THE ROOTS OF *Dictamnus angustifolius*

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The genus *Dictamnus* L. (family Rutaceae) is represented world-wide by six species [1]. Of the plants of the species growing abroad, *Dictamnus albus* L. has been studied intensively since 1923, and from it have been isolated the alkaloids dictamnine [2], skimmianine [3], γ-fagarine [4], preskimmianine [5, 6], and isomaculosidine [6], limonoids [7], anthocyanins [8] monoterpenes [8], coumarins [9], and flavonoid glycosides [8, 10].

In the flora of the Soviet Union, five species of the genus *Dictamnus* are known [11], two of which grown in Uzbekistan [12] and are used in folk medicine [13]. Four of these species have been subjected to chemical investigation. From *D. angustifolius* G. Don. have been isolated the alkaloids dictamnine, skimmianine, dubinidine, and evoxine [14], and from *D. caucasicus* Fisch. ex Grossh. dictamine, skimmianine, γ-fagarine, robustine, isodictamine, isopteleine, and isomaculosidine [15]. In *D. dasycarpus* Turcz. and *D. gymostylus* Stev. the furocoumarins psoralen and xanthoxin have been detected; limonin and obacunoic acid have been isolated from the former plant [16].

We have begun an investigation of the chemical composition of *D. angustifolius* growing in the mountains of Chimgan, Tashkent oblast. Plants of the genus *Dictamnus* are described as poisonous, causing burns on contact [6, 12, 13]. However, during the collection of the raw material in the end-of-fruit-bearing phase (July 1, 1977) we observed that the plant is readily eaten by animals and does not possess a burning effect. The toxicity of the plant and its capacity for causing burns are probably connected with certain periods of its vegetation. The roots of *D. angustifolius* were extracted with methanol. The extract was separated into basic, acidic, and neutral fractions. From the main fraction we obtained five alkaloids which, on the basis of spectral characteristics and a direct comparison with samples obtained previously from *D. caucasicus* [15], were identified as dictamnine, γ-fagarine, skimmianine, isodictamnine, and isopteleine.

From the neutral fraction we obtained three substances, with mp 116-117°C (I), 141-142°C (II), and 154-155°C (III). From its UV, IR, NMR, and mass spectra, (I) was identified as the limonoid fraxinellone. From its melting point, specific rotation, and a mixed-melting point with an authentic sample [17], compound (II) was identified as β-sitosterol.

Substance (III) proved to be an alkaloid. Its IR spectrum contained the absorption bands of an amide group. The UV spectrum did not change on acidification, which is characteristic of quinolin-2-one compounds [18]. The NMR spectrum coincided with that published for preskimmianine [5, 6] and with that of a synthetic sample of it — 3-isopentenyl-4,7,8-trimethoxyquinolin-2-one [19]. The main peaks of the ions in the mass spectrum of (III) with m/e (%) 303 (M^+, 100), 288 (M − 15, 99), 272 (M − 31, 20), 260 (M − 43, 78), 258 (M − 45, 26), 248 (M − 55, 52), 234 (M − 69, 38) were also close to those for preskimmianine [6]. The facts given above show that (III) is preskimmianine.

In the literature [6], the formation of a fragment with m/e 260 is represented as the splitting out of a NHCO group from M^+. With the aim of confirming this, we obtained the N-methyl derivative of preskimmianine (IV). Its mass spectrum contained the peaks of ions with m/e (%) 317 (M^+, 47), 302 (M − 15, 64), 286 (M − 31, 12), 275 (M − 42, 20), 274 (M − 43, 100), 272 (M − 45, 26), 262 (M − 55, 29), 248 (M − 69, 20), 244 (M − 73, 26). The very low intensity of the peak of the ion with m/e 260 (5%) and the fact that the peak of the $(M - 43)^+$ ion has the maximum intensity in the spectrum of (IV) shows that the ejection of 43 m.u. from M^+ of (III) most probably takes place through the splitting out of C_3H_7 and not of the amide group. It is also interesting to note that in the spectrum of (IV) the intensity of the peak of the $(M - 42)^+$ ion is five times smaller than the intensity of the peak of the $(M - 43)^+$

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ion, while in the majority of cases [20] in the spectra of the 3-isopentenyl-N-methylquinolin-2-one alkaloids the peak of $(M - 42)^+$ ion formed through the cleavage of the double bond of the isopentenyl chain by the mechanism suggested by Reisch et al. [21] has the maximum intensity.

With the exception of dictamnine and skimmianine, this is the first time that any of the substances mentioned have been isolated from *D. angustifolius*. Attention is merited by the fact that plants of the genus *Dictamnus* contain the N-methylfuranoquinolin-4-one alkaloids, which are rarely found in plants, being known previously only as products of the isomerization of furanoquinoline bases [22]. In this connection, isopteleine, together with simmianine and dictamnine, is the main component of the combined alkaloids of *D. angustifolius*, while it has not been detected in *D. albus* and is present in only very small amount in *D. caucasicus*.

EXPERIMENTAL

For the conditions of recording the spectra, see [23]. For TLC (KSK silica gel with 5% of gypsum) we used the following solvent systems: toluene–ethyl acetate–formic acid (5:4:1) and ethyl acetate.

Isolation of the Total Alkaloids. The comminuted air-dry roots of *D. angustifolius* (8.5 kg) were treated with methanol until the alkaloids had been extracted completely. The solvent was driven off by vacuum distillation. The extract was distributed between 10% sulfuric acid and ether–chloroform (2:1). The acid solution was made alkaline with concentrated ammonia and was extracted with ether and chloroform. After treatment with 4% caustic soda, the extracts were washed with water, dried over potassium carbonate, filtered, and concentrated. The concentrated ethereal solution deposited crystals of isopteleine (0.15 g), mp 208-209°C (from acetone). Distillation of the solvents gave ether-extracted (3.86 g) and chloroform-extracted (0.58 g) combined non-phenolic alkaloids, and the ether–chloroform (2:1) solution previously treated with 4% caustic soda gave, on distillation, a neutral fraction.

Separation of the Combined Alkaloids. When the combined ether-extracted material was treated with acetone, skimmianine separated out (0.34 g), mp 176-177°C (from methanol). The remainder of the combined material (3.52 g) was chromatographed on a column of alumina (1:100). The ethereal eluates yielded dictamnine (0.2 g), mp 132-133°C (from acetone); γ-fagarine (0.015 g) mp 140-141°C (from acetone); skimmianine (0.05 g); isodictamnine (0.03 g), mp 182-183°C (from water); and isopteleine (0.07 g). Chromatography of the combined chloroform-extracted material on a column of alumina (1:100) and elution with ether gave isopteleine (0.15 g).

Separation of the Neutral Fraction. The neutral fraction was chromatographed on a column of alumina (1:10). The ethereal eluates yielded fraxionellone (0.25 g), β-sitosterol (0.13 g), and preskimmianine (0.18 g).

Fraxinellone (I), mp 116-117°C (from ether) $[\alpha]_D$ −44° (c 1.5, ethanol). UV spectrum: λ_{max} 217 nm (log ε 4.05). IR spectrum, cm^{-1}: 3135 (furan ring), 1750 (lactone CO), 1678 (C=C). Mass spectrum, m/e (%): 232 (M^+, 30), 136 (100), 108 (43), 93 (41). NMR spectum ($CDCl_3$, scale): 2.59 and 3.72 (2 H, multiplet, and 1 H, doublet, J = 2.5 Hz, 2 H_α and H_β of a furan ring, respectively), 5.16 (1 H, singlet, CH–OCO); 7.92 (3 H, singlet, CH_3–C=); 9.20 (3 H, singlet, CH_3–C); and 7.70-8.80 ppm (6 H, multiplet, $3CH_2$).

β-Sitosterol (II), mp 141-142°C (from methanol), $[\alpha]_D$ −35°C (c 1.0; chloroform).

Preskimmianine (III), mp 154-155°C (from acetone). UV spectrum, λ_{max}, nm: 219, 232 inflection, 250, 258, 310 shoulder, 322, 335 (log ε 4.53, 4.31, 4.07, 4.08, 3.82, 3.98, 3.83). IR spectrum, cm^{-1}: 3100-3160 and 1635 (NHCO). NMR spectrum ($CDCl_3$, τ scale, ppm): 2.60 and 3.23 (doublets, 1 H each, J = 9 Hz, ortho aromatic protons); 4.75; 6.69; 8.25 and 8.35 [triplet, 1 H, J = 6.5 Hz; doublet, 2 H, J = 6.5 Hz; two singlets, 3 H each; CH_2–CH=C(CH_3)$_2$]; 6.12 and 6.15 ppm (singlets, 6 H and 3 H, respectively, 3 OCH_3).

N-Methylpreskimmianine (IV). Freshly calcined potassium carbonate (0.5 g) and methyl iodide (1 ml) were added to a solution of preskimmianine (0.04 g) in dry acetone (15 ml). The mixture was boiled in the water bath for 20 h, cooled, and filtered. The residue obtained after the solvent had been distilled off was chromatographed on a column of silica gel (1:100). The first ethereal eluate yielded (IV) (0.01 g), mp 80-81°C (from hexane), and the last yielded (III) (0.02 g). IR spectrum of (IV): 1638 cm^{-1} (NCO).

SUMMARY

From the roots of *Dictamnus angustifolius* G. Don. collected in Chimgan at the end-of-fruit-bearing stage have been isolated alkaloids dictamnine, skimmianine, γ-fagarine, isodictamnine, isopteleine, and preskimmianine, the limonoid fraxinellone, and the steroid β-sitosterol. This is the first time that any of these substances, with the exception of dictamnine and skimmianine, have been found in this plant.

LITERATURE CITED

1. R. Hegnauer, Chemotaxonomie der Pflanzen, Vol. 6, Birkhäuser Verlag, Basel (1973), p. 217.
2. R. H. S. Manske and H. L. Holmes, The Alkaloids, Vol. 3, Academic Press, New York (1953), p. 69.
3. H. Gertig and H. Grabarczyk, Acta Polon. Pharm., 18, 97 (1961); Chem. Abstr., 56, 7424 (1962).
4. Ha-huy-ke and M. Luckner, Pharmazie, 12, 771 (1966).
5. R. Storer and D. W. Young, Tetrahedron Lett., 2199 (1972).
6. R. Storer and D. W. Young, Tetrahedron, 29, 1217 (1973).
7. M. Pailer, G. Schaden, G. Spiteller, and W. Fenzl, Monatsh. Chem., 96, 1324 (1965).
8. W. Renner, Pharmazie, 12, 763 (1962).
9. L. Berrens and E. Dijk, Experimenta, 20, 615 (1964); J. Reisch, K. Szendrei, E. Minker, and I. Novak, Planta Medica, 15, 320 (1967).
10. H. Grabarczyk, Dissertationes Pharm. (Pol.), 16, 177 (1964); Chem. Abstr., 62, 817 (1965).
11. Flora of the USSR [in Russian], Vol. 14, Moscow (1949), p. 227.
12. Flora of Uzbekistan [in Russian], Vol. 4, Tashkent (1959), p. 75.
13. Kh. Kh. Khalmatov, Wild-Growing Medicinal Plants of Uzbekistan [in Russian], Tashkent (1964), p. 137.
14. S. A. Sultanov and S. Yu. Yunusov, Khim. Prirodn. Soedin., 195 (1969).
15. I. M. Kikvidze, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 675 (1971).
16. N. F. Komissarenko, Khim. Prirodn. Soedin., 377 (1968); G. K. Nikonov, Med. Prom. SSSR, 12, 15 (1964).
17. E. F. Nesmelova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 289 (1977)
18. A. W. Sangster and K. L. Stuart, Chem. Rev., 65, 97 (1965).
19. J. F. Collins, G. A. Grey, M. F. Grundon, D. M. Harrison, and C. G. Spyropoulos, J. Chem. Soc., Perkin Trans. 1, 94 (1973).
20. J. Reisch, K. Szendrei, I. Novak, E. Minker, J. Korosi, and K. Csedo, Tetrahedron Lett., 449 (1972); F. Bohlmann and V. S. B. Rao, Chem. Ber., 102, 1774 (1969).
21. J. Reisch, K. Szendrei, I. Novak, and E. Minker, Acta Pharm. Hung., 44, 107 (1974).
22. H. G. Boit, Ergebnisse der Alkaloid-Chemie bis 1960, Academie Verlag, Berlin (1961), pp. 715-717.
23. V. I. Akhmedzhanova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 320 (1976).