

Role of Diet in Drug Pharmacokinetics and Therapeutic Outcomes: An Overview

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Abstract

Diet is an important but frequently underestimated determinant of drug pharmacokinetics and therapeutic response. Food can influence the absorption, distribution, metabolism, and elimination of drugs through changes in gastrointestinal physiology, gastric pH, gastrointestinal transit, bile secretion, intestinal blood flow, drug solubility, transporter activity, and drug-metabolizing enzymes. The magnitude and direction of these effects depend on the physicochemical characteristics of the drug, pharmaceutical formulation, meal composition, quantity of food, timing of food intake, and individual patient characteristics. High-fat meals, for example, may increase the bioavailability of some poorly soluble drugs, whereas minerals and other food components can reduce absorption through complex formation. Certain foods and beverages, particularly grapefruit, can alter intestinal cytochrome P450 and transporter activity and consequently modify systemic drug exposure. Dietary vitamin K is clinically relevant in patients receiving warfarin, while foods containing high concentrations of tyramine may interact with monoamine oxidase inhibitors. Enteral nutrition can also interfere with the absorption of selected medications. Recent research has expanded the concept of food–drug interactions to include food texture, viscosity, volume, and interactions involving the gut microbiome. Regulatory agencies increasingly emphasize systematic assessment of food effects during drug development because changes in drug exposure can influence efficacy, adverse effects, and treatment safety. A comprehensive understanding of diet–drug interactions is therefore essential for individualized medication counseling, rational prescribing, medication safety, and optimization of therapeutic outcomes.

Keywords: Diet, food–drug interaction, pharmacokinetics, bioavailability, drug absorption, drug metabolism, therapeutic outcomes, CYP450, drug transporters, nutrition.

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1. Introduction

Drug therapy does not occur independently of dietary intake. Most orally administered medicines encounter food and gastrointestinal contents before reaching the systemic circulation, making diet an important environmental factor capable of modifying drug exposure. Food can alter gastrointestinal pH, gastric emptying, intestinal transit, bile secretion, gastrointestinal and hepatic blood flow, drug dissolution, and intestinal transporter and enzyme activity. These physiological changes can consequently influence the rate and extent of oral drug absorption and may produce clinically relevant changes in systemic drug exposure and therapeutic response (Kambayashi & Shirasaka, 2023; Shirasaka & Kambayashi, 2024). Recent pharmacokinetic research has further demonstrated that food effects depend not only on the nutrient composition of a meal but also on its physical characteristics, including meal volume, viscosity, fat content, and other properties, as well as on the physicochemical characteristics and formulation of the administered drug (Shirasaka &

Kambayashi, 2024). Physiologically based pharmacokinetic approaches have consequently been explored to quantitatively predict changes in drug absorption under fed and fasted conditions.

Food–drug interactions may influence pharmacokinetics through changes in drug release, absorption, distribution (Wang et al., 2025), metabolism, and elimination, or may produce pharmacodynamic interactions in which food modifies the clinical effect of a medicine without necessarily producing a proportional change in drug concentration (Ngcobo, 2025). Clinically recognized interactions include those involving grapefruit and other fruit juices, dairy products, vitamin K-containing foods, tyramine-rich foods, alcohol, and selected herbal products (Winkle, 2025). Such interactions may decrease therapeutic effectiveness or increase drug exposure and adverse effects, with particular clinical importance for medicines with a narrow therapeutic index (Sarkar et al., 2023). Food constituents can also influence cytochrome P450 enzymes and drug transporters,

providing important mechanisms for alterations in drug bioavailability and systemic exposure (Kambayashi & Shirasaka, 2023). A recent comprehensive review further emphasized that food, beverages, alcohol, herbs, phytochemicals, nutraceuticals, and micronutrients can modify pharmacokinetic or pharmacodynamic responses and recommended comprehensive dietary assessment in patients who are particularly vulnerable to food–drug interactions (2026).

The importance of food effects has also been recognized in contemporary drug-development and regulatory practice. The U.S. Food and Drug Administration (FDA) issued the final guidance “Assessing the Effects of Food on Drugs in INDs and NDAs—Clinical Pharmacology Considerations” in May 2026. The guidance recommends systematic evaluation of food effects for orally administered drug products during development to determine whether food alters drug absorption and to establish appropriate administration instructions, including whether a medicine should be taken with food, under fasting conditions, or in relation to specific meal conditions (U.S. Food and Drug Administration [FDA], 2026). The FDA further emphasizes that increases or decreases in drug exposure caused by food may affect both safety and effectiveness, highlighting the importance of appropriately designed food-effect studies in the development and labeling of orally administered medicines (FDA, 2026).

2. Pharmacokinetic Basis of Food–Drug Interactions

Pharmacokinetics describes the processes of absorption, distribution, metabolism, and elimination (ADME). Diet can potentially affect each of these processes, although absorption and metabolism are particularly susceptible to food-related changes (Gangadhar et al., 2025). The magnitude of an interaction depends on the drug's physicochemical properties, formulation, dose, meal composition, timing of administration, and patient-specific physiological characteristics (Assiri, 2026). For orally administered drugs, bioavailability is especially important. Food may increase or decrease the area under the concentration–time curve (AUC), maximum plasma concentration (C_{max}), time to maximum concentration (T_{max}), and sometimes the overall duration of drug exposure. Such changes can be clinically relevant when the therapeutic window is narrow (Bácskay et al., 2025).

3. Effect of Food on Drug Absorption

3.1 Gastric pH and Drug Dissolution

Food temporarily modifies gastric pH and the physicochemical environment of the gastrointestinal tract. These changes may influence the dissolution and ionization of drugs, particularly compounds whose solubility is strongly pH-dependent. The presence of food can therefore either enhance or

reduce the amount of drug available for absorption (Wang et al., 2025).

Changes in gastrointestinal pH, bile acid concentrations, and luminal conditions can be especially important for poorly water-soluble drugs. Recent research has emphasized that the effect of food is closely linked to the biopharmaceutical properties of the drug and its formulation (Sen et al., 2026).

3.2 Gastric Emptying and Intestinal Transit

Food generally modifies gastric emptying and intestinal transit. A substantial meal may delay gastric emptying and consequently delay the arrival of a drug at the primary site of absorption. This may increase T_{max} without necessarily changing total exposure. In other circumstances, delayed transit can enhance dissolution or provide additional time for absorption (Jalleh et al., 2026).

The relationship between food intake and absorption is therefore not uniform; food may produce reduced, delayed, increased, accelerated, or negligible absorption depending on the drug and formulation (Dunga et al., 2026).

3.3 Influence of Dietary Fat

Dietary fat is one of the most important nutritional factors affecting oral drug absorption (Liang et al., 2026). A high-fat meal can stimulate bile secretion and increase the solubilization of lipophilic compounds (Löbenberg et al., 2026). It may consequently increase the bioavailability of some poorly water-soluble drugs. However, the effect varies considerably among medications (Nicolaescu et al., 2025).

The FDA's current food-effect guidance recommends a high-fat meal as an important standardized condition for evaluating food effects during drug development because high-fat meals can produce substantial changes in the absorption of some orally administered drugs (O'Shea et al., 2019).

3.4 Dietary Fibre and Drug Absorption

Dietary fibre can influence drug absorption through several mechanisms, including adsorption, increased gastrointestinal viscosity, altered transit, and changes in the intestinal environment. These effects can be particularly relevant when medicines are administered simultaneously with fibre-rich meals or supplements (Canga et al., 2010).

The physical properties of food, including viscosity and volume, are increasingly being recognized as potentially important determinants of oral drug absorption. Unlike conventional food-effect studies that primarily focus on nutrient composition, emerging evidence suggests that the rheological and physical characteristics of meals can influence gastrointestinal physiology, gastric emptying, drug disintegration and dissolution, intestinal drug diffusion, and ultimately the rate and extent of drug absorption. In particular, increased food viscosity may alter gastrointestinal motility and fluid

movement and can interfere with the penetration of gastrointestinal fluids into pharmaceutical formulations, whereas meal volume may influence gastric distension, gastric emptying, and the gastrointestinal environment available for drug dissolution and absorption. These effects may vary according to the physicochemical properties of the drug and its Biopharmaceutics Classification System (BCS) category (Wang et al., 2025). Recent research has also highlighted the potential for incorporating food physical properties, particularly viscosity and volume, into **physiologically based pharmacokinetic (PBPK) models** to improve quantitative prediction of food-related changes in oral drug absorption (Wang et al., 2025).

3.5 Minerals and Chelation

Minerals such as calcium, magnesium, iron, and aluminium may interact with certain medicines within the gastrointestinal tract and thereby alter their oral absorption. A major mechanism is chelation, in which multivalent metal cations form poorly soluble or poorly absorbable complexes with susceptible drugs. This interaction is particularly important for tetracycline-class antibiotics and fluoroquinolones, for which calcium, magnesium, aluminium, iron, and other polyvalent cations can decrease gastrointestinal absorption and consequently reduce systemic drug exposure (Sarkar et al., 2021; Vuong et al., 2023). Experimental and pharmacokinetic modeling studies have further demonstrated that calcium, magnesium, and aluminium can form complexes with fluoroquinolones and substantially affect their absorption and bioavailability (Sarkar et al., 2021). A recent systematic review of dietary interventions involving macrolides and tetracyclines also demonstrated that food, antacids, and mineral supplements can modify the pharmacokinetic characteristics of several antibiotics, although the magnitude of the interaction varies according to the individual drug and dietary condition (Wiesner et al., 2024).

Accordingly, the timing of mineral-containing foods, dietary supplements, antacids, and medications may need to be separated when clinically indicated. For example, regulatory labeling for several oral fluoroquinolones recommends separating administration from antacids containing aluminium or magnesium and from iron-containing products because of the potential for reduced antibiotic absorption. Similarly, FDA information for doxycycline advises attention to concurrent calcium-, iron-, and magnesium-containing products because these minerals can decrease drug effectiveness when taken too closely together (U.S. Food and Drug Administration [FDA], 2018). However, separation intervals should be drug-specific, because not every medicine containing a susceptible chemical group exhibits the same magnitude of interaction.

4. Influence of Food on Drug Metabolism

Diet can modify drug metabolism by affecting metabolic enzymes and transport proteins in the intestine and liver. Cytochrome P450 enzymes, particularly CYP3A4, are important examples.

4.1 Grapefruit and CYP3A4

Grapefruit and grapefruit juice are among the best-characterized examples of food–drug interactions. Bioactive constituents of grapefruit, particularly furanocoumarins, can inhibit intestinal CYP3A4, thereby reducing presystemic first-pass metabolism and increasing the systemic exposure of susceptible drugs. The magnitude of this interaction varies according to the specific drug, grapefruit preparation and concentration, amount consumed, dosing conditions, and individual differences in intestinal CYP3A4 activity (Bailey et al., 1998; Hanley et al., 2011). Current regulatory information also identifies grapefruit juice as an important inhibitor of CYP3A-mediated drug metabolism, although its inhibitory strength can vary substantially depending on the preparation and dose (U.S. Food and Drug Administration [FDA], 2026).

Several therapeutic classes can be affected, including certain statins, calcium-channel blockers, immunosuppressants, antiarrhythmic agents, and other CYP3A substrates. For example, grapefruit juice may increase exposure to susceptible statins such as simvastatin and atorvastatin and may consequently increase the risk of concentration-related adverse effects. Similarly, interactions with certain calcium-channel blockers, immunosuppressants, and antiarrhythmic drugs may increase systemic drug exposure. However, grapefruit does not interact with all medicines within these therapeutic classes, and the magnitude of the interaction varies substantially among individual drugs (Bailey et al., 1998; FDA, 2025).

Importantly, grapefruit may also decrease, rather than increase, the systemic exposure of certain drugs through effects on intestinal drug transporters. Grapefruit and other fruit juices can inhibit organic anion-transporting polypeptide (OATP)-mediated uptake of certain medicines. A well-characterized example is fexofenadine, for which grapefruit juice has been shown to reduce oral bioavailability by decreasing intestinal transporter-mediated drug uptake (Dresser et al., 2002). The FDA similarly notes that grapefruit juice can reduce fexofenadine concentrations and potentially decrease its therapeutic effectiveness (FDA, 2025). Thus, grapefruit represents an important example of how a single dietary component can produce opposite pharmacokinetic effects depending on the drug and the underlying metabolic or transporter pathway.

4.2 Herbal Foods and Phytochemicals

Herbs, spices, botanicals, and concentrated phytochemical preparations may influence drug-metabolizing enzymes and transporters. Compounds such as curcumin, garlic-derived constituents,

ginseng-related compounds, and other phytochemicals have been investigated for their potential to modify pharmacokinetic or pharmacodynamic pathways.

Because the concentration of active constituents can vary considerably between foods and commercial supplements, the clinical significance of individual interactions may differ substantially (Dillard and German, 2000).

5. Role of Food in Drug Transporter Activity

Drug transporters are membrane proteins that regulate the uptake, efflux, and distribution of medicines across the intestinal, hepatic, renal, and other cellular membranes, thereby contributing substantially to drug absorption, disposition, and systemic exposure. Dietary components can modify transporter activity through inhibition, induction, altered expression, or changes in transporter localization, potentially resulting in clinically relevant changes in drug bioavailability (Giacomini et al., 2010; Kato, 2016). Increasing evidence indicates that intestinal transporters, particularly members of the organic anion-transporting polypeptide (OATP) family and ATP-binding cassette transporters such as P-glycoprotein (P-gp), can contribute to food–drug interactions (Giacomini et al., 2010; Tamai, 2015). A systematic review of intestinal OATP-mediated interactions identified several drugs, including fexofenadine, atenolol, and celirolol, as clinically relevant transporter substrates and demonstrated that dietary or natural products can inhibit intestinal OATP-mediated drug uptake (Izzo et al., 2017).

Grapefruit provides an important example because its constituents can affect both drug-metabolizing enzymes and membrane transport systems. In addition to inhibition of intestinal CYP3A4, grapefruit and grapefruit juice can inhibit intestinal uptake transporters such as OATP1A2 and OATP2B1, thereby reducing the absorption of susceptible drugs. Fexofenadine represents a well-characterized example: grapefruit juice has been shown to decrease fexofenadine exposure, an effect attributed primarily to inhibition of intestinal OATP-mediated uptake (Dresser et al., 2002; Glaeser et al., 2007). More broadly, systematic evidence indicates that grapefruit, apple, and orange juices can inhibit intestinal OATP activity and decrease the bioavailability of selected transporter substrates, although the clinical significance varies according to the specific drug and interaction conditions (Izzo et al., 2017).

The growing understanding of transporter-mediated interactions has therefore expanded food–drug interaction research beyond the traditional focus on cytochrome P450 enzyme inhibition and induction. Contemporary research considers coordinated effects on metabolic enzymes, uptake transporters, and efflux transporters as important determinants of oral drug disposition. Recent literature further

indicates that dietary polyphenols and other food-derived bioactive compounds can interact with intestinal transporters and may contribute to interindividual variability in drug exposure (2026). Consequently, transporter-mediated food effects should be considered when evaluating the pharmacokinetic profile and potential therapeutic consequences of orally administered medicines.

6. Food and Drug Distribution

The effect of diet on drug distribution is generally less direct than its effect on absorption and metabolism. Nevertheless, nutritional status can modify plasma protein concentrations, body composition, tissue perfusion, and the availability of binding sites.

Malnutrition, obesity, severe protein deficiency, and altered body composition can potentially influence the distribution of highly protein-bound or lipophilic medicines. Consequently, nutritional status may contribute to interindividual differences in drug exposure and therapeutic response (Umutoni et al., 2026).

7. Diet, Drug Elimination, and Renal Function

Diet can indirectly influence drug elimination by modifying renal physiology, hydration, electrolyte balance, and acid–base status. Dietary patterns may also affect urinary pH, which can influence the renal excretion of some weakly acidic or weakly basic drugs.

In patients with kidney disease, dietary restrictions and altered nutritional status may coexist with impaired drug clearance. Such patients therefore require careful consideration of both medication and dietary factors when therapeutic regimens are designed (Zhu et al., 2026).

8. Clinically Important Food–Drug Interactions

Clinically important food–drug interactions occur when dietary components alter the pharmacokinetic or pharmacodynamic properties of medicines, potentially affecting treatment efficacy and safety. Grapefruit and grapefruit juice can inhibit intestinal CYP3A4 and certain drug transporters, increasing or decreasing exposure to susceptible medicines such as selected statins, calcium-channel blockers, immunosuppressants, and antihistamines (Bailey et al., 1998; Dresser et al., 2002). Calcium, magnesium, iron, and aluminium may form poorly absorbable complexes with drugs such as tetracyclines and fluoroquinolones, thereby reducing their gastrointestinal absorption (Sarkar et al., 2021). Dietary vitamin K is clinically relevant for patients receiving warfarin because substantial changes in vitamin K intake can alter anticoagulant response, whereas tyramine-rich foods may cause potentially serious pharmacodynamic interactions in patients receiving monoamine oxidase inhibitors (Vuong et al., 2023). High-fat meals may increase the absorption of selected lipophilic drugs through enhanced bile secretion and gastrointestinal solubilization, while high-fibre foods may modify

drug absorption through adsorption, increased viscosity, and changes in gastrointestinal transit (Shirasaka & Kambayashi, 2024; Wang et al., 2025). Alcohol can additionally produce pharmacokinetic and pharmacodynamic interactions with several medicines, potentially increasing sedation, toxicity, or alterations in drug metabolism. Herbal products and concentrated botanical preparations may also influence drug-metabolizing enzymes and transporters, although the clinical magnitude of individual interactions varies. Therefore, assessment of dietary habits, supplements, beverages, meal timing, and relevant food components should form part of medication counseling, particularly for patients receiving drugs with a narrow therapeutic index or those taking multiple medications.

Table 1. Clinically Relevant Food–Drug Interactions: Dietary Factors, Mechanisms, Pharmacokinetic Effects, and Therapeutic Implications (Vuong et al., 2023; Wang et al., 2025)

Dietary factor / component	Representative drug(s)	Primary mechanism	Effect on drug disposition	Potential therapeutic implication
Grapefruit / grapefruit juice	Simvastatin, atorvastatin, cyclosporine, selected calcium-channel blockers	Intestinal CYP3A4 inhibition	Increased systemic exposure of susceptible drugs	Increased risk of concentration-related adverse effects
Grapefruit / apple / orange juice	Fexofenadine and other OATP substrates	Inhibition of intestinal OATP-mediated uptake	Reduced drug absorption and bioavailability	Potential reduction in therapeutic effectiveness
High-fat meals	Selected poorly water-soluble/lipophilic drugs	Increased bile secretion and gastrointestinal solubilization	Increased absorption and/or systemic exposure in susceptible drugs	May enhance bioavailability; may also increase adverse-effect risk

Calcium-rich foods / supplements	Tetracyclines, fluoroquinolones	Chelation and formation of poorly absorbable complexes	Reduced gastrointestinal absorption	Reduced systemic exposure and possible reduction in antimicrobial effectiveness
Iron-containing foods / supplements	Tetracyclines, fluoroquinolones	Chelation/complex formation	Reduced drug absorption	Potential treatment failure if interaction is clinically significant
Magnesium- or aluminum-containing antacids	Fluoroquinolones, tetracyclines	Formation of insoluble complexes	Markedly reduced absorption of susceptible drugs	Reduced therapeutic effectiveness
High-fibre foods / supplements	Selected orally administered medicines	Adsorption, increased viscosity, and altered gastrointestinal transit	Delayed or reduced absorption in susceptible drugs	Possible reduction in systemic drug exposure
Vitamin K-rich foods	Warfarin	Pharmacodynamic antagonism of vitamin K-dependent anticoagulation	Altered anticoagulant response	Changes in INR and anticoagulant control when intake changes

				substantially
Tyramine-rich foods	Monoamine oxidase inhibitors (MAOIs)	Reduced tyramine metabolism during MAO inhibition	Increased sympathetic response	Potential marked elevation of blood pressure
Alcohol	Sedatives, opioids, hypoglycemic agents, anticoagulants and others	Pharmacodynamic and metabolic interactions	Altered drug effects and, for some drugs, altered metabolism	Increased sedation, toxicity, or other adverse effects
Herbal products / concentrated botanicals	Various prescription medicines	Modulation of CYP enzymes and drug transporters	Altered drug metabolism, absorption, or clearance	Variable effects on efficacy and toxicity
Enteral nutrition	Selected orally administered medicines	Binding to nutrients, altered gastrointestinal conditions, formulation interaction	Reduced or delayed absorption of susceptible drugs	Potentially reduced therapeutic response
High-volume / viscous meals	Selected orally administered drugs	Changes in gastric emptying, fluid movement, dissolution, and intestinal environment	Altered rate and/or extent of absorption	Variable changes in drug exposure

These interactions are not universally applicable to every drug within a therapeutic class. Therefore,

medication-specific guidance is necessary rather than broad dietary restrictions.

9. Vitamin K and Anticoagulant Therapy

Vitamin K-containing foods are particularly important in patients receiving vitamin K antagonists such as warfarin. Sudden changes in vitamin K intake can influence anticoagulant response. The clinically relevant principle is generally dietary consistency rather than complete avoidance of vitamin K-rich foods (Fusaro et al., 2026).

Green leafy vegetables and other vitamin K-containing foods can therefore be incorporated into a balanced diet when intake is stable and medication monitoring is appropriately performed (Leivaditis et al., 2026).

10. Tyramine-Rich Foods and Monoamine Oxidase Inhibitors

Tyramine-containing foods can interact pharmacodynamically with monoamine oxidase inhibitors (MAOIs). Under conditions of MAO inhibition, tyramine metabolism can be impaired, potentially resulting in excessive sympathetic activity and substantial increases in blood pressure. Foods traditionally associated with high tyramine concentrations include aged cheeses, fermented products, and certain cured or processed foods. The risk depends on the particular MAOI, dose, dietary exposure, and individual circumstances (Yuan, 2026).

11. Alcohol and Medication Outcomes

Alcohol can interact with medicines through both pharmacokinetic and pharmacodynamic mechanisms. It may influence hepatic metabolism, central nervous system activity, gastrointestinal function, and adherence. Concomitant use with sedatives, opioids, hypoglycemic medicines, anticoagulants, and other drugs can have clinically important consequences.

Alcohol-related nutritional deficiencies and chronic changes in hepatic function may further complicate medication management. Thus, alcohol consumption should be considered as part of the overall dietary and lifestyle assessment of patients receiving long-term pharmacotherapy (Nieto et al., 2026).

12. Enteral Nutrition and Medication Administration

Enteral feeding is particularly important in hospitalized and critically ill patients. Administration of medication through feeding tubes or alongside enteral nutrition can alter drug absorption because of binding to nutrients, changes in gastric emptying, altered gastrointestinal conditions, or interactions with the feeding formulation.

Medication administration schedules may therefore need to be coordinated with enteral feeding. Crushing or dispersing medications without confirming formulation suitability can also affect

drug release and absorption (Steele and Smith, 2026).

13. Nutritional Status and Therapeutic Outcomes

The effect of diet on medication outcomes extends beyond individual food–drug interactions. Nutritional status itself can influence pharmacokinetics and pharmacodynamics. Protein-energy malnutrition, obesity, micronutrient deficiencies, dehydration, and altered body composition may modify drug distribution, metabolism, and elimination (Habtemariam et al., 2026).

Recent literature emphasizes that food–drug interactions should be considered alongside patient nutritional status, particularly among older adults, children, pregnant individuals, and patients receiving medicines with narrow therapeutic windows (Reytor-González et al., 2026). A detailed dietary history may therefore provide clinically relevant information during medication review.

14. Gut Microbiota as a Link Between Diet and Drug Response

The gut microbiome represents an emerging interface between nutrition and pharmacology. Dietary patterns influence microbial composition and metabolic activity, while intestinal microorganisms can metabolize certain drugs and drug metabolites.

Food-induced changes in the gut microbiota may consequently modify drug bioavailability or activity indirectly. Recent research on food properties and drug absorption has identified gut microbiota composition as one of several physiological factors potentially contributing to variability in oral drug absorption (Kumar et al., 2026).

This field may become increasingly important as precision nutrition and precision pharmacotherapy develop.

15. Role of Meal Timing

The timing of medication relative to meals can be as important as the composition of the meal. Drugs may be prescribed on an empty stomach, with food, immediately after meals, or at a specified interval before or after eating (Hristakeva et al., 2026).

Meal timing can influence gastric emptying, dissolution, intestinal exposure, and metabolic processes. For drugs for which food substantially changes exposure, consistent administration conditions are particularly important (Jalleh et al., 2026).

The FDA's 2026 guidance emphasizes the importance of translating food-effect studies into practical dosing instructions that account for real-world meal patterns and patient adherence (Löbenberg et al., 2026).

16. Food Effects in Drug Development

Food-effect studies are an important component of oral drug development. Conventional studies commonly compare pharmacokinetic parameters after administration under fasting and fed

conditions. Contemporary approaches increasingly incorporate physiologically based pharmacokinetic modeling and in vitro systems to predict food effects and reduce uncertainty.

The FDA recommends evaluating food effects early in development and subsequently conducting appropriately designed studies with the intended commercial formulation. High-fat meals remain an important standardized condition, while additional meal conditions may be evaluated when clinically relevant (Zhang et al., 2026).

Recent experimental approaches such as dynamic gastrointestinal models, including Tiny-TIM, have also been investigated to understand and predict food-related changes in oral drug absorption.

17. Personalized Nutrition and Precision Pharmacotherapy

Interindividual variability in diet, genetics, gut microbiota, nutritional status, gastrointestinal physiology, and medication use means that the same food may not produce an identical effect in every patient.

Precision pharmacotherapy seeks to integrate these variables to optimize treatment. In the future, dietary assessment, pharmacogenomic information, microbiome profiles, therapeutic drug monitoring, and PBPK modeling may contribute to individualized medication recommendations (Jamai et al., 2026).

Such approaches could be particularly valuable for patients taking multiple medicines, individuals receiving narrow-therapeutic-index drugs, and populations with substantial dietary variability (Nicoletti et al., 2026).

18. Future Perspectives

Future research should move beyond the traditional concept of food as simply a fed or fasted condition. Meal composition, food matrix, viscosity, volume, temperature, processing, fibre content, fat quality, phytochemical content, microbiome interactions, and dietary patterns may all influence drug disposition.

The integration of PBPK models, artificial intelligence, dynamic gastrointestinal models, pharmacomicrobiomics, and real-world dietary data may improve prediction of food effects. Recent literature indicates increasing interest in incorporating physical food properties into quantitative models of oral drug absorption.

Another important area is the development of standardized dietary databases and clinical decision-support systems that can alert healthcare professionals to potentially important food–drug interactions.

Conclusion

Diet is a significant determinant of drug pharmacokinetics and therapeutic outcomes. Food can modify drug absorption through changes in gastrointestinal pH, gastric emptying, intestinal transit, bile secretion, drug solubility, and physical

characteristics of the gastrointestinal environment. Dietary constituents can additionally influence drug-metabolizing enzymes and transporters, while nutritional status, meal timing, gut microbiota, and enteral nutrition may further contribute to variability in treatment response. Clinically recognized examples include grapefruit interactions, mineral-related reductions in drug absorption, vitamin K effects on anticoagulant therapy, and tyramine interactions with monoamine oxidase inhibitors. Importantly, food effects are drug- and formulation-specific and should not be generalized across therapeutic classes. Current regulatory approaches emphasize systematic assessment of food effects during drug development, while emerging technologies such as PBPK modeling and dynamic gastrointestinal systems are improving prediction of these interactions. Integrating dietary assessment into medication management can therefore support safer prescribing, improve adherence, reduce avoidable adverse effects, and optimize therapeutic effectiveness. Future research should focus on personalized food–drug interaction prediction by integrating dietary patterns, nutritional status, pharmacogenomics, gut microbiota, and individual pharmacokinetic characteristics.

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