ABSTRACT

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The blood-brain barrier (BBB) has a prominent role in regulation of the transport of substances into and out of the central nervous system (CNS). Partly, the BBB inhibits the entrance of substances harmful for the brain, it regulates the delivery of needed substances and it takes part in efflux of useless substances as well. The equilibrium of these regulation systems is essential for the correct function of the CNS, without which the homeostasis would be disturbed.

Non-steroidal anti-inflammatory drugs (NSAIDs) are very well known for their anti-inflammatory effect, for reduction of fever and pain. Due to their bright, everyday usage, some side effects on the brain were observed (sleepiness, giddiness, nausea). This has evoked the question, how NSAIDs can cross the BBB.

PBMEC/C1-2 cell monolayer was used as an *in vitro* model of the BBB. The transport of following NSAIDs was investigated: celecoxib, diclofenac, ibuprofen, lornoxicam, meloxicam, piroxicam and tenoxicam. The experiments were carried out using only one NSAID (single transport studies) or more substances (group transport studies) at once. Different conditions (diverse transport mediums, serum contest, adding of transport inhibitors verapamil or probenecid, excluding of some NSAIDs substances) during group studies were simulated to observe a possible influence on the transport properties of NSAIDs. Internal standards diazepam (transcellular marker) and carboxyfluorescein (CF) (paracellular marker) were added to normalize the obtained data.

Ranking of single substance studies were similar to ranking of corresponding group study. Rankings of group studies were mostly influenced by using serum-free medium, by adding transport inhibitors verapamil or probenecid or by using astrocyte-conditioned medium. Serum-free study confirmed a strong binding ability of some NSAIDs to the serum proteins and its influence on the transport abilities. Group studies with transport inhibitors pointed to transport proteins, which are involved in permeation properties of the chosen substances. And finally, the suggestion that all substances can interact with each other was also proven.

Explicitly it was confirmed that most NSAIDs could cross the BBB significantly and consequently can influence the function of the CNS.