Abstract

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Title of diploma thesis: Testing of the cytotoxicity of potential drugs in the cell lines together with the measurement of their passage through the blood brain barrier by the PAMPA method

This master thesis focuses on the prediction of tacrine derivatives permeability through blood-brain barrier and their cytotoxicity. We studied tacrine-benzothiazole and tacrine-thiaquinazoline derivates as potential drugs for treatment of Alzheimer´s disease. The reason of testing new tacrine derivates was effort to find substances with same effect and lower toxicity, for which was the tacrine discarded from clinical practice. The probable permeability of the studied substances was determined *in vitro* by the PAMPA method. Based on the permeation coeficient values we have identified that tacrine-benzothiazole derivates A-D (Pe= 8,31-16,9×10^{-6} cm/s) and tacrine-thiaquinazoline derivates 1, 3, 4 (Pe= 8,59-14,9×10^{-6} cm/s) were permeable through blood-brain barrier, tacrine-thiaquinazoline derivate 2 (Pe= 3,79×10^{-6} cm/s) had uncertain permeability and tacrine-thiaquinazoline derivate 5 (Pe= 2,0×10^{-6} cm/s) was not permeable. In the pre-clinical evaluation of potential drugs their cytotoxicity should also be determined. Cytotoxicity evaluation was studied in this master thesis using MTT-test. Based on IC_{50} values we found that studied benzothiazole/thiaquinazoline derivates showed higher cytotoxicity than tacrine alone.