Research Article ISSN 2689-1050

Chemical & Pharmaceutical Research

A New Flavanone from *Cinnamumom Subavenium*

Chang C.T[1], Kao C.L[2], Yeh H.C[1], Song P.L[3], Liu S.L[4], Li H.T[3] and Chen C. Y[5]*

[1]*Department of Clinical Microbiology Laboratory, Yuan's General Hospital, Kaohsiung, Taiwan.*

[2]*Tzu Hui Institute of Technology, Pingtung County, Taiwan.*

[3]*Department of Medical Laboratory Science and Biotechnology, Fooyin University, Kaohsiung, Taiwan.*

[4]*Experimental Forest, College of Bio-Resources and Agriculture, National Taiwan University, Nantou County, Taiwan.*

[5]*School of Medical and Health Sciences, Fooyin University, Kaohsiung, Taiwan.*

***Correspondence:**
Chen C. Y., School of Medical and Health Sciences, Fooyin University, Kaohsiung, Taiwan.

Received: 20 Jan 2022; **Accepted:** 22 Feb 2022; **Published:** 26 Feb 2022

Citation: Chang CT, Kao CL, Yeh HC, et al. A New Flavanone from *Cinnamumom Subavenium*. Chem Pharm Res. 2022; 4(1): 1-3.

ABSTRACT

*One new flavanone, 6,7,4′-triydroxy-3′-methoxyflavanone (**1**), was isolated from barks of Cinnamomum subavenium Miq (Lauraceae). The structure of **1** was characterized and identified by spectral analysis.*

Keywords

Cinnamomum subavenium, *Lauraceae*, Flavanone.

Introduction

Cinnamomum subavenium Miq (Lauraceae) is a medium-sized evergreen tree, found in central to southern mainland China, Burma, Cambodia, Taiwan, Malaysia and Indonesia [1]. In the course of screening for biologically and chemically novel agents from Formosan Lauraceous plants [2-13], *C. subavenium* was chosen for further phytochemical investigation. They have identified a novel cytotoxic monoterpenoid, subamone, a novel sesquiterpenoid, subamol, five new butanolides, subamolide A-E, two new secobutanolides, secosubamolide and secosubamolide A, one new diphenyl ether, 2,2',7a,7a',7b,7b'- hexamethyldiphenyl ether, along with 47 known compounds from the stems, roots and leaves of *C. subavenium* [14-20]. In the course of screening for biologically and chemically novel agents from Formosan plants in the *Cinnamoum* species, *C. subavenium* was chosen for further phytochemical investigation. A new flavanone, 6,7,4′-triydroxy-3′-methoxyflavanone (**1**) was isolated and identified from these barks. In this paper, we report the isolation and structural elucidation of this new compound.

6,7,4′-Triydroxy-3′-methoxyflavanone (**1**) was obtained as a yellow amorphous powder and its molecular formula was deduced as $C_{16}H_{14}O_6$ by HRESIMS (*m/z* 325.0689 $[M + Na]^+$; calc. 325.0688). The UV spectrum showed a λ_{max} at 242 and 284 nm typical for a flavanone skeleton [21]. The IR spectrum exhibited strong absorption bands at 3400, 1680 and 1515 cm^{-1} due to the hydroxyl, α,β-unsaturated ketone and aromatic C=C functionalities, respectively, in the molecule. ^1H and ^{13}C NMR spectra showed the presence of three hydroxyl and one methoxy groups on the flavanone skeleton. The aromatic region of its ^1H NMR spectrum showed two singlet protons at δ 7.24 and 6.51, two *ortho*-coupled protons at δ 7.02 and 6.89 and a *meta*-coupled proton at δ 7.22. The two singlet signals were assigned to H-5 and H-8 respectively. This suggested that ring A was substituted at C-6 and C-7. In the proton NMR, a pair of double-doubles at δ 2.70 (1H, dd, J = 16.8, 3.0 Hz) and 3.06 (1H, dd, J = 16.8, 13.0 Hz) due to H-3a/H-3b and an oxy-methine proton signal at δ 5.37 (1H, dd, J = 13.0, 3.0 Hz, H-2) further attested the flavanone skeleton [21]. Significant correlations between OMe-3′, H-2′ H-6′, and H-5′, as well as H-2, and H-3, were observed in the NOESY spectrum. Therefore, the methoxy group should be located on the B-ring. The *ortho*-coupled shielded proton resonating at δ 6.87 (d, J = 8.0 Hz) was assigned at H-5′ while the other proton signal at δ

7.02 (dd, J = 8.0, 2.0 Hz) was assigned at H-6′ with the help of COSY and HMBC correlations. Further, the *meta*-coupled proton signal at δ 7.21 was assigned at H-2′. The ^{13}C NMR spectrum of **1** displayed characteristic signals of a flavanone skeleton at δ 190.5 due to an α,β-unsaturated ketone, a methylene carbon resonance at δ 44.7 (C-3) and an oxymethine carbon signal at δ 79.5 (C-2) [21]. This conclusion was reinforced by the peak correlating signals at 2.70/3.06 and 5.37 ppm observed in the ^{1}H-^{1}H COSY spectrum. In the long-range HETCOR spectrum, H-3 (δ 2.70/3.06) shows ^{2}J correlation to C-2 (δ 80.9) and C-4 (δ 190.5) and ^{3}J correlation to C-1′ (δ 131.2) and C-10 (δ 113.5). The methane proton H-2 (δ 5.37) shows ^{2}J correlation to C-1′ (δ 131.2) and C-3 (δ 44.7) and ^{3}J correlation to C-2′ (δ 112.9), C-6′ (δ 120.2) and C-4 (δ 190.5). Elucidation of the absolute configuration at C-2 was based on the values of the coupling constants with the methylenic protons H-3α,β ($J_{ax\text{-}ax}$ = 13.0 and $J_{ax\text{-}eq}$ = 3.0 Hz). The close similarity of the H-2 chemical shifts with those of the literature thus confirmed the *S*-configuration of C-2 [22,23]. Thus the structure of this compound was determined to be 6,7,4′-triydroxy-3′-methoxyflavanone (**1**).

Experimental

General: IR, Hitachi 260-30 spectrophotometer; 1D and 2D NMR, Varian (Unity Plus) NMR spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR); Low-resolution ESI-MS, API 3000 (Applied Biosystems); High-resolution ESI-MS, Bruker Daltonics APEX II 30e spectrometer; Silica gel 60 for CC and precoated silica gel plates (Merck) were used for TLC, visualized with 10% H_2SO_4.

Plant material: The specimen of *C. subavenium* was collected from Taipei, Taiwan, February 2013. A voucher specimen was identified by Dr. Fu-Yuan Lu (Department of Forestry and Natural Resources College of Agriculture, National Chiayi University) and was deposited in the School of Medical and Health Sciences, Fooyin University, Kaohsiung, Taiwan.

Extraction and isolation: The barks (2.6 kg) of *C. subavenium* were extracted repeatedly with CH_2Cl_2 at room temperature for 24-48 hrs. The CH_2Cl_2 extract was dried and evaporated to root a viscous residue (34.1 g). The residue was placed on a silica gel column and eluted with CH_2Cl_2 gradually enriched with MeOH to afford 8 fractions. Fraction 7 (2.3 g) was purified by silica gel chromatography (CH_2Cl_2–MeOH, 20:1) to give 6,7,4′-triydroxy-3′-methoxyflavanone (**1**) (6 mg).

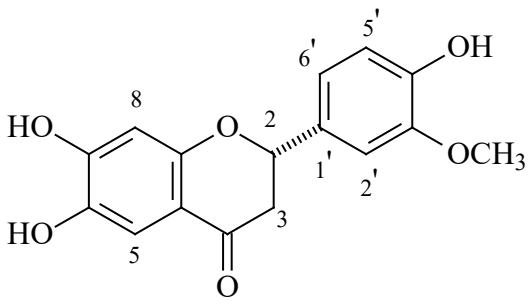

Figure 1: Structure of 6,7,4′-triydroxy-3′-methoxyflavanone (**1**).

6,7,4′-Triydroxy-3′-methoxyflavanone (1): Yellow amorphous powder; $[\alpha]_D^{24}$ – 22.8°(c = 0.22; $CHCl_3$); IR (neat) ν_{max}: 3400 (br, OH), 1680 (C=O), 1515 (C=O) cm^{-1}; UV/Vis (CH_3CN): λ_{max} (log ε): 242 (3.75), 284 (3.90) nm; MS (ESI): *m/z* (%): 325 $[M + Na]^+$; HRMS-ESI: *m/z* $[M + Na]^+$ calcd for $C_{16}H_{14}O_6Na$: 325.0689; found: 325.0688; ^{1}H NMR (400 MHz, $CDCl_3$): 2.70 (1H, dd, J = 16.8, 3.0 Hz, H-3a), 3.06 (1H, dd, J = 16.8, 13.0 Hz, H-3b), 5.37 (1H, dd, J = 13.0, 3.0 Hz, H-2), 3.90 (3H, s, OMe-3′), 6.51 (1H, s, H-8), 6.87 (1H, d, J = 8.0 Hz, H-5′), 7.02 (1H, dd, J = 8.0, 2.0 Hz, H-6), 7.21 (1H, d, J = 2.0 Hz, H-2′), 7.24 (1H, s, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.7 (C-3), 56.2 (3-O*C*H$_3$), 80.9 (C-2), 104.3 (C-8), 108.2 (C-5), 112.9 (C-2′), 113.5 (C-10), 115.3 (C-5′), 120.2 (C-6′), 131.2 (C-1′), 144.6 (C-6), 147.2 (C-4′), 148.5 (C-3′), 155.1 (C-7), 159.1 (C-9), 190.5 (C-4, C=O).

References

1. Lee CH, Kuo CN, Chen HL, et al. Review on pharmacological activities of Cinnamomum subavenium. Nat Prod Res. 2013; 27: 988-991.
2. Chen CY, Chen CH, Lo YC, et al. Anticancer activity of isoobtusilactone A from Cinnamomum kotoense: involvement of apoptosis, cell-cycle dysregulation, mitochondria-regulation and reactive oxygen species. J Nat Prod. 2008; 71: 933-940.
3. Kuo PL, Chen CY, Tzeng TF, et al. Involvement of reactive oxygen species/c-Jun NH2-terminal kinase pathway in kotomolide A induces apoptosis in human breast cancer. Toxicol Appl Pharm. 2008; 229: 215-226.
4. Chen CY, Hsu YL, Tsai YC, et al. Kotomolide A arrests cell cycle progression and induces apoptosis through the induction of ATM/p53 and the initiation of mitochondrial system in human non-small cell lung cancer A549 cells. Food Chem Toxicol. 2008; 46: 2476-2484.
5. Liu TZ, Cheng JT, Yiin SJ, et al. Isoobtusilactone A induces both caspase–dependent and–independent apoptosis in Hep G2 cells. Food Chem Toxicol. 2008; 46: 321-327.
6. Chen CY, Hsu YL, Chen YY, et al. Isokotomolide A, a new butanolide extracted from the leaves of Cinnamomum kotoense, arrests cell cycle progression and induces apoptosis through the induction of p53/p21 and the initiation of mitochondrial system in human non-small cell lung cancer A549 cells. Eur J Pharmacol. 2007; 574: 94-102.
7. Kuo PL, Chen CY, Hsu YL. Isoobtusilactone A induces cell cycle arrest and apoptosis through reactive oxygen species/apoptosis signal-regulating kinase 1 signaling pathway in human breast cancer cells. Cancer Res. 2007; 67: 7406-7420.
8. Chen CY, Liu TZ, Chen CH, et al. Isoobtusilactone A-induces apoptosis in human hepatoma Hep G2 cells is mediated via increased NADPH oxidase-derived reactive oxygen species (ROS) production and the mitochondria-associated apoptotic mechanisms. Food Chem Toxicol. 2007; 45: 1268-1276.
9. Chen CH, Lo WL, Liu YC, et al. Chemical and cytotoxic constituents from the leaves of Cinnamomum kotoense. J Nat Prod. 2006; 69: 927-933.

10. Mancera M, Roffe I, Rivas M, et al. Synthesis of d-mannitol and l-iditol derivatives as monomers for the preparation of new regioregular AABB-type polyamides. Carbohydr Res. 2002; 337: 607-611.
11. Hsieh TJ, Chen CH, Lo WL, et al. Lignans from the stems of Cinnamomum camphora. Nat Prod Commun. 2006; 1: 21-25.
12. C. Y. Chen. Butanolides from the stems of Cinnamomum kotoense. Nat Prod Commun. 2006; 1: 453-455.
13. Hsieh TJ, Su CC, Chen CY, et al. Using experimental studies and theoretical calculations to analyze the molecular mechanism of coumarin, p-hydroxybenzoic acid, and cinnamic acid. J Mo Stru. 2005; 741: 193-199.
14. Chen CY, Chen CH, Wong CH, et al. Cytotoxic constituents of the stems of Cinnamomum subavenium. J Nat Prod. 2007; 70: 103-106.
15. Kuo SY, Hsieh TJ, Wang YD, et al. Cytotoxic constituents from the leaves of Cinnamomum subavenium. Chem Pharm Bull. 2008; 56: 97-101.
16. Chen CY, Wang HM, Chung SH, et al. Chemical constituents from the roots of Cinnamomum subavenium. Chem Nat Compd. 2010; 46: 474-476.
17. Chen CY, Wang YD. A novel sesquiterpenoid from the leaves of Cinnamomum subavenium. Chem Nat Compd. 2011; 47: 215-217.
18. Chen CY, Wang YD. Norcadinane sesquiterpene from the roots of Cinnamomum subavenium Miq. Chem Nat Compd. 2011; 47: 461-462.
19. Lin RJ, Lo WL, Wang YD, et al. A novel cytotoxic monoterpenoid from the leaves of Cinnamomum subavenium. Nat Prod Res. 2008; 22: 1055-1059.
20. Huang GC, Kao CL, Li WJ, et al. A new diphenyl ether from Cinnamomum subavenium. Chem Nat Compd. 2018; 54: 869-871.
21. Uriburu ML, Gil RR, Sosa VE, et al. Prenylflavonoids from Flourensia fiebrigii. Phytochemistry. 2007; 68: 1295-1299.
22. Singh VP, Bineeta Y, Pandey VB. Flavanone glycosides from Alhagi pseudoalhagi. Phytochemistry. 1999; 51: 587-590.
23. Kang TH, Jeong SJ, Ko WG, et al. Cytotoxic lavandulyl flavanones from Sophora flavescens. J Nat Prod. 2000; 63: 680-681.