Abstract
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Title of Disertation: Testing of new potencial substances for the treatment of Alzheimer´s Disease
Alzheimer´s disease (AD) is the most common form of dementia which is manifested especially by loss of short-term memory, spatial disorientation, progressive loss of cognitive function and progressive deterioration of intellect. It is estimated about 36 million (mostly AD) people worldwide suffer from dementia and this number continues to grow.
AD is unpredictable, multifactorial disease of unknown origin and casual therapy. In most *post-mortem* investigated brains, loss of nerve tissue, oxidative damage induced by inflammation and neuronal decay, extracellular aggregated amyloid beta in amyloid plaque and hyperphosphorylated tau protein tangles were discovered. This disease always ends lethally after 2-10 years from diagnosis. At present, the only available drugs for AD are for symptomatic treatment and most treated patients build a tolerance to them over time. The effect of drugs used in the treatment of AD is based on inhibition of acetylcholinesterase (AChE) (donepezil, galantamine, rivastigmine) or on inhibition of N-methyl-D-aspatate (NMDA) receptors (memantine).
In this work, existing AChE inhibitors used in the treatment of AD, precursors for the synthesis or renewal of existing AChE inhibitors and new potential inhibitors of AChE inhibitors synthesized at the Faculty of Military Health Sciences, the Department of Toxicology (University of Defense) were tested. Standard methods for measuring inhibition of AChE and for determining antioxidant properties of the tested substances were selected for the experiment. These used methodologies have been enriched by a new method for measuring inhibition betasecretase (BACE) and inhibition aggregation of amyloid beta, which have not been yet established at the Faculty of Military Health 8

Sciences. Based on the results of the experiment, a number of new substances with a multi-target effect (inhibition of AChE, inhibition of BACE and inhibition of the aggregation of amyloid beta) associated with a probable incidence of AD was selected and recommended for further *in vivo* testing.