Journal of Medicinal Materials, 2026, Vol. 31, No. 1+2 (pp. 29 - 35)

CHEMICAL PROFILING AND ANTI-INFLAMMATORY EFFECTS OF *PHYSALIS ANGULATA* IN LIPOPOLYSACCHARIDE-STIMULATED BONE MARROW–DERIVED DENDRITIC CELLS

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Received February 20th, 2026 Accepted March 1st, 2026

Summary

Physalis angulata is an important medicinal plant that has been widely used in traditional medicine for the treatment of inflammation and various inflammatory-related disorders. Despite its medicinal relevance, comprehensive chemical profiling of the fruits of *P. angulata* collected in Vietnam has not yet been systematically investigated. In this study, a comprehensive chemical characterization of the methanolic extract of *P. angulata* was performed using high-resolution quadrupole time-of-flight mass spectrometry (HR-QTOF-MS), enabling rapid and accurate profiling of its bioactive constituents. Furthermore, the anti-inflammatory activity of the isolated compounds was evaluated by measuring lipopolysaccharide (LPS)-induced production of pro-inflammatory cytokines, including interleukin (IL)-12p40, IL-6, and tumor necrosis factor-α (TNF-α), in bone marrow-derived dendritic cells. Consistent with this, compound **1** exhibited potent anti-inflammatory activity against IL-12p40, IL-6, and TNF-α, with IC_{50} values of 1.17 ± 0.02, 7.52 ± 0.03, and 2.93 ± 0.05 μM, respectively, compared with the positive control adezmapimod (IC_{50} = 5.00 ± 0.01, 3.50 ± 0.01, and 7.20 ± 0.01 μM, respectively). Overall, this study provides the first comprehensive chemical profile of *P. angulata* from Vietnam and offers scientific evidence supporting its traditional use as a source of anti-inflammatory agents.

Keywords: *Physalis angulata;* Solanaceae; *Chemical profile; Anti-inflammatory agents.*

1. Introduction

Physalis angulata L. (Solanaceae), commonly known as cutleaf groundcherry, is a medicinal plant broadly distributed in tropical and subtropical regions, particularly in Southeast Asia, Africa, and South America [1]. The species has been extensively employed in traditional medicine for the treatment of various ailments, including inflammatory disorders, fever, malaria, liver diseases, and cancer-related conditions [2]. In recent years, *P. angulata* has gained increasing scientific interest due to its chemically diverse secondary metabolites and accumulating evidence of its broad pharmacological potential [3]. Phytochemical investigations have identified *P. angulata* as a rich source of bioactive compounds, including physalins, withanolides, flavonoids, phenolic acids, and steroids [4]. Among these, physalins-highly oxygenated seco-steroidal lactones-are recognized as the major characteristic constituents of the species. Substantial experimental evidence has demonstrated that physalins possess a wide range of biological activities, such as anti-inflammatory, immunomodulatory, antitumor, antimalarial, and antimicrobial effects [5].

Despite these advances, the correlation between the phytochemical composition of *P. angulata* and its biological activities has not yet been fully elucidated. In particular, comprehensive chemical profiling remains limited, and the effects of geographical origin, plant parts, and extraction conditions on its chemical constituents are poorly understood. Addressing these knowledge gaps is crucial for the standardization of *P. angulata*-derived materials and for providing scientific validation of its traditional medicinal uses. Therefore, the present study aims to characterize the chemical profile of *P. angulata* collected in Vietnam using LC–MS/MS, thereby providing supportive evidence for a scientific basis for future investigations into its pharmacological potential and potential applications in pharmaceutical and functional food development.

2. Materials and methods

2.1. General experimental procedures

Open-column chromatographic separations were carried out using *silica gel* (Kieselgel 60, 70–230 and 230–400 mesh; Merck, Darmstadt, Germany) as well as reversed-phase C-18 (YMC*GEL ODS-A packing, 12 nm pore size, S-150 μm; YMC Co., Ltd., Japan). The progress of fractionation and compound purity was monitored by thin-layer chromatography performed on pre-coated *silica gel* 60 F_{254} and RP-C18 $F_{254}S$ plates (Merck). Chromatographic spots were visualized under ultraviolet illumination at 254 and 365 nm, followed by spraying with 10% (v/v) aqueous sulfuric acid and subsequent heating. All chemicals and solvents employed in this study were of

analytical or HPLC grade and were obtained from Aldrich Chemical Co. (St. Louis, MO, USA). Nuclear magnetic resonance (NMR) analyses, including ^{1}H, ^{13}C, and two-dimensional experiments, were performed using a Bruker Avance III spectrometer operating at 500 MHz.

2.2. Plant material

The whole plant of *P. angulata* was collected in Me Linh, Hanoi, Vietnam, in July 2024. The plant material was taxonomically authenticated by Dr. Nguyen Cao Cuong, and a voucher specimen (QTB 005) was deposited in the herbarium of Yersin University of Da Lat, Faculty of Medicine and Pharmacy, Lam Dong.

2.3. Extraction and isolation

Fresh aerial parts of *P. angulata* were collected, cut into small pieces, air-dried, and pulverized to yield 2.0 kg of dry powder. The material was extracted with methanol (3 × 5 L) under ultrasonic assistance at 50°C for 3 h each time. The combined extracts were filtered and evaporated under reduced pressure to afford a MeOH extract (90 g). This extract was suspended in water (1.5 L) and successively partitioned with chloroform and EtOAc, yielding the chloroform (C, 24.5 g), EtOAc (PAE, 4.5 g), and water layer (PAW, 61.0 g) fractions. The chloroform fraction (C, 24.5 g) was subjected to *silica gel* column chromatography and eluted with a gradient of chloroform–methanol (100:1 → 1:100, v/v) to afford five subfractions (C1 - C5). Fraction C2 wasfurther separatedn over *silica gel* (CH_2Cl_2–MeOH, 20:1, v/v) yielded three subfractions (C2A–C2C). Subfraction C2A was fractionated on RP-18 column chromatography with acetone–water (1.8:1, *v/v*), affording C2A1–C2A3. Repeated RP-18 chromatography of C2A1 with MeOH–H_2O (1:1, v/v) gave compound **1** (4.6 mg). *Silica gel* chromatography of C2A3 (CH_2Cl_2–acetone, 10:1, v/v) afforded compounds **2** (7.1 mg) and **3** (4.9 mg).

2.4. Liquid chromatography quadrupole time-of-flight mass spectrometry (LC-Q-TOF MS/MS) conditions

The secondary metabolite composition of *P. angulata* was characterized using an optimized analytical strategy adapted from our earlier work [6]. Chromatographic analyses were carried out on an Agilent 1260 Infinity liquid chromatography platform (Agilent Technologies, Santa Clara, CA, USA) equipped with a binary solvent delivery system, an inline degassing unit, an automated sample injector, a thermostated column oven, and a photodiode array detector. Compound separation was achieved using a CAPCELL PAK UG C_{18} column (150 × 4.6 mm, 5 μm; Shiseido, Japan), protected by a C_{18} guard cartridge (4.0 × 3.0 mm; Phenomenex, Torrance, CA, USA).

Chromatographic separation was performed using a binary solvent system consisting of solvent A (0.1% formic acid in water, v/v) and solvent B (0.1% formic acid in acetonitrile, v/v). To achieve adequate separation of the metabolite components, a gradient elution program was applied as follows: 5% B from 0 to 5 min; a linear increase from 5% to 80% B over 5–10 min; 80–85% B from 10 to 15 min; 85–90% B from 15 to 25 min; and finally 90–95% B from 25 to 30 min. The mobile phase was delivered at a constant flow rate of 0.6 mL/min, and the injection volume was set to 5 μL. Mass spectrometric analysis was conducted using an Agilent 6530 quadrupole time-of-flight (Q-TOF) mass spectrometer (Agilent Technologies, Santa Clara, CA, USA) equipped with an electrospray ionization (ESI) source. Data acquisition was carried out in both positive and negative ionization modes to ensure comprehensive detection of metabolites. The mass spectrometer was operated under optimized conditions, with the capillary voltage set to 4000 V, fragmentor voltage to 175 V, skimmer voltage to 65 V, and OCT 1 RF Vpp to 750 V. The nebulizer pressure was maintained at 40 psi, while the drying gas and sheath gas temperatures were set at 325 °C and 350 °C, respectively. High-accuracy mass data were acquired in centroid mode over an *m/z* range of 50–1000, ensuring mass measurement errors below 5 ppm. Instrument operation and data analysis were performed using MassHunter Workstation software (version B.05.00; Agilent Technologies). The combination of high-resolution chromatographic separation and accurate mass detection enabled rapid and reliable profiling of secondary metabolites in complex plant extracts, providing excellent sensitivity and reproducibility.

2.5. Cell culture and reagents

Bone marrow-derived dendritic cells (BMDCs) were generated from wild-type C57BL/6 mice obtained from Orient Bio Inc. (Seoul, Korea) [7]. All animal experiments were conducted in accordance with the ethical guidelines approved by the Institutional Animal Care and Use Committee of Jeju National University (approval no. 2016-0059). For BMDC preparation, bone marrow cells were harvested

from the femurs and tibias by flushing with Dulbecco's Modified Eagle Medium (DMEM; Welgene, Gyeongsan, Korea). The collected cells were subsequently cultured in RPMI 1640 medium supplemented with 10% heat-inactivated fetal bovine serum (FBS; Gibco, New York, NY, USA), 50 μM 2-mercaptoethanol, and 2 mM L-glutamine. To promote dendritic cell differentiation, the culture medium was further enriched with 3% conditioned medium from J558L hybridoma cells as a source of granulocyte–macrophage colony-stimulating factor (GM-CSF). The culture medium supplemented with GM-CSF was refreshed at two-day intervals. After six days of differentiation, loosely attached dendritic cell clusters and non-adherent cells were harvested, washed, and resuspended in RPMI 1640 medium containing 5% FBS. The cells were then seeded into 48-well plates at a density of 1 $\times$ 10^5 cells per 0.5 mL and preincubated with the isolated compounds at the indicated concentrations for 1 h. Subsequently, dendritic cells were stimulated with lipopolysaccharide (LPS; 10 ng/mL) derived from *Salmonella minnesota* (Alexis, New York, USA). Following an 18 h incubation period, culture supernatants were collected, and the levels of murine IL-12p40, IL-6, and TNF-α were quantified using enzyme-linked immunosorbent assay (ELISA) kits (BD PharMingen, San Diego, CA, USA) in accordance with the manufacturer's protocols. Data represent the mean ± SD obtained from three independently repeated experiments.

2.6. Cytokine production measurements

BMDCs were seeded into 48-well culture plates at a density of 1 $\times$ 10^5 cells in 0.5 mL per well and allowed to equilibrate prior to treatment. The cells were pretreated with the isolated compounds at the specified concentrations for 1 h, followed by stimulation with lipopolysaccharide (LPS; 10 ng/mL) from *S. minnesota* (Alexis, NY, USA) for 18 h. After incubation, culture supernatants were collected, and the levels of murine IL-12p40, IL-6, and TNF-α were quantified using ELISA kits (BD PharMingen, CA, USA) according to the manufacturer's instructions.

2.7. Cell viability assay and statistical analysis

Cell viability was evaluated using an MTT-based colorimetric assay to determine the cytotoxic effects of the isolated compounds on BMDCs [7]. Cells were exposed to the test compounds at concentrations ranging from 1 to 50 μM for a period of 18 h. All data are expressed as mean values with corresponding standard deviations. Statistical evaluation was performed using one-way analysis of variance (ANOVA), with significance thresholds set at $P < 0.05$ and $P < 0.01$. Each experiment was independently repeated at least three times to ensure reproducibility.

3. Results and discussion

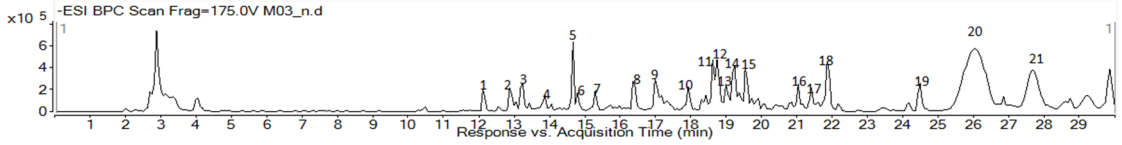

Fig. 1. MS chromatograms of *P. angulata* extract analyzed by LC–MS/MS

The chemical constituents of *P. angulata* in the methanol extract were systematically characterized using liquid chromatography coupled with tandem mass spectrometry (LC–MS/MS). This analytical approach enabled comprehensive profiling of the secondary metabolites present in the extract. A total of thirteen major compounds were detected and tentatively identified based on their chromatographic and spectrometric characteristics.

Specifically, the detected peaks (**Table 1**) were tentatively assigned to chlorogenic acid [8], esculetin [9], rutin [10], kaempferol 3-*O*-α-L-arabinopyranosyl-7-*O*-α-L-rhamnopyranoside [11], isorhamnetin 3-*O*-β-rutinoside [12], physalins D, E, G, and W [13], physagulin H [14], withaminimin [15], kaempferol-3-*O*-β-rutinoside [16], and 9,12,13-trihydroxyoctadec-10-enoic acid [17]. These compounds were tentatively identified by comparing their retention times, deprotonated molecular ions ([M–H]$^-$), characteristic MS/MS fragmentation patterns, and maximum UV absorption wavelengths with those reported in the literature and available reference data. The LC–MS/MS results revealed that flavonoids and physalin-type withanolides constituted the predominant classes of

compounds in the methanol extract of *P. angulata*. In particular, the presence of multiple physalin derivatives highlights the chemical complexity of the extract and is consistent with previous phytochemical investigations of the genus *Physalis*. A detailed summary of the identified compounds, including their retention times, observed and calculated mass-to-charge ratios, and proposed molecular formulas, is presented in Table 1. Although most compounds were reliably identified, several showed noticeable mass deviations (ppm), suggesting the need for further calibration and quantitative validation of the LC–MS method to ensure greater analytical robustness.

In particular, esculetin, physagulin H, withaminimin, and kaempferol-3-*O*-*β*-rutinoside were tentatively identified. Although relatively high mass errors (ppm) were observed for the precursor ions, the MS/MS fragmentation patterns were consistent with those previously reported in the literature, thereby supporting the proposed assignments. Further isolation of the major constituents will be conducted to validate the identification and confirm the analytical method.

Table 1. LC-QTOF MS/MS analysis of secondary metabolites from *P. angulata*

Peak No	Expected compounds	t_R (min)	Observed (*m/z*)	Calculated (*m/z*)	Molecular formula $[M-H]^-$	MS/MS fragment (*m/z*)	Collision energy (eV)	UV (λmax, nm	Error (ppm)
1	-	11.10	471.2481	–			10	214	7.36
2	Chlorogenic acid	12.85	353.0904	353.0878	$C_{16}H_{18}O_9$	191[M-$C_9H_6O_8$-H]$^-$			7.36
3	-	13.22	421.1667	–			10	215	
4	Esculetin	13.85	177.0277	177.0193	$C_9H_6O_4$	133 $[M-CO_2-H]^-$	10	215	47.45
5	Rutin	14.66	609.1509	609.1461	$C_{27}H_{30}O_{16}$	300[M-$C_{12}H_{20}O_9$-H]$^-$	10	215	7.88
6	Kaempferol 3-*O*-*α*-L-Arabinopyranosyl-7-*O*-*α*-L-Rhamnopyranoside	14.79	563.1437	563.1406	$C_{26}H_{28}O_{14}$	431$[M-H-Ara]^-$	10	216	5.50
7	Isorhamnetin 3-*O*-*β*-rutinoside	15.29	623.1649	623.1618	$C_{28}H_{32}O_{16}$	593$[M-H-HCHO]^-$			4.97
8	-	16.35	549.1922	–			10	220	
9	Physalin D	16.97	579.1679	579.1639	$C_{28}H_{32}O_{11}$[a]	543$[M-H]^-$	10	220	6.91
10	Physagulin H	17.91	543.1899	543.1620	$C_{30}H_{32}O_8$[b]	525$[M-H]^-$	10	220	51.36
11	Physalin E	18.60	579.1687	579.1639	$C_{28}H_{32}O_{11}$[a]	543$[M-H]^-$	10		8.29
12	Withaminimin	18.72	527.1963	527.2650	$C_{20}H_{40}O_8$[c]	507$[M-H-H_2O]^-$	10	220	130.29
13	Physalin W	18.97	579.1669	579.1639	$C_{28}H_{32}O_{10}$	523 $[M-H-H_2O]^-$			5.18
14	Diterpene lactone	19.22	581.1049	–			10		
15	-	19.53	597.1337	–			10		
16	Fatty acids (9,12,13-trihydroxyoctadec-10-enoic acid)	21.03	329.3259	–	$C_{18}H_{34}O_5$		10		
17	Kaempferol-3-*O*-*β*-rutinoside	21.41	593.1322	593.1512	$C_{27}H_{30}O_{15}$[b]	557$[M-H-2H_2O]^-$	10	254	32.03
18	Physalin G	21.85	561.1573	561.1533	$C_{28}H_{32}O_{10}$[b]	525$[M-H]^-$	10	214	7.13
19	-	23.47	479.1771	–	–				
20	-	26.03	657.4546	–	–		10		
21	-	27.66	301.2197	–	–				

[a] $[M + Cl]^-$; [b] $[M + OH]^-$; [c] $[M + Cl+H_2O]^-$.

The methanolic extract of *P. angulata* was sequentially fractionated using chloroform and EtOAc to afford solvent-partitioned extracts. Subsequent phytochemical investigations were carried out through an integrated separation strategy employing multiple chromatographic methods, including repeated *silica gel* column chromatography, RP-C_{18} chromatography, Sephadex LH-20 gel filtration, and preparative high-performance liquid chromatography (prep-HPLC). This systematic approach led to the isolation of three compounds (**1**–**3**).

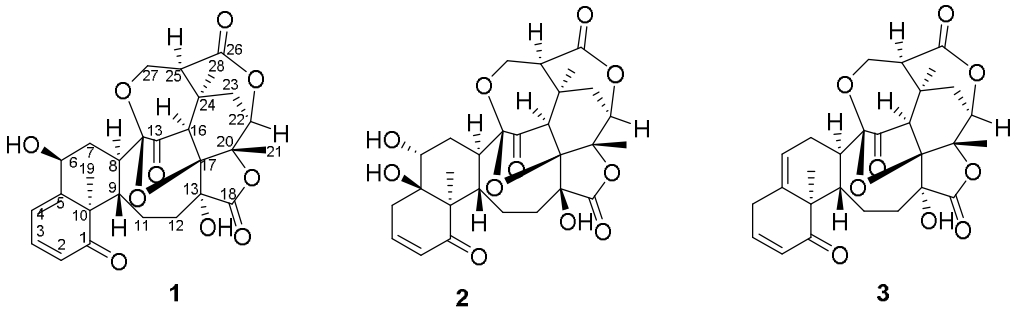

Fig. 2. Chemical structures of compounds isolated from the fruits of *P. angulata*.

Compound **1** was obtained as a white amorphous powder. It corresponded to peak 18 with a retention time of 21.85 min. The molecular formula was determined to be $C_{28}H_{30}O_9$ based on the HRESI-MS ion at *m/z* 561.1573 ([M+Cl]$^-$, calcd for $C_{28}H_{33}O_{12}Cl^-$, 561.1533). The NMR spectroscopic data of compound **1** were typical of physalin-type withanolides, which are major constituents of the genus *Physalis*. The ^{1}H NMR ($CDCl_3$) spectrum of compound **1** showed signals for three singlet methyl groups at δ_H 1.52 (s, H-19), 1.29 (s, H-28), and 1.99 (s, H-21), each integrating for three protons; one oxygenated methine proton; three olefinic protons; and two geminally coupled protons of an oxygenated methylene. The ^{13}C NMR spectrum of compound **1** displayed 28 carbon signals, which, in combination with ^{1}H–^{13}C HSQC analysis, were assigned to four carbonyl carbons at δ_C 166.7, 172.3, 208.1, and 205.7. The 16,24-cyclo-13,14-seco-steroidal skeleton was assigned based on the characteristic A/B steroidal ring system and a lactone ring between C-22 (δ_C 77.1) and C-26 (δ_C 167.0), together with the presence of both δ- and γ-lactone moieties. An intramolecular ether bridge between C-14 (δ_C 107.1) and C-27 (δ_C 60.8), along with a conjugated α,β-unsaturated carbonyl system, further supported its identification as a physalin-type framework. Moreover, the carbonyl signal at δ_C 210 was assigned to the C-1 ketone, forming an α,β-unsaturated enone system with C-2 (δ_C 125.5) and C-3 (δ_C ~139.9), whereas the signals corresponding to C-18 and C-26 were attributed to lactone carbonyls. The resonance at δ_C 107.1 confirmed the presence of the characteristic C-14 acetal carbon of physalins, and the cleavage of the C-13/C-14 bond supported the 13,14-seco feature. These structural assignments of **1** were further confirmed by key HMBC correlations. The HMBC correlations from H-27 to C-14 and C-25 confirmed the presence of an ether bridge between C-14 and C-27. Additionally, key HMBC cross-peaks from H-2 to C-4 and C-10, from H-3 to C-1 and C-5, and from H-6 to C-8 and C-10 further supported the proposed carbon framework. Other key HMBC correlations are shown in Fig. 2. Therefore, on the basis of comprehensive analysis of ^{1}H NMR, ^{13}C NMR, ^{1}H–^{1}H COSY, ^{1}H–^{13}C HSQC, and ^{1}H–^{13}C HMBC data, together with comparison with reported literature, compound **1** was identified as physalin G [18]. The relative configuration of **1** was tentatively assigned based on comparison of NMR data with literature values of physalin G. The absolute configuration was not determined in the present study due to the lack of CD or X-ray analysis. Similarly, compounds **2** and **3** were identified as physalins D and B, respectively, based on the same analytical approach. The detailed NMR data of compounds are presented in Table 2. The isolation and structural elucidation of the compounds were validated and used for the chemical profiling of *P. angulata*.

Table 2. NMR data of compounds **1**–**3**

No.	1		2		3	
	δ_C[a,b]	δ_H[a,c] (mult., *J* in Hz)	δ_C[a,b]	δ_H[a,c] (mult., *J* in Hz)	δ_C[a,b]	δ_H[a,c] (mult., *J* in Hz)
1	210.7	-	207.3	-	205.7	-
2	125.5	5.92 (d, 10.0)	127.9	5.84 (dd, 2.0, 10.0)	127.4	5.91 (dd, 2.0, 10.0)
3	139.9	6.88 (dd, 6.0, 10.0)	144.0	6.67 (m)	146.2	6.78 (ddd, 2.5, 5.0, 10.0)
4	119.4	6.08 (d, 5.5)	35.6	3.26 (d, 20.0)/2.06*	32.7	2.86 (d, 4.5)/3.27*
5	156.4	-	77.8	-	134.0	-

No.	1		2		3	
	δ_C[a,b]	δ_H[a,c] (mult., *J* in Hz)	δ_C[a,b]	δ_H[a,c] (mult., *J* in Hz)	δ_C[a,b]	δ_H[a,c] (mult., *J* in Hz)
6	71.4	4.53*	73.6	3.64 (br s)	124.5	5.58 (d, 6.5)
7	25.7	2.38*/1.53*	26.7	2.08*/ 2.00*	24.2	2.19*/2.37 (m)
8	38.6	2.69 (t, 8.5)	38.8	2.43 (dt, 3.5, 12.5)	40.0	2.20*
9	36.0	2.96 (dd, 8.5, 10.5)	30.8	3.04 (dd, 8.5, 11.0)	33.2	2.92 (m)
10	54.1	-	54.9	-	52.7	-
11	24.3	2.36* 1.26*	25.5	1.16 (m) 1.86 (t, 16.5)	24.8	1.22* 2.03 (d, 2.0)
12	32.9	2.06 (brs)	26.0	1.00 (dd, 10.0, 16.5) 2.34*	25.8	1.60 (m) 2.40 (m)
13	79.7	-	80.0	-	79.67	-
14	107.1	-	108.0	-	107.5	-
15	208.2	-	208.9	-	208.1	-
16	55.6	2.29 (br s)	55.9	2.32*	56.4	2.22 (br s)
17	81.1	-	81.2	-	80.3	-
18	172.3	-	173.1	-	172.3	-
19	21.0	1.52 (s)	14.2	1.30 (s)	17.9	1.22 (s)
20	80.6	-	81.4	-	81.0	-
21	21.6	1.99 (s)	21.8	1.99 (s)	21.5	1.97 (s)
22	77.1	4.53*	77.8	4.58 (br s)	76.9	4.55 (d, 2.0)
23	31.4	2.49 (br s)/1.56*	33.0	2.10*/ 2.13 (dd, 3.0, 14.5)	33.1	2.04 (m)
24	31.0	-	31.3	-	31.1	-
25	50.9	2.45 (br d, 3.0)	51.0	2.58 (d, 4.0)	51.0	2.45 (d, 4.0)
26	167.0	-	168.6	-	166.7	-
27	60.8	3.79 (d, 13.0)/4.51 (d, 4.5)	61.0	3.78 (d, 13.5)/4.47 (dd, 4.5, 13.5)	60.7	3.79 (d, 13.5)/4.51 (dd, 4.5, 13.5)
28	26.5	1.29 (s)	26.3	1.29 (s)	26.5	1.27 (s)

*Data was identified based on 1D and 2D NMR experiments (500 MHz, $CDCl_3$). *Overlapped signals.*

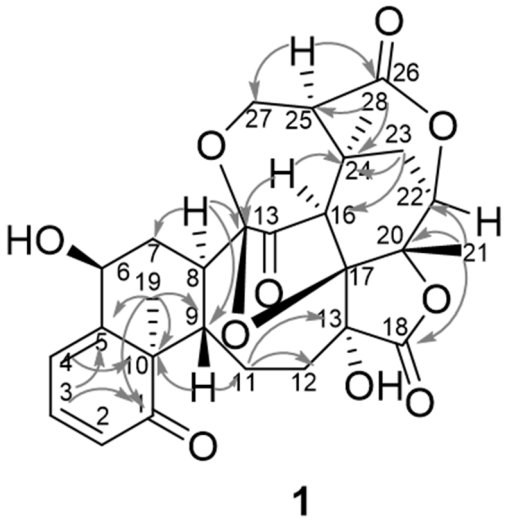

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Fig. 3. Important HMBC cross-peaks of compound **1**

Elucidating the mechanisms by which bioactive compounds suppress key pro-inflammatory mediators, including IL-12p40, IL-6, and TNF-α, provides critical insights into molecular pathways that may be exploited for the development of novel anti-inflammatory strategies in disease prevention and health promotion. Consistent with this, compound **1** exhibited potent anti-inflammatory activity against IL-12p40, IL-6, and TNF-α, with IC_{50} values of 1.17 ± 0.02, 7.52 ± 0.03, and 2.93 ± 0.05 μM, respectively, compared with the positive control Adezmapimod (IC_{50} = 5.00 ± 0.01, 3.50 ± 0.01, and 7.20 ± 0.01 μM, respectively). In contrast, the remaining compounds were inactive. The strong inhibition of IL-12p40 and TNF-α production suggests that compound **1** may interfere with upstream signaling events in LPS-activated BMDCs. Given that these cytokines are primarily regulated by NF-κB and MAPK pathways, physalin G may suppress phosphorylation of IKK or p38 MAPK, thereby preventing nuclear translocation of NF-κB. The presence of an α,β-unsaturated carbonyl moiety in physalin G could enable covalent interaction with cysteine residues of signaling proteins, a mechanism previously reported for several withanolides. Further mechanistic studies involving Western blot analysis of p-p38, p-IKK, and NF-κB nuclear translocation would be necessary to confirm this hypothesis.

4. Conclusions

In this study, the methanolic extract of *P. angulata* collected in Vietnam was chemically characterized for the first time using HR-QTOF-MS, enabling rapid profiling of its major constituents. Several secondary metabolites (**1–3**) were identified and validated. Biological evaluation showed that compound **1** significantly inhibited LPS-induced production of IL-12p40, IL-6, and TNF-α in bone marrow–derived dendritic cells, indicating notable anti-inflammatory activity. These findings support the traditional medicinal use of *P. angulata* and provide a basis for further pharmacological investigation. However, this study was limited to *in vitro* assays, and additional *in vivo* studies are required to confirm the therapeutic potential. Moreover, further calibration and quantitative validation of the LC–MS method are necessary to improve accuracy and reproducibility for future applications.

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