Phytomolecules-drug interactions: clinical and nutritional implications

Phytomolecules from herbal products, as well as bioactive phytochemicals from plant foods and food dressings, have potential health effects [1-4]. However, it is known that herbal products and nutraceuticals could affect drug-metabolizing enzymes and transporters [5, 6].

In susceptible patients, phytomolecules–drug interactions may result in significant therapeutic changes for some drugs with a narrow therapeutic index and there is a growing interest on food-drug interactions. From a search in the MEDLINE database (20/11/2022) with the search terms "food-drug interactions" 2,918 results were retrieved (from 1976 to 2022; 110 case reports from 1995), of which 1,220 in the last ten years.

Moreover, in special populations, such as individuals with a spinal cord injury [3, 4, 7] the evaluation of risk for potential food or nutraceutical interactions with drugs should be monitored also considering the sedentary habit imposed by their condition [7]. Many bioactive compounds have non-linear dose–response effects, acting in the context of the hormetic-based lifestyle medicine [8]. Different health, nutritional, and training status could affect the interactions among phytochemicals and microbiota [8]. The latter is involved in the metabolism of some phytochemicals, such as flavonoids, having low bioavailability and some metabolites can have bioactivities [9]. Therefore, genetic polymorphisms of the detoxification systems, epigenetic mechanisms and differences in gut microbiome could account the inter-individual variability in both efficacy and toxicity [9]. From that, phytochemicals can act as drugs or pro-drugs and it is difficult to establish a therapeutic index [9, 10].

Moreover, some antioxidants from plant sources have antinutrient effects [11]. Despite the potential adverse effects of high doses of phytomolecules, nutraceuticals are considered safe. In this context was the neglected potential interaction between monacolin K (structurally identical to lovastatin) and some plant foods [12]. From that, the European Commission concluded: "considering the significant harmful effect on health associated with the use of monacolins from red yeast rice at levels of 10 mg/day, and individual cases of severe adverse health reactions at levels as low as 3 mg/day, the use of monacolins from red yeast rice at levels of 3 mg and more per portion of the product recommended for daily consumption should be prohibited".

Therefore, the potential risk of interaction between herbal products, dietary supplements and drugs should be evaluated considering the overall lifestyle and nutritional status by using a patient-centered approach.

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