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ISOLATION OF ROEMERINE USING ION-EXCHANGE RESINS

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Roemerine from Roemeria refracta D. C. [1] possesses valuable pharmacological properties [2].

We have studied the possibility of isolating roemerine both from the dry plant and from the fresh plant R. refracta using cation-exchangers.

The comminuted air-dry plant (100 kg) was extracted with 1% hydrochloric acid at 80–90° C by the counter-current-battery method. 1200 *l* of extract was filtered through a suction funnel and passed through a battery of three adsorbers connected in series. Each adsorber was charged with 1.5 kg of air-dry KU-1 cation-exchanger in the H-form.

The alkaloid saturated columns were washed with water and the alkaloids were desorbed with a 1.5% solution of ammonia in 85% ethanol. The amount of eluate was 45 *l*. The eluate was evaporated in vacuum.

The alkaloids were extracted from the aqueous residue with ether (20 *l*). The ether was distilled off. This gave the combined alkaloids, which were treated with hydrochloric acid, forming 19.6 g of roemerine hydrochloride (0.020% of the weight of the raw material). From the batch of raw material indicated, extraction with chloroform by the usual method yielded 0.07% of combined alkaloids and from these roemerine hydrochloride was obtained (0.021% on the weight of the raw material). The results obtained in the treatment of the fresh plant R. refracta proved interesting. 100 kg of the plant (3–4 hr after gathering) was ground in a two-roll crusher and extracted under the same conditions as the air-dry plant. On air-drying, the fresh plant decreased in weight by approximately five times.

From 100 kg of the fresh plant we isolated 41.5 g of combined alkaloids and from this, by treatment with hydrochloric acid we obtained 22.1 g of roemerine hydrochloride. Consequently, the yield of combined alkaloids is 0.21% and that of roemerine hydrochloride 0.11% of the weight of the raw material calculated to the air-dry plant (100 kg of fresh plant gives 20 kg of air-dry material).

The marked difference in the yield of roemerine isolated from the freshly-prepared and dried plant (of one and the same batch) can apparently be explained by chemical processes taking place on drying. Consequently, the production of roemerine can be organized directly from the fresh plant R. refracta.

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THE ALKALOIDS OF THALICTRUM ISOPYROIDES. STRUCTURE OF THALISOPINE

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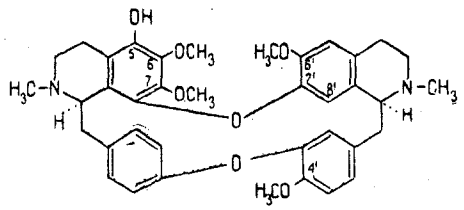
From the roots of Th. isopyroides collected in Zarkent (Tashkent Oblast), we have isolated thalicmine and thalicminine, and from the roots collected in Kaplanbek we have isolated kryptopine, thalisopine, and a new alkaloid thalisopidine. The mother liquors have been shown chromatographically (TLC) to contain O-methylthalisopine.

Thalisopidine $C_{37}H_{40}N_2O_7$ (I) forms needle-like crystals with mp 215–216° C (acetone), $[\alpha]_D^{19}$ −9° (c 0.96; ethanol). Its IR spectrum—λ_{max} 285 mμ (log ε 4.04)—is characteristic for benzyltetrahydroisoquinoline bases; IR spectrum: 3540–3300 cm^{-1} (hydroxy group); NMR spectrum (JNM-4H-100/100 MHz, τ scale): 7.56 (3H), 7.51 (3H)—two N-methyl groups—, 7.04 (3H), 6.70 (3H), and 6.30 (3H)—three methoxy groups—3.6–2.8 (9H)—aromatic protons. The methylation of (I) with diazomethane yielded the O,O-dimethyl ether with mp 238–239° C. These results show that substance (I) has the following developed formula: $C_{32}H_{23}(N{-}CH_3)_2(OCH_3)_3(OH)_2(-O-)_2$.

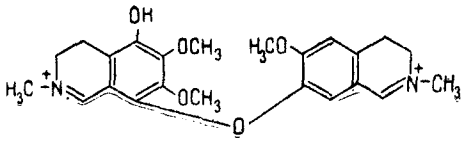
As was shown earlier [1], thalisopine $C_{38}H_{42}N_2O_7$ (II) belongs to the bisbenzylisoquinoline bases. Its IR spectrum has a band at 3500–3400 cm^{-1} (hydroxy group); in the spectrum of O-acetyl-(II) (III) there is the band of a phenol ester at 1770 cm^{-1}. When (II) was methylated with diazomethane, amorphous O-methyl-(II) with mp 163–166° C (decomp.); $[\alpha]_D^{19}$ −54° (c 1.0; chloroform), was obtained. The NMR spectrum of (II) has the signals of the protons of two N-methyl groups at 7.57 and 7.52. The signals of the protons of OCH_3 groups appear at 7.00 (C-7), 6.71 (C-6'), 6.30 (C-6), and 6.14 (C-4'). The one-proton signal at 4.90 is due to the proton of the hydroxy group. In the weak-field region there are the signals of nine aromatic protons at 3.69; 3.62; 3.43; 3.23; 3.15; 2.94. The signal at 3.69 relates to the C-8' proton. In the spectrum of (III) the signal of the three protons of a CH_3—COO group appear at 7.75.

Since the methoxy group in position 6' resonates in the strong field, the two asymmetric atoms possess the same configuration [2]. When thalisopine was decomposed with sodium in liquid ammonia, L-6-methoxy-1-(4'-methoxybenzyl)-2-methyltetrahydroisoquinoline was obtained [1]. Consequently, thalisopine has the L,L-configuration.

In the mass spectrum of thalisopine (II), the peak of the molecular ion with m/e 638 makes up 11% of the main peak. The peak with m/e 206 (100%) corresponds to the doubly-charged ion *a*. The splitting off of dimethyl ester from the ion *a* leads to a fragment with m/e 183 (17). Fragment *a* corresponds to a singly-charged ion radical with m/e 412 (89). The latter, losing a methyl radical, gives a fragment with m/e 397 (38). In addition, the peaks of ions with m/e 221 (18), 174 (18), 173 (29), 172 (89), 90 (9), 89 (20) are recorded.



II



a

On the basis of what has been said above, we proposed for thalisopine structure (II) as the most probable.

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INVESTIGATION OF GLOBULIN A

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From the seeds of the type 108-F cotton plant we have isolated by chromatography on DEAE-cellulose a homogeneous globulin component which we have called globulin A. The same component was obtained from Acala glandless [1] as acalin A, and its homogeneity was shown. We have confirmed the homogeneity of globulin A by electrophoresis in polyacrylamide gel and by chromatography on DEAE cellulose.

The molecular weight was determined by gel filtration through Sephadex G-200 (column 2.5 × 50 cm) [2]. The protein was dissolved and eluted with 1M sodium chloride solution (pH 7.6). To construct the calibration curve, we used the proteins γ-globulin, blood serum albumin, hemoglobin, and ribonuclease. The elution curves were constructed after the determination of the amount of protein on an SF-4a instrument. The molecular weight of globulin A proved to be ≈170 000.

The N-terminal amino acids were determined by the fluorodinitrobenzene method [3]. A solution of 10 mg of globulin A in 5 ml of 0.1 M ammonium acetate (pH 8.7) was treated with 0.2 g of FDNB and the mixture was stirred at 40° C for 2 hr. The excess of reagent was eliminated with peroxide-free ether. To eliminate the dinitrophenol, the reaction mixture was dialyzed against water and freeze-dried. The dry FDN-protein was hydrolyzed in tubes with 5.7 N