Aust. J. Chem., 1976, **29**, 229–30

The Occurrence of Senkirkine in *Tussilago farfara*

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Abstract

The medicinal herb, *Tussilago farfara* L., is shown to contain the hepatotoxic pyrrolizidine alkaloid, senkirkine.

Tussilago farfara L. is a herb of the tribe Senecioneae, family Compositae, species of which commonly contain hepatotoxic pyrrolizidine alkaloids.[1] We have investigated the alkaloids present in the young (pre-blooming) flowers of *T. farfara* which are used for medicinal purposes in Japan and presumably in China where the drug is prepared.

We find that the alkaloid content is low (0·015%) and that the only constituent detectable by gas chromatography–mass spectrometry is senkirkine. Senkirkine has previously been isolated from several other genera of the tribe Senecioneae[1–3] as well as from a *Crotalaria* species (family Leguminosae),[4] and is known to be hepatotoxic.[5]

An earlier tentative identification of senecionine in the roots and flowering stems of *T. farfara* from Norway was made on the basis of comparative R_F values.[1] Since senkirkine and senecionine have similar R_F values in the system used, it is possible that the alkaloid encountered in the Norwegian material was also senkirkine.

Additional interest in the present finding relates to the use of *T. farfara* as an alternate larval food plant by the cinnabar moth [*Callimorpha jacobaea* L. (Arctiidae)] which normally feeds on the pyrrolizidine alkaloid-containing species *Senecio jacobaea* L.[6] The cinnabar moth, and other Arctiids, appear to require pyrrolizidine alkaloids which are stored in the body tissues as predator deterrents[7,8] and metabolized by the males of some Arctiid species to dihydropyrrolizine derivatives which are secreted on the moth's coremata.[9]

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Experimental

The n.m.r. data were measured in $CDCl_3$ solution, with tetramethylsilane as internal reference, on a Varian T-60 spectrometer. Mass spectra were measured with a Varian MAT-111 gas chromatograph–mass spectrometer (g.c.–m.s.) with samples introduced by direct insertion or through a 6 ft by 1/8 in. glass column packed with 3% OV17 on Gaschrom Q mesh size 100–120. The carrier gas was helium flowing at 15 ml/min and the column temperature was programmed from 70°C to 230°C at 6°/min. The thin-layer plates were prepared from a slurry of silica gel (Merck Silica Gel G) and 0·1 N NaOH, and developed with methanol or chloroform–methanol–concentrated ammonia (85 : 14·5 : 0·5).

Extraction of Tussilago farfara

Dried, milled young flowers (the herbal drug as imported from China into Japan; 1030 g) were extracted with 0·5 N H_2SO_4. One-tenth of the acid extract was made alkaline with aqueous ammonia and extracted with chloroform for determination of free base content. The remainder was made 2 N with respect to H_2SO_4, reduced with zinc for 3 h, filtered, made alkaline with aqueous ammonia and extracted with chloroform. Titration of aliquots of the two crude base fractions with standard 4-toluenesulphonic acid in chloroform solution showed that the plant contained 0·015% free base and no *N*-oxide.

Examination of the crude alkaloid extracts by g.c.–m.s. established that there was essentially only one component, retention time 26·5 min, which exhibited the same mass spectrum as authentic senkirkine (see below).

Characterization of Senkirkine

The crude base was crystallized from acetone to give colourless prisms (25 mg), m.p. 196–197°, undepressed on admixture with authentic senkirkine, R_F 0·29 (MeOH), 0·51 ($CHCl_3$–MEOH–NH_3) (senkirkine, R_F 0·29 and 0·51 respectively). Mass spectrum (*m/e* (*I*%)): $M+1^+$ 366 (2), M^+ 365 (3), 337 (4), 321 (6), 294 (10), 266 (18), 250 (16), 222 (16), 211 (15), 168 (46), 167 (26), 153 (57), 151 (59), 149 (100), 123 (47), 122 (40), 110 (74), 83 (58), 82 (63), 81 (60), 71 (50), 70 (59), 69 (39). Authentic senkirkine gave an identical mass spectrum including the M+1 peak which we find present in the mass spectra of several pyrrolizidine alkaloids and their esterifying acids measured in the Varian MAT-111 spectrometer.

N.m.r. spectrum (60 MHz, $CDCl_3$): δ 0·91 (3H, d, $CH_3CH<$); 1·35 (3H, s, $CH_3C(OH)$; 1·91 (3H, d, $CH_3CH=$); 2·11 (3H, s, NCH_3); 5·01 (1H, m, H7); 4·38 5·44 (2H, AB quartet, H9); 6·14 (1H, t, H2), identical in all essential respects with the spectrum reported by Briggs *et al.*[10]

Acknowledgment

We thank Professor R. C. Cambie, University of Auckland, for an authentic sample of senkirkine.

Manuscript received 9 September 1975

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