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

Mellado, M., Salas, C. O., Uriarte, E., Viña, D., Jara-Gutiérrez, C., Matos, M. J., & Cuellar, M. (2019). Design, Synthesis and Docking Calculations of Prenylated Chalcones as Selective Monoamine Oxidase B Inhibitors with Antioxidant Activity. ChemistrySelect, 4(26), 7698-7703. <10.1002/slct.201901282> Accessed 14 Nov 2020.

Abstract

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 μM 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.

Keywords

Antioxidant activity; Claisen-schmidt reaction; Molecular docking; Monoamine oxidase B inhibitors; Prenyl-chalcones