Trimeric and Tetrameric A-Type Procyanidins from Peanut Skins

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ABSTRACT: Peanut skins are a rich source of oligomeric and polymeric procyanidins. The oligomeric fractions are dominated by dimers, trimers, and tetramers. A multistep chromatographic fractionation led to the isolation of four new A-type procyanidins of tri- and tetramer structures. The structures of the new trimers were defined by NMR, electronic circular dichroism, and MS data as epicatechin-(4β→8,2β→O→7)-epicatechin-(4β→8,2β→O→7)-catechin, peanut procyanidin B (3), and epicatechin-(4β→8,2β→O→7)-epicatechin-(4β→6)-catechin, peanut procyanidin C (4). The new tetramers were defined as epicatechin-(4β→8,2β→O→7)-epicatechin-(4β→6)-epicatechin-(4β→8,2β→O→7)-catechin, peanut procyanidin E (1), and epicatechin-(4β→8,2β→O→7)-epicatechin-(4β→6)-epicatechin-(4β→8,2β→O→7)-epicatechin, peanut procyanidin F (2). In addition, both A-type dimers A1, epicatechin-(4β→8,2β→O→7)-catechin, and A2, epicatechin-(4β→8,2β→O→7)-epicatechin, as well as two known peanut trimers, ent-epicatechin-(4β→6)-epicatechin-(4β→8,2β→O→7)-catechin, peanut procyanidin A (5), and epicatechin-(4β→8)-epicatechin-(4β→8,2β→O→7)-catechin, peanut procyanidin D (6), were also isolated. Dimer A1, the four trimers, and two tetramers were evaluated for anti-inflammatory activity in an in vitro assay, in which LPS-stimulated macrophages were responding with secretion of TNF-α, a pro-inflammatory cytokine. Tetramer F (2) was the most potent, suppressing TNF-α secretion to 82% at 8.7 μM (10 μg/mL), while tetramer E (1) at the same concentrations caused a 4% suppression. The results of the TNF-α secretion inhibition indicate that small structural differences, as in peanut procyanidin tetramers E and F, can be strongly differentiated in biological systems.

Procyanidins are common phenolic plant metabolites with antioxidant properties and comprise epicatechin (EC) and catechin (C) constituent units. In the more common B-type procyanidins, the flavan-3-ol units are connected through a single bond between C-4 of the upper unit and C-6 or C-8 of the lower unit. The B-type procyanidins dominate in dietary important sources such as apples, pears, and cocoa-containing foods. The A-type procyanidins differ from the B-types by having an additional bond between adjacent flavan-3-ol units that connects C-2 of the upper unit via an oxygen atom to C-7 of the lower unit. Such a “bridge” imposes conformational rigidity to both units. In addition, in the A-type procyanidins, the crowding around the B-type connected units often produces rotational restrictions favoring one conformation (rotamer) over another, as is evidenced by the 1H NMR spectroscopic analysis. The presence of A-type procyanidins has been well established in cranberries, cinnamon, and peanut skins. To a significant degree, the position of the A-type bond is characteristic for the plant source. For example, in cinnamon it involves the top unit, but in cranberries the bottom unit. Data on the biological activity of individual procyanidins, especially of the A-type, are rare, reflecting mainly the poor commercial availability of these compounds. However, the available data indicate that biological systems can differentiate between structurally similar procyanidins.

Thus, it appears that A-type procyanidins, as a result of their rigid 3D shape, should interact with biological macromolecules more specifically, leading to potential therapeutic applications. Among the documented pharmacological effects, procyanidins were shown to exert cardiovascular, neuroprotective, antidiabetic, and hypotensive activities. A protective effect of these polyphenols in ischemia-induced cell swelling was also observed. Recent advances in medical sciences increasingly indicated that many degenerative diseases are associated with increased oxidative stress levels. Thus, a higher intake of procyanidins could be beneficial by lowering excessive levels of harmful reactive oxygen species generated during oxidative stress. This postulate seems to be true as more therapeutic applications of procyanidins are explored. Besides...