

A 4,5-Dioxoaporphine from the Aerial Parts of *Stephania tetrandra*

Duan Yun Si, Shou Xun Zhao, and Jing Zhen Deng

J. Nat. Prod., **1992**, 55 (6), 828-829 • DOI:
10.1021/np50084a023 • Publication Date (Web): 01 July 2004

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Chemical Society, 1155 Sixteenth Street N.W., Washington,
DC 20036

A 4,5-DIOXOAPORPHINE FROM THE AERIAL PARTS
OF *STEPHANIA TETRANDBRA*DUAN YUN SI*¹, SHOU XUN ZHAO, and JING ZHEN DENG*Phytochemistry Division, China Pharmaceutical University, Nanjing 210009, People's Republic of China*

ABSTRACT.—Chromatographic separation of the EtOH extract from the aerial parts of *Stephania tetrandra* resulted in the isolation of a novel 4,5-dioxoaporphine alkaloid, stephadione [1], together with six known alkaloids: corydione, oxonantenine, cassameridine, nantenine, cassythicine, and tetrandrine. The structure of stephadione was determined to be 6a,7-didehydro-1,2;9,10-dimethylenedioxy-4,5-dioxo-N-methylaporphine by a consideration of spectral evidence.

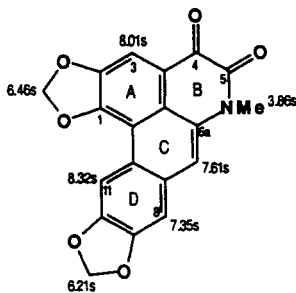
Many reports have dealt with the phytochemistry of the traditional Chinese medicine, Fen Fang Ji. This drug is the dried root of *Stephania tetrandra* S. Moore (Menispermaceae), which is widely distributed in Southern China. Twenty-one compounds, including nineteen alkaloids, have been determined (1–4). The aerial part of *S. tetrandra* appears to have escaped the attention of chemists. It was therefore thought desirable to investigate the constituents of the aerial parts of *S. tetrandra*. From the EtOH extract, one novel compound, stephadione [1], one well-known component, tetrandrine, and five other alkaloids previously unreported from *S. tetrandra* were isolated and purified.

The new optically inactive base, stephadione [1], was obtained as an amorphous red powder with mp >300°.

Its hreims exhibited a molecular ion peak at *m/z* 349, corresponding to its molecular formula of C₁₉H₁₁NO₆ (found 349.0564, calcd 349.0582). The uv spectrum had five bands at 239, 271, 312.5, 326, and 466 nm and its ir spectrum showed the presence of a conjugated ketone at 1647 and a six-membered lactam at 1588 cm⁻¹. These data suggested that 1 was a 4,5-dioxoaporphine-type alkaloid.

In the ¹H-nmr spectrum of 1, there were signals for one N-Me group at δ 3.86 and two methylenedioxy groups at δ 6.21 and 6.64. The four protons in the aromatic region resonated as four singlets at δ 7.35, 7.61, 8.01, and 8.32, indicating that both rings A and D had a methylenedioxy group and the oxygenated pattern of ring D must be at 9,10. The bonded site of the methylenedioxy group in ring A was assumed to be at 1,2, because all the aporphine compounds previously reported from natural sources possess a 1,2-oxygenation pattern (5–8). An nOe differentiation analysis further confirmed the bonded site of the oxygenation group in ring A. As no enhancement was observed through irradiation of H-11, which always appeared as a signal in the lowest field, the chemical structure of 1 was established as 6a,7-didehydro-1,2;9,10-dimethylenedioxy-4,5-dioxo-N-methylaporphine.

The six other compounds were shown to be the known alkaloids corydione (9), cassameridine (5), nantenine (5), tetran-



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¹Permanent Address: Department of Pharmacology, Jining Medical College, Jining 272113, People's Republic of China.

drine (4), and cassythicine (5), based on direct comparisons (mp, uv, ms, ^1H nmr, and co-tlc) with the respective authentic samples.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All mp's were uncorrected. Uv spectra were obtained on a Shimadzu UV-300 spectrophotometer with 95% EtOH as solvent. Ir spectra in KBr disk were recorded on Nicolet 5S XC and Perkin-Elmer 983 spectrometers. ^1H -nmr spectra were taken on JEOL FX-90Q and VARIAN XL-400 spectrometers in CDCl_3 with TMS as internal standard. Mass spectra were obtained on Nicolet FTMS-2000 and JMS DX300 spectrometers.

PLANT MATERIAL.—The aerial parts of *S. tetrandra* were collected in July 1988 in Jingdezhen, Jiangxi Province, China. A voucher specimen was deposited in the Phytochemistry Division, China Pharmaceutical University, Nanjing, China.

EXTRACTION AND ISOLATION.—Air-dried, ground, plant material was extracted exhaustively with boiling EtOH, and the extract was evaporated in vacuo to afford a residue which was extracted successively with refluxing with petroleum ether, CHCl_3 , EtOAc, and MeOH. The CHCl_3 fraction was concentrated to give a gum which was treated with 2% HCl. The insoluble mass was subjected to a column of Si gel H with an elution gradient of C_6H_6 and Me_2CO to provide two chromatographically homogeneous components, corydione, and stephadione [1]. The aqueous acidic solution was fractionated between aqueous acid and CHCl_3 . The upper layer was adjusted to pH 9 with NH_4OH and extracted with CHCl_3 . Both CHCl_3 extracts were chromatographed separately on columns of Si gel H. Stepwise elution of the columns with petroleum ether/ CHCl_3 , CHCl_3 , and $\text{CHCl}_3/\text{MeOH}$ afforded corydione, oxonantenine, cassameridine, and nantenine from the first column and cassameridine, tetrandrine, and cassythicine from

the second column.

Stephadione [1].—Amorphous red powder: mp $>300^\circ$; CHCl_3 solution showed strong green fluorescence; uv λ max (EtOH) nm (log ϵ) 239 (4.54), 271 (3.99), 312.5 (4.13), 326 (4.47), 366 ± 3 (4.13); ir ν max (KBr) cm^{-1} 3077, 3029, 2916, 1647 (conjugated carbonyl), 1588 (lactam), 1499, 1467, 1363, 1305, 1247, 1191, 1079, 1045, 939; eims m/z [M] $^+$ 349.0564 (78.3), 321 (100), 304 (31.1), 292 (16.2), 263 (19.8), 207 (8.0), 206 (62.1), 190 (14.2); ^1H nmr see text and structure.

ACKNOWLEDGMENTS

The authors thank Mr. Hao An Chen, Laboratory of Traditional Chinese Medicine, Guangdong Institute for Drug-control, China, for the identification of the plant material. Acknowledgment is also made to the National Natural Science Foundation of China for financial support of this work.

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Received 26 November 1991