Abstract

Pancreatic cancer is one of the most aggressive cancers, with a low survival rate. In most cases, it is diagnosed in an advanced stage of the disease, when surgical treatment is no longer feasible. Nowadays, the only available curative treatment is surgery followed by chemotherapy. Such a low prognosis for this type of cancer is due to the very vague or sometimes even lack of clear symptoms of the disease. Despite the constantly developing knowledge of tumorigenesis processes, there is an urgent need to come up with an effective treatment strategy. Over the last few years, there has been a significant increase in interest in substances exhibiting anticancer properties that occur naturally in food. However, the consumption of a sufficient amount of these substances with food which would be effective in therapy is usually not possible. The main reason is low bioavailability which comes from the physical and chemical properties of the compounds.

The aim of this doctoral dissertation was to develop an effective delivery system for phenethyl isothiocyanate and curcuminoids, which exhibit a broad spectrum of anticancer properties. Phenethyl isothiocyanate was encapsulated in the lipid core of the nanoemulsion, while curcuminoids were encapsulated in the phospholipid bilayer of the liposomes. The developed nanocarriers allow for the encapsulation of hydrophobic compounds, which are also characterized by high reactivity. The particle diameter, polydispersity index and zeta potential of nanoformulations were determined. Then, the carriers containing active substances were imaged using microscopic techniques. Long-term stability, as well as the effect of the presence of fetal calf serum on the obtained nanoformulations were investigated. Both nanoemulsions and liposomes did not cause significant damage of red blood cells (hemolysis < 5%).

The further studies demonstrated high biological activity of nanocarriers *in vitro*. Tests were conducted to determine the cytotoxic/cytostatic effects of nanoemulsions and liposomes against two pancreatic cancer cell lines. The nanoemulsion containing phenethyl isothiocyanate caused a decrease in intracellular adenosine-5'-triphosphate levels, as well as glutathione levels. Moreover, it was responsible for the generation of reactive oxygen species. A pharmacokinetic profile was additionally determined for the nanoemulsion. The pharmacokinetic studies showed that after intravenous administration, elimination of the compound was slow, with a half-life of about 22h. A high degree of distribution of phenethyl isothiocyanate in nanoemulsion form in the body was also observed.

In the last stage of the study, the effect of active compounds in the form of nanoformulations applied in a 1:1 v/vand combination index were analyzed.

Based on the studies conducted within the framework of the doctoral project, the biological potential of the developed nanocarriers was demonstrated. The obtained nanoformulations, characterized in this work, represent a promising drug delivery system that may find application in pancreatic cancer therapy.