ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Pharmaceutical Chemistry and Control of Pharmaceuticals

Student: Markéta Krejčiová

Supervisor: Prof. PharmDr. Martin Doležal, Ph.D.

Supervisor specialist: Mjr. PharmDr. Jana Žďárová Karasová, Ph.D.

Title of diploma thesis: Monitoring of basic pharmacokinetic parameters of acetylcholinesterase inhibitors used in the treatment of Alzheimer´s disease

Alzheimer's disease is a progressive irreversible neurodegenerative disorder that is globally associated with the most frequent cause of dementia. The pathophysiology of this illness is not fully understood yet. The commonly used treatment is still symptomatic, based on IAChE and memantine. Great attention is paid particularly to IAChEs and their derivatives, which arise from the basic structure of tacrine and 7-MEOTA. These two molecules were used as a reference for comparison with newly synthetized IAChE derivatives KB-36 and KB-38.

Changes in plasma and brain tissue concentration levels were studied. The *in vivo* study was performed on rats (male, tribe Wistar). Equimolar doses were administered intramuscularly. Samples of plasma and brain tissue were evaluated by using HPLC techniques. The main aim was to determine the real concentration levels of all IAChE in both compartments.

Our results showed that tacrine had a better blood-brain barrier permeation than 7-MEOTA. Maximal concentration of tacrine in brain tissue, 18.86 ng/ml, was achieved in the 30^{th} minute. Maximal concentration of 7-MEOTA in brain tissue was 14.17 ng/ml and in was achieved in the 15^{th} minute. New derivatives, KB-36 and KB-38, did not achieved brain tissue in therapeutic concentration order. Therefore it is unlikely that these new molecules could relieve Alzheimer's disease symptoms.