

Editorial



MAGIC-OL Resveratrol

Resveratrol from red wine has long been associated with the so-called “French Paradox”, reflecting the low incidence of heart disease among the French despite their relatively high-fat diet. It is a polyphenolic compound found in the skins of such red fruits as grapes, plums or peanuts. Plants do not produce resveratrol routinely, but in order to combat environmental stresses or attack by pathogenic organisms. Such defensive molecules are known as phyto-alexins, from the Greek words for “plant” and “protector”. However scientists are more and more tempted to classify resveratrol as a human or “anthro-” alexin too, considering what it does to protect our health and even, perhaps, extend our lifespan by mimicking caloric restriction, as evidenced in recent studies on *Saccharomyces cerevisiae* or *Coenorhabditis elegans*. From *in vitro* experiments, the most striking health benefits of resveratrol might be, firstly, cardio- and vascular-protective effects through a variety of mechanisms: it inhibits platelet aggregation, the proliferation of smooth muscle cells, and the oxidation of LDL-cholesterol; it reduces the synthesis of certain lipids and eicosanoids that tend to promote inflammation and atherosclerosis; and it suppresses certain cardiac arrhythmias. Some of these effects may be due in part to resveratrol being a phytoestrogen, *i. e.*, a plant compound that has biological activities similar to those of estrogens.

Second, neuroprotective effects have been reported and, third, resveratrol has demonstrated anticarcinogenic, chemopreventive activity: it inhibits cellular events associated with the initiation,

promotion, and progression of tumors through a wide range of actions that are still relatively poorly understood. It appears to help detoxify carcinogens, to inhibit the synthesis of various cancer-related compounds, and to stimulate the genetic mechanism for the apoptosis (programmed death) of cancer cells.

Much of the scientific evidence for resveratrol's benefits is based on *in vitro* studies in which the diastereomers trans- or cis-resveratrol have been tested. However, from animal studies and human trials investigating the metabolic transit of plant-derived resveratrol, we know that the predominant isomer that is orally ingested with foods like grapes or red wine is trans-resveratrol-glucoside (piceid) which is degraded in the small intestine and subsequently glucuronidated and sulfated in enterocytes therein. These resveratrol derivatives might be less biologically active due to their esterified hydroxyl groups. Although this might be an explanation for some contradictory results from animal feeding studies on the anti-oxidative effects of dietary resveratrol *in vivo*, the chemopreventive activity of orally administered trans-resveratrol has almost consistently been demonstrated in animal models of induced cancer. This is the actual mystery of dietary resveratrol and its derivatives. We definitely need well-controlled human trials to confirm the cardio-protective and chemopreventive results, also in comparison with other dietary polyphenols.

Clearly, none of the huge number of supplements available as grape extracts can be recommended, as very little is known about the toxicity of dietary resveratrol. The toxicological data available so far have revealed a NOAEL (no observed adverse effect level) of 300 mg/kg body weight. Considering a maximum of 10 mg of plant-derived resveratrol ingested with a normal diet on a daily basis, this NOAEL seems inaccessible. But still, nothing is known about the effective dose required to achieve the health benefits evidenced in cell culture studies or in animal trials. Nonetheless, there is no doubt that resveratrol is a genuinely promising molecule for good health and there is some hope that future studies will resolve the mystery of this “anthro-alexin”.

V. Somoza

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