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# A new veratramine alkaloid from the bulbs of *Fritillaria hupehensis*

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**Abstract**

A new highly conjugated alkaloid of veratramine type, 22*S*,25*S*,5α-veratramine-7(8),12(14)-diene-3β,13β,23β-triol-6-one (**1**), was isolated from the bulbs of *Fritillaria hupehensis* Hsiao *et* K.C. Hsia. Its structure was determined on the basis of spectroscopic evidences.


*Keywords:* *Fritillaria hupehensis*; Alkaloid; Veratramine group

*Fritillaria hupehensis* Hsiao *et* K.C. Hsia, a well-known medicinal plant grown in Northwest of Hubei province, China, is used as antitussive in local folk. It has been recorded in the Pharmacopoeia of the People's Republic of China, named Hubeibeimu [1]. Phytochemical investigations had led to the isolation of 11 C-*nor*-D-homo steroidal alkaloids [2]. As a continuation of our research on the bioactive constituents from *Fritillaria* species, we reinvestigated the chemical constituents of *F. hupehensis* collected from Enshi district of Hubei Province, recently. As a result, a new highly conjugated veratramine alkaloid, named 22*S*,25*S*,5α-veratramine-7(8),12(14)-diene-3β,13β,23β-triol-6-one (**1**), was obtained.

Compound **1**, white amorphous powder from MeOH, $[\alpha]_D^{20}$ −0.006 (c 0.001, $CHCl_3$), m.p. 132.0–133.1 °C, possessed a molecular formula of $C_{27}H_{41}NO_4$ concluded from its HRFABMS (calcd. 443.3035, found 443.3042), which was consistent with the NMR data. The UV absorption peaks at 242 (4.28), 348 (3.56) nm indicated the presence of α, β-unsaturated ketene group. The IR spectrum exhibited strong absorptions due to hydroxy (3392 $cm^{-1}$) and carbonyl (1608 $cm^{-1}$) functions. The NMR spectra of **1** indicated the presence of six quaternary carbons (including one ketonic carbon, one oxygenated carbon and three olefinic carbons), nine tertiary carbons (including two oxygenated carbons and one olefinic carbons), eight secondary carbons and four primary carbons. Analysis of NMR spectra of **1**, combining with the correlation of biosynthesis between the natural products in the same plant, led to the conclusion that **1** was a C-*nor*-D-homo-steroidal alkaloid of veratramine group [3,4]. The HMBC experiment revealed

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Table 1
The $^{1}H$, $^{13}C$ NMR data and HMBC, $^{1}H$–$^{1}H$ COSY, ROESY correlations of **1** (400 MHz, in $CDCl_3$)

| No. | $\delta_H$ | $\delta_C$ | HMBC | H–H COSY | ROESY |
|---|---|---|---|---|---|
| 1α | 1.32 (m) | 37.5 | C-2, 3, 10, 19 | H-1β, 2α | H-2α, 3, 5, 9 |
| 1β | 1.61[a] (m) | | C-2, 3, 5, 10 | H-1α, 2β | H-2β, 19 |
| 2α | 2.01[a] (m) | 31.3 | C-1, 3, 4, 10 | H-1α, 2β, 3 | H-1α, 3 |
| 2β | 2.35[a] (m) | | C-1, 3, 4, 10 | H-1β, 2α | H-1β |
| 3 | 3.88 (m) | 70.6 | C-1, 2, 4, 5 | H-2α, 4α, 4β | H-1α, 2α, 4α, 5 |
| 4α | 2.88[a] (m) | 31.9 | C-2, 3, 5, 6, 10 | H-3, 4β, 5 | H-3, 4β, 5 |
| 4β | 1.73 (m) | | C-3 | H-3, 4α, 5 | – |
| 5 | 2.29 (dd, 2.7, 8.8) | 54.9 | C-4, 6, 7, 10, 19 | H-4α, 4β | H-1α, 3, 4α, 9 |
| 6 | – | 199.3 | – | – | – |
| 7 | 5.96 (s) | 114.5 | C-5, 6, 8, 9, 14 | H-9 | H-15α |
| 8 | – | 171.0 | – | – | – |
| 9 | 2.81 (br.s) | 53.8 | C-8, 10, 11, 14, 19 | H-7, 11α | H-1α, 5 |
| 10 | – | 40.3 | – | – | – |
| 11α | 2.73 (br.s) | 30.9 | C-9, 12, 14 | H-9, 11β | H-18, 19 |
| 11β | 2.19[a] (br.s) | | C-9, 12 | H-11α | – |
| 12 | – | 163.0 | – | – | – |
| 13 | – | 73.4 | – | – | – |
| 14 | – | 135.4 | – | – | – |
| 15α | 2.23[a] (m) | 22.8 | C-8, 12, 14, 16, 17 | H-15β, 16α | H-16α |
| 15β | 1.15[a] (m) | | C-14, 16, 17 | H-15α, 16β | H-16β |
| 16α | 2.02 (m) | 24.1 | C-13, 15, 17 | H-15α, 16β,17 | H-15α, 17 |
| 16β | 1.61[a] (m) | | C-13, 15, 17 | H-15β, 16α | H-15β |
| 17 | 2.37 (m) | 43.1 | C-13, 15, 16, 18, 20, 21, 22 | H-16α, 22 | H-16α, 20, 23 |
| 18 | 1.50 (s) | 21.5 | C-12, 13, 17 | – | H-11α, 20 |
| 19 | 0.59 (s) | 12.3 | C-1, 5, 9, 10 | – | H-1, 11α |
| 20 | 2.91 (m) | 29.5 | C-13, 16, 17, 21, 22 | H-21 | H-17, 18, 21, 22 |
| 21 | 1.18 (d, 7.3) | 15.4 | C-17, 20, 22 | H-20 | H-20 |
| 22 | 2.51(dd, 2.1, 7.4) | 71.0 | C-20, 21, 23, 24, 26 | H-17, 23 | H-20, 21, 24α |
| 23 | 3.74 (m) | 68.6 | C-20, 22, 24, 25 | H-22, 24α, 24β | H-17 |
| 24α | 2.20[a] (m) | 43.1 | C-22, 23, 25, 26, 27 | H-23, 24β, 25 | H-24β |
| 24b | 1.30 (m) | | C-23, 25 | H-23, 24α | H-24α |
| 25 | 1.62[a] (m) | 32.4 | C-23, 24, 26, 27 | H-24α, 26α, 26β, 27 | H-26α, 27 |
| 26α | 3.05(dd, 2.4, 8.2) | 55.3 | C-22, 24, 25, 27 | H-25, 26β | H-25, 26β |
| 26β | 2.21[a] (br.d) | | C-22, 24, 25 | H-25, 26α | H-26α, 27 |
| 27 | 0.72 (d, 8.2) | 19.2 | C-24, 25, 26 | H-25 | H-25, 26β |

[a] Overlapped.

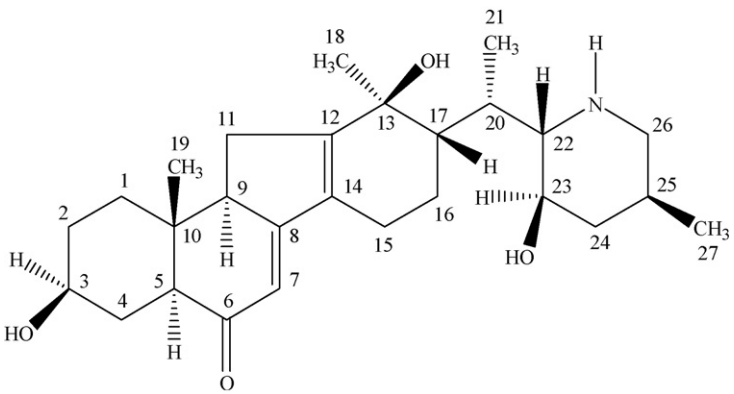


Fig. 1. The structure of compound **1**.

indicating the existence of the veratramine-7(8),12(14)-diene-6-one fragment (the correlations of H-4α/C-6, H-5/C-6, H-7/C-6, H-5/C-7, H-9/C-8, H-9/C-14, H-11α, β/C-12, H-11α/C-14, H-15α, β/C-14 and H-15α/C-12). The absence of H-17/H-23 COSY correlation and the absence of C-17/H-23, H-17/C-23 HMBC correlations suggested the 17, 23-seco group. The chemical shifts of C-13 ($\delta$ 73.4) indicated that C-13 connected a hydroxyl group. The relative stereochemistry of **1** was assigned on the base of ROESY spectrum. The protons at C-3, 5, 9, 17, 20, 22, 23 and 25 were determined to be α, α, α, β, β, β, α and α oriented, respectively. The NMR data and the correlations of HMBC, H–H COSY and ROESY were listed in Table 1. Thus, the structure of **1** was elucidated as 22*S*,25*S*,5α-veratramine-7(8),12(14)-diene-3β,13β,23β-triol-6-one (Fig. 1).

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