

## **Study on effects of resveratrol and quercetin on inflammation and insulin resistance**

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A study was carried out to examine the extent to which quercetin and trans-resveratrol (RSV) prevented inflammation or insulin resistance in primary cultures of human adipocytes treated with tumor necrosis factor-a (TNF-a)—an inflammatory cytokine elevated in the plasma and adipose tissue of obese, diabetic individuals.

Cultures of human adipocytes were pretreated with quercetin and trans-RSV followed by treatment with TNF-a. Subsequently, gene and protein markers of <u>inflammation</u> and <u>insulin resistance</u> were measured. The authors report that quercetin, and to a lesser extent trans-RSV, attenuated the TNF-a-induced expression of inflammatory genes such as interleukin (IL)-6, IL-1b, IL-8, and monocyte chemoattractant protein-1 (MCP-1) and the secretion of IL-6, IL-8, and MCP-1.

Forum members were concerned about certain aspects of the study, especially the extrapolation of in vitro results to in vivo situations. The in vitro conditions the authors describe are minimally representative of an in vivo condition. In vivo, after consumption of quercetin or resveratrol, these compounds undergo extensive metabolism, leading to glucuronidated, sulphated or methylated compounds. In a previous study, quercetin 3-glucoside was transformed to 3,4-dihydroxyphenylacetic acid, acetate and butyrate in cells from human gut; only 3'-methylquercetin has been detected in human plasma, present at a concentration of 0.1 to 0.2  $\mu$ M after 3 h. The authors of the current paper are using concentrations up to 60  $\mu$ M, concentrations which have not been found in vivo.



There were also concerns with the work on cell uptake of quercetin and resveratrol. Primary adipocytes were incubated with the polyphenols, but it is not clear whether or not the concentrations used were subtoxic. Our current knowledge is limited about local concentration of the molecules we are studying in subcellular compartments, their interaction with alternative targets, and eventually their transformation into products that could be more or less active on a given specific pathway. The real difficult and important issue is the identification of a reasonable convergence -- if not agreement -- between data originating from extremely distant approaches. In this case, the notion that metabolic diseases are related to a homeostatic imbalance in adipose tissue, linked to a different redox status, linked to activation of specific pathways, and that different redox sensitive polyphenols do have a protective effect, encompasses the evidence produced by extremely distant approaches.

From a clinical point of view, the role of phytochemicals acting as antioxidants and anti-inflammatory agents could be extremely important in inflammation-associated chronic conditions such as cardiovascular disease, diabetes, and cancer. Quercetin and resveratrol may indeed play an important role in this regard, and need to be investigated further to establish the clinical importance of natural dietary compounds in the prevention of chronic degenerative conditions.

## Provided by Boston University Medical Center

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