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Computatinal study of the monoamin oxidase B mechanism-based irreversible inhibitors

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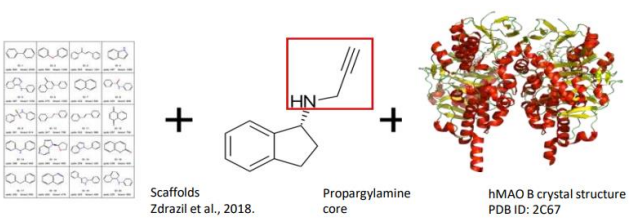
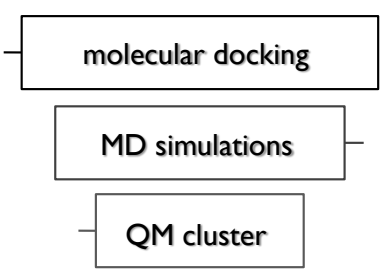
Monoamine oxidase B (MAO B) is a flavoenzyme responsible for the metabolism of endogenic and exogenic amines such as monoamine neurotransmitters who's disturbed homeostasis is implicated in the wide range of neurodegenerative pathogenesis. MAO B represents primary pharmacological target for the treatment of the Alzheimer's and Parkinson's disease. Commercial drugs, selegiline and rasagiline, are administrated with dietary restrictions and in high doses are associated with more frequent and greater intensity side effects. [1] There is a constant market pressure for the development of new, mechanism-based MAO B inhibitors with more favourable pharmacokinetic profiles.
Innovative approach was developed for the drug design which involves binding of the scaffolds [2] with propagylamine core which is present in commerical drugs which target MAO enzymes. [3] More favourable thermodynamic profiles are obtained using methods ofscript based molecular docking and molecular dynamics simulations. More favourable kinetic profile of the inhibitory activity was obtained and characterized *via* the quantum chemical cluster approach.





[1] T. Tandarić, A. Prah, J. Stare, J. Mavri, R. Vianello, *Int. J. Mol. Sci.* **21** (2020) 6151.
[2] B. Zdrazil, R. Guha, *J. Med. Chem.* **61** (2018) 4688–4703.
[3] T. Tandarić, R. Vianello, *ACS Chem. Neurosci.* **10** (2019) 3532–3542.