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Antiatherogenic effect of quercetin is mediated by proteasome inhibition in the aorta and circulating leukocytes

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Abstract:
Quercetin, a plant-derived flavonoid, has attracted considerable attention as promising compound for heart disease prevention and therapy. It has been linked to decreased mortality from heart disease and decreased incidence of stroke. Here, we report new data showing the angioprotective properties of quercetin mediated by its effect on proteasomal proteolysis. This study was designed to investigate the ability of quercetin to modulate proteasomal activity in a rabbit model of cholesterol-induced atherosclerosis. First, we show proteasomal trypsin-like (TL) activity increased up to 2.4-fold, chymotrypsin-like (CTL) activity increased by up to 43% and peptidyl-glutamyl peptide-hydrolyzing (PGPH) activity increased by up to 10% after 8 weeks of a cholesterol-rich diet. A single intravenous injection of the water-soluble form of quercetin (Corvitin) significantly decreased proteasomal TL activity 1.85-fold in monocytes, and decreased the CTL and PGPH activities more than 2-fold in polymorphonuclear leukocytes (PMNL) after 2 h. Prolonged administration (1 month) of Corvitin to animals following a cholesterol-rich diet significantly decreased all types of proteolytic proteasome activities both in tissues and in circulating leukocytes and was associated with the reduction of atherosclerotic lesion areas in the aorta. Additionally, the pharmacological form of quercetin (Quertin) was shown to have an antiatherogenic effect and an ability to inhibit proteasome activities.

Key words:
proteasome inhibition, atherosclerosis, flavonoids