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Design of prototypes of nootropic drugs based on racetams and ampakines

Rustam Suleiman[1*], Nataliia Kobzar[1], Vitaliy Yaremenko[1], Lina Perekhoda[1]

[1] *National University of Pharmacy, Kharkiv, Ukraine*
* *suleiman.nfau@outlook.com*

Introduction. The evolution of the creation of nootropics from the racetam group is based on the modification of the structure of Piracetam, thanks to which analogues with better pharmacokinetic properties and an expanded spectrum of pharmacological effects were created [1]. That is why the selection of the already existing racetam of the new generation of Nebracetam for further modification will make it possible to create a potential series of derivatives with nootropic properties. Modern approaches to the search for new drugs involve the combination of different pharmacophores in one molecule, which can lead to synergistic effects. That is why, in our opinion, the search for a pharmacophore among ampakines [2] has great prospects. Most of the racetams and ampakines have a common mechanism of action, in particular, due to the effect on AMPA and acetylcholine receptors [1, 3], which will allow for a purposeful search for substances according to the chosen direction.

Materials and methods. The base for virtual screening was generated using the Marvin Sketch 20.5 program.

Results and discussion. Logico-structural analysis and a hybrid-pharmacoform approach was used to select the basic structure and pharmacophores for the design of effective prototypes. As such "building blocks", we proposed Nebracetam and previously obtained synthetic frameworks with a 5-sulfonylidene-4,5-dihydro-1*H*-1,2,4-triazole ring [4], which were combined with benzofurazan-5-yl-carbonyl fragment (pharmacophore of benzofurazan ampakines CX717 and CX1739). In fig. 1 shows the structures of basic compounds and potential nootropics (I and II).

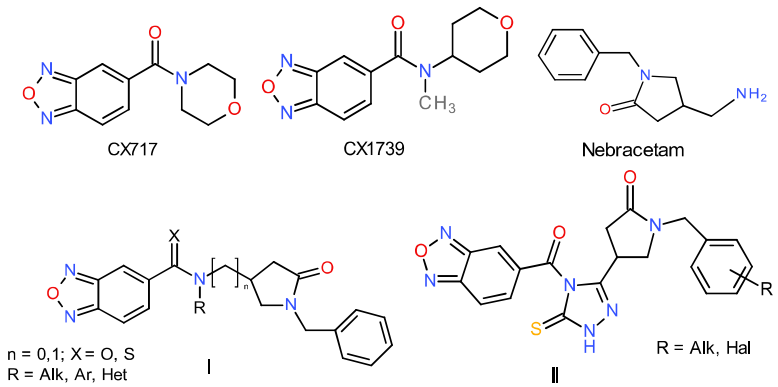

Fig. 1. Structures of basic compounds and potential nootropics

Conclusions. As a result of the design of potential nootropic molecules, pharmacophore frames were used among racetams and benzofurazan ampakines. Such a combination can lead to additive and synergistic effects that will give a positive response in experimental screening.

References

1. Malykh A.G., Sadaie M.R. Piracetam and piracetam-like drugs: from basic science to novel clinical applications to CNS disorders. Drugs. 2010;70(3):287-312.
2. Timm D.E., Benveniste M., Weeks A.M., Nisenbaum E.S., Partin K.M. Structural and functional analysis of two new positive allosteric modulators of GluA2 desensitization and deactivation. Mol Pharmacol. 2011;80:267-280.
3. Kadriu B., Musazzi L., Johnston J.N. et al. Positive AMPA receptor modulation in the treatment of neuropsychiatric disorders: A long and winding road. Drug Discovery Today. 2021;26(12):2816-2838.
4. Semenets A.P., Suleiman M.M., Fedosov A.I., Shtrygol S.Yu., Havrylov Ih.O., Mishchenko M.V/ et al. Synthesis, docking, and biological evaluation of novel 1-benzyl-4-(4-(R)-5-sulfonylidene-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)pyrrolidin-2-ones as potential nootropic agents. European Journal of Medicinal Chemistry. 2022;244:114823.