Searching for novel synthetic MAO inhibitors

Panagiou Mavroeidi [1], Aggeliki Syriopoulou[1], Nikitas Georgiou[1], Nikolaos Tzouras[1], Stavros Neofotistos[1], Georgios Vougioukalakis[1], Serdar Durdagi[2] and Thomas Mavromoustakos[1]

[1]Department of Chemistry, Laboratory of Organic Chemistry, National and Kapodistrian University of Athens, Zografou GR-15771, Greece

[2]Department of Biophysics School of Medicine, Bahcesehir University, Istanbul

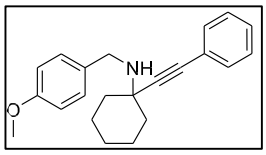
e-mail: gmavroeidi@hotmail.com

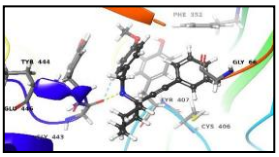
Non-selective monoamine oxidase inhibitors (MAO-I) belong to the earliest drugs tried in the therapy of Parkinson's disease but they present several side-effects that limit their efficacy. Propargylamines consist a heterogeneous family of organic compounds with unique properties. A series of propargylamine compounds bearing tetrasubstituted carbon centers demonstrate very strong inhibitory effect as novel synthetic MAO inhibitors with remarkable selectivity and therapeutic effects.

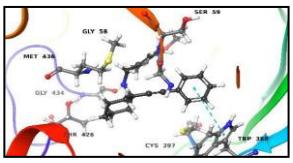
Thirty-two propargylamine derivatives synthesized by Prof. G. Vougioukalakis' research group, were investigated via molecular docking. Propargylamine derivative compounds tested for their binding to the active site of 1s3b and 2z5x proteins.

Using AutoDock Tools, the molecules were prepared in their three-dimensional form to produce the autogrid and autodock parameter files. Compounds N-4-methoxybenzyl-1-phenylethynyl cyclohexan-1- amine and N-benzyl-1- phenylethynyl cyclohexan-1-amine showed the most favorable ΔG values during molecular docking *in silico* experiments. (Figures 1-3).

Docking results designated also some promising binding to MAO enzymes with some molecules showing high selectivity. The *in vitro and in silico* results show that the synthetic propargylamine derivatives may serve as a useful pharmacological tool with high selectivity for the active site of the MAO receptor.







Images 1-3: (left) Synthetic compound structure. (medium) The active site of 2z5x (MAO-A.) and the interactions of the compound with the enzyme active site aminoacids. (right) The active site of 1s3b (MAO-B) and the interactions of the compound with the enzyme active site aminoacids.

References

1. Tzouras NV, ACS Omega. (2019)
2. Neofotistos, S P, Adv. Synth. Catal. (2020)