

## ABSTRACT

At the present time many types of treatment are used for curing of different cancer diseases. Among the most common types of such treatment belong a surgery, radiotherapy, chemotherapy, and immunotherapy. In the case of chemotherapy, there is used a wide (broad) spectrum of chemotherapeutics such as alkylating agents, platinum compounds, antimetabolites, anthracyclines and, at the present time, also inhibitors of tyrosine kinases. The bachelor thesis describes different types of tyrosine kinase inhibitors and their use in treatment of several cancers. They become popular because of their high specificity and minimal side effects. The first successful use of a tyrosine kinase inhibitor was treatment of the patients suffering from chronic myelogenous leukemia (CML) with imatinib. Vandetanib is another inhibitor of tyrosine kinases that is now used for treatment of another cancer, the medullary thyroid cancer. During treatment, vandetanib is biotransformed with cytochromes P450, which are the terminal oxidases of a mixed function oxidase (MFO) system, into the less efficient metabolites. In the practical part of the bachelor thesis we isolated enzymes, which metabolize xenobiotics, including vandetanib. Rat liver tissue was used for isolation of NADPH:cytochrome P450 reductase, which was isolated as a homogeneous protein and NADH:cytochrom b<sub>5</sub> reductase, which however needs to be further purified to homogeneity. These isolated enzymes will be used in the reconstitution experiments with the enzymes of the MFO system (cytochromes P450) to study metabolism of tyrosine kinase inhibitor vandetanib as well as other xenobiotics.

**Keywords:** tyrosine kinase inhibitors, xenobiotics, vandetanib, cytochrome P450; NADPH:cytochrome P450 reductase; NADH:cytochrom b<sub>5</sub> reductase