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# DIHYDROFLAVONOLS FROM *CEDRUS DEODARA**

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**Key Word Index**—*Cedrus deodara*; Pinaceae; wood extractives; taxifolin; cedeodarin, 5, 7, 3′, 4′-tetrahydroxy-6-methyl-2, 3-dihydroflavonol; cedrin, 5, 7, 3′, 4′, 5′-pentahydroxy-6-methyl-2, 3-dihydroflavonol; dihydromyricetin; cedrinoside; dihydroflavonols.

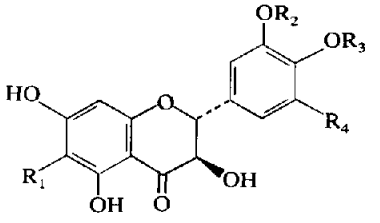
**Absract**—The identification of taxifolin and structure elucidation of cedeodarin (6-methyltaxifolin), dihydromyricetin, cedrin (6-methyldihydromyricetin) and cedrinoside from cedar wood are described.

*Cedrus deodara* (Roxb.)Loud. (Pinaceae) is reputed [1] to be useful in various ailments in indigenous systems of medicine. So far the characterization and biological evaluation for spasmolytic activity of five sesquiterpenoids from this taxon [2–5] have been described. Recently, it was observed that the butanol-soluble fraction of the plant extract showed marked anti-inflammatory activity in carrageenin-induced edema in mice, which prompted a detailed chemical investigation.

## RESULTS AND DISCUSSION

The defatted alcoholic extract of the plant wood was separated into chloroform and butanol-soluble fractions. The latter fraction was purified by lead acetate precipitation. The dark brown viscid material obtained by decomposing the lead salts was repeatedly chromatographed over cellulose which led to the isolation of five constituents A, B (cedeodarin), C (cedrin), D and E (cedrinoside). The residue obtained after removing Pb ions from the filtrate, showed the presence of nine phenolic constituents which will be described subsequently.

Substance A, mp 232–234°, $C_{15}H_{12}O_7$, $M^+$304.0592, gave a violet colour with aqueous $FeCl_3$ and a yellow colour with alkali which suggested it to be a phenolic compound with a chromone moiety. It gave a violet–red colour with Mg in HCl. The $UV_{max}$ at 291 and 332 nm (infl.) were closely related to dihydroflavonol [6]. A bathochromic shift (24 nm) on addition of $AlCl_3$ and IR absorption at 1630 $cm^{-1}$ indicated the presence of a chelated hydroxyl group *peri* to carbonyl. The $^1$H NMR spectrum indicated a pair of doublets at $\delta$ 4.93 and 4.47 typical of the AB system of the vicinal protons at C-2 and C-3 of 3-hydroxy flavanone [7]. The remaining features of the $^1$H NMR spectrum defined 5,7- and 3′,4′-dihydroxylations in rings A and B, respectively. The formation of a pentaacetate, a tetramethyl ether (mp 187°) and tetramethyl ether monoacetate (mp 168°) confirmed its identity as the known taxifolin **1**.




**1** $R_1 = R_2 = R_3 = R_4 = H$
**2** $R_1 = Me$; $R_2 = R_3 = R_4 = H$
**3** $R_1 = Me$; $R_2 = R_3 = H$; $R_4 = OH$
**4** $R_1 = R_2 = R_3 = H$; $R_4 = OH$
**5** $R_1 = Me$; $R_2 = Glc$; $R_3 = H$; $R_4 = OH$

Substance B (cedeodarin), $C_{16}H_{14}O_7$, mp 216–218°, $M^+$318.0741, was an analogue of substance A from its similar colour reactions, UV and IR spectra. Its $^1$H NMR spectrum exhibited an extra singlet at $\delta$ 2.02 for an aryl methyl and only one proton singlet at 6.06 which suggested that it was either C-6 or C-8 methyl-substituted taxifolin. The MS pattern of cedeodarin showed fragments by the losses of $H_2O$, CO, HCO and the base peak was obtained by RDA fragmentation which gave rise to ions *m/e* 167 and 152 and were in accord with the above deductions.

The $^1$H NMR of the pentaacetyl and tetramethyl monoacetate (mp 138°) derivatives confirmed the presence of four aryl hydroxyls and a secondary carbinol functions. Further confirmation of the presence of C-3 OH group was obtained from $^1$H NMR of cedeodarin tetramethyl ether which showed distinct $J_{H_3H_{3OH}}$ coupling (2 Hz) as evidenced by a double doublet at $\delta$ 4.48 which was lost on addition of $D_2O$. The chemical shift of aryl methyl ($\delta$ 2.02) fixed its placement [8, 9] at C–6. This was also confirmed by the proton noise-decoupled $^{13}$C NMR spectrum of **1** showing the signals at 95.60 and 97.03 ppm [10] due to C-8 and C-6, respectively; which appeared in the case of **2** at 95.12 and

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104.80 ppm [11] respectively; further, the splitting pattern in the proton-coupled spectra showed the C-8 signal as a sharp doublet and the C-6 signal as an unresolved multiplet. Cedeodarin is thus 6-methyltaxifolin **2**. It may be mentioned that a *C*-methyldihydroflavonol [12] (mp 194–195°, $[\alpha]_D$ +7.42°) isolated from *Populus deltoides* has been formulated as 6-methyltaxifolin without any spectral evidence but on the basis of its dehydrogenation to 6-methylquercetin. 8-Methyltaxifolin [13] (deodarin) has also been reported from *C. deodara* which could not be confirmed in these studies. It would appear that cedeodarin is racemic 6-methyltaxifolin.

Substance C (cedrin), mp 165°, $C_{16}H_{14}O_8$, $M^+$334, IR and UV indicative of dihydroflavonols and its $^1$H NMR spectrum showed the characteristic AB pair of doublets ($J$ = 11 Hz) at δ 4.95 and 4.57 due to C-2,3 vicinal protons, two singlets at 6.05 (1H) and 6.65 (2H) assignable to ring A (H-8) and ring B (H-2′,6′) protons, respectively. An aryl methyl singlet at δ 2.01 established C-6 as the site for *C*-methylation in the molecule. The $M^+$ and other fragment ions characteristic of dihydroflavonols were observed in the MS spectrum at rather low relative intensities and the base peak at *m/e* 332 ($M^+ - 2$) could be explained by the thermal loss of $H_2$ from the *ortho*-dihydroxyls giving rise to a quinonoid structure. The $^1$H NMR spectrum of the hexaacetyl derivative exhibited signals for one alcoholic and five phenolic acetoxy methyls (δ 1.99, 2.27, 2.36) with a concurrent paramagnetic shift (δ 1.10) of the carbinolic proton in addition to other structural features. Moreover, methylation led to a pentamethyl ether ($^1$H NMR, MS) which yielded a monoacetate on subsequent acetylation. Cedrin was, therefore, confirmed as 6-methyldihydromyricetin **3**.

Substance D, mp 245–248°, $C_{15}H_{12}O_8$, $M^+$320. Its colour change with $FeCl_3$, IR and UV indicated close resemblance with cedrin. The $^1$H NMR specrum established the absence of an aryl methyl signal, instead an additional proton (δ 5.88) ascribable to C-6, was observed. Its MS showed a base peak at *m/e* 318 ($M^+ - 2$) and other prominent ions at *m/e* 152 (84%) and 135 (54%). The pattern of hydroxylation was confirmed by the formation of hexaacetate, a pentamethyl ether which sustained one acylable secondary alcoholic function, evident by its conversion to monoacetate (mp 159°). Hence substance D must be dihydromyricetin [14] **4**.

Substance E (cedrinoside), mp 238–240°, gave $FeCl_3$, Mg–HCl and Fiegel tests for flavonoid glycosides. Its acid hydrolysis yielded an aglycone which was identified as cedrin **3** and D-glucose (coPC.). The $^1$H NMR of peracetate displayed signals for five alcoholic acetoxy methyls (δ 1.82–2.06) and four phenolic acetoxy methyls (δ 2.18–2.31) and a paramagnetic shift (δ 0.88) of C-3 carbinolic methine suggesting the presence of only one glucose molecule which was not attached at C–3. The characteristic bathochromic shift of UV absorption by addition of NaOAc and $AlCl_3$ indicated that C-5,7 OH of ring A was free. Therefore, glucose was linked to a ring B hydroxyl function. The site of glucosylation must be C-3′ because H-2′,6′ equivalent protons of cedrin were now found to exhibit different chemical shifts in the $^1$H NMR of cedrinoside and its nonaacetate. Since the anomeric proton of cedrinoside appeared as *m* ($W_{1/2}$ = 9 Hz) at δ 5.16, the structure of cedrinoside is cedrin 3′-*O*-β-D-glucopyranoside **5**.

## EXPERIMENTAL

Mps (uncorr.) were determined on a Kofler hot stage apparatus. $^1$H NMR spectra were recorded on 60 or 90 MHz instruments in $CDCl_3$ (TMS as int. standard) unless otherwise specified. TLC on cellulose layers was developed in $I_2$ vapour or with 3% $FeCl_3$–$K_3Fe(CN)_6$. The plant material was collected from Nainital Hills, U.P., by Dr. B. Gupta of the Botany Section. A voucher specimen No. 27 has been preserved in the Institute's herbarium.

*Isolation procedure.* Powdered dry wood (36 kg) was extracted with EtOH (300 l.) and concd to a dark brown semisolid. The concentrate (1.96 kg) was exhaustively macerated to get hexane (280 g), $CHCl_3$ (245 g), *n*-BuOH (820 g) and $H_2O$-soluble (180 g) portions successively. The residue of BuOH fraction (100 g) was dissolved in alcohol, precipitated with $Pb(OAc)_2$ and the lead salts were decomposed with $H_2S$ in alcoholic suspension. PbS was filtered and the filtrate was concd to a residue (20.3 g) which showed 5 major spots on TLC. It was chromatographed on cellulose (2 kg) and eluates were mixed on basis of TLC results (Table 1).

The repeated partition chromatography of the residue from eluate 4 on cellulose ($CHCl_3$–MeOH–$H_2O$, 35:3:2→35:5:2) afforded compounds A(0.45 g) and B (0.57 g). The residue from combined eluates 5–7 was similarly separated on cellulose ($CHCl_3$–MeOH–$H_2O$; 35:3:2→35:9:2) to give compounds B, (0.32 g), C (0.39 g), D (0.40 g) and E (0.15 g).

*Substance A* (**1**) Mp 232–234° ($CHCl_3$–MeOH). $[\alpha]_D$ +1.90° (*c*′ 1.05, MeOH). $\lambda_{max}^{MeOH}$ nm (log ε): 229, 291, (4.48, 4.49), 332 (infl.); MeOH–$AlCl_3$: 227, 315 (4.6, 4.61); MeOH–NaOMe: 223, 326 (4.53, 4.76). $^1$H NMR $Me_2CO$: δ 4.47

Table 1. Chromatography of fraction A (20.3 g) on cellulose

| Fraction No. | Eluant | Elution volume (l) | Weight (g) | Constituents | TLC* |
|---|---|---|---|---|---|
| 1 | $CHCl_3$–$H_2O$ | 2.85 | 0.10 | — | |
| 2 | $CHCl_3$–MeOH–$H_2O$ | | | | |
| | 35: 1:2 | 5.72 | 0.97 | — | |
| 3 | 35: 3:2 | 9.85 | 2.18 | — | |
| 4 | 35: 5:2 | 11.25 | 2.33 | A, B | 0.50, 0.65 |
| 5 | 35: 7:2 | 10.25 | 0.97 | A, C | 0.50, 0.29 |
| 6 | 35: 9:2 | 12.50 | 1.43 | C, D | 0.29, 0.17 |
| 7 | 35:11:2 | 15.20 | 1.23 | D, E, st | 0.17, 0.12 |
| 8–9 | 35:15:2 | 18.50 | 0.93 | st | |

*Solvent: $CHCl_3$–MeOH–$H_2O$, 35:7:2.

(1H, *d*, $J = 11$ Hz, H-3), 4.93 (1H, *d*, $J = 11$ Hz, H-2), 5.89 (2H, *br s*, H-6, 8), 6.82 (2H, *s*, H-2′,5′), 7.00 (1H, *s*, H-6′). MS *m/e* (%rel.int.): 304.0592 (52), 276 (65), 275 (10), 223 (5), 166 (7), 165 (21), 154 (13), 153 (100), 152 (31), 150 (28), 143 (10), 124 (7) and 123 (44). (Found: C, 58.7; H, 3.96. $C_{15}H_{12}O_7$ requires: C, 59.2; H, 3.94%). The penta-acetate was purified by chromatography Si gel in $C_6H_6$–hexane (1:1). $^1$H NMR: δ 2.05 (3H, *s*, C-3 OAc), 2.32 (9H, *s*, C-7,3′,4′ OAc), 2.39 (3H, *s*, C-5 OAc), 5.69 (1H, *d*, $J =$ 11 Hz, H-3), 6.38, 6.72 (2H, *m*, H-6,8), 7.25–7.43 (3H, *m*, H-2′,5′,6′).

*Substance B* (**2**). Mp 216–218° (MeOH–$CHCl_3$) $[\alpha]_D + 0°$ (*c*, 1.20, MeOH). It gave green colour with $FeCl_3$ and light orange colour with conc $H_2SO_4$. $\lambda_{max}^{MeOH}$ nm (log ε): 228, 295, (4.21, 4.24), 334, (infl); MeOH–$AlCl_3$: 227, 318 (4.29, 4.30); MeOH–$AlCl_3$–HCl: 228, 319 (4.37, 4.33); NaOAc–$H_3BO_3$–MeOH: 228, 295 (4.26, 4.26). $^1$H NMR ($Me_2CO$–$d_6$, 100 MHz): δ 2.02 (3H, *s*, C-6, Me), 4.62 (1H, *d*, $J =$ 11 Hz, H-3), 5.02 (1H, *d* $J = 11$ Hz, H-2), 6.06 (1H, *s*, H-8), 6.83–7.10 (3H, *m*, H-2′,5′,6′). MS *m/e* (% rel.int.): 318 ($M^+$, 40), 300 (5), 289 (16), 179 (13), 168 (7), 167 (100), 165 (5), 152 (15), 151 (7), 150 (54), 138 (5), 137 (3), 124 (5), 123 (21), 122 (5). (Found: C, 60.35; H, 5.57. $C_{16}H_{14}O_7$ requires: C, 60.37; H, 5.24%). It yielded a pentaacetate on reaction with $Ac_2O$–$C_5H_5N$, as an amorphous powder. $^1$H NMR: δ 1.93 (3H, *s*, C-3 OAc), 2.00 (3H, *s*, C-6 Me), 2.26 (6H, *s*, C-3′,4′ OAc), 2.28 (3H, *s*, C-7 OAc), 2.37 (3H, *s*, C-5 OAc), 5.31 (1H, *d*, $J = 12$ Hz, H-2), 5.63 (1H, *d*, $J = 12$ Hz, H-3), 6.73 (1H, *s*, H-8), 7.27 (3H, *m*, H-2′,5′,6′). Substance B was methylated with $Me_2SO_4/K_2CO_3/Me_2CO$ to yield tetra-methyl ether which crystallized from MeOH as needles, mp 225°. $^1$H NMR (100 MHz): δ 2.09 (3H, *s*, C-6 Me), 3.85 (6H, *s*, C-3′,4′, OMe), 3.91 (3H, *s*, C-7 OMe), 3.94 (3H, *s*, C-5 OMe), 4.48 (1H, *dd*, $J = 2$, 12 Hz, H-3), 5.00 (1H, *d*, $J =$ 12 Hz, H-2), 6.32 (1H, *s*, H-8), 6.78–7.18 (3H, *m*, H-2′,5′,6′). (Found:C, 64.08; H, 5.75. $C_{20}H_{22}O_7$ requires: C, 64.16; H, 5.75%).

*Substance C* (*cedrin* **3**). Mp 165°. It gave orange–brown colour with $FeCl_3$. $\lambda_{max}^{MeOH}$ nm (log ε): 231, 296, (4.86, 4.75), 342 (infl); MeOH–$AlCl_3$: 231, 318 (5.64, 4.86); MeOH–NaOAc: 231, 296 (5.27, 4.68). $^1$H NMR ($Me_2CO$–$d_6$, 100 MHz): δ 2.01 (3H, *s*, C-6 Me), 4.57, 4.95 (1H each, *d*, $J = 11$ Hz, H-3,2), 6.05 (1H, *s*, H-8), 6.65 (2H, *s*, H-2′,6′). MS *m/e* (% rel.int.): 334 $M^+$ (21), 333 (10), 332 (100), 331(7), 303 (4), 302 (3), 180 (2), 167 (2), 166 (2), 143 (2). (Found: C, 57.50; H, 4.80. $C_{16}H_{14}O_8$ requires: C, 57.54; H, 4.79%). Acetylation with $Ac_2O$–$C_5H_5N$ yielded a hexa-acetate as an amorphous powder. $^1$H NMR: δ 1.99 (3H, *s*, C-3 OAc), 2.08 (3H, *s*, C-5 OAc), 2.27 (9H, *s*, C-3′,5′,7 OAc), 2.30 (3H, *s*, C-4′ OAc), 2.36 (3H, *s*, C-5 OAc), 5.33, 5.60 (1H each, *d*, $J = 12$ Hz, H-2,3), 6.75 (1H, *s*, H-8), 7.21 (2H, H-2′,6′). Methylation of cedrin with $Me_2SO_4/K_2CO_3/Me_2CO$ afforded pentamethyl ether which crystallized as needles (MeOH), mp 194°. $^1$H NMR: δ 2.14 (3H, *s*, C-6 Me), 3.89 (6H, *s*, C-7,4′ OMe), 3.91 (3H, *s*, C-5 OMe), 3.95 (6H, *s*, C-3′,5′ OMe), 4.47, 5.01 (1H each, *d*, $J = 11$ Hz, H-3,2), 6.3 (1H, *s*, H-8), 6.62 (2H, *s*, H-2′,6′). MS: *m/e* 404 ($M^+$), 389, 380, 362, 210, 203, 197, 195, 187, 183, 182 (base), 152, 151, 140, 137, 136, 135, 121, 120, 109. Pentamethyl ether was acetylated with $Ac_2O$–$C_5H_5N$ to yield its monoacetate, mp 135°. $^1$H NMR: δ 2.01 (6H, *s*, C-6 OAc), 5.13 (1H, *d*, $J = 12$ Hz, H-2), 5.51 (1H, *d*, $J = 12$ Hz, H-3). (Found: C, 62.33; H, 5.83. $C_{23}H_{26}O_9$ requires: C, 62.35; H, 5.82%).

*Substance D* (**4**). Mp 245–248° (MeOH–$CHCl_3$), $[\alpha]_D +$ 18.08° (*c* 0.94, MeOH). $\lambda_{max}^{MeOH}$ nm (log ε): 229, 293 (4.00, 4.70); MeOH–$AlCl_3$: 229, 315 (4.97, 4.90). $^1$H NMR ($Me_2CO$–$d_6$): δ 4.43 (1H, *d*, $J = 11$ Hz, H-3), 4.89 (1H, *d*, $J = 11$ Hz, H-2), 5.88 (2H, *s*, H-6, 8), 6.55 (2H, *s*, H-2′,6′). MS *m/e* (% rel.int.): 320 (2), 319 (10), 318 (100), 317 (5), 288 (5), 260 (4), 244 (8), 243 (6), 165 (12), 158 (5), 152 (84), 151 (10), 149 (14), 136 (7), 135 (54), 125 (7), 124 (6), 123 (5). Hexa-acetate, needles (MeOH), mp 108°. $^1$H NMR δ 2.12 (3H, *s*, C-3, OAc), 2.33 (12H, *s*, C-3′,4′,5′,7 OAc), 2.40 (3H, *s*, C-5 OAc), 5.44 (1H, *d*, $J = 11$ Hz, H-2), 5.65 (1H, *d*, $J = 11.5$ Hz, H-3), 6.65 (1H, *d*, $J = 2$ Hz, H-8), 6.84 (1H, *d*, $J = 2$ Hz, H-6), 7.39 (2H, *s*, H-2′,6′). Pentamethyl ether, mp 190°(lit. [15] mp 192°). $^1$H NMR (ppm): δ 3.85 (3H, *s*, C-7 OMe), 3.88 (3H, *s*, C-4′ OMe), 3.93 (9H, *s*, C-5,3′,5′ OMe).

*Substance E* (*cedrinoside* **5**). Mp 238–240° (MeOH–$CHCl_3$), brownish–green colour with $FeCl_3$, red–violet colour with Mg–HCl $\lambda_{max}^{MeOH}$ nm (log ε): 231, 296, 333 (5.32, 5.29, 4.69). MeOH–$AlCl_3$: 231, 319 (5.69, 5.63); MeOH–$AlCl_3$–HCl: 231, 319 (5.72, 5.72); MeOH–NaOAc: 228, 298, 333 (5.63, 4.66, 5.29). $^1$H NMR (DMSO): δ 1.80 (3H, *s*, C-6 Me), 3.0–3.90 (6H, *m*, H-2″,3″,4″,5″,6″), 4.31 (1H, *d*, $J = 11$ Hz, H-3), 4.77 (1H, *d*, $J = 11$ Hz, H-2), 5.16 (1H, *m*, $W_{1/2} = 9$ Hz, H-1″), 5.55 (1H, *s*, H-8), 6.85, 7.16 (2H, H-2′,6′). Acetylation with $Ac_2O$–$C_5H_5N$ gave nonaacetate as amorphous powder. $^1$H NMR: δ 1.82–2.06 (18H, 5 × OCOMe, C-6Me), 2.18 (6H, *s*, C-3′,4′,2 × OCOMe), 2.26 (3H, *s*, C-7 OCOMe), 2.31 (3H, *s*, C-5 OCOMe), 4.07 (2H, *m*, C-6″$CH_2$OAc), 5.07 (4H, *m*, CHOAc), 5.38 (1H, *d*, $J = 12$ Hz, H-2), 5.63 (1H, *d*, $J =$ 12 Hz, H-3), 6.60 (1H, *s*, H-8), 6.90, 7.10 (2H, H-2′,6′). Cedrinoside (50 mg) was heated at 100° with 5% HCl (5 ml) for 2 hr. The reaction mixture was worked up as usual to give an aglycone (25 mg) which was purified by cellulose chromatography, mp 165° (cedrin). The aq. hydrolysate showed a single spot for sugar identical with glucose (coTLC and coPC).

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