

PhD thesis: Modifications of selected cytostatics in genitourinary cancers

The growing mortality rate resulting from the incidence of cancer requires the search for new methods of treatment. One of the most common cancers are cancers of the genitourinary system, including bladder and prostate, which are the cause of about 3.8% of all deaths caused by cancer in men.

The aim of the research was to search for new methods of treating cancers of the genitourinary system and to use biotechnology in the development of modifications of anticancer drugs. Moreover, the research was aimed at examining the effect of biomaterials and substrates of natural origin on cancerous cells of the genitourinary system *in vitro* in a 2D and 3D model of cell culture. Second and third generation fluoroquinolones: ciprofloxacin and levofloxacin were used in the study. The first biomaterial used in the research was chitosan. For many years, it was considered as a useful bioadhesive material due to its ability to form non-covalent bonds with biological tissues, moreover, it is considered biocompatible and non-toxic, biodegradable by enzymes. The research used another current trend in medicine - natural extracts and the reuse of raw materials. Polyphenols, including flavonoids, are organic compounds. These compounds are found in large amounts in plants and trees (popularly growing in Poland). Norway spruce (*Picea abies*) extract was used in this study. Commercially available cell lines T24 (bladder cancer) and DU145 (prostate cancer) were selected as cell models. Metabolic activity, rate of proliferation, growth kinetics, apoptosis level, changes in pH of culture medium, ratio of live/dead cells were studied. In response to the need to develop new *in vitro* test models, an additional analysis was also performed on the 3D model of the T24 line.

Depending on the analysis, the most toxic drugs turned out to be combinations of ciprofloxacin in concentrations of 1000 μM with 5% *Picea abies* extract. All combinations of drugs had a very large impact on the tested parameters of cancer cells, showing particularly cytotoxic effects in the last time points of the modified drugs. The highest sensitivity in detecting changes indicating the cytotoxic nature of drugs was observed on multicellular spheroids, which seem to be a promising model for future research.

The conducted analyzes proved that the modification of drugs with biopolymers and natural extracts may be a promising direction in the fight against cancers of the genitourinary system. However, it is necessary to carry out further analyses, also based on new methods of chemical modification of drugs and their optimization for further *in vitro* studies on 3D models.

Key words: *fluoroquinolones, bladder cancer, prostate cancer, chitosan, polyphenols.*