Summary of the doctoral dissertation

„Selected carriers for the preparation of a therapeutic formulation of a chemotherapeutic agent useful in oncology.”

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Cancer is one of the key challenges of modern medicine. It is characterized by the uncontrolled growth and division of cells in the body, leading to the formation of tumors and changes in tissues. Oncological diseases often have an unfavorable prognosis due to the lack of an appropriate strategy for drug delivery to the tumour site. A major challenge in introducing a new drug substance into therapy is its poor solubility, limited bioavailability, toxicity, or difficulty in reaching the target cells. The development of innovative drug delivery systems based on biomaterials and nanotechnology can not only increase the stability and bioavailability of a drug, but also reduce the toxicity of a potential drug substance. For this reason, there has recently been an intensely growing interest in targeted therapy using various types of active substance carriers that facilitate the transport of the drug from the site of administration to the site of action.

The main objective of the present study was to search for and select carriers for the preparation of a therapeutic formulation of a chemotherapeutic useful in oncology. In the first stage of the study, potential carriers were synthesized and analyzed. Graphene oxide derivatives, polymer carriers-chitosan-based hydrogels, exosomes, and liposomes were obtained in this way.After initial testing, liposomes were selected for further study. Eighteen new liposomal systems were developed as part of the research, providing an innovative solution for targeted therapy. Each of the systems was investigated over a temperature range of 37^0C and 41^0C and in four environments with pH values of 5.50; 6.00; 6.50; 7.40. Two FDA-approved drugs (Binimetinib and Doxorubicin) and a new synthesized chemical substance with confirmed biological activity (9-(N-piperazinyl)-5-methyl-12(H)-chino[3,4-b][1,4]benzothiazine chloride). Subsequently, HSA and dHSA proteins were attached to the test their effects on the drug release profile. Six mathematical models were used to compare experimental results with theoretical values. Lipophilicity values were calculated using appropriate computer programs, and then these values were compared with empirical data to determine the correlation of the obtained results. In addition, the clustering tendency of liposomal combinations was examined using principal component analysis (PCA) and hierarchical cluster analysis (HCA). Finally, an analysis of variance (ANOVA) was applied, which confirmed the statistical effect of pH and changing temperature on the drug release characteristics of liposomes. The study shows that within the physiological range of the patient's body temperature, the best drug release occurs in a slightly acidic environment. The newly created formulations offer hope for use as potential carriers in anticancer therapy.