

# ABSTRACT

No treatment that would completely stop the progression of Alzheimer's disease has not been found yet. Recently used tacrine showed good results in the treatment of Alzheimer's disease, however long-term use led to chronic hepatotoxicity due to its metabolites.

This master thesis deals with the compound 7-phenoxytacrine, one of the promising tacrine derivatives, which is one of the candidates for potential use in the therapy of Alzheimer's disease. Due to the formation of hepatotoxic metabolites of tacrine after the biotransformation in human liver, it appears necessary to identify the emerging metabolites of 7-phenoxytacrine molecule. Within this master's thesis *in vitro* biotransformation study of 7-phenoxytacrine using human liver microsomes was performed. High performance liquid chromatography with tandem mass spectrometry was used to determine the parent substance and the seventeen 7-phenoxytacrine metabolites. The analytical method showed the formation of six monohydroxylated and eleven dehydroxylated metabolites of 7-phenoxytacrine. Thus, we concluded that hydroxylation is the major metabolic reaction after *in vitro* microsomal biotransformation. In addition to the identification of metabolites, a quantification and microsomal stability study, including the determination of the amount of parent substance after biotransformation in defined time points, was performed. Furthermore, the biological half-life and intrinsic clearance of 7-phenoxytacrine were determined and we classified this compound to the group of rapidly biotransformed molecules.