Coumarin derivatives as promising xanthine oxidase inhibitors

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Xanthine oxidase (XO) is an interesting target for the synergic treatment of several diseases. Coumarin scaffold plays an important role in the design of efficient and potent inhibitors. In the current work, twenty 3-arylcoumarins and eight 3-heteroarylcoumarins were evaluated for their ability to inhibit XO. Among all the candidates, 5,7-dihydroxy-3-(3?-hydroxyphenyl)coumarin (compound 20) proved to be the best inhibitor with an IC50 of 2.13 ?M, being 7-fold better than the reference compound, allopurinol (IC50 = 14.75 ?M). To deeply understand the potential of this compound, the inhibition mode was also evaluated. Compound 20 showed an uncompetitive profile of inhibition. Molecular docking studies were carried out to analyze the interaction of compound 20 with the studied enzyme. The binding mode involving residues different from the catalytic site of the binding pocket, is compatible to the observed uncompetitive inhibition. Compound 20 was not cytotoxic at its IC50 value, as demonstrated by the viability of 99.1% in 3 T3 cells. Furthermore, pharmacokinetics and physicochemical properties were also calculated, which corroborated with the potential of the studied compounds as promising XO inhibitors. © 2018

Coumarin derivatives

Molecular docking

Xanthine oxidase inhibition

3 heteroarylcoumarin derivative

5,7 dihydroxy 3 (3' hydroxyphenyl)coumarin

allopurinol

arylcoumarin derivative

coumarin derivative

molecular scaffold

unclassified drug

xanthine oxidase

xanthine oxidase inhibitor

allopurinol

coumarin

coumarin derivative

enzyme inhibitor

3T3 cell line

amino acid sequence

animal cell

Article

binding site

controlled study

drug safety

enzyme active site

enzyme binding

enzyme inhibition

IC50

molecular docking

mouse

nonhuman

pharmacokinetics

physical chemistry

antagonists and inhibitors

chemical structure

chemistry

structure activity relation

Allopurinol

Catalytic Domain

Coumarins

Enzyme Inhibitors

Molecular Docking Simulation

Molecular Structure

Structure-Activity Relationship

Xanthine Oxidase