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TECHNOLOGY****INTERACTION OF FOODS AND DRUGS INVOLVING  
NUTRIENTS AND ENZYMES****Trupti Tambe\***

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**ABSTRACT**

Healthcare providers, such as physicians, pharmacists, nurses, and dietitians, have to be aware of important food-drug interactions in order to optimize the therapeutic efficacy of prescribed and over-the-counter drugs. Here, we review some of the most widely consumed fruits and vegetables to inform healthcare providers of possible nutrient-drug interactions and their potential clinical significance. A Thousands of drugs are commercially available and a great percentage of the population takes at least one pharmacologically active agent on a regular basis. Given this magnitude of use and variability in individual nutritional status, dietary habits and food composition, there is a high potential for drug-nutrient interactions. However, there is a relatively short list of documented fruit-drug or vegetable-drug interactions, necessitating further and extensive clinical evaluation.

There are currently few studies that combine a nutrient-based and detailed pharmacological approach, or studies that systematically explore the risk and benefits of fruit and vegetables. There are numerous patients who encounter increased risks of adverse events associated with drug-nutrient interactions. These include elderly patients, patients with cancer and/or malnutrition, gastrointestinal tract dysfunctions, acquired immunodeficiency syndrome and chronic diseases that require the use of multiple drugs, as well as those receiving enteral nutrition or transplants. Therefore, the main reason for devoting a major review to nutrient-drug interactions is the enormous importance of fruits and vegetables used for their beneficial effects as nutrients and as components in folk medicine

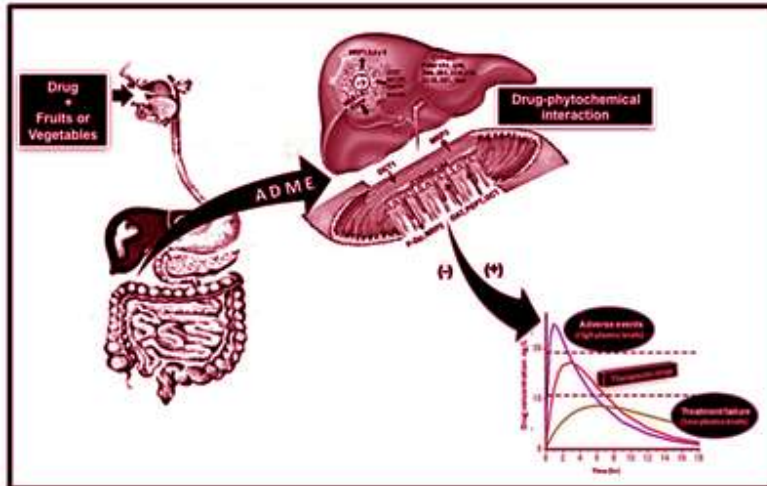
**KEYWORDS:** Enzymes, drug-nutrient, Nutrients.

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**INTRODUCTION****Food-drug interactions:**

A drug-nutrient interaction is defined as the result of a physical, chemical, physiological, or pathophysiological relationship between a drug and a nutrient. An interaction is considered significant from a clinical perspective if it alters the therapeutic response. Food-drug interactions can result in two main clinical effects: the decreased bioavailability of a drug, which predisposes to treatment failure, or an increased bioavailability, which increases the risk of adverse events and may even precipitate toxicities (See Figure).

Drug-drug interactions are widely recognized and evaluated as part of the drug-approval process, whether pharmaceutical, pharmacokinetic, or pharmacodynamic in nature, For healthy-treatment intervention, it is necessary to understand how these drug-food interactions can induce a beneficial result or lead to detrimental therapeutic conditions (less therapeutic action or more toxicity). Equal attention must be paid to food-drug interactions, Drug metabolizing enzymes and drug transporters play important roles in modulating drug absorption, distribution, metabolism, and elimination. Acting alone or in concert with each other, they can affect the pharmacokinetics and pharmacodynamics of a drug. The interplay between drug metabolizing enzymes and transporters is one of the confounding factors that have been recently shown to contribute to potential complex drug interactions.



### Fruit/Vegetables and drug transporters:

Drug absorption across the gastrointestinal tract is highly dependent on affinity for membrane transporters as well as lipophilicity. On the other hand, the liver plays a key role in the clearance and excretion of many drugs. Hepatic transporters are membrane proteins that primarily facilitate nutrient and endogenous substrate transport into the cell via uptake transporters, or protect the cell by pumping out toxic chemicals via canalicular transporters. Oral administration of drugs, however, may lead to limited and variable oral bioavailability because of absorption across the intestinal barrier.

The major uptake transporters responsible for nutrient and xenobiotic transport, both uptake and efflux transporters, belong to the two solute carrier (SLC and SLCO) superfamilies.

### Nutrient-drug interactions: examples with clinical relevance

According to the World Health Organization (WHO), increased daily fruit and vegetable intake could help prevent major chronic non-communicable diseases [2].

#### 1) Orange (*Citrus sinensis*):

Previous studies in humans using fexofenadine as a probe showed that oral coadministration with orange juice decreased the oral bioavailability of fexofenadine [4]. Orange juice and its constituents were shown to interact with members of the OATP transporter family by reducing their activities. Orange juice might reduce the intestinal absorption of substrates of OATP-B (e.g., digoxin, benzylpenicillin, and hormone conjugates), resulting in a decrease in concentration in the blood. It has been previously shown that consumption of a single 240 mL serving of Sevilla orange juice resulted in a 76% increase in felodipine exposure, comparable to what is observed after grapefruit juice consumption [3].

#### 2) Grapes (*Vitis vinifera*):

The grape is considered a source of unique and potentially useful medicinal natural products; they are also used in the manufacturing of various industrial products. Resveratrol is an electron-rich molecule with two aromatic benzene rings linked by an ethylene bridge. CYP3A-mediated aromatic hydroxylation and epoxidation of resveratrol are possible, resulting in a reactive p-benzoquinone methide metabolite which is capable of binding covalently to CYP3A4, leading to inactivation and potential drug interactions.

#### 3) Pomegranate (*Punica granatum*):

It has been reported that pomegranate juice influenced the pharmacokinetics of carbamazepine in rats by inhibiting enteric CYP3A activity. Such inhibition of the enteric CYP3A activity by a single exposure to pomegranate juice appears to last for approximately 3 days [5].

**4) Guava (*Psidium guajava* L)**

There is only one report about the effect of guava extracts on drug transport: guava extract showed a potent inhibitory effect on P-gp mediated efflux in Caco-2 cells. It was also found to inhibit efflux transport from serosal to mucosal surfaces in the rat ileum. This means that guava could interact with P-gp substrates such as digoxin, fexofenadine, indinavir, vincristine, colchicine, topotecan, and paclitaxel in the small intestine. For this reason, this fruit should be consumed with caution by patients taking medicines.

**5) Apple (*Malus domestica*)**

It has been found that apple juice extract inhibits CYP1A1 at levels of CYP1A1 mRNA, protein, and enzymatic activity. On the other hand, it has also been reported that apple juice and its constituents can interact with members of the OATP transporter family (OATP-1, OATP-3 and NTCP) by reducing their activities *in vitro*. The functional consequence of such an interaction was a significant reduction in the oral bioavailability of fexofenadine in human plasma levels, possibly by preferential direct inhibition of intestinal OATP activity.

**6) Grapefruit (*Citrus paradisi*)**

Several findings showed that grapefruit juice had a major effect on the intestinal CYP system with a minor effect at the hepatic level. The predominant mechanism for this interaction is the inhibition of cytochrome P-450 3A4 in the small intestine, which results in a significant reduction of drug presystemic metabolism. The interaction of grapefruit with certain drugs was unintentionally discovered two decades ago. Since then, there have been numerous reports on the effects of grapefruit and its components on CYP450 drug oxidation and transportation.

**CONCLUSION**

As a consequence, there is an increased global consumer demand for fruits and vegetables, and some consumers purchase organic foods with the understanding that they are healthy. WHO and the Food and Agriculture Organization of the United Nations (FAO) recommend a daily intake of at least 400 grams or five servings of fruits and vegetables to aid in the prevention of chronic illnesses such as heart disease, cancer, diabetes, and obesity. In industrialized countries, fruits and vegetables tend to have been subjected to some sort of processing (e.g., refrigeration, acidification, fermentation, and thermal, high pressure, chemical, or physical processing) that might have an effect on the bioactive compound. All of these factors could have an impact on the metabolism or transport of drugs in an individual, potentially altering pharmacological responses. Although the significance of interactions between drugs is widely appreciated, little attention has been given to interactions between drugs and nutrients. We have to prevent undesired and harmful clinical consequences.

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