

Abstract

Six different substances blocking ion channels were chosen (verapamil, diltiazem, nifedipine, phenobarbital, memantine, amantadine) for the purpose of this work. All these substances are routinely used in clinical practice and it is well known that adverse effects on the central nervous system can occur during therapy with them. Therefore, both single and group transport studies were carried out to investigate and compare the transport abilities of chosen ion channel antagonists to penetrate the BBB and to find out the interference between them.

The required data for each substance used in single and group studies were determined using the Transwell BBB *in vitro* model based on EVC304 cell line. Diazepam and carboxyfluorescein were used as internal standards for normalization of permeability data.

According to the obtained data from single studies nifedipine as drug acting in periphery passes the BBB faster than internal standard diazepam (acting in CNS) and much more faster than other ion channel blockers acting in periphery, too. In clinical practice it can mean that nifedipine used for concrete clinical problem can have more CNS adverse effects in comparison to verapamil or diltiazem. The permeability data also demonstrate that verapamil, diltiazem, nifedipine and diazepam permeate through the BBB according to their lipophilicity in contrast to phenobarbital, which must be actively transported. This fact is supported by the results from group studies, where it was found that the permeability of the CNS drug phenobarbital was significantly increased by co-administration of peripherally acting Ca²⁺-channel blockers verapamil and diltiazem. Consequently, we have confirmed the concept that phenobarbital can be substrate of P-gP, which functionality is influenced by verapamil and diltiazem.