ABSTRACT

This work deals with the problem of searching for effective derivatives of 1,2-dideoxy-2´-methyl-α-D-glucopyranoso-[2,1-d]-Δ2´-thiazoline (NGT), potential inhibitors of human β-*N*-acetylhexosaminidases. The work is targeted to production of inhibitors derived from NGT by the modification of its structure by free and immobilised lipases. Potential inhibitors of β-*N*-acetylhexosaminidases may be potent tools for studying of enzymes in cell processes and also open possibility to the discovery of new possible drugs for the treatment of some neurodegenerative diseases, such as Alzheimer disease.

The thesis is focused on brief characterization of β-*N*-acetylhexosaminidases, e.g., glycosidases from enzymatic groups GH 20 and GH 84. β-*N*-Acetylhexosaminidases from microorganisms *Bacteroides thetaiotaomicron, Aspergillus oryzae, Streptomyces plicatus, Talaromyces flavus* and humans[1] were used in the experiments. The enzymes produced were purified and then tested for their activity.

We also tested inhibitory activity of potential inhibitor 6-*O*-acetyl-1,2-dideoxy-2´-methyl-α-D-glucopyranoso-[2,1-d]-Δ2´-thiazoline. Starting compound, NGT, was synthesized by the modified process (originally created by prof. Knapp[2]) using 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose in the reaction with Lawesson´s reagen.

In the second part of this work we explored some biochemical properties of lipases used and their action in NGT acetylation reactions in selected enviroment. Some lipases (Lipase CV Amano, Lipase PL Amano, Novozyme®435 Sigma Aldrich), which showed higher efficiency in NGT acetylation were investigated also from kinetic point of view.