THE ISOQUINOLONE ALKALOIDS

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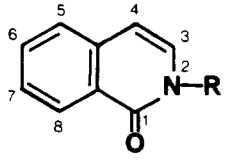
Fifteen isoquinolone alkaloids are presently known. They may be found either in the fully aromatic form *A*, or else in the partially reduced form *B*. The numbering system is as indicated in expression *A*. The R substituent on the nitrogen atom may be either hydrogen or methyl, and carbons 6 and 7 usually possess oxygenated substituents. Three dimeric isoquinolone alkaloids are known; these are baluchistanamine (**1**), revolutinone (**9**), and punjabine (**15**).

Isoquinolone alkaloids have been found among the Ranunculaceae, Menispermaceae, Berberidaceae, Papaveraceae, Hernandiaceae, Fumariaceae, Lauraceae, and Monimiaceae. The alkaloid siamine (**11**), found in a leguminaceous plant, has an exceptional oxygenation pattern and also bears a methyl substituent at C–3. It, thus, differs markedly from the other naturally occurring isoquinolones.

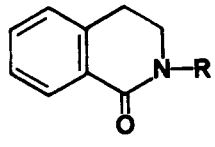
Isoquinolones may originate in nature from the oxidation of benzylisoquinolines. It is possible, however, that they may also be formed from the *in vivo* oxidation of protoberberines, phthalideisoquinolines, or even spirobenzylisoquinolines. The biogenesis of siamine (**11**) is clearly different from that of the fourteen other isoquinolone alkaloids.

Nmr chemical shifts are in δ values. References to nmr data that are immediately followed by a double asterisk (**) indicate that the original spectral assignments may have been slightly modified in the present listing. Chemical shifts possessing identical superscripts are interchangeable. All ^{1}H nmr values are at 60 MHz unless indicated otherwise. If more than one reference is cited for nmr spectral data, it is always the first reference which is the one actually quoted in the present review.

Uv wave-lengths are in nm, and log ϵ values are between parentheses. Only values for λ max are given, unless specifically indicated otherwise. Ir values are in cm^{-1}.

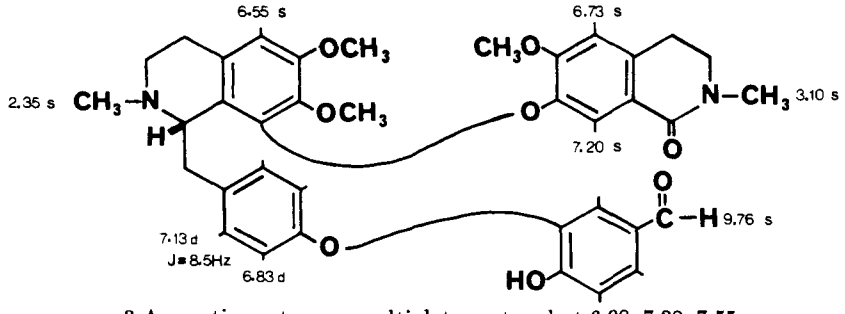


A



B

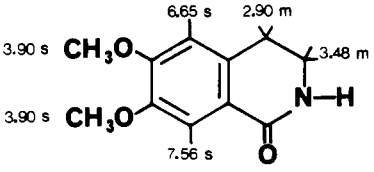
1 BALUCHISTANAMINE $C_{37}H_{38}N_2O_8$: 638.716



3 Aromatic protons as multiplets centered at 6.98, 7.38, 7.55
3 Methoxy singlets at 3.62, 3.85, and 3.90

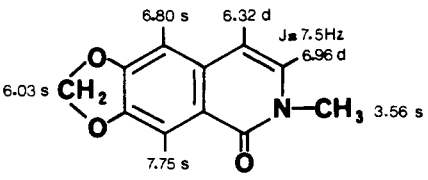
MP: 122–124° (cyclohexane-benzene) (1,2)
UV: (EtOH) 224 (4.57), 260 (4.05), 270 (4.06), 282 sh (3.97), 294 sh (3.90), 305 sh (3.80) (1,2);
(EtOH, OH^-) 227 (4.71), 263 sh (3.93), 274 sh (3.65), 302 (3.42), 350 (3.90) (2)
IR: ($CHCl_3$) 1600, 1640, 1700 (2); 1640, 1720 (1)
NMR: ($CDCl_3$) (2**,1)
MS: 638 (M^+), 411 (100), 365, 227, 206, 204, 120 (1,2)
CD: (MeOH, 0.5 mg/ml) $[\theta]_{290}$ 0, $[\theta]_{263}$ 2560, $[\theta]_{253}$ 0, $[\theta]_{231}$ −14,000, $[\theta]_{220}$ 0 (1,2)
SOURCES: Berberidaceae: *Berberis baluchistanica* Ahrendt (1,5,3,2); *Berberis lycium* Royle (39)

2 CORYDALDINE



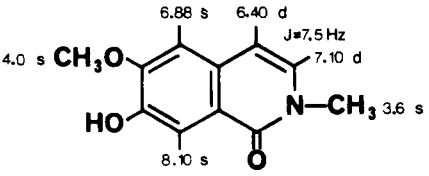
$C_{11}H_{13}NO_3$: 207.228
MP: 173° (benzene-ether) (4);
163–164° (cyclohexane-benzene) (2);
173–174° (ethyl acetate) (2)
UV: (EtOH) 228 (4.26), 270 (3.94), 304 (3.77) (2)
IR: ($CHCl_3$) 1660, 2925, 2995 (2)
NMR: ($CDCl_3$) (2**)
MS: 207 (M^+, 100), 178, 150, 135, 104, 76 (2)
SOURCES: Berberidaceae: *Berberis baluchistanica* Ahrendt (1,2)

3 DORYANINE



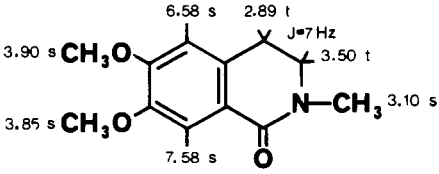
$C_{11}H_9NO_3$: 203.197
MP: 160–162° (acetone and petroleum ether) (6);
162–163° (acetone and petroleum ether) (9);
159–160° (benzene and *n*-hexane) (7)
UV: (EtOH) 231 (4.39), 248 (4.44), 258 (4.34), 284 (3.77), 294 (3.83), 325 (3.58), 338 (3.45) (6,8);
(MeOH) 230 (4.46), 245 (4.49), 258 (4.41), 283 (3.81), 294 (3.85), 326 (3.63), 340 (3.50), (9); see also (7)
IR: (Nujol) 1580, 1610, 1658 (7)
NMR: ($CDCl_3$) (8,6,10); (CF_3CO_2H) (7)
MS: 203 (M^+) (10)
SOURCES: Monimiaceae: *Doryphora sassafras* Endlicher (6,7,8,11)

4 DORYPHORNINE



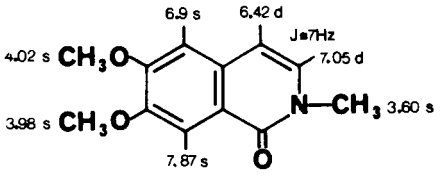
$C_{11}H_{11}NO_3$: 205.212
MP: 215–217° ($CHCl_3$) (9)
UV: (MeOH) 242 (4.64), 271 (3.48), 282 (3.53), 292 (3.55), 325 (3.34) (9);
(MeOH, OH^-) 305 (4.83), 341 (4.40) (9)
IR: (KBr) 1635, 3200 (9)
NMR: ($CDCl_3$) (9**)
MS: 205 (M^+, 100), 199 (19), 162 (31) (9)
SOURCES: Monimiaceae: *Doryphora sassafras* Endlicher (9)

5 N-METHYLCORYDALDINE



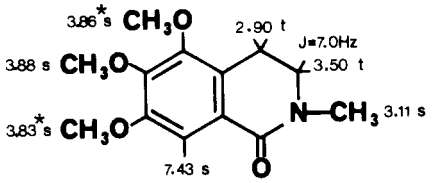
$C_{12}H_{15}NO_3$: 221.255
MP: 120.5° (EtOH) (12);
122° (MeOH) (13);
125–126° (petroleum ether) (14)
IR: ($CHCl_3$) 1590, 1630, 2820, 2920, 2980, 3200–3600 (broad) (15); see also (16)
NMR: ($CDCl_3$) (16**,15,17)
MS: 222 (14), 221 (M^+, 71), 220 (10), 179 (13), 178 (88), 163 (8), 151 (12), 150 (100), 135 (12), 110.5 (9), 107 (8), 92 (11), 126.5 and 143.5 (m) (18); see also (16,15)
SOURCES: Hernandiaceae: *Hernandia ovigera* L. (11,19);
Papaveraceae: *Papaver bracteatum* Lindl. var. 'Arya I' (18);
Papaver urbanium Fedde. (18);
Ranunculaceae: *Thalictrum fendleri* Engelm. ex Gray (16,18)

6 N-METHYL-6,7-DIMETHOXY-ISOQUINOLONE



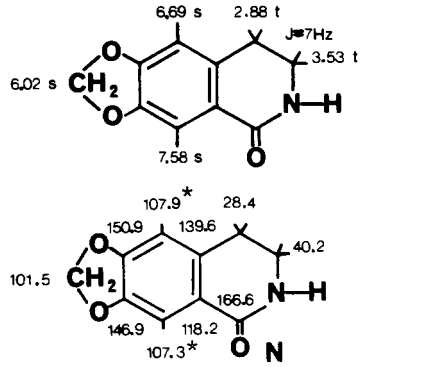
$C_{12}H_{13}NO_3$: 219.240
MP: 112–113° (methanol-chloroform, 1:1) (20); 109–110° (n-hexane) (21); 104–105° (ether) (22)
UV: (MeOH) 245 (3.8), 270 (3.11), 280 (3.18), 290 (3.18), 335 (2.9) (21); (EtOH) 249, 268 sh, 271, 283, 294, 324, 330 infl. (22)
IR: (potassium bromide) 1490, 1590, 1640 (21); see also (22)
NMR: ($CDCl_3$) (21**,17,20,22,23)
MS: 219 (M^+, 100), 204, 190, 176, 109.5 (M^{++}) (20,22)
SOURCES: Hernandiaceae: *Hernandia ovigera* L. (16,21,22);
Menispermaceae: *Stephania sasakii* Hayata (40);
Ranunculaceae: *Thalictrum alpinum* L. (20);
Thalictrum isopyroides C.A.M. (22)

7 N-METHYLTHALIDALDINE



$C_{13}H_{17}NO_4$: 251.282
MP: 104–106° (23)
IR: ($CHCl_3$) 1630 (16)
NMR: ($CDCl_3$) (16**,8,17)
MS: 251 (M^+), 221 (100), 208, 180, 165, (172, 156, 151 metastable peaks) (16)
SOURCES: Ranunculaceae: *Thalictrum fendleri* Engelm. ex Gray (8,16)

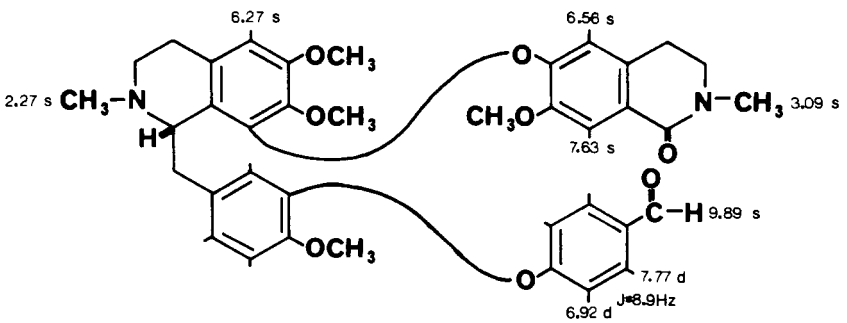
8 NOROXYHYDRASTININE



$C_{10}H_9NO_3$: 191.186
MP: 182–183° (MeOH) (11,24); see also (25)
UV: (MeOH) 223 (4.31), 261 (3.58), 304 (3.67) (8,11,24)
IR: (KBr) 925, 1670, 2800, 3040, 3175 (8,11)
NMR: ($CDCl_3$) (11**)
^{13}C-NMR: (38)
MS: 191 (M^+), 162, 134 (100), 104, 76, 43. Metastable peaks: 137, 111, 81, 56 (8,11)
SOURCES: Fumariaceae: *Fumaria parviflora* Lam. (41)
Ranunculaceae: *Thalictrum alpinum* L. (20)
Thalictrum glaucum Desf. (25);
Thalictrum minus L. var. adiantifolium Hort. (11,24);
Thalictrum rugosum Ait. (25)

9 REVOLUTINONE

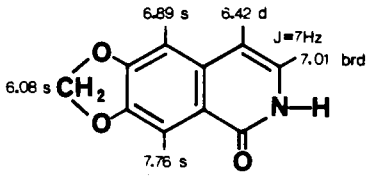
$C_{38}H_{40}N_2O_8$: 652.743



3 Aromatic protons as multiplets centered at 6.79–7.04
4 Methoxy groups at 3.67, 3.73, 3.85, 3.86
$[\alpha]^{28}D$: −10° (c 0.5, MeOH) (26)
UV: (MeOH) 205 sh (5.13), 250 (4.78), 258 (4.76), 272 (4.69), 280 sh (4.66), 301 sh (4.31) (26)

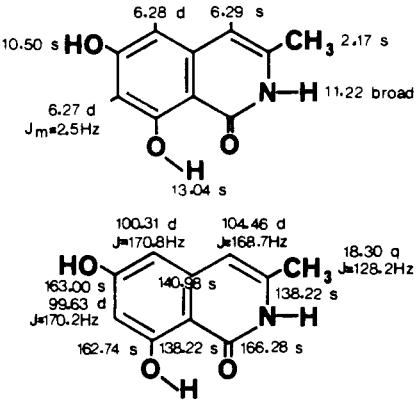
IR: ($CHCl_3$) 1644, 1694, 2720 (26)
NMR: (90 MHz, $CDCl_3$) (26**)
MS: 652 (M^+, 0.15), 411 (100), 241 (4), 221 (3), 205 (2), 203 (2), 190 (3) (26)
CD: (c 7.7x10^{-3}M, MeOH) $[\theta]_{595}$ −2,600, $[\theta]_{260}$ −14,000, $[\theta]_{230}$ 26,000 (26)
SOURCE: Ranunculaceae: *Thalictrum revolutum* DC. (26)

10 6,7-METHYLENEDIOXY-ISOQUINOLONE



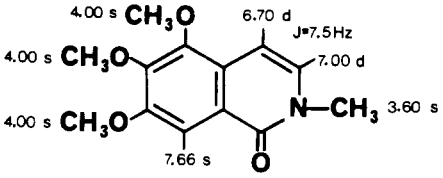
$C_{10}H_7NO_3$: 189.170
MP: 268–270° (decomp.) ($CHCl_3$) (25,27)
UV: (MeOH) 268 sh (3.60), 282 (3.58), 293 (3.59), 312 sh (3.37), 326 (3.47), 340 (3.36) (25)
IR: ($CHCl_3$) 1660, 3400 (25)
NMR: ($CDCl_3$, 90 MHz) (25)
MS: 189 (M^+, 100), 162 (3), 131 (4), 103 (2), 76 (2) (25);
(CI, *i*-butane) 190 (M+1) (100) (25)
SOURCES: Ranunculaceae: *Thalictrum glaucum* Desf. (25);
Thalictrum minus Ait. (25);
Thalictrum rugosum (27)

11 SIAMINE



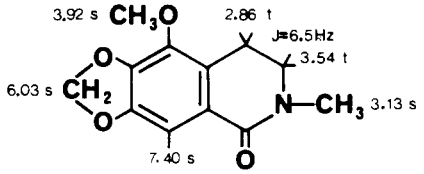
$C_{10}H_9NO_3$: 191.186
MP: 264–268° (MeOH) (28)
UV: (MeOH) 245, 262 sh, 272 sh, 282, 294, 321, 330 (29,30)
IR: 840, 1635 (29,30)
NMR: (30,29)
^{13}C-NMR: (29)
SOURCES: Leguminoseae: *Cassia siamea* (28)

12 THALACTAMINE



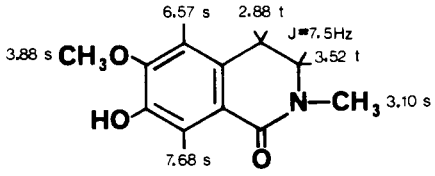
$C_{13}H_{15}NO_4$: 249.266
MP: 111–112° (light petroleum) (21); see also (23)
UV: (MeOH) 245 (3.78), 270 (3.09), 280 (3.17), 290 (3.16), 335 (2.92) (21); see also (8,23)
IR: (KBr) 1600, 1610, 1650 (21); see also (23)
NMR: ($CDCl_3$) (21**,8,17,23)
MS: 249 (M^+) (23)
SOURCES: Ranunculaceae: *Thalictrum minus* (8,21,23)

13 THALFLAVINE



$C_{12}H_{13}NO_4$: 235.239
MP: 140° ($CHCl_3$) (13);
136–137° (MeOH) (31); see also (32,33)
UV: (MeOH) 216 (4.64), 280 (4.13) (31)
IR: (KBr) 940, 1035, 1500, 1600, 1640 (31); see also (32)
NMR: ($CDCl_3$) (31**,17,32)
MS: 235 (M^+, 85), 204 (2), 192 (100), 164 (79), 149 (2), 134 (2), 121 (2), 119 (2), 106 (2), 91 (3), 63 (7), 44 (6) (31); see also (32)
SOURCES: Ranunculaceae: *Thalictrum flavum* L. (32)

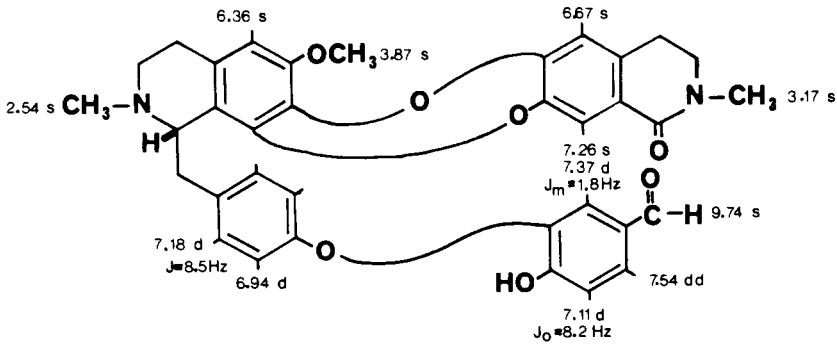
14 THALIFOLINE



$C_{11}H_{13}NO_3$: 207.229
MP: 210–211° (MeOH) (11,24); see also (34);
208–210° ($CHCl_3$) (9);
211–212° ($CHCl_3$) (37); see also (36);
210–211° ($CHCl_3$-MeOH, v/v 99.5:0.5) (35)
UV: (MeOH) 224 (4.41), 261 (3.87), 302 (3.77) (8,24,37); see also (11);
(0.01N methanolic KOH) 238 (4.40), 270 (3.73), 330 (3.65) (11); see also (24)
IR: (KBr) 1640, 3150 (11); (KBr) 1640, 3700–3800 (9);
($CHCl_3$) 1640, 3500 (37,36)
NMR: ($CDCl_3$) (37**,9,11,17,36)
MS: 207 (M^+), 164 (100), 136 (11,37)
X-RAY: (27)
SOURCES: Lauraceae: *Cryptocarya longifolia* Kostermans (27);
Ranunculaceae: *Thalictrum minus* L. var. *adiantifolium* Hort. (11,24,37)

15 PUNJABINE

$C_{35}H_{32}N_2O_7$: 592.647



[α]D: −40° (c 0.48, MeOH) (39)
UV: (MeOH) 231 (4.81), 270 min (4.31), 274 (4.32), 325 sh (3.98) (39);
(MeOH), OH^+) 213 (4.82), 223 min (4.77), 228 (4.78), 253 sh (4.57), 276 min (4.09), 295 (4.11), 339 (4.50) (39)
IR: ($CHCl_3$) 1620, 1645, 1690, 2740, 2850 (39)
NMR: ($CDCl_3$) (39)
MS: 592 (M^+, 0.3), 365 (100), 279 (14), 227 (12) (39)
CD: (MeOH), c 3.04x10^{-5}M) $[\theta]_{350}$ 0, $[\theta]_{300}$ −3300, $[\theta]_{280}$ −11,800, $[\theta]_{271}$ −12,500, $[\theta]_{247}$ −41,450, $[\theta]_{232}$ 0, $[\theta]_{222}$ 34,200 (39)
SOURCES: Berberidaceae: *Berberis lycium* Royle (39)

Occurrence of Isoquinolones by Plant Sources

Family Berberidaceae	
Genus *Berberis*	
B. baluchistanica Ahrendt	Baluchistanamine
	Corydaldine
B. lycium Royle	Baluchistanamine
	Punjabine
Family Fumariaceae	
Genus *Fumaria*	
F. parviflora Lam.	Noroxyhydrastinine
Family Hernandiaceae	
Genus *Hernandia*	
H. ovigera L.	N-Methylcorydaldine
	N-Methyl-6,7-dimethoxyisoquinolone

Family Lauraceae	
Genus *Cryptocarya*	
C. longifolia Kostermans	Thalifoline
Family Leguminoseae	
Genus *Cassia*	
C. siamea	Siamine
Family Menispermaceae	
Genus *Stephania*	
S. sasakii Hayata	N-Methyl-6,7-dimethoxyisoquinolone
Family Monimiaceae	
Genus *Doryphora*	
D. sassafras Endlicher	Doryanine
	Doryphornine
Family Papaveraceae	
Genus *Papaver*	
P. bracteatum Lindl. var. 'Arya I'	N-Methylcorydaldine
P. urbanium Fedde	N-Methylcorydaldine
Family Ranunculaceae	
Genus *Thalictrum*	
T. alpinum L.	N-Methyl-6,7-dimethoxyisoquinolone
	Noroxyhydrastinine
T. fendleri Engelm. ex Gray	N-Methylcorydaldine
	N-Methylthalidaldine
T. flavum L.	Thalflavine
T. glaucum Desf.	Noroxyhydrastinine
	6,7-Methylenedioxyisoquinolone
T. isopyroides C.A.M.	N-Methyl-6,7-dimethoxyisoquinolone
T. minus	Thalactamine
T. minus Ait.	Noroxyhydrastinine
T. minus L. var. adiantifolium Hort.	Noroxyhydrastinine
	Thalifoline
T. revolutum DC.	Revolutinone
T. rugosum Ait.	Noroxyhydrastinine
	6,7-Methylenedioxyisoquinolone

Botanical Distribution of Isoquinolone Alkaloids

1 Baluchistanamine
Berberidaceae: *Berberis baluchistanica* Ahrendt (1,5,3,2)
Berberis lycium Royle (39)

2 Corydaldine
Berberidaceae: *Berberis baluchistanica* Ahrendt (1,2)

3 Doryanine
Monimiaceae: *Doryphora sassafras* Endlicher (6,7,8,11,1)

4 Doryphornine
Monimiaceae: *Doryphora sassafras* Endlicher (9)

5 N-Methylcorydaldine
Hernandiaceae: *Hernandia ovigera* L. (11,19)
Papaveraceae: *Papaver bracteatum* Lindl. var. 'Arya I' (18)
Papaver urbanium Fedde (18)
Ranunculaceae: *Thalictrum fendleri* Engelm. ex Gray (16,18)

6 N-Methyl-6,7-Dimethoxyisoquinolone
Hernandiaceae: *Hernandia ovigera* L. (16,21,22)
Menispermaceae: *Stephania sasakii* Hayata (40)
Ranunculaceae: *Thalictrum alpinum* L (20);
Thalictrum isopyroides C.A.M. (22)

7 N-Methylthalidaldine
Ranunculaceae: *Thalictrum fendleri* Engelm. ex Gray (8,16)

8 Noroxyhydrastinine
Fumariaceae: *Fumaria parviflora* Lam. (41)
Ranunculaceae: *Thalictrum alpinum* L. (20); *Thalictrum glaucum* Desf. (25);
Thalictrum minus L. var. adiantifolium Hort. (11,24);
Thalictrum rugosum Ait. (25)

9 Revolutionone
Ranunculaceae: *Thalictrum revolutum* DC. (26)

10 6,7-Methylenedioxyisoquinolone
Ranunculaceae: *Thalictrum glaucum* Desf. (25);
Thalictrum rugosum Ait. (25)

11 Siamine
Leguminoceae: *Cassia siamea* (28)

12 Thalactamine
Ranunculaceae: *Thalictrum minus* (8,21,23)

13 Thalflavine
Ranunculaceae: *Thalictrum flavum* L. (32)

14 Thalifoline
Lauraceae: *Cryptocaria longifolia* Kostermans (27)
Ranunculaceae: *Thalictrum minus* L. var. adiantifolium Hort. (11,24,37)

15 Punjabine
Berberidaceae: *Berberis lycium* Royle (39)

ACKNOWLEDGMENT

This compilation was carried out in conjunction with research supported by grant No. CA-11450 awarded by the National Cancer Institute, USPHS, USDHHS.

Received 3 September 1981

Notes Added to Proof: The new amorphous alkaloid oxyhydrastinine, which corresponds to N-methyl-3,4-dihydro-6,7-methylenedioxyisoquinolone, $C_{11}H_{11}O_3N$, has been found in two members of the Papaveraceae family, *Argemone mexicana* L. and *Papaver dubium* L., var. *glabrum*. The $CDCl_3$ nmr spectrum shows H-5 and H-8 as singlets at δ6.61 and 7.54, respectively. The methylenedioxy singlet is at δ5.99 and the N-methyl singlet is at δ3.13. The C-3 and C-4 protons appear as triplets at δ3.51 (J_A=6.5 Hz) and 2.90 (J_B=7.0 Hz), respectively (42).

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