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FLAVONOIDS FROM *DODONAEA VISCOSA**

KUSUM SACHDEV and DINESH K KULSHRESHTHA

Central Drug Research Institute, Lucknow, India

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Key Word Index—*Dodonaea viscosa*, Sapindaceae, 6-methoxyflavonols, flavanone, isorhamnetin 3-rhamnosylgalactoside, aliarin, 5,7-dihydroxy-3′-(3-hydroxymethylbutyl)-3,6,4′-trimethoxyflavone

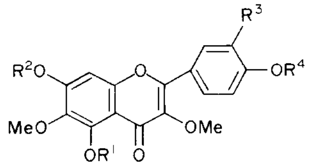
Abstract—An investigation of *Dodonaea viscosa* afforded a new flavonoid having an isoprenoid side chain along with the seven known flavonoids· 5-hydroxy-3,6,7,4′-tetramethoxyflavone, pinocembrin, santin, penduletin, 5,7,4′-trihydroxy-3,6-dimethoxyflavone, aliarin and isorhamnetin 3-rhamnosylgalactoside The structure of the new flavonoid was elucidated as 5,7-dihydroxy-3′-(3-hydroxymethylbutyl)-3,6,4′-trimethoxyflavone

INTRODUCTION

As a part of our investigation on *Dodonaea viscosa* L [1], we report here the isolation of eight flavonoids including one new compound (3) The structural elucidation of the latter is described.

RESULTS AND DISCUSSION

The chloroform fraction of the alcoholic extract of the aerial part of *Dodonaea viscosa* afforded, on chromatographic separation, 5-hydroxy-3,6,7,4′-tetramethoxyflavone (**1**), 5,7-dihydroxyflavanone, (pinocembrin), 5,7-dihydroxy-3,6,4′-tetramethoxyflavone (santin) (**2**), a new flavonoid (**3**) and 5,7,4′-trihydroxy-3′(3-hydroxymethylbutyl)-3,6-dimethoxyflavone (aliarin) (**4**). The *n*-butanol fraction was resolved into ethyl acetate and water fractions. The ethyl acetate fraction yielded 5,4′-dihydroxy-3,6,7-trimethoxyflavone (penduletin) (**5**) and 5,7,4′-trihydroxy-3,6-dimethoxyflavone (**6**), whereas isorhamnetin 3-rhamnosylgalactoside was obtained from the water fraction after repeated chromatography over Si gel



1 $R^2 = R^4 = Me$, $R^1 = R^3 = H$

2 $R^4 = Me$, $R^1 = R^2 = R^3 = H$

3 $R^4 = Me$, $R^3 = CH_2CH_2CH{<}^{CH_2OH}_{Me}$, $R^1 = R^2 = H$

4 $R^3 = CH_2CH_2CH{<}^{CH_2OH}_{Me}$, $R^1 = R^2 = R^4 = H$

5 $R^2 = Me$, $R^1 = R^3 = R^4 = H$

6 $R^1 = R^2 = R^3 = R^4 = H$

7 $R^2 = Me$, $R^3 = CH_2CH_2CH{<}^{CH_2OH}_{Me}$, $R^1 = R^4 = H$

8 $R^1 = R^2 = R^4 = Me$, $R^3 = CH_2CH_2CH{<}^{CH_2OH}_{Me}$

Flavonoid **3**, M$^+$ 430, gave a positive Shinoda test and a negative Quastel test which indicated it to be a flavonoid without free *ortho*-dihydroxyl functions Its solubility in 10 % aqueous sodium carbonate suggested the presence of a free hydroxyl group at C-7 In its UV spectrum (Table 2) the aluminium chloride–hydrochloric acid shift of band I by 21 nm indicated the presence of a free 5-OH function along with 6-OR grouping [2] The presence of an oxygen function at C-6 is also corroborated by the suppression of band II for a free 7-OH [3]. Moreover, the position of band II in **3** at 272 nm was almost identical with the corresponding band of the other 6-methoxy flavonoids isolated from this plant This observation also suggested a common oxygenation pattern of ring A in these flavonoids, i e at positions C-5–C-7

The ¹H NMR spectrum showed a set of signals that could be assigned to a side chain of the type $-CH_2CH_2CH{<}^{CH_2OH}_{Me}$, viz a 3H doublet ($J = 7$ Hz) at δ 0.91 for a methyl group located adjacent to a methine group, a 2H doublet ($J = 7$ Hz) at 3 43 due to resonance of $-CH_2OH$ protons attached to the same methine carbon, a broad multiplet at 1.55 integrating for three protons assigned to $-CH_2-CH{<}$ part and a 2H triplet ($J = 7$ Hz) at 2 61 due to a benzylic $-CH_2$ group This spectrum also revealed the presence of three methoxyl groups appearing as 3H singlets at δ 3 71, 3 78 and 3 9 The aromatic region had a 1 H singlet at δ 6.42 ascribable to the proton at C-8, the only unsubstituted position in ring A Ring B protons displayed a 3H ABX pattern of splitting, resulting in the appearance of an *ortho*-coupled 1H doublet ($J = 9$ Hz) at δ 6 88, a *meta*-coupled 1H doublet ($J = 3$ Hz) at 7 75 and a 1H double doublet ($J = 3$ 9 Hz) at 7.8 assigned to H-5′, H-2′ and H-6′, respectively These data required the placement of the remaining substituents, viz two methoxyl groups and one isoprenoid side chain at C-3, C-3′ and C-4′

The side chain was placed in ring B on the basis of its mass spectrum It showed losses of 73 and 72 a.m u from

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$[M]^+$ as well as from $[M-Me]^+$, $[M-H_2O]^+$ and $[B_2]^+$ Occurrence of benzylic cleavage explained the loss of 73 a m u Loss of 72 a.m u was explainable by the β-cleavage of the side chain accompanied by hydrogen transfer to the aromatic nucleus which takes place via a 1,6-rearrangement. This kind of rearrangement requires at least one free *ortho* position [4], therefore, the choice of placing the side chain was narrowed down to either C-3′ or C-4′ Facile loss of a methyl radical followed by the loss of 28 a m u favoured methoxyl groups at C-3 and C-6 [3] Besides the fragmentation pattern, the relative intensities of $[M]^+$, $[M-H]^+$, $[M-Me]^+$ and $[M-H_2O]^+$ (see Experimental) were also in conformity with the placement of two hydroxyl groups at C-5 and C-7 and two of the three methoxyl functions at C-3 and C-6, respectively [5].

The relative disposition of the side chain and methoxyl group in ring B of 3 was settled by its correlation with aliarin (**4**), a compound reported earlier from this plant [1] Thus, aliarin was methylated with ethereal diazomethane but this methylating agent failed to react upon the C-4′ hydroxyl group presumably due to the steric hindrance caused by the bulky side chain As a consequence, it gave 5,4′-dihydroxy-3′-(3-hydroxymethylbutyl)-3,6,7-trimethoxyflavone (**7**) which, although being a monomethyl ether of aliarin, was found to be different from **3** on the basis of its UV and mass spectra However, when both **3** and **4** were separately methylated with dimethylsulphate–potassium carbonate in dry acetone, they furnished permethylated products (**8**), (M^+, 458) which were identical in all respects (co-chromatography and superimposable IR and mass spectra) This result led to the conclusion that the side chain in **3** was present at C-3′, as in aliarin, with the remaining methoxyl group at C-4′ Thus, the structure of **3** was established as 5,7-dihydroxy-3′-(3-hydroxymethylbutyl)-3,6,4′-trimethoxyflavone

Other products isolated from the plant. 5-hydroxy-3,6,7,4′-tetramethoxyflavone (**1**), pinocembrin, santin (**2**), penduletin (**5**), and 5,7,4′-trihydroxy-3,6-dimethoxyflavone (**6**) were identified by UV (Table 2), ^{1}H NMR (Table 3) and mass spectra (Table 1) Flavonoids **2**, **5** and **6** were correlated with each other by their conversion into **1** on treatment with ethereal diazomethane The identity of isorhamnetin 3-*O*-rhamnosylgalactoside was determined by UV, ^{1}H NMR, FDMS, acid hydrolysis and finally by comparison of its

Table 1 Mass spectral data of 6-oxygenated flavonoids from *Dodonaea viscosa**†

	1	**2**	**4‡**	**5**	**6**
$[M]^+$	358 (100)	344 (100)	416 (100)	344 (100)	330 (100)
$[M-H]^+$	357 (35 8)	343 (31 5)	415 (27)	343 (30)	329 (28 2)
$[M-Me]^+$	343 (60)	329 (39 4)	401 (42 9)	329 (55 2)	315 (41 9)
$[M-H_2O]^+$	340 (30)	326 (21)	398 (20 7)	326 (7 7)	312 (16)
$[M-HCO]^+$	329 (5 8)	— —	— —	315 (10 3)	301 (4 3)
$[M-Me-H_2O]^+$	325 (6 3)	311 (10 5)	383 (5)	311 (4 3)	297 (5 2)
$[M-MeCO]^+$	315 (15)	301 (25 2)	373 (11 7)	301 (11 1)	287 (19 5)
$[M-MeCO-H_2O]^+$	297 (8 3)	283 (14)	355 (7)	283 (4 2)	269 (9 2)
$[M-MeCO-MeCO]^+$	272 (3 3)	258 (7 8)	330 (4 5)	258 (2 7)	244 (5 4)
$[A_1+H]^+$	197 (1 6)	– —	183 (4 4)	197 (1 6)	183 (1 6)
$[A_1-Me]^+$	181 (10 8)	167 (5 2)	167 (4 5)	181 (10 5)	167 (5 6)
$[A_1-MeCO]^+$	153 (10 3)	139 (3 2)	139 (5)	167 (3 3)	139 (2 4)
$[A_1-MeCO-CO]^+$	125 (3 1)	— —	- —	139 (1 1)	— —
$[B_2]^+$	135 (20)	135 (13 1)	207 (2 5)	121 (18 5)	121 (16 2)

*Mass spectra were run at 70 eV, source temp from 180° to 200° and probe temp from 200° to 230°. Values in m/z are followed by rel int of the peaks in parentheses For A_1 and B_2 terminology see ref [3]

†Mass spectrum of **3** is given in the Experimental

‡Peaks at m/z (rel int) 344 $[M-72]^+$ (4 5), 343 $[M-73]^+$ (9 1), 329 $[M-Me-72]^+$ (9 9), 328 $[M-Me-73]^+$ (4 9), 135 $[B_2-72]^+$ (2 5), 134 $[B_2-73]^+$ (3 5), 107 $[B_2-72-CO]^+$ (2 5) and 106 $[B_2-73-CO]^+$ (3 5) were also observed

Table 2 UV spectral data of 6-oxygenated flavonoids from *Dodonaea viscosa** †

	1	2	3	4	5	6
MeOH	338 275	340 274	335, 300sh 272	350, 305sh 270	340 272	340 273
NaOMe	— 275	375, 297sh, 276	370, 300sh 272	402 285	390 275	410, 327sh 274
$AlCl_3$	358 287	360, 305sh, 283	362, 305sh, 276	366, 308sh, 275, 255	367 284	258 278
$AlCl_3$–HCl	356 287	357, 305sh 284	356, 305sh 280	361, 308sh 278, 252	358 282	355 275
NaOAc	338 275	368, 305sh 275	370, 300sh 273	370, 305sh 275	388, 340sh 270	392, 300sh 274
NaOAc–H_3BO_3	338 273	340 273	342 271	350, 305sh 272	340 272	343 272

* λ_{max} in nm

† All UV spectra were recorded using standard procedures [13]

Table 3 ^1H NMR spectral data of 6-oxygenated flavonoids from *Dodonaea viscosa** †

	1	2	4	5	6
H-8	6 6 *s*	6 41 *s*	6.42 *s*	6 75 *s*	6 49 *s*
H-2′	7 94 *dd* (2, 10)	7 96 *dd* (3 5, 10)	7.83 *d* (2 5)	8 0 *dd* (2, 10)	7 94 *dd* (3.5, 10)
H-3′	6 95 *dd* (2, 10)	6 97 *dd* (3 5, 10)	—	6 92 *dd* (2, 10)	6 93 *dd* (3 5, 10)
H-5′	6 95 *dd* (2, 10)	6 97 *dd* (3 5, 10)	6 88 *d* (9)	6 92 *dd* (2, 10)	6 93 *dd* (3 5, 10)
H-6′	7 94 *dd* (2, 10)	7 96 *dd* (3 5, 10)	7 72 *dd* (2 5, 9)	8 0 *dd* (2, 10)	7 94 *dd* (3.5, 10)
OMe	3 68, 3 76 3 79, 3 80 *s*	3 8, 3 78 (6H) *s*	3 76, 3 78 *s*	3 77, 3 85 3 95 *s*	3 83, 3 95 *s*
$-CH_2CH_2CH{<}^{CH_2OH}_{Me}$	—	—	Me, 0 93, *d* (7), $-CH_2CH{<}$, 1 7, *m*, $-CH_2$, 2 68, *d* (7), $-CH_2OH$, 3 39, *d* (7)	—	—

*Spectra were recorded in Me_2CO-d_6 Values are given in δ-values (ppm) downfield from TMS as internal standard *J* values in Hz are given in parentheses

† ^1H NMR of **3** is given in text

data with those reported in the literature [6, 13].

Interestingly, the characterizations of aliarin (**4**) and 5,7-dihydroxy-3′-(3-hydroxymethylbutyl)-3,6,4′-trimethoxyflavone constitute the first report of *C*-prenylation in ring B in the area of flavones and flavonols Previously, *C*-prenylation in ring B has been noticed in flavanones, isoflavanones and isoflavones only. It is also noteworthy that in the family Sapindaceae, 6-oxygenated flavonoids have been isolated only from the genus *Dodonaea*: 5-hydroxy-3,6,7,4′-tetramethoxyflavone from *Dodonaea lobulata* [14] and santin from *Dodonaea attenuata* var. *linearis* [15] and *Dodonaea viscosa* var *angustifolia* [16]. Both of these flavonoids have also been isolated in the present studies.

EXPERIMENTAL

All mps are uncorr. IR spectra were recorded in KBr, UV spectra were obtained in MeOH, CC employed Si gel and polyamide The isolation of flavonoids was monitored by TLC over Si gel using the following solvents (1) C_6H_6–MeOH (9 5 0 5), (2) $CHCl_3$–MeOH (9.5 0.5), and (3) EtOAc–MeOH–H_2O (8 1 1). The compounds were visualized by spraying with 1 % ceric sulphate in 2 N H_2SO_4 Sugars were chromatographed over Whatman No 1 paper using *n*-BuOH satd with H_2O.

Extraction and isolation 14 kg of air-dried, ground aerial parts of *Dodonaea viscosa* L (voucher specimen deposited in CDRI) was extracted with alcohol The alcoholic extract was concd under red pres at *ca* 50° and resolved into *n*-hexane, $CHCl_3$, *n*-BuOH and H_2O soluble fractions The *n*-BuOH fraction was further partitioned into EtOAc and H_2O The gross fractionation of the $CHCl_3$ fraction was effected over Si gel using *n*-hexane, C_6H_6 and EtOAc The C_6H_6–EtOAc (3 1) eluate, on further chromatography over Si gel, yielded **1**, pinocembrin and **2** The EtOAc eluate gave **3** and **4** by repeated column and prep TLC over Si gel in solvent 2

The EtOAc fraction of the *n*-BuOH soluble material was repeatedly chromatographed over Si gel and polyamide to yield a mixture of **5** and **6** which were further separated by chromatography over Si gel using gradient elution with $CHCl_3$–MeOH The H_2O fraction of the same material was chromatographed over Si gel using EtOAc (satd with H_2O)- MeOH in the sequence of increasing polarity, this resulted in the elution of isorhamnetin 3-rhamnosylgalactoside in EtOAc (satd with H_2O)- MeOH (9 8 0 2)

5-Hydroxy-3,6,7,4′-tetramethoxyflavone (**1**) was crystallized from *n*-hexane–Me_2CO as yellow needles, mp 176°, TLC in solvent 1 It was identified by UV, MS and ^1H NMR as **1** [7, 14] (Tables 1 3)

Pinocembrin was crystallized from *n*-hexane–Me_2CO as white needles, mp 201°, TLC in solvent 1 It was characterized from its UV, ^1H NMR and MS data [8, 9]

Santin (**2**) was also crystallized from *n*-hexane–Me_2CO, mp 163 , TLC in solvent 1 On the basis of UV, ^1H NMR, MS and solubility in 10% aq Na_2CO_3 its structure was established as **2** [10, 15] (Tables 1–3)

Penduletin (**5**) was crystallized from Me_2CO, mp 212–214°, TLC in solvent 2 Its UV, ^1H NMR and MS data (Tables 1 3) were in agreement with those of **5** [11]

5,7,4′-Trihydroxy-3,6-dimethoxyflavone (**6**) was obtained as dark yellow crystals mp 217°, TLC in solvent 2 It was identical with **6** (UV, MS and ^1H NMR, Tables 1–3) [12]

Isorhamnetin 3-rhamnosylgalactoside was crystallized from $CHCl_3$ MeOH, mp 187°, TLC in solvent 3 It was hydrolysed with 2 N HCl at 100° for 4 hr and the aglycone identified by its spectral data [13] and sugars by PC The UV, ^1H NMR and MS data of the glycoside were identical with those reported in the lit [6]

5,7-Dihydroxy-3′-(3-hydroxymethylbutyl)-3,6,4′-trimethoxyflavone (**3**) TLC in solvent 2 IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3485, 3000, 2920, 1650, 1605 and 1250, UV in Table 2, ^1H NMR in the text, MS *m/z* (rel int) 430 $[M]^+$ (100), 429 $[M-H]^+$ (27 3), 415 $[M-Me]^+$ (43 6), 412 $[M-H_2O]^+$ (26 9), 397 $[M-Me-H_2O]^+$ (9 4), 387 $[M-MeCO]^+$ (17 3), 369 $[M-MeCO-H_2O]^+$ (14 5), 358 $[M-72]^+$ (5 4), 357 $[M-73]^+$ (11 6), 343 $[M-Me-72]^+$ (18 2), 342 $[M-Me-73]^+$ (2 4), 340 $[M-H_2O-72]^+$ (2 4), 339 $[M-H_2O-73]^+$ (3 8), 221 $[B_2]^+$ (8 2), 206 $[B_2-Me]^+$ (3 6), 193 $[B_2-CO]^+$ (3 3), 183 $[A_1+H]^+$ (10 0), 182 $[A_1]^+$ (3 4), 167 $[A_1-Me]^+$ (18 2), 155 $[A_1-CO]^+$ (9 1), 149 $[B_2-72]^+$ (39 9), 148 $[B_2-73]^+$ (6 9), 140 $[A_1+H-MeCO]^+$ (5 3), 139 $[A_1-MeCO]^+$ (9 3), 135 (11 0), 134 $[B_2-72-Me]^+$ (8 2), 133 $[B_2-73-Me]^+$ (9 1), 121 $[B_2-72-CO]^+$ (9 4), 120 $[B_2-73-CO]^+$ (5 6), 112 $[A_1+H-MeCO-CO]^+$ (12 5), 111 $[A_1-MeCO-CO]^+$ (21), 106 $[B_2-72-MeCO]^+$ (4 5), 105 $[B_2-73-MeCO]^+$ (18 7)

5,4′-Dihydroxy-3′-(3-hydroxymethylbutyl)-3,6,7-trimethoxyflavone (**7**) TLC in solvent 2 UV λ_{max}^{MeOH} nm 272, 300 (sh), 338, + NaOMe 274, 406, + $AlCl_3$ 278, 305 (sh), 368, + $AlCl_3$–HCl 276, 305 (sh), 355, + NaOAc 270, 345, + NaOAc–H_3BO_3 270, 345 MS *m/z* 430 (M^+, base peak), 429 $[M-H]^+$, 415 $[M-Me]^+$ 412 $[M-H_2O]^+$ 398 $[M-Me-H_2O]^+$ 387 $[M-MeCO]^+$, 369 $[M-MeCO-H_2O]^+$, 358 $[M-72]^+$, 357 $[M-73]^+$, 343 $[M-Me-72]$ 342 $[M-Me-73]^+$ 340 $[M-H_2O-72]^+$ 339 $[M-H_2O-73]^+$, 207 $[B_2]^+$, 197 $[A_1+H]^+$, 181 $[A_1-Me]^+$, 168 $[A_1-CO]^+$ 155 153 $[A_1-MeCO]^+$, 149, 135 $[B_2-72]^+$, 134 $[B_2-73]^+$, 125 $[A_1-MeCO-CO]^+$ 107 $[B_2-72-CO]^+$, 106 $[B_2-73-CO]$

3′-(3-Hydroxymethylbutyl)-3,5,6,7,4′-pentamethoxyflavone (**8**) TLC in solvent 2 IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3400, 3000, 2920, 1625, 1600 and 1248, ^1H NMR (60 MHz, CCl_4) δ 0 91 (3H *d*, *J* = 7 Hz Me), 1 50 (3H, m, $C\underline{H}_2$ CH<), 2 57 (2H, *t*, *J* = 7 Hz benzylic protons), 3 4 (2H, *d*, *J* = 7 Hz, CH_2OH), 3 70 (6H, s 2 × OMe), 3 78 (3H, s, OMe) 6 51 (1H s, H-8) 5 72 (1H *d*, *J* = 10 Hz, H-5′), 7 66 (1H, *d* *J* = 3 Hz H-2′), 7 73 (1H, *dd*, *J* = 3, 10 Hz, H-6′), MS *m/z* 458 $[M]^+$, 457 $[M-H]^+$, 443 $[M-Me]^+$, 440 $[M-H_2O]^+$ 439 $[M-H_2O-H]^+$ 425 $[M-Me-H_2O]^+$ 415 $[M-MeCO]^+$ 397 $[M-MeCO-H_2O]^+$, 386 $[M-72]^+$, 385 $[M-73]^+$ 371 $[M-Me-72]^+$ 370 $[M-Me-73]$, 221 $[B_2]^+$, 211 $[A_1+H]^+$, 196 $[A_1-H-Me]^+$ 195 $[A_1-Me]^+$, 167 $[A_1-MeCO]^+$, 149 $[B_2-72]$, 148 $[B_2-73]^+$ 139 $[A_1-MeCO-CO]^+$ 134 $[B_2-72-Me]^+$, 133 $[B_2-73-Me]^+$ 121 $[B_2-72-CO]$, 120 $[B_2-73-CO]^+$, 106 $[B_2-72-MeCO]^+$ 105 $[B_2-73-MeCO]^+$

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