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GENETICKÁ TOXIKOLOGIE A PREVENCE RAKOVINY

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Comparison between silibinin-conjugated gold nanospheres and nanobipyramids impacts on the treatment of liver fibrosis *in vivo*

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Chronic liver diseases are associated with approximately two million deaths per year worldwide. Of this, one million have been linked to complications of cirrhosis and the other to viral hepatitis and hepatocellular carcinoma. Globally, liver cirrhosis is the 11th most common cause of death today and, together with liver cancer (16th most common cause of death), accounts for 3.5% of all deaths worldwide. Liver cirrhosis has actually become the most common cause of death in the 35-44 age group in Slovakia [1].

The development of chronic inflammation leads to chronic liver damage. This damage can progress into liver fibrosis, which progressively results in liver cirrhosis. Nowadays, active pharmacological research is focused on the therapeutical strategies for inhibiting chronic inflammation. Reduction in the progression of hepatic fibrogenesis is one of the key approaches to the treatment of chronic liver disease. It is necessary to support the research and development of new effective and safe antifibrotic drugs as, despite growing knowledge of the molecular mechanisms of liver fibrogenesis, to date, there is no effective therapy for the treatment of hepatic fibrosis.

One of the most effective antifibrotic drugs could be silibinin - the part of the lipophilic extract of Milk thistle (Silybum marianum). Lipophilic extract from the seeds of this plant - silymarin, is composed mainly of one flavonoid (taxifolin) and seven flavonolignans (isosilybin A, isosilybin B, isosilychristin, silybin A, silybin B, silychristin and silydianin). About half of the silymarin mixture consists of silibinin (silybin A and silybin B in a ratio of 1: 1). Silibinin also has the highest antioxidant activity of all silymarin components [2] and has been shown its antifibrotic effects *in vitro* in renal cells by reducing the number of proteins such as collagen type I, fibronectin, a-SMA, p-IkB, MMP9, p-Smad2, p-Smad3, and p-p65, as well as *in vivo* in fibrotic kidneys in mouse [3-4].

A problem with using silibinin as a drug lies in its insolubility in water and the need of using higher doses of the drug if administered orally. Gold nanomaterials seem to be the ideal solution to this problem. They are a suitable carrier for the use in targeted therapies, biocompatible, and show lower toxicity compared to other inorganic nanomaterials. They have almost no acute toxicity and their unique optical features enable to monitor them in the body. In this study, we use the two types of gold nanomaterials: nanospheres and nanobipyramids. Spherical nanomaterials are suitable candidates for targeted drug delivery due to the high surface area to volume ratio. On the other hand, differently shaped nanomaterials (e.g., nanobipyramids) are more appropriate for biomedical diagnostics due to their physical-optical properties.

The combination of silibinin-coated gold nanoparticles thus represents a potentially successful anti-fibrotic drug that could also be used in the treatment of liver diseases.

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