Abstract

Ellipticine is a plant alkaloid, which exhibits significant antitumor activity; therefore it was a center of interest since 60's of 20th century. There were a lot of ways published to obtain this anticancer drug. Ellipticine is actually a pro-drug, whose pharmacological efficiencies are dependent on the activation of two groups of enzymes, cytochrome P450 and peroxidases. The resulting effect of these groups of enzymes is either detoxification or activation of ellipticine metabolites. 13-Hydroxyellipticine and 12-hydroxyellipticine are products of activation reactions, which subsequently spontaneously cleave to carbenium ions, which in this form are bound to deoxyguanosine while generating DNA adducts.

13-Hydroxyellipticine may have potentially higher biological efficiencies than ellipticine, because it does not need enzymes for its activation and formation of DNA adducts. The aim of the diploma thesis was to synthesize this ellipticine derivative. 9-Nitroellipticin (another derivative of ellipticine) is an intermediate product of the 13-hydroxyellipticine synthesis. Results of this diploma thesis show that 9-nitroellipticine is oxidized by liver microsomal systems, which contain cytochromes P450, forming at least 4 metabolites. 9-Nitroellipticine shows similar behavior as ellipticine. Another ellipticine derivative, 9-aminoellipticine was prepared by reduction of the nitro group in position C-9 of ellipticine. This 9-aminoderiative of ellipticine, similar to 9-hydroxyellipticine, is not oxidized by rat liver microsomes. Properties of functional groups present at the C-9 of ellipticine affects the hydrophobicity of molecule and its metabolism.

Key words

Ellipticine, 13-hydroxyellipticine, 9-nitroellipticine, cytochrome P450, rat liver microsomes