**Flavonoids from almond skins are bioavailable and act synergistically with Vitamins C and E to enhance hamster and human LDL resistance to oxidation.**

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**Abstract:**
Consumption of tree nuts such as almonds has been associated with a reduced risk of coronary heart disease. Flavonoids, found predominantly in the skin of almonds, may contribute to their putative health benefit, but their bioactivity and bioavailability have not previously been studied. Almond skin flavonoids (ASF) were extracted with HCl:H2O:methanol (1:19:80) and their content of catechins and flavonols identified by HPLC with electrochemical detection. ASF bioactivity was assessed in vitro by their capacity to increase the resistance of human LDL to oxidation induced by 10 mmol/L Cu2+. ASF from 0.18 to 1.44 mmol gallic acid equivalent (GAE)/L increased the lag time to LDL oxidation in a dose-dependent manner ($P \leq 0.0001$). Combining ASF with vitamin E or ascorbic acid extended the lag time >200% of the expected additive value ($P \leq 0.05$). The bioavailability and in vivo antioxidant activity of 40 mmol ASF were examined in BioF1B hamsters. Peak plasma concentrations of catechin, epicatechin, and flavonols (quercetin, kaempferol, and isorhamnetin) occurred at 60, 120, and 180 min, respectively. The concentration of isorhamnetin was significantly elevated in liver at 180 min. Absorbed ASF enhanced the ex vivo resistance of hamster LDL collected at 60 min to oxidation by 18.0% ($P = 0.028$), and the in vitro addition of 5.5 mmol/L vitamin E synergistically extended the lag time of the 60-min sample by 52.5% ($P \leq 0.05$). Thus, ASF possess antioxidant capacity in vitro; they are bioavailable and act in synergy with vitamins C and E to protect LDL against oxidation in hamsters.