Abstract

Absorption of drugs from the gastrointestinal tract after oral administration is a key pharmacokinetic process co-determining the subsequent pharmacodynamic response of the organism and therapeutic efficacy. This dissertation thesis is devoted to the study of factors that influence this parameter. Special emphasis is placed on the study of lymphatic absorption, i.e. the rate of absorption of the active substance via the intestinal lymphatic system.

A number of *in vivo* studies have been carried out in laboratory rats. Pharmacokinetic studies have been performed by means of regular blood sampling from vascular catheters after oral administration of the drug. Lymphatic absorption was investigated in an anaesthetized mesenteric lymphatic duct cannulated rat model. Modern drugs were tested that were incorporated into innovative dosage forms by collaborating chemical and technological institutions.

Abiraterone acetate, a lipophilic agent used in the therapy of prostate cancer, was well absorbed from the gastrointestinal tract after administration in the form of oil marbles. This technology also succeeded in reducing the otherwise very significant positive food-effect. Abiraterone acetate was not absorbed to any significant extent via the intestinal lymphatic system.

In contrast, lymphatic absorption of cinacalcet, a substance used to treat hyperparathyroidism, was significant. The relative contribution of lymphatic absorption to the total systemic bioavailability was 20%. This means that one fifth of the substance that appeared in the systemic circulation had previously passed through the intestinal lymph.

The bioavailability of cannabidiol, an important cannabinoid and a substance registered for the treatment of some particular forms of childhood epilepsy, was significantly increased by the preparation of micro- and nanoemulsion dosage forms. Lymphatic absorption played a significant role. Absorption of cannabidiol was roughly half and half via the portal bloodstream and the intestinal lymphatic system.

Nilotinib, a modern tyrosine kinase inhibitor used for the treatment of chronic myeloid leukaemia, was administered in a dosage form based on encapsulation of the active substance in glucan particles derived from yeast cells. This led to a slight increase in bioavailability. Lymphatic absorption was low.

The pharmacokinetics of selected modern drugs and dosage forms, including the contribution of lymphatic absorption, have been described in detail in the studies summarized and commented in this thesis. This information will be used in the development of novel active substances and dosage forms with improved absorption properties, possibly specifically targeting the intestinal lymphatic system.

Key words:

Bioavailability, lymphatic absorption, abiraterone acetate, cinacalcet, cannabidiol, nilotinib