chloroform extract was shaken with a 5% solution of sulfuric acid. With cooling, the acid solution was made alkaline with sodium carbonate, and the alkaloids were exhaustively extracted with chloroform (3.9 g). The alkaloids so obtained were chromatographed on silica gel (Czechoslovakia, L, 100/160) in a ratio of 1:25. Elution was performed with hexane, ether, and ether–ethyl acetate (initially 10:1, with a successive increase in the concentration of the latter), 300-ml fractions of the eluates being collected. The ether–ethyl acetate eluates 8-13 deposited crystals of acosanine, mp 78-80°C (from petroleum ether). The substance dissolved well in chloroform, acetone, and ethanol, and less well in ether. Mass spectrum, m/z (%): 467 (M^+, 4.6), 452(4), 450(2), 449(2), 337(30), 436(100), 420(6), 418·(4.5), 71(1.5), 58(2).

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ALKALOIDS OF Haplophyllum perforatum

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The alkaloid composition of the seeds and roots of the plant Haplophyllum perforatum growing in Tadzhikistan (Karateg range) has been studied for the first time. In addition to the known furoquinoline alkaloids, the new alkaloid haplosine has been isolated and it has been shown to be identical with the product of the hydrogenolysis of haplopine. Among natural compounds, this is the first representative of derivatives of the 3-ethyl-4-methoxyquinolin-2-one series.

The chemical composition of Haplophyllum perforatum (M. B.) Kar et Kir. (family Rutaceae) [1] depends greatly on its conditions of growth. Of the 30 alkaloids isolated from this plant growing in various sites [2], only evoxine was present in all the samples studied. Skimmianine – the main alkaloid of H. perforatum from the foothills of the Babatag [3, 4] and the most widely distributed in representatives of the Rutaceae family [5] – was not found in the epigeal part of the plant gathered in the Dzhungarian Ala-Tau [6] and seeds collected in the Samarkand province [3]. Modified furoquinoline derivatives were found in

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the latter [7]. Glycoalkaloids were present mainly in the epigeal part of the plant collected in the Dzhungarian Ala-Tau [6] and the foothills of Babatag [4, 8].

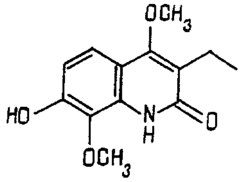
This incomplete list of the results that have been obtained shows that many alkaloids are produced in this plant only at certain growth sites, and therefore the plants from new collection points form an independent object of chemical study.

We have studied alkaloids of the seeds and roots of H. perforatum gathered in the gorge of the R. Faizabab (Tadzhikistan, Karateg range). By the usual method, a methanolic extract of the seeds was separated into basic and neutral fractions [6]. Chromatography of the basic fraction yielded 7-isopentyloxy-γ-fagarine, skimmianine, evoxine, methylevoxine, and glycoperine, while the neutral fraction yielded haplamine, flindersine, and the lignan eudesmin [9]. Similarly, basic, acidic, and neutral fractions were obtained from a methanolic extract of the roots. The basic fraction yielded robustine, dictamine, skimmianine, and evoxine; the neutral fraction haplamine and flindisine, and the acid fraction robustine, haplamine, and a base with mp 155-156°C (I). The total amounts of alkaloids were 0.5 and 0.15% on the weight of the dry seeds and roots, respectively.

The known substances were identified by direct comparison with authentic samples. With the exception of robustine, all the alkaloids had been isolated from this plant previously.

Base (I) was new, and had been called haplosine. Haplosine has the composition $C_{13}H_{15}NO_4$. According to its UV and IR spectra it belongs to the quinolin-2-one series [10]. The PMR spectrum of (I) showed the following signals (δ, ppm): 1.15 and 2.6 (3H, t, and 2H, q, respectively, J = 7.5 Hz, ethyl group); 3.84 (6H, s, 2 × OCH_3); and 6.79 and 7.31 (two doublets, 1H each, J = 8.8 Hz, ortho-aromatic protons). These facts permitted us to put forward for this base the structure of 3-ethyl-7-hydroxy-4,8-dimethoxyquinolin-2-one. This substance had been obtained previously by the catalytic hydrogenation of 7-isopentyloxy-γ-fagarine and of haplopine [11]. A direct comparison of haplosine with tetrahydrohaplopine (TLC, mixed melting point, mass spectra) showed their identity.

It is interesting to note that isomerization and hydrogenolysis reactions leading to the formation of N-methylfuroquinolin-4-one (iso-compounds) and 3-ethyl-4-methoxyquinolin-2-ones (tetrahydro derivatives of furoquinoline), respectively, are characteristic for 4-methoxyfuroquinoline alkaloids [12]. Somewhat later, iso-compounds obtained synthetically were isolated from plants but there is no information on the isolation of tetrahydro derivatives of furoquinoline. The isolation of haplosine is the first case of the detection of tetrahydro derivatives of furoquinoline in plants.



EXPERIMENTAL

The spectra of the substances were obtained on Hitachi EPS-3T (ethanol), UR-20, and MKh-1303, and 100 MHz ($CDCl_3$, 0 – HMDS) instruments. For TLC were used silica gel containing 5% of gypsum and the following solvent systems: 1) toluene–ethyl acetate–acetic acid (5:4:1); 2) benzene–methanol (4:1); 3) ethyl acetate; and 4) chloroform–acetone (6:1).

Isolation of the Alkaloids. The dry comminuted seeds (284 g) were extracted with methanol eight times. The evaporated methanolic extract was shaken with petroleum ether and with 10% sulfuric acid. The part that had not then dissolved was separated off and was dissolved in chloroform. The alkaloids were extracted from the chloroform solution with 10% sulfuric acid. The acid solutions were combined and made alkaline with ammonia, and the alkaloids were extracted with ether (0.74 g) and with chloroform (0.63 g). After concentration of the ethereal solution, the crystals of evoxine that had deposited were separated off (0.18 g).

Chromatography on alumina of the remaining ether-extracted alkaloids (0.56 g) gave 7-isopentenyloxy-γ-fagarine, mp 105-106°C (20 mg); skimmianine, mp 175-176°C (15 mg); methylevoxine, mp 105-106°C (15 mg); and evoxine, mp 154-155°C (0.3 g). A similar separation of the chloroform-extracted alkaloids (0.63 g) gave evoxine (0.25 g) and glycoperine (0.12 g). The neutral fraction yielded eudesmin (0.2 g), haplamine (20 mg), and flindersine (11 mg). No alkaloids were isolated from the petroleum ether extract.

The dry comminuted roots (540 g) were extracted similarly. Basic (0.45 g), acidic, (0.58 g) and neutral (2.03 g) fractions were obtained. Chromatography of the basic fractions on silica gel yielded robustine, mp 147-148°C (4 mg); dictamnine, mp 130-132°C (8 mg); skimmianine (120 mg); and evoxine (170 mg). The acid fraction yielded robustine (80 mg); haplopine, mp 204-205°C (200 mg), and haplosine (21 mg); and the neutral fraction haplamine (50 mg), and flindersine (30 mg).

Haplosine, mp 155-156°C (from benzene and ethyl acetate). UV spectrum: $\lambda_{max}^{C_2H_5OH}$, nm: 217, 252, 322, 344 (log ε 4.57; 4.24; 4.24; 4.22); $\lambda_{max}^{C_2H_5OH+OH^-}$, nm: 205, 225, 273 (log ε 4.55; 4.62; 4.28). The spectrum did not change on acidification.

IR spectrum: ν_{max}^{KBr}, cm^{-1}: 3570, 3480 (OH), 3100, 1650, 1500, 1450.

Mass spectrum, m/z (%): 249(M^+, 98), 248(14), 235(17), 234(100), 233(10), 221(10), 220(72), 219(58), 218(27), 204(14), 202(14).

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