Abstract

Reliably functional animal models for *in vivo* drug studies are essential for preclinical research. This thesis describes several rat models which were implemented and optimized for the studies on pharmacokinetic and pharmacodynamic properties of selected medical substances and innovative dosage forms.

An *in vivo* model for the studies on the progression of pharmacokinetic parameters of drugs during postnatal ontogenesis was used for studying of rosuvastatin, a drug used in the treatment of hypercholesterolemia. In comparison with rat pups of age corresponding to approximately twelve-year-old children in whom rosuvastatin pharmacokinetics is similar to adults, significantly lower values of volume of distribution and clearance and significantly higher rosuvastatin exposition were observed in rat pups of age corresponding to approximately two years in humans. Based on these results, it is possible to estimate that rosuvastatin in adequately reduced doses could be administered to children older than two years who suffer from familial hypercholesterolemia.

Cross-over design is considered the most reliable model for studies of drug bioavailability. Innovative drug formulations containing rivaroxaban, abiraterone acetate, and cannabidiol were tested using this model.

Significantly higher exposure of anticoagulant agent rivaroxaban was achieved after its administration in the form of cocrystals with oxalic acid, when compared with a standard commercial dosage form.

Administration of abiraterone acetate, prodrug of abiraterone used in the treatment of prostate cancer, in the form of oil marbles led to significantly higher abiraterone bioavailability in comparison with a standard commercial dosage form. Moreover, typical food effect observed after the administration of standard commercial dosage form was reduced when the technology with oil marbles was used.

Oral administration of cannabidiol, a natural substance with a huge potential for the treatment of various diseases, leads to very low bioavailability. Because of cannabidiol lipophilicity, various cannabidiol oil solutions are used. Significantly higher bioavailability was achieved when cannabidiol was administered in the form of microemulsion in comparison with a standard oil solution.

The microemulsion of cannabidiol was also tested on anti-inflammatory effects that could be useful in the treatment of rheumatoid arthritis. A rat model of collagen-induced

arthritis was used for this purpose. Clinical, histological, and laboratory evaluation of cannabidiol in the form of microemulsion showed moderate anti-inflammatory effects.