

Exploration of umbelliferone based derivatives as potent MAO inhibitors

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Monoamine oxidase (MAO) inhibitors are potential drug candidates for treating neurological disorders such as anxiety, Alzheimer's disease and Parkinson's disease.

This review presents information about MAO inhibitory effects of the umbelliferone based derivatives. The potential antioxidant effects of the derivatives were evaluated by DPPH and H2O2 scavenging methods. The derivatives were screened for hMAO-A and hMAO-B inhibition through a series of different umbelliferone derivatives was designed and synthesized for experimental conditions. Through docking simulation, the mechanistic insight for enzyme- compound infractions was achieved. By two spectrophotometric titration methods, the antioxidant potential was dually assessed.

A remarkable hMAO-A inhibitory potential was exhibited by $(7.473\pm0.035~\mu\text{M}$ and the selectivity index of 0.14) Compound 5 with bromo 5-bromo-isatin, revealing the impact of hybrid coumarin and 5-bromo-2-oxoindolin-3-yl ring with hydrazine linker on the hMAO-A active site. With an exceptional selectivity index of 8.55, compound 13 exhibited significant hMAO-B inhibition with an IC50 value of $10.32\pm0.044\mu\text{M}$. Incorporation of 2-hydroxy-2-phenylacetate moiety on 2-oxo-2H-chromen ring led the important binding infractions within the hMAO active site.

A good correlation was revealed between experimental MAO <u>inhibition</u> and docking score by computational studies. Notably, the compounds



with remarkable MAO inhibitory potential were also observed as potential antioxidants which have implications for therapy of neuropsychological and neurodegenerative diseases.

More information: Priyanka Dhiman et al, Exploration of Umbelliferone based Derivatives as Potent MAO inhibitors: Dry Vs Wet lab Evaluation, *Current Topics in Medicinal Chemistry* (2018). DOI: 10.2174/1568026618666181115095204

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