Ellipticine, an alkaloid isolated from Apocynaceae plants, exhibits significant antitumor and HIV activities. Ellipticine is a pro-drug, whose pharmacological and genotoxic effects depend on activation by cytochromes P450 (CYP) and peroxidases (Px) to a reactive species generating DNA adducts. To elucidate contribution of CYPs (and which of them) and Px to ellipticine activation, we used rat and mouse models, mice with deleted gene of NADPH:CYP reductase in the liver, thus absenting this enzyme in the liver (HRN^{TM}) and a control mouse line (WT), rats treated with ellipticine, and microsomal systems isolated from the liver of mouse lines and from the liver, kidney and lung of rats. The purified enzymes, CYP1A1 and 3A4, reconstituted with NADPH:CYP reductase were also used. The effect of cytochrome b_5, a facultative component of the mixed function monooxygenase system, on ellipticine oxidation by CYP1A1 and 3A4 was also investigated. Carcinogenic benzo(a)pyrene (BaP), known to covalently bind to DNA after its activation with CYPs, was investigated for its potential to generate DNA adducts and to induce CYP and NADPH:CYP reductase enzymes in mouse livers. We investigated an influence of each of components of the mixed function oxidases (MFO) system on metabolism of BaP. CYP1A1 is widely accepted to be the most important enzyme activating BaP. In the present study, microsomal systems of rats and mice and purified enzymes CYP1A1 reconstituted with NADPH:CYP reductase were used. We investigated a production of BaP metabolites and BaP-DNA adducts. HPLC separation of metabolites formed by oxidation of ellipticine and/or BaP was performed. For quantification of DNA adducts generated by these compounds, the ^{32}P-postlabeling method was used. The results found in the study investigating ellipticine metabolism shows that cytochrome b_5 affects oxidation of ellipticine by CYP1A1/2, favoring formation of 12-hydroxy- and 13-hydroxyellipticine metabolites implicated in ellipticine–DNA adduct formation, at the expense of 9-hydroxy- and 7-hydroxyellipticine that are detoxication products. In the case of CYP3A4, cytochrome b_5 stimulates formation of 9-hydroxyellipticine and one of the activation metabolites, 13-hydroxyellipticine. We found an increase in activation metabolites of ellipticine and DNA adduct formation in liver microsomes of rats treated with ellipticine. CYP1A1 is induced by ellipticine in the liver, and this feature leads to “switching” of the main activation enzyme activating ellipticine from CYP3A4 to CYP1A1. In contrast to situation in the liver, ellipticine is detoxicated by CYP1A1 in lung and kidney, whereas is activated by Px in these extrahepatic tissues. The study investigating BaP metabolism shows that BaP is oxidized by hepatic microsomal system of rats and mice; six metabolites (9,10-diOH-; 4,5-diOH-; ?; 3,6-quinone-; 1,6-quinone and 3-OH-BaP) are formed by these microsomes. However, only three of them, 3,6-quinone-; 1,6-quinone and 3-OH-BaP, are generated by purified CYP1A1 reconstituted with NADPH:CYP reductase. A low concentration of NADPH:CYP reductase in the reconstituted system is sufficient for BaP oxidation, being stimulated by cytochrome b_5. Two BaP-derived DNA adducts (1 and 2, formed from 9-hydroxy-4,5-epoxy-BaP and 7,8-diol-9,10-epoxy-BaP, respectively) are generated by hepatic microsomes. Epoxide hydrolase is essential for formation of adduct 2, whereas adduct 1 is generated in the system containing only CYP1A1 with reductase. Cytochrome b_5 influences formation of both DNA adducts.