Editorial

Resveratrol – Current status and outlook

The stilbene resveratrol gained scientific interest in the early 90s when its presence was reported in red wine, leading to speculations that resveratrol might help explain the ''French Paradox'' [1]. This is described by significant reduction in cardiovascular disease risk and low mortality from coronary heart disease in France despite relatively high levels of dietary saturated fat and cigarette smoking. Moderate consumption of alcoholic beverages, red wine in particular, in France was associated with that risk reduction and resveratrol had been hypothesized to be the active principle by eliciting antioxidant, anti-inflammatory, and other potential anti-atherogenic effects *in vitro* and in some animal models of atherosclerosis. However, it is not yet known whether increased consumption of polyphenols from red wine provides any additional protection from cardiovascular disease beyond that associated with its alcohol content.

''.....resveratrol might help explain the ''French Paradox''

The most striking finding in recent years was that resveratrol protects overfed mice from weight gain and extends the lifespan of mice on a high-calorie diet [2]. Here, Baur et al. showed that resveratrol shifts the physiology of middle-aged mice on a high-calorie diet towards that of mice on a standard diet and significantly increases their survival by mimicking mechanisms of calorie restriction. The underlying mechanisms discussed include increased insulin sensitivity, reduced insulin-like growth factor-1 (IGF-I) levels, increased AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor-gamma coactivator 1-α (PGC-1α) activity, increased mitochondrial number, and improved motor function after resveratrol administration. However, it is not known whether resveratrol has similar effects in humans.

Clinical trials are also needed to prove other potential health benefits of resveratrol for which cellular mechanisms point to cancer- and chemo-preventive effects, anti-inflammatory effects, and the prevention of obesity, cardiovascular diseases and type II diabetes mellitus. Bearing in mind that oral resveratrol is not known to be toxic or cause adverse effects in humans at doses up to 5 g per day for 29 days [3], its use as a dietary supplement is widely studied.

The still growing interest in the biological activity of resveratrol is demonstrated by the number of annual citations since 1990, when its intake with red wine was associated with the French Paradox: Entering ''resveratrol'' into the ISI Web of Knowledge data base resulted in 15 hits in 1990 and gave 1381 hits in 2010 – a raise by almost a factor of 100, compared with numbers of 235 and 1635 (increase of a factor of 6) for quercetin within the same period of time.

This issue provides the latest results on resveratrol's efficacy in human trials, its bioavailability and cellular transport mechanisms, and recent findings that support its beneficial impact on osteoporosis, atherosclerosis, type II diabetes mellitus and cancer prevention.

Future research in this field will not only need to clarify the efficacy of resveratrol in humans but will also be focused on strategies to (i) improve its bioavailability by optimized galenic preparations or by limiting the extensive metabolisation of resveratrol into less active compounds, and to (ii) enhance the formation of the most active metabolites of resveratrol formed after oral intake. One approach here could be the concomitant administration of other phenolic compounds that compete with resveratrol for phase-I/II metabolising enzymes, resulting in higher systemic concentrations of non-metabolised free resveratrol.

Nonetheless, research in the past 30 years has provided convincing evidence that resveratrol is a genuinely promising molecule for good health, although the cellular mechanisms of action have not yet been fully understood and clinical and epidemiological data are still needed.

V. Somoza

Veronika Somoza

References

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