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PLANT ANTITUMOUR AGENTS. XII. TEXENSINE, A NEW PEPTIDE ALKALOID FROM COLUBRINA TEXENSIS[1,2]

M. C. Wani*, H. L. Taylor and M. E. Wall
Chemistry and Life Sciences Laboratory
Research Triangle Institute
Research Triangle Park, N. C. 27709

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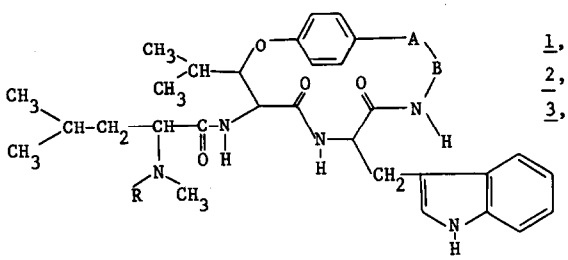
Recently, a number of peptide alkaloids have been isolated from the plants of the Rhamnaceae family.[3,4] In the course of our continuing study of Colubrina texensis (Gray) (Rhamnaceae) for tumour inhibitory substances, we have isolated a new peptide alkaloid texensine (1).[5]



1, A-B = CH = CH, R = CH_3
2, A-B = CH_2-CH_2, R = CH_3
3, A-B = CH = CH, R = H

The alcoholic extract of the dried aerial parts of the plant was partitioned between chloroform and water and the residue from the chloroform layer was partitioned between 10% aqueous methanol and petroleum ether. Chromatography of the residue from the aqueous methanol layer on Florisil using 25% methanol in chloroform followed by repeated preparative tlc on silica gel (15% acetone in chloroform) and crystallization from ethyl acetate gave texensine (1) (0.0005%), M^+ at m/e 573.3318, calcd. for $C_{33}H_{43}N_5O_4$, m/e 573.3315; mp 249-252°; $[\alpha]_D^{25}$ - 144° (C 0.50, $CHCl_3$). The infrared spectrum of texensine showed absorption bands at 3475, 3385 (NH), 1685 (amide I) and 1495 (amide II) cm^{-1} suggesting a peptide.

The structure of texensine was deduced from its mass spectrum (Figure 1) which showed the characteristic peptide decomposition pattern.[6] The molecular compositions of fragment ions were determined by high-resolution mass spectroscopy. Thus the most intense peak at m/e 114 ($C_7H_{16}N$, Chart 1) corresponding to the ion 4 indicated that the basic terminal amino acid was N,N-dimethylleucine (5).[4] This was further supported by the ion at m/e 516 ($M-C_4H_9$) and the presence of nmr signals at δ 2.27 [S, 6 $N(CH_3)_2$] and 0.99 [d, 6, J = 6.5H_z, $HC(CH_3)_2$].

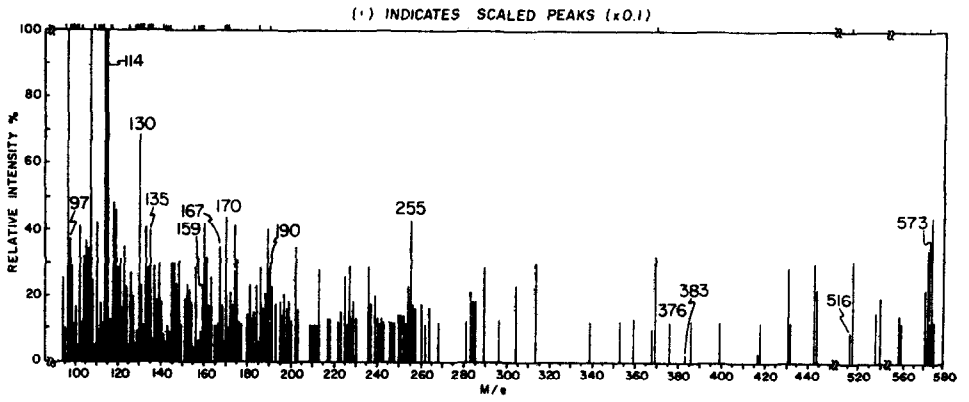


Figure 1. Mass Spectrum of Texensine

The peaks at m/e 130 (C_9H_8N), 159 ($C_{10}H_{11}N_2$), and 170 ($C_{11}H_8NO$) corresponded to ions 6, 7, and 8, respectively and are typical for tryptophan (9) containing peptide alkaloids.[7] The presence of tryptophan moiety was further confirmed by the absorption maxima at 281 and 290 nm in the ultraviolet spectrum of texensine (1).

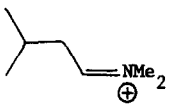
The peak at m/e 97 (C_6H_9O) corresponding to the ion 10 suggested the presence of β-hydroxyleucine (11) moiety in the molecule. This was further substantiated by the presence of a pair of doublets ($J = 6H_z$) centered at δ0.89 and 1.24 due to the methyl groups of this moiety.

Finally the peak at m/e 135 (C_8H_9NO) corresponding to the ion 12 suggested the presence of p-hydroxystyrylamine (18) moiety which is characteristic of these peptide alkaloids.[4]

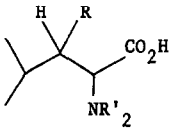
The joining of the four units--N,N-dimethylleucine (5), tryptophan (9), β-hydroxyleucine (11), and p-hydroxystyrylamine (18)--was evident from other fragmentation peaks. Thus the peak at m/e 190 ($C_{12}H_{16}NO$) corresponding to the ion 13 showed that the phenolic oxygen was etherified with β-hydroxyleucine (11). The ion at m/e 376 ($C_{23}H_{26}N_3O_2$) corresponding to the formula 14 showed that the styrylamine was acylated by the tryptophan carboxyl. The two ions at m/e 283 ($C_{17}H_{19}N_2O_2$) and 255 ($C_{16}H_{19}N_2O$) represented by formulas 15 and 16 respectively indicated that β-hydroxyleucine and tryptophan were directly linked to complete the macrocyclic ring. The ion at m/e 167 ($C_9H_{15}N_2O$) corresponding to the formula 17 proved that N,N-dimethylleucine was attached to the macrocyclic ring through the nitrogen of β-hydroxyleucine.

In agreement with the assigned structure hydrogenation of 1 gave dihydrotexensine (2) (Required for $C_{33}H_{45}N_5O_4$: m/e 575. Found: m/e 575) which upon acid hydrolysis gave p-tyramine.[8]

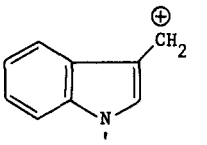
Chart 1



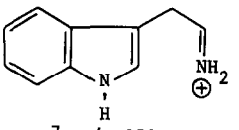
4 m/e 114



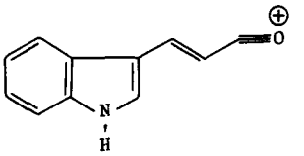
5, R=H, R'=Me
11, R=OH, R'=H



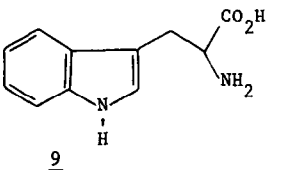
6 m/e 130



7 m/e 159



8 m/e 170



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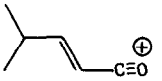
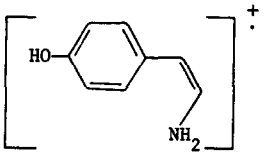
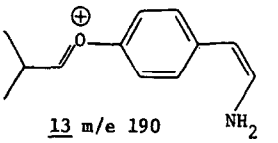


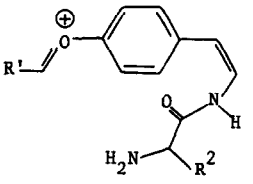
10 me/97



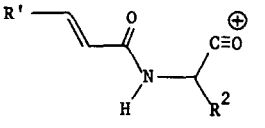
12 m/e 135



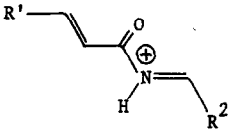
13 m/e 190



14 m/e 376

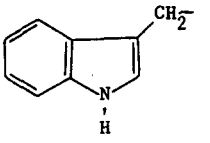


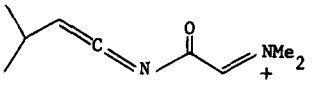
15 m/e 283



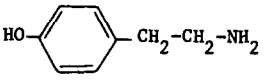
16 m/e 255

In 14, 15, and 16; R' =  and R^2 =





17 m/e 167



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It appears that texensine is an N-methylated derivative of homoamericine (3).[9] It should, however, be pointed out that the latter has only been reported as a contaminant (4%) of americine and has never been isolated in pure state.[9]

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