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ABSTRACT BOOK



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Promising biological targets for the design of multitarget neuromodulatory agents

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Background: Neuropsychiatric and neurodegenerative disorders, including depression and cognitive impairment, are characterized by complex multifactorial pathophysiology involving dysregulation of multiple neurotransmitter systems, impaired neuroplasticity, and neuroinflammatory processes. Traditional pharmacotherapy targeting a single biological target often demonstrates limited therapeutic efficacy. Therefore, increasing attention has been paid to the concept of multitarget-directed ligands (MTDLs), which involves the design of compounds capable of modulating several key biological targets within the central nervous system simultaneously [1].

Aim: The aim of this work was to analyse recent literature data on promising biological targets for the development of multitarget neuromodulators and to evaluate their relevance for modern drug design strategies.

Methods: A comprehensive review of scientific publications in the fields of medicinal chemistry and neuropsychopharmacology published between 2020 and 2025 was conducted. Attention was given to studies describing molecular mechanisms of CNS targets, pharmacophore features of ligands, molecular docking, pharmacophore modelling, and in silico ADMET predictions. Additionally, studies addressing structure–activity relationship analysis and CNS drug-likeness parameters, including blood–brain barrier permeability, were considered.

Results: Literature analysis indicates that several biological targets are particularly promising for the development of multitarget neuromodulators. Among them, 5-HT_{1A} serotonin receptors, sigma-1 receptors, NMDA receptors, and the enzymes monoamine oxidase A (MAO-A) and acetylcholinesterase (AChE) play key roles in the regulation of neurotransmission, neuroplasticity, and cognitive processes. The 5-HT_{1A} receptor is widely recognized as an important target for antidepressant drug development [2]. The sigma-1 receptor has emerged as a promising target due to its involvement in neuroprotection and cellular stress regulation [3]. The NMDA receptor of the glutamatergic system is closely associated with mechanisms underlying rapid antidepressant effects [4]. Enzymatic targets such as MAO-A and AChE are also crucial because they regulate neurotransmitter metabolism and cognitive functions [5].

Conclusions: Current research supports the effectiveness of multitarget strategies for the development of novel neuromodulators for complex CNS disorders. Simultaneous modulation of receptor systems (5-HT_{1A}, sigma-1, NMDA) and enzymatic targets (MAO-A, AChE) may provide improved therapeutic outcomes. The integration of target-based drug design, computational modeling, and SAR analysis represents a promising approach for identifying novel heterocyclic compounds with optimal pharmacological and pharmacokinetic properties.

References

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