AN INVESTIGATION OF THE ALKALOIDS OF Ammothamnus lehmanni

THE STRUCTURE OF LEHMANNINE

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UDC 547.944/945

The present paper gives the results of an investigation of the alkaloids in the organs of Ammothamnus lehmanni in various periods of the development of the plant (Table 1) collected in the Bukhara oblast of the Uzbek SSR.

TABLE 1. Dynamics of the Accumulation of Alkaloids in the Plant Ammothamnus lehmanni Bge.

Time of collection	Phase of development	Organ investigated	Total %	Alkaloids found
Young plant	6-week	Epigeal part	1.56	Matrine N-oxide, sophocarpidine
15.V 1972	Flowering	Leaves	2.2	Sophocarpine, cytisine, lehmannine, sophocarpidine
		Stems	1.47	Matrine N-oxide. Sophocarpine, lehmannine, matrine, and N-oxide were isolated.
		Root	0.72	Matrine N-oxide, sophocarpidine
10.VI 1972	Fruit-bearing	Epigeal part	1.6	Matrine N-oxide, cytisine, sophocarpine, lehmannine, matrine, sophocarpidine
1.VII 1972	Ripening of the fruit	Epigeal part	1.0	Matrine N-oxide, cytisine, sophocarpine, lehmannine, matrine, sophocarpidine
10.VII 1972	Ripening of the fruit	Epigeal part	0.6	Matrine N-oxide, cytisine, sophocarpine, lehmannine, matrine, sophocarpidine
		Epigeal part (March, 1973)	1.3	Matrine N-oxide, cytisine, sophocarpine, lehmannine, matrine, sophocarpidine
June, 1970	Fruit-bearing	Epigeal part (April, 1972)	1.5	Matrine N-oxide, cytisine, sophocarpine, lehmannine, matrine, sophocarpidine
		Root	0.35	Matrine N-oxide. Sophocarpidine
June, 1970	Ripe fruit	Seeds	3.74	Matrine N-oxide, sophocarpidine, cytisine, lehmannine, matrine, sophocarpine.

V. I. Lenin Tashkent State University. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 377-380, May-June, 1975. Original article submitted February 1, 1974.

TABLE 2. Change in the Alkaloid Content on Storage

Plant	Time of analysis	Alkaloid content, %		
		Sophocarpine	Matrine N-oxide, sophocarpidine	other alkaloids
Ammothamnus Lehmanni (coll. (1970)	1972 April	59	40	1
Ammothamnus Lehmanni	1973 March	11	88	1

In the periods of development of the plant considered we found no pachycarpine, which has been found in this plant previously [1]. Apparently, this alkaloid is synthesized in a later period. Furthermore, it has been shown that when the plant is stored the alkaloids are oxidized to the N-oxides (Table 2).

In the investigation of the combined alkaloids, apart from known alkaloids we isolated a new base which we have called lehmannine. It has mp 93-94° C, $[\alpha]_D^{24}$ + 37.03° (c 0.54; ethanol), $C_{15}H_{22}ON_2$, and forms a monopicrate with mp 144-145° C.

The IR spectrum of lehmannine showed absorption bands in the 2680, 2750, 2770, and 2180 cm^{-1} regions, which are characteristic of trans-quinolizidine and in the 1650 cm^{-1} region characteristic of a six-membered lactam.

The form of the bands of the stretching vibrations of the >N–CO group of lehmannine differs sharply from those for sophocarpine [2], where these signals are found in the form of two strong bands at 1625, 1680 cm^{-1}; in lehmannine, a single strong band appears.

The UV spectrum of lehmannine lacks the characteristic absorption for the (–CH=CH–C=O) chromophore, and only a weak inflection is observed at 255-260 nm. Consequently, in this base the double bond is isolated from the lactam.

The mass spectrum of lehmannine has, in addition to the peak of the molecular ion (M^+ 246) (100 %), confirming the composition of the alkaloid, peaks of ions with m/e 245 (M–1), (62 %), 232, 217, 203, 190, 188, 177, 159, 150, 136, 122, 110, 98, 97, 96, 83, 55, which are characteristic for alkaloids of the matrine series with one double bond in ring D [3].

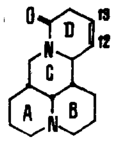
In the NMR spectrum of lehmannine, the signals of two olefinic protons in the 5.6-5.9 ppm region with close values of the chemical shifts form a second-order spectrum. In the 4.2-4.5 ppm region there are the signals of two other protons which, by analogy with the spectra of lactam-containing alkaloids of the matrine series, are assigned to the H_{17e} and H_{11} protons [4].

At 2.95 ppm there is a signal in the form of a triplet the splitting of which is due to spin–spin coupling constants of 12 Hz and 11 Hz. The very small number of spin–spin couplings shows that this signal is due to the H_{17a} proton. In the 2.60-2.85 ppm region there are the signals of two equatorial protons H_{2e} and H_{10e} present in the α-position to the N_1 nitrogen. The signals of the other protons form an unresolved multiplet in the 2.1-1.0 ppm region.

It follows from double-resonance experiments that the olefinic protons are connected by spin–spin coupling with H_{11}. Consequently the double bond is located in the $C_{12,13}$ position in ring D.

The position of the H_{17a} signal in weaker fields as compared with the corresponding signals in the spectra of allomatrine derivatives showed that this base belongs to the matrine series. In actual fact, when lehmannine was hydrogenated over Raney nickel it absorbed 1 mole of hydrogen and formed matrine.

Thus, the structure of 12,13-dehydromatrine may be proposed for lehmannine.



EXPERIMENTAL METHOD

The UV spectrum was taken on an SF-4-A instrument (in methanol), the IR spectrum on a UR-10 instrument (in the form of a film), the mass spectrum on an MKh-1303 instrument, and the NMR spectrum on a Varian XL-100-15 instrument (carbon tetrachloride).

For paper chromatography we used "Leningradskaya No. 2" chromatographic paper (fast) and the following solvent systems: 1) butan-1-ol–water–hydrochloric acid (100 : 27 : 15) and 2) butan-1-ol–5% acetic acid (1 : 1); for chromatography in a fixed thin layer we used KSK and Merck silica gels and, in addition, the solvent systems 3) chloroform–benzene–methanol (20 : 4 : 3) and 4) chloroform–cyclohexane–methanol (20 : 5 : 3). The spots were revealed with Dragendorff's reagent and with iodine vapor.

Determination of the Amount of Alkaloids in the Plant. The air-dry plant (collected in May, 1972) (100 g) was extracted with methanol for 15 h in a Soxhlet apparatus. The methanol was distilled off and the residue was dissolved in 15% sulfuric acid; the solution was washed with chloroform to eliminate ballast substances, brought to pH 9 with 25% ammonia, and exhaustively extracted with chloroform.

The extract was dried and the solvent was distilled off, giving 2.2 g (2.2%) of total alkaloids.

Separation of the Total Alkaloids. The total alkaloids (2.2 g) were dissolved in 15% sulfuric acid and the solution was washed with chloroform. Then the acid layer was brought to pH 9 with 25% ammonia and exhaustively extracted with petroleum ether, benzene, and chloroform. Yields: petroleum ether fraction 0.7 g; benzene fraction 0.3 g; and chloroform fraction 1.2 g.

All three fractions were chromatographed in system 4 on a fixed thin layer of silica gel. The petroleum ether fraction contained mainly sophocarpine, and the chloroform fraction mainly matrine N-oxide and sophocarpidine. Seven alkaloids were found in the benzene fraction (sophocarpine, sophocarpidine, lehmannine, matrine, matrine N-oxide, cytosine, and a base with R_f 0.59).

Separation of the Benzene Fraction. On each of 20 plates (200 × 200 mm) with a fixed layer of silica gel was deposited 7 mg of the benzene fraction, and chromatography was performed in system 4. Then the plates were dried and sprayed with Dragendorff's reagent. The zones corresponding to the new alkaloid were collected. The alkaloid was extracted from the sorbent with methanol, 25% ammonia was added, and the methanol was distilled off. The residue was treated with petroleum ether, and from this extract lehmannine was obtained with the formula $C_{15}H_{22}ON_2$, mp 93-94° C (petroleum ether), mol. wt. 246 (mass spectrometry). Yield 70 mg (3.18% of the total alkaloids).

SUMMARY

1. The qualitative and quantitative composition of the combined alkaloids from the leaves, stems, seeds, and roots of Ammothamnus lehmanni Bge. according to its vegetation periods have been studied.

2. It has been found that the young plant contains predominantly the N-oxide forms of the matrine alkaloids, and as the plant develops these are reduced to the free bases.

3. A new base lehmannine, $C_{15}H_{22}ON_2$ has been isolated for which 12,13-dehydromatrine is proposed as the most probable structure.

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