Abstract

Tumour-related diseases are the second most common cause of death in the Czech Republic, right after cardiovascular diseases. Nanomedicine – a novel scientific discipline – shows captivating potential in anticancer treatment with help of so called nanotranporters – nanoparticles capable of transporting other molecules. Encapsulation of a cytostatic drug into a nanoparticle improves its pharmacokinetical and pharmacodynamical properties which helps to reduce adverse side effects on non-tumour healthy tissue.

In the scope of this diploma thesis apoferritin – apo-form of ferritin – was studied, since this nanotransporter shows promise for clinical use in anticancer treatment. Effect of hepatic microsomes from premedicated and control rats on biotransformation of doxorubicin cytostatic *(Dox)* in free and apoferritin nanoparticle-bound forms was investigated at pH 7,4. Over the course of biotransformation two types of metabolites – M1 and M2 – were observed. Regardless of the employed inductor all studied microsomes have exhibited similar metabolism of free doxorubicin and its apoferritin encapsulated form *(ApoDox)*. Our results also imply that doxorubicin can be metabolically processed by rat hepatic microsomes in both free and ApoDox form with similar efficiency. We have also studied biotransformation of ellipticine as both free molecule and apoferritin encapsulated nanoparticle by hepatic microsomes and cytochrome P450 3A4 in Supersomes™ by itself and with co-expressed cytochrome b_5 at pH 7,4 and 6,5. Results show that ellipticine oxidation is pH dependent. On the other hand, ellipticine release from apoferritin carrier is affected primarily by the structure of supersome microsomal membrane. At the same time, important role of cytochrome b_5 in ellipticine biotransformation by cytochrome P450 from 3A4 family was revealed.

Key words

Doxorubicin, ellipticine, cytochrome P450, apoferritin