

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

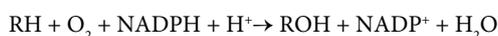
Afaf Kamal-Eldin*

Department of Food Science, United Arab Emirates University, UAE

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



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, —NH₂, 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 glucuronidation 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.

References

1. Won CS, Oberlies NH, Paine MF (2012) Mechanisms underlying food-drug interactions: inhibition of intestinal metabolism and transport. *Pharmacol Ther* 136: 186-201.
2. Pirmohamed M (2013) Drug-grapefruit juice interactions: two mechanisms are clear but individual responses vary. *BMJ* 346: f1.
3. He K, Iyer KR, Hayes RN, Sinz MW, Woolf TF, et al. (1998) Inactivation of cytochrome P450 3A4 by bergamottin, a component of grapefruit juice. *Chem Res Toxicol* 11: 252-259.
4. Hidaka M, Okumura M, Fujita K, Ogikubo T, Yamasaki K, et al. (2005) Effects of pomegranate juice on human cytochrome p450 3A (CYP3A) and carbamazepine pharmacokinetics in rats. *Drug Metab Dispos* 33: 644-648.
5. Iwata H, Tezuka Y, Kadota S, Hiratsuka A, Watabe T (2004) Identification and characterization of potent CYP3A4 inhibitors in Schisandra fruit extract. *Drug Metab Dispos* 32: 1351-1358.
6. Kim H, Yoon YJ, Shon JH, Cha IJ, Shin JG, et al. (2006) Inhibitory effects of fruit juices on CYP3A activity. *Drug Metab Dispos* 34: 521-523.
7. Rettie AE, Korzekwa KR, Kunze KL, Lawrence RF, Eddy AC, et al. (1992) Hydroxylation of warfarin by human cDNA-expressed cytochrome P-450: a role for P-450C9 in the etiology of (S)-warfarin-drug interactions. *Chem Res Toxicol* 5: 54-59.
8. Eagle K (2012) Toxicological effects of red wine, orange juice, and other dietary SULT1A inhibitors via excess catecholamines. *Food Chem Toxicol* 50: 2243-2249.

*Corresponding author: Afaf Kamal-Eldin, Department of Food Science, United Arab Emirates University, UAE, Tel: 00971 50 1389 248; E-mail: Afaf.Kamal-Eldin@uaeu.ac.ae

Received March 29, 2014; Accepted May 03, 2014; Published May 10, 2014

Citation: Kamal-Eldin A (2014) Food, Supplements and Drugs: Pharmacokinetics Interactions and their Implications. *J Bioequiv Availab* 6: e51 doi:10.4172/jbb.10000e51

Copyright: © 2014 Kamal-Eldin A. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.