A new lignan from the stem bark of *Fagraea fragrans* Roxb.

Rattanaburi S., Kaikaew K., Watanapokasin R., Phongpaichit S., Mahabusarakamb W. (2022) Natural Product Research, 36 (7), pp. 1851-1856.

มีบทความอ้างอิง 2 บทความ

Biochemical Systematics and Ecology 117 (2024) 104899

Contents lists available at ScienceDirect

Biochemical Systematics and Ecology

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

A new benzoic acid derivative from *Gentiana davidi* and its chemotaxonomic significance

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ARTICLE INFO

Keywords:
Gentiana davidi
Benzoic acid derivative
Iridoid
Flavonoid
Structural identification
Chemotaxonomy

ABSTRACT

Phytochemical investigation of *Gentiana davidi* led to isolation of a total of 21 compounds, including seven benzoic acid derivatives (**1**–**7**), one alkaloid compound (**8**), seven iridoids (**9**–**15**), and six flavonoids (**16**–**21**). The chemical structures of these compounds were characterized by spectroscopic analysis, and their NMR data were compared with those reported in the literature. Among them, compound **1** was identified as a new benzoic acid derivative, and compounds **2**–**21** are identified and reported for the first time from this plant. The chemotaxonomic significance of these isolated compounds from the *G. davidi* is discussed.

1. Subject and source

The genus *Gentiana* belonging to the family Gentianaceae consists of over 400 species, with most species growing (Huang et al., 2020) at high altitudes; it is distributed in many countries in the Northern Hemisphere (Pan et al., 2016). Some *Gentiana* plants have long been used in traditional Chinese medicine, including *G. scabra*, *G. manshurica*, *G. triflora*, and *G. rigescens* (Chinese Pharmacopoeia Commission, 2020). *Gentiana davidi* Franch. is a traditional Chinese herb that is widely used as a folk Chinese in China (Peng et al., 2022). It is commonly used as a whole herb to treat postpartum mania, hernia, suppurative osteomyelitis, urinary tract infections, conjunctivitis and carbuncles (Peng et al., 2022).

In the present study, *G. davidi* was collected in December 2019 from Dawei Mountain, Hunan Province, People's Republic of China, and identified by Professor Ta-si Liu (Hunan University of Chinese Medicine). A voucher specimen (no. 20191211) was deposited at the Hunan Province Engineering Research Center of Bioactive Substance Discovery of Chinese Medicine, Hunan University of Chinese Medicine, China.

2. Previous work

Previous phytochemical investigations have shown that more than 500 compounds have been isolated from different parts, including rhizomes, roots, stems, leaves, aerial parts, whole plants, and flowers, of species of *Gentiana*. (Pan et al., 2016). Diverse classes of compounds have been identified from *Gentiana*, including iridoids, xanthones, flavonoids, triterpenes and steroids (Yang et al., 2010). Some compounds exhibit remarkable biological activities, such as liver protection, anti-inflammatory, antioxidant, antitumor, and immunomodulatory activities (Jiang et al., 2021). Previous studies on *G. davidi* demonstrated the presence of triterpenoids, phenylpropanoids, sterols and fatty acids (Peng et al., 2022, 2023). Pharmacological studies have indicated that *G. davidi* possesses anti-inflammatory and antibacterial activities (Peng et al., 2022, 2023). This study was designed to enrich the chemical profile of *G. davidi* and provide additional evidence for the chemotaxonomic analysis of the genus *Gentiana*.

3. Present study

3.1. General experimental procedures

Nuclear magnetic resonance (NMR) spectra were recorded using Bruker INOVA-600 MHz spectrometer (Bruker, Germany). High-resolution electrospray ionization mass spectrometry (HR-ESI-MS) was performed using quadrupole time-of-flight (Q-TOF) mass spectrometer equipped with an ESI source (Waters, USA). Ultraviolet visible (UV) spectra were recorded using Hewlett-Packard 8452A spectrophotometer (Hewlett-Packard, USA). Infrared (IR) spectroscopy was performed

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https://doi.org/10.1016/j.bse.2024.104899
Received 13 June 2024; Received in revised form 2 September 2024; Accepted 5 September 2024
Available online 8 September 2024

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DOI 10.1007/s10600-024-04481-6
Chemistry of Natural Compounds, Vol. 60, No. 5, September, 2024

SECONDARY METABOLITES OF *Cinnamomum burmanni*

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Cinnamomum burmanni (Nees & T. Nees) Blume (Lauraceae) is a source of Indonesia cinnamon, and is widely used as a spice in Indonesia [1]. The chemical constituents of the roots of this plant have not yet been reported. Previously, we isolated 19 compounds, including one triterpenoid, one coumarin, two steroids, and four benzenoids from the leaves of this plant [2]. In the course of screening for biologically and chemically novel agents from Formosan plants in the family Lauraceae [3–6], *C. burmanni* was chosen for further phytochemical investigation. In this paper, we reinvestigated the constituents in the stems of *C. burmanni*. The MeOH extract of its stems was subjected to solvent partitioning and chromatographic separation to afford 22 pure substances. A chemical investigation of the stems of *C. burmanni* afforded 22 phytochemicals including a diazetidin, cinnatenuifolin (**1**) [7]; nine benzenoids, (*E*)-1,2,3-trimethoxy-5-(prop-1-enyl)benzene (**2**) [8], 3-(3′,4′,5′-trimethoxyphenyl)-prop-2-en-1-al (**3**) [9], *β*-hydroxypropiovanillone (**4**) [10], *β*-hydroxypropioisovanillone (**5**) [11], syringic acid (**6**) [12], salicylic acid (**7**) [13], ferulic acid (**8**) [14], salicylaldehyde (**9**) [15], and *p*-hydroxybenzylalcohol (**10**) [16]; eight lignans, (+)-yangambin (**11**) [17], (+)-syringaresinol (**12**) [18], (+)-*dia*-syringaresinol (**13**) [19], (+)-*epi*-syringaresinol (**14**) [20], (+)-medioresinol (**15**) [21], (+)-pinoresinol (**16**) [22], (+)-lariciresinol (**17**) [23], and (+)-5,5′-dimethoxylariciresinol (**18**) [24]; two oxysporones, (4-oxo-4*H*-pyran-3-yl)-acetic acid (xylaric acid) (**19**) [25], and (4-oxo-4*H*-pyran-3-yl)-acetic acid methyl ester (**20**) [26]; two apocarotenoids, burmannic acid (**21**) [27], and burmanic acid A (**22**) [28]. All compounds, except **6**, **8**, **12**, **21**, and **22**, were found for the first time from this plant.

General. UV spectra were obtained in MeCN, IR spectra were measured on a Hitachi 260-30 spectrophotometer. ^{1}H NMR (400 MHz, CD_3OD) and NOESY spectra were obtained on a Varian (Unity Plus) NMR spectrometer. Low-resolution ESI-MS spectra were obtained on an API 3000 (Applied Biosystems) and high-resolution ESI-MS spectra on a Bruker Daltonics APEX II 30e spectrometer. Silica gel 60 (Merck, 70–230 mesh, 230–400 mesh) was used for column chromatography. Precoated Silica gel plates (Merck, Kieselgel 60 F-254), 0.20 mm and 0.50 mm, were used for analytical TLC and preparative TLC, respectively, visualized with 50% H_2SO_4.

Plant Material. The specimen of *C. burmanni* (Nees & T. Nees) Blume was collected from Chiayi County, Taiwan in January 2019. A voucher specimen (Cinnamo. 10) was identified by Dr. Fu-Yuan Lu (Department of Forestry and Natural Resources College of Agriculture, National Chiayi University) and was deposited in the Department of Medical Laboratory Sciences and Biotechnology, School of Medical and Heath Science, Fooyin University, Kaohsiung, Taiwan.

Extraction and Isolation. The stems of *C. burmanni* (7.6 kg) were extracted with MeOH (10 L × 3) at room temperature and a MeOH extract (312 g) was obtained upon concentration under reduced pressure. The MeOH extract was placed on a silica gel column and eluted with CH_2Cl_2 gradually enriched with MeOH to afford ten fractions. Part of fraction 1 (21.3 g) was subjected to silica gel chromatography by eluting with *n*-hexane–EtOAc (100:1), enriched with EtOAc to furnish four further fractions (1-1–1-4). Fraction 1-2 (3.1 g) eluted with *n*-hexane–EtOAc (50:1) was further purified using silica gel column chromatography using the same solvent system to give cinnatenuifolin (**1**, 8 mg). Part of fraction 2 (13.4 g) was subjected to silica gel chromatography by eluting with *n*-hexane–EtOAc (100:1), enriched with EtOAc to furnish five further fractions (2-1–2-5). Fraction 2-2 (1.1 g) eluted with *n*-hexane–EtOAc (40:1) was further purified using silica gel column chromatography using the same solvent system to give (*E*)-1,2,3-trimethoxy-5-(prop-1-enyl) benzene (**2**, 5 mg) and 3-(3′,4′,5′-trimethoxyphenyl)-

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