

REVIEW

RESVERATROL, A NATURAL CHEMOPREVENTIVE AGENT AGAINST DEGENERATIVE DISEASES

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Resveratrol, a natural chemopreventive agent against degenerative diseases. E. IGNATOWICZ, W. BAER-DUBOWSKA. Pol. J. Pharmacol., 2001, 53, 557–569.

Resveratrol (3,5,4'-trihydroxystilbene) is a naturally occurring compound shown to modulate the risk of cardiovascular degenerative diseases (atherosclerosis) and inhibit chemical carcinogenesis in rodents. Various studies have demonstrated the effect of this phytoalexin on biological mechanisms involved in cardioprotection. These include modulation of lipid turnover, inhibition of eicosanoid production, prevention of the low-density lipoprotein oxidation and inhibition of platelet aggregation. Carcinogenesis in animal models can be divided at least into three stages: initiation, promotion and progression. Initiation occurs as result of interaction of a reactive form of carcinogen with DNA. Chemical carcinogens like polycyclic aromatic hydrocarbons are metabolized to reactive species by cytochrome P450 dependent enzymes activated through aryl hydrocarbon (Ah) receptor. The inhibition of tumor initiation by resveratrol most probably occurs through preventing the activation of Ah receptor. Resveratrol affects also several factors involved in tumor promotion and progression. Since tumor promoting agents alter the expression of genes whose products are associated with inflammation, chemoprevention of cardiovascular diseases and cancer may share the same common mechanisms. This includes principally modulation of the expression of growth factors and cytokines. Recently, chemopreventive properties of resveratrol have been associated with the inhibition of NF- κ B. This transcription factor is strongly linked to inflammatory and immune responses, regulation of cell proliferation and apoptosis, thus it is important for tumor development and many other diseases including atherosclerosis. Although the mechanisms by which resveratrol interferes with the activation of NF- κ B are not clear, it seems that inhibition of its degradation which is necessary for its cellular activation is the principal target. Based on the quantity and diversity of data available on the biological activity of resveratrol, it has to be considered a very promising chemoprotector and chemotherapeutic. Urgent investigations on its bioavailability and effects on *in vivo* systems, especially in humans, are necessary.

Key words: *resveratrol, cardioprotection, chemoprevention, reactive oxygen species, multistage carcinogenesis, transcription factor NF- κ B, atherosclerosis, low density lipoprotein oxidation*

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