Biological Properties of Monomeric and Polymeric Catechins: Green Tea Catechins and Procyanidins

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Abstract

There is an increasing interest in the disease preventing and/or therapeutic properties of green tea and red wine. Major biologically active constituents in green tea and red wine are tea catechins and procyanidins, respectively. Tea catechins are monomers of flavan-3-ol, and procyanidins are polymers of the flavan-3-ol units such as catechin and epicatechin. These structurally related catechin compounds have extensively been studied for their various biological activities. Tea catechins and procyanidins are known as very strong antioxidants, which can scavenge various forms of free radicals. They may prevent cardiovascular diseases, probably through their ability to inhibit oxidation of low-density lipoprotein (LDL), to lower the plasma cholesterol level, and to prevent platelet aggregation. In addition, there is increasing evidence of the cancer chemopreventive properties of catechins and procyanidins. Understanding the molecular and cellular mechanisms of their beneficial properties, in particular their roles in the signal transduction pathways and gene expression, are of interest. This review discusses our current knowledge and understanding of the biological activities of tea catechins and procyanidins, including their basic chemistry, occurrence, antioxidant activity, effect on heart disease, and effects on signal transduction pathways. Together, these may provide better insights into their possible beneficial effects in human.

Keywords: Antioxidant, catechins, chemopreventive compounds, heart disease, procyanidins.

Introduction

Polyphenolic compounds from natural sources such as foods and edible plants have widely been studied because of their potential health promoting and/or curative properties. Of the naturally occurring polyphenolic compounds, catechins and their polymers, procyanidins have gained much attention. Catechins and procyanidins are found mainly in green tea and red wine, respectively. Health benefits associated with these compounds include the prevention and treatment of a number of chronic diseases, including cardiovascular diseases and cancers. The mechanisms underlying their biological properties are not fully understood.

Catechins, members of the flavanol group of polyphenols, are the best known biologically active components of green tea. Tea catechins are known as strong antioxidants. These compounds have long been consumed primarily in Asian countries including China and Japan (Graham, 1992). Consumption of tea in these cultures has been associated with prevention of many diseases including cancer and heart disease and cataracts (Lambert & Yang, 2003). Procyanidins are oligomers and polymers of flavan-3-ols units, mainly found in grape seeds and red wine. Procyanidins have gained much attention since the finding of the so-called French Paradox, which shows a low mortality rate from coronary heart disease in the French population despite their high consumption of fat. It is believed that the high intake of wine, especially red wine, in France may provide an explanation of this paradox (Leger et al., 1979; Renaud & de Lorgeril, 1992). Major constituents of red wine, which are absent from white wine, include various forms of procyanidins.

These structurally related catechin compounds are of great interest because of their various proven biological activities in vitro and promising health benefits in vivo.
This review will describe the basic biological and chemopreventive properties of catechins and procyanidins, as it relates to their basic chemistry, occurrence, antioxidant activity, effect on heart disease, and effects on signal transduction pathways.

**General background: Basic chemistry and occurrence**

Catechins are classified as flavan-3-ol monomers and are the major flavonoid constituents in green tea leaves, which account for 60% to 80% of the total flavonoids in green tea (Graham, 1992; Balentine et al., 1997). Four major catechins in fresh tea (*Camellia sinensis*) leaves are (−)-epicatechin (EC), (−)-epigallocatechin (EGC), (−)-epicatechin gallate (ECG), and (−)-epigallocatechin gallate (EGCG). The structures of representative catechins are shown in Figure 1. Other minor catechins present in tea are epigallocatechin digallates, epicatechin digallate, 3-0-methyl EC and EGC, catechin gallate, and galloallocatechin gallate, among others. Among these catechins, EGCG accounts for about 50% to 80% of total catechins in green tea (Yang et al., 2002). Besides green tea, catechins are also found in various food sources such as apples, peaches, buckwheat, red wine, and cocoa beans (Aucamp et al., 1997; Peterson & Dwyer, 1998; Watanabe, 1998; Weisburger, 2001; Van Der Sluis et al., 2002).

Procyanidins are also called proanthocyanidins because they produce colored anthocyanidins when heated under acidic conditions (Haslam, 1989; Scalbert et al., 2000). Another well-known name for procyanidins is condensed tannins, which differ from the hydrolyzable tannins in their chemical structure. Procyanidins are oligomers and polymers of flavan-3-ols units, whereas the hydrolyzable tannins have a form of phenolic acids esters and a polyol, which is usually a glucose moiety (Santos-Buelga & Scalbert, 2000). Procyanidins are reported to be far more common in the human diet and have recently received more attention than hydrolyzable tannins because of their purported health beneficial properties (Santos-Buelga & Scalbert, 2000). They are widely found in the plant kingdom and in food sources, especially fruits, vegetables, nuts, seeds, wines, hops, teas, and pine bark (Haslam, 1989; Chung et al., 1998; Packer et al., 1999; Stevens et al., 2002).

Figure 1 lists the general structures of procyanidin polymers and procyanidin dimers. So far, more than 200 procyanidin oligomers with a polymerization degree less than 5 have been identified, but polymers with degrees higher than that are also found in nature (Santos-Buelga & Scalbert, 2000). Most common flavan-3-ols units of procyanidins are (+)-catechin and (−)-epicatechin. These units are generally linked by interflavan carbon-carbon bonding (Haslam, 1989). They are linked by C4-C8 or by C4-C6 in some rare cases, and sometimes are esterified by gallic acid (Ricardo da Silva et al., 1991; Prieur et al., 1994; Labarbe et al., 1999). Among the oligomeric procyanidins, procyanidin dimers possessing C4-C8 or C4-C6 bond are classified into B-type and trimers are C-type procyanidins (Santos-Buelga & Scalbert, 2000). However, procyanidins that contain additional carbon-oxygen bonds in their structure are also found in nature, and they are categorized into A-type procyanidins (Haslam, 1989; Santos-Buelga & Scalbert, 2000). A-type procyanidins are dimeric and have carbon-oxygen bonds between C2 of the upper unit and oxygen at the C7 of the lower unit. A-type procyanidins have been found in various fruits and plants including mountain cranberry, shells of horse chestnut, litchi, and peanut skins (Haslam, 1989; Le Roux et al., 1994; Lou et al., 1999).

**Biological activities**

**Antioxidant activity**

Free-radical damage has been postulated to contribute to the etiology of aging, and many chronic health problems such as cardiovascular, inflammatory diseases, and cancer (Rice-Evans & Diplock, 1993; Spiteller, 2001). Free radicals including reactive oxygen species (ROS) are capable of chemically altering major classes of biomolecules (e.g., lipids, proteins, nucleic acids), resulting in changes in their structure and function, which may be the mechanism that leads to aging and the development of chronic diseases (McCall & Frei, 1999).

Like other polyphenolic compounds, catechins and procyanidins have an antioxidant property, which may partially account for their beneficial role in heart diseases. Catechins and procyanidins have been shown to scavenge various forms of free radicals such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical, singlet oxygen (O2•), superoxide anion (O2−), hydroxy (OH−), nitric oxide (NO•) and alkyl peroxyl radicals (Sichel et al., 1991; Santos-Buelga & Scalbert, 2000; Sang et al., 2003; Sano et al., 2003). The antioxidant activities of the four major tea catechins on lipid peroxidation in synaptosomes were compared using various assays (Guo et al., 1996). In most assays, ECG and EGCG displayed better antioxidant activity than EC and EGC; however, the antioxidant activity of tea catechins may be dependent on the type of assay. The galloyl moiety of tea catechins appears to be required for the antioxidant and the antiproliferative effects in Caco-2 cells (Salucci et al., 2002). The presence of 3′,4′,5′-trihydroxyl groups attached to the B-ring has been shown to enhance the superoxide radical scavenging efficiency displayed by the catechin family in comparison to those with 3′,4′- dihydroyxyl groups, and the insertion of a galloyl moiety into three positions of the C-ring has exerted a synergistic effect on superoxide radicals scavenging activity...
Green tea catechins have been shown to regenerate \( \alpha \)-tocopherol in human low-density lipoprotein (LDL), which functions as a major antioxidant in human LDL (Zhu et al., 1999). EGCG and ECG show potent inhibitory effects on LDL oxidation \textit{in vitro}, and consumption of 300 mg of green tea polyphenol extract twice daily for 1 week delayed the oxidation of human LDL \textit{ex vivo} (Miura et al., 2000).

**Figure 1.** Structures of tea catechins and procyanidins.
However, other tea studies have shown little or no effect on plasma antioxidant potential after drinking even up to six cups of green tea (Riemsma et al., 2001). The potential explanations for the difference between these studies could be attributed to the different tea preparations, bioavailability, variable absorption from the gut with the resultant differences in blood concentrations of the active constituents, and/or differences in the study populations. Tea catechins also inhibit xanthine oxidase, a liver enzyme that produces uric acid and ROS during the catabolism of purines (Aucamp et al., 1997).

Studies on the antioxidant activity of procyanidins have been reported. The antioxidant activity of procyanidins from grape (Vitis vinifera) seeds has been extensively studied since the finding of the French Paradox. The antioxidant properties of procyanidins from grape seeds have been shown to inhibit superoxide anion and lipid peroxidation and to reduce or delay the formation of conjugated dienes during all phases of lipid peroxidation including induction, propagation, and breakdown (Facino et al., 1996). Sorghum (Sorghum bicolor Moench) grain procyanidin (B-1 type procyanidin, which comprised 16 epicatechin extension units and a catechin terminal unit) is 15- to 30-times more effective as an antioxidant against peroxyl radicals than simple monomeric phenolics or Trolox (Hagerman et al., 1998). Procyanidins are known to have little or no pro-oxidant activity, whereas many small phenolics are pro-oxidants (Yamanaka et al., 1997; Hagerman et al., 1998). The effects of polymerization of catechin-related compounds on the antioxidant activity may depend on the assay environment. Antioxidant activity decreased with polymerization in the lipid phase, whereas the activity in the aqueous phase increased from monomer to trimer and then decreased from trimer to tetramer (Plumb et al., 1998).

Procyanidin B2, a dimer from buckwheat (Fagopyrum esculentum Moench), has been reported to be more effective than (−)-epicatechin and rutin in hydrogen peroxide (H2O2) and superoxide anion (O2•−) scavenging when considered on a molar basis, although it was less effective in scavenging hypochlorous acid (HOCl) (Quettier-Deleu et al., 2000). The oligomeric procyanidins from hops are potent inhibitors of neuronal nitric oxide synthase activity, while procyanidin B2 is the most potent and procyanidin B3, catechin, and epicatechin are not effective (Stevens et al., 2002). Among hop procyanidins, however, procyanidin B3 shows the highest antioxidant activity against 3-morpholinosydnonimine-induced oxidation of LDL. In addition to reactive oxygen species, procyanidins are also shown to have antioxidant activities by inhibiting xanthine oxidase (Hatano et al., 1990).

Although the bioavailability of procyanidins is still not clear, several studies have reported the antioxidant activity of procyanidins in vivo. Oligomeric and polymeric procyanidins from grape seeds increased blood plasma antioxidant activity in rats after oral administration (Koga et al., 1999). The protective effect of grape seed procyanidins on hepatic and brain lipid in a mouse model has been tested and compared with antioxidant vitamins such as vitamin C, vitamin E, and β-carotene (Bagchi et al., 1998). The grape seed procyanidins exhibit a dose-dependent inhibition against not only 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced hepatic and brain lipid peroxidation and DNA fragmentation, but also peritoneal macrophage activation in mice. Although the antioxidant vitamins show significant activities in these tests, grape seed procyanidins display significantly better activities in all tests. A human feeding study with a commercial procyanidin product (Leucoselect Phyto-some) has been reported (Nuttall et al., 1998). Human subjects who were given two capsules containing 300 mg of grape procyanidin extracts showed increased serum total antioxidant capacity as measured by Trolox equivalent antioxidant capacity assay using a chemiluminescent detection method on day 5. The authors also indicated that the procyanidin extract had no effect on serum vitamins C and E levels.

Effects on heart disease

The oxidation of low-density lipoproteins is thought to be a key step in the development of atherosclerosis (Ross, 1999). Green tea catechins have been shown to protect LDL from oxidation and regenerate α-tocopherol in LDL particles (Salah et al., 1995; Zhu et al., 1999). Lowering LDL cholesterol and increasing high-density lipoprotein (HDL) cholesterol in plasma is believed to enhance the removal of lipids from the arterial wall and peripheral tissues and to be protective against coronary heart diseases (Ross, 1999). Consumption of green tea or green tea catechins has been reported to lower the plasma cholesterol level in animal and in human studies (Muramatsu et al., 1986; Imai & Nakachi, 1995). Green tea catechins have been reported to have a potent antithrombotic activity due to their antiplatelet effects by inhibition of cytoplasmic calcium increase (Kang et al., 2001). Although there are many studies regarding the effects of green tea or green tea catechin mixtures on heart disease, studies on the effect of individual catechins are limited. EGCG has been shown to reduce significantly total cholesterol and LDL plasma levels in Wistar rats fed a diet containing 1% EGCG for 4 weeks when compared to the no treatment group (Raederstorff et al., 2003). EC displayed stronger LDL oxidation when catalyzed by mammalian 15-lipoxygenase than ascorbic acid, α-tocopherol, and flavone (da Silva et al., 2000).

Red wine, but not white wine, has been shown to decrease dramatically blood platelet aggregation in a rat feeding study (Ruf et al., 1995). In the production of red wine, the fermentation process includes juice as
well as skins and seeds, whereas white wine is obtained by fermentation of grape juice only (Bombardelli & Morazzoni, 1995). Phenolic substances rich in red wine, grape seeds, and skins were thought to be responsible for the prevention of coronary heart disease and therefore have received much attention because of their various biological activities. Procyanidins from grape seeds have been compared with monomers for their anti-hypercholesterolemic effect in rats fed with hypercholesterolemic diets (Tebib et al., 1994). In that study, rats fed polymeric tannins had significantly lower plasma total cholesterol, triacylglycerol, LDL, and very low density lipoprotein (VLDL) cholesterol concentrations than rats fed with monomers. The polymer-fed group also showed a higher plasma HDL cholesterol level and a greater fecal excretion of cholesterol than did the monomer-fed group. The anti-atherosclerotic effect of a procyanidin-rich extract (74.3% procyanidins) from grape seeds was studied in cholesterol-fed rabbits (Yamakoshi et al., 1999). Procyanidin-rich extracts diet (0.1% and 1% in the diet) decreased the number of oxidized LDL-derived atherosclerotic foam cell lesions in the aorta of the rabbits. The authors detected procyanidins in the plasma of rats but not in the lipoproteins including LDL and VLDL, indicating that procyanidins might inhibit LDL oxidation by scavenging reactive oxygen species in aqueous phases such as the plasma and the interstitial fluid of the arterial wall. Beside grape seeds procyanidins, oligomeric procyanidins present in chocolate and cocoas have been reported to inhibit LDL oxidation in vitro as well (Pearson et al., 2001).

Cancer chemopreventive properties: NF-κB, AP-1, and MAPKs

Many natural products, including polyphenolic compounds, have been demonstrated to possess chemopreventive effects in various human cancer cell lines as well as in carcinogen-induced tumor models in experimental animals (Yang et al., 2002). Inhibitory activities of tea catechins against tumorigenesis in animal models on various organs have extensively been studied and are well documented (Yang et al., 2002). However, information on the potential role of procyanidins in cancer prevention, particularly in vivo, is limited. Moreover, a composite of signal transduction pathways involved in the preventive mechanisms has only recently been addressed, and little is known regarding the roles of catechins and procyanidins on the cellular signal transduction pathways in cancers, which need to be elucidated.

Nuclear factor-kappa B (NF-κB) is a transcription factor that plays a crucial role in several signal transduction pathways involved in various cancers as well as in chronic inflammatory diseases (Barnes & Karin, 1997; Amit & Ben-Neriah, 2003). It consists of homo- and heterodimeric complexes formed from the Rel family of proteins (Siebenlist et al., 1994; Baeuerle & Baltimore, 1996). In vertebral cells, there are five members of the Rel/NF-κB proteins including p65 (Rel A), p50/p105, p52/100, c-Rel, and Rel B (Siebenlist et al., 1994; Baeuerle & Baltimore, 1996; Ghosh et al., 1998). The most common NF-κB is a heterodimer composed of p65 and p50. In most cells, NF-κB is sequestered in the cytosol, associated with inhibitor proteins, IκBs. A variety of extracellular stimuli lead to the activation of the upstream IκB kinases (IKKs), resulting in rapid phosphorylation and proteolytic degradation of IκB, with the subsequent release of NF-κB from the IκB, and NF-κB complex then translocates to the nucleus where it regulates gene transcription (Karin & Ben-Neriah, 2000; Li et al., 2001; Yamamoto & Gaynor, 2001). Activation of NF-κB has been linked to apoptotic cell death; either promoting or inhibiting apoptosis, depending on the cell types and the environmental conditions (Baichwal & Baeuerle, 1997). In most cells, activation of NF-κB protects the cells from apoptotic stimuli, presumably through the induction of survival genes (Karin & Ben-Neriah, 2000).

Activator protein-1 (AP-1) has been implicated to play important roles in various biological processes including apoptosis and cancer development. It is known to bind to a palindromic DNA sequence such as TPA-responsive element (TRE) present within the regulatory region of many genes, including c-jun (Angel et al., 1987). AP-1 activity has been involved in many diverse cellular processes including biological apoptosis, proliferation, transformation, and differentiation, although the exact outcome may be highly dependent on tissue and developmental stage (Angel & Karin, 1991; Huang et al., 1998; Li et al., 2003).

AP-1 activity can be regulated by many mechanisms, one of which is the activation of mitogen-activated protein kinase (MAPK) pathways (Karin, 1995). MAPKs are activated in response to a wide variety of extracellular stimuli and mediate signal transduction cascades that play an important regulatory role in cell growth, differentiation, and apoptosis (Chan-Hui & Weaver, 1998). Three of the MAPKs have been well studied: extracellular signal-regulated protein kinases (ERK), c-jun N-terminal kinases (JNK), and p38.

EGCG has been reported to inhibit NF-κB activation by blocking the binding of NF-κB to DNA and disappearance of IκB from the cytosolic fraction in peritoneal macrophages (Lin & Lin, 1997). EGCG has been found to exhibit differential dose-responses on the inhibition of NF-κB in cancer skin cells versus normal skin cells (Ahmad et al., 2000). The inhibition of NF-κB constitutive expression and activation required much higher doses of EGCG in normal skin cells as compared to cancer skin cells. In the JB6 mouse epidermal cell lines, EGCG has been shown to inhibit TPA-induced NF-κB activity, phosphorylation of IκBζ at Ser32, and the NF-κB
sequence-specific DNA-binding activity (Nomura et al., 2000). Inhibition of NF-κB activation by EGCG also has been found through inhibiting IKK in an intestinal epithelial cell line IEC-6 (Yang et al., 2001). A recent study has demonstrated the inhibitory activity of EGCG on ultraviolet B (UVB)-mediated activation of NF-κB in normal human epidermal keratinocytes (Afaq et al., 2003). We have recently studied the effects of catechins on the activation of NF-κB induced by LPS in HT-29 colon adenocarcinoma cells, using luciferase reporter gene assay and immunoblotting. Among the catechins tested in this study, only EGCG decreased the LPS-induced IkBα phosphorylation, whereas NF-κB-reporter gene activity was unaffected or slightly activated by all the catechin compounds tested (Jeong et al., 2004a).

In a human keratinocyte cell line HCL14 that contains signature UVB mutations in both p53 alleles, EGCG has been shown to inhibit UVB-induced AP-1 trans-activation nearly to the basal level (Barthelman et al., 1998). In normal human keratinocytes, however, EGCG markedly increases AP-1 factor-associated responses through a MAPK signaling mechanism, which is similar to our recent findings in HT-29 cells (Jeong et al., 2004a), suggesting that the signaling mechanism of EGCG action could be markedly different between cell types (Balasubramanian et al., 2002).

Our laboratory has shown that EGCG potently induced the activations of MAPKs including JNK1, p38, and ERK2 activities in several human cancer cell lines such as HepG2 (hepatoma), HT-29 (colon), and HeLa (cervical squamous) in a time- and dose-dependent manner (Chen et al., 2000, 2003). Many chemotherapeutic drugs have been reported to activate JNK and p38, and their activation has been suggested to be an important component of the cellular response to several anticancer drugs and to play a crucial role in apoptosis (Hannun, 1996; Osborn & Chambers, 1996). However, the activation of MAPK pathways can lead to either cell survival or cell death, which may depend on cell types, concentration of the agents, as well as time of treatments.

Procyanidin-rich extracts from pine (Pinus maritima) bark, called pycnogenol, inhibit in a dose-dependent manner the increase of capillary permeability induced by UV radiation in the shaved back of the rats (Blazso et al., 1997). However, the effect of procyanidins on the activation of NF-κB is not clear. The extract has been shown to inhibit the activation, the binding to DNA, and the NF-κB-dependent gene expression in HaCaT cells, an immortalized human keratinocyte (Packer et al., 1999). It also protected GSH levels and suppressed partially the cytotoxicity induced by UV treatment, both in human primary keratinocytes and in HaCaT cells. In contrast to these results, however, the pine bark extract had no effect on the activation on NF-κB in a murine macrophage RAW 264.7 cell line (Virgili et al., 1998).

Catechin monomers, catechin and epicatechin, dimeric and trimeric procyanidins, and the pine bark extract have been compared for their activity on NF-κB gene expression in macrophage cells (Park et al., 2000). Catechin monomers and procyanidin dimers repress interferon-γ-induced NF-κB-dependent gene expression, whereas the trimeric procyanidin C2 and the pine bark extract induce the expression. Results obtained from our laboratory with human colon HT-29 cells stably transfected with NF-κB reporter gene have demonstrated little or no effect of procyanidin dimers B1 and B2 on LPS-induced NF-κB transcription activation up to concentrations of 50 μM (Jeong et al., 2004a). Therefore, the biological roles of procyanidins in NF-κB signaling pathways may be dependent on the degree of polymerization of the procyanidins, the extracellular stimuli, as well as the cell types.

Currently, there is no report on the effects of individual procyanidins on AP-1 activity. Our laboratory has recently found that procyanidins B1 and B2 have no effect on AP-1 reporter gene activity in HT-29 cells, and hence it appears that the potential chemopreventive effects of procyanidins may not use the AP-1 signaling pathway under the conditions that were studied. However, more studies would be needed in other cell lines/types, especially in vivo conditions, in order to understand fully the mechanism of actions of procyanidins. Procyanidins-rich grape seed extract has recently been shown to inhibit the growth and induction of apoptotic cell death in a human prostate carcinoma DU145 cell line (Agarwal et al., 2000). Follow-up studies by this research group have revealed that the grape seed extract inhibits both epidermal growth factor (EGF)-induced and constitutively active Elk1 phosphorylation and AP-1 activation in a human prostate carcinoma DU145 cell line (Tyagi et al., 2003). It also causes a strong increase in phospho-JNK1/2 levels, JNK activity, and phospho-c-Jun levels in the same cell line, while the JNK activation induced by the grape seed extract was blocked by a JNK inhibitor SP600125, implicating the involvement of JNK activation by the grape seed extract in its apoptotic response (Tyagi et al., 2003).

Conclusions

Various biological activities have been studied for tea catechins and procyanidins, which are structurally related and based on the flavan-3-ol unit. Despite a number of studies on their potential health benefits, the exact mechanisms underlying their biological activities remain to be elucidated. For tea catechins, biological functions of both tea itself and individual tea catechin compounds, especially EGCG, have widely been explored. Tea catechins have been shown to scavenge a variety of free radicals including ROS in vitro, but in vivo, plasma
antioxidant capacity after consumption of tea or tea catechins is equivocal. Although EGCG is known as the most potent bioactive compound among the tea catechins, its in vivo bioavailability is much less than that of EGC and EC (Lambert & Yang, 2003), which may explain the discrepancy between various in vitro and in vivo results. Bioavailability of procyanidins is still unclear. Metabolites of procyanidins after oral administration to mice and rats have been found in plasma and various tissues (Bombardelli & Morazzoni, 1995; Koga et al., 1999). Procyanidin dimers and trimers have been reported to be absorbed through the intestinal epithelia cell monolayer in vitro, but polymers are reported to be unabsorbable in vivo in chicken and sheep (Deprez et al., 2000). Studies on the biological activities of procyanidins have largely been made with the procyanidin mixtures or procyanidin-rich extracts rather than a single compound. The biological potential of procyanidins in vivo has been suggested to be through their degradation by the colonic microflora into low-molecular-weight phenolic compounds that might contribute to the beneficial properties (Deprez et al., 2000). Due to the highly complex structure of polymeric procyanidins, it might be difficult to prepare or isolate pure procyanidins with high polymerization degree. Nevertheless, the biological consequences and effects of the individual compounds should be elucidated in the future in order to better understand the underlying molecular mechanism after exposure to these compounds in our everyday diet.

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References


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