

Isoplanchol A, a New Phenolic Stereoisomer from *Uncaria Gambir* Sap with Antioxidant and Predicted Cyclin-Dependent Kinase 1 Binding Potential

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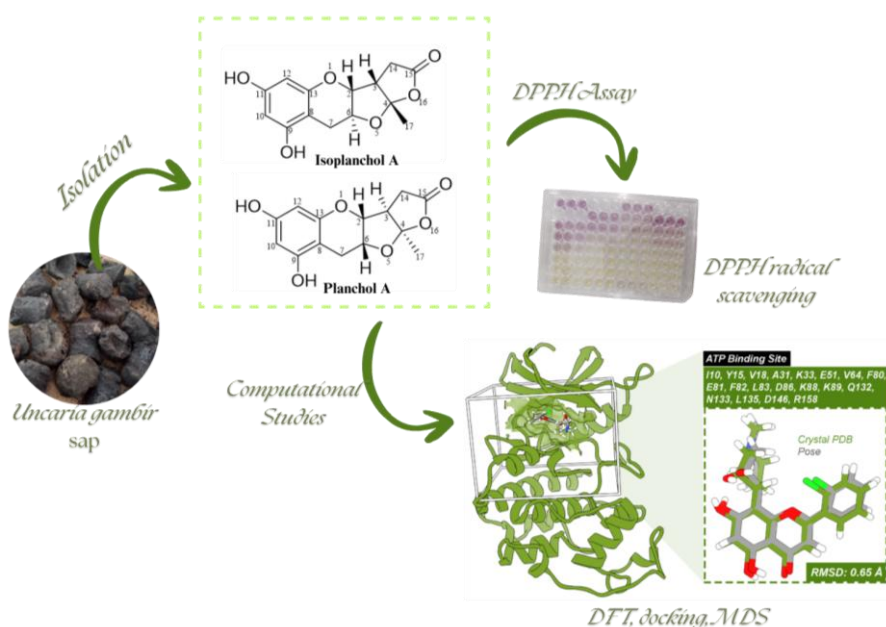
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Abstract

Phenolic compounds of *Uncaria gambir* Roxb. are known for their antioxidant properties. The methanolic extract of gambir sap yielded the known planchol A (**1**) and a new stereoisomer, isoplanchol A (**2**), whose structures were elucidated by Ultraviolet–visible spectroscopy (UV-Vis), Fourier-transform infrared spectroscopy (FT-IR), One-dimensional nuclear magnetic resonance/Two-dimensional nuclear magnetic resonance (1D/2D NMR), and Direct analysis in real time–high-resolution mass spectrometry (DART-HRMS). In the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay, Half-maximal inhibitory concentration (IC₅₀) values were 91.86 ± 0.50 µg/mL for the extract, 162.11 ± 1.65 µg/mL for **1**, and 89.67 ± 0.74 µg/mL for **2**. In the 2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic

acid) (ABTS) assay, IC_{50} values were $79.76 \pm 0.36 \mu\text{g/mL}$ for the extract, $14.53 \pm 0.21 \mu\text{g/mL}$ for 1, and $20.22 \pm 0.50 \mu\text{g/mL}$ for 2, comparable to catechin ($17.02 \pm 0.08 \mu\text{g/mL}$); the isomers' order was reversed relative to DPPH, indicating assay-dependent activity. Density functional theory calculations gave similar Highest occupied molecular orbital-Lowest unoccupied molecular orbital (HOMO-LUMO) gaps (5.73–5.85 eV) for both. Molecular docking and 300 ns molecular dynamics simulations predicted stable binding of both compounds in the Adenosine triphosphate (ATP)-binding pocket of cyclin-dependent kinase 1 (CDK1), with a more favorable Molecular mechanics-Generalized born surface area (MM-GBSA) binding free energy for 2 ($\Delta G_{\text{bind}} = -29.95 \text{ kcal/mol}$) than for 1 (-26.44 kcal/mol). These in silico results are hypothesis-generating and require experimental validation. Gambir sap is a source of antioxidant phenolics, and isoplanchol A (**2**) is a candidate for further biological investigation.

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Innovative Description: The discovery of isoplanchol A, a novel antioxidant phenolic stereoisomer from gambir sap with predicted Cyclin-dependent kinase 1 inhibitory activity, is reported.