

## Abstract

This doctoral thesis is focused on the synthesis and characterization of novel hybrid polysaccharide-based polymers applicable for biomedicine, specifically for a conceptually new bimodal cancer treatment – immunoradiotherapy. For this purpose, polysaccharides  $\beta$ -glucan from *Auricularia auricula-judae* and  $\kappa$ -carrageenan from *Kappaphycus alvarezii*, exhibiting immunostimulatory and anticancer activities, were chosen to be grafted with thermoresponsive poly(2-isopropyl-2-oxazoline-co-2-butyl-2-oxazoline)s (POXs) (with different graft lengths and grafting densities) that induced a lower critical solution temperature of the final polymers. The thermoresponsive behavior of resulting polymers was studied with temperature-dependent light scattering methods, fluorescence measurements and also nuclear magnetic spectroscopy to select a polymer material with the most suitable properties for the intended application, aiming at a polymer depot formation after the injection of a polymer solution into the body. The chosen polymer,  $\beta$ -glucan-*graft*-POX with graft length of 2500 Da, was then modified to bear 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid and a fluorescent dye Dyomics-615 at the graft ends and tested first *in vitro* to investigate its immunostimulatory properties and also the cellular uptake. Subsequently, the polymer was radiolabeled with yttrium-90(III) and used in the *in vivo* antitumor efficiency experiment on mice with EL4 lymphoma, demonstrating an extraordinary treatment success (~ 50 % cured mice), which was probably caused by a considerable synergistic effect of using immunoradiotherapy compared to separate use of immunotherapy or radiotherapy.

Furthermore, a special attention was dedicated to the characterization of  $\kappa$ -carrageenan-*graft*-POXs, which showed except for the above mentioned desired biological properties also a sensibility to the presence of potassium cations and an interesting “schizophrenic” thermoresponsive behavior with both lower and upper critical solution temperatures in aqueous environment.

**Keywords:**  $\beta$ -glucan,  $\kappa$ -carrageenan, poly(2-alkyl-2-oxazoline), multimodal cancer therapy, immunotherapy, radiotherapy.