

Prevention of vascular damage with Lisosan G wheat extract: the *in vitro* basis for a clinical investigation

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Abstract. – Vascular damage and impairment play a crucial role in the pathogenesis of nonalcoholic fatty liver disease (NAFLD). Nutraceutical supplements might have a role in reducing vascular damage, provided that their efficacy is proven by controlled studies and is supported by a mechanistic rationale. Therefore, the use of nutraceutical supplements can have some effects also in the prevention of NFLD.

Epidemiological evidence correlates the intake of whole grain and whole-grain products with a reduced occurrence of vascular disease. Lisosan G is a powder obtained from *Triticum Sativum* (wheat), which is registered with the Italian Ministry of Health as a nutritional supplement. In vivo, Lisosan G has been shown to protect against cisplatin induced toxicity, and the use of this compound in the prevention of cirrhosis and steatosis has been recently been proposed thanks to its marked anti-oxidant activity.

We discuss here the rationale for further investigation on this compound in the prevention of NAFLD.

Key Words:

Lisosan G, Oxidative stress, NAFLD, Vascular damage.

Introduction

Increased vascular damage, at least in part associated with oxidative stress, is a major cause of nonalcoholic fatty liver disease (NAFLD) including cirrhosis, fibrosis and steatosis¹⁻³.

Mounting evidence suggests that single and component nutraceutical supplements, vitamins, antioxidants, and minerals might have a role – if coupled with other lifestyle modification and medical therapy – in the prevention of vascular damage, provided that their efficacy is proven by controlled studies and is supported by a mechanistic rationale⁴.

For instance, extracts from *Ginkgo biloba* (ginkgolide B) protect endothelial cells from H₂O₂-induced cell death by acting on the AKT/endothelial NO synthase and MAPK/P38 signaling pathways⁵. Moreover, *Ginkgo biloba* extract increases SOD activity and decreases apoptosis in a dose-dependent manner in endothelial progenitor cells (EPC), the pivotal players in the servicing of the endothelial cell lining⁶, and other examples of the efficacy of nutraceuticals in the prevention of oxidative stress and vascular damage are uncountable. Noteworthy, recent evidence suggests the role of whole grain and whole-grain products in the prevention and treatment of NAFLD^{7,8}.

Lisosan G is a powder obtained from *Triticum Sativum* (wheat), which is registered with the Italian Ministry of Health as a nutritional supplement. It contains vitamins, minerals and polyunsaturated fatty acids and it does not interfere with the drug metabolizing system⁹. The production process is performed by Agrisan SRL (Larciano, PT). First, the wholegrain is grounded to a rough powder; the bran and germ are then collected. Water is added to moisten the mix, then a mix of lacto-bacillus and natural yeast strains is inoculated to initiate fermentation. Once the product is

sufficiently fermented, it is dried. The resulting dry powder is Lisosan G. *In vivo*, Lisosan G has been shown to protect against cisplatin-induced toxicity¹⁰.

We have recently reported that Lisosan G presents protective effects on human microvascular endothelial cells exposed to ox-LDL through reduction of oxidative/inflammatory processes¹¹. More in detail, the incubation with ox-LDL significantly increased ICAM-1, IL-6 and ET-1 levels compared with baseline levels, while in presence of Lisosan G, ICAM-1 and ET-1 levels were significantly reduced compared with ox-LDL-treated cultures and controls. The reduced expression of ICAM-1 and ET-1 was also associated with a diminished formation of malondialdehyde, a marker of oxidative stress. Further to the above-described evidence, recent data suggest a protective effect of Lisosan G on EPCs exposed to oxidative stress by stimulating the activity of endogenous antioxidant systems. Lisosan G seems to activate the Nrf-2/ARE pathway, an endogenous system deputed to the antioxidant protection and up-regulation of the redox-sensitive genes^{12,13}.

On these bases, we speculate that Lisosan G might play a role in the prevention of liver vascular damage, thanks to its action on a number of mediators of oxidative stress and inflammation, and therefore may have a role in the prevention of NAFLD. We are currently planning clinical investigation on this issue which, as previously reported^{1,14}, is necessary to fully explore the efficacy of nutraceuticals in the prevention of cardiovascular diseases. In fact, we do believe that only well-designed and well-conducted studies should represent the source of evidence for recommending nutritional supplementations¹⁵⁻¹⁸.

Conflict of Interest

Luigi Pellegrini is the CEO of Agrisan srl. Luca Giacomelli is a scientific consultant of Agrisan. The other authors have no conflicts of interest to disclose.

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