Send Orders for Reprints to reprints@benthamscience.net

Letters in Organic Chemistry, 2020, *17*, 000-000

RESEARCH ARTICLE

Cytotoxic Prenyl and Geranyl Coumarins from the Stem Bark of *Casimiroa edulis*

Khun Nay Win Tun[1,2], Nanik Siti Aminah[3,*], Alfinda Novi Kristanti[3], Rico Ramadhan[3] and Yoshiaki Takaya[4]

[1]*Natural Science, Faculty of Science and Technology, Universitas Airlangga, Surabaya, Indonesia;* [2]*Department of Chemistry, Taunggyi University, Taunggyi, Myanmar;* [3]*Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga, Surabaya, Indonesia;* [4]*Faculty of Pharmacy, Universitas Meijo, 150 Yagotoyama, Tempaku, Nagoya, 468-8503 Japan*

ARTICLE HISTORY

Received: June 12, 2019
Revised: September 15, 2019
Accepted: October 04, 2019

DOI:
10.2174/1570178616666191019121437

Abstract: Phytochemical investigation of the methanolic extract of the stem bark of *Casimiroa edulis* afforded four coumarins. Various spectroscopic experiments were used to characterize the isolated coumarins. The structures were identified as auraptene (**K-1**), suberosin (**K-2**), 5-geranyloxypsoralen (bergamottin) (**K-3**), and 8-geranyloxypsoralen (**K-4**), based on the chemical and spectral analysis. Among these compounds, suberosin (**K-2**) and 5-geranyloxypsoralen (bergamottin) (**K-3**) were isolated for the first time from this genus, and auraptene (**K-1**) was isolated from this plant for the first time. Cytotoxicity of pure compound **K-4** and sub-fraction MD-3 was evaluated against HeLa and T47D cell lines and moderate activity was found with an IC_{50} value in the range 17.4 to 72.33 µg/mL.

Keywords: *Casimiroa edulis*, coumarins, HeLa, spectroscopic experiments, stem bark, T47D.

1. INTRODUCTION

Nature is a good source of potential chemotherapeutic drugs [1]. The isolation process is a key step in discovering new biologically active substances from complex natural extracts [2]. A large number of bioactive compounds are isolated from research studies and screened each year, thus realizing the intrinsic therapeutic potential of natural products, and providing vast resource for further research [3]. Despite significant developments in the extraction and separation techniques, it is still a challenging task to isolate natural products from plants, animals, marine organisms or micro-organisms [4].

Coumarins (2*H*-1-benzopyran-2-ones) are a class of naturally occurring compounds found in various plants with an extensive pharmacological profile. To date, approximately 1500 coumarin derivatives have been identified from plants [5]. They have been identified as potent anti-inflammatory [6,10], anti-oxidant [7], anti-melanogenic [8], anti-bacterial [9], anti-viral [10], anti-coagulant [11], and cytotoxic agents [12].

A number of coumarins from *Casimiroa* spp. have been found by several researchers. Phellopterin, isopimpinellin, imperatorin, xanthotoxol, 8-hydroxy-5-methoxypsoralen, 8-[(6,7-dihydroxy-3,7-dimethyl-2-octen-1-yl)oxy]-5-methoxypsoralen, 8-[(4-hydroxy-3-methyl-2-buten-1-yl)oxy]psoralen, 8-[(6,7-dihydroxy-3,7-dimethyl-2-octen-1-yl)oxy]psoralen, 8-geranyloxypsoralen (**K-4**), 8-[(4-hydroxy-3-methyl-2-buten-1-yl)oxy]-5-methoxypsoralen, are reported to belong to the furanocoumarins, a class of chemical compounds produced by the roots, seeds, and leaves of *Casimiroa* spp. Another report has shown that simple coumarins (umbelliferone, esculetin, herniarin) are present in the leaves and seeds of *Casimiroa* spp. Some isolated furanocoumarins and simple coumarins have been reported to show anticoagulant and antimutagenic activity. In addition, the structure modification of some furanocoumarins was also reported [13-20].

This paper outlines the isolation and structure elucidation of compounds **K-1** to **K-4** (Figs. **1-4**) from the stem bark of *Casimiroa edulis*, as well as the cytotoxicity of sub-fraction MD-3 (section **3.3**) and pure compound **K-4**.

2. RESULTS AND DISCUSSION

2.1. Structure Elucidation

Consecutive chromatographic purification of the MeOH soluble fraction of the stem bark of *C. edulis* yielded four compounds. The molecular structures of isolated compounds were identified on the basis of their UV, IR, ^{1}H NMR, ^{13}C NMR, DEPT (**D**istortionless **E**nhancement by **P**olarization

*Address correspondence to this author at the Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga; Tel/Fax: +62-31-5936501; Fax +62-31-5936502; E-mail: nanik-s-a@fst.unair.ac.id

1570-1786/20 $65.00+.00