Politechnika Śląska
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# PRACA DOKTORSKA

"Badania nad syntezą kopolimerów liniowych i szczepionych zawierających jednostki pochodnych choliny z wybranymi anionami o działaniu terapeutycznym jako nowych układów biofunkcyjnych"

"Studies on the synthesis of linear and grafted copolymers containing ionic units of choline derivatives with selected therapeutic anions as novel biofunctional systems"

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Gliwice 2019

## Załącznik 2 Summary of the doctoral dissertation

In this work, new, amphiphilic copolymers containing trimethylammonium moieties were synthesized for use as carriers of biologically active substances of anionic or non-ionic nature. The key in the proposed research was the use of methacryloyl derivative of choline as a monomer enabling the introduction of a biologically active substance into the polymer already at the stage of its synthesis.

Thanks to the modification of choline methacrylate, it was possible to obtain new monomers in the form of bis (trifluoromethanesulfonyl)imide or salicylate. Synthesis of polymers was carried out using the ATRP technique for a different proportions of initial comonomers. The use of both low molecular weight initiator, as well as a multifunctional macroinitiator based on bromoacyloxy derivatives of poly(2-hydroxyethyl methacrylate) allowed to obtain linear and graft copolymers, respectively.

The obtained polymers were characterized and compared in the means of the size of the polymer particles formed in solutions and the glass transition temperature. A significant effect of anions on copolymer properties has been demonstrated. The presence of chlorides enabled the formation of smaller nanoparticles than in the case of salicylates. Graft copolymers were self-assembled to form smaller nanoparticles than their linear analogues (16-60 nm vs. 171-290 nm).

In the further part of the study, salicylate copolymers were tested for the release of anion in phosphate buffer solutions as an anion exchange, and then diffusion from the polymer matrix. Both linear and graft copolymers showed a burst-release effect in the first hours of the process, in which up to 50% of the biologically active substance was released, followed by an additional 20% within 80 hours.

Amphiphilic linear copolymers containing chloride, salicylate or sulfacetamide anions were also employed in the encapsulation of the selected nonionic drug (quercetin, indomethacin, erythromycin). The aromatic nature of the biologically active substance prevented it from being loaded into the polymer matrix due to repulsive interactions with ionic polymer moieties, while the efficiency of erythromycin encapsulation was satisfactory regardless of the type of anion. Erythromycin was released only from salicylate systems, for which, similarly to the release of the ionic drug, in the initial stage burst-release was observed up to about 60%.

Biological studies have shown that the copolymers did not inhibit epithelial cell proliferation. It has been proven that, with the exception of copolymers with sulfacetamide anions, proposed polymer systems inhibit the expression of genes responsible for proinflammatory action. An additional advantage was the antibacterial activity of linear copolymers and some graft copolymers against E. coli.

The conducted research confirmed that the obtained polymers can be used as effective carriers of biologically active substances.