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Memantine–cinnamic acid hybrids: Synthesis and in vitro evaluation of their effects against Alzheimer's disease

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Despite of extensive investigations of finding causes for Alzheimer's disease (AD), the etiology of this neurological disorder is rather complicated. Currently, the only drug approved for a treatment for moderate to severe Alzheimer's disease is memantine (1-amino-3, 5-dimethyladamantane). This clinical drug is known as an open-channel, non-competitive N-methyl-D-aspartate (NMDA) receptor inhibitor.

Considering the multifactorial nature of AD, the monotherapy concerning one-compound - one-target has not reached the desired effect. Therefore, in the recent years the hybrid-based approach has emerged as a promising therapy for Alzheimer's disease. Following the multitarget approach, herein, amide-modified memantine with different substituted cinnamic acids were designed in order to investigate their effects in an in vitro AD model.

Methodology and Theoretical Orientation: **Synthesis: The target memantine amides (Fig. 1) were obtained in moderate yields (40–70%) based on the N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC) as coupling agent and HOBt as catalyst (SHEEHAN, 1961).**

Neuroprotective effects of memantine derivatives: **APPswe cells injured by copper, which triggers β-amyloid toxicity, were served as an AD model in vitro. The MTS assay was used to examine the protective effects of the memantine derivatives on copper injured APPswe cells. EC50 value was used to evaluate the efficacies for neuroprotection of the memantine hybrids as well as the positive drug memantine hydrochloride.**

Conclusion and Significance: **The results demonstrated that the tested hybrid compounds showed protective effects on improving APPswe cell viability due to copper-induced toxicity. The EC50 ranging from (18.23 ± 1.08) μM to (35.24 ± 1.84) μM**

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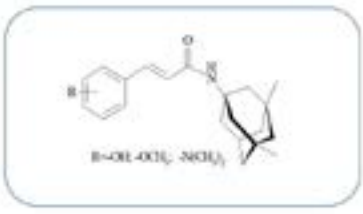

Biography

Aleksandra Tencheva is a PhD student in Organic chemistry at South-West University "Neofit Rilski", Bulgaria. She has been evaluating her PhD thesis under the supervision of Prof. Ivanka Stankova, PhD. Tencheva's research interest is in design of drugs with potentional neuroprotective activity. She has been taken part in young project (MU-23/2018) entitled "Newly memantine analogues with potential protective effects for the treatment of dementia of the Alzheimer's type".

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