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Editorial

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A Key to Understanding the Effects of Food Bioactives in Health, Gut Microbiota

In the past few years there has been a renewed interest in the study of the relationship between food and health, where plant-derived food has been in the focus of interest by food scientists and nutritionists. The evidence of the biological effects, however, has been very difficult to validate as there are large discrepancies between the effects observed in vitro and the response observed in vivo, which is generally subjected to large interindividual variability.[1,2] A relevant part of this variability can be explained by differences in the metabolism of dietary constituents by the gut microbiota,[3] as specific bacterial communities with distinct metabolic capabilities are found in different volunteers. The metabolism of food constituents by the gut microbiota has been revealed to be a key factor for the biological effects of many food constituents, and the interaction of constituents with gut microbiota is an emerging field of research that will add to our understanding of the role of food constituents in human health.[1,2]

Recent studies have demonstrated the complexity of the microbial populations that colonize the human gut, in which trillions of cells[4] and thousands of bacterial species[5] occur. A human microbial gene catalog has been recently published,[5] and the collective genome of these gut bacteria, named "microbiome", contains at least a hundred times as many genes as the human genome.[4] These bacteria contribute up to 2 kg of our body weight, and differences in gut microbiota communities have been associated with health status.[6−8] Evidence of correlations between specific gut microbiota compositions and obesity,[9,10] cardiovascular diseases,[11] and type 2 diabetes[12] has been reported. It has also recently been demonstrated that individuals can be stratified by their metagenomic profile into different "enterotypes".[13] Therefore, there has been an interest in modulating gut microbiota to modify health status either by dietary treatments[14,15] or by microbiota transfers that have proved useful in animals[9] and humans.[16]

During food digestion, a large number of food chemical constituents, and particularly in plant-derived foods, are not digested and absorbed in the small intestine and reach the colon, where they are metabolized by the gut microbiota to different metabolites that can either be absorbed or remain in the gut and then exert effects on health. This has been known for a long time for fiber, but now it has also been demonstrated for other food constituents, particularly phytochemicals.[3]

The dietary modification of gut microbiota by dietary constituents has traditionally been attempted by the supply of live bacteria in food, "probiotics", by indigestible or limited-digestible food constituents ("prebiotics"), or by both ("synbiotics").[17] Recent studies have opened new opportunities to study the interaction of food constituents with gut microbiota. This is considered a dual interaction as food constituents can modulate gut microbiota and the gut microbes can transform food constituents, providing different metabolites and biological effects depending on the microbial strains that colonize the gut.[1,2]

It is known that food constituents can promote the growth of specific bacterial strains while they prevent the growth of others. This type of interaction includes the prebiotic effect, which has been known for a long time, by which prebiotic constituents of food (some dietary fibers, etc.) can promote the growth of "beneficial" bacteria including lactobacilli and bifidobacteria. There is an increasing knowledge on how different gut bacteria can have effects on human health and different functions, and therefore the role of food constituents on bacterial strains will be much wider than the well-known prebiotic effect. Little is known, however, on the mechanisms by which food constituents modulate gut microbiota. Some suggestions are as follows:

(1) Bacterial strains are able to metabolize some food constituents and can get nutrients from an indigestible material and therefore can grow better than other bacteria that cannot use these food constituents as a source of energy.

(2) Food constituents can be toxic to some bacterial strains, and therefore those that are more resistant to these toxic compounds (e.g., phenolics, sulfur-containing compounds) can grow better in the presence of these food constituents.

(3) Gut bacteria can communicate using chemical signals (i.e., homoserinlactones) known as "quorum sensing" phenomenon. Thus, food constituents can interact with this communication system, modulating the production of these signals and/or the interaction with the receptors, which affects the growth of specific bacteria and the way they colonize the colon.

(4) Interaction of chemical constituents with nutrients and growth factorsis required for the growth of some bacteria.

In a second way, gut microbiota can transform food constituents, and this metabolism will be different depending on the microbial strains that compose our gut. This has already been demonstrated for some phenolic food constituents, as the transformation of soy isoflavones into equol, a more active metabolite of daidzein, depends on the gut microbiota, and volunteers that are either equol producers or non-equol-producers have been described. This has also been found in the metabolism of lignans, hops flavanones, ellagitannins, and ellagic acid.[3] Gut microbiota can also affect the rate of hydrolysis of rhamnosides, glycosides that cannot be hydrolyzed by human enzymes and that need gut bacteria for hydrolysis before absorption. This is the case of orange juice flavanones and many other flavonoid rutinosides.

Therefore, it is essential to understand how these food constituents are metabolized by gut microbiota, the metabolites produced (advanced analytical methods), and the bacteria responsible for specific biochemical transformations and production of specific bioactive metabolites from food constituents (combinations of microbiology and metabolites analysis) and how these food constituents can modulate the gut

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microbiota (microbiology) and therefore induce changes in the gut microbial populations to optimize microbial communities for human health (nutritional studies).

The *Journal of Agricultural and Food Chemistry* has identified gut microbiota research as an important topic in the area of food science and nutrition and, therefore, is committed to increase the knowledge in the field of the interactions of food chemical constituents and gut microbiota. In this Virtual Issue on Gut Microbiota, the perspectives of food and nutrition on gut microbiota are highlighted (Slupsky). The modification of gut microbiota, and particularly lactobacilli and biffidobacteria, by different food constituents (galacto-oligisaccharides, polyphenols, pyroglutamylleucine, and yeast and blueberry extracts) has also been covered. The study of the effect of food constituents on both luminal and mucosal microbiota is shown to be a very promising research topic. In addition, the analysis of the urine microbial metabolite fingerprinting after the intake of specific food products has been identified as a relevant tool; results can be directly associated with the metabolism of food constituents in the gut. Microbial metabolite fingerprinting of feces is also a relevant point of interest in this field, as it reflects the events taking place in the gut without the introduction of the interindividual variability due to absorption (presence or absence of specific transporters) and human metabolism. The analysis of specific metabolic changes of food constituents by probiotic strains (lactobacilli and biffidobacteria) is also identified as a promising field of research, as these bacteria could be easily incorporated as food ingredients in food formulations. Thus, probiotic strains with specific hydrolytic or metabolic capabilities can lead to a better absorption of bioactive food constituents and, therefore, could lead to the development of new food products and formulations with better health properties. The transformations of dietary constituents by gut microbiota and the identification of the metabolites produced are also active fields of research studying the changes in polyphenols (ellagitannins and wine polyphenols), carbohydrates (arabinoxylans), lignans, and other phytochemicals.

Advances in this field will allow the development of new food products with specific health effects, either to modulate the gut microbiota or to incorporate specific bacteria responsible for the interaction of food constituents to improve the health effects of food.

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Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.

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