

## ABSTRACT

Despite all the progress made in the treatment of cancer in recent years, it is still necessary to continue with the research of more effective and specific drugs. In recent years, there has been a growing interest in personalized medicine and its application through drug delivery systems, which could help increase the specificity of cancer treatment and subsequently its effectiveness.

Drug delivery systems can use different platforms for their design, whether they are liposomes, micelles, nano crystals or others. A very interesting platform for the construction of drug delivery systems are polysaccharides, which were, as carriers of contrast agents in order to effectively display tumours, characterized in this doctoral thesis. But polysaccharides are interesting for more reasons. Both by its availability, and by its biocompatibility and non-toxic character. In this doctoral thesis we deal with two types of polysaccharides conjugates with linked contrast agents for magnetic resonance and fluorescent imaging. The first type of polysaccharide is glycogen, the second is mannan. Both constructs - glycogen and mannan based, were synthesized in a version with and without polymethyloxazolin, which should prolong their circulation in the organism. Both types of polysaccharide conjugates used passive targeting into the tumour using the Enhanced Permeability and Retention (EPR) effect. Mannan conjugate was passively targeted through EPR and actively via DC-SIGN (Dendritic Cell - Specific Intercellular adhesion molecule 3 - Grabbing Nonintegrin binding receptor) receptors into the sentinel lymph nodes, where the first metastatic tumour cells are most commonly found.

The doctoral thesis used various methods for *in vitro* and *in vivo* characterization of both types of polysaccharide conjugates. The localization of conjugates was monitored by confocal microscopy, the level of cytotoxicity of the conjugates was tested, and tests for determination the type of endocytosis used by the cell for externally administered glycogen were performed. The rate of relaxation of conjugates or fluorescence of phantoms *in vitro* was also characterized. *In vitro* tests were followed by pilot *in vivo* experiments on non-tumour models. In final phase, for both types of polysaccharide constructs, glycogen and mannan based, extensive *in vivo* measurements were made on animals with tumours, where magnetic resonance imaging (MRI) and fluorescence were used to monitor biodistribution and accumulation of constructs according to the extent of modification of polymetyloxazolin, we compared constructs without and with linked polymetyloxazolin. At the end of the experiments, histological examinations were also performed to determine the effect of the conjugates administered on the internal organs.

The results showed that glycogen and mannan-based conjugates are a very promising platform for future use as carriers of drugs. Especially due to its non-toxic character and in the case of mannan also due to active targeting via DC-SIGN receptors. It was also found that by adjusting the degree of modification by polymetyloxazoline, the properties of both conjugates can be changed to obtain optimal results, i.e., the ratio of the rate of accumulation in the tumour to the duration of circulation.