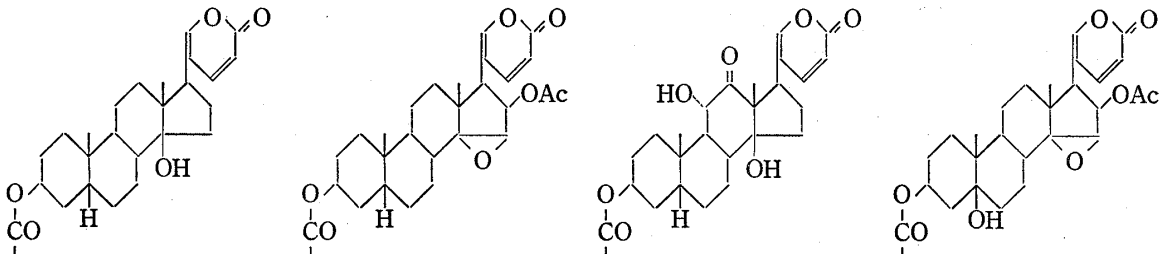

Chart 1

are being conducted in these laboratories and the details will be reported in the near future.

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Fukinotoxin, a New Pyrrolizidine Alkaloid from *Petasites japonicus*[1)]

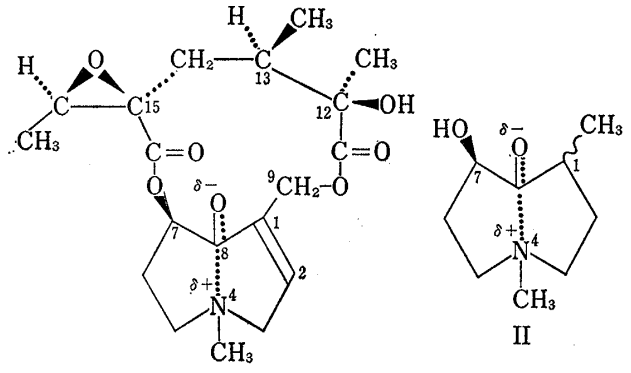
Fukinotoxin (I), a novel pyrrolizidine alkaloid, was isolated from young scape of *Petasites japonicus* and its structure has been shown to be (12*R*,13*R*,15*R*,3'*R*)-12-hydroxy-4,12,13-trimethyl-4,8-secosenec-1-enine-15-spiro-2'-(3'-methyl)oxiran with the aid of chemical and X-ray crystallographic analyses.

In the course of the studies on carcinogenic activity of pyrrolizidine alkaloids in Compositae plants,[2)] a new alkaloid, named fukinotoxin (I) which has highly cytotoxic activity,[3)] was isolated from young scape of *Petasites japonicus* MAXIM. (Japanese name: Fuki-no-toh). The present paper deals with the structural determination of (I) by discussing the result of chemical study and X-ray analysis.

(I) was isolated from the MeOH extract of the young scape using silica gel column chromatography and showed mp 129.0—131.0° (from acetone), $[\alpha]_D$ +63.8° ($CHCl_3$), $[\theta]^{21°}_{max}$ (methylcyclohexane) +12900(239 nm), +17500 (278 nm),[4)] OH(3300 cm^{-1}), and CO(1735 cm^{-1}, broad)

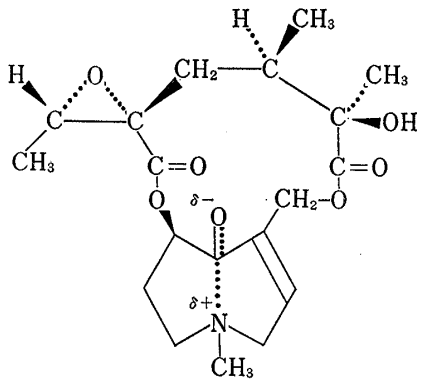
1) Part VI in the series "Studies on Constituents of Crude Drug". For Part V see 2).
2) M. Hikichi and T. Furuya, *Tetrahedron Letters*, **1974**, 3657.
3) M. Saito, Private Communication.
4) K.B. Birnbaum, A. Klasek, P. Sedmere, G. Snatzke, L.F. Johnson, and F. Santavy, *Tetrahedron Letters*, **1971**, 3421.

and is very soluble in H_2O. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum [ppm in $CDCl_3$] displayed signals at δ 1.04 (3H, d, J=8.5 Hz), 1.33 (3H, s), 1.44 (3H, d, J=7.5, 2.10 (3H, s), 3.45 (2H, d of d, J=18.5 and 15.0), 5.18 (1H, broad s), 6.16 (1H, broad s), 4.33 (1H, d, J=11.5), 5.47 (1H, d, J=11.5) and 1.80 to 3.10 (7H, complicated peaks), indicating 12-membered macrocyclic secopyrrolizidine alkaloid.[5] The hydrogenolysis and hydrolysis of (I) gave necine, (7*R*)-dihydrodesoxyotonecine (II)[2,6] which was identical with the authentic sample by direct comparison with mixed melting point (m. mp), $[\alpha]_D$ and infrared (IR) spectrum.



I

II



III

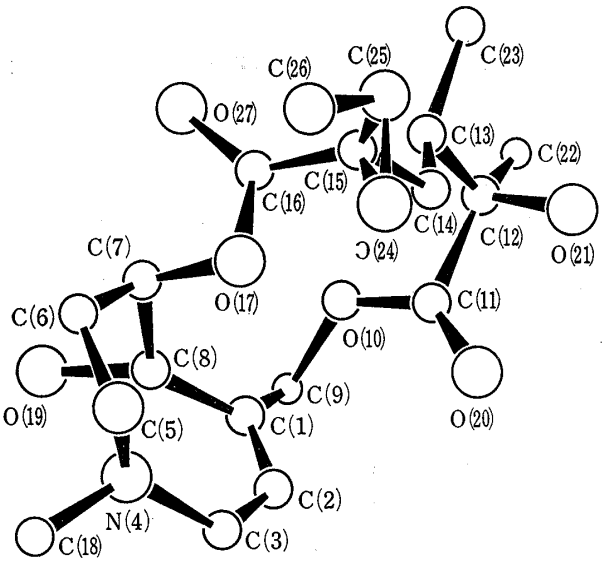


Fig. 1. Structure of Fukinotoxin (I)

Crystal data: Colorless prisms orthorhombic, space group $P2_12_12_1$ with four molecules of $C_{19}H_{27}O_7N$ in a unit cell of the dimensions a=9.252, b=24.372, and c=8.762A. Unique reflections (1595) were observed on a Rigaku four-circle X-ray diffractometer ($2\theta \leq 140°$) using Cu-Kα radiation monochromated by a graphite crystal. The intensities were corrected for Lorentz and polarization factors. The structure was solved by direct method using the Multan program[7] and completed by Fourier method. The refinement by the block-diagonal least-squares calculation gave an R value of 9.7%.

From the experimental results, the absolute molecular structure of (I) was determined to be (12*R*,13*R*,15*R*,3′*R*)-12-hydroxy-4,12,13-trimethyl-4,8-secosenec-1-enine-15-spiro-2′-(3′-methyl)oxiran, a stereoisomer of otosenine (III)[8] as shown in the Fig.

(I) seems likely to be main carcinogen in the young scape which is recently noticed as one of carcinogenic human foods[9] and the H_2O solubility and characteristic conformation of (I)

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bring up the significant problems in the carcinogenesis. The carcinogenic test of (I) is now in progress.

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