POLITECHNIKA ŚLĄSKA

WYDZIAŁ CHEMICZNY

KATEDRA CHEMII ORGANICZNEJ, BIOORGANICZNEJ
I BIOTECHNOLOGII

ROZPRAWA DOKTORSKA

Synteza heterocyklicznych pochodnych monosacharydów i ich wpływ na żywotność komórek nowotworowych

mgr inż. Katarzyna Żurawska

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SUMMARY OF THE DOCTORAL DISSERTATION

Synthesis of heterocyclic monosaccharide derivatives and their effects on cancer cell viability

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The increasing occurrence of cancer makes it necessary to search for new therapeutics that act selectively on the affected cells. The diverse types of cancer and their location in the body determine the use of different treatment methods. In addition to surgical removal of cancerous tumours, chemotherapy is used, which can target cell receptors and enzymes involved in cellular processes that affect the survival of cancer cells. Among the enzymes essential for normal cell function is fucosyltransferase 8 (FUT8), an enzyme responsible for transferring the L-fucose moiety to molecular acceptor, which can be another sugar molecule, lipids, or proteins. Overexpression of FUT8 has been indicated in several types of cancer cells. Currently only few effective inhibitors of this enzyme are known.

In the dissertation, there were obtained a set of heteroaromatic compounds, and their glycosides and glycoconjugates, capable of acting as FUT8 inhibitors. In this research work there were obtained sugar intermediates, derivatives mainly of L-fucose and L-rhamnose, non-sugar intermediates such as derivatives of purpurin, anthraquinone, 1,3,5-triazine, 1,3,4-thiadiazole, furan-2(5*H*)-one, 2*H*-pyrrol-2-one and 1,2,4-triazole, which were then used in the synthesis of complex sugar derivatives, inly L-rhamnose and L-fucose.

The obtained sugar derivatives were preliminarily evaluated for their biological activity on HCT116 and MCF-7 cell lines. The lowest IC_{50} values on the tested cell lines were obtained for the **Ram38** derivative (4-(3,4-dichloro-5-hydroxy-1*H*-pyrrol-2(5*H*)-on-1-yl)methylene)-1-(4-*O*-acetyl-2,3,6-trideoxy-L-*erythro*-hex-2-enepyranosyl)-1*H*-1,2,3-triazole), also was found to interact with FUT8 bacterial origin.

The results of the analyses allowed the preliminary determination of the structure of the fragments from which a potential inhibitor should be composed to interact with the FUT8 protein, which is a starting point for further research in this area.