

## 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.

### Dr. Ilaria Peluso

Research Centre for Food and Nutrition, Council for Agricultural Research and Economics, Rome 00178, Italy.

E-mail: [ilaria.peluso@crea.gov.it](mailto:ilaria.peluso@crea.gov.it)

<https://orcid.org/0000-0002-6210-5241>

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