DRUG-FOOD INTERACTIONS: THE HIDDEN FRONTIER IN CLINICAL PRACTICE

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A drug interaction is a situation in which a substance affects the activity of a drug, i.e., the effects are either increased decreased, or a new effect is produced that neither substance causes on its own.[1] It represents an important source of medication errors.[2] In contemporary clinical practice, drug-drug interactions (DDIs) are a well-established concern, and there are protocols, alerts, and clinical guidelines in place to reduce harm.[3] In contrast, drug-food interactions (DFIs) have long been under-recognised and frequently overlooked in pharmacotherapy. Several factors contribute to the neglect of DFIs. Firstly, DFIs receive little attention in most clinical medicine curricula. While students are trained to screen for DDIs, few are taught about DFIs. Secondly, most electronic medical record systems and pharmacy software offer limited or weak alerts for drug-food interactions. This creates a blind spot in prescribing and dispensing practices. Thirdly, clinical workloads and time constraints often prevent clinicians and pharmacists from providing dietary guidance. Moreover, significant food effects complicate the development of new drugs, especially when clinical plans require controlled or monitored food intake during dosing. So, predicting whether a drug or its product will exhibit a food effect in humans remains a challenge.

Clinically significant DFIs may result from changes in pharmaceutical, pharmacokinetic, or pharmacodynamic properties. These interactions can influence the absorption, metabolism, distribution, or elimination of drugs in various ways. For example, a high-fat meal can increase the solubility and, therefore, the absorption of lipophilic drugs, potentially enhancing their effects. Conversely, certain components of food may inhibit or induce drug-metabolising enzymes or transporters, such as cytochrome P450 enzymes or P-glycoprotein**,** which can lead to increased toxicity or reduced therapeutic efficacy. Moreover**,** DFIs can alter pharmacodynamics by directly affecting the mechanism of drug action at its site of effect. These interactions may result in additive, synergistic, or antagonistic outcomes. Despite this complexity and potential clinical impact, DFIs are often given less attention in clinical discussions and prescribing practices compared to drug-drug interactions. The most important drug-food interactions are those associated with a high risk of treatment failure due to reduced bioavailability in the fed state. These interactions are observed between milk and other dairy products, as well as iron salts, tetracycline derivatives, and antacids containing polyvalent cations, resulting in a significant reduction in their bioavailability of 50–90% or more.[4,5] Numerous reports have documented interactions between drugs and grapefruit juice (GFJ). GFJ contains furanocoumarins that inhibit intestinal CYP3A4, significantly increasing the oral bioavailability of drugs such as felodipine, midazolam, and cyclosporine, which may potentially raise their plasma concentrations to toxic levels. Furanocoumarins also increase the bioavailability of certain statins, including simvastatin and atorvastatin, thereby increasing the risk of myopathy and rhabdomyolysis.[6] Tyramine-containing foods such as cheese, red wine, overripe bananas, yoghurt, etc., can trigger hypertensive crises in patients taking monoamine oxidase inhibitors (MAOIs) by promoting excessive norepinephrine release.[7] Warfarin, one of the most commonly prescribed oral anticoagulants, are affected by foods high in vitamin K. Leafy greens like spinach, lettuce, parsley, and fenugreek can reduce the effectiveness of warfarin, potentially resulting in sub-therapeutic INR levels and a higher risk of clot formation.[8]

As healthcare continues to shift toward precision medicine and patient-centred care, there is an urgent need to revisit the pharmacological implications of food. Addressing this overlooked area requires a multipronged approach, including the incorporation of DFIs into undergraduate and postgraduate medical education, as well as the embedding of food interaction warnings and management strategies into clinical guidelines, particularly for high-risk or commonly prescribed medications. This approach also involves incorporating DFI alert modules into electronic health record systems and providing dietary guidance through patient counselling. In addition, supporting research into unrecognised DFIs, including those involving nutraceuticals, herbal supplements, and nutritional trends, is essential for identifying new risks. As medical educators, we need to bring drug-food interactions from the footnotes to the forefront of clinical care. "It‘s time we regard food as a pharmacological variable, not an afterthought. A meal can be medicine or a mistake when taken with certain drugs".

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