

Anti-inflammatory Diterpenoid Alkaloids from *Aconitum taipeicum*

Lanrun Yang , Yanni Liang  and Dongbo Zhang  *

*Co-construction Collaborative Innovation Center for Chinese Medicine Resources
Industrialization by Shaanxi & Education Ministry, State Key Laboratory of Research &
Development of Characteristic Qin Medicine Resources (Cultivation), Shaanxi Innovative Drug
Research Center, Shaanxi University of Chinese Medicine, Xianyang 712046, P. R. China*

(Received June 16, 2025; Revised July 17, 2025; Accepted July 18, 2025)

Abstract: Aconitamine A, a new hetidine-type C₂₀-diterpenoid alkaloid (**1**), and three known aconitine-type C₁₉-diterpenoid alkaloids (**2-4**) were isolated from the roots of *Aconitum taipeicum*. The structures of all isolates were identified by spectroscopic methods and comparison with literature data. Compounds **1** and **2** showed inhibition of nitric oxide production in RAW 264.7 macrophages stimulated by lipopolysaccharide with IC₅₀ values of 30.5 and 4.7 μM compared to positive control (dexamethasone, IC₅₀ = 12.9 μM).

Keywords: *Aconitum taipeicum*; Ranunculaceae; diterpenoid alkaloids; NO inhibitory activity. © 2025 ACG Publications. All rights reserved.

1. Plant Source

Fresh roots of *Aconitum taipeicum* Hand.-Mazz. (Ranunculaceae) were collected in the Taibai Mountains of Shaanxi Province in China (107°89' E, 34°12' N) in October 2018 and identified by senior experimentalist Jitao Wang, Shaanxi University of Chinese Medicine, Xianyang, P. R. China. A voucher specimen (No. 20181015) was deposited at room temperature in the Herbarium of the Natural Product Research Centre of Shaanxi University of Chinese Medicine.

2. Previous Studies

Aconitum taipeicum, commonly known as "Jin-Niu-Qi", is a perennial herb around an altitude of 2600–3400 meters in the Southern Shaanxi Province and in Western Henan Province in China, and its roots have long been used as an anti-inflammatory and analgesic drug in Chinese folk medicine [1]. This species is well known to be a rich source of diterpenoid alkaloids (DAs) with a diverse range of

* Corresponding author: E-Mail: symensu@163.com

pharmacological activities [1–5], mainly focusing on analgesic, anticancer, anti-inflammatory, and cardiac effects [6].

In our previous research on this plant, aconicumines A–D, an advanced class of norditerpenoid alkaloids were isolated [5]. Further investigation on the constituents of *A. taipeicum* resulted in the isolation of one unprecedented hetidine-type C₂₀-DA (**1**) along with three previously identified aconitine-type C₁₉-DAs (**2–4**). Herein, the isolation, structure elucidation and nitric oxide (NO) inhibition of these alkaloids are described.

3. Present Study

The fresh roots of *A. taipeicum* (4.0 kg) were cut and soaked with a 2% H₂SO₄ solution (3 × 25 L, 24 h each) under ambient temperature, and the H₂SO₄ aqueous solution was concentrated and extracted with EtOAc (2.0 L × 4). The acidic water-soluble materials were adjusted to pH 9–10 with NH₄OH solution and extracted with CHCl₃ (2.0 L × 4). The CHCl₃ extract (14.7 g) was fractionated by MCI gel medium pressure liquid chromatography with MeOH–H₂O (0, 50%, 100%) to afford fractions A–C. Fr.C was separated by an ODS column and eluted with MeOH–H₂O (1:1–1:0) to give six subfractions (Fr.C.1–Fr.C.6). Fr.C.6 was subjected to silica gel CC eluted with CHCl₃–MeOH (40:1–1:1) to give six subfractions (Fr.C.6.1–Fr.C.6.6). Fr.C.6.3 was subjected to silica gel CC eluted with petroleum ether/acetone (40:1–0:1) to give compounds **2** (8.0 mg), **3** (5.0 mg) and subfractions (Fr.C.6.3.1–Fr.C.6.3.4). Fr.C.6.3.2 was purified using preparative HPLC (ACN/H₂O, 76:24; flow rate, 7.0 mL/min) to give **1** (1.3 mg, *t_R* = 22.7 min). Fr.C.6.3.3 was separated by silica gel CC eluted with petroleum ether/EtOAc (40:1–1:1) to afford **4** (2.8 mg).

Aconitaimine A (1): White powder; IR ($\nu_{\max}$): 3405, 2921, 2853, 1724, 1659, 1582, 1457, 1387, 1183, 1025 cm^{−1}; HRESIMS *m/z* 344.2587 [M + H]⁺ (calcd for C₂₂H₃₄NO₂, 344.2590). ¹H (400 MHz) and ¹³C NMR (100 MHz) data, see Table 1.

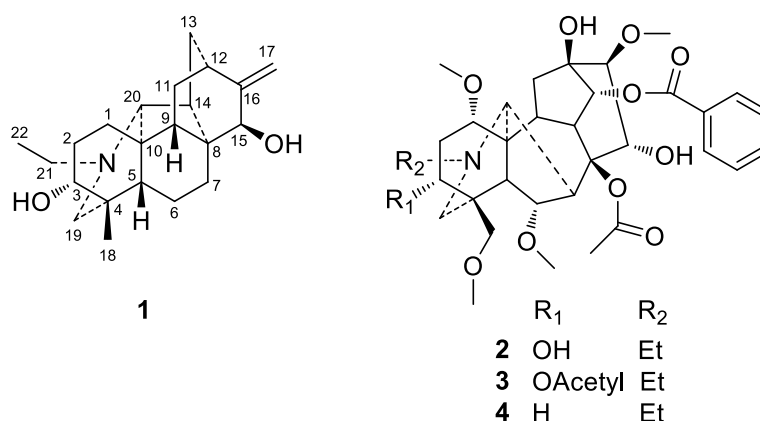


Figure 1. Chemical structures of compounds **1–4**

Compound **1**, a white powder, displayed a molecular formula of C₂₂H₃₃NO₂ as determined by positive HR-ESI-MS (*m/z* 344.2587 [M + H]⁺, calcd. 344.2590), requiring 7 indices of hydrogen deficiency. The absorption band at 3405 cm^{−1} in the IR spectrum indicated the presence of hydroxyl group. The ¹H NMR spectrum (Table 1) exhibited signals for an *N*-ethyl side chain [δ_H 1.03 (3H, t, *J* = 7.2 Hz, H-22), 2.38 (1H, m, H-21a) and 2.62 (1H, m, H-21b)], a methyl group at δ_H 1.05 (3H, s, H-18), an isolated methylene attached to the *N*-atom [δ_H 2.45, 2.46 (2H, ABq, *J* = 12.1 Hz, H-19)], an *N*-containing methine at δ_H 2.33 (1H, br s, H-20), two *O*-containing methines [δ_H 3.21 (1H, dd, *J* = 11.3, 4.9 Hz, H-3) and 4.01 (1H, t, *J* = 2.0 Hz, H-15)], and an exocyclic double bond [δ_H 4.83, 4.93 (each 1H, br s, H-17)]. The ¹³C NMR, DEPT, and HSQC spectroscopic data displayed 22 carbon signals (Table 1), including two methyls [δ_C 23.1 (C-18) and 12.4 (C-22)], eight methylenes [two nitrogen-

A new diterpenoid alkaloid

bearing at δ_C 50.6 (C-19) and 50.0 (C-21)], seven methines [two oxygenated at δ_C 77.7 (C-3) and 72.4 (C-15), one nitrogen-containing at δ_C 76.3 (C-20)], three quaternary carbons [δ_C 39.4 (C-4), 44.3 (C-8) and 44.4 (C-10)] and an exocyclic double bond [δ_C 158.3 (C-16) and 104.2 (C-17)]. The above NMR features suggested that **1** possessed a hetidine-type C₂₀-diterpenoid alkaloid carbon skeleton, similar to trabzonine, which has been previously observed from *Aconitum nasutum* (Ranunculaceae) [7]. Comparison of the ¹³C NMR data of **1** with those of trabzonine suggested that the hydroxymethyl at C-22 (δ_C 58.9, t) in trabzonine was reduced to methyl group (δ_C 12.4, q) in **1**, which was verified by the HMBC (Figure 2) correlation from H-22 [δ_H 1.03 (3H, t, J = 7.2)] to C-21 (δ_C 50.0) and a spin system (H₂-22/H-21/N) deduced from analysis of the ¹H–¹H COSY spectrum. Another difference was that the hydroxyl group located at C-7 in trabzonine was connected to C-3 in **1**, which was confirmed by the HMBC cross-peaks of H-1, H-18 and H-19 to C-3. Thus, the planar structure of **1** was determined as shown (Figure 1).

The relative configuration of **1** was assigned on the basis of the NOESY analysis (Figure 2). The NOESY correlations of H-5 with H-1 β , H-3, H-7 β , H-9 and H-18 indicated that these protons were β -oriented. The cross-peaks from H-7 α to H-15 and H-14 suggested these hydrogens were on the sameface. Furthermore, the correlation between H-1 α and H-20 in the NOESY spectrum indicated that H-1 α and H-20 possessed identical orientations. The calculated ECD curve of 3*R*,4*R*,5*S*,8*S*,9*S*,10*R*,12*R*,14*R*,15*R*,20*S*-**1** was consistent with the experimental curve (Figure 3). Therefore, the absolute configuration of **1** was assigned, and named as aconitamine A.

Table 1. ¹H (400 MHz) and ¹³C (100MHz) NMR data for **1** (δ in ppm, J in Hz) in CDCl₃

No.	δ_H	δ_C
1a	1.18 (1H, m)	31.2 (t)
1b	1.87 (1H, m)	—
2a	1.43 (1H, m)	29.1 (t)
2b	1.75 (1H, m)	—
3	3.21 (1H, dd, J = 11.3, 4.9)	77.7 (d)
4	—	39.4 (s)
5	1.02 (1H, m)	44.2 (d)
6a	1.66 (1H, m)	22.2 (t)
6b	2.21 (1H, m)	—
7a	1.43 (1H, m)	31.0 (t)
7b	1.98 (1H, m)	—
8	—	44.3 (s)
9	1.44 (1H, m)	45.2 (d)
10	—	44.4 (s)
11a	1.56 (1H, m)	29.3 (t)
11b	1.85 (1H, m)	—
12	2.20 (1H, m)	34.7 (d)
13a	1.57 (1H, m)	36.6 (t)
13b	1.78 (1H, m)	—
14	1.65 (1H, m)	50.1 (d)
15	4.01 (1H, t, J = 2.0)	72.4 (d)
16	—	158.3 (s)
17a	4.83 (1H, br s)	104.2 (t)
17b	4.93 (1H, br s)	—
18	1.05 (3H, s)	23.1 (q)
19	2.45, 2.46 (2H, ABq, J = 12.1)	50.6 (t)
20	2.33 (1H, br, s)	76.3 (d)
21a	2.38 (1H, m)	50.0 (t)
21b	2.62 (1H, m)	—
22	1.03 (3H, t, J = 7.2)	12.4 (q)

Recorded in CDCl₃. Assignments were based on DEPT, ¹H–¹H COSY, HSQC, and HMBC experiments.

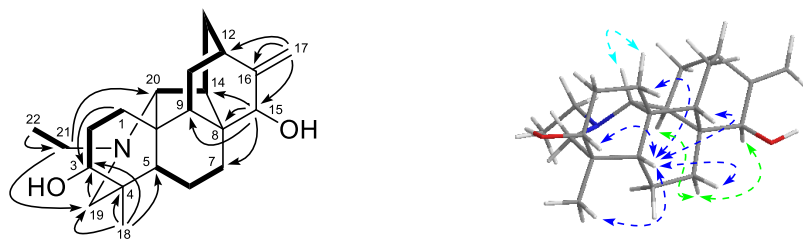


Figure 2. Key ^1H - ^1H COSY (—), HMBC (—→), and NOESY (↔) correlations of **1**

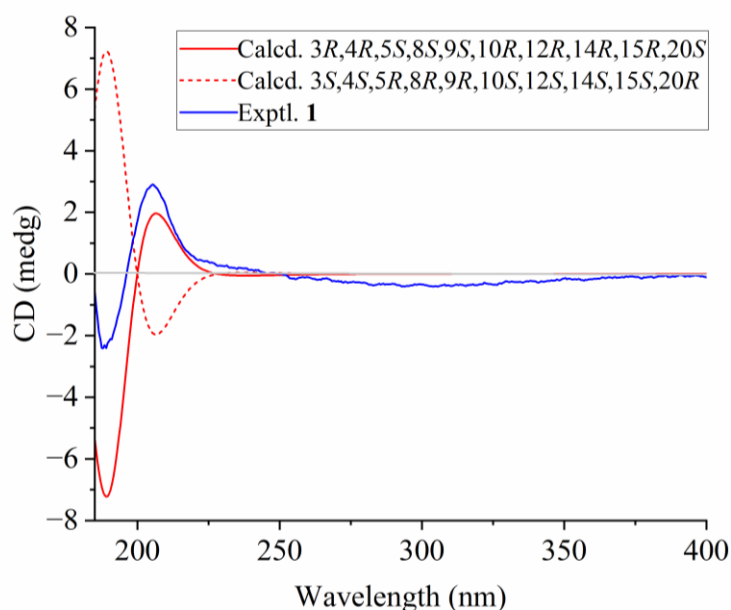


Figure 3. Experimental and calculated ECD spectra of **1**

Three known aconitine-type C_{19} -DAs (**2-4**) (Figure 1) were also isolated and identified as aconitine (**2**) [8], 3-acetylaconitine (**3**) [8] and 3-deoxyaconitine (**4**) [9] by comparison of their physical and spectroscopic data with those reported in the literature.

Considering the folkloric uses of *A. taipeicum*, the primary anti-inflammatory activities of compounds **1-4** were evaluated by inhibition of NO production in RAW 264.7 macrophages induced by LPS. Cell culture, Griess and MTT procedures, and data analysis for the inhibition of NO production were the same as in the previous protocol [5]. The results showed that compounds **1** and **2** potentially inhibited NO production with IC_{50} values of 30.5 and 4.7 μM compared to positive control (dexamethasone, $\text{IC}_{50} = 12.9 \mu\text{M}$), while others showed no obvious activities ($\text{IC}_{50} > 50.0 \mu\text{M}$). All isolates were non-cytotoxic to RAW 264.7 macrophages at the tested concentrations.

Acknowledgments

The work was supported financially by the Youth Innovation Team Research Project of Education Department of Shaanxi Province (23JP033) and Basic Research Project of Natural Science of Shaanxi Province (2025JC-YBMS-843).

A new diterpenoid alkaloid

Supporting Information

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

ORCID

Lanrun Yang: [0009-0004-7963-5697](https://orcid.org/0009-0004-7963-5697)

Yanni Liang: [0000-0002-8002-6555](https://orcid.org/0000-0002-8002-6555)

Dongbo Zhang: [0000-0002-5108-9514](https://orcid.org/0000-0002-5108-9514)

References

- [1] Y. Q. He, Z. Y. Ma, Q. Yang, B. H. Yao and L. M. Gao (2008). A new norditerpenoid alkaloid from *Aconitum taipaicum*, *Acta Pharmacol. Sin.* **43**(9), 934-937.
- [2] Z. J. Guo, Y. Xu, H. Zhang, M. Y. Li and K. Xi (2014). New alkaloids from *Aconitum taipaicum* and their cytotoxic activities, *Nat. Prod. Res.* **28**(3), 164-168.
- [3] J. Singhuber, M. Zhu, S. Prinz and B. Kopp (2009). *Aconitum* in traditional Chinese medicine-a valuable drug or an unpredictable risk?, *J. Ethnopharmacol.* **126**(1), 18-30.
- [4] Y. Xu, Z. J. Guo and N. Wu (2010). Two new amide alkaloids with anti-leukaemia activities from *Aconitum taipaicum*, *Fitoterapia* **81**(8), 1091-1093.
- [5] D. B. Zhang, Y. N. Liang, Z. Wang, L. K. Shi, Z. Zhang, Z. S. Tang and L. Q. Huang (2023). Aconicumines A-D, an advanced class of norditerpenoid alkaloids with an unprecedented *N*, *O*-diacetal motif from *Aconitum taipaicum* Hand.-Mazz., exhibit anti-inflammatory properties in vitro, *Phytochemistry* **210**, 113675.
- [6] C. S. Peng and F. P. Wang (2000). Advances in chemistry of norditerpenoid alkaloids, *Acta Pharmacol. Sin.* **35**(12), 932-938.
- [7] A. H. Mericli, F. Mericli, H. K. Desai, B. S. Joshi, Q. Tong, K. Bhattacharyya, G. Melikoglu, M. Kucukislamoglu, A. Ulubelen and S. W. Pelletier (2000). Norditerpenoid and diterpenoid alkaloids from the roots of *Aconitum nasutum* Fisch. ex Reichb., *Heterocycles* **53**(9), 1987-1996.
- [8] Y. J. Wang, J. Zhang, C. J. Zeng, Z. Yao and Y. Zhang (2011). Study on the diterpene alkaloids from processed roots of *Aconitum pendulum*, *West China J. Pharm. Sci.* **26**(1), 11-13.
- [9] W. Pelletier, N. V. Mody and N. Katsui (1977). The structures of sachaconitine and isodelphinine from *Aconitum miyabei* Nakai, *Tetrahedron Lett.* **18**(46), 4027-4030.

A C G
publications

© 2025 ACG Publications