Synthesis of N- substituted amino acid amino amides and their study as possible treatment of Alzheimer disease

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According to WHO annually millions of people all over the world are suffering from Alzheimer's disease (AD). Clinical symptoms of AD are extracellular accumulation of senile plaques which are consists with β-amyloid, hyperphosphorylation of tau protein twist into abnormal tangles inside brain cells [1]. It is known that the main cause of AD is misfolding of Aβ-peptides, which leads to formation of extracellular aggregates of Aβ [2]. Thus, we sought to develop new agents that can effectively inhibit the formation of β-amyloid aggregates. From this viewpoint compounds such as N-substituted amino acids dialkyl-amino alkylamides has special interest. Therefore, we synthesized novel compounds N-benzoyl-DL-valine dimethylamino-ethylamine iodmetilate (TVA) and 1-diethylaminoethyl-2-phenyl-4-benzylidene-5-imidazolone (TVS), which are posses prominent anticholinesterase and antibutyrylcholinesterase activities and have a high selection to butyrylcholinesterase that reaches to 10000-39000 unit. The latter is very remarkable, as the butyrylcholinesterase promotes the formation of Aβ 25-35 and amyloid aggregates [3]. The synthesis of compound TVA was performed by the method of active aesthers, whereas, the synthesis of the second compound TVS was implemented by the azlactone method (Fig. 1).

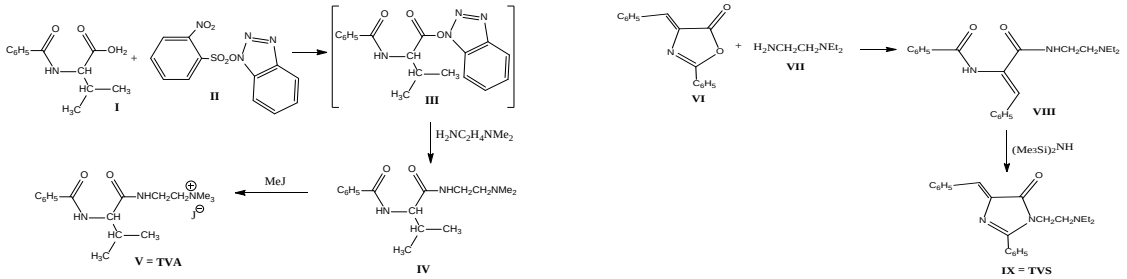

Figure1. Synthesis of TVA and TVS

Morphological and histochemical investigation of mentioned compounds in experimental models of AD showed that destructive and dystrophic processes in the hippocampus were significantly reduced compared with the control group.

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