Chinese Herbal Medicines 18 (2026) 487–490

Contents lists available at ScienceDirect

Chinese Herbal Medicines

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

Research Letter

Diverse alkaloids with anti-inflammatory activity discovered from *Thalictrum baicalense*

To the Editor,

The genus *Thalictrum*, a member of Ranunculaceae family distributed in Asia, Europe, Africa, North and South America. There are 99 species throughout China (Wang, 2018). Among them, more than 43 species have been used medicinally in China, of which the roots of the plants are often used as traditional folk medicines to treat esoenteritis, cancer, dysentery, and conjunctivitis (Li et al., 2014). The main bioactive components of the genus *Thalictrum* plants are isoquinoline alkaloids, which showed the significant pharmacological effects such as anti-tumor, antibacterial, anti-inflammatory, antiviral, antimalarial, anti-arrhythmia, anti-silicosis, anti-platelet aggregation, immunomodulatory, antihypertensive and hypolipidemic effects (Li et al., 2014). In our previous work, a series of isoquinoline alkaloids with novel structures and potent anti-tumor activity were isolated from the plants of *Thalictrum baicalense* Turcz. ex Ledeb. (Xue et al., 2020; Xue et al., 2022). For example, baicalensine A, a new class of dimeric alkaloid, exhibited antiproliferative activities against Caco-2 (human colorectal adenocarcinoma cells) and HL-60 (human acute promyelocytic leukemia cells) cancer cells with IC_{50} values of 9.24 and 10.15 μmol/L, respectively (Xue et al., 2020). Thalicultratine M was more active in inhibiting the growth of both Caco-2 and HepG-2 (human hepatocellular carcinoma cells) cancer cells than the positive drug 5-FU (Xue et al., 2022). Additionally, a non-alkaloid compound, (7*R*, 8*S*, 7′*R*, 8′*S*)-9*E*-feruloylneoolivill, demonstrated significant inhibitory activity on NO production in LPS-induced mouse monocyte/macrophage cell line Raw 264.7 with an IC_{50} value of 9.56 μmol/L (Yang et al., 2025). According to published literature, isoquinoline alkaloids exert anti-inflammatory effects by inhibiting key pro-inflammatory pathways (Yang et al., 2021). Plants of the genus *Thalictrum* are rich in alkaloid constituents, prompting our investigation into the anti-inflammatory potential of alkaloids isolated from *T. baicalense*. In our continuous study, a phytochemical investigation of the roots of *T. baicalense* led to the isolation of 41 alkaloids (Fig. 1). These compounds encompass a wide spectrum of structural types. Notably, this study identified four previously undescribed alkaloids. Their chemical structures were determined by spectroscopic analysis, and their anti-inflammatory activities were also evaluated.

Compound **1** was obtained as a yellow amorphous powder. Its molecular formula was deduced as $C_{19}H_{15}NO_6$ with 13 degrees of unsaturation from the quasi-molecular ion peak at *m*/*z* 354.097 9 $[M + H]^+$ (calcd. For $C_{19}H_{16}NO_6$, 354.097 8) in HRESIMS (Fig. S1.1). The ^{1}H-NMR data (Fig. S1.3 and Table S1) of **1** exhibited a pair of *ortho*-coupled aromatic protons at δ_H 7.29 (1H, d, J = 8.5 Hz, H-12) and 7.27 (1H, d, J = 8.5 Hz, H-11), two isolated aromatic protons at δ_H 7.50 (1H, s, H-1) and 7.01 (1H, s, H-4), one olefinic proton at δ_H 7.11 (1H, s, H-13), two methylenedioxyl protons at δ_H 6.09 and 6.08 (1H, d, J = 1.1 Hz, 2-OCH_2O-3), two hydroxyl protons at δ_H 9.43 (1H, s, 10-OH) and 5.58 (1H, d, J = 4.3 Hz, 5-OH), one methoxy signal at δ_H 3.78 (3H, s, 9-OCH_3) and three protons linked to the oxygenated or nitrogenated carbons at δ_H 4.74 (1H, dd, J = 6.1, 3.5 Hz, H-5), 4.26 (1H, dd, J = 13.6, 6.1 Hz, H-6) and 3.98 (1H, dd, J = 13.6, 3.5 Hz, H-6). Comprehensive interpretation of the ^{13}C-NMR and HSQC data (Table S1, Fig. S1.4 and Fig. S1.5) revealed nineteen carbon resonances classified as one carbonyl carbon, 14 aromatic or olefinic carbons, and four aliphatic carbons (including one methylenedioxy carbon at δ_C 101.4). The above NMR data suggested that **1** was a berberine-type alkaloid. Analyses of its 1D NMR data revealed that the structure of **1** was closely similar to that of 5-hydroxyl-8-oxyberberine (**5**) (Wang et al., 2014) with the difference of the methoxyl at C-10 replaced by a hydroxyl group. The 10-hydroxyl substitution was determined by the cross peaks from H-12 to C-8a, C-10, and C-13, from H-11 to C-9 and C-12a, and from the methoxy at δ_H 3.78 to C-9 in HMBC spectrum (Fig. S1.6 and Fig. S5). Its specific optical rotation $[\alpha]_D^{20}$: +44.44 (*c* 0.18, CH_3OH) was comparable to that of (+)-5-hydroxyl-8-oxyberberine suggesting 5*S* configuration (Wang et al., 2014). Hence, the structure of **1** was determined as (+)-5-hydroxyl-8-oxythalifendine.

Compound **17** was obtained as a white amorphous powder. Its molecular formula was deduced as $C_{26}H_{31}NO_{10}$ with 12 degrees of unsaturation from the quasi-molecular ion peak at *m*/*z* 518.203 1 $[M + H]^+$ (calcd. For $C_{26}H_{32}NO_{10}$, 518.202 6) in HRESIMS (Fig. S2.1). The ^{1}H-NMR data (Fig. S2.3 and Table S2) of **17** exhibited a pair of *ortho*-coupled aromatic protons (δ_H 6.71 and 6.70, both 1H, d, J = 7.9 Hz, H-12, H-11), two isolated aromatic protons (δ_H 6.95 and 6.94, both 1H, s, H-1, 4), one methylenedioxyl signal at δ_H 5.96 (2H, s), one methoxy signal at δ_H 3.75 (3H, s), and one *N*-methyl signal at δ_H 1.80 (3H, s). Two sets of methylene proton signals were overlapped by the water peak in DMSO d_6, which were observed at δ_H 3.45 (2H, m, H-6) and 3.35 (2H, s, H-8) in its ^{1}H-NMR spectrum tested in CD_3OD (Fig. S2.4). The ^{13}C-NMR and HSQC data (Fig. S2.5; Fig. S2.6 and Table S2) of **17** showed 26 carbon resonances, which were classified as one carbonyl carbon, 12 aromatic carbons, one methylenedioxyl carbon, one methoxy carbon, one *N*-methyl carbon, and four methylene carbons, as well as a set of a glucopyranosyl carbons. The anomeric signal at δ_H 4.93 (1H, d, J = 7.2 Hz, H-1′) was suggestive of β-configuration of the glucosyl moiety. The above NMR data suggested that **17** was a protopine type alkaloid glucoside. The ^{1}H- and ^{13}C- NMR data of the

https://doi.org/10.1016/j.chmed.2026.02.013
1674-6384/© 2026 Tianjin Press of Chinese Herbal Medicines. Published by ELSEVIER B.V.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

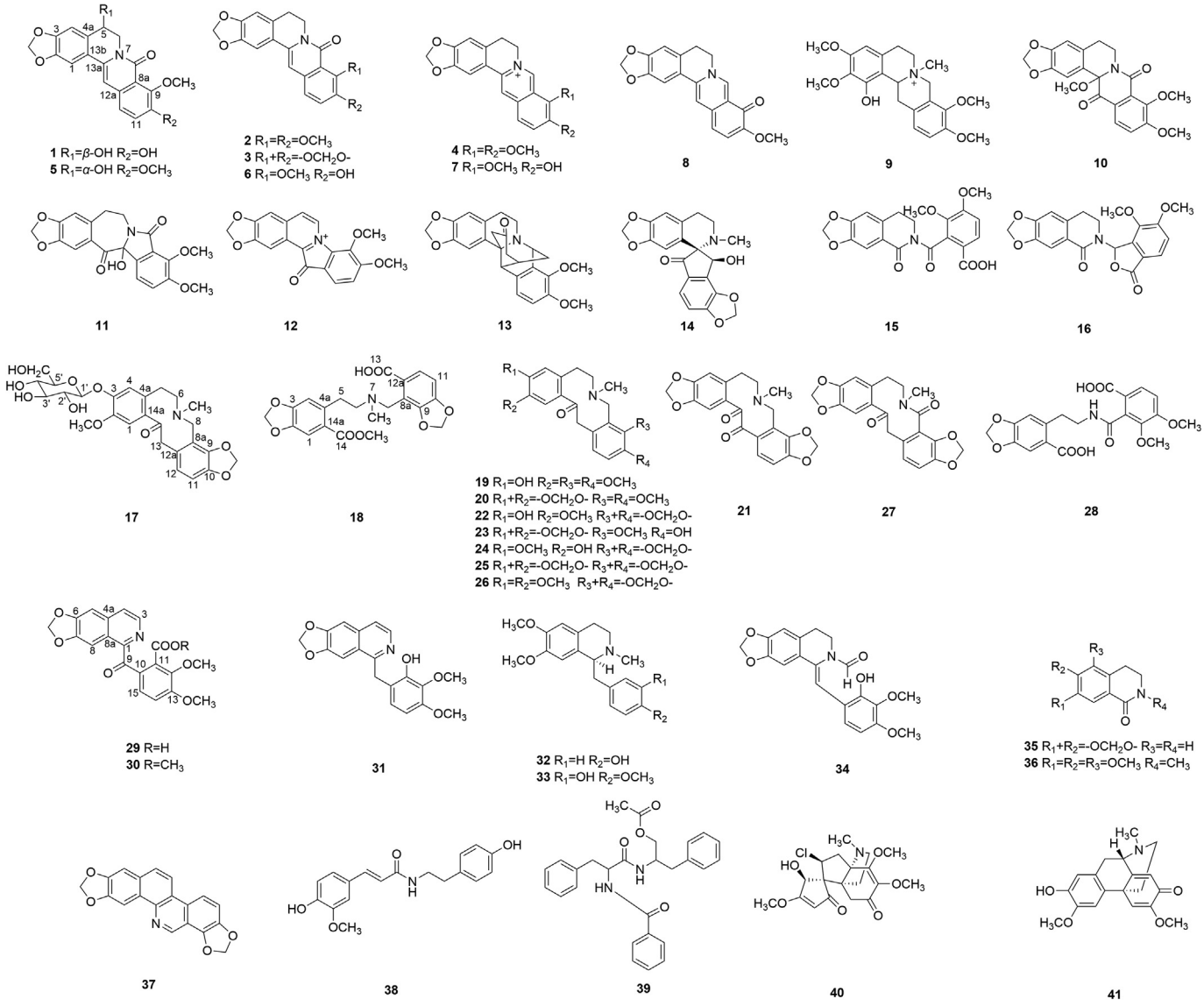


Fig. 1. Structures of compounds **1**–**41**.

aglycone of **17** showed close similarity with those of izmirine (Guinaudeau, Shamma, & Gözler, 1983) suggesting its aglycone as izmirine, which was supported by analyses of the HMBC (Fig. S2.7) and NOESY (Fig. S2.8) data as shown in Fig. S5. The *β*-glucopyranosyl group was located at position C-3 of the aglycone determined by the HMBC correlation from H-1′ to C-3, as well as the NOESY correlations of H-1′/2-OCH_3 and H-4/H-1′. Compound **17** was inferred to be izmirine 3-*O*-*β*-glucopyranoside.

Compound **18** was obtained as a white amorphous powder. Its molecular formula was deduced as $C_{21}H_{21}NO_8$ with 12 degrees of unsaturation from the quasi-molecular ion peak at *m*/*z* 416.134 6 $[M + H]^+$ (calcd. For $C_{21}H_{22}NO_8$, 416.134 5) in HRESIMS (Fig. S3.1). The ^{1}H-NMR data of **18** (Fig. S3.2 and Table S2) revealed a pair of *ortho*-coupled aromatic proton signals (δ_H 7.78 and 6.84, both 1H, d, *J* = 8.3 Hz, H-12, 11), two isolated aromatic proton signals (δ_H 7.42 and 6.66, both 1H, s, H-1, 4), two methylenedioxyl signals (δ_H 6.04 and 6.01, both 2H, s), one methoxy signal at δ_H 3.83 (3H, s), one *N*-methyl signal at δ_H 2.59 (3H, s), and three methylene signals at δ_H 3.93, 3.26 and 2.94. The ^{13}C-NMR and HSQC data of **18** (Fig. S3.3; Fig. S3.4 and Table S2) showed 21 carbon resonances assigned as two ester carbonyls, 12 aromatic carbons, two methylenedioxyls, one methoxyl, one *N*-methyl and three methylenes. By comparison of NMR data with berberilic acid (**28**) (Dobbie & Lauder, 1902), compound **18** possessed one more methyl ester and a methylenedioxyl substitution instead of two methoxys in **28**, which was confirmed by analyses of the HMBC and NOESY data (Fig. S3.5; Fig. S3.6 and Fig. S5). The structure of compound **18** was assigned as shown and named seco-13-oxoprotopine.

Compound **29** was obtained as a brown amorphous powder. HRESIMS (Fig. S4.1) exhibited a quasi-molecular ion peak at *m*/*z* 382.092 6 $[M + H]^+$ (calcd. For $C_{20}H_{16}NO_7$, 382.092 7), supporting the molecular formula $C_{20}H_{15}NO_7$ with 14 degrees of unsaturation. The ^{1}H-NMR (600 MHz, $CDCl_3$) spectrum (Fig. S4.3 and Table S3) displayed six aromatic proton signals, including a pair of *ortho*-coupled protons at δ_H 8.35 (1H, d, *J* = 5.5 Hz, H-3) and 7.53 (1H, d, *J* = 5.5 Hz, H-4) indicative of a six-membered nitrogen-containing aromatic ring, two singlet aromatic protons at δ_H 7.62 (1H, s, H-8) and 7.09 (1H, s, H-5), a pair of *ortho*-coupled aromatic protons at δ_H 7.17 (1H, d, *J* = 8.6 Hz, H-15) and 6.69 (1H, d, *J* = 8.6 Hz, H-14), a methylenedioxy signal at δ_H 6.06 (2H, s), and two methoxy signals at δ_H 3.91 (3H, s) and 3.87 (3H, s). The ^{13}C-NMR (150 MHz, $CDCl_3$)

spectrum (Fig. S4.4 and Table S3) revealed 20 carbon resonances, including 15 aromatic carbons (four of which were oxygenated), a ketone carbonyl, an ester carbonyl, a methylenedioxy carbon, and two methoxy carbons. Based on the NMR data, compound **29** was identified as a benzylisoquinoline alkaloid. Comparison with 2,3-dimethoxybenzoic acid methyl ester (**30**) (Min, Yang, Lee, Kim, Choi, & Lee, 2006) indicated that **30** was the methyl ester of **29**, which was supported by the HMBC correlations (Fig. S4.6 and Fig. S5). Compound **29** was named 11-carboxylic-12-methoxy-pulcheotine A.

The known compounds were identified as oxyberberine (**2**), 8-oxocoptisine (**3**), berberine (**4**), (−)-5-hydroxyl-8-oxyberberine (**5**), 8-oxythalidendine (**6**), thalifendine (**7**), berberrubine (**8**), 9-*O*-methylstecepharine (**9**), dioxomethoxycanadine (**10**), chilenine (**11**), coptisonine (**12**), (+)-valachine (**13**), sibiricine (**14**), anhydroberberillic acid (**15**), berberal (**16**), demethylated muramine (**19**), allocryptopine (**20**), 13-oxoprotopine (**21**), izmirine (**22**), thalictrisine (**23**), 6,8,9,15-tetrahydro-12-hydroxy-11-methoxy-7-methylbenzo[g][1,3]benzodioxolo[4,5-c]azecin-14(7*H*)-one (**24**), protopine (**25**), cryptopine (**26**), leptocarpine (**27**), berberilic acid (**28**), 6-([1,3]dioxolo[4,5-g]isoquinoline-5-carbonyl)-2,3-dimethoxybenzoic acid methyl ester (**30**), berbitine (**31**), (*S*)-armepavine (**32**), (*S*)-laudanidine (**33**), ployberbine (**34**), noroxyhydrastineine (**35**), *N*-methylthalidaldine (**36**), norsanguinarine (**37**), *N*-*trans*-feruloyltyramine (**38**), autantiamide (**39**), acutumine (**40**), and pallidine (**41**). Detailed NMR data and complete references for all compounds are provided in the Supporting Information.

The cytotoxic activities of compounds **1–11**, **14**, **17–18**, **20**, **22–24**, **27–29**, **31–33**, **35**, **37–39** and **41** were evaluated against RAW 264.7 cells. The cell viability assay indicated that the majority of tested compounds were well tolerated at 50 μmol/L, showing that cell viability remained above 80% (Dai et al., 2024). Cytotoxicity was observed only for compounds **3**, **18**, and **31**, as shown in Fig. 2A. It is noteworthy that at 25 μmol/L compounds **3** and **18** showed cell survival rates above 80%, as shown in Fig. 2B. The NO production assay, using dexamethasone (Dex, 10 μmol/L) as the positive control, was conducted in lipopolysaccharide (LPS, 500 ng/mL)-stimulated RAW 264.7 cells and was carried out on the compounds with more than 80% of cell viability (Dai et al., 2024). Notably, compounds **1**, **3**, **4**, **6–10**, **18**, **22**, **29** and **38** demonstrated inhibitory effects on NO production in LPS-induced RAW264.7 cells. Among them, compound **29** exhibited more potent inhibitory effect with an IC_{50} value of IC_{50} = (8.35 ± 0.76) μmol/L (Table S4). Furthermore, we observed that most berberine-type alkaloids demonstrated favorable inhibitory activity. Therefore, we selected compound **6** with the strongest activity, along with the newly identified compound **1** displaying comparable potency, for further evaluation of their effects on the pro inflammatory cytokines TNF α and IL 6. The results demonstrated that both compounds significantly suppressed the production of TNF α and IL 6 (Fig. 2C and Fig. 2D).

Among the tested isolates, most of berberine-type alkaloids (**1**, **3–4**, **6–10**) consistently demonstrated superior inhibitory activity compared to other structural types. Notably, the new berberine-type alkaloid (+)-5-hydroxy-8-oxothalidendine (**1**) displayed considerable potency, and the analogues (**6**, **7**) with the same 9-methoxy-10-hydroxy substitution also showed similar activity. Most of the protopine- and benzylisoquinoline-type alkaloids exhibited no effects on NO production except for **18**, **22**, and **29**. It is worth noting that compound **29** displayed the most potent inhibition. Structurally, compound **29** belongs to the benzylisoquinoline alkaloid. However, biogenetically, it is the ring C cleavage product of an 8,13-dioxo-berberine derivative.

Conclusion

Our phytochemical investigation of *T. baicalense* roots has led to the isolation and structural elucidation of forty-one alkaloids covering seven structural classes deriving from phenylalanine or tyro-

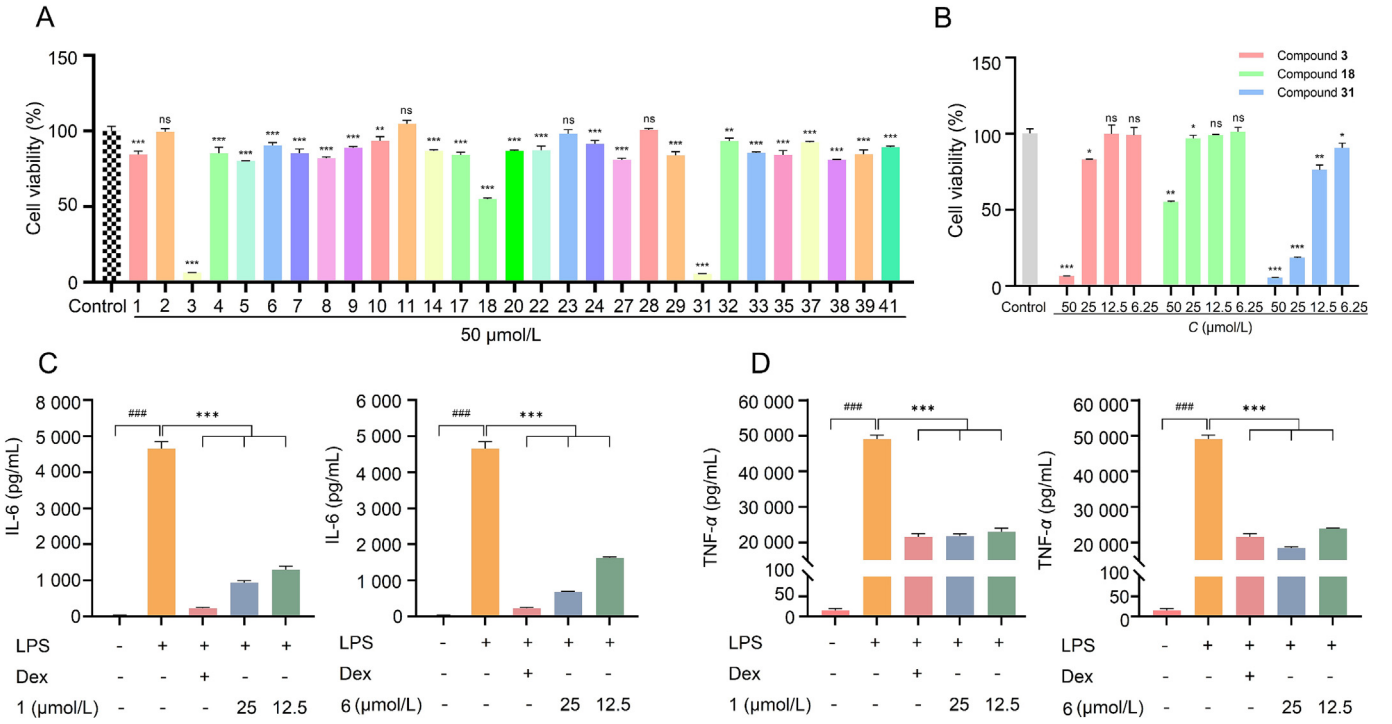


Fig. 2. Influence of all tested compounds on RAW 264.7 cell viability (A). Influence of compounds **3**, **18**, and **31** on RAW 264.7 cell viability (B). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ *vs* Control group, ns: not significant. Effects of compounds **1** and **6** on IL-6 levels in LPS induced RAW 264.7 cells (C). Effects of compounds **1** and **6** on TNF α levels in LPS induced RAW 264.7 cells (D). Data are presented as means ± standard deviations (n = 3, independent experiments). $^{###}P < 0.001$ *vs* Control group; $^{***}P < 0.001$ *vs* LPS group.

sine pathway biogenetically, including four previously undescribed compounds (**1**, **17–18**, **29**), along with 19 compounds isolated from this genus for the first time (**5–6**, **8–16**, **19**, **21**, **24**, **27**, **28**, **38–40**). This work significantly expands the chemical library of the *Thalictrum* genus. More importantly, the anti-inflammatory evaluation of these isolates unequivocally identified berberine-type alkaloids as the primary anti-inflammatory constituents in this plant, which provides a direct chemical and pharmacological justification for the traditional use of *T. baicalense* in treating inflammatory ailments. The pronounced activity of the berberine-type analogues highlights their potential as valuable lead compounds for the development of novel anti-inflammatory agents. Consequently, this study not only contributes to the chemotaxonomy and phytochemistry of *Thalictrum* but also paves the way for further drug discovery efforts based on these natural scaffolds.

CRediT authorship contribution statement

Jinyuan Yang: Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Zhaojing Chen:** Software, Methodology, Formal analysis, Data curation. **Jingjing Xue:** Software, Methodology, Formal analysis, Data curation. **Yikun Ren:** Visualization, Software, Methodology. **Zhanlin Li:** Visualization. **Dahong Li:** Visualization. **Yating Sun:** Visualization, Validation, Resources, Investigation. **Huiming Hua:** Writing – review & editing, Resources, Project administration, Methodology, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was supported by National Natural Science Foundation of China (No. 82173715).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chmed.2026.02.013.

References

Dai, L. T., Yang, L., Guo, J. C., Ma, Q. Y., Xie, Q. Y., Jiang, L., et al (2024). Anti-diabetic and anti-inflammatory indole diterpenes from the marine-derived fungus *Penicillium* sp. ZYX-Z-143. *Bioorganic Chemistry, 145* 107205.

Dobbie, J. J., & Lauder, A. (1902). XIV.—Corydaline. Part VII. the constitution of corydaline. *Journal of the Chemical Society, Transactions, 81*, 145–156.

Guinaudeau, H., Shamma, M., & Gözler, T. (1983). Izmirine: A new protopine alkaloid. *Journal of Natural Products, 46*(6), 934–935.

Li, S. G., Su, Y. Q., Ma, D. K., Li, J. Y., Guo, J., Li, D. H., et al (2014). Research progress on chemical constituents and pharmacological activities of alkaloids from plants in *Thalictrum* L. *Drugs & Clinic, 29*(3), 312–321.

Min, Y. D., Yang, M. C., Lee, K. H., Kim, K. R., Choi, S. U., & Lee, K. R. (2006). Protoberberine alkaloids and their reversal activity of P-gp expressed multidrug resistance (MDR) from the rhizome of *Coptis Japonica* Makino. *Archives of Pharmacal Research, 29*(9), 757–761.

Wang, L., Zhang, S. Y., Chen, L., Huang, X. J., Zhang, Q. W., Jiang, R. W., et al (2014). New enantiomeric isoquinoline alkaloids from *Coptis chinensis*. *Phytochemistry Letters, 7*, 89–92.

Wang, W. C. (2018). *Thalictrum (Ranunculaceae) In China*. Beijing: Peking University Press. Chapter 4.

Xue, J. J., Jiang, C. Y., Zou, D. L., Li, B. J., Lu, J. C., Li, D. H., et al (2020). Baicalensines a and B, two isoquinoline alkaloids from the roots of *Thalictrum baicalense*. *Organic Letters, 22*(19), 7439–7442.

Xue, J. J., Wang, Y. T., Liu, F. S., Yang, H. G., Lin, B., Li, Z. L., et al (2022). Alkaloid dimers isolated from *Thalictrum baicalense* have antitumor activities. *Chinese Journal of Chemistry, 40*(15), 1831–1841.

Yang, J. Y., Chen, Z. J., Ren, Y. K., Yuan, C. L., Hu, S. H., Liu, Y. Y., et al (2025). Isoflavones and lignans with anti-inflammatory activity from *Thalictrum baicalense* Turcz. *Fitoterapia, 183* 106587.

Yang, M. L., Wang, Y. D., Fan, Z. F., Xue, Q. W., Njateng, G. S. S., Liu, Y. P., et al (2021). Chemical constituents and anti-inflammatory activity of the total alkaloid extract from *Melodinus cochinchinensis* (Lour.) Merr. and its inhibition of the NF-κB and MAPK signaling pathways. *Phytomedicine, 91* 153684.

Jinyuan Yang [a]
Zhaojing Chen [a]
Jingjing Xue [a]
Yikun Ren [a]
Zhanlin Li [a]
Dahong Li [a]
Yating Sun [b,*]
Huiming Hua [a,*]

[a] *Key Laboratory of Structure-Based Drug Design & Discovery, Ministry of Education, School of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, Shenyang 110016, China*
[b] *School of Pharmacy, Shenyang Medical College, Shenyang 110034, China*
[*] Corresponding authors.
E-mail addresses: sunyatingna@163.com (Y. Sun), huimhua@163.com (H. Hua).

Received 14 October 2025
Revised 11 February 2026
Accepted 11 February 2026

Available online 13 February 2026