WYDZIAŁ CHEMICZNY
KATEDRA FIZYKOCHEMII I TECHNOLOGII POLIMERÓW

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ROZPRAWA DOKTORSKA

Badania nad otrzymywaniem, charakterystyką i możliwościami aplikacyjnymi polibezwodników, opartych na betulinie i jej pochodnych

Przewodnik po monotematycznym cyklu publikacji

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SUMMARY OF THE DOCTORAL DISSERTION

The research planned as a part of the doctoral dissertation covers mainly the synthesis of a new polyanhydrides, based on dicarboxylic derivative of betulin, and their detailed characterization, including tests for their antitumor activity and hydrolytic degradation in conditions similar to physiological (37^oC, pH = 7.4).

Betulin is a naturally occurring pentacyclic triterpene that is obtained on the large scale from the outer layer of birch bark. Both betulin and its numerous derivatives exhibit a broad spectrum of biological relevance, including antitumor activity, while being non-toxic to normal cells. Due to the proven pharmacological activity, betulin derivatives can be used as new potential therapeutic agents. Additionally, due to the presence of functional groups, betulin is also an ideal substrate for the polymer's preparation.

Polyanhydrides, based on betulin disuccinate (DBB), were obtained by a melt polycondensation with the use of acetic anhydride. The method used allows to obtain polyanhydrides in a short time, without the need to purify the intermediate products. Due to the proven biological activity of DBB, including cytostatic effect, the polyanhydrides obtained therefrom can be used as polymer prodrugs that release the active substance as a result of polymer hydrolysis under physiological conditions. The rate of hydrolysis of the obtained polymers, and thus the release of DBB, was controlled by the copolymerization of DBB with other polycarboxylic compounds, e.g. sebacic acid or polyethylene glycol.

The main problem with the use of betulin as a therapeutic substance is its poor water solubility, limiting the possibility of introducing it into the body and its bioavailability. This problem can be solved by obtaining polymeric betulin derivatives and forming micro- and nanoparticles from them. The polyanhydrides obtained in the work were successfully used to obtain polymer microspheres and nanospheres as well as self-assembled micellar structures. The synthesized polymers have a cytostatic effect on cancer cells but are not toxic to healthy cells, therefore they can be used as carriers of other biologically active compounds. The obtained structures have been tested for their suitability in drug controlled release systems, including inhalation systems.

The conducted research confirmed the possibility of using the obtained polyanhydrides in the pharmaceutical industry as polymer prodrugs and as matrices in controlled drug delivery systems.