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DRUG FOOD INTERACTIONS A REVIEW OF CONTEMPORARY EVIDENCE

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Abstract

Food–drug interactions can alter drug absorption, metabolism and effect, influencing the efficacy and safety of therapy, yet they remain less studied than drug–drug interactions. This narrative review summarises mechanisms, clinically relevant examples and practical recommendations reported in sources published from 2021 to 2026. We searched open-access scientific sources and selected 15 publications, including narrative, systematic and scoping reviews, cross-sectional studies, a database, regulatory guidance and a conference abstract. The evidence indicates that interactions arise mainly through altered absorption, intestinal enzyme or transporter activity, chelation with cations and pharmacodynamic effects. Grapefruit irreversibly inhibits intestinal CYP3A4, while calcium and iron can reduce fluoroquinolone and tetracycline absorption; in one hospital study, 74.5% of 47 patients receiving both an antibiotic and a cation-containing product took them at the same time. For warfarin, a consistent vitamin K intake is recommended. Most newer cardiovascular and antidiabetic medicines can be taken with or without food, although oral semaglutide is an exception. Evidence concerning phenytoin remains limited: only 3 of 12 studies in the reviewed systematic review were rated as having moderate certainty. Clinical assessment should consider a medicine's bioavailability and metabolic pathway alongside the patient's dietary habits. The review is narrative and its findings are limited by the breadth of the search and the variable quality of included evidence.

Keywords: food–drug interaction; pharmacokinetics; CYP3A4; grapefruit; warfarin; chelation; patient awareness.

Introduction

A food–drug interaction (FDI) is a situation in which a food product or dietary supplement changes the pharmacokinetics or pharmacodynamics of a drug [1]. Such effects are especially common with orally administered drugs [1]. Their consequences range from loss of drug efficacy to severe adverse reactions.

Data on FDIs are far scarcer and more fragmented than data on drug–drug interactions. People eat very differently, which makes it hard to assess the effect of food on a drug precisely [2]. During drug development, European guidelines recommend studying interactions with food only when in vivo evidence requires it [1]. Available resources are also limited: for example, one database compiles more than 1,700 interactions from online sources, and the POMELO corpus contains 5,752 manually annotated sentences from 639 Medline articles [1].

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Interactions are classified in several ways. One classification divides them into types I–IV according to their effect on the pharmaceutical state of the drug, its absorption (enzyme, transporter protein, chelation), distribution and elimination [2]. A recent review names milk, grapefruit juice and alcoholic beverages as products that may cause specific interactions and recommends taking a full dietary history that covers foods taken together with medication [3]. Regulatory attention is also growing: in May 2026 the U.S. Food and Drug Administration (FDA) published revision 1 of its guidance on assessing the effects of food on drugs, which stresses the need to evaluate the rate and extent of absorption, variability of exposure, and differences between meals of varying fat and calorie content [4].

Gathering the evidence accumulated in recent years in one place is therefore of practical value. **The aim of this study** was to summarise, on the basis of scientific sources published in 2021–2026, the main mechanisms of food–drug interactions, clinically relevant examples, and data on the awareness of patients and health professionals, and to formulate practical recommendations.

Materials and Methods

This study was designed as a narrative review and was not registered under the PRISMA protocol. In October 2026, we searched a general web search tool and consulted results from PubMed, PubMed Central and publisher platforms. The English-language search terms included “food-drug interactions,” “drug-food interactions,” “grapefruit juice CYP3A4,” “warfarin vitamin K diet,” “food effect bioavailability,” “levothyroxine coffee,” “fluoroquinolone tetracycline calcium” and “knowledge of food-drug interactions survey.” The search was limited to publications from 2021 through 2026.

We included English-language peer-reviewed articles, databases and regulatory documents published between 2021 and 2026 that addressed an interaction between a medicine and a food, beverage or supplement. Dissertations, popular websites and articles published before 2021 were excluded. One exception was a 2022 conference abstract on levothyroxine and coffee, identified through a press report; this source is explicitly qualified in the text. Reviews published during the search period may summarise older primary studies, which are identified separately in the results.

For each included source, we extracted the study design, population, principal findings and authors’ conclusions. Findings were grouped by interaction mechanism and medicine class and synthesised narratively; no meta-analysis was conducted. We did not independently apply formal risk-of-bias instruments such as AMSTAR 2 or GRADE. Where the phenytoin systematic review reported GRADE assessments, we present the authors’ ratings.

The search was conducted by one reviewer and did not use a prespecified database strategy in Scopus or Web of Science, so relevant studies may have been missed. Full texts were analysed only for sources [2], [5], [6] and [11]; for the other sources, analysis was limited to abstracts and results sections. Because this review analyses published sources and includes no new human or animal research, ethical approval was not required.

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Results

Fifteen sources were included in the analysis: 5 narrative reviews, 3 systematic or scoping reviews, 4 cross-sectional studies, 1 database, 1 regulatory document and 1 conference abstract (Table 1).

Table 1. Sources included in the analysis

	Source	Type	Topic
	Lacruz-Pleguezuelos et al., 2023 [1]	Database	FooDrugs: text and transcriptomic data
	Roy et al., 2022 [2]	Review	Classification of FDIs, information resources, personalised medicine
	Tolou-Ghamari, 2026 [3]	Review	Interactions of drugs with food, beverages, alcohol, herbal products
	FDA, 2026 [4]	Regulatory document	Assessing the effects of food on drugs
	Abu Dayyih et al., 2024 [5]	Review	Grapefruit and intestinal CYP3A4
	Eljaaly et al., 2021 [6]	Cross-sectional study (hospital)	Fluoroquinolones, tetracyclines and cations
	Talasaz et al., 2024 [7]	Evidence review	Oral anticoagulants and food, herbal products
	Grześk et al., 2021 [8]	Review	Direct oral anticoagulants and food
	Scoping review [9]	Scoping review	Novel cardiovascular and antidiabetic drugs
0	Review on antifungals, 2025 [10]	Systematic review, meta-analysis	14 oral antifungal drugs
1	Orellana-Paucar et al., 2026 [11]	Systematic review	Phenytoin and food, herbs
2	Washington et al., 2022 [12]	Conference abstract	Levothyroxine oral solution and coffee
3	Kuźbicka et al., 2024 [13]	Cross-sectional survey	Patient awareness, Poland
4	Megaw et al., 2025 [14]	Cross-sectional survey	Dietitians' knowledge, South Africa
5	Saleh and Mohammed, 2026 [15]	Cross-sectional survey	Public awareness, Baghdad

The reviews divide interactions into pharmacokinetic and pharmacodynamic types [1, 2]. Roy et al. distinguish four types [2]:

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- **Type I** — the drug and food interact before entering the body, at the stage of preparation or administration (for example, with enteral feeding, levothyroxine dissolves poorly and may stick to the tube).
- **Type II** — the most common with oral administration; subtype A is a change in enzyme activity (grapefruit and cyclosporine), subtype B a change in transporter protein activity, and subtype C chelation or complex formation (ciprofloxacin and calcium).
- **Type III** — changes in volume of distribution, metabolism and tissue penetration (for example, with rasagiline, tyramine-rich food may cause an acute hypertensive episode known as the "cheese reaction").
- **Type IV** — competition in the elimination pathways of the drug or food components.

The reviews also note that the volume and composition of a meal may slow gastric emptying and delay drug absorption [2], and that changes in drug transporters may lead to toxicity or therapeutic failure [3].

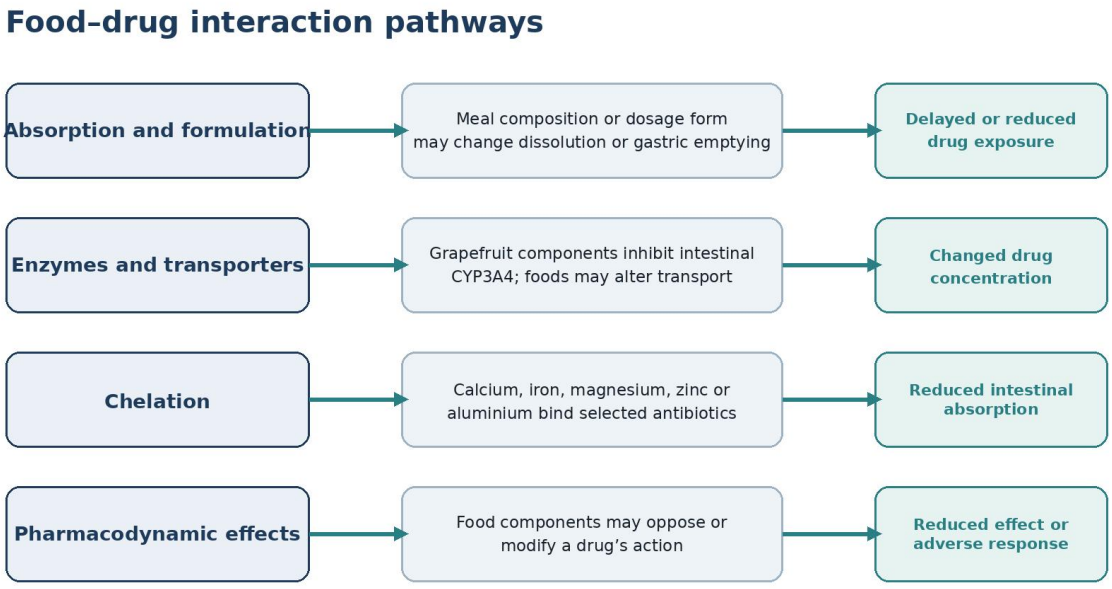


Figure 1. Principal pathways of food–drug interaction. Conceptual synthesis of the mechanisms described in sources [1–3, 5–11].

Naringin, bergamottin and 6,7-dihydroxybergamottin in grapefruit juice inhibit intestinal CYP3A4 [5]. Furanocoumarins are the most potent components and inactivate the enzyme irreversibly; recovery of activity requires synthesis of new enzyme [5]. According to the review's author, the interaction begins 30 minutes after a single glass of juice, and CYP3A4 activity recovers 2–3 days after the last intake [5]. The interaction affects the intestinal rather than the hepatic enzyme: the disposition of intravenously administered drugs does not change [5]. The clinical significance of the interaction depends on the oral bioavailability of the drug: drugs with low bioavailability that undergo extensive intestinal CYP3A4 metabolism are affected most [5]. A rule of thumb has three conditions: the drug is taken orally, its bioavailability is incomplete, and it is extensively

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metabolised by CYP3A4; a pharmacokinetic interaction is expected only if all three are met [5]. Examples include felodipine (with 250 ml of juice the concentration rose about 3-fold, with 0–8-fold variation between patients), simvastatin, atorvastatin, immunosuppressants, midazolam and triazolam [5]. Serious events described in the review include rhabdomyolysis with statins, a rise of tacrolimus concentration of up to 500% after grapefruit marmalade, and acute renal dysfunction; however, the author also notes that clinical toxicity cases are rare [5]. A time gap between juice and drug does not fully remove the effect: for felodipine, a 4-hour interval gave the maximal effect, a 10-hour interval about half of it, and 24 hours about 25% [5].

Oral fluoroquinolones and tetracyclines form insoluble chelates with di- and trivalent cations (calcium, iron, magnesium, zinc, aluminium) in the gut and are poorly absorbed [6]. According to Eljaaly et al., the mean AUC of ciprofloxacin falls by up to 42% with calcium and by up to 64% with iron [6]. In one teaching hospital in Jeddah (2019), 47 of 177 patients (26.6%) who received an oral fluoroquinolone or tetracycline also received a cation-containing product. In 35 of them (74.5%) the two were given at the same time, and in 1 (2.1%) the interval was chosen incorrectly; patients took a mean of 8 oral drugs [6]. The most frequent antibiotics were ciprofloxacin (61.7%), moxifloxacin (25.5%) and doxycycline (12.8%), and among cations iron (59.6%) and calcium (31.9%) predominated [6]. As interval criteria the authors considered correct: for ciprofloxacin, 2 hours before or 6 hours after the cation; for doxycycline, at least 1–2 hours before aluminium-, calcium- and magnesium-containing products; and for iron products, at least 3 hours before or 2 hours after doxycycline [6]. It should be noted that this study examined cation-containing drug products rather than food; the same chelation mechanism applies to dairy products, but directly measured results are not reported in that study.

Patients taking warfarin are advised not to restrict vitamin K-rich food but to consume it in a steady amount every day [7]. Direct oral anticoagulants (DOACs) were initially thought to have no interaction with food, but clinical observations have shown that such effects exist [8]. The absolute bioavailability of dabigatran is about 6%; food does not change it but delays the time to Cmax by about 2 hours [8]. Rivaroxaban 10 mg is absorbed independently of food, whereas a 20 mg tablet taken after a meal increased AUC by a mean of 39% [8]. The bioavailability of apixaban is about 50% [8]. Grześk et al. advise patients on anticoagulants to avoid products containing *Hypericum perforatum* (St John's wort) and to pay particular attention to other food components [8]. Talasaz et al. note that food interactions are widely recognised for warfarin, may also be clinically relevant for DOACs, and that knowledge gaps remain in this area [7].

A scoping review searched in PubMed, Scopus and Cochrane up to May 2024 included 36 publications and covered sacubitril/valsartan, vericiguat, rivaroxaban, edoxaban, apixaban, dabigatran, empagliflozin, dapagliflozin and other drugs [9]. For most drugs, food lowered the maximum concentration (Cmax) and delayed absorption but did not significantly change total exposure (AUC); these drugs can therefore usually be taken irrespective of meals [9]. SGLT2 inhibitors showed a similar pharmacokinetic profile regardless of food; for vericiguat, exposure improved when taken with food [9]. Exceptions: the effect of oral semaglutide falls sharply when taken with food, and it is recommended on an empty stomach; the bioavailability of pitavastatin was higher in the fasted state [9].

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A systematic review and meta-analysis searched in three databases (Medline, Embase, Cochrane) up to June 2024 assessed the effects of food, beverages, antacids and mineral supplements on 14 oral antifungals; it included 73 studies from 68 reports, 58% of which were open-label crossover studies [10]. The authors concluded that the degree of interaction depends on the physicochemical properties of the drug, the type of food, the dosage form and patient characteristics [10]. The abstract gives no figures for individual drugs.

A systematic review on phenytoin (search period 1960–2024) found 826 articles, of which 12 were included (4 randomised trials, 4 quasi-experimental studies and 4 case reports) [11]. By GRADE, only 3 (one RCT, one quasi-experimental study and one case report) were of moderate certainty and the other 9 of very low certainty [11]. Three studies found no interaction, five found increased absorption, one found improved efficacy and three found reduced efficacy [11]. The authors concluded that folic acid may prevent folate deficiency without changing plasma phenytoin concentration (a moderate-quality RCT); that phenytoin levels should be monitored when it is taken with piperine; that taking it together with noni juice should be avoided (based on one case report); and that evidence on interactions with food is insufficient for firm conclusions [11].

An abstract presented at the 2022 meeting of the Endocrine Society described a crossover study in 40 healthy adults in which 600 µg of levothyroxine oral solution was taken 5 minutes before coffee and, separately, fasting [12]. Compared with fasting, the geometric mean ratio was 93.98% for AUC0–48 and 95.99% for Cmax, and the 90% confidence intervals lay within the FDA bioequivalence range [12]. This result applies only to the liquid form, not to tablets; because the study was conducted by the drug manufacturer and exists only as a conference abstract, it should be interpreted with caution [12].

In a survey of 127 patients in Poland, most patients took medicine with water, and some used tea or juice; taking medicine with tea was more common among men and older people, and higher education reduced that likelihood; the authors recommend starting education on safe pharmacotherapy in primary school [13]. In South Africa, an online cross-sectional survey of dietitians was conducted in August–September 2022 (70 valid responses; a 12-item knowledge test) [14]. In Baghdad, an online survey assessing the public's knowledge, awareness and attitudes was conducted in March–May 2024; the authors attribute under-reporting of FDIs to insufficient documentation of dietary history, lack of follow-up or low awareness [15]. In the parts we reviewed of [14, 15], no scores or percentages are reported. Among information resources, the FooDrugs database combines text documents and transcriptomic data [1]; the reviews mention interaction checkers such as Drugs.com, Medscape and WebMD [2] and food-component networks (NutriChem), and point to nutrigenomics and pharmacomicrobiomics as future possibilities [2]. The 2026 FDA guidance revises part of the 2022 guidance [4].

Discussion

The clinical significance of food–drug interactions depends on the medicine’s properties, while the strength of evidence varies across interactions. The mechanism linking grapefruit with intestinal CYP3A4 inhibition is well described; evidence concerning phenytoin is substantially less certain. The three-condition framework for

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grapefruit—oral administration, incomplete bioavailability and extensive CYP3A4 metabolism—can help identify medicines at risk [5]. Because the enzyme is irreversibly inhibited and activity recovers over 2–3 days, separating grapefruit juice and a medicine by only a few hours may not reliably prevent an interaction. For affected medicines, avoiding grapefruit or considering an alternative medicine is therefore more consistent with the reported mechanism [5].

Food does not alter the total exposure of many newer cardiovascular and antidiabetic medicines, although it may delay absorption or reduce peak concentrations; oral semaglutide and pitavastatin are reported exceptions [9]. The effect may also depend on dosage form: the available levothyroxine–coffee finding concerns an oral solution and comes from a manufacturer-sponsored conference abstract, so it cannot be generalised to tablets [12]. For antifungal medicines, the interaction varies with the drug's physicochemical properties, formulation, food type and patient characteristics [10].

The main challenge with chelation is its prevention in routine care. In the Jeddah hospital study, fluoroquinolones or tetracyclines and cation-containing products were administered simultaneously in 74.5% of the relevant cases [6]. The authors describe the difficulty of maintaining dose intervals in older patients taking multiple medicines, as well as alert fatigue and possible schedule changes for cation-containing products. They also report that an educational intervention in a U.S. study reduced simultaneous administration from 72.5% to 10% [6]. Although the same chelation mechanism is expected with dairy products, this analysis did not identify direct clinical measurements for those foods.

For warfarin, current advice favours a consistent daily intake of vitamin K rather than eliminating vitamin K-rich foods [7]. Food effects on direct oral anticoagulants are less fully characterised, although they may be clinically relevant [7, 8].

The evidence base also limits firm recommendations. In the phenytoin review, half of the 12 included studies involved 5–24 healthy volunteers, and four were single-patient case reports; most did not control for confounding factors [11]. Limited evidence does not rule out an interaction, so monitoring remains appropriate for medicines with a narrow therapeutic index when a relevant interaction is suspected.

Surveys of patients and health professionals in several countries point to the value of documenting dietary history and providing education [3, 13–15]. Databases and interaction-checking resources are also developing, while regulatory guidance continues to be updated [1, 2, 4].

When prescribing, ask about foods, beverages such as grapefruit, dairy products, tea, coffee and alcohol, and dietary supplements taken with the medicine [3]. Assess the medicine's bioavailability and metabolic pathway; when the three grapefruit-risk conditions are met, advise avoiding grapefruit or consider an alternative medicine [5]. Separate fluoroquinolones and tetracyclines from calcium- or iron-containing products according to the relevant product instructions, and adjust the schedule of the cation-containing product when needed [6]. For warfarin, recommend a consistent vitamin K intake [7]. Follow the product instructions for newer medicines, including taking oral semaglutide on an empty stomach [9]. When evidence is insufficient, as for some phenytoin interactions, consider monitoring drug concentrations where clinically appropriate [11]. Patient education should reinforce these steps [13].

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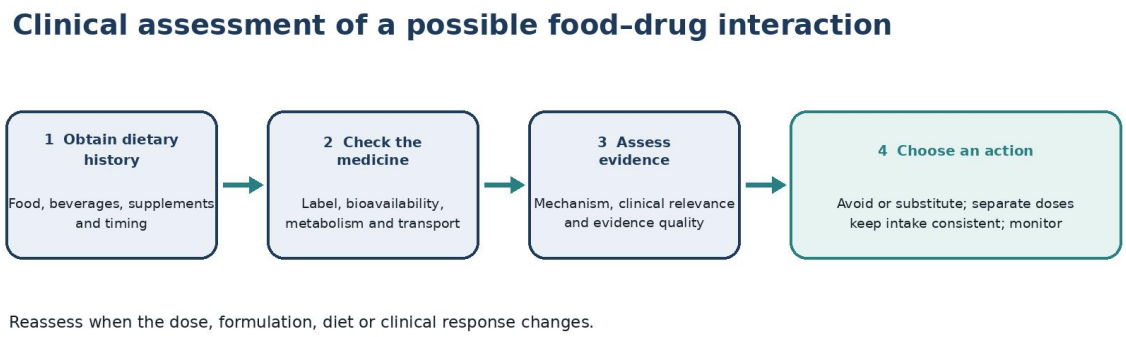


Figure 2. A practical sequence for assessing and managing a possible food–drug interaction. Synthesised from sources [3–11, 13].

The narrative design, the absence of formal risk-of-bias assessment, the limited breadth of the search, and the fact that only abstracts were analysed for many sources may affect the completeness and accuracy of the results (see Section 2). Many pharmacokinetic studies were done in healthy volunteers, so caution is needed when extrapolating them to sick and elderly patients. None of the included sources was conducted in Uzbekistan; studies on local dietary habits are needed.

Conclusion

Food–drug interactions arise through changes in absorption, intestinal enzyme or transporter activity, chelation and pharmacodynamic effects; their clinical significance depends on the medicine's bioavailability and metabolic pathway. The clearest evidence in this review concerns grapefruit-mediated intestinal CYP3A4 inhibition, chelation between cations and fluoroquinolones or tetracyclines, and maintaining a consistent vitamin K intake during warfarin therapy. Most newer cardiovascular and antidiabetic medicines can be taken irrespective of meals, although oral semaglutide and pitavastatin are exceptions. Evidence concerning phenytoin, antifungal medicines and levothyroxine remains limited or uncertain; for medicines with a narrow therapeutic index, concentration monitoring may be appropriate. In practice, clinicians should obtain a dietary history, follow medicine-specific instructions for dose timing, educate patients and consider local studies that reflect dietary habits in Uzbekistan.

References

1. Lacruz-Pleguezuelos B, Piette O, Garranzo M, et al. FooDrugs: a comprehensive food–drug interactions database with text documents and transcriptional data. Database (Oxford). 2023;2023:baad075. doi:10.1093/database/baad075
2. Roy R, Marakkar S, Vayalil MP, et al. Drug-food interactions in the era of molecular big data, machine intelligence, and personalized health. Recent Adv Food Nutr Agric. 2022;13(1):27–50. doi:10.2174/2212798412666220620104809

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www.jadr.co.in

Volume 17, Issue 05 | Received 23.10.2026 | Accepted 28.10.2026 | Online 2.11.2026

3. Tolou-Ghamari Z. Interactions among drugs, food, beverages, alcohol, herbs, phytochemicals, nutraceuticals, and micronutrients: a current and updated review. Cardiovasc Hematol Agents Med Chem. 2026;24(2). [pages and DOI to be completed]
4. U.S. Food and Drug Administration, CDER. Assessing the effects of food on drugs in INDs and NDAs — clinical pharmacology considerations: guidance for industry, revision 1. May 2026. https://www.fda.gov/media/121313/download
5. Abu Dayyih W, Al-Ani I, Hailat M, et al. Review of grapefruit juice–drugs interactions mediated by intestinal CYP3A4 inhibition. J Appl Pharm Sci. 2024;14(05):059–068. doi:10.7324/JAPS.2024.160197
6. Eljaaly K, Helal A, Almandeel T, Algarni R, Alshehri S. Multivalent cations interactions with fluoroquinolones or tetracyclines: a cross-sectional study. Saudi J Biol Sci. 2021;28(12):6929–6932. doi:10.1016/j.sjbs.2021.07.065
7. Talasaz AH, McGonagle B, HajiQasemi M. Pharmacokinetic and pharmacodynamic interactions between food or herbal products and oral anticoagulants: evidence review, practical recommendations, and knowledge gaps. Semin Thromb Hemost. 2024. doi:10.1055/s-0044-1790258
8. Grześk G, Rogowicz D, Wołowiec Ł, et al. The clinical significance of drug–food interactions of direct oral anticoagulants. Int J Mol Sci. 2021;22(16):8531. doi:10.3390/ijms22168531
9. Food-drug interactions of novel drugs used in cardiologic and diabetic patients — a PRISMA scoping review. [authors and journal to be completed]. PMID: 42124949
10. [Authors]. The impact of dietary interventions on the pharmacokinetics of antifungal drugs: a systematic review with meta-analyses. Clin Pharmacokinet. 2025. doi:10.1007/s40262-025-01511-6. PMID: 40347349
11. Orellana-Paucar AM, Mosquera-Lopez ET, Bustamante-Alvarez NM, et al. Optimizing phenytoin therapy: a systematic review of clinically relevant food and herb interactions. Front Pharmacol. 2026;16:1676685. doi:10.3389/fphar.2025.1676685
12. Washington K, et al. Levothyroxine sodium oral solution administered with coffee versus fasting: bioavailability study [conference abstract; verify full title]. ENDO 2022, Endocrine Society annual meeting, Atlanta, 11–14 June 2022. Reported by: HealthDay News, 17 June 2022 (Endo: coffee doesn't mar bioavailability of levothyroxine solution).
13. Kuźbicka K, Pawłowska I, Pawłowski L, Kocić I. Awareness and knowledge of drug-drug and food-drug interactions among adults in Poland — a questionnaire-based survey. Eur J Transl Clin Med. 2024;7(2):40–49.
14. Megaw C, Olivier N, Cordier W. South African dietitians' knowledge and perceptions of food-drug interactions and factors affecting it. J Hum Nutr Diet. 2025. doi:10.1111/jhn.70010
15. Saleh MA, Mohammed SS. Knowledge, awareness, and attitudes toward food–drug interactions among a sample of the Iraqi population in Baghdad: a cross-sectional study. J Nutr Food Secur. 2026;11(3):386–392.