New insights into highly potent tyrosinase inhibitors based on 3-heteroarylcoumarins: Anti-melanogenesis and antioxidant activities, and computational molecular modeling studies

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Melanogenesis is a physiological pathway for the formation of melanin. Tyrosinase catalyzes the first step of this process and down-regulation of its activity is responsible for the inhibition of melanogenesis. The search for molecules capable of controlling hyperpigmentation is a trend topic in health and cosmetics. A series of heteroarylcoumarins have been synthesized and evaluated. Compounds 4 and 8 exhibited higher tyrosinase inhibitory activities (IC50= 0.15 and 0.38 ?M, respectively), than the reference compound, kojic acid (IC50= 17.9 ?M). Compound 4 acts as competitive, while compound 8 as uncompetitive inhibitor of mushroom tyrosinase. Furthermore, compounds 2 and 8 inhibited tyrosinase activity and melanin production in B16F10 cells. In addition, compounds 2?4 and 8 proved to have an interesting antioxidant profile in both ABTS and DPPH radicals scavenging assays. Docking experiments were carried out in order to study the interactions between these heteroarylcoumarins and mushroom tyrosinase.

3-Heteroarylcoumarins

B16F10 melanoma cells

Melanogenesis

Tyrosinase inhibitors

3 (4 bromothiophen 2 yl) 5,7 dihydroxycoumarin

3 (4 bromothiophen 2 yl) 6 methoxycoumarin

3 (4 bromothiophen 2 yl) 7 hydroxycoumarin

3 (4 bromothiophen 2 yl) 7,8 dihydroxycoumarin

3 (4 bromothiophen 2 yl) 8 hydroxycoumarin

3 heteroarylcoumarin derivative

5,7 dihydroxy 3 (thiophen 2 yl)coumarin

6 hydroxy 3 (thiophen 2 yl)coumarin

6 methoxy 3 (thiophen 2 yl)coumarin

7 hydroxy 3 (thiophen 2 yl)coumarin

antioxidant

coumarin derivative

kojic acid

trolox C

unclassified drug

antioxidant

enzyme inhibitor

melanin

monophenol monooxygenase

ABTS radical scavenging assay

animal cell

antimelanogenesis activity

antioxidant activity

Article

controlled study

DPPH radical scavenging assay

drug activity

drug design

drug synthesis

EC50

IC50

limit of quantitation

molecular docking

molecular model

mouse

nonhuman

animal

antagonists and inhibitors

biosynthesis

carbon nuclear magnetic resonance

mass spectrometry

proton nuclear magnetic resonance

tumor cell line

Animals

Antioxidants

Carbon-13 Magnetic Resonance Spectroscopy

Cell Line, Tumor

Enzyme Inhibitors

Mass Spectrometry

Melanins

Mice

Models, Molecular

Molecular Docking Simulation

Monophenol Monooxygenase

Proton Magnetic Resonance Spectroscopy