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### Conjugates of $\gamma$ -Carbolines and phenothiazine as new selective inhibitors of butyrylcholinesterase and blockers of NMDA receptors for Alzheimer Dementia

Alzheimer's disease is a multifactorial pathology and the development of new multitarget neuroprotective drugs is promising and attractive. We synthesized a group of original compounds, which combine in one molecule  $\gamma$ -carboline fragment of dimebon and phenothiazine core of Methylene Blue (MB) linked by 1-oxo- and 2-hydroxypropylene spacers. Inhibitory activity of the conjugates towards Acetylcholinesterase (AChE), Butyryl Cholin Esterase (BChE) and structurally close to them Carboxylesterase (CaE), as well their binding to NMDA-receptors were evaluated *in vitro* and *in silico*. These newly synthesized compounds showed significantly highest inhibitory activity towards BChE with IC<sub>50</sub> values in submicromolar and micromolar range and exhibited selective inhibitory action against BChE over AChE and CaE. Kinetic studies for the 9 most active compounds indicated that majority of them were mixed-type BChE inhibitors. The main specific protein-ligand interaction is  $\pi$ - $\pi$  stacking of phenothiazine ring with indole group of Trp82. These compounds emerge as promising safe multitarget ligands for the further development of a therapeutic approach against aging-related neurodegenerative disorders such as Alzheimer and/or other pathological conditions.

#### Biography

Gjumrakch Aliev, MD, PhD is President of "GALLY" International Biomedical Research Institute Inc., San Antonio, Texas, USA. He also holds appointment with the University of Atlanta, Atlanta, Georgia, USA as a Professor of Cardiovascular, Neuropathology, Gerontology, Health Science and Healthcare Administration, and Leading Researcher in the Institute of Physiologically Active Compounds, Russian Academy of Sciences, Chernogolovka, Moscow Region, Russia. He received his MD in 1982, from the Baku Medical University (former USSR) with *cum laude*. Then, he accomplished his PhD in Cardiovascular Diseases from the prestigious Russian Academy of the Medical Sciences, Moscow, Russia in 1988 with *cum laude*. He received Post-doctoral Training with Professor G. Burnstock in the University College of the London. He authored and coauthored more than 500 publications in the fields of neurodegenerative diseases research (Alzheimer's disease), as well as cardio- and cerebrovascular disease, cancer and electron microscopy. He is an outstanding Teacher, Scholar and a Renowned Scientist in the area of cellular molecular physiology, and cardiovascular and neurodegeneration-mediated pathologies and drug development including Alzheimer's disease. He is nationally and internationally reputed in his area.

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