

Abstract

Hepatocellular carcinoma (HCC) is one of the most common primary liver cancers and typically develops in the setting of chronic liver injury, in which inflammation, oxidative stress, disturbances in xenobiotic biotransformation, and structural remodelling of the organ coexist. Consequently, considerable attention has been directed towards identifying agents capable of mitigating the adverse consequences of these processes. Lisosan G (LG) is a nutraceutical with antioxidant and cytoprotective properties. However, its effects on the course of HCC have not yet been sufficiently elucidated. The aim of this study was to evaluate the effects of LG on hepatocarcinogenesis in rats, with particular emphasis on the activity of biotransformation systems, oxidative stress, inflammatory processes, markers of cellular differentiation and cell death, and the functional activity of isolated hepatocytes.

The study was conducted on 90 female Wistar rats randomly assigned to nine experimental groups comprising healthy animals, animals subjected to partial hepatectomy, and animals with HCC. Within these groups, the animals were fed either a standard diet or a diet supplemented with 2.5% or 5% LG. HCC was induced using a model combining partial hepatectomy with exposure to diethylnitrosamine.

The results demonstrated that the effects of LG were most pronounced in livers affected by neoplastic transformation. In HCC, LG increased the activity of antioxidant and detoxification enzymes, including GST, SOD, and catalase, while reducing the concentrations of MDA and protein carbonyls. In addition, the HCC groups receiving LG exhibited lower concentrations of IL-6 and RIPK3, as well as reduced levels of NO and superoxide anion. Dietary supplementation with LG was also associated with increased expression of HNF4 α and TP53, together with reduced levels of AFP and PKM2.

The obtained results confirmed the antioxidant activity of LG, evidenced by the attenuation of lipid peroxidation and oxidative protein damage. Although LG inhibits tumor cell dedifferentiation, it exerts no beneficial effect on the pathways regulating programmed cell death, namely apoptosis and necroptosis. The lack of an unambiguous effect of LG in the course of HCC justifies the need for further studies prior to the application of this nutraceutical in the adjuvant treatment of liver cancer.