Design and synthesis of 4-aminoquinoline derivatives with adamantane scaffold as inhibitors of human cholinesterases

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Lecture title: Design and synthesis of 4-aminoquinoline derivatives with adamantane scaffold as inhibitors of human cholinesterases

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Abstract

Quinoline heterocycle as example a privileged pharmacophore ensue numerous of descendants with diverse biological activities. 4-Aminoquinolines (4-AQ) as the most representative family, exhibit a broad spectrum of biological activity, including antimalarial, antibacterial, antifungal and antiviral. In the last 40 years, this scaffold has attracted attention as potentially CNS active agent, important for treating neurodegenerative disorders, such as Alzheimer's disease (AD). Based on the findings that compound which poses adamantyl group in the side chain expressed promising activity against both human cholinesterases, the main targets in developing drugs for treating AD, we designed and synthesized a series of 4-aminoquinoline derivatives with adamantane moiety to further examine potential of this group of compounds. Starting from the corresponding 4-chloroquinoline combining various experimental conditions and directions in the synthetic pathway, we obtained corresponding 4-aminoquinoline derivatives. In the final step, adamantyl moiety was linked to terminal amino group by reductive amination. Alternatively, previously synthesized side chains were directly coupled with the corresponding 4-chloroquinoline. Structure-activity analysis of first series of compounds, shown that n-octenyl as a linker is the most promising for the inhibition of both acetyl- and butyrylcholinesterase. Agreeing to this result, a new series of n-octenyl derivatives with adamantane was synthesized, where terminal amino-group was further modified by connecting different heterocyclic structures via reductive amination.

Curriculum Vitae

Katarina Komatović (née Bogojević), born in Belgrade, Serbia, graduated BSc studies in 2014. and MSc studies in 2015. at University of Belgrade – Faculty of Chemistry (UBFC). The same year she started her PhD studies at Department of Organic Chemistry, UBFC. From 2017. to 2018. she worked as Junior Teaching assistant, and in 2018. she became Teaching Assistant at Department of Organic Chemistry, UBFC. Her teaching experience includes laboratory work and theoretical practice in several courses in Organic chemistry for students at Faculty of Chemistry, Faculty of Biology and Faculty of Physical Chemistry.

She co-authored three reviewed scientific publications and participated in four projects. The research area is organic synthesis and medicinal chemistry.

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