Abstract of the thesis

RŮŽIČKOVÁ M.; **INVESTIGATION OF SUGAR MODIFIED PYRIMIDINE NUCLEOSIDES AS POTENTIAL INHIBITORS OF THYMIDINE (TP) AND URIDINE (UP) PHOSPHORYLASE**

Key words: uridine phosphorylase, thymidine phosphorylase, nucleoside, inhibitor, anticancer chemotherapy, substrate specifity

The work deals with the investigation of novel potential inhibitors of recombinant thymidine and uridine phosphorylases from *E. coli* and *Salmonella typhimurium.* The main goals of this study are the determination of kinetic parameters for natural substrates (thymidine and uridine) for recombinant TP and UP, assessment of the role of phosphate anion in the enzymatic transformations and search for new inhibitors of TP and UP. Study of UP and TP substrate specifity and activity under the various reaction conditions is desired to obtain better view to their functions and to design novel structures of potencial inhibitors.

The determination of the Michaelis constant K_M and reaction rate V_{max} was performed at the spectrophotometer *Varian Cary-300 Bio.* The representation of obtained kinetic data we used the Lineweawer-Burk plot. The next point of my work was the determination of the enzymatic activity and their substrate specifity for some pyrimidine analogues by HPLC analysis of reaction mixtures. Tested compounds 2´-O-methyluridine, 1-(ß-D-fructofuranosyl)uracil, 2´-deoxy-2´-fluorouridine, 2´-amino-2´-deoxyuridine, 3´-amino-3´-deoxyuridine and 3´-amino-3´-deoxythymidine showed various abilities to be phosphorylated.