3-Arylcoumarins as highly potent and selective monoamine oxidase B inhibitors: Which chemical features matter?

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Monoamine oxidase B inhibitory activity is closely regulated by the interaction of the small molecules with the enzyme. It is therefore desirable to use theoretical approaches to design rational methods to develop new molecules to modulate specific interactions with the protein. Here, we report such methods, and we illustrate their successful implementation by studying six synthetized 3-arylcoumarins (71?76) based on them. Monoamine oxidase B inhibition is essential to maintain the balance of dopamine, and one of its major functions is to combat dopamine degradation, a phenomenon linked to Parkinson's disease. In this work, we study small-molecule inhibitors based on the 3-arylcoumarin scaffold and their monoamine oxidase B selective inhibition. We show that 3D-QSAR models, in particular CoMFA and CoMSIA, and molecular docking approaches, enhance the probability to find new interesting inhibitors, avoiding very costly and time-consuming synthesis and biological evaluations. © 2020 Elsevier Inc.

3-Arylcoumarins

3D-QSAR models

Drug design

Molecular docking

Monoamine oxidase B inhibitors

3 (2',4' dimethoxyphenyl) 6 methylcoumarin

3 (3',4' dihydroxyphenyl) 6 methylcoumarin

3 (3',4' dimethoxyphenyl) 6 methylcoumarin

3 (3',5' dimethoxyphenyl) 8 methylcoumarin

3 (5' bromo 2',4' dimethoxyphenyl) 6 methylcoumarin

3 arylcoumarin derivative

8 ethoxy 3 (3',4' dimethoxyphenyl)coumarin

8 ethoxy 3 (3',4',5' trimethoxyphenyl)coumarin

8 methoxy 3 (3 tolyl)coumarin

amine oxidase (flavin containing) isoenzyme B

coumarin derivative

dopamine

monoamine oxidase B inhibitor

monoamine oxidase inhibitor

unclassified drug

animal cell

Article

biological activity

comparative molecular field analysis

comparative molecular similarity indices analysis

drug design

drug potency

drug selectivity

drug synthesis

enzyme inhibition

IC50

molecular docking

nonhuman

Parkinson disease

priority journal

probability

protein database

protein degradation

protein function

three dimensional quantitative structure activity relationship