Absorption and metabolism of tea catechin in humans.

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Green tea is consumed as a popular beverage in Japan and throughout the world. During the past decade, epidemiological studies have shown that tea catechin intake is associated with lower risk of cardiovascular disease [1,2]. In vitro biochemical studies have reported that catechins, particularly epigallocatechin-3 gallate (EGCg), help to prevent oxidation of plasma low-density lipoprotein (LDL) [3-5]. LDL oxidation has been recognized to be an important step in the formation of atherosclerotic plaques and subsequent cardiovascular disease [6].

Metabolic studies have shown that EGCg supplement is incorporated into human plasma at a maximum concentration of 4400 pmol/mL [7-10]. Such concentrations would be enough to exert antioxidative activity in the blood stream. The potent antioxidant property of tea catechin may be beneficial in preventing the oxidation of LDL. It is of interest to examine the effect of green tea catechin supplementation on antioxidant capacity of plasma in humans by measuring plasma phosphatidylcholine hydroperoxide (PCOOH) as a marker of oxidized lipoproteins.

1. Absorption and metabolism of tea catechin

A large part of tea catechin ingested orally is distributed in intestinal mucosa, and is excreted finally into feces. A part of catechin receives conjugation reactions (glucuronide and sulfate formations) in the intestinal mucosa, liver and kidney, and substancial levels of catechin is incorporated into human body as in non-conjugated form. EGCg is actually incorporated into human plasma after an intake of green tea drink. Five % of catechin ingested is incorporated and the absorption maximum reached around 1-2 hr. No harmful effect has been found clinically or biochemically in any of the subjects taking EGCg supplement. Serum aspartate aminotransferase, creatinine, total cholesterol, and iron levels are not changed after consumption of tea catechin at concentrations up to 1000 mg/day for 3 months [13]. A substancial level of EGCg is confirmed to be present in human plasma after 60 min of ingestion, though the basal level after 12 hr of fasting is below the detection limit (< 2 pmol/mL). In humans the half-life in kinetics of tea catechin metabolism is relatively short, as has

been reported in rats [9, 11, 12]. In the study by Van Het Hof et al. [14], human plasma antioxidant activity and oxidation marker were measured after overnight fasting, i.e. at least 12 hr of fasting after their most recent tea consumption. Therefore, it is likely that the plasma catechins disappeared in their study, even though the subjects consumed 6 cups of green tea daily for 4 weeks, or by due to lower sensitivity of their methodology. The plasma EGCg concentration is increased to 122 ng/mL at 60 min after an oral intake of 82 mg of EGCg. The concentrations of endogenous plasma antioxidant molecules such as α -tocopherol, γ -tocopherol, β -carotene, and lycopene show no change before and after the EGCg ingestion. Regarding the metabolites, Lee et al. [17] reported glucuronide and sulfate conjugates of catechins in human plasma, in which a phenolic hydroxyl group of the catechins is supposed to be substituted for glucuronide or sulfate. Since the antioxidant activity of catechins is closely dependent on the number of phenolic hydroxyl groups [15], catechins in the free form (non-conjugated form) would be most important to the antioxidant action. Because of their high polarity, glucuronide and sulfate conjugates would be excreted rapidly from the blood stream. The antioxidant contribution of these metabolites in blood plasma seems to be less effective than that of the non-conjugated free from catechins.

2. Antioxidative effect of tea catechin

PCOOH (phosphatidylcholine hydroperoxide) is a marker of oxidative injury of plasma lipoproteins. Since phosphatidylcholine is generally located as a major constituent on the outer surface of the amphipathic lipid monolayer of the lipoprotein particle, the occurrence of PCOOH directly indicates an increase of oxidative challange in monolayer membranes of lipoprotein in plasma. PCOOH is the predominant membrane lipid hydroperoxide in human plasma [16-18]. Because PCOOH is a primary oxidation product of phosphatidylcholine, an increase in PCOOH concentration reflects stimulation of in vivo peroxidation of plasma lipoprotein phospholipid. Tea catechin supplementation clearly lowers plasma PCOOH concentrations in humans. The decrease in PCOOH correlates with plasma EGCg increase. Generally PCOOH level is individually rather stable in plasma throughout the day, keeping certain levels between 40 and 90 pmol PCOOH/mL of plasma in a healthy donor. The rapid decline of plasma PCOOH level after the catechin supplementation suggests the increase of the plasma antioxidative capacity resulting from EGCg absorption. This may indicate that the EGCg incorporated into plasma prevents spontaneously occurring membrane phospholipid peroxidation of the plasma lipoproteins. The beneficial effect of daily tea catechin intake in reducing the risk of cardiovascular disease [1, 2] could be mediated in part through protection of oxidative modification of plasma lipoproteins. In the study of in vitro peroxidation caused by CuSO4, the catechin-incorporated plasma shows significantly less production of PCOOH and TBARS. The reactivity of EGCg with

oxygen radicals and the chelating activity with Cu2+ would be important for such reduction of PCOOH and TBARS. The effect of plasma endogenous antioxidants, such as ascorbic acid, tocopherols, and carotenoids, on Cu2+-mediated oxidation of plasma or the synergistic reaction between these antioxidants and EGCg shuld be considerable. Other antioxidative function of tea catechin may inclide inhibition of hydrolytic and oxidative enzymes (phospholipases, cyclooxygenase, and lipoxygenases) relating to anti-inflammatory activity.

Drinking green tea contributes to a high antioxidant capacity in humans. The taking of tea catechin as an antioxidative nutrient can be recommended as a way to reduce the risk of cardiovascular disease [19, 20]. Most recent prospective cohort study also concluded that catechins may reduce the risk of ischemic heart disease mortality [21].

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