Bialystok, 10.06.2025 r.

ABSTRACT

"Polymeric drug carriers containing lithocholic acid derivatives"

The main goal of this doctoral dissertation was the synthesis and characterization of polymeric materials containing lithocholic acid (LCA) derivatives as potential carriers for anticancer drugs. The main motivation behind the study was the unique structure of LCA, which possesses reactive functional groups – carboxylic and hydroxyl - located on opposite sides of the steroid backbone. This spatial arrangement enables selective chemical modifications and makes LCA an attractive model compound for designing carriers intended for targeted and combination therapies.

The research was divided into two main areas: (1) the synthesis of magnetic polymer-inorganic hybrids with iron oxide (Fe_3O_4) nanoparticle cores and polymeric shells containing LCA derivatives, and (2) the preparation of water-soluble or water-dispersible linear homo- and copolymers with LCA moieties, modified with fluorescent labels. The obtained materials were characterized using a range of analytical techniques, including spectroscopic methods (FTIR, UV-Vis, NMR, fluorescence spectroscopy), chromatographic techniques (SEC), microscopic techniques (TEM), thermal analysis (DSC, TGA), and light scattering methods (DLS, ELS).

In the part focused on magnetic hybrids, a total of 14 systems with polymeric shells containing bile acid derivatives were synthesized and characterized. These systems were further functionalized with biologically active molecules, including folic acid and doxorubicin. RAFT polymerization enabled the synthesis of block copolymer structures. The resulting hybrids exhibited good colloidal stability, high selectivity toward cancer cells, and improved anticancer activity compared to free drug forms.

In the second research area, a series of linear homo- and copolymers soluble in water and containing LCA derivatives at the chain ends or in side chains was obtained. These polymers were used to prepare stable nanoparticles via nanoprecipitation. Selected systems were fluorescently labeled, resulting in materials capable of simultaneous drug delivery and imaging. Fluorescence analysis confirmed emission in the blue and orange regions and the possibility of selective excitation of the fluorophores. The systems also demonstrated the ability to encapsulate or covalently bind doxorubicin.

Dawid Szymczuk
10.06.25.