

Cytochromes P450 (CYP) are a superfamily of heme proteins distributed widely throughout nature, involved in metabolism of a broad variety of substrates and catalyzing a variety of interesting chemical reactions. They play a central role in metabolism of chemotherapeutic agents. Several prodrug antitumor agents have been found as CYP substrates. Ellipticine, an alkaloid found in Apocynaceae plants, is an example of such type of pro-drug.

Here, we investigate the efficiencies of human recombinant CYPs expressed in eukaryotic and prokaryotic expression systems, namely in SupersomesTM, microsomes isolated from insect cells transfected with baculovirus construct containing cDNA of human CYP1A1, 1A2 and 3A4 with NADPH:CYP reductase or in Bactosomes, the membrane fraction of *E. coli* transfected with cDNA of the same human CYP enzymes and NADPH:CYP reductase to oxidize their marker substrates and ellipticine. Cytochrome b₅, an additional component of the mixed function oxidase system, which metabolize xenobiotics was also expressed in some of the systems.

The results found in this work demonstrate that human CYP1A1, 1A2 or 3A4 expressed in both eukaryotic and prokaryotic systems oxidize their marker substrates (EROD for CYP1A1/2, MROD for CYP1A2 and testosterone 6 β -hydroxylation for CYP3A4). They also oxidize ellipticine, forming up to five metabolites, 7-hydroxy-, 9-hydroxy-, 12-hydroxy-, 13-hydroxyellipticine and N²-oxide of ellipticine. Their efficiencies, however, differ in individual systems. In the case of ellipticine oxidation, the CYP1A1 expressed in prokaryotic system with reductase and cytochrome b₅ was efficient, forming predominantly 13-hydroxyellipticine and 9-hydroxyellipticine. Human CYP3A4 exhibit different capability of oxidizing ellipticine in eukaryotic and prokaryotic systems, being higher in the later one. In the presence of cytochrome b₅, a pronounced increase in formation of 13-hydroxyellipticine by CYP3A4 was found in the eukaryotic system, whereas this heme protein decreased ellipticine oxidation catalyzed by this enzymes expressed in the membrane of *E.coli*.

Keywords: cytochrome P450, ellipticine, cytochrome b₅, prokaryotic expression system, eukaryotic expression system