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Editorial Open Access

Food, Supplements, and Drugs: Pharmacokinetics Interactions and their Implications

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Editorial

The bioavailability and bioactivity of xenobiotic molecules of foods, supplements and drugs are affected by two sets of transforming enzymes (Phase 1 and Phase 2) resulting in their conversion to polar metabolites that are more readily excreted in the bile or urine and by their efflux and uptake transporters (Phase 3) [1].

(1) Phase 1 metabolism is catalyzed by microsomal oxygenase enzymes, mainly the CYP 450 superfamily (50-200 isozymes in animals and *ca* 30 characterized in humans) exist in the liver and intestine and catalyze oxidation reactions such as

$$RH + O_2 + NADPH + H^+ \rightarrow ROH + NADP^+ + H_2O$$

as well as dealkylation, dehalogenation, epoxidation, and reduction reactions.

(2) Phase 2 metabolism is catalyzed by conjugation enzymes that add a polar conjugate (e.g. glucuronic acid, sulfate, or glycine) with certain chemical groups on the xenobiotic molecules such as —OH, —COOH, —NH_2, and —SH groups.

(3) Phase 3 metabolism, involving uptake and efflux transporters mediating the transport of xenobiotics between the intestinal lumen and the enterocytes.

The pharmacokinetic interaction between xenobiotics in foods, supplements, and drugs happen when these xenobiotics share metabolic enzymes and when they interact with the enzymes by enhancing or inhibiting their activities, which may affect the metabolism of other xenobiotics. The typical examples for food-drug interactions are those of grapefruit juice (*Citrus x paradisi* Macfad.) with cholesterol-lowering statin drugs, anticoagulants, calcium channel blockers, central nervous system drugs, cytotoxics, and immunosuppressants [2]. Some of these interactions are clinically significant especially the irreversible inhibition, by grapefruit furanocoumarins such as 6′,7′-dihydroxybergamottin, of the cytochrome P450 enzyme CYP3A4, which metabolizes about 50% of the drugs either in the small intestine or the liver [3]. Other fruit juices that interact with CYP 3A4 include *inter alias* pomegranate (*Punica granatum* L.) [4], Schisandra fruit (*Schisandra chinensis* (Turcz.) Baill.) [5], wild grape (*Vitis spp.*), black mulberry (*Morus nigra* L.), and black raspberry (*Rubus spp.*) [6]. Cranberry juice (*Vaccinium macrocarpon*) interacts with warfarin because of its high level of flavonoids that inhibit CYP P450 CYP2C9 the predominant enzymes in warfarin metabolism [7].

Besides food, supplement and drug interactions *via* CYP 450 isozymes, xenobiotics from these sources may affect each other's metabolism through interactions with phase 2 conjugating enzymes, mainly glucuronosyl transferases (UGTs), and sulfotransferases (SULTs). Cruciferous vegetables, citrus fruits, soy foods enhance the glucurinidation of relevant xenobiotics. In addition, ingestion of coffee (including decaffeinated), tea, chocolate, bananas, and citrus fruits can inhibit sulfation of certain xenobiotics, increases catecholamine, and elicit increases in blood pressure, migraine headaches, and/or atrial fibrillation in susceptible individuals [8]. In addition, certain xenobiotics interact by affecting the uptake and efflux transporters.

In summary, xenobiotics from food or supplement origin can alter, *via* physiologic and physicochemical mechanisms, drug absorption, distribution, metabolism, and/or excretion (ADME) and thereby, affect their bioavailability and biopotency. So far, studies have focused on the interactions between certain fruit juices and major drugs of chronic diseases. Besides fruit juices, xenobiotic molecules are concentrated in several herbs and spices and their interactions with drugs and supplements have not been studied. The study of these interactions are timely as the demography of the world is witnessing steady increase in the proportion of the elderly and middle age individuals who are on permanent medications. At the same time, there a tremendous increase in the number of nutraceutical supplements claimed for improved life quality. At the same times, trials are ongoing to produce "tailored foods" or "functional foods", in which the concentrations of certain phytochemicals are increased agronomically, by gene modification, or by food processing. This is an open area for future research and bioinformatics.

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