# ANTIOXIDANT EFFECT OF RESVERATROL IN A MOUSE MODEL OF CHRONIC ETHANOL ADDICTION

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**Background:** Chronic alcohol consumption has dramatic consequences on the entire organism. Long-term alcohol abuse can cause a number of clinical conditions, including: cirrhosis of the liver, chronic pancreatitis, epilepsy, polyneuropathy, heart disease, nutritional deficiencies. Chronic alcohol consumption determines metabolic and pathological changes in the liver, documented both in humans and in experimental models, due to ethanol metabolism, which mainly occurs in this organ. These alterations are generally associated with the oxidation process of alcohol and more particularly with the oxidative stress resulting in the production of free radicals and consequent lipid peroxidation. Between dietary components, antioxidants are considered interesting in the context of alcohol related disorders. Resveratrol (3,5,4'-trihydroxy-trans-stilbene), a non-flavonoid phenol, naturally produced by several plants has several well-documented favourable actions in humans, as well as in experimental models. Powerful antioxidant action, common to the chemical class of polyphenols to which it belongs, makes the resveratrol an extremely interesting substance for its potential use in pathologies where the redox system is altered. The present study aims to investigate the effect of Resveratrol consumption in a mouse model of chronic alcohol addiction. In particular, we have evaluated the potential antioxidant ability of this natural compound, by measuring serum free oxygen radicals defence (FORD) and free oxygen radicals (FORT) levels, in mice chronically addicted. Moreover, we measured the formation of serum metabolites of Resveratrol to support the hypothesis that effects would be related to the compound. Secondly, we analysed BDNF levels in different tissue in order to assess the putative protective effect of Resveratrol, by modulating neurotrophic factors after prolonged treatment.

**Materials and methods:** 40 male CD-1mice were randomly divided into four groups (n=10 for each one): (i) control group (CTR) received sucrose dissolved in water at equivalent caloric intake of the ethanol group; (ii) Ethanol group (EtOH) received ad libitum, after an habituation period, ethanol 11% dissolved in water for 60 d; (iii) Resveratrol group (RESV) received Resveratrol (10 mg/kg//d) dissolved in sucrose; and (iv) a further group of mice (EtOH+RESV) received Resveratrol (10 mg/kg//d) dissolved in ethanol 11%. Animals were sacrificed by a guillotine. The blood was collected and quickly centrifuged for serum preparation. Tissues were processed for BDNF analysis. FORD and FORT tests were carried out using two specific kits (Callegari, Parma, Italy). Quantitative on-line HPLC-ESI-MS/MS analyses were performed using HPLC system interfaced to an Applied Biosystems, to determine serum Resveratrol metabolites. BDNF evaluation was carried out with ELISA kit by Promega.

**Results:** Alcoholic mice showed a worse oxidative status than non-alcoholic mice (higher FORT and lower FORD) but Resveratrol supplementation partially counteracted the alcohol pro-oxidant effects, as evidenced by FORT. Resveratrol supplementation is, also, able to counteract the altered BDNF levels in liver and testis of addicted mice. Metabolites of Resveratrol were found only in the serum of mice treated with the natural compound.

**Conclusion:** The antioxidant protection provided by Resveratrol might be of primary interest for drug discovery and dietary-based prevention of the damage associated with chronic alcohol abuse.