Design, Synthesis and Docking Calculations of Prenylated Chalcones as Selective Monoamine Oxidase B Inhibitors with Antioxidant Activity

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Different natural and synthetic chalcones have exhibited selective inhibition on monoamine oxidase B (MAO?B) activity, demonstrating potential interest for the treatment of neurodegenerative diseases. Herein we report the synthesis of seven new prenylated chalcones (7a-g) obtained from the natural compound 5 (4-hydroxy-3-(3-methylbut-2-en-1-yl)phenylethanone), previously isolated from S. graveolens. Five of these compounds exhibit high inhibition and selectivity against MAO?B, with IC50 values in the low micromolar range. In addition, the antioxidant activity of this series was measured, being three compounds better than the reference, butylated hydroxytoluene (BHT). Compound 7 f [(2E)-3-(4-(dimethylamino)phenyl)-1-(4-hydroxy-3-(3-methylbut-2-en-1-yl)phenyl)prop-2-en-1-one] proved to be the best compound within the studied series (IC50 MAO-B=8.19 ?M and k DPPH=3.73). Finally, molecular docking was performed to better understand the binding properties of these derivatives. Important features for MAO?B inhibitory activity were observed: hydrogen-bonding interaction between Tyr435 and nearness with Tyr398 and FAD co-factor. Therefore, these molecules are good candidates for the design of a lead compound for Parkinson's disease.

Antioxidant activity

Claisen-Schmidt reaction

Molecular docking

Monoamine oxidase B inhibitors

Prenyl-chalcones