QUINOLINE ALKALOIDS OF Haplophyllum

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The genus Haplophyllum A. Juss. (family Rutaceae) is represented on the world scale by 50 species [1], 32 of which are known in the Soviet Union, including 23 in Central Asia [2], which is a center of species diversity of these plants.

Systematic investigations of alkaloids of the genus Haplophyllum were begun by S. Yu. Yunusov and G. P. Sidyakin in 1948 [3]. Alkaloids were found in all the plants of this species investigated: 12 Central Asian [4, 5], and four Azerbaidzhanian [6]. Abroad, the alkaloids of Haplophyllum hispanicum [7], H. suaveolens [8], and H. tuberculatum [9], which are taxonomically close to the Central Asian plants, have been studied. From these 19 species of Haplophyllum alone, 46 alkaloids have been obtained (see below), including 34 new ones. With the exception of acetylevoxine [7] and 3-dimethylallyl-4-dimethylallyloxy-2-quinolone [9], all the new alkaloids have been isolated from Central Asian plants of the genus Haplophyllum.

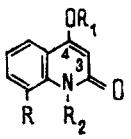
Haplophyllum alkaloids belong to the quinoline derivatives and only two of them have proved to be amides [10] (see below). The majority of the alkaloids (furanoquinoline, dihydropyrano-4-quinolone, 2-alkyl- and 2-phenyl-4-quinolone alkaloids, and others) are weak bases, and because of the hydrolysis of their salts they pass into an organic solvent from an acid solution. This enables them to be separated from the stronger bases such as, for example, the dihydrofuranoquinoline alkaloids. A number of compounds (pyrano-2-quinolones, some modified furanoquinoline derivatives, and amides) do not exhibit basic properties, and if a phenolic hydroxyl is present they show acidic properties. Consequently, alkaloids can be found not only in the basic but also in the neutral and acidic fractions of a plant extract.

An investigation of plants of the genus Haplophyllum has shown that they contain new representatives of almost all the known varieties of quinoline alkaloids, in which plants of the family Rutaceae are rich [11, 12]. Together with these, in Haplophyllum species peculiar quinoline alkaloids not found in plants of other genera of the family Rutaceae have been discovered: quinoline alkaloids containing a fragment of two isoprene units (Ie, IIa, and XVI), glycoalkaloids of the furanoquinoline series (IXj and IXk) and modified furanoquinole derivatives (XIa, XIb-XIII) (see below).

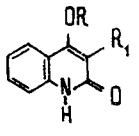
We have subdivided the quinoline alkaloids isolated up to the present time from plants of the genus Haplophyllum into seven groups. In this review we discuss the characteristic reactions and spectral properties of each group.

Below we give the alkaloids obtained from plants of the genus Haplophyllum (alkaloids isolated previously from other genera of the family Rutaceae are marked with an asterisk):

4-HYDROXY-2-QUINOLONE DERIVATIVES



I



II

Alkaloid	Plant
1. Robustinine (edulitine) Ia, R=OCH_3; $R_1=CH_3$; $R_2=H$	H. bungei [13], H. foliosum [14], H. robustum [15]
2. Folifidine, Ib, R=OH; $R_1=R_2=CH_3$	H. dubium [16], H. foliosum [14]
3. Folimine, Ic, R=OCH_3; $R_1=R_2=CH_3$	H. foliosum, [17] H. perforatum [18]

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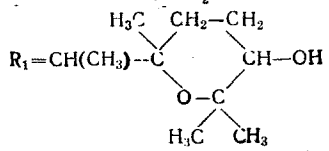
Alkaloid	Plant
4. Foliosidine, Id $R=OCH_2CH(OH)C(OH)(CH_3)_2$; $R_1=R_2=CH_3$	H. dubium [16], H. foliosum [19], H. perforatum [18]
5. Bucharaine, Ie, $R=R_2=H$; $R_1=CH_2CH=$ $=C(CH_3)CH_2CH_2CH(OH)C(OH)(CH_3)_2$	H. bucharicum [20]
6. **Bucharidine, IIa,** $R=R_2=H$	H. bucharicum [21]



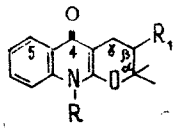
7. 3-Dimethylallyl-4-dimethylallyloxy-2-quinolone, IIb, $R=R_1=CH_2CH=$ $=C(CH_3)_2$	H. tuberculatum [9]

PYRANO-2-QUINOLONE DERIVATIVES

III

8. Flindersine,* IIIa, R=H	H. bucharicum [22], H. perforatum [23]
9. Haplamine, IIIb, $R=OCH_3$	H. perforatum [24]

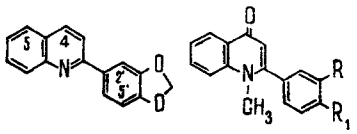
DIHYDROPYRANO-4-QUINOLONE DERIVATIVES



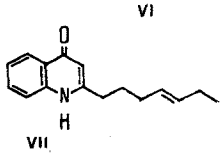
IV

10. Haplofoline, IVa, $R=R_1=H$	H. foliosum [25], H. suaveolens [8]
11. Folifine (ribalinine), IVb, $R=CH_3$; $R_1=OH$	H. bucharicum [14, 20], H. foliosum [14].
12. Haplobucharine, IVc, $R=CH_2CH=C(CH_3)_2$; $R_1=H$	H. bucharicum [22]

2-PHENYLQUINOLINE AND 2-PHENYL- AND 2-ALKYL-4-QUINOLONE DERIVATIVES



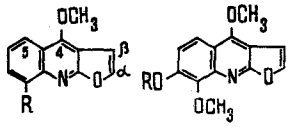
V VI



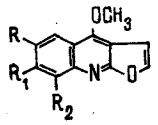
VII

13. Dubamine, V	H. dubium [26], H. latifolium [5]
14. 1-Methyl-2-phenyl-4-quinolone,* VIa, $R=R_1=H$	H. foliosum [27], H. perforatum [18]
15. Graveoline (foliosine),* VIb, $R+R_1=O_2CH_2$	H. dubium [16, 28], H. foliosum [19] H. perforatum [18]
16. Folimidine, VIc, $R=OCH_3$, $R_1=OH$	H. foliosum [29]
17. Acutine, VII	H. acutifolium [30]

FURANOQUINOLINE DERIVATIVES



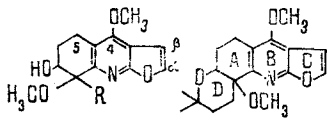
VIII IX



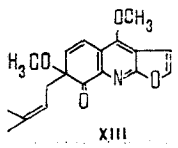
X

Alkaloid	Plant
18. Dictamine,* VIIIa, R=H	H. bucharicum [31], H. bungei [13], H. perforatum [18], H. robustum [4], H. ramosissimum [32], H. suaveolens [8]
19. Robustine, VIIIb, R=OH	H. bucharicum [31] H. pedicellatum [31], H. dubium [16], H. robustum [33]
20. γ-Fagarine,* VIIc, R=OCH_3	H. bucharicum [31], H. kowalenskyi [6], H. pedicellatum [34], H. robustum [33], H. schelkovnikovii [6], H. tenue [6], H. villosum [6]
21. Haplofidine, VIIId, R=$OCH_2CH=C(CH_3)_2$	H. perforatum [35]
22. Haplopine, IXa, R=H	H. bucharicum [20], H. dubium [16], H. foliosum [14], H. latifolium [5], H. pedicellatum [31], H. perforatum [36], H. robustum [33]
23. Skimmianine,* IXb, R=CH_3	H. acutifolium [30], H. bucharicum [3, 20], H. bungei [13], H. dubium [28], H. foliosum [19, 34], H. kowalenskyi [6], H. latifolium [5], H. obtusifolium [31], H. pedicellatum [3], H. perforatum [3], H. popovii [37], H. ramosissimum [32], H. robustum [33], H. schelkovnikovii [6], H. suaveolens [8], H. tenue [6].
24. 7-Isopentenyloxy-γ-fagarine,* IXc, R=$CH_2CH=C(CH_3)_2$	H. latifolium [10], H. perforatum [38]
25. Haplatine, IXd, R=$CH_2CH=C(CH_3)(CH_2OH)$	H. latifolium [39]
26. Evodine,* IXe, R=$CH_2CH(OH)C(CH_3)=CH_2$	H. perforatum [40]
27. Evoxoidine,* IXf, R=$CH_2COCH(CH_3)_2$	H. perforatum [40]
28. Evoxine (haploperine),* IXg, R=$CH_2CH(OH)C(OH)(CH_3)_2$	H. dubium [16, 28], H. hispanicum [7], H. latifolium [5], H. obtusifolium [31], H. perforatum [3], H. popovii [37], H. ramosissimum [13], H. suaveolens [8].
29. Methylevoxine, IXh, R=$CH_2CH(OH)C(OCH_3)(CH_3)_2$	H. perforatum [41]
30. Acetylevoxine, IXi, R=$CH_2CH(OCOCH_3)C(OH)(CH_3)_2$	H. hispanicum [7]
31. Glycoperine, IXj, R= α-L-rhamnose	H. perforatum [42]
32. Triacetylglycoperine, IXk, R= triacetyl-α-L-rhamnose	H. perforatum [43]
33. Kokusaginine,* Xa, $R=R_1=OCH_3$, $R_2=H$	H. suaveolens [8]
34. Folifinine, Xb, R=H, $R_2=OH$, $R_1=CH_2CH_2C(OH)(CH_3)_2$	H. foliosum [44]
35. Foliminine, Xc, R=H, $R_1+R_2=CH_2CH_2C(CH_3)_2O$—	H. foliosum [45]

MODIFIED FURANOQUINOLINE DERIVATIVES



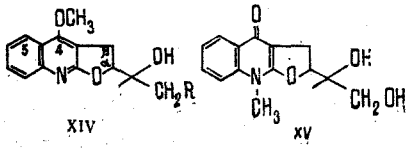
XI XII



XIII

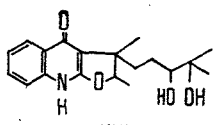
36. Haplofilidine, XIa, R=$CH_2CH=C(CH_3)_2$	H. perforatum [46]
37. Perforine, XIb, R=$CH_2CH_2C(OH)(CH_3)_2$	H. perforatum [47]
38. Anhydroperforine, XII	H. perforatum [48]
39. Perfamine, XIII	H .perforatum [49]

DIHYDROFURANOQUINOLINE AND DIHYDROPYRANO-4-QUINOLONE DERIVATIVES



XIV

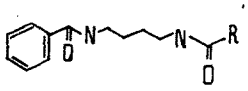
XV



XVI

Alkaloid	Plant
40. Platydesmine,* XIVa, R=H	H. perforatum [18]
41. Dubinidine, XIVb, R=OH	H. dubium [26, 28], H. foliosum [19, 34]
42. Dubinine, XIVc, R=OCOCH$_3$	H. perforatum [18]
43. Folisine, XV	H. dubium [26]
44. Bucharaminol, XVI	H. foliosum [50]
	H. bucharicum

AMIDES



XVII

45. Haplamide, XVIIa, R=C$_6$H$_5$	H. latifolium [10]
46. Haplamidine, XVIIb, R=CH=CH—C$_6$H$_5$	H. latifolium [10]

4-Hydroxy-2-quinolone Derivatives

In plants of the family Rutaceae, 38 alkaloids of this group have been found, seven of them in representatives of the genus Haplophyllum.

A common property of 4-methoxy-2-quinolones is their capacity for undergoing demethylation in an acid medium with the formation of the corresponding 4-hydroxy-2-quinolones [15, 51]. 4-Hydroxy-2-quinolones unsubstituted at C_3 give nitroso derivatives [15]. The fusion with alkali of compounds containing a hydroxylated O-isoprenoid chain in the homocyclic ring leads to the cleavage of the ether bond [51]. Alkaloids with a 4-O-allylalkyl side chain undergo hydrogenolysis when subjected to Adams hydrogenation [9, 20], when there is no substituent in position 3 they undergo the Claisen rearrangement [52].

The UV spectra of 4-hydroxy-2-quinolone derivatives (Fig. 1a) are characterized by three absorption regions: ≈210-260 nm (log ε 4.4), 260-295 nm (log ε 3.9), and 310-360 nm (log ε 3.5-4.0) [15, 17, 51, 53]. The bands are frequently split into two and do not change on acidification and alkalinization [17]. Angular dihydrofurano- and dihydropyrano-2-quinolones have similar spectra (Fig. 1a) [54, 55]. The values of λ_{max} and log ε in the spectra of these compounds depend on the position of the alkoxy substituent in the homocyclic ring (Fig. 1b) [51, 55, 56]. The band at 260-295 nm appears in the longer-wave region for alkaloids of type II than for compounds of type I having no substituent in position 3 (Fig. 1c) [20, 21]. In contrast to the 4-alkoxy-2-quinolones, the spectra of the 4-hydroxy-2-quinolones show a characteristic hypsochromic displacement of the curve in an alkaline medium (Fig. 1c) [57, 58].

In the IR spectra of the 4-alkoxy-2-quinolones and also in those of the angular dihydrofurano- and dihydropyrano-2-quinolone derivatives an absorption band is found in the 1670-1630 cm^{-1} region (amide carbonyl), the intensity of which far exceeds the intensity of the absorption bands in the 1610-1500 cm^{-1} region.

In the mass spectra of compounds (Ia-Ic) the peak of the molecular ion has the maximum intensity. The main fragments are formed as the result of the detachment of a methyl radical from the methoxy group at C_4 followed by the elimination of carbon monoxide. The presence of a methoxy group at C_8 leads to the appearance of the peaks of the ions $(M-1)^+$, $(M-29)^+$, and $(M-30)^+$, which have diagnostic value [59]. In the mass spectrum of foliosidine, the peak of the ion $(M-102)^+$ formed through the detachment of the isoprenoid chain is three times stronger than the peak of the molecular ion. The mass spectra of bucharaine and bucharidine are almost identical, which is a consequence of the conversion of bucharaine into bucharidine by a Claisen rearrangement taking place in the mass spectrometer [60].

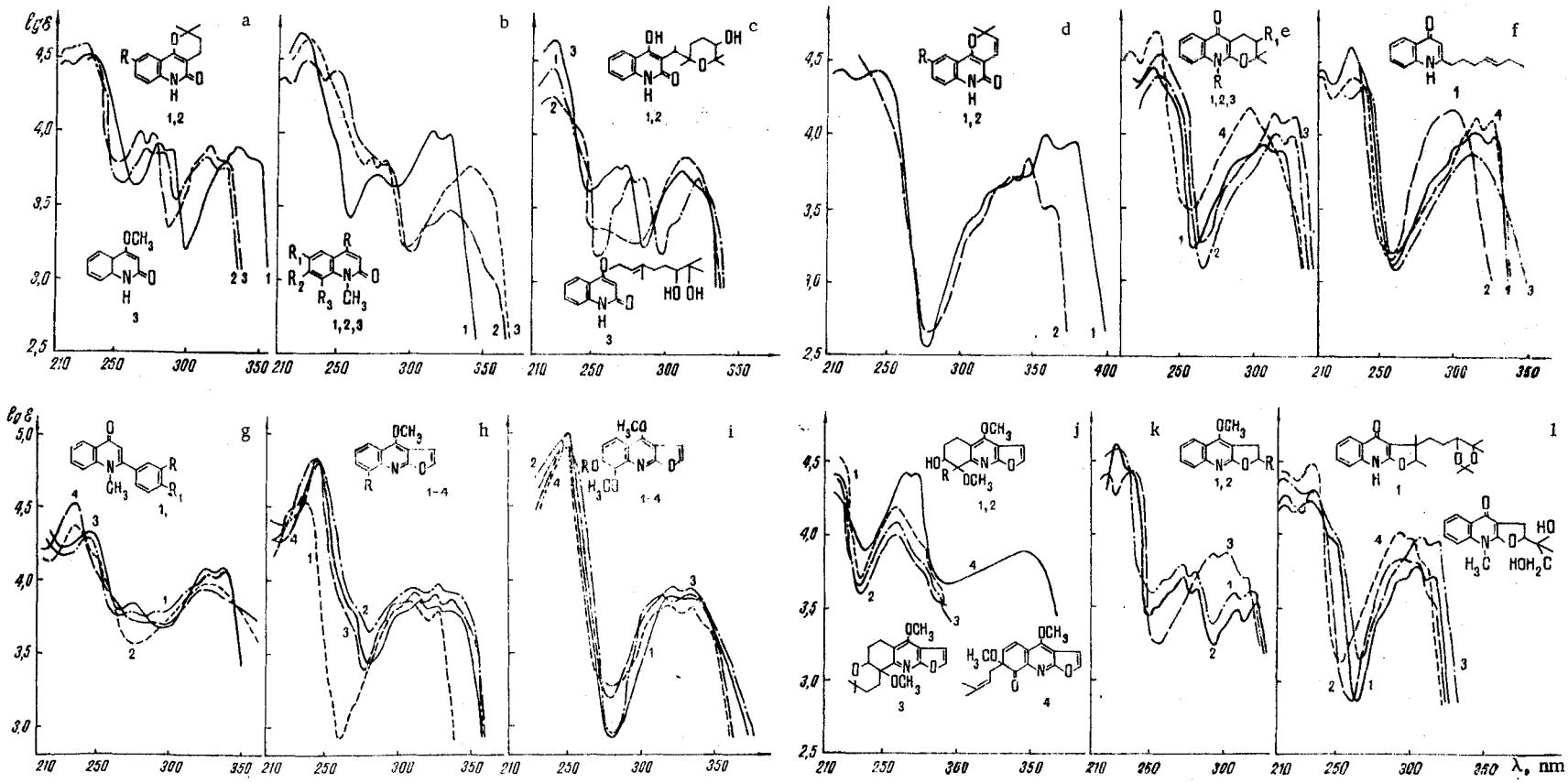
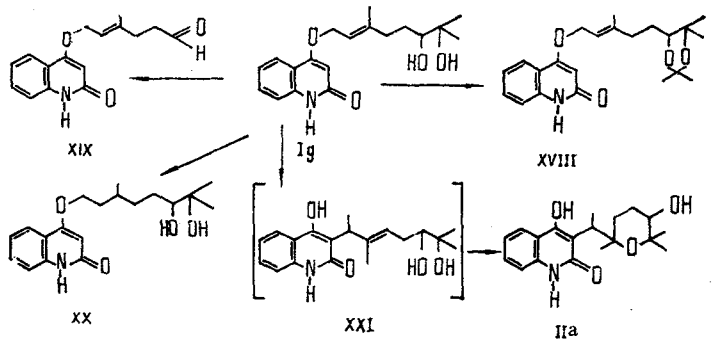


Fig. 1. UV spectra of the quinoline alkaloids of Haplophyllum in ethanol: a) 1) dihydrohaplamine ($R = OCH_3$); 2) dihydroflindersine ($R = H$); 3) 4-methoxy-2-quinolone; b) 1) ($R_1 = R_3 = H$; $R = R_2 = OCH_3$); 2) folimine ($R_1 = R_2 = H$; $R = R_3 = OCH_3$); 3) ($R_2 = R_3 = H$; $R = R_1 = OCH_3$); c) 1) bucharidine; 2) bucharidine (ethanol $+OH^-$); 3) bucharaine; d) 1) haplamine ($R = OCH_3$); 2) flindersine ($R = H$); e) 1) haplofoline ($R = R_1 = H$); 2) folifine ($R = CH_3$; $R_1 = OH$); 3) N-methylhaplofoline ($R = CH_3$, $R_1 = H$); 4) N-methylhaplofoline (ethanol $+H^+$); f) 1) acutine; 2) acutine (ethanol $+H^+$); 3) acutine (ethanol $+OH^-$); 4) dihydroacutine; g) 1) graveoline ($R + R_1 = O_2CH_2$); 2) graveoline (ethanol $+H^+$); 3) folimidine ($R = OCH_3$); $R_1 = OH$); 4) folimidine (ethanol $+H^+$); h) 1) dictamnine ($R = H$); 2) robustine ($R = OH$); 3) γ-fagarine ($R = OCH_3$); 4) haplofidine ($R = OCH_2CH=C(CH_3)_2$); i) skimmianine ($R = CH_3$); 2) 7-isopentenyloxy-γ-fagarine ($R = CH_2CH=C(CH_3)_2$); 3) evoxine ($R = CH_2CH(OH)C(OH)(CH_3)_2$); 4) methylevoxine ($R = CH_2CH(OH)C(OCH_3)(CH_3)_2$); j) 1) haplofilidine ($R = CH_2CH=C(CH_3)_2$); 2) perforine ($R = CH_2CH_2C(OH)(CH_3)_2$); 3) anhydroperforine; 4) perfamine; k) 1) dihydrodictamine ($R = H$); 2) platydesmine ($R = C(OH)(CH_3)_2$); 3) platydesmine (ethanol $+H^+$); l) 1) bucharamine; 2) bucharamine (ethanol $+H^+$); 3) folisine; 4) folisine (ethanol $+H^+$).

In the NMR spectra of (Ia-Ie) a singlet in the 4.00-4.07 ppm region indicates the absence of a substituent at C_3 [17, 54, 61]. When deuterochloroform is replaced by trifluoroacetic acid, a paramagnetic shift of the H_3 signal by 1.05 ppm in the spectrum of (Id) [62] and by 0.40 ppm in the spectrum of (Ic) is observed. A methoxy group at C_8 descreens the protons of the methylimide group by 0.15-0.20 ppm.

Bucharaine and Bucharidine

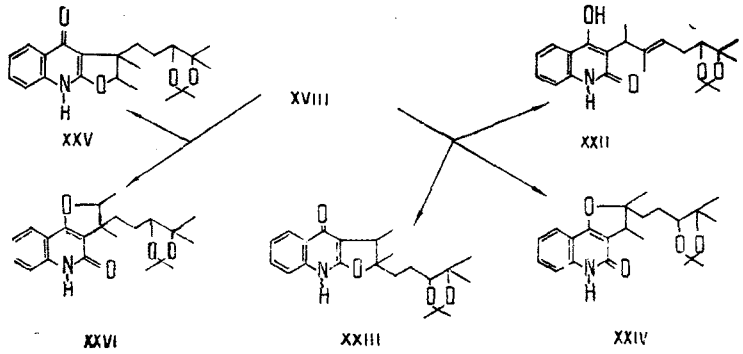
The 4-geranyloxy-2-quinolone structure of bucharaine, established on the basis of the NMR and mass spectra of its isopropylidene derivative (XVIII) [63, 64] and of bucharainal (XIX) [52], obtained by the periodate oxidation of the base, is in harmony with the formation of 4-hydroxy-2-quinolone [20] and of dihydrobucharaine (XX) in the Adams reduction of (Ic) (Scheme 1).



Scheme 1

The chemical properties of bucharidine, the characteristics of its NMR and mass spectra [21], and also the possible biogenetic link with bucharaine on the basis of an anomalous Claisen rearrangement and subsequent cyclization at the expense of the tertiary hydroxy group and the double bond of the side chain have permitted structure (IIa) to be put forward for bucharidine (see Scheme 1) [52].

The heating of bucharaine in tetralin or its pyrolysis [52, 54] forms bucharidine. The pyrolysis of (XVIII) leads to anomalous products of the Claisen rearrangement: compound (XXII) (isopropylidene derivative of (XXI)) and substances (XXIII) and (XXIV), formed by the linear and angular cyclizations of (XXII) (Scheme 2).



Scheme 2

The isolation of (XXIV) (yield 93%) in the form of racemic diastereomers in approximately equal amounts shows the nonstereodirected nature of the cyclization.

When (XVIII) is fused with alkali, the normal Claisen rearrangement products are formed: (XXV) and (XXVI) (see Scheme 2). One of the stereomers of (XXV) has proved to be identical with bucharamine.

Quinoline alkaloids with isoprene substituents containing an α-glycol system frequently form isopropylidene derivatives in the process of separating mixtures of bases with the aid of acetone [61]. The separation of the combined alkaloids of H. bucharicum without acetone leads to the isolation of, in addition to bucharamine (XXV), the diol (XVI), the isopropyl derivative of which is identical with bucharamine. Consequently, the plant does not contain bucharamine, which is an artifact, but (XVI), which has been called bucharaminol.

Pyrano-2-quinolone Derivatives

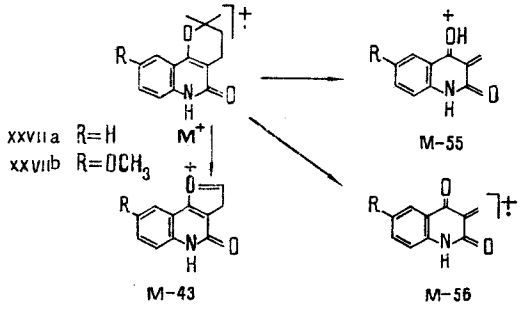
This group of substances, represented in the family Rutaceae by four alkaloids, is based on the skeleton of flindersine, first isolated from the plant Flindersia australis [65]. Flindersine and the new alkaloid haplamine have been found in Haplophyllum species.

The presence of an α,α-dimethylpyran ring in these compounds explains a number of reactions characteristic for this group of alkaloids: hydrogenation of the double bond of the pyran ring in the presence of platinum or nickel catalysts, the cleavage of the pyran ring on distillation with a 30% solution of alkali to give 4-hydroxy-2-quinolone derivatives and acetone; and oxidation with potassium permanganate in an acid medium with the formation of α-hydroxyisobutyric acid [65].

The UV spectra of flindersine and haplamine (Fig. 1d) contain two absorption bands, at 210-260 nm (log ε 4.4) and at 300-380 nm (log ε 4.0), and a minimum at 280 nm (log ε 2.6); the second band is split into several peaks. The spectra of the dihydro derivatives (Fig. 1a) are similar to those of the 4-alkoxy-2-quinolones [55, 65].

The IR spectra of (IIIa) and (IIIb) have the strong absorption band of an amide carbonyl in the 1640-1660 cm^{-1} region and a weak maximum at 3160 cm^{-1} (NH group) [23, 24].

The main peaks in the mass spectra of flindersine and haplamine are those of the ions M^+ and $(M-15)^+$. The ejection of a methyl radical favors the formation of a stable pyrylium ion [9, 23, 24]. The mass spectra of the dihydro derivatives (XXVIIa) and (XXVIIb) are characterized by strong peaks of the molecular ions and of peaks of the ions formed by the elimination of isopropyl and isobutylene radicals and of an isobutylene molecule (Scheme 3) [55].



Scheme 3

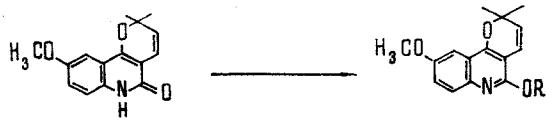
Such decomposition is characteristic of compounds containing an α,α-dimethyldihydropyran ring [66].

In the NMR spectra of (IIIa) and (IIIb), the protons of the pyran ring resonate in the form of two doublets at 3.23-3.28 ppm (Hγ) and 4.44-4.57 ppm (Hβ) (J = 10 Hz) and of a six-proton singlet at 8.45-8.50 ppm (gem-dimethyl group). In the spectra of (XXVIIa) and (XXVIIb) in place of the signals of the olefinic protons two two-proton triplets are observed in the regions of 7.25-7.53 ppm ($CH_2\gamma$) and 8.12-8.32 ppm ($CH_2\beta$) (J = 6.5 Hz) [23, 24, 55, 67].

Haplamine

The structure of haplamine, which was established on the basis of the spectral characteristics of compounds (IIIb) and (XXVIIb) and the production of 4-hydroxy-6-methoxy-2-quinolone by the distillation of the alkaloid with 30% caustic soda solution [24, 55] has been confirmed by synthesis [68].

It follows from the IR spectra of (IIIb) taken in chloroform solution and in a tablet with KBr [55] that haplamine exists in the lactam form in the crystalline state and in chloroform solution. However, in methylation and acetylation haplamine reacts in the lactim form, yielding O-methyl and O-acetyl derivatives (XXVIIIa, XXVIIIb) (Scheme 4).



Scheme 4

The capacity of haplamine for reacting in the lactim form is probably due to a redistribution of the electron density under the influence of the electron-donating substituent, which increases the delocalization of the double bonds in the system. The electronic effect of the methoxy group in position 6 in haplamine and dihydrohaplamine is also shown on the UV spectrum, the long-wave band of which undergoes a bathochromic shift (by ≈20 nm) in comparison with its position in the spectra of flindersine and dihydroflindersine (Fig. 1a and d). A similar shift is characteristic of 4,6-dimethoxy-2-quinolone [56], of 5-hydroxy- and 5-methoxy-2-oxindoles and of 4-methoxyacetanilide [69], in which, as in haplamine, the methoxy group is located in the para position to the nitrogen atom.

Dihydropyrano-4-quinolone Derivatives

Six compounds of this type are found in the family Rutaceae and three of them (IVa-IVc) have been shown to be present in representatives of the genus Haplophyllum.

The racemic form of folifine (the alkaloid ribalinine) has been detected in the plant Balfourodendron riedelianum [70]. The structure of folifine and ribalinine was established in 1967 [14, 70] on the basis of spectral characteristics and has been confirmed by the synthesis of ribalinine. Syntheses of haplofoline [71] and of haplobucharine [10] have also been effected.

On acetylation, haplofoline forms an O-acetyl derivate (ν_{max} 1762 cm^{-1}), and on methylation gives a N-methyl derivative. The oxidation of haplofoline with potassium permanganate in acetone leads to oxalylanthranlic acid [25].

The UV spectra of (IVa-IVc) (Fig. 1e), like the spectra of other alkaloids containing a 4-quinolone system [53], contain two absorption bands at 220-260 nm (log ε 4.5) and 295-340 nm (log ε 4.0). Absorption in the 260-290 nm region, which is characteristic of 2-quinolones and, especially, dihydropyrano-2-quinolones (Fig. 1a) is absent. A second band, frequently split into two or more maxima, undergoes a hypsochromic shift in an acid medium and is observed in the form of a single maximum at ≈300 nm.

The absorption curve of haplofoline, like that of other 4-quinolones containing NH groups [30, 72], shows a hypsochromic displacement in an alkaline medium, which enables haplofoline to be distinguished from its N-alkyl analog by means of their UV spectra. Furthermore, the spectrum of haplofoline is shifted in the short-wave direction by 5-7 nm in comparison with those of (IVb) and (IVc) (Fig. 1e).

The IR spectra of the dihydropyrano-4-quinolones have absorption bands at 1635, 1605, 1585, 1555, and 1515 cm^{-1} of approximately equal intensities which are typical for 2-alkoxy-4-quinolone derivatives [73].

The mass spectrum of haplofoline [66] is almost identical with that of its angular isomer – dihydroflindersine [9]. The fragmentation of haplobucharine [22] begins with the ejection of an isoprene molecule and the formation of an ion with m/e 227, which then decomposes in the same way as the molecular ion of haplofoline [66].

In the NMR spectra of (IVa-IVc), the signal of the proton at C_5 is observed in the form of a quartet at 1.55-1.73 ppm in a weaker field than the signals of the other aromatic protons, which appear in the form of a multiplet in the 2.50-3.03 ppm region. The descreening of H_5 is due to the influence of the anisotropic field of the peri-carbonyl group [74]. The protons of the dihydropyran ring in the spectra of (IVa and IVc), like those of (XXVIIa) and (XXVIIb) resonate at 7.31-7.46 ppm (2 Hγ) and 8.22-8.25 ppm (2 Hβ) in the form of triplets (J = 7 Hz) and of a singlet at 8.59-8.63 ppm (6 H, gem-dimethyl group) [14, 22]. In the spectrum of (IVb), which has a hydroxy group in the β position of the dihydropyran ring, the β- and γ-protons are observed in the form of a one-proton triplet at 6.14 and a two-proton doublet at 7.12 ppm, and because of the magnetic nonequivalence of the methyl groups the gem-dimethyl group appears in the form of singlets at 8.52 and 8.65 ppm [14].

2-Phenylquinoline and 2-Phenyl- and 2-Alkyl-4-quinolone Derivatives

This group of alkaloids is represented in Haplophyllum plants by five compounds (see above), of which graveoline and (VIa) were first isolated from Ruta graveolens [75] and B. riedelianum [73], respectively.

Dubamine is the only representative of Haplophyllum alkaloids which lacks a substituent in position 4. Its oxidation with potassium permanganate in an acid medium forms quinaldinic acid, while oxidation in acetone solution gives oxalylanthranilic acid [76]. The 2-piperonylquinoline structure of dubamine has been confirmed by synthesis [77].

The structure of folimidine (VIc) has been established by a correlation with graveoline and by the production of a monodeutero derivative on its deuteration [29].

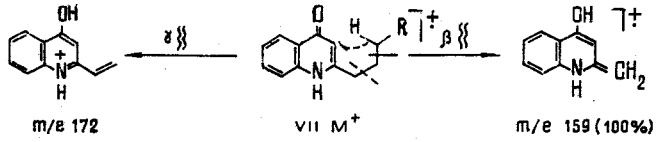
On Adams hydrogenation, acutine forms a dihydro derivative which has been found to be identical with a synthetic sample of 2-heptyl-4-quinolone. The position of the double bond in (VII) has been deduced by a comparative study of the mass and NMR spectra of acutine and its dihydro derivative [78].

The UV spectra of the 2-alkyl-4-quinolones and 2-phenyl-4-quinolones (Fig. 1f, g), each containing two absorption bands at ≈210-240 nm (log ε 4.4) and 290-350 nm (log ε 4.0), each of which is split into two and more maxima, differ by the fact that in place of the minimum at 260 nm characteristic of the 2-alkyl-4-quinolones the spectra of the 2-phenyl-4-quinolones have a number of peaks in the 260-300 nm region (log ε 3.8). The double maximum of the long-wave band undergoes a hypsochromic shift on acidification similar to that in the spectra of the 2-alkoxy-4-quinolones (Fig. 1e, *l*) and it is observed in the form of a single maximum at ≈ 300 nm in the case of the 2-alkyl-4-quinolones and ≈ 328 nm in the case of the 2-phenyl-4-quinolones. The spectrum of acutine (Fig. 1f) undergoes a hypsochromic shift on alkalinization, which is typical for 4-quinolones containing no alkyl group on the nitrogen atom [72].

In the IR spectrum of acutine there are four bands in the 1635-1500 cm^{-1} region, at 1635, 1577, 1560, and 1510 cm^{-1}, and the intensity of the absorption band of the 4-quinolone carbonyl group (1635 cm^{-1}) does not exceed the intensity of the absorption bands of the aromatic system. A similar pattern is observed in the spectra of (VIa-VIc) with the only difference that the absorption maximum of the carbonyl group in the spectra of the 2-phenyl-4-quinolones is found in a lower-frequency region (≈1624 cm^{-1}).

Distinguishing features of the mass spectra of the 2-phenyl-4-quinolones are the maximum intensity of the peak of the molecular ion, the high intensity of the peak of the ion $(M - 28)^+$, corresponding to the ejection of carbon monoxide, and the presence of the peak of the ion $(M - 1)^+$, having a considerable intensity (10-16%) [29].

The main pathway for the fragmentation of the 2-alkyl-4-quinolones is due to the cleavage of the C−C bonds present in the β and the γ positions to the 4-quinolone nucleus, β-cleavage being accompanied by the migration of the γ-hydrogen atom through a six-membered transition state (Scheme 5) [30].



Scheme 5

In the NMR spectra of the 2-alkyl- and 2-phenyl-4-quinolones, the proton at C_3 resonates in the form of a singlet in the 3.51-3.79 and 3.81-3.83 ppm regions, respectively [29, 30]. When deuterochloroform is replaced by trifluoroacetic acid, there is a paramagnetic shift of the H_3 signal in the spectra of the alkaloids of the 2-phenyl-4-quinolone series by 0.66 ppm.

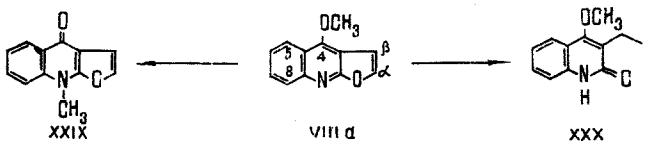
Furanoquinoline Derivatives

This group of compounds is found in the majority of species of the family Rutaceae that have been investigated [11]. The number of alkaloids of the furanoquinoline series known is 36, 18 of which, including 10 new ones, have been found in representatives of the genus Haplophyllum. All the alkaloids of this genus are derivatives of dictamine, and in the majority of them the substituents are present in positions 7 and 8.

A methoxy group at C_4 in the alkaloids of this group is demethylated in an acid or alkaline medium [79], and therefore when phenolic alkaloids of the furanoquinoline series are detected, their presence in the native state is usually a matter of doubt in those cases where the phenolic hydroxyl is located at C_4 [80]. A study of the properties of the Haplophyllum alkaloids has shown that the hydrolysis of (VIIId), (IXc), and (IXj), containing O-prenyl [35, 38] and O-carbohydrate [42]) substituents takes place more readily. For example, 7-isopentenyloxy-γ-fagarine is converted into haplopine on standing in 1% sulfuric acid solution at room temperature, and even during the recording of the NMR spectrum in CF_3COOH. Consequently, doubt about the native nature of the phenolic alkaloids of the furanoquinoline nucleus with the hydroxy group in the homocyclic ring is just as justified as when this group is present at C_4. The fact that in some plants we can easily detect phenolic alkaloids in the acid fractions of an ethanolic extract [10] and in others they are absent even when bases with O-prenyl and O-carbohydrate substituents are present in the plants (robustine is not isolated when haplo-

fidine is present [35], nor is haplopine when glycoperine and 7-isopentenyloxy-γ-fagarine are present [35]), permits the assumption that phenolic alkaloids do actually exist in plants, playing the role of intermediates in the synthesis of O- derivatives of the quinoline series.

The furanoquinoline alkaloids have been the subject of numerous papers and reviews [79, 81], and we shall therefore limit ourselves to giving the most important of the characteristic reactions of this series of substances: Isomerization on interaction with methyl iodide and on hydrogenolysis under the conditions of Adams reduction, leading to the formation of the iso compound (XXIX) and the tetrahydro derivatives (XXX), respectively (Scheme 6).



Scheme 6

Hydrogenation over a palladium catalyst leads to α,β-dihydro derivatives (XXXI) and over Raney nickel to a mixture of (XXX) and (XXXI) [81]. At the present time, characteristic features of the spectral behavior of compounds of the furanoquinoline and of their iso (XXIX), tetrahydro (XXX), and dihydro (XXXI) derivatives have been determined which are used in establishing the structures of new furanoquinoline alkaloids.

The UV spectra of the furanoquinoline alkaloids (Fig. 1h, i) have two absorption bands in the ≈ 230-260 nm (log ε 4.7) and 280-350 nm (log ε 3.8) regions. The second band is frequently split into two and more peaks and is separated from the first maximum by a deep minimum at 260-280 nm (log ε 3.00). A comparison of the absorption spectrum of dictamnine – the simplest representative of this group – with that of the O-substituted analogs shows that the bands of the latter are present in the longer-wave region. The spectra of alkaloids with different alkoxy substituents in one and the same position of the homocyclic ring almost coincide. Isomerization in the 1-methyl-4-quinoline compounds (XXIX) causes a bathochromic shift of the bands by ≈ 10 nm and their change on acidification [45, 53]. The absorption spectra of the tetrahydro derivatives (XXX) are characterized by the appearance of maxima in the 260-295 nm region that are typical for the 2-quinolones and do not change on acidification or alkalinization [45].

The IR spectra of the alkaloids of the dictamnine group contain two bands of low to medium intensity at 3175-3145 and 3140-3112 cm^{-1} [35, 38-41, 43-45] which are characteristic of the unsubstituted furan ring [82]. A number of other bands has been reported [82] at 1639-1616, 1274-1253, 1109-1088, and 885-816, the presence of which the authors concerned connect with the presence of the furan ring. However, these bands are unsuitable for identification purposes since they appear in the spectra of many quinoline alkaloids containing no furan ring.

In the mass spectra of the majority of furanoquinoline alkaloids the peak of the molecular ion has the maximum intensity. Its fragmentation begins in each case with the loss of a methyl radical followed by the elimination of carbon monoxide at the expense of the OCH_3 group at C_4. Compounds containing an OCH_3 group at C_8 undergo fragmentation with the formation of the ions $(M-1)^+$, $(M-29)^+$, and $(M-30)^+$ [83, 84], which are characteristic of all quinoline alkaloids with an OCH_3 group at C_8. The mass-spectrometric fragmentation of the bases (IXc-IXk) begins with the ejection of the substituent at C_7 and the formation of the stable ion of the phenolic compound [38-42], the further fragmentation of which does not differ from that of haplopine [85]; the fragmentation of haplofidine [35], after the ejection of 68 mass units, is correspondingly similar to the fragmentation of robustine [84].

The NMR spectra of the furanoquinoline alkaloids (VIII)-(X) is characterized by the presence in the aromatic region of, in addition to the signals of the protons of the benzene ring, the doublets of the protons of the furan ring at 2.42-2.47 ppm (Hα) and 2.98-3.07 ppm (Hβ) (J = 2.5-3 Hz), which correlates qualitatively with the calculated values of the π-electron densities on the corresponding carbon atoms [86]. Passage to the isofuranoquinolines (XXIX) causes no appreciable shift in the signal of the β proton, while the signal of the α proton undergoes a diamagnetic shift by 0.25 ppm.

The protons of the methoxy group at C_4 resonate in a weaker field (5.54-5.70 ppm) than the protons of the other methoxy groups, which appear in the form of singlets at 5.90-6.30 ppm.

The signal of the proton at C_5, which is present in the peri position with respect to the methoxy group at C_4, in the alkaloids (VIII-X) is observed in a weaker field than the signals of the other aromatic protons. Its assignment may be confirmed by a comparative study of the spectra of the base and of its iso compound

in which the proton at C_5 is selectively descreened by the peri-carbonyl group at C_4, while the signals of the other aromatic protons, particularly that at C_8, undergo a diamagnetic shift [45, 87].

Modified Furanoquinoline Derivatives

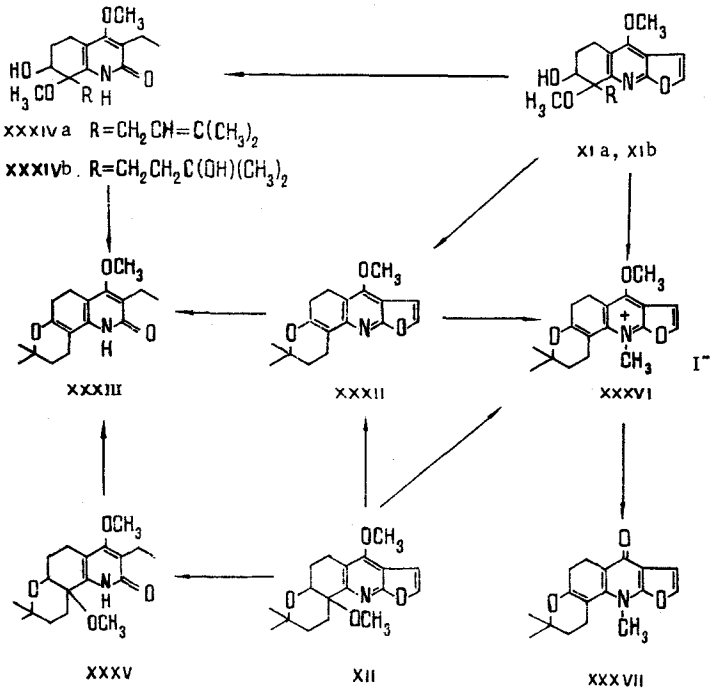
This group of compounds, which have been found only in the plant H. penforatum, differs from the furanoquinoline alkaloids by the structure of the homocyclic ring A.

Haplofilidine, perforine, and anhydroperforine are derivatives of 5,6,7,8-tetrahydrofuranoquinoline, and perfamine is the only representative among the furanoquinoline alkaloids in which the homocyclic ring A is modified to a gem-disubstituted cyclohexadienone ring.

The alkaloids (XIa), (XIb), and (XII) are stable to the action of alkalis, but when they are heated with mineral acids [88], cyclization takes place with the subsequent elimination of a molecule of methanol, leading to the formation of (XXXII) (Scheme 7). The Adams hydrogenation of (XXXII) leads to the hydrogenolysis of the furan ring and the formation of the tetrahydro derivative (XXXIII). We have also made the passage to (XXXIII) by heating with mineral acids tetrahydrohaplofilidine (XXXIVa), tetrahydroperforine (XXXIVb), and tetrahydroanhydroperforine (XXXV), obtained by the reduction of the corresponding bases (XIa, XIb, and XII, respectively) over a platinum catalyst.

In contrast to the situation in the case of furanoquinoline derivatives, a methoxy group at C_4 in compounds with a partially hydrogenated homocyclic ring is not demethylated on being heated with solutions of acids or alkalis and is not isomerized under the action of methyl iodide. The heating of haplofilidine, perforine, and anhydroperforine with methyl iodide in a sealed tube leads to the methiodide (XXXVI) which is also formed in a similar manner from (XXXII). Under the action of an ethanolic solution of alkali the methiodide is converted into the iso compound (XXXVII).

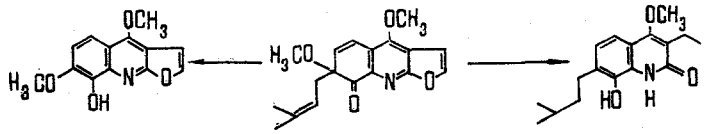
Such behavior of compounds with a partially hydrogenated homocyclic ring (XIa, XIb, XII, and XXXII) permits them to be distinguished by chemical means from the furanoquinoline alkaloids.



Scheme 7

In addition to the correlation of haplofilidine with perforine and with anhydroperforine, transitions have also been effected from perforine to anhydroperforine [48, 88] and to haplofilidine [89].

Perfamine, like compounds with a gem-disubstituted cyclohexadienone ring, tends to undergo a transition to substance with an aromatic structure in an acid medium [90], and on being heated with acid in dioxane solution it is converted into 8-hydroxy-4,7-dimethoxyfuranoquinoline (XXXVIII) and on hydrogenation over a platinum catalyst in glacial acetic acid into 3-ethyl-8-hydroxy-7-isopentyl-4-methoxy-2-quinolone (XXXIX) (Scheme 8) [85].



XXXVIII XIII XXXIX

Scheme 8

Consequently, on the reduction of perfamine in an acid medium, in addition to the hydrogenolysis of the furan ring and the hydrogenation of the double bond of the isopentenyl chain, the hydrogenolytic splitting out of the methoxy group takes place, accompanied, as in the case of the cleavage of perfamine in an acid, by enolization to form a phenolic compound.

The UV spectra of (XIa), (XIb), and (XII) have an absorption band in the 250-290 nm region (log ε 4.1) which is split to several maxima and a minimum at 235 nm (log ε 3.6), and (XIII) has a double maximum at 265 and 273 nm (ε 4.4) and a broad band with its maximum at 345 nm (log ε 3.9) (Fig. 1j) [85, 88].

The IR spectra of (XI-XIII) contain the bands of the stretching vibrations of C – H bonds of the furan ring at 3165-3145 and 3145-3115 cm^{-1} [85, 88]. The total integral intensity of the bands of the skeletal vibrations of the heteroaromatic nucleus in the 1630-1480 cm^{-1} region in the spectra of compounds with a 5.6-7.8 tetrahydro furanoquinoline nucleus is less than that in the spectra of the furanoquinoline alkaloids (ΣA 4.25-3.10 and 6.84-4.90, respectively) [91].

In the mass spectra of perforine and haplofilidine [92], the most intense peaks of the ions with m/e 248, 216 (100%) and 188 are formed as a result of the splitting off of the side chain and the subsequent elimination of molecules of methanol and carbon monoxide. The methoxy group at C_8 and the hydroxy group at C_7 take part in the formation of the latter ions.

A feature of the fragmentation of the molecular ion of anhydroperforine [92] is due to the presence in its molecule of an allyl methoxy group at the nodal point of rings A and D, through which ions with m/e 288, 287, 286, and 285 arise, the m/e 287 ion being the maximum ion in the spectrum.

In the mass spectrum of (XXXII) (M^+, 285, 100%) [92], the strongest peaks, of ions with m/e 242 (62), 230 (72), and 229 (72), arise as the result of the elimination of isopropyl and isobutenyl radicals and an isobutylene molecule, which is typical for compounds containing dimethyldihydropyran rings.

The main fragmentation pathway of the molecular ion of perfamine is the elimination of an isoprene molecule with the formation of an ion with m/e 245 (100%) the further fragmentation of which is analogous to that of haplopine [85].

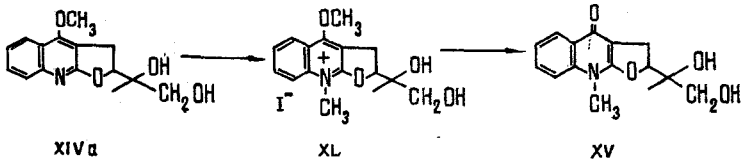
In the NMR spectra of (XIa), (XIb), (XII), and (XIII), in the region of aromatic protons only doublets (J = 3 Hz) of the protons of a furan ring in the 2.53-2.61 (Hα) and 3.13-3.24 ppm (Hβ) regions are observed. In the spectrum of perfamine in this region – in addition to the doublets at 2.36 and 2.92 ppm (J = 3 Hz) of the protons of the furan ring – doublets at 2.10 and 3.88 ppm (J = 9 Hz) of the olefinic protons of the cyclohexadienone ring are observed [85, 88, 92].

In the spectrum of perfamine, the protons of the methoxy group at C_4 (singlet at 5.66 ppm) are found in a weaker field than in the spectra of haplofilidine, perforine, and anhydroperforine (5.78-5.85 ppm region). The protons of the allyl methoxy group in ring A in the spectra of all the compounds are observed in the form of a singlet at 6.87-6.96 ppm [85, 88].

Dihydrofuranoquinoline and Dihydrofurano-4-quinolone Derivatives

Of the 17 compounds of this group known in the family Rutaceae, five are found in representatives of the genus Haplophyllum (see above). With the exception platydesmine, which was first isolated from Platydesma campanulata [93], all the alkaloids are new.

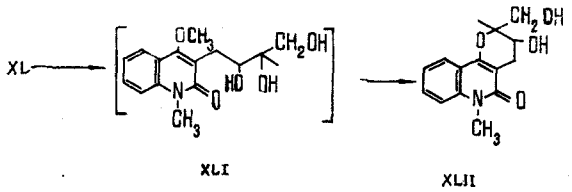
In contrast to the furanoquinoline alkaloids, the dihydrofuranoquinoline alkaloids are not reduced with the opening of the dihydrofuran ring and on being heated with methyl iodide they form methiodides (XL) [19], which are converted into the iso compounds on pyrolysis or on being heated with anhydrous pyridine (Scheme 9) [50].



Scheme 9

Quaternary bases of the dihydrofuranoquinoline series are found in the family Rutaceae, but they have not been detected in Haplophyllum species.

A characteristic property of the quaternary salts of the dihydrofuranoquinoline alkaloids is their capacity for being converted in an alkaline medium into 2-quinolone derivatives (XLI) by the hydrolysis of the dihydrofuran ring [94]. However, in the case of dubinidine methiodide under these conditions isodubinidine (XLII) is formed (Scheme 10) [95]. It was not possible to isolate the intermediate 2-quinolone compound (XLI) even when an alkaline solution of (XL) was heated with a 1 N solution of caustic soda for one minute.



Scheme 10

Being vinyl ethers, 4-methoxy-2-quinolone compounds (XLI), unlike the initial bases (XIVa-XIVc) are readily demethylated to 4-hydroxy-2-quinolone derivatives, and therefore the formation of isodubinidine can be explained by the cyclodehydration of (XLI) through the tertiary hydroxy group of the side chain and the phenolic hydroxyl formed as a result of the saponification of the methoxy group at C_4.

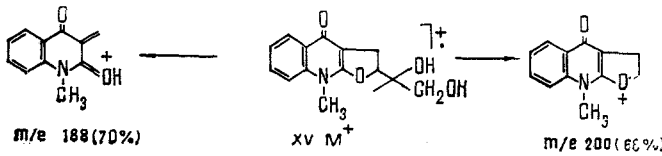
The UV spectra of (XIVa-XIVc) (Fig. 1k) contain three absorption bands in the regions 220-245 nm (log ε 4.5), 250-290 nm (log ε 3.7), and 300-330 nm (log ε 3.5), and those of (XV) and (XVI) (Fig. 1*l*) contain two bands in the ranges 210-240 nm (log ε 4.3) and 290-325 nm (log ε 3.8) and also an inflection at 250 nm (log ε 4.0) [50, 93, 96].

The spectra of the dihydrofuranoquinoline and dihydrofurano-4-quinolone compounds taken in an acid medium are almost identical (Fig. 1k, *l*).

In their IR spectra, both groups of alkaloids give absorption bands in the 1640-1630 cm^{-1} region. But the dihydrofuranoquinoline bases can be distinguished from the isomeric dihydrofurano-4-quinolones by the absence of the strong maximum at 1550 cm^{-1} that is characteristic for the 2-alkoxy-4-quinolone compounds [73].

In the mass spectra of (XIVa-XIVc), the main peaks of the ions with m/e 200 is formed as a result of the splitting out of a side chain [93, 95].

The main directions of fragmentation of folisine are the splitting off of the side chain and the cleavage of the $C_\alpha-C_\beta$ and $O-C_\alpha$ bonds, which leads to stable ions with m/e 200 and 188 (Scheme 11) [50].

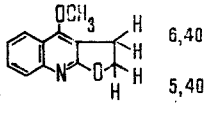


Scheme 11

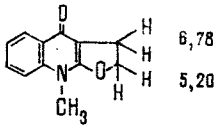
In the mass spectrum of bucharamine (XXV), which is the acetonide of bucharaminol (XVI), the maximum peak of the ion with m/e 214 is formed by the splitting off of the side chain. To this ion corresponds an ion with m/e 215 (80%) arising as a result of the migration of a hydrogen atom to the position of detachment of the side chain. The elimination of one of the methyl groups from the ion with m/e 215 leads to an ion with m/e 200 (18%) [31, 64].

Thus, the mass-spectrometric behavior of the alkaloids of this group depends on the structure of the nucleus (dihydrofurano-4-quinolone or dihydrofurano-4-methoxyquinolone) at the position of the substituents in the dihydrofuran ring.

In the NMR spectra of (XIV-XVI), the protons of the dihydrofuran ring resonate in approximately the same region [31, 50, 94, 97] as the corresponding protons of dihydrodictamnine (XXXI) and dihydroisodictamnine (XLIII) [67].



XXXI



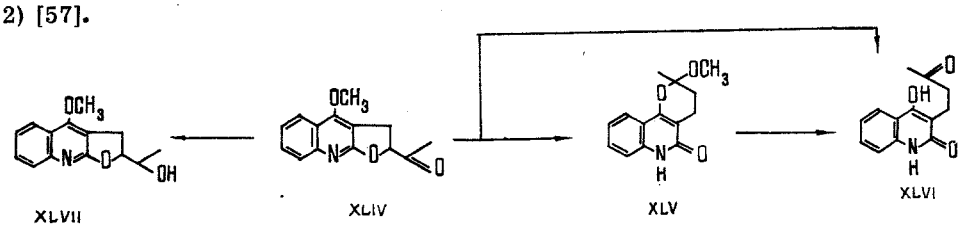
XLIII

The characteristic nature of the chemical shifts of the α- and β-protons of the dihydrofuran ring is used as a criterion in determining the position of substituents in this ring [31, 50, 97]. Trifluoroacetic acid affects the chemical shifts of these protons, shifting them downfield [72].

Dubinidine

The structure of dubinidine (XIVb) proposed on the basis of chemical reactions and spectral characteristics [97] has been confirmed by synthesis [98]. In contrast to all other known α-isopropyldihydrofuranoquinoline and the isomeric 4-quinolone alkaloids, dubinidine contains two adjacent hydroxy groups in the isopropyl substituent. This led to an unusual method of proving its structure, permitting the revelation of properties unknown in this series of compounds. Thus, when dubinidinone (XLIV), obtained by the oxidation of dubinine with periodic acid, is subjected to Clemmensen reduction, the dihydrofuran ring undergoes hydrogenolysis, which is not characteristic for the dihydrofuranoquinoline alkaloids, accompanied by the migration of the methyl radical from the methoxy group to the keto group, which leads to the ketal (XLV) (Scheme 12) [57].

From the products of reduction of (XLIV), we isolated negligible amounts of (XLVI), formed by hydrolysis of the ketal via heating in dioxane in the presence of sulfuric acid, or by the action of trifluoroacetic acid (Scheme 12) [57].



Scheme 12

The Adams hydrogenation of dubinidinone leads to (XLVII). On attempted reduction over a platinum catalyst or amalgamated zinc in hydrochloric acid, dubinidine is recovered unchanged. Consequently, hydrogenolysis of the dihydrofuran ring under the conditions of Clemmensen reduction takes place when there is a keto group in the α position to the ring.

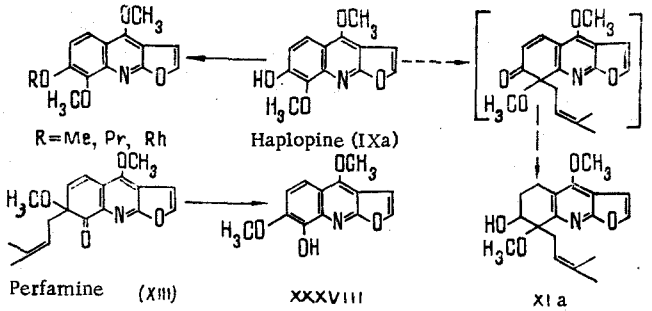
* *
*

At the present time, more than 150 quinoline alkaloids are known which have been found in 64 genera of the family Rutaceae, which numbers about 150 genera [99]. Almost one third of them have been found in the representatives of the genus Haplophyllum.

Furanoquinoline alkaloids have been found in all the plants of this genus with the exception of H. tuberculatum. Among the plants studied, particular interest is presented by H. bucharicum and H. perforatum, which contain peculiar structural modifications of this class of compounds. The biogenetic link of the alkaloids of H. bucharicum, which contain a fragment of two isoprene units, is obvious, since experiments with labelled compounds have shown that the Claisen rearrangement, with the aid of which the transitions from bucharaine to bucharidine and bucharaminol take place, occurs in the plant [100].

The plant H. perforatum is marked by the presence of furanoquinoline compounds the diversity of which is due not only to differences in the structure of the substituents and their positions in the homocyclic ring but also to a modification of the latter into a gem-disubstituted cyclohexadienone ring or into partially hydrogenated rings. The structural similarity and the combined presence of furanoquinoline and modified furanoquinoline alkaloids in the plant permit the assumption that in the alkylation of haplopine transition from an aromatic structure to a cyclohexadienic structure is possible under certain conditions. The isolation of perfamine from the plant shows that this alkylation route is apparently followed in vivo. Perfamine is capable, by the elimination of the alkyl substituent, of being reconverted into a compound of aromatic structure. The

formation of alkaloids with a 5,6,7,8-tetrahydrofuranoquinoline skeleton can be represented through a reduction of compounds of a perfamine type (Scheme 13). It follows from this Scheme that the perculiar alkaloids of Haplophyllum containing no anthranilic acid fragment can be formed by the general anthranilic acid mechanism of biosynthesis.



The detection in plants of the genus Haplophyllum of specific quinoline alkaloids together with representatives of almost all the known modifications of this class of compounds permits the conclusion that among the plants of the family Rutaceae that have been studied this genus is unique as a source of various quinoline substances.

LITERATURE CITED

1. I. Mester and E. C. Vicol, Rev. Roum. Biol., 16, 221 (1971).
2. Flora of the USSR [in Russian], Moscow–Leningrad, Vol. XIV (1949), p. 198.
3. S. Yu. Yunusov and G. P. Sidyakin, Dokl. Akad. Nauk UzSSR, No. 12, 15 (1950); No. 12, 22 (1953); Zh. Obshch. Khim., 22, 1055 (1952).
4. S. Yu. Yunusov, Alkaloids [in Russian], Tashkent (1974), p. 171.
5. E. F. Nesmelova and G. P. Sidyakin, Khim. Prirodn. Soedin., 548 (1973).
6. N. Ya. Isaev and I. A. Bessonova, Khim. Prirodn. Soedin., 815 (1974).
7. A. G. Gonzalez, R. M. Ordonez, and F. R. Luis, An. Quim., 68, 1133 (1972).
8. M. Ionescu, I. Mester, and M. Vlassa, Rev. Roum. Chim., 13, 1641 (1968); M. Ionescu and I. Mester, Phytochem., 9, 1137 (1970).
9. D. Lavie. N. Danieli, R. Weitman, and E. Glotter, Tetrahedron, 24, 3011 (1968).
10. E. F. Nesmelova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 427 (1977) [in this issue]; Khim. Prirodn. Soedin., 289 (1977).
11. P. G. Waterman, Biochem. Syst. and Ecol., 3, 149 (1975).
12. R. Hegnauer Chemotaxonomie der Pflanzen, Birkhauser Verlag, Basel-Stuttgart, Vol. 6 (1973), p. 181.
13. D. Kurbanov and S. Yu. Yunusov, Khim. Prirodn. Soedin., 289 (1967).
14. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 257 (1967).
15. I. M. Saitbaeva, G. P. Sidyakin, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 443 (1966).
16. S. A. Sultanov and S. Yu. Yunusov, Khim. Prirodn. Soedin., 131 (1969).
17. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 133 (1972).
18. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 682 (1976).
19. G. P. Sidyakin, M. Eskairov, and S. Yu. Yunusov, Zh. Obshch. Khim., 30, 338 (1960).
20. S. M. Sharafutdinova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 198 (1968); 264 (1968); 394 (1969).
21. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 455 (1969).
22. E. F. Nesmelova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 815 (1975).
23. V. I. Akhmedzhanova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 262 (1974).
24. V. I. Akhmedzhanova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 109 (1974).
25. I. M. Fakhrutdinova, G. P. Sidyakin, and S. Yu. Yunusov, Uzb. Khim. Zh., No. 4, 41 (1963).
26. S. Yu. Yunusov and G. P. Sidyakin, Dokl. Akad. Nauk UzSSR, No. 10, 19 (1954).
27. D. Durbanov, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 58 (1968).
28. S. A. Sultanov, V. I. Pastukhova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 355 (1967).
29. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 755 (1972).
30. D. M. Gulyamova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 850 (1971).
31. K. Ubaidullaev, A. I. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 343 (1972).
32. D. Kurbanov, G. P. Sidyakin, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 67 (1967).
33. I. M. Fakhrutdinova, G. P. Sidyakin, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 107 (1965).
34. S. Yu. Yunusov and G. P. Sidyakin, Zh. Obshch. Khim., 25, 2009 (1955).

35. Kh. A. Abdullaeva, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 684 (1974).
36. G. P. Sidyakin and S. Yu. Yunusov, Dokl. Akad. Nauk UzSSR, No. 4, 39 (1962).
37. Z. Sh. Faizutdinova, G. P. Sidyakin, and S. Yu. Yunusov, Dokl. Akad. Nauk UzSSR, No. 1, 35 (1966).
38. I. A. Bessonova, V. I. Akhmedzhanova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 677 (1974).
39. E. F. Nesmelova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 666 (1975).
40. V. I. Akhmedzhanova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 289 (1977).
41. V. I. Akhmedzhanova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 272 (1975).
42. V. I. Akhmedzhanova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 680 (1974).
43. Kh. A. Abdullaeva, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 425 (1977) [in this issue].
44. D. K. Kurbanov, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 373 (1968).
45. I. A. Bessonova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 52 (1974).
46. T. T. Shakirov, G. P. Sidyakin, and S. Yu. Yunusov, Dokl. Akad. Nauk UzSSR, No. 6, 28 (1959); No. 9, 40 (1960); No. 8, 47 (1961).
47. G. P. Sidkyakin, I. A. Bessonova, and S. Yu. Yunusov, Dokl. Akad. Nauk UzSSR, No. 10, 33 (1959).
48. I. A. Bessonova, Kh. A. Abdullaeva, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 682 (1974).
49. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 812 (1975).
50. I. A. Bessonova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 629 (1971).
51. V. I. Pastukhova, G. P. Sidyakin, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 27 (1965).
52. Z. Sh. Faizutdinova, I. A. Bessonova, Ya. V. Rashkes, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 239 (1970).
53. A. W. Sangster and K. L. Stuart, Chem. Rev., 65, 97 (1965).
54. I. A. Bessonova, Ya. V. Rashkes, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 358 (1974).
55. V. I. Akhmedzhanova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 320 (1976).
56. T. Sato and M. Ohta, Bull. Chem. Soc. Japan, 31, 157 (1957).
57. I. A. Bessonova, Ya. V. Rashkes, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 217 (1976).
58. R. Storer and D. W. Young, Tetrahedron Lett., 1555 (1972).
59. D. M. Clugston and D. B. McLean, Can. J. Chem., 44, 781 (1966).
60. Ya. V. Rashkes, Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 577 (1970).
61. V. A. Tel'nov, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 724 (1970).
62. K. L. Seitanidi and M. R. Yagudaev, Khim. Prirodn. Soedin., 755 (1974).
63. Ya. V. Rashkes, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 336 (1972).
64. Ya. V. Rashkes, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 364 (1974).
65. R. F. C. Brown, J. J. Hobbs, G. K. Hughes, and E. Ritchie, Aust. J. Chem., 7, 348 (1954).
66. Ya. V. Rashkes, Z. Sh. Faizutdinova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 107 (1970).
67. A. V. Robertson, Aust. J. Chem., 16, 451 (1963).
68. P. Venturella, A. Bellino, and F. Piozzi, Heterocycles, 3, 367 (1975).
69. A. H. Beckett, R. W. Daisley, and J. Walker, Tetrahedron, 24, 6093 (1968).
70. R. A. Corral and O. O. Orage, Tetrahedron Lett., 583 (1967).
71. R. M. Bowman and M. F. Grundon, J. Chem. Soc., (C), 1084 (1966).
72. R. Tschesche and W. Werner, Tetrahedron, 23, 1873 (1967).
73. H. Rapoport and K. G. Holden, J. Amer. Chem. Soc., 82, 4395 (1960).
74. S. Goodwin, J. N. Schoolery, and L. F. Johnston, J. Amer. Chem. Soc., 81, 3065 (1959).
75. H. R. Arthur and H. T. Cheung, Aust. J. Chem., 13, 510 (1960).
76. G. P. Sidyakin, I. A. Bessonova, V. I. Pastukhova, and S. Yu. Yunusov, Zh. Obshch. Khim., 32, 4091 (1962).
77. G. P. Sidyakin, V. I. Pastukhova, and S. Yu. Yunusov, Uzb. Khim. Zh., No. 3, 56 (1962).
78. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 206 (1973).
79. H. G. Boit, Ergebnisse der Alkaloid-Chemie bis 1960, Akademie Verlag, Berlin (1961), p. 708.
80. I. T. Eshiet and D. A. H. Taylor, J. Chem. Soc., (C), 481 (1968); S. R. Johns, J. A. Lamberton, and A. A. Sioumis, Aust. J. Chem., 21, 1897 (1968); I. J. Pachter, R. F. Raffauf, G. E. Ullyot, and O. Ribeiro, J. Amer. Chem. Soc., 82, 5181 (1960).
81. H. T. Openshaw, in: The Alkaloids (ed. R. H. Manske and H. L. Holmes), Academic Press, New York, Vol. III (1953), p. 69; Vol. VII (1960), p. 329; Vol. IX (1967), p. 226; S. C. Parkashi and J. Bhattacharyye, J. Sci. Ind. Res. (India), 24, 226 (1965); P. J. Scheur, in: Chemistry of the Alkaloids (ed. S. W. Pelletier), Van Nostrand/Reinhold, New York (1970), p. 355.
82. L. H. Briggs and L. D. Colebrook, J. Chem. Soc., 2458 (1960).

83. D. M. Clugston and D. B. MacLean, Can. J. Chem., 43, 2516 (1965).
84. Z. Sh. Faizutdinova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 260 (1967).
85. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 791 (1976).
86. M. R. Yagudaev and S. Yu. Yunusov, Khim. Prirodn. Soedin., 55 (1974).
87. S. R. Johns, J. A. Lamberton, and A. A. Sioumis, Aust. J. Chem., 20, 1975 (1967).
88. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 360 (1968).
89. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 356 (1967).
90. V. V. Ershov, A. A. Volod'kin, and G. N. Bogdanov, Usp. Khim., 32, 154 (1963).
91. E. L. Kristallovich, M. R. Yagudaev, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 223 (1976).
92. I. A. Bessonova, Z. Sh. Faizutdinova, Ya. V. Rashkes, M. R. Yagudaev, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 273 (1969).
93. F. Werny and P. J. Scheuer, Tetrahedron, 19, 1293 (1963).
94. S. R. Johns and J. A. Lamberton, Aust. J. Chem., 19, 1991 (1966).
95. I. A. Bessonova, Z. Sh. Faizutdinova, Ya. V. Rashkes, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 446 (1970).
96. I. A. Bessonova, G. P. Sidyakin, and S. Yu. Yunusov, Zh. Obshch. Khim., 34, 347 (1964).
97. I. A. Bessonova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 29 (1969).
98. M. F. Grundon and K. J. James, Tetrahedron Lett., 4724 (1971).
99. A. L. Takhtadzhyan, Systemics in the Physiology of Flowering Plants [in Russian], Moscow–Leningrad (1966), p. 318.
100. T. R. Chamberlain, J. F. Collins, and M. F. Grundon, Chem. Commun., 1269 (1969).

MOLECULAR COMPOSITION OF COTTONSEED PHOSPHATIDYLCHOLINES

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Biological membranes consist mainly of proteins and lipids, and the bulk of the latter are composed of phospholipids, of which phosphatidylcholine (PC) predominates. The structure and a number of important properties of biomembranes depend on the molecular structure of the PC.

In recent years, the structural elements of biomembranes, particularly the phospholipids (PLs) of animal origin, have been studied extremely intensively, but investigations devoted to the PLs of plants and their molecular structure are still inadequate; consequently, the analysis of plant PLs is of great interest.

We have reported [1-3] possible molecular forms of the main groups of PLs of the cotton plant determined by calculation on the basis of the position distribution of the fatty acids in their molecules. In the present paper we give the results of experimental investigations of the fine molecular structure of the PC of the seed kernels of the cotton plant of variety S-6029 [4]. The total fatty-acid composition and position distribution of the fatty acid radicals of the glyceride part of the PC molecule of this variety of cotton plant has been reported previously [3].

The phosphatidylcholines were studied by means of the scheme shown. For better separation into molecular types, the PC was converted by the action of phospholipase into diglyceride (DG) and also into monoacetyldiglyceride (MADG) derivatives. The DG and MADG were separated according to their degree of unsaturation on argentized plates in systems 1 and 2. The yields of the individual fractions are given in Tables 1 and 2.

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