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Review

Basic biochemical mechanisms behind the health benefits of polyphenols

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ABSTRACT

Polyphenols and consequently many flavonoids have several beneficial actions on human health. However, the actual molecular interactions of polyphenols with biological systems remain mostly speculative. This review addresses the potential mechanisms of action that have been so far identified, as well as the feasibility that they could occur in vivo. Those mechanisms include: i) non specific actions, based on chemical features common to most polyphenols, e.g. the presence of a phenol group to scavenge free radicals; and ii) specific mechanisms; based on particular structural and conformational characteristics of select polyphenols and the biological target, e.g. proteins, or defined membrane domains. A better knowledge about the nature and biological consequences of polyphenol interactions with cell components will certainly contribute to develop nutritional and pharmacological strategies oriented to prevent the onset and/or the consequences of human disease.

Contents

Abbreviations: AH, antioxidant; A·, antioxidant radical; CVD, cardiovascular disease; EC, (−)–epicatechin; EGCG, (−)–epigallocatechin gallate; LH, lipid; L·, lipid radical; LOOH, lipid hydroperoxide; LOO·, lipid peroxyl radical; NF-κB, nuclear factor kappa-B; PO·, polyphenol radical; POH, polyphenol.

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1. Introduction

A large number of studies has identified cellular targets that could be involved in the health promoting actions of dietary plant polyphenols. However the actual molecular interactions of polyphenols with those cellular targets remain mostly speculative. This paper summarizes the most important mechanisms proposed for the actions of polyphenols in animal settings. Although the particular focus will be on the effects of polyphenols on cardiovascular disease (CVD), the same potential mechanisms could occur in other animal tissues and systems. It is important to mention that this paper was mostly written based on the positive aspects of fruits and vegetables, and hence that polyphenol interactions with animal tissues provide beneficial effects. However, negative effects of polyphenols cannot be totally disregarded. In this regard, caution should be taken when the supplementation of polyphenols is beyond an upper limit that could be set as a generous intake of fruits and vegetables, e.g. 10 servings a day.

2. Polyphenols and cardiovascular disease

Epidemiological evidence demonstrates that diets rich in fruits and vegetables promote health and attenuate, or delay, the onset of CVD (Hertog et al., 1993; Appel et al., 1997; Liu et al., 2000; Joshipura et al., 2001; Hung et al., 2004; Buijsse et al., 2006; Lichtenstein et al., 2006; Iqbal et al., 2008; Mursu et al., 2008; Holt et al., 2009). The beneficial effects of fruits and vegetables have been largely ascribed to polyphenols, since the ingestion of foods rich in polyphenols is associated in humans and experimental animals with diminutions in: i) dyslipidemia and atherosclerosis; ii) endothelial dysfunction and hypertension; iii) platelet activation and thrombosis; iv) the inflammatory process associated with the induction and perpetuation of CVD. This evidence has been revised by different authors (Dohadwala and Vita, 2009; Bertelli and Das, 2009; Corti et al., 2009; Desch et al., 2010; Galleano et al., 2009). A definitive understanding of the mechanisms behind the health effects of polyphenols will allow to identify the fruits and vegetables, and the chemical compounds, responsible for those effects, and finally define the best health promoting diets.

3. Chemical aspects of dietary polyphenols

Plants produce polyphenols as secondary metabolites involved in diverse processes, such as growth, lignification, pigmentation, pollination, and resistance against pathogens, predators, and environmental stresses (Duthie et al., 2003). Chemically, polyphenols are compounds having one or more hydroxyl groups attached to a benzene ring. Edible plants provide to the human diet with more than 8000 different polyphenols that can be categorized as flavonoids and non-flavonoid compounds.

Flavonoids have a common C6–C3–C6 structure consisting of two aromatic rings (A and B) linked through a three carbon chain, usually organized as an oxygenated heterocycle (ring C) (Fig. 1). Flavonoids can be divided into several subfamilies according to the degree of oxidation of the oxygenated heterocycle, being flavanols, flavanones, flavones, flavonols (essentially, flavan-3-ols), isoflavones, and anthocyanidins, the most relevant for human diets (Scalbert and Williamson, 2000). Starting from a basic chemical structure, plant biosynthetic pathways introduce different hydroxyl group patterns, methyl groups, and sugars (Jaganatah and Crozier, 2010). In certain cases, oligomerization and polymerization of the flavonoid units occur. Oligomers and polymers of flavonoids are called tannins and are classified in two groups, condensed tannins and hydrolyzable tannins. Condensed tannins (also known as proanthocyanidins or procyanidins) are oligomers of flavanols, and their chemical structures are defined not only by the kind of monomer, but also according to the kind of link among monomers. There are several oligomerization patterns and some plants present characteristic manners of oligomerization, e.g. in cocoa the monomeric units are linked through 4→8 carbon–carbon bonds forming mostly B-type dimers (Jaganatah and Crozier, 2010). Hydrolyzable tannins are polymers readily hydrolyzed by acids into their components: a central core constituted by a polyol (a sugar, generally D-glucose, or a flavonoid, as catechin) and a phenolic carboxylic acid esterifying partially or totally that core molecule. These tannins are classified according to the phenolic carboxylic acids present that could be gallic acid (gallotannins) or ellagic acid (ellagitannins) (Jaganathan and Mandal, 2009).

Among the non-flavonoid polyphenols, stilbenes have gained attention due to their proposed biological actions in animals. Stilbenes have a common C6–C2–C6 structure, consisting in two aromatic rings linked through a two carbon bridge with a double bond. The parent compound of this family is resveratrol (Fig. 1) that occurs i) in *trans* and *cis* configurations; ii) as free forms (aglycones) and as glucosides; and iii) as monomers, oligomers and polymers (viniferins). As it can be inferred from the above brief description of the chemical structures of plant polyphenols, although the phenol group is the base of their classification, its relevance for chemical reactions in animals is as important as that of other chemical groups that are part of the polyphenol molecule.