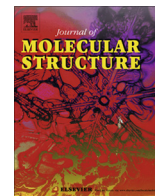


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Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Design and synthesis of chalcone derivatives as potent tyrosinase inhibitors and their structural activity relationship



Muhammad Nadeem Akhtar ^{a,*}, Nurshafika M. Sakeh ^b, Seema Zareen ^a, Sana Gul ^c, Kong Mun Lo ^d, Zaheer Ul-Haq ^c, Syed Adnan Ali Shah ^{e,f,*}, Syahida Ahmad ^b

^a Faculty of Industrial Sciences & Technology, Universiti Malaysia Pahang, Lebuhraya Tun Razak 26300, Kuantan, Pahang, Malaysia

^b Department of Biochemistry, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia

^c Dr. Panjwani Center for Molecular Medicine & Drug Research, International Center for Chemical & Biological Sciences, University of Karachi, Karachi 75270, Pakistan

^d Department of Chemistry, University of Malaya, 50603 Kuala Lumpur, Malaysia

^e Faculty of Pharmacy, Universiti Teknologi MARA, Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor Darul Ehsan, Malaysia

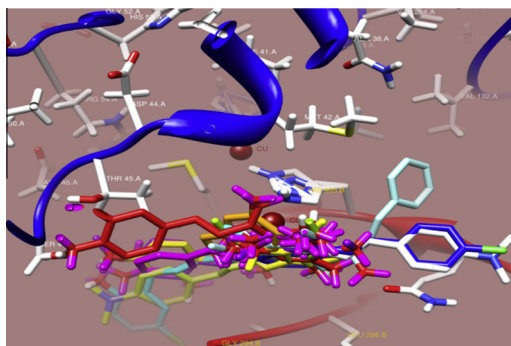
^f Atta-ur-Rahman Institute for Natural Products Discovery (AuRIns), Universiti Teknologi MARA, Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor Darul Ehsan, Malaysia

HIGHLIGHTS

- Chalcones derivatives were prepared through the Claisen–Schmidt condensation reaction.
- Compounds were characterized by detailed spectroscopic techniques and single-crystal X-ray structural analysis.
- Flavokawain B (**1**), flavokawain A (**2**) and compound **3** were found to be potential tyrosinase inhibitors.
- Detailed molecular docking and SARs studies were correlated well with the tyrosinase inhibition studies *in vitro*.

GRAPHICAL ABSTRACT

In this study, a series of chalcones (**1–10**) have been synthesized and examined for their tyrosinase inhibitory activity. The results showed that flavokawain B (**1**), flavokawain A (**2**) and compound **3** were found to be potential tyrosinase inhibitors, indicating IC₅₀ 14.20–14.38 μM values. This demonstrates that 4-substituted phenolic compound especially at ring A exhibited significant tyrosinase inhibition. Additionally, molecular docking results showed a strong binding affinity for compounds **1–3** through chelation between copper metal and ligands.



ARTICLE INFO

Article history:

Received 5 September 2014

Received in revised form 3 December 2014

Accepted 23 December 2014

Available online 31 December 2014

Keywords:

Chalcones

1D and 2D NMR spectroscopy

Tyrosinase inhibitors

Flavokawain A

ABSTRACT

Browning of fruits and vegetables is a serious issue in the food industry, as it damages the organoleptic properties of the final products. Overproduction of melanin causes aesthetic problems such as melisma, freckles and lentigo. In this study, a series of chalcones (**1–10**) have been synthesized and examined for their tyrosinase inhibitory activity. The results showed that flavokawain B (**1**), flavokawain A (**2**) and compound **3** were found to be potential tyrosinase inhibitors, indicating IC₅₀ 14.20–14.38 μM values. This demonstrates that 4-substituted phenolic compound especially at ring A exhibited significant tyrosinase inhibition. Additionally, molecular docking results showed a strong binding affinity for compounds **1–3** through chelation between copper metal and ligands. The detailed molecular docking and SARs studies correlate well with the tyrosinase inhibition studies *in vitro*. The structures of these compounds were elucidated by the 1D and 2D NMR spectroscopy, mass spectrometry and single X-ray crystallographic

* Corresponding authors. Tel.: +60 9 5492393; fax: +60 9 5492766 (M.N. Akhtar). Tel.: +60 3 32584616; fax: +60 3 32584602 (S.A.A. Shah).

E-mail addresses: nadeemupm@gmail.com (M.N. Akhtar), syedadnan@salam.uitm.edu.my, benzene301@yahoo.com (S.A.A. Shah).