# Combined 3D-QSAR and docking analysis for the design and synthesis of chalcones as potent and selective monoamine oxidase B inhibitors

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Abstract
Monoamine oxidases (MAOs) are important targets in medicinal chemistry, as their inhibition may change the levels of different neurotransmitters in the brain, and also the production of oxidative stress species. New chemical entities able to interact selectively with one of the MAO isoforms are being extensively studied, and chalcones proved to be promising molecules. In the current work, we focused our attention on the understanding of theoretical models that may predict the MAO-B activity and selectivity of new chalcones. 3D-QSAR models, in particular CoMFA and CoMSIA, and docking simulations analysis have been carried out, and their successful implementation was corroborated by studying twenty-three synthetized chalcones (151–173) based on the generated information. All the synthetized molecules proved to inhibit MAO-B, being ten out of them MAO-B potent and selective inhibitors, with $IC_{50}$ against this isoform in the nanomolar range, being (E)-3-(4-hydroxyphenyl)-1-(2,2-dimethylchroman-6-yl)prop-2-en-1-one (152) the best MAO-B inhibitor ($IC_{50}$ of 170 nM). Docking simulations on both MAO-A and MAO-B binding pockets, using compound 152, were carried out. Calculated affinity energy for the MAO-A was +2.3 Kcal/mol, and for the MAO-B was −10.3 Kcal/mol, justifying the MAO-B high selectivity of these compounds. Both theoretical and experimental structure–activity relationship studies were performed, and substitution patterns were established to increase MAO-B selectivity and inhibitory efficacy. Therefore, we proved that both 3D-QSAR models and molecular docking approaches enhance the probability of finding new potent and selective MAO-B inhibitors, avoiding time-consuming and costly synthesis and biological evaluations.

Author keywords
3D-QSAR models
Chalcone derivatives
Drug design
Molecular docking
Monoamine oxidase B inhibitors