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

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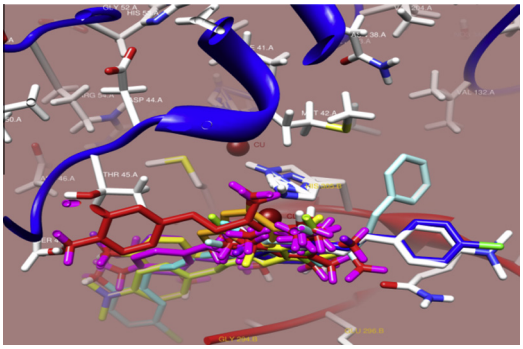
HIGHLIGHTS

- 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 tryrosinase inhibitory activity. The results showed that flavokawain B (**1**), flavokawain A (**2**) and compound **3** were found to be potential tyrosinase inhibitors, indicating IC_{50} 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.



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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 tryrosinase inhibitory activity. The results showed that flavokawain B (**1**), flavokawain A (**2**) and compound **3** were found to be potential tyrosinase inhibitors, indicating IC_{50} 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

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