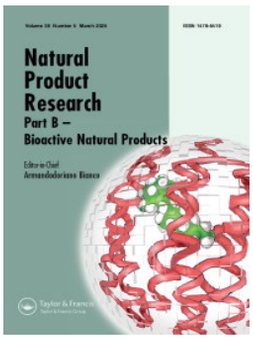

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RAPID COMMUNICATION

One anti-tumour C21 steroidal glycoside from *Cynanchum wallichii* Wight

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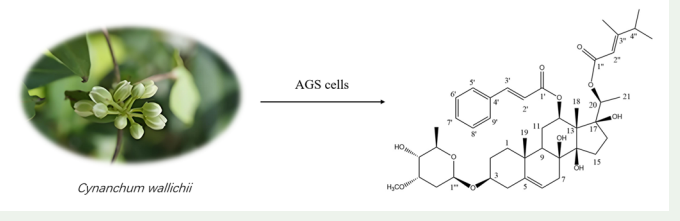
ABSTRACT

The roots of *Cynanchum wallichii* Wight is rich in C21 steroidal glycosides according to previous research. In this study, a systematic chemical study was performed on the roots of *C. wallichii*, leading to the isolation of one previously undescribed C21 steroidal glycoside compound (**1**) and a known compound, gagamine (**2**). *In vitro* bioassay indicated that compound **1** showed a strong inhibitory effect on AGS cells, with the IC_{50} value 7.8 μM.



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KEYWORDS
Cynanchum wallichii Wight; anti-tumour effect; C21 steroidal glycoside; structural identification

1. Introduction

Natural products, especially those derived from plants, have long been recognised as a wellspring of bioactive compounds with diverse therapeutic potential. *Cynanchum wallichii* Wight has been recognised to possess a certain status in the traditional medicinal realm. Previous studies have unequivocally indicated that its roots are rich in C21 steroidal glycosides (Chen et al. 2010; Zhang et al. 2022a). As a significant class of natural products, C21 steroidal glycosides have exhibited extensive potential value in anti-tumour, thus attracting extensive attention from researchers (Zhang et al. 2022b). A number of investigations have disclosed that the C21 steroidal glycoside components in plants have significant anti-tumour activities. The C21 steroidal glycosides isolated from the roots of *Cynanchum otophyllum* can induce apoptosis and

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G0/G1-phase cell-cycle arrest in HepG2 cells (Li et al. 2021). The C21 steroidal glycosides isolated from the roots of *Marsdenia tenacissima* can inhibit the proliferation of HepG2 (human hepatocellular cancer), A549 (lung cancer), and MCF-7 (human breast cancer) cells (Liu et al. 2023).

In the course of our unremitting exploration for anticancer active constituents among natural products, a systematic chemical investigation was carried out on the roots of *C. wallichii*, leading to the isolation of an unreported C21 steroidal glycoside compound (**1**) (Figure 1) and the known compound gagamine (**2**). In this paper, we report the isolation and structural identification of the isolated compounds by means of spectroscopic methods, as well as the *in vitro* bioactivity assays of these compounds against AGS tumour cells.

2. Results and discussion

Compound **1** was obtained as a white powder. The molecular formula of **1** was deduced to be $C_{44}H_{62}O_{11}$ according to its pseudo-molecular ion peak m/z 767.4361 $[M+H]^+$ (767.4365 calcd for $C_{44}H_{63}O_{11}^+$). The proton and carbon spectrum of **1** gave one anomeric proton and carbon signals at δ_H 4.84 and δ_C 93.7, respectively. NMR data and HSQC correlation determined a β-cymaropyranosyl moiety (Supplementary Table 1) compared with that in the literature (Ma et al. 2007). Acid hydrolysis experiment showed that the absolute configuration of the cymarose was *D*-from. Combined with previous studies reporting that the C21 steroidal glycoside with deoxy-sugars was the characteristic constituent of this plant, compound **1** was preliminarily deduced to be a C21 steroidal monoglycoside, which was further confirmed by the following NMR data analysis. First, benzyl proton signals δ_H 7.63 (2H, m) 7.41 (2H, m), a group of double bond signals δ_H 6.64 (1H, d, 16.0) 7.78 (1H, d, 16.0), and a carbonyl carbon signal δ_C 168.5 were all typical signals of cinnamoyl (Li et al. 2015), which was substantiated by HMBC correlations from δ_H 7.78 (H-3′) to δ_C 168.5 (C-1′), δ_C 129.5 (C-5′/9′) and from δ_H 6.64 (H-2′) to δ_C 135.9 (C-4′). Second, a group of ikemaoyl signals [δ_C 167.7, 165.9, 115.6, 39.3, 21.3, 21.3, 16.3; δ_H 5.74 (1H, brs), 2.38(1H, m), 1.07 (6H, d, 6.5), 2.10 (3H, s)] were identified from the NMR spectrum of **1** by comparing with

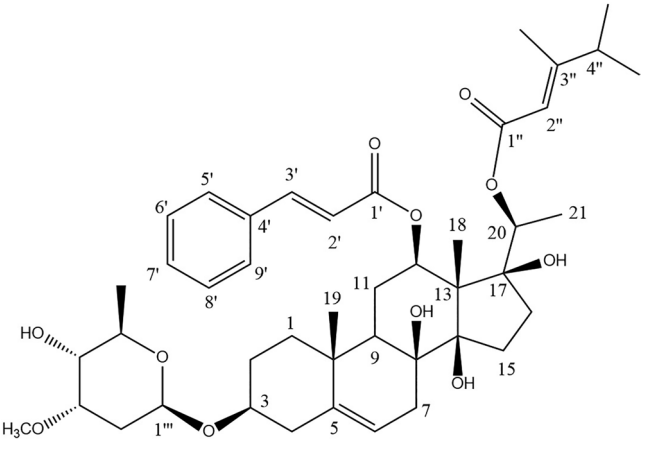

Figure 1. Chemical structure of compound **1.**

the NMR data in the literature (Li et al. 2015). Additionally, there were still 21 carbon signals remaining in the ^{13}C spectrum of **1**, suggesting that the aglycone of **1** was a C21 steroid. The structure of the aglycone moiety was established by HMBC correlation analysis and comparing NMR data with those in the literature. In the HMBC spectrum, correlation from one Me-19 (δ_H 1.17) to C-1, C-5, C-9, C-10, from Me-18 (δ_H 1.59) to C-12, C-13, C-14, C-17, and from H-6 to C-7 and C-8 afforded a typical C-21 steroidal skeleton. Among those correlations, Me-18 (δ_H 1.59) to C-12 (δ_C 75.6), C-14 (δ_C 89.2), C-17 (δ_C 88.8) and H-6 to C-8 (δ_C 75.0) determined that C-8, C-12, C-14, C-17 were oxygenated. Moreover, the chemical shift of C-20 was δ_C 75.1, indicated that the typical C-20 carbonyl for the C21 steroidal skeleton was reduced to a hydroxyl. In addition to the C-3 (δ_C 79.3), the structure of the aglycone moiety of **1** was deduced to be 12-*O*-cinnamoyl-20-*O*-ikemaoylsarcostin. HMBC correlations from H-1′ to C-12 and from from H-1′′ to C-20 determined the location of the ikemaoyl and cinnamoyl groups, respectively. Correlation from H-1′′′ of the cymarose to C-3 of the aglycone determined the location of the sugar moiety (Supplementary Figures 1-6). Therefore, the structure of **1** was established as 12-*O*-cinnamoyl-20-*O*-ikemaoylsarcostin 3-*O*-*β*-D-cymaropyranoside.

The known compound **2** was determined by comparing its NMR data with those in the literature (Mu et al. 1992).

In vitro bioassay was conducted in AGS tumour cells. The results indicated that compound **1** showed a strong inhibitory effect on AGS cells with the IC_{50} value 7.8 μM, while the positive gedunin showed an IC_{50} value 21.6 μM.

3. Conclusion

In summary, *via* the continuous exploration of natural anticancer constituents, we intensively investigated the roots of *Cynanchum wallichii* and isolated an unreported C21 steroidal glycoside compound (**1**) along with gagamine (**2**). *In vitro* biological experiments demonstrated that compound **1** exerted a significant inhibitory effect on AGS cells, potentially providing novel natural lead compounds for the development of anticancer drugs.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

Chen G, Xu N, Li ZF, Zhang QH, Wu HH, Pei YH. 2010. Steroidal glycosides with anti-tumor activity from the roots of *Cynanchum wallichii* Wight. J Asian Nat Prod Res. 12(6):453–457. doi:10.1080/10286020.2010.489821.

Li JL, Zhou J, Chen ZH, Guo SY, Li CQ, Zhao WM. 2015. Bioactive C steroidal glycosides from the roots of that suppress the seizure-like locomotor activity of zebrafish caused by pentylenetetrazole. J Nat Prod. 78(7):1548–1555. doi:10.1021/np501058b.

Li XS, Yang XM, Ding WJ, Xu ZP, Zhang CM, Long J, Liu L, Lu CY, Tang JS. 2021. New C-steroidal aglycones from the roots of and their anticancer activity. Fitoterapia. 149:104833. doi:10.1016/j.fitote.2021.104833.

Liu JL, Xu HT, Mu DD, Han X, Du TT, Wang YL, Wei XH, Chou GX. 2023. C21 steroids from the roots of *Marsdenia tenacissima*. Phytochemistry. 213:113782. doi:10.1016/j.phytochem.2023.113782.

Ma XX, Jiang FT, Yang QX, Liu XH, Zhang YJ, Yang CR. 2007. New pregnane glycosides from the roots of *Cynanchum otophyllum*. Steroids. 72(11-12):778–786. doi:10.1016/j.steroids.2007.06.001.

Mu QZ, Shen YM, Zhou QL, Wang SQ, Wu B, Zheng QT. 1992. Studies on the Constituents of *Adelostemma gracillimum*. Planta Med. 58(2):200–204. doi:10.1055/s-2006-961429.

Zhang LD, Lin YF, Huang M, Chen WB, Duan LX, Liu ZQ, Lu LL, Zhang RR. 2022a. Six C21 steroidal glycosides from *Cynanchum wallichii* Wight roots and their multidrug resistance reversal activities. Phytochemistry. 199:113172. doi:10.1016/j.phytochem.2022.113172.

Zhang X, Gao M, Rao ZL, Lei ZQ, Zeng JS, Huang ZJ, Shen CH, Zeng N. 2022b. The antitumour activity of C21 steroidal glycosides and their derivatives of Baishouwu: a review. J Ethnopharmacol. 293:115300. doi:10.1016/j.jep.2022.115300.