Streszczenie w języku angielskim I Summary

Hematopoietic neoplasms are a heterogeneous disease group and a major challenge for contemporary medicine. Acute myeloid leukemia accounts for the largest proportion among adult leukemias. Multiple myeloma is the second most common hematopoietic malignancy. Myeloablative therapy with high – dose melphalan followed by autologous stem cell transplantation is considered the standard of treatment for multiple myeloma patients who are eligible for transplantation. Problems associated with the use of this therapy include lack of selectivity, high toxicity and the development of drug resistance. All this leads to the search for new therapeutics with higher anti–tumor efficacy and a better safety profile.

One way to improve the therapeutic efficacy of drugs is to regulate their pharmacological activity by modifying their chemical structure. The aim of this dissertation was to analyze the biological properties of new melphalan derivatives obtained by chemical synthesis and to select this modification of its structure which exhibits higher anticancer activity than the parent compound against multiple myeloma cells (RPMI8226), acute monocytic (THP1) and promyelocytic (HL60) leukemia cells.

In vitro studies have identified the most effective structural modification of melphalan. It was shown that the key to enhancing cytotoxic, genotoxic and proapoptotic activity in leukemia and multiple myeloma cells is the modification of the carboxyl group by its esterification and the replacement of the di–*N*–propylamine group with an amidine group containing a heterocyclic ring (morpholine or thiomorpholine one). Simultaneously, such a change in the structure of melphalan causes a reduction in cytotoxic activity against normal cells — peripheral blood mononuclear cells. The mechanism of activation of molecular death pathways by melphalan and the derivatives studied was investigated. The study allowed us to understand the relationship between the chemical structure of melphalan and the new derivatives and their biological activity. The obtained results are an important contribution to the knowledge of the currently used drug — melphalan, as well as its new analogues.

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