Abstrakt v anglickém jazyce

Cancer disease is a group of clinically diverse diseases characterized by uncontrolled proliferation of cancer cells incapable of differentiation. Tumor therapy consists of a combination of surgery, radiotherapy and chemotherapy utilizing cytostatic agents. The plant alkaloid ellipticine ranks among a group of cytostatic agents. Its mode of action is based on DNA intercalation, inhibition of topoisomerase II and formation of covalent DNA adducts. Ellipticine is oxidized through cytochromes P450 catalysis into detoxication metabolites 9-hydroxyellipticine and 7-hydroxyellipticine, and into activation metabolites 12-hydroxyellipticine, 13-hydroxyellipticine and ellipticine N^2-oxide. The aim of practical part of this work was to compare the efficiency of human cytochromes P450 1A1/2 and 3A4 expressed in prokaryotic and eukaryotic systems in the process of ellipticine oxidation. Ellipticine metabolites were analysed using high performance liquid chromatography. It was found that cytochrome P450 1A1 expressed in the prokaryotic system catalyses predominantly the formation of 9-hydroxyellipticine and 7-hydroxy-ellipticine. The difference is minimal in the production of ellipticine metabolites catalysed by cytochromes P450 1A2 expressed in both cellular systems. The formation of 13-hydroxyellipticine and 12-hydroxyellipticine, the metabolites generating covalent DNA adducts, is catalysed predominantly by cytochrome P450 3A4 expressed in the prokaryotic system. The results found in this work show that human cytochromes P450 1A1/2 and 3A4 expressed in the prokaryotic system catalyse ellipticine oxidation more efficiently than the same cytochromes P450 expressed in the eukaryotic system.

Key words:
anti-tumor chemotherapy, ellipticine, covalent DNA adducts, cytochrome P450, oxidation, prokaryotic and eukaryotic systems