in the absorption, distribution, metabolism, or excretion of a drug:

Absorption: Food may delay gastric emptying, alter stomach pH, stimulate bile flow, or physically interact with the drug.

Distribution: Changes in plasma protein levels-often affected by nutritional status-can alter the distribution of highly protein-bound drugs.

Metabolism: Foods can inhibit or induce hepatic and intestinal enzymes, particularly cytochrome P450 (CYP) isoforms.

Excretion: Foods that affect urine pH or kidney function can modify drug elimination

- **Pharmacodynamics Interactions**

These occur when foods influence the drug's clinical effects directly, either enhancing or diminishing its intended outcome.

ROLE OF DRUG TRANSPORTERS AND ENZYMES

Drug transporters such as P-glycoprotein and OATP proteins regulate the movement of drugs across cellular membranes. Many foods contain natural compounds capable of inhibiting or inducing these transporters. Similarly, CYP enzymes are responsible for the metabolism of most prescription medications. Foods like grapefruit, cruciferous vegetables, garlic, and herbs can modify enzyme activity, leading to substantial variations in drug levels.

Examples of Significant Food–Drug Interactions

Fruit–Drug Interactions

Grapefruit juice strongly inhibits intestinal CYP3A4 and P-glycoprotein, increasing blood concentrations of statins, calcium channel blockers, immunosuppressants, and some psychiatric drugs.

Seville orange and pomelo show similar inhibitory effects on CYP and transporter activity.

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Apples, grapes, and mangoes interact with drug transporters and CYP enzymes, affecting medications such as antihistamines, sedatives, and cardiovascular drugs.

Vegetable–Drug Interactions

Broccoli and other cruciferous vegetables induce phase I and phase II enzymes, potentially lowering drug levels.

Spinach, tomatoes, carrots, and peppers may alter enzyme pathways and modify drug metabolism.

Influence of Nutritional Status on Drug Response

A person's nutritional status has a strong influence on drug behavior. Malnutrition can reduce plasma protein levels, increasing the free fraction of drugs and raising toxicity risks. Conversely, obesity may alter drug distribution volumes and affect dosing requirements. Micronutrient deficiencies can also impair metabolic functions necessary for processing medications.

Effects of Drugs on Nutritional Health

Many medications alter appetite, nutrient absorption, or metabolism:

Appetite changes: Steroids and psychotropic drugs may increase appetite, while some chemotherapeutics cause severe anorexia.

Digestive disturbances: NSAIDs and antibiotics may cause nausea, vomiting, diarrhea, or intestinal irritation.

Nutrient malabsorption: Antacids reduce mineral absorption; laxatives decrease transit time, impairing fat-soluble vitamin uptake.

Increased nutrient excretion: Diuretics enhance the loss of potassium, magnesium, and sodium.

Food Interactions with Common Drug Classes

Antihistamines

Certain antihistamines cause drowsiness, and alcohol or sedative herbs increase this effect. Rupatadine becomes more bioavailable when taken with food.

Analgesics

Acetaminophen is absorbed more slowly when taken with meals, while NSAIDs should generally be taken with food to reduce gastric irritation. Alcohol consumption significantly increases the risk of liver damage when combined with acetaminophen.

Antihypertensive Agents

Propranolol levels increase with high-protein meals.

Celiprolol absorption decreases with orange juice.

ACE inhibitors such as captopril absorb better when taken before meals.

Grapefruit juice increases exposure to calcium channel blockers.

Antibiotics

Dairy products, mineral supplements, and certain fruit juices bind with antibiotics like ciprofloxacin and tetracycline, reducing their absorption. Azithromycin levels drop significantly when taken with food.

DIET AND DRUG INTERACTIONS

Antidiabetics

Glimepiride should be taken with the first major meal of the day. Acarbose is most effective when taken at the beginning of a meal.

Thyroid Hormones

Levothyroxine absorption decreases when taken with certain foods. Dosing on an empty stomach is recommended.

Anticoagulants

Warfarin effectiveness depends heavily on consistent vitamin K intake. Sudden dietary changes can destabilize INR values. Many supplements and herbs increase bleeding risk.

Bronchodilators

Theophylline absorption varies with meal composition. Caffeine-containing products intensify stimulant effects.

Statins

Grapefruit juice significantly raises levels of atorvastatin, simvastatin, and lovastatin, increasing the risk of muscle toxicity.

RESULTS:

A recent single-dose, fed study evaluated a new test formulation developed as a fixed-dose combination (FDC) of Dolutegravir, Emtricitabine, and Tenofovir Alafenamide (50 mg/200 mg/25 mg tablets). The primary objective was to compare its performance against a reference formulation in healthy adult male and female volunteers under fed conditions.

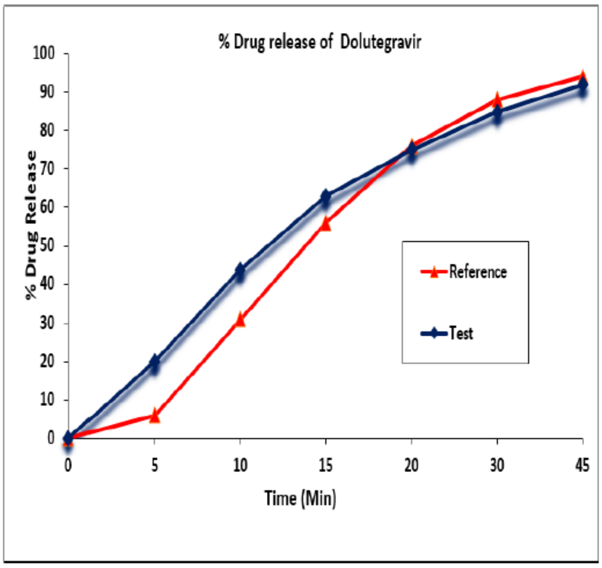

Fig 1: Dolutegravir in vitro drug release profile of test and reference formulations. Each point represents mean (SD).

The results demonstrated that the test FDC formulation was bioequivalent to the reference product with respect to all three active pharmaceutical ingredients: Dolutegravir, Emtricitabine, and Tenofovir Alafenamide. Statistical analysis confirmed no significant differences were observed across key parameters, including in vitro dissolution profiles, relative bioavailability, and overall pharmacokinetic metrics.

Furthermore, the study concluded that the test formulation exhibits similar in vitro characteristics to the reference formulation. The in vivo behavior was also found to be consistent between both formulations for Emtricitabine and Tenofovir Alafenamide, with a predictive outcome noted specifically for

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Dolutegravir bioequivalence. Both the test and reference formulations were confirmed to be safe and well-tolerated among all participants during the trial.

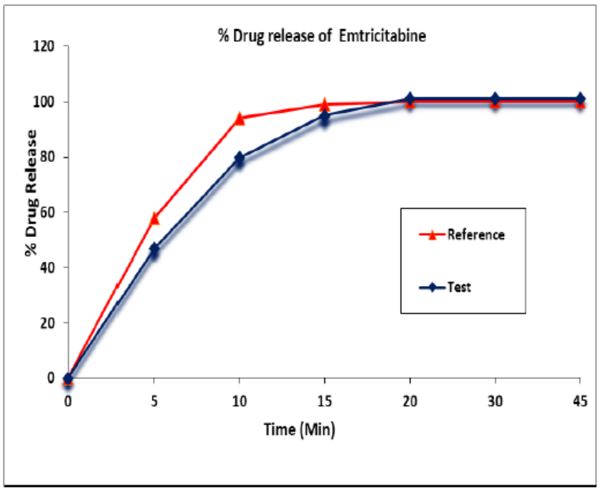

Fig 2: Emtricitabine in vitro drug release profile of test and reference formulations. Each point represents mean (SD).

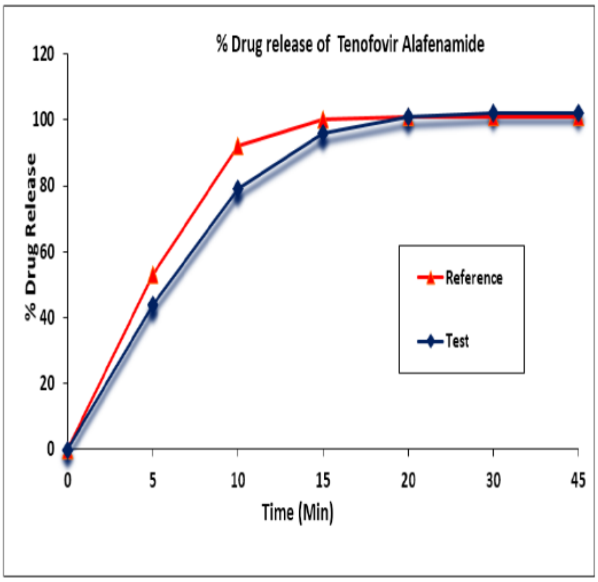

Fig 3: Tenofovir Alafenamide in vitro drug release profile of test and reference formulations. Each point represents mean (SD).

The Importance of Food-Drug Interaction Awareness

The introduction of numerous new pharmaceutical products annually underscores the ongoing challenge of managing potential food-drug interactions. Such interactions can negatively impact the safety and efficacy of drug therapy, as well as the patient's nutritional status. Generally, minimizing these interactions is crucial to avoid poor or unexpected therapeutic outcomes.

Oral medications require absorption through the gastrointestinal tract (stomach or small intestine). The presence of food can significantly influence this process, potentially reducing drug absorption rates. A common strategy to mitigate this is advising patients to take medication either one hour before or two hours after a meal.

While prescription and over-the-counter drugs undergo rigorous testing, the comprehensive testing of various foods for potential interactions is less standardized. Healthcare providers should proactively counsel patients to disclose all details regarding their dietary intake and the use of dietary supplements to their doctors and pharmacists. This practice allows healthcare teams to better anticipate and help patients avoid adverse interactions.

CONCLUSION

Food–drug interactions are a critical yet often overlooked component of therapeutic management. They can influence drug safety,

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efficacy, and patient outcomes. Understanding these interactions enables clinicians to make informed decisions about prescribing and counseling. As dietary behaviors evolve and the use of supplements expands, awareness and monitoring of food–drug interactions remain essential for optimal healthcare delivery.

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