Immunoregulatory effects of the flavonol quercetin in vitro and in vivo

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Author(s) Nickel, Thomas; Hanssen, Henner; Sisic, Zeljka; Pfeiler, Susanne; Summo, Claudia; Schmauss, Daniel; Hoster, Eva; Weis, Michael
Author(s) at UniBasel Hanssen, Henner ;
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Atherosclerosis is known to be an inflammatory disease. Dendritic cells (DCs) are essential for the regulation of the immune system. Up to 10% of the cells in atherosclerotic plaques are DCs. The cardiovascular protective effects of flavonoids (tea, wine) may be mediated by anti-inflammatory mechanisms that affect DC regulation. We aimed to characterize the impact of the flavonol quercetin on DC activity and differentiation in vitro and in vivo.; For the in vitro experiments, we used murine DCs and endothelial cells to study adhesion properties. For all other experiments (DC phagocytosis capacity, DC maturation, DC differentiation (BDCA-1/-2) and NF-kB-activation), human monocyte-derived DCs were used. The cells were incubated with quercetin (10ăμmol/L) ś oxLDL (10ăμg/mL) between 24 and 48ăh. For in vivo experiments, eight healthy male volunteers took 500ămg of quercetin twice daily over 4ăweeks, five healthy male volunteers served as control. Before and after intake, blood samples were collected. Peripheral blood leukocytes were isolated (analyses of DC differentiation), and plasma was immediately frozen.; Quercetin reduced DC adhesion (-42%; pă<ă0.05) and expression of CD11a (-21%; pă<ă0.05). OxLDL-induced DC differentiation was partially inhibited by quercetin (BDCA-1-29%; BDCA-2-33%; pă<ă0.05). These effects were achieved by compensation of oxLDL-induced up-regulation of NF-kB by quercetin. The 4-week treatment with quercetin resulted in relevant plasma levels (2.47ăμmol/L) and reduced BDCA-2ă+ăDCs in the peripheral blood by 42% (pă<ă0.05) as well as systemic levels of the NO-synthase inhibitor asymmetric dimethylarginine (-31%, pă<ă0.05).; In vitro, quercetin reduced DC adhesion and oxLDL-induced DC differentiation. In vivo, quercetin reduced circulating plasmacytoid DCs and systemic ADMA-levels. The immunoregulatory effects of quercetin may contribute to the anti-atherosclerotic potential of flavonols.
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