

A STUDY OF THE ALKALOIDS OF KIRGHIZ OPIUM

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At the present time, more than 40 alkaloids have been isolated from various types of opium. In an investigation of the Kirghiz poppy, the authors were mainly occupied with the development of a method for the quantitative isolation of the main opium alkaloids [1]. The mother liquors from Kirghiz opium have not been studied previously, and therefore we have investigated the opium raw material and the first mother liquor after the separation of the morphine and narcotine obtained from the Chimkent pharmaceutical chemicals factory.

I. The opium raw material was extracted with water and then with acid. This gave 21.8% of combined alkaloids, from which, by virtue of their basicities and by chromatography, morphine, codeine, thebaine, papaverine, narcotine, cryptopine, protopine, and also bases with mp 267-268°C and 263°C were isolated. The two latter alkaloids were nonphenolic (mol. wts. 299 and 313) and their IR spectra and mass spectrometric decompositions resembled those of alkaloids of the morphine type [2].

II. Kirghiz opium gives the red color reaction characteristic for papaverrubine bases [3]. Since the alkaloids of this type are sensitive to the action of acids, the extraction of the opium was carried out with organic solvents by Pfeifer's method [4]. This gave 20% of total bases (calculated on the moist opium), and from them were isolated morphine, codeine, thebaine, narcotine, papaverine, xanthaline, and a base with mp 187-189°C. The physicochemical properties of this base are similar to those of porphyroxine [5]. All the known alkaloids with the exception of porphyroxine were shown to be identical with authentic samples in respect to melting point, IR spectra, and TLC.

III. From the ethanolic-ammoniacal mother liquors remaining after the extraction of the morphine and narcotine, a nonphenolic base with mp 138-139°C was obtained by chromatography on silica gel. The substance gives one spot on TLC in various solvent systems and has a positive reaction for a methylenedioxy group with gallic acid. The IR spectrum lacks absorption bands of hydroxy and carbonyl groups, and the UV spectrum of the base is characteristic of alkaloids of the tetrahydroberberine series [6]. The nature of the fragmentation of the alkaloid on electron impact shows that the methylenedioxy group is located in ring A and two methoxy groups in ring D of the tetrahydroberberine skeleton [7]. The NMR spectrum shows the presence of four aromatic protons resonating in the τ 3.44-3.74 region, two protons of a methylenedioxy group (τ 4.33, singlet), and six protons of two methoxy groups (two three-proton singlets at τ 6.32 and 6.35). The protons at C₈ appear in the form of a characteristic AB quartet at τ 6.03 and 6.73 ($J = 16$ Hz). The other protons are found in the τ 6.60-7.70 region.

What has been said above shows that our base is identical with *l*-canadine, which was confirmed by comparing the IR spectra of tetrahydroberberine and our base, taken in chloroform. This is the first time that this alkaloid has been isolated from opium. It is interesting to note that the canadine precursor cryptopine has also been found in Kirghiz opium.

EXPERIMENTAL

Five hundred grams of opium was extracted with water (5 × 2 l). The extract was evaporated to 1 liter and diluted with isopropanol (600 ml) and 240 ml of a mixture of ammonia solution and isopropanol (1 : 1) was added to the solution over 1 h to give pH 9.2. The precipitate of morphine and narcotine that

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deposited (25 g) was filtered off with suction, and the alkaloids were extracted from the filtrate with chloroform. The chloroform solution was extracted with citrate-phosphate buffer solutions at pH values from 8 to 2. This gave eight fractions which were chromatographed on silica gel. The fractions with pH 8 and 7 yielded morphine, that with pH 5 codeine and a base with mp 267–268°C, that with pH 4 codeine, protopine, and thebaine, that with pH 3 papaverine, a base with mp 263°C, thebaine, and cryptopine, and that with pH 2 thebaine and papaverine. The remaining chloroform extract consisted of narcotine and papaverine. The total weight of bases from the eight fractions was 55 g. After its extraction with water, the opium residue was treated with 0.5% sulfuric acid and the alkaloids were extracted from the latter by means of KU-2 ion-exchanger. This gave a total of 29 g of alkaloids from which narcotine, papaverine, and morphine were isolated by chromatography on silica gel.

The base with mp 267–268°C from the ethereal-chloroformic eluates crystallizes from ethanol and is insoluble in water and alkalis. UV spectrum: $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$ 214, 245 inflection, 287 nm (log ϵ 4.30; 3.36; 3.29). IR spectrum, cm^{-1} : 3280 (active hydrogen); mass spectrum: 299 (M) (100%), 284 (6), 282 (7), 270 (3), 256 (5), 242 (7), 229 (18), 214 (6), 202 (9), 188 (9), 175 (4), 162 (20), 137 (6), 124 (20), 71 (18), 69 (19), 57 (30), 43 (22).

The base with mp 263°C was obtained from the chloroformic eluates; it crystallizes from ethanol and is insoluble in water and alkalis. UV spectrum: $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$ 243 inflection: 283 nm (log ϵ 3.75; 3.27). IR spectrum, cm^{-1} : 3320, 1675; mass spectrum: 313 (M) (100%), 298 (2), 270 (4), 256 (5), 242 (3), 229 (13), 214 (9), 200 (4), 188 (11), 178 (6), 175 (3), 161 (3), 138 (4), 115 (3), 70 (9), 58 (6).

178 g of opium was dried to constant weight and was extracted with ether, into which the narcotine and papaverine passed. Then the opium was made alkaline with a solution of sodium carbonate, and further alkaloids were extracted with ether. The second ethereal extract was shaken with citrate-phosphate buffer, pH 6.2, and with tartaric acid. This gave three fractions: a buffer solution (I), a tartaric acid extract (II), and an ethereal extract (III), from the last of which 5.5 g of combined bases was obtained. The buffer solution I was extracted with ether and with chloroform to give 6.1 g of ethereal and 3 g of chloroformic alkaloids. From the ethereal alkaloids thebaine, cryptopine, and protopine were isolated.

The chloroform extraction of the tartaric acid fraction II gave 5.3 g of total alkaloids from the acid solution and 2.6 g from the solution after it had been made alkaline. The separation of the 5.3 g of combined alkaloids on alumina yielded narcotine and papaverine. The mother liquors after the separation of the narcotine were treated with acetone, which precipitated crystals of xanthaline with mp 205–206°C (chloroform-ethanol, 1 : 1); hydrochloride with mp 200°C; picrate with mp 201–203°C.

The combined alkaloids (2.6 g) from the alkaline solution were separated on alumina. The ethereal eluates yielded porphyroxine with mp 187–190°C, which gave a red color reaction with mineral acids and dissolved in alkaloids. IR spectrum, cm^{-1} : 3460, 2925, 2835, 1600, 1518, 1468, 1375, 1330, 1290, 1255, 1220, 1200. Mass spectrum (main peaks): 371 (M) (75%), 356 (100), 179 (55).

The total amount of bases extracted by ether was 22.5 g. Then the opium was extracted with chloroform and the latter was distilled off. This gave 13.2 g of combined alkaloids, consisting of 11 g of morphine and 2 g of codeine.

The alcoholic ammoniacal mother liquor (400 ml), by passage through a column containing KU-1 ion-exchange resin, yielded 35 g of combined alkaloids. The fraction soluble in benzene (7 g) was separated on silica gel. The ethereal eluates deposited a substance crystallizing from ethanol in the form of thin lemon-yellow prisms and darkening in the air, readily soluble in acids, acetone, ether, chloroform, and carbon tetrachloride, and insoluble in alkali $[\alpha]_{\text{D}}^{28} - 222^\circ$ (c 1.529; acetone); UV spectrum, λ , nm: inflection 228, min 255, max 288 (log ϵ 3.91, 2.83, 3.51, respectively); mass spectrum 339 (M) (100%), 176 (8), 174 (12), 164 (69), 149 (36), picrate with mp 168–169°C, hydrochloride with mp 221°C (with foaming).

The NMR spectrum was taken in carbon tetrachloride on a JNM-4H-100/100 MHz instrument (with HMDS as internal standard), and the mass spectra on an MKh-1303 instrument fitted with a system for the direct introduction of the sample into the ion source.

SUMMARY

Morphine, codeine, narcotine, thebaine, papaverine, protopine, xanthaline, prophyroxine, bases with mp 267 and 263°C, *l*-canadine, and cryptopine have been isolated from Kirghiz opium.

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