

Interactions of gut microbiota with functional food components and nutraceuticals

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15 **Keywords:** gut microbiota; functional foods; nutraceuticals; prebiotics;
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Abstract

The human gut is populated by an array of bacterial species, which develop important metabolic and immune functions, with a marked effect on the nutritional and health status of the host. Dietary component also play beneficial roles beyond basic nutrition, leading to the development of the functional food concept and nutraceuticals. Prebiotics, polyunsaturated fatty acids (PUFAs) and phytochemicals are the most well characterized dietary bioactive compounds. The beneficial effects of prebiotics mainly relay on their influence on the gut microbiota composition and their ability to generate fermentation products (short-chain fatty acids) with diverse biological roles. PUFASs include the ω -3 and ω -6 fatty acids, whose balance may influence diverse aspects of immunity and metabolism. Moreover, interactions between PUFAs and components of the gut microbiota may also influence their biological roles. Phytochemicals are bioactive non-nutrient plant compounds, which have raised interest because of their potential effects as antioxidants, antiestrogens, anti-inflammatory, immunomodulatory, and anticarcinogenics. However, the bioavailability and effects of polyphenols greatly depend on their transformation by components of the gut microbiota. Phytochemicals and their metabolic products may also inhibit pathogenic bacteria while stimulate the growth of beneficial bacteria, exerting prebiotic-like effects. Therefore, the intestinal microbiota is both a target for nutritional intervention and a factor influencing the biological activity of other food compounds acquired orally. This review focuses on the reciprocal interactions between the gut microbiota and functional food components, and the consequences of these interactions on human health.

Keywords: gut microbiota; functional foods; nutraceuticals; prebiotics; polyunsaturated fatty acids; phytochemicals

Introduction

The intestinal tract harbours a complex bacterial community (microbiota), integrated by more than 800 different bacterial species, which have an enormous impact on the nutritional and health status of the host. The metabolic activity developed by the gut microbiota contributes to the digestion of dietary compounds, salvage of energy, supply of (micro)nutrients and transformation of xenobiotics. Overall, a balanced gut microbiota composition confers benefits to the host, while microbial imbalances are associated with metabolic and immune-mediated disorders (1, 2). The composition of the gut microbiota is influenced by endogenous and environmental factors (diet, antibiotic intake, xenobiotics, etc.). Of these factors, the diet is considered a major driver for changes in gut bacterial diversity that may affect its functional relationships with the host (3). In fact, the microbiome of the adult-type and infant-type microbiota has distinct gene contents to accommodate nutrient acquisition strategies to different diets (4).

The primary role of diet is providing sufficient nutrients to meet the basic nutritional requirements for maintenance and growth, while giving the consumer a feeling of satisfaction and well-being. In addition, some food components exert beneficial health effects beyond basic nutrition, leading to the concept of functional foods and nutraceuticals (5). Functional foods are those foods that provide benefits beyond basic nutrition when consumed as part of the regular diet. Nutraceuticals are extracts containing the biologically active food components supplied in other than a food form. Dietary components with biological effects are susceptible to be metabolized by intestinal bacteria during the gastrointestinal passage, prior being absorbed. The colon has the highest bacterial load and constitutes an active site of metabolism rather than a simple excretion route (6). The metabolic activity of the gut microbiota on bioactive

food components can modify the host exposure to these components and their potential health effects. Furthermore, some functional food components influence the growth and/or metabolic activity of the gut microbiota and, thereby, its composition and functions (7, 8). Therefore, the intestinal microbiota is both a target for nutritional
5 intervention to improving health and a factor influencing the biological activity of other food compounds acquired orally. This review focuses on the reciprocal interactions between the gut microbiota and functional food components, and the consequences of these interactions on human health (Figure 1).

10 **Gut microbial ecology**

The human gut is populated by a vast number of bacterial species (more than 800) that reach the highest concentrations in the colon (up to 10^{12} cells per gram of faeces). The gut colonization process starts immediately after birth and the development and establishment of the infant's microbiota highly depend on environmental factors. The
15 infant's microbiota initially shows low diversity and instability, but evolves into a more stable adult-type microbiota over the first 24 months of life (9). In general, *Bifidobacterium* populations are dominant in the first months of life, especially in breast-fed infants (up to 90% of the total faecal bacteria) due to the bifidogenic effect of breast milk, while a more-diverse microbiota is found in formula-fed infants, weaning
20 children and adults (10). Metagenomic analyses show that in adults and weaned children the major constituents of the colonic microbiota are *Bacteroides*, followed by several genera belonging to the division *Firmicutes*, such as *Eubacterium*, *Ruminococcus* and *Clostridium*, and the genus *Bifidobacterium*. By contrast, in infants the genus *Bifidobacterium* is predominant and also a few genera from the family
25 *Enterobacteriaceae*, such as *Escherichia*, *Raoultella*, and *Klebsiella* (4). The

composition of this bacterial ecosystem is dynamic and susceptible to changes driven by dietary factors and diverse disease conditions (11, 12).

Roles of the gut microbiota in host physiology and health

5 The gut microbiota develops a number of protective, immune and metabolic functions, which altogether have an enormous impact on the nutritional and health status of the host. The indigenous gut microbiota and transient bacteria (food-associated and probiotics) are known to influence the development and regulation of the host's defences, of immune and non-immune nature, via interaction with the epithelium and
10 the gut-associated lymphoid tissue (13). The intestinal epithelium constitutes a physical barrier that regulates the transcellular and paracellular transit of exogenous substances and impairs the entry of most of luminal antigens; this barrier is strengthened by the mucus layer integrated by glycoproteins (mucins) and the synthesis of antimicrobial peptides and other secretions (bile, acids, enzymes, etc.). The commensal microbiota
15 constitutes part of this primary line of defence, and participates in regulation of paracellular permeability, mucin gene expression by goblet cells and secretion of antimicrobial peptides (defensins and angiogenins) by intestinal Paneth cells. Moreover, the intestinal microbiota is essential to the postnatal development of the immune system, influencing the content of lamina propria T cells, immunoglobulin A producing
20 B cells, intraepithelial T cells and serum immunoglobulin levels (14). Based on these protective and immunomodulatory roles, some probiotic strains are acknowledged for their beneficial effects on the treatment of acute diarrhoea, prevention of antibiotic associated-diarrhoea, eradication of *Helicobacter pylori* infection together with antibiotics and in prevention of atopic eczema in humans (13, 15).

The intestinal microbiota also affects the host metabolism, providing additional enzymes and regulating the expression of genes involved in the utilization of carbohydrates and lipids, and in drugs bioconversion (16-18). The number of genes of the collective genome (microbiome) of the microbiota exceeds by far those of the human genome, encoding additional metabolic features (17, 19). Genomic and physiologic studies have demonstrated that the gut microbiota provides enzymes specialized in the utilization of non-digestible carbohydrates and host-derived glycoconjugates (e.g. mucin), deconjugation and dehydroxylation of bile acids, cholesterol reduction, biosynthesis of vitamins (K and B group) and isoprenoids and metabolism of amino acids and xenobiotics (4, 16, 17).

The microbiome is particularly enriched in genes involved in carbohydrate metabolism and uptake, indicating that complex polysaccharides are the primary energy source for the colonic microbiota (4). The genome sequence of *Bifidobacterium longum* also has a large number of predicted proteins (more than 8%) related to the catabolism of oligo- and poly-saccharides released from non-digestible plant polymers (20). Some of the most abundant bacterial enzymes involved in the degradation of complex polysaccharides and xenobiotics are β -glycosidases and β -glucuronidases, which may play both beneficial and harmful roles (21). Glycosidase activities present in the human colonic microbiota act on plant glucosides contributing to nutrient utilization and, in some cases, to the generation of biologically active aglycones with other health benefits (e.g. from isoflavones). The utilization of complex dietary polysaccharides by the microbiota seems to contribute to harvest energy from the diet, which may represent 10% of the daily energy supply (22). Fermentation of dietary polysaccharides leads to the generation of short-chain fatty acids (SCFAs) (e.g. acetate, butyrate and propionate) and other gases (e.g. carbon dioxide and hydrogen). The principal SCFAs (acetate,

propionate and butyrate) are metabolized by the colonic epithelium (butyrate), liver (propionate) and muscle (acetate) and exert different functions. Butyrate is utilized by enterocytes and generally regarded as a healthy metabolite, since it positively influences cell growth and differentiation, and exerts anti-inflammatory effects (23). Acetate and propionate can access the portal circulation and oppositely impact lipid metabolism. While acetate seems to contribute to lipid and cholesterol synthesis in the liver, propionate can inhibit the effects of acetate. Unlikely β -glycosidases, β -glucuronidases usually liberate toxins and mutagens that have been glucuronated in the liver and excreted into the gut with the bile. This can lead to the accumulation high local concentrations of carcinogenic compounds within the gut, thus increasing the risk of carcinogenesis. Furthermore, reuptake of the deconjugated compound from the gut and re-glucuronidation in the liver lead to an enterohepatic circulation of xenobiotic compounds, which increases their retention time in the body. In the colonic microbiota, bacterial β -glucosidases seem to be more widespread than β -glucuronidases. Studies carried out in 40 bacterial strains, which are representative of dominant bacteria in human faeces, show that more than half of the low G+C% Gram-positive *Firmicutes* have β -glucosidase activity, while β -glucuronidase activity is only present in some *Firmicutes*, within the clostridial clusters XIVa and IV (21). Most of the *Bifidobacterium* spp. and *Bacteroides thetaiotaomicron* have β -glucosidase activity. Moreover, the level of exposure to glycosides in the colon, which is dependent on the type of diet consumed, could affect the induction of enzyme activity levels in some members of the gut microbiota and, therefore, influence their functions (21). Specific glycosidases (xylanases, arabinofuranosidases and xylosidases) required for complete degradation of complex polysaccharides present in plant cell walls, such as arabinans and arabinoxylans, are also encoded by the total faecal microbiota and by strains of the

main bacterial genera (*Bifidobacterium* and *Bacteroides*) (24, 25). *Bifidobacterium longum* subsp. *infantis* ATCC 15697, an isolate from the infant gut, is also equipped with genes and enzymes allowing the preferential consumption of small mass oligosaccharides, which represent 63.9% of the total human milk oligosaccharides available (26, 27). In addition, genes coding for an endo-alpha-N-acetylgalactosaminidase and a 1,2-alpha-L-fucosidase, which hydrolyse high-molecular weight mucin, are present in several *Bifidobacterium bifidum* strains (28).

Gut bacterial enzymes are also involved in the metabolism of cholesterol and bile acids. Cholesterol can be reduced to coprostanol by the commensal microbiota, increasing its secretion in faeces. Bile acids are synthesized from cholesterol in the liver mostly as the primary bile acids, cholic acid and chenodeoxycholic acid. Intestinal bacteria are also able to convert these acids into various types of secondary bile acids by catalysing their deconjugation and dehydroxylation, thereby limiting the solubilization and absorption of dietary lipids throughout the intestine (29). However, these activities can also lead to the generation of secondary bile acids, some of which (deoxycholic acid and lithocholic acid) are considered possible carcinogens. *Bacteroides intestinalis* and secondarily *Bacteroides fragilis* and *E. coli* are potentially involved in the generation of secondary bile acids in the colon (30).

The metabolic activity of the microbiota can also contribute to the supply of amino acids required by humans. In the presence of fermentable carbohydrate substrates (e.g. non-starch polysaccharides, resistant starch and oligosaccharides), colonic bacteria grow and actively synthesize protein, which can be a source of amino acids for the host (31). Although it is difficult to quantify the protein synthesis and turnover within the large intestine, at least from 1 to 20% of circulating plasma lysine and threonine in adult human subjects is derived from the intestinal microbiota, as estimated by using labelled

amino acids (16). Nevertheless, the metabolic activities of the microbiota involved in the degradation of food related nitrogen compounds (e.g. nitrocompounds, sulphur-containing compounds and amino acids) can lead to the generation of potentially carcinogenetic substances (32).

5 The commensal microbiota also regulates the expression of genes involved in the processing and absorption of dietary carbohydrates and complex lipids by the host, which altogether lead to body weight gain and increased fat storage. Gut colonization by commensal bacteria increases the expression of an intestinal monosaccharide transporter and key enzymes (acetyl-CoA carboxylase and fatty acid synthase) of *de novo* fatty acid
10 biosynthetic pathways (33, 34). The colonization of germ-free mice also reduces the levels of circulating fasting-induced adipose factor (Fiaf) and the skeletal muscle and liver levels of phosphorylated AMP-activated protein kinase, contributing to fat storage (35). Furthermore, comparisons between germ-free and colonized rat demonstrated that the intestinal microbiota affect levels of xenobiotic-metabolizing enzymes in large
15 intestine and liver, including glutathione transferases, gastrointestinal glutathione peroxidase, epoxide hydrolases, N-acetyltransferases, and cytochrome P450 activities, which might affect the host ability to detoxify different compounds (36, 37).

Therefore, the intestinal tract is inhabited by a complex microbiota that develops strategies to regulate nutrient acquisition and utilization in symbiosis with the host and
20 in response to the diet. The biochemical activity this complex ecosystem generates healthy as well as potentially harmful compounds from the diet and their balance is essential to maintain a healthy status. This could be achieved by diverse nutritional strategies, including the administration of probiotic bacteria and other functional food components, whose roles and interactions with the microbiota are reviewed in the
25 following sections.

Prebiotics and gut microbiota

Prebiotics are nondigestible food ingredients, mostly oligosaccharides, which beneficially affect the host by stimulating growth, activity or both of specific intestinal bacteria (38). The criteria that have to fulfil a prebiotic include, (1) resistance to gastric acidity and mammalian enzymes; (2) susceptibility to be fermented by gut microbiota; and (3) ability to stimulate the growth and/or activity of beneficial intestinal bacteria. The possible beneficial effects of prebiotics include the control intestinal transit time and bowel habits, and reduction of risk of atherosclerosis, osteoporosis, obesity, type-2 diabetes, cancer, infections and allergies, although their effectiveness in humans is still controversial (38). The biological effects of prebiotics mainly depend on their influence on the gut microbiota composition and derived metabolites; although some roles could be due to their own structure and direct action (e.g. inhibition of pathogen adhesion by homology with bacterial receptors).

Galacto-oligosaccharides (GOS) and inulin-derivatives (e.g. fructo-oligosaccharides [FOS]) are the prebiotics most commonly commercialized in Europe. GOS are non-digestible oligosaccharides derived from lactose that are found naturally in human milk and consist of chains of galactose monomers. These prebiotics provide beneficial effects in the gastrointestinal tract by stimulating growth of specific members of the intestinal microbiota (e.g. bifidobacteria). GOS alone or combined with FOS are mainly added to infant formula to promote the prevalence of a microbiota composition similar to that resulting from breast-feeding during both milk-feeding and the weaning period. This dietary strategy may increase the total amount of faecal bifidobacteria and favour a *Bifidobacterium* species composition resembling that of breast-fed infants (39, 40). Moreover, GOS may structurally mimic the pathogen binding sites that coat the surface

of gastrointestinal epithelial cells and thereby may inhibit enteric pathogen adhesion and infection (41).

Inulin and its hydrolytic product (oligofructose) are fructans that are linked by β -(2-1) linkages and differentiated by the number of fructose monomers. Inulin has a high number (10-60) and oligofructose derivatives have a low (3-7) number of fructose monomers. They naturally occur at high concentrations in plant-foods such as onion, asparagus, wheat, artichoke, etc. (42), and exhibit different functional attributes (43), including modulation of the gut microbiota, prevention of pathogens adhesion and colonization, induction of anti-inflammatory effects, reduction of food intake, modulation of bowel habits and regulation of alterations in lipid and glucose metabolism. Most of these effects are derived from their structural resistance to mammalian digestive enzymes and their ability to stimulate the growth of beneficial bacteria (e.g. bifidobacteria and lactobacilli) in the colon and to increase the generation of SCFAs with diverse biological roles (38, 44-47). The effects of these prebiotics on immune functions may be due to the induced changes on the gut microbiota and/or to the effects of the generated SCFAs via binding to SCFA receptors on leucocytes (48). Studies using long-chain inulin have evidenced beneficial effects on bowel inflammation reducing the production of pro-inflammatory biomarkers, along with an increase in intestinal bifidobacteria and lactobacilli (49-53). SCFA may also regulate intestinal fat absorption since butyrate, for instance, impairs lipid transport *in vitro* in Caco-2 cells (54-55). In addition, inulin and inulin-type fructans, are considered dietary soluble fiber, and directly modulate bowel habits slowing gastric emptying and intestine transit time, delaying absorption of glucose and improving alterations in glucose metabolism (56).

Furthermore, dietary fibre including some non-starch polysaccharides, such as cellulose, dextrans, chitins, pectins, beta-glucans, and waxes, and lignin can modulate the transit time through the gut providing similar beneficial effects as those of inulin-type fructans. These compounds are found in many foods such as cereal, nuts, etc. They are also partially susceptible to bacterial fermentation and may induce changes in bacterial populations, particularly in number of bifidobacteria and lactobacilli. These dietary soluble fibers have been shown to exert additional beneficial effects, for instance improving gut barrier function *in vitro* (57) and *in vivo* (58-60), which could be partially a consequence of their effect on the microbiota composition.

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Polyunsaturated fatty acids (PUFAs) and gut microbiota

PUFA are fatty acids that contain more than one double bond, which are separated from each other by a single methylene group. The ω -3 fatty acids (linolenic, eicosapentaenoic and docosahexaenoic acids) and ω -6 fatty acids (linoleic and arachidonic acids) are the best characterized so far. The biological effects of the ω -3 and ω -6 fatty acids are largely mediated by their mutual interactions. The possible underlying mechanisms by which PUFA exert their beneficial effects on health are diverse, involving the formation of prostacyclins and thromboxanes, pro-inflammatory cytokine production (tumor necrosis factor alpha and interleukin-1), modulation of the hypothalamic-pituitary-adrenal anti-inflammatory responses, and induction of the release of acetylcholine (61). Thus, diets rich in PUFAs have been shown to positively influence immune function, blood pressure, cholesterol and triglycerides levels, and cardiovascular function in animals and humans (62-65).

The adult microbiome is not particularly enriched in genes involved in fatty acid metabolism (4); however, some interactions of PUFAs with the indigenous microbiota

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and some probiotics have been reported, which might affect the biological roles of both. *In vitro* studies on the effects of PUFAs (linoleic, gamma-linolenic, arachidonic, alpha-linolenic and docosahexaenoic acids) on the growth and adhesion of different *Lactobacillus* strains (*Lactobacillus rhamnosus* GG, *Lactobacillus casei* Shirota and 5 *Lactobacillus delbrueckii* subsp *bulgaricus*) have shown different results depending on the strain. High concentrations of PUFA (10-40 µg/ml) inhibited growth and adhesion to mucus of all tested bacterial strains, whilst low concentrations of gamma-linolenic acid and arachidonic acid (5 µg/ml) promoted growth and mucus adhesion of *L. casei* Shirota (66). PUFAs supplemented into the growth medium can also be utilized by 10 *Lactobacillus* strains, generating different products (67). Interconversions were detected in octadecanoic acids (18:1), their methylenated derivatives (19:cyc), conjugated linoleic acid and eicosapentaenoic acid proportions. These results suggest that *Lactobacillus* may have a potential as regulators of PUFA absorption *in vivo*. The administration of PUFAs has also positively influenced the adhesion of *Lactobacillus* to 15 the jejunal mucosa of gnotobiotic piglets, indicating that the intake of these fatty acids may influence the intestinal levels of this bacterial group (68). In fish fed diets containing PUFAs, lactic acid bacteria dominated among the Gram-positive bacteria within the epithelial mucosa, suggesting that dietary fatty acids affect the attachment sites for the gastrointestinal microbiota, possibly by modifying the fatty acid 20 composition of the intestine wall. In a small clinical trial, the administration of an infant formula supplemented with *Bifidobacterium* Bb-12 or *Lactobacillus* GG to infants with atopic eczema (n=15) exerted some effects on plasma lipids (69). Of neutral lipids, alpha-linolenic acid (18:3 n-3) proportions were reduced by the probiotic supplementation and, in relation to phospholipids, only *Bifidobacterium* Bb-12 25 supplementation increased the proportion of alpha-linolenic acid. Therefore, the

evidence suggests that some physiological effects of probiotics could be associated with the interactions between probiotics and dietary PUFA, although further studies are needed to confirm this hypothesis *in vivo*.

5 **Phytochemicals and gut microbiota**

Phytochemicals are defined as bioactive non-nutrient plant compounds present in fruits, vegetables, grains, and other plant foods, whose ingestion has been linked to reductions in risk of major chronic diseases (70). The different compounds included in this group can be classified according to common structural features into carotenoids, phenolics, alkaloids and nitrogen-containing and organosulfur compounds. Phenolics, flavonoids and phytoestrogens have raised particular interest because of their potential effects as antioxidants (71), antiestrogens (72), anti-inflammatory and immunomodulatory (73-77), cardioprotectives and anticarcinogenics (70, 71, 78) compounds (Table 1).

The bioavailability and effects of polyphenols greatly depend on their transformation by specific components of the gut microbiota via esterase, glucosidase, demethylation, dehydroxylation and decarboxylation activities (6). Many dietary polyphenols are glycosides that are transformed into aglycones by commensal bacterial glycohydrolases, thereby modifying their bioavailability and affecting positive or negatively their activities and/or functional effects on the mammalian tissues (79, 80). Polyphenols are commonly present in plant foods as a bound form, most often conjugated as glycosides, and most of them are metabolized by gut microbiota resulting in formation of aglycones (81, 82). The microbiota metabolites of polyphenols are better absorbed in the intestine, and their entero-hepatic circulation ensures that the

residence time in plasma for the metabolites is extended compared to that of their parent compounds, and finally are excreted via urine.

The gut microbiota has proved to be essential for the production of active isoflavone metabolites with oestrogen-like activity; additionally, the metabolites produced exhibit
5 different anti-inflammatory properties (73). Similarly, the flavonoid quercetin generated by gut microbial enzymes exerts a higher effect in the down-regulation of the inflammatory responses than the glycosylated form present in vegetables (quercitrin or 3-rhamnosylquercetin) (83). This effect is exerted by inhibiting cytokine and inducible
10 nitric oxide synthase expression through inhibition of the NF-kappaB pathway both *in vitro* and *in vivo* (83). In contrast, the ellagitannin punicalagin that is the most potent antioxidant found in pomegranate juice is extensively metabolized to hydroxy-6H-dibenzopyran-6-one derivatives, which did not show significant antioxidant activity compared to punicalagin (84).

Phytochemicals and their derived products can also affect the intestinal ecology as a
15 significant part of them are not fully absorbed and are metabolised in the liver, excreted through the bile as glucuronides and accumulated in the ileal and colorectal lumen (85). For example, the intake of flavonol-rich foods has been shown to modify the composition of the gut microbiota, exerting prebiotic-like effects (86). Unabsorbed dietary phenolics and their metabolites have been shown to exert antimicrobial or
20 bacteriostatic activities (87). These metabolites selectively inhibit pathogen growth and stimulate the growth of commensal bacteria, including also some recognized probiotics (87, 88), thus influencing the microbiota composition. Plant phenolic compounds from olives (89), tea (87), wine (88) and berries (90, 91) have demonstrated antimicrobial
25 properties. Tea phenolics have shown to inhibited the growth of *Bacteroides* spp., *Clostridium* spp. (*C. perfringens* and *C. difficile*), *Escherichia coli* and *Salmonella*

typhimurium (87). The level of inhibition was related to the chemical structure of the compound and bacterial species. In this sense, caffeic acid generally exerted a more significant inhibitory effect on pathogen growth than epicatechin, catechin, 3-*O*-methylgallic acid, and gallic acid. Another *in vitro* study showed that (+)-catechin increased the counts of *Clostridium coccooides*-*Eubacterium rectale* group and *Escherichia coli*, but inhibited those of *Clostridium histolyticum* (86). The effects of (-)-epicatechin were less pronounced increasing the growth of *Clostridium coccooides*-*Eubacterium rectale* group (86). Interestingly, the growth of beneficial bacteria (*Bifidobacterium* spp and *Lactobacillus* spp) was relatively unaffected or favoured (86, 87). Resveratrol, a potent antioxidant found in wine, favoured the increase of *Bifidobacterium* and *Lactobacillus* counts (88) and abolished the expression of virulence factors of *Proteus mirabilis* to invade human urothelial cells (92). Anthocyanins from berries also have proved to inhibit the growth of pathogenic *Staphylococcus* spp, *Salmonella* spp, *Helicobacter pylori* and *Bacillus cereus* (90, 91). Phenolics, and flavonoids may also reduce the adhesion ability of *L. rhamnosus* to intestinal epithelial cells (93). Tea catechins have also been shown to modify mucin content of the ileum which could modulate bacterial adhesion and colonization (94). Therefore, polyphenols appear to have potential to confer health benefits via modulation the gut microecology. However, the effects of interplay between polyphenols and specific gut microbiota functions remain largely uncharacterized.

Conclusions and future perspectives

The gut microbiota exerts an enormous impact on the nutritional and health status of the host via modulation of the immune and metabolic functions. The microbiome provides additional enzymatic activities involved in the transformation of dietary

compounds. Food bioactive compounds also exert significant effects on the intestinal environment, modulating the gut microbiota composition and probably its functional effects on mammalian tissues. This evidence is changing the way the biological roles of functional food components are being investigated since their metabolites and effects
5 may depend on the gut microbiota and even change from one individual to another. Advances on the knowledge of the interactions between bioactive food compounds and specific intestinal bacteria could contribute to a better understanding of both positive and negative interactions *in vivo* and to the identification of new functional microorganisms inhabiting our intestinal tract.

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Table 1. Phytochemicals and physiological function

Phytochemical	Compound	Physiological function	Reference	
Phenolics	Hydroxy-cinnamic acids	p-coumaric acid	Bacteriostatic or antimicrobial activities	87
		caffeic acid	Bacteriostatic or antimicrobial activities	86
Flavonoids	Flavonols	quercetin, 3-rhamnosyl quercetin	down-regulation of inflammatory response(s), modulation of proliferative response(s)	83, 77
		kaempferol	Anti-inflammatory, modulation of proliferative response(s)	77
		resveratrol	Prebiotic effect, and abolition of the expression of virulence factors, modulation of proliferative response(s)	88, 77
		Flavones	apigenin, luteolin	Inhibition of LPS-induced
	Flavanols	catechins	Antimicrobial properties, Modulation of mucins	87-91, 94
	Flavanones	hesperitin, naringenin	Anti-inflammatory	77
	Isoflavonoids	genistein, daidzein	Antiadhesive properties	93
		equol (der. from daidzein)	Oestrogen effects	72
	Anthocyanidins	cyanidin	Antimicrobial properties	90, 91
		hydroxyl-6H-dibenzopyran-6-one (der. from ellagitanin)	Poor antioxidant capacity	84

Figure legends

Figure 1. Interactions between functional food components and the gut microbiota.

