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Flavones from *Combretum Quadrangulare* Growing in Vietnam and Their Alpha-Glucosidase Inhibitory Activity

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Abstract: *Combretum quadrangulare* Kurz is widely used in folk medicine in Eastern Asia and is associated with various ethnopharmacological properties including hepatoprotective, antipyretic, analgesic, antidiarrheal, and anthelmintic activities. Previous phytochemical investigations reported the presence of numerous triterpenes (mostly cycloartanes, ursanes, lupanes, and oleananes) along with dozens of flavonoids. However, the extracts of *C. quadrangulare* and isolated flavonoids have not been evaluated for their alpha-glucosidase inhibition. In the frame of our efforts dedicated to the chemical investigation of Vietnamese medicinal plants and their biological activities, a phytochemical study of the MeOH extract of the leaves of *C. quadrangulare* using bioactive guided isolation was undertaken. In this paper, the isolation and structure elucidation of twelve known compounds, 5-hydroxy-3,7,4'-trimethoxyflavone (**1**), ayanin (**2**), kumatakenin (**3**), rhamnocitrin (**4**), ombuin (**5**), myricetin-3,7,3',5'-tetramethyl ether (**6**), gardenin D (**7**), luteolin (**12**), apigenin (**13**), mearnssetin (**14**), isoorientin (**15**), and vitexin (**16**) were reported. Bromination was applied to compounds **2** and **3** to provide four new synthetic analogues **8–11**. All isolated and synthesized compounds were evaluated for alpha-glucosidase inhibition and antibacterial activity. Compounds **4** and **5** showed moderate antibacterial activity against methicillin-resistant *Staphylococcus aureus* while others were inactive. All compounds failed to reveal any activity toward extended spectrum beta-lactamase-producing *Escherichia coli*. Compounds **2**, **4**, **6–9**, and **11–14** showed good alpha-glucosidase inhibition with IC₅₀ values in the range of 30.5–282.0 μM. The kinetic of enzyme inhibition showed that **8** and **11** were noncompetitive type inhibition against alpha-glucosidase. In silico molecular docking model indicated that compounds **8** and **11** were potential inhibitors against enzyme α-glucosidase.

Keywords: *Combretum quadrangulare* Kurz; flavonoid; alpha-glucosidase; antibacterial; molecular docking

1. Introduction

Combretum quadrangulare Kurz is widely used in folk medicine in Eastern Asia. The traditional uses have been corroborated by in vitro data of hepatoprotective, antipyretic,