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Interaction between Phenolics and Gut Microbiota: Role in Human Health

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Dietary phenolic compounds are often transformed before absorption. This transformation modulates their biological activity. Different studies have been carried out to understand gut microbiota transformations of particular polyphenol types and identify the responsible microorganisms. Although there are potentially thousands of different phenolic compounds in the diet, they are typically transformed to a much smaller number of metabolites. The aim of this review was to discuss the current information about the microbial degradation metabolites obtained from different phenolics and their formation pathways, identifying their differences and similarities. The modulation of gut microbial population by phenolics was also reviewed in order to understand the two-way phenolic−microbiota interaction. *Clostridium* and *Eubacterium* genera, which are phylogenetically associated, are other common elements involved in the metabolism of many phenolics. The health benefits from phenolic consumption should be attributed to their bioactive metabolites and also to the modulation of the intestinal bacterial population.

KEYWORDS: *Eubacterium*; *Clostridium*; polyphenols; phenolics; flavonoids; tannins; human metabolism; gut microflora; microbial metabolism; bioavailability

INTRODUCTION

Phenolic compounds are currently receiving much attention because of their beneficial health effects related to their antioxidant, anti-inflammatory, antiestrogenic, cardioprotective, cancer chemopreventive, and neuroprotective properties (*1*−*6*). Most dietary polyphenols are transformed in the colon by the intestinal microbiota before absorption. This conversion is often essential for absorption and modulates the biological activity of these dietary compounds (*7*, *8*). Furthermore, dietary polyphenols are substrates for several enzymes located in the small intestine and colon and in the liver (hydrolyzing and conjugating enzymes) (*9*−*16*). Therefore, the colon has to be considered as an active site for metabolism rather than a simple excretion route and deserves further attention from the scientific community (*17*). Recent studies have investigated the relevance of the intestinal microbial activation of polyphenols in human health.

Gut bacteria can hydrolyze glycosides, glucuronides, sulfates, amides, esters, and lactones. They also carry out ring-cleavage, reduction, decarboxylation, demethylation, and dehydroxylation reactions (*17*−*19*). The hydrolysis of glycosides results in metabolites that are potentially more biologically active than the parent compounds. Further bacterial transformation of aglycones can lead to production of more or less active compounds, depending on the substrate being metabolized and the products formed (*18*, *19*). Several studies have been carried out to understand the transformations of particular polyphenol types and to identify the microorganisms involved during their colonic fermentation, which varies depending on the chemical structure.

On the other hand, phenolic compounds are also antimicrobial and can interact with the gut microbiota, producing a modulation of the microbial population of the gastrointestinal (GI) tract. This has effects on GI health and also in the metabolism of dietary phenolics (*20*, *21*).

The aim of this review was to summarize the current information about the microbial degradation metabolites and their formation pathways obtained from the different groups of dietary phenolic compounds, identifying their differences and similarities. The modulation of gut microbial population by phenolics has also been reviewed in order to understand the two-way phenolic−microbiota interaction. Recent progress in the identification of colonic microbial species responsible for phenolic metabolism and novel tools used to identify them and the effects of polyphenol microbial metabolism on their bioavailability and bioactivity were also reviewed.

MICROBIAL METABOLIC PATHWAYS AND METABOLITES OF THE DIETARY PHENOLIC COMPOUNDS

In nature, phenolics are usually found conjugated to sugars and organic acids and can be classified into two major types: flavonoid and nonflavonoid phenolics. All flavonoid phenolics share a basic structure consisting of two benzene rings (A and B) linked through a heterocyclic pyrone C ring (**Figure 1**). In contrast, nonflavonoid phenolics include a more heterogeneous group of compounds (**Figure 2**) including from the simplest of the class such as C_6-C_1 benzoic acids and C_6-C_3 hydroxycinnamates to

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