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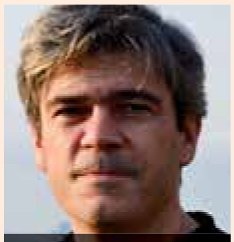
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Complex foods
versus functional foods, nutraceuticals and dietary supplements: differential health impact (Part 2)

KEYWORDS: complex foods, functional foods, nutraceuticals, food structure, synergy, human studies, health potential.

Abstract What differentiates natural complex foods from nutraceuticals and dietary supplements is food structure, this latter involving nutrient interaction and synergism, and a complex mixture at nutritional doses. Scientific evidence showed that functional foods, nutraceuticals and dietary supplements (FND) have failed stopping chronic diseases epidemics: most conclusions of recent meta-analyses and systematic reviews are lack of significant health effect and needs for further studies. Why such disappointing results? Probably because FND results from a curative and reductionist nutritional approach while complex foods participates in a preventive and holistic approach. Indeed, reductionism has led to fractionate foods, isolating compounds from them for use at supra-nutritional doses in FND. Holism considers foods as complex systems in which the whole is more than sum of the parts leading to more sustainable health effects, and technological treatments more respectful of food structure.

An emphasis on synergism
Synergy means that 1 + 1 is not equal to 2 but is higher than 2, e.g., as eloquently shown in vitro with a mix of rutin, *p*-coumaric acid, abscisic acid (1). In other words, the whole is more than the sum of the parts. For example, the strength of a cable is higher than the sum of the strengths of each steel rope constitutive of the cable and taken separately. Examples could be multiplied indefinitely.
In addition, there are more and more papers showing convincing results about this issue.

Thus, Rayalam et al. have studied synergism between resveratrol and other phytochemicals and the implications for obesity and osteoporosis. They concluded that "combining resveratrol with other phytochemicals may provide an extraordinary potential for preventing obesity and osteoporosis by not only decreasing the dose of each compound, thereby avoiding potential toxic side effects, but also by targeting multiple signaling pathways affecting adipogenesis, apoptosis, lipolysis and osteogenesis simultaneously" and added that "these phytochemical synergies may make possible novel safe, potent and efficacious therapies"(2). Further, Wang et al. concluded that "combining foods across food categories was more likely to create an antioxidant synergism" (3).

In another study, authors have investigated the effect of botanical diversity on antioxidant status in healthy women. The reduction in urinary isoprostanes is higher following consumption of eighteen fruits and vegetable species than with only five botanical species. Authors concluded that "botanical diversity plays a role in determining the bioactivity of high-vegetable and fruit diets and that smaller amounts of many phytochemicals may have greater beneficial effects than larger amounts of fewer phytochemicals" (4). The second study is an observational study in which authors have tested the effect of fruit and vegetable variety *versus* quantity consumed: the consumption of a high variety of fruits and vegetables, but not quantity, was associated with significant better cognitive test scores (5).

These examples well illustrate that increasing botanical varieties within diets increases the number and diversity of bioactive compounds rather than their amount, leading to beneficial synergetic effects which are less predominant when increasing the quantity of only a few food compounds. This may have important implications for nutritional policies. For example, it is not sufficient recommending increasing fruit and vegetable consumption - such as in the French Programme National Nutrition Santé guidelines marks -, one must also recommend to increase botanical diversity.

The role of food structure

After synergy effect, the beneficial roles played by structure of complex foods must be emphasized. The number of human studies illustrating the role played by food structure is many (6). The first having emphasized this point was led in 1977: intact apple, apple purée and apple juice were tested in healthy subjects for their effect on post-prandial glycaemia, insulinaemia and satiety. Results showed that the more the original apple is destructured or refined, the less it is satiating and the higher the insulinemic response, while no significant effect on glycaemia (7). There is also another interesting study by Granfeldt et al. in 1991 about durum wheat and the influence of processing on food structure: pasta and bread made of the same ingredients, i.e., durum wheat, exhibited different glycaemic and insulinaemic responses due to their different food structure (8). In addition to food form, food cohesiveness or density may also play an important role on food health effect. For example, breads with different crumb density have not the same glycaemic and satiety responses. Thus, in the studies by Burton et al. and by Saulnier et al., a significant correlation between bread crumb density and glycaemic response has been found (9-10).

Besides the role of food structure characteristics on physiology, there is also the role played by nutrient interaction within the complex food matrix: they can be either deleterious as for antinutrients or beneficials as for other kinds of interactions, e.g., with fiber.

Antinutrients

Antinutrients are well known to chelate minerals and to limit their bioavailability (11). They are polyphenols, phytic acid and other phytochemicals such as lectins and some saponins. They are generally accumulated in the plant under stress conditions or pro-oxidative conditions, e.g., to fight against insects. So, plant-based micronutrients, in their natural form, are generally only partially bioavailable. For example, iron in cereal products is no more than 20% bioavailable in humans, magnesium no more than 30% and zinc no more than 20% (12). Therefore, processing is an important means 1) to reduce anti-nutrients levels, e.g., legume and cereal pre-fermentation and pre-germination as used in developing countries; but also 2) to release bound form of some micronutrients into more bioavailable free form (13).

The fiber co-passengers

In addition to interaction with phytic acid, there are also interactions with the fiber fraction. The concept of 'fiber co-passengers' has been developed recently, apparently first by Vitaglione et al. in 2008: fiber co-passengers are all the non-energy nutrients bound to fiber and that arrive at colonic level where they exert their physiological effect, e.g., phenolic antioxidants bound to fiber (14). According to Vitaglione et al., antioxidants bound to fiber would be protected by them within food structure to reach the colon where they can exert their full potential, i.e., the trapping of free radicals released by bacteria metabolism (protection against colon cancer?), and the progressive release of antioxidants that pass through the intestinal barrier to reach bloodstream where they can protect from LDL oxidation, then from cardiovascular disease risk such as atherosclerosis (14).

Food structure and bioavailability

In a nutritional supplement, micronutrients are generally almost 100% bioavailable. Therefore, complex foods and supplements do not lead to the same kinetics of micronutrient release within organism; but for which effects? Indeed, the differential health effects of different kinetics of micro- and phyto-nutrients release are not known on a long term. Therefore, I think this is the most important and urgent research issue to address. However, in some specific nutritional situations, this is undoubtedly useful to increase micronutrient bioavailability, as for example through vitamin A supplementation in some developing countries where severe deficiencies can occur. Indeed, in population that mainly consumes vegetable products, there may be problem with micronutrient bioavailability to organism.

So, according to food matrix characteristics, nutrients are not equally bioavailable and released at the same kinetic within digestive tract. This is true for starch, but also for lipids and proteins. The same is also true for fiber: according to their physico-chemical characteristics such as solubility, degree of polymerization, water-holding capacity, porosity, viscosity, etc., they are not fermented equally: thus, soluble fiber are rapidly fermented, releasing a high amount of short-chain fatty acids at a given colonic site while insoluble fibre are partially and more progressively fermented.

In addition to macronutrients and fiber, there are also free and bound micronutrients. For example, free and bound ferulic acid have not the same nutritional effect due to different kinetics of release: free ferulic acid (1-5%) is released in the upper digestive tract where it may play a role in cell signaling while bound ferulic acid (95-99%) is more progressively released and would play a major antioxidant role at colonic level.

TOWARD NEW TECHNOLOGICAL PROCESSES

However, between supplements and natural food products, maybe there is a golden mean to find? Indeed, technological processes may well play the role to modify nutrient bioavailability, provided it is for the best (15). For example, gelatinization of starch increases its digestibility. One can also beneficially search to increase bioavailability of vitamins and polyphenols. For example, degrading phytates and increasing mineral absorption may be very interesting in developing countries where there are mineral deficiencies. Thus, pre-fermentation, soaking and germination are very used in developing countries to improve nutritional density of grain products; and to increase micronutrient bioavailability (13). Here, regarding fermentation and germination of rye, results clearly show that fermentation plus germination is the most efficient in increasing amount of bioactive compounds (some bound compounds being initially physiologically inactive) (16).

This leads to the concept of 'minimal processing' that is a good compromise between highly refined processed foods and natural foods, sometimes not edible as such (17). I think that the main issue of processing is to preserve both food structure and nutrient density, but also palatability (because it has been shown that a highly nutritious food will not be consumed if its organoleptic properties are low). Finally, processing may help to reach the following objective: to be a 'friend' of natural foods and help them to give the best! For example, cereal micronutrient density can be preserved via less refined flours and less drastic thermal treatments.

CONCLUSIONS AND PERSPECTIVES

Functional foods, nutraceuticals and dietary supplements do not really succeed in stopping obesity and diabetes epidemics and in preventing from cancers and cardiovascular diseases in developed and emerging countries; but they remain very useful in some circumstances. Besides, there is today a body of evidence showing that the whole is best than the sum of the parts, because of synergism, interactions with digestive environment and satiety effect. Therefore, it is now time to develop new minimal processes, because processing is probably the most significant lever to rapidly improve food nutritional quality (e.g., more rapid than genetic selection, and more efficient on a long term than dietary supplements).

Otherwise, while the last decades were characterized by a reductionist and pharmacologic approach applied to human nutrition, the future should include a more holistic approach applied to foods and diets and complementary to the reductionist approach (6). Focus should be put more on preventive nutrition and complex foods. A holistic view of food will help preserve more its complex and natural matrix. Consequently, this will help improving nutritional recommendations (6).

Concerning the reductionist approach, it is well characteristic from Western societies (18). It has led to major scientific discoveries. Reductionism aims at isolating components of a system to better understand how it works. Therefore, its major drawback is to see the system through a reduced view with the risk to conclude that this partial view explain the whole. Thus, during these last twenty years of research, one has mainly focused on the physiological and health effect of food nutrient taken one by one; which has led to associate one compound with one physiological mechanism. This has led to think that only one compound may prevent the organism from chronic diseases, as for isolated antioxidants. Obviously, this is not true: foods are complex systems and not drugs, and human organism is complex as well: so, there is today a real need for more holistic approaches, historically originating from Asia. For this, we need more generalist, holistic and transversal researchers to work together with highly specialized and reductionist researchers (18).

This questioning is not really new as we can read in the paper of Visioli in 2011: "In summary, the development of new experimental paradigms to appropriately study the effects of food items on human health should be actively sought after, and public health authorities should reconsider their approach to regulations and guidelines" (19).

In the end, foods being not drugs, it is now urgent to shift from a reductionist and pharmacological approach to a holistic and integrative approach in nutrition research.

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