SHORT REPORT

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A New Acyclic Compound from the Medicinal Plant *Tinospora sinensis*

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Abstract: In this study, chemical investigation of the aerial parts of the medicinal plant *Tinospora sinensis* yielded five compounds (**1**–**5**), including a new acyclic compound (**1**) and four known compounds (**2**–**5**). Their structures were determined by extensive analysis of the spectroscopic data, including 1D (^{1}H and ^{13}C NMR) and 2D NMR data (HSQC, COSY, and HMBC). Compounds **3**–**5** were identified to be stearic acid (**3**), abscisic acid (**4**), and blumenol A (**5**) based on comparisons of the NMR data with those reported in the literature. The NMR data for 2-hydroxy methyl stearate (**2**) were reported for the first time in $CDCl_3$ in this study. The compounds were evaluated for their antitumor potential against A549 cell line, while all were inactive (25 μM). Besides, compound **1** demonstrated marginal inhibition (19.35%) of LPS-induced NO production in RAW 264.7 cells (50 μM).

Keywords: *Tinospora sinensis*; acyclic compound; NMR.

1. Plant Source

The aerial parts of *Tinospora sinensis* (Lour.) Merr. investigated in this study were collected in September 2021 from Qingyuan City, Guangdong Province of China. A corresponding voucher specimen with the accession number Tinsin202109ap has been deposited in the herbarium of the First Affiliated Hospital, Nanchang Medical College. The herbarium specimen was preserved in the Fairy Lake Botanical Garden with Herbarium number of SZG00006527.

2. Previous Studies

Tinospora sinensis (Lour.) Merr. (Menispermaceae) is a deciduous liana belonging to the genus *Tinospora* [1], native to the southern provinces of Guangdong, Guangxi, and Yunnan in China. In traditional medicine, it is highly esteemed for its pharmacological properties, including relaxing tendons, activating collaterals, calming the mind, and soothing the nerves [1]. Previous studies of this plant yielded sesquiterpenes, alkaloids, lignans, and phenol glycosides [2-6].

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3. Present Study

In our study, a chemical investigation of the medicinal plant *Tinospora sinensis* yielded compounds **1**–**5** (Figure 1).

Fresh aerial parts of *Tinospora sinensis* (800 g) were dehydrated, pulverized, and exhaustively extracted through percolation using 95% ethanol over seven days for four times. After removing the solvent under reduced pressure, the resulting crude extract (76 g) underwent sequential liquid-liquid partitioning with ethyl acetate and *n*-butanol. The ethyl acetate-soluble fraction (26 g) was then fractionated on a D101 macroporous resin column using programmed water:ethanol gradients (90:10, 70:30, 50:50, 20:80, 10:90, 0:100, v/v), resulting in six fractions (F1–F6, 10 %, 30 %, 50 %, 80%, 90%, 100%).

The 80% ethanol-eluted segment (F4, 4.8 g) was subsequently processed through ODS reverse-phase chromatography using methanol-water gradients (20–100% MeOH, v/v), resulting in the isolation of seven subfractions (Fr.1–Fr.7).

Fr. 6 (1.2 g) was re-fractionated on ODS silica gel with incremental methanol concentrations (10-100%) to afford five subfractions (Fr. 6a–Fr. 6e). Isolation of SubFr6c (300 mg) via isocratic semi-preparative HPLC (40% methanol) yielded compound 4 (3 mg, t_R 41 min), while resolution of Fr.6f on normal-phase silica columns (PE/EtOAc 10:1) produced compounds **3** (4.1 mg) and **2** (2.3 mg).

Fr. 7 was purified by semi-preparative HPLC with a mobile phase of MeOH/H_2O (50%, *v/v*) to yield six fractions (Fr.7a–Fr.7f). Fr. 7c was further subjected to semi-preparative HPLC eluted with a mobile phase of MeOH/H_2O (35/65 %, *v/v*) to yield compound **5** (1.7 mg, t_R = 47.5 min).

8-Methoxy-3-methylene-4,8-dioxooctanoic acid (**1**): Colorless oil; UV (MeOH) λ_{max} (log ε) 204 (4.09), nm; ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m*/*z* 213.0766 $[M - H]^-$ (calcd. for $C_{10}H_{14}O_5^-$, 213.0768).

2-Hydroxy methyl stearate (**2**): Colorless oil; ^{1}H and ^{13}C NMR data, see Table 1; ESIMS *m*/*z* 301.2734 $[M + H]^+$ (calcd. for $C_{18}H_{37}O_3^+$, 301.2737).

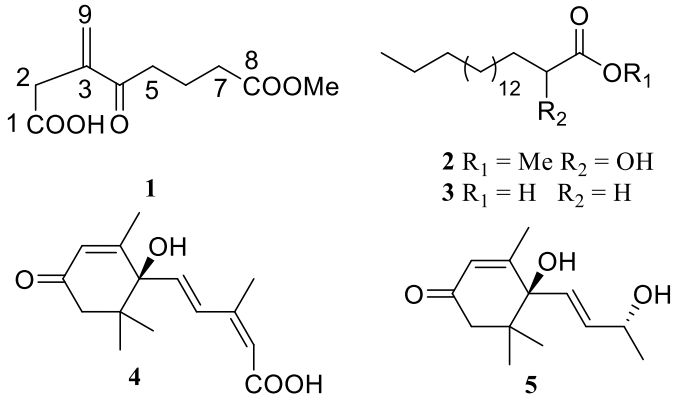

Figure 1. The structures of compounds **1**–**5** from the aerial parts of *Tinospora sinensis*

The molecular formula of compound **1** was established as $C_{10}H_{14}O_5$ based on the HRESIMS ion peak at 213.0766 $[M - H]^-$ (calcd. for $C_{10}H_{14}O_5^-$, 213.0768), which corresponds to 4 degrees of unsaturation. The ^{1}H NMR and HSQC spectra displayed signals for a methoxy group [δ_H 3.65 (3H, s)], a methylene group [δ_H 3.43 (2H, s)], two olefinic singlets [δ_H 6.28 (1H, s), 5.67 (1H, s)], two methylene triplets [δ_H 2.59 (2H, t, *J* = 7.2 Hz), 2.34 (2H, t, *J* = 7.2 Hz)], and a methylene quintet [δ_H 1.84 (2H, quint, *J* = 7.2 Hz)]. The ^{13}C NMR data disclosed a total of 10 carbons, which were attributed to a methoxy carbon (δ_C 52.0), three carbonyl carbons (δ_C 209.5, 175.5, 169.7) including a ketone

carbon, four methylene carbons (δ_C 46.7, 42.0, 33.8, 20.0), two olefinic carbons assigned to a terminal double bond (δ_C 137.1, 129.0) by the HSQC spectrum. The three carbonyl carbons and the double bond accounted for all four degrees of unsaturation, suggesting that compound **1** is acyclic [7]. The COSY relationship of H_2-5 (δ_H 2.59)/H_2-6 (δ_H 1.85)/H_2-7 (δ_H 2.34) defined a spin system CH_2-5–CH_2-6–CH_2-7, this was also supported by the splitting patterns and coupling constants (J = 7.2 Hz) [8]. The HMBC correlations from H_2-6 and H_2-7 and the methoxy group (δ_H 3.65) to C-8 (δ_C 175.5) indicated a methyl ester was linked to C-7. Additional HMBC correlations from the vicinal methylenes H_2-5 and H_2-6 to the ketone carbon C-4 (δ_C 209.5), from H_2-5 to C-3 (δ_C 137.1) and C-4, and from the olefinic methylene protons (δ_H 6.28, 5.67) to C-4 confirmed the connection of the α,β-methylene unsaturated ketone moiety to C-5 *via* C-4 [9]. The remaining signals were assigned to a carboxymethylene group (-CH_2COOH) evidenced by the HMBC correlation from H_2-2 (δ_H 3.43) (a methylene singlet shifted downfield due to adjacent electronegative groups) to the carbonyl carbon C-1 (δ_H 169.7), consistent with the molecular formula. Crucially, HMBC correlations from H_2-2 to the olefinic carbon C-3 (δ_H 137.1), the ketone carbonyl C-4 (δ_H 209.5), and the olefinic methylene carbon C-9 (δ_C 129.0) established the connection of this carboxymethyl group to C-3. Therefore, the structure of **1** was determined to be 8-methoxy-3-methylene-4,8-dioxooctanoic acid.

Compound **2** was determined to have the molecular formula $C_{19}H_{38}O_3$ based on HRESIMS data analysis. Comparison of its ^{1}H and ^{13}C NMR spectra with those of compound **3** revealed striking similarities, with key differences attributable to the presence of a methoxy group (δ_H 3.78; δ_C 52.5) and an oxymethine moiety (δ_H 4.19; δ_C 70.5), along with the absence of one methylene group. These observations suggested that **2** represents a hydroxylated and esterified derivative of **3**. This structural assignment was further corroborated by HMBC correlations, which showed key interactions from the methoxy protons (δ_H 3.78) and the oxymethine proton (δ_H 4.19) to the carbonyl carbon at δ_C 175.9 (Figure 2). Thus, the structure of **2** was determined to be 2-hydroxy methyl stearate.

Table 1. ^{1}H and ^{13}C NMR Data of **1–3** (^{1}H NMR at 400 MHz and ^{13}C NMR at 100 MHz)

No.	**1** [a]		No.	**2** [b]		**3** [b]
	δ_H	δ_C		δ_H	δ_C	
1		169.7	1		175.9	173.5
2	3.43, s	46.7	2	4.19, dd (7.4, 4.2)	70.5	33.7
3		137.1	3	1.77, m; 1.63, m	34.4	24.7
4		209.5	4	1.40, m	24.7	28.9
5	2.59, m	42.0	5–15	1.17–1.36, o	29–30	29–30
6	1.85, quint (7.2)	20.0	16	1.28, o	31.9	31.9
7	2.34, t (7.2)	33.8	17	1.25, o	22.7	22.7
8		175.5	18	0.88, t (6.6)	14.1	14.1
9	6.28, s 5.67, s	129.0				
OMe	3.65, s	52.0		3.78, s	52.5	

[a] In CD_3OD, [b] In $CDCl_3$.

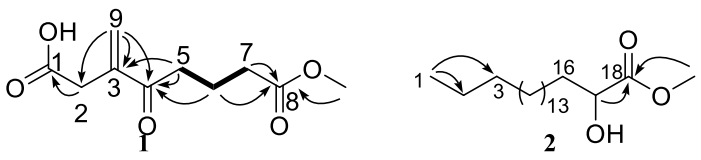

Figure 2. Key COSY (—) and HMBC correlations (⤳) of **1** and **2**

Compounds **3**–**5** were identified to be stearic acid (**3**) [10], abscisic acid (**4**) [11], and blumenol A (**5**) [12] based on comparisons of the NMR data with those reported in the literature.

A new acyclic compound from the medicinal plant *Tinospora sinensis*

Literature reports indicate that *Tinospora sinensis* has yielded 241 distinct chemical constituents upon isolation and characterization [1]. These encompass 58 diterpenoids, 20 sesquiterpenes and triterpenes, 14 phenylpropanoids, 37 alkaloids, 12 flavonoids and flavonoid glycosides, 29 phenolic compounds, 13 steroids, and 58 miscellaneous compounds. Notably, terpenoids (78 compounds, based on 13 phytochemical studies of this plant) represent the most extensively researched and frequently documented class, constituting approximately one-third of the total. The biosynthetic pathways of terpenoids employ isoprene units (C_5) as their fundamental building blocks, these terpenoid classes may serve as chemosystematic markers for *Tinospora sinensis*, supporting its taxonomic placement within the genus *Tinospora.* While compound **4** and the glucoside of **5** (corchoionoside C) had been previously reported from this species [1, 13], this study reported the aglycone of corchoionoside C (**5**) and compound **2** for the first time.

The antitumor potential of compounds **1**–**5** was investigated through viability screening against A549 at the concentration of 25 μM following procedures in the literature [14–15]. No substantial growth suppression was observed, with reductions in cell viability remaining below the 30% threshold in all experimental groups. Additionally, these compounds were assessed for their inhibitory effects on LPS-induced NO production in RAW 264.7 cells at 50 μM. The results indicated that only compound **1** demonstrated marginal inhibition (19.35%), while the other four compounds exhibited inhibition rates of 13.47% (**2**), 10.30% (**3**), 8.19% (**4**), 16.03% (**5**), respectively.

Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

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