

PLENARY PRESENTATIONS

NOVEL γ -CARBOLINES AND CARBAZOLES DERIVATIVES AS A PROMISING DRUG CHEMOTYPES FOR THE NEURODEGENERATIVE DISEASE TREATMENT

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The search of effective drugs for the treatment of neurodegenerative diseases such as Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD) is an extremely complex challenge. It is explained by both the multifactorial nature of such pathologies and the difficulties in modeling CNS diseases *in vitro* and *in vivo*. The actual trends in developing drugs for the neurodegenerative diseases treatment are the targeted search for the agents that directly affect the pathogenesis of diseases, the creation of multi-target structures, and the repositioning of already known drugs^{1,2}.

Previously, neuroprotective activity of the antihistamine drug Dimebon (γ -carboline derivative) was discovered. This compound has pronounced therapeutic properties in the 2nd phase of clinical trials (CT) in Alzheimer's disease patients³, and currently is on the Phase 3 CT in Russia. We carried out a targeted modification of the parent γ -carboline and carbazole derivatives to find new neuroprotective properties in various cellular and animal models of neurodegenerative disorders⁴⁻⁷. Pronounced anti-aggregation and mitochondria stabilizing properties were found in a group of novel γ -carboline/carbazole and aminoadamantane conjugated structures in different AD, PD models. Fluorine derivatives of the reference agent Dimebon demonstrated strong disease modification action in cell and animal ALS models. It allows to consider these groups of compounds as promising neuroprotective drug-candidates for the broad spectrum of neurodegenerative diseases.

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References:

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