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TERPENIC GLYCOSIDES FROM *PLUCHEA INDICA*

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Key Word Index—*Pluchea indica*; Compositae; monoterpene glycoside; sesquiterpene glycoside; ionone derivative glycoside; lignan.

Abstract—Investigation of the aerial parts of *Pluchea indica* afforded five new terpenic glycosides, linaloyl glucoside, linaloyl apiosyl glucoside, 9-hydroxylinaloyl glucoside, plucheosides A and B, in addition to 15 known compounds. The structures of new compounds were elucidated on the basis of chemical and spectral data.

INTRODUCTION

In connection with a study on the glycosides in some plants of the Compositae, we have now studied the aerial parts of *Pluchea indica* and isolated five new terpenic glycosides together with nine previously known glycosides and six polar compounds. The glycosides are the first isolation from the genus *Pluchea*. Characteristic constituents of the genus [1–13] are eudesmanolide sesquiterpenes. The sesquiterpene glycosides showed considerable biological activity in a survival test [14].

RESULTS AND DISCUSSION

Careful separation of the polar fraction of *P. indica* afforded 20 polar compounds. The known compounds were identified as stigmasteryl glucoside (**1**), eugenyl glucoside (citrucin C) (**2**) [15], 4-allyl-2,6-dimethoxyphenyl glucoside (**3**) [16], methyl salicylate glucoside (**4**), benzyl glucoside (**5**) [17], phenylethyl glucoside (**6**) [18], (*Z*)-3-hexenyl glucoside (**7**) [18], pinoresinol monoglucoside (**8**) [19], syringaresinol monoglucoside (**9**) [20], 1,2-bis-(4-hydroxy-3-methoxyphenyl)-propane-1,3-diol (*erythro*) (**10**) [21], 1,2-bis-(4-hydroxy-3-methoxyphenyl)-propane-1,3-diol (*threo*) (**11**) [21], hedyotisol A (**12**) [22], hedyotisol B (**13**) [22], 1-(4-hydroxy-3-phenyl)-2-{2-methoxy-4-[1-(*E*)-propene-3-ol]-phenoxy}-propane-1,3-diol (*erythro*) (**14**) [15] and 1-(4-hydroxy-3-phenyl)-2-{2-methoxy-4-[1-(*E*)-propene-3-ol]-phenoxy}-propane-1,3-diol (*threo*) (**15**) [15] by spectral data and direct comparison of their physical properties with those reported previously for these compounds.

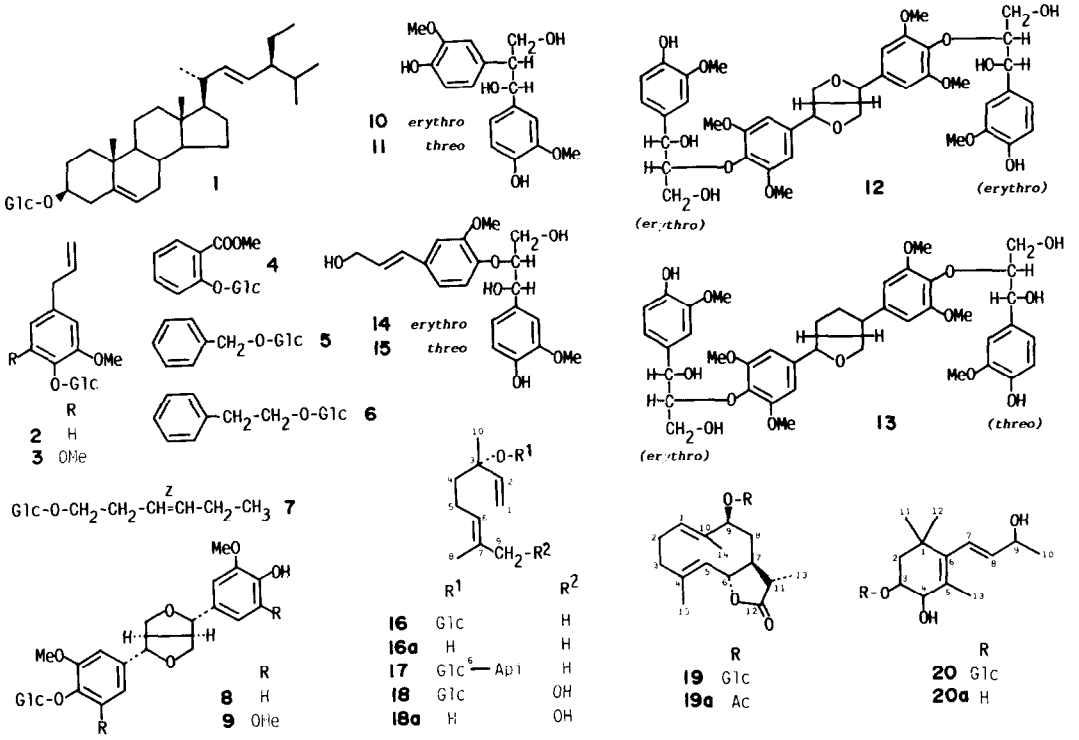
The ^{1}H NMR spectrum of linaloyl glucoside (**16**) indicated the presence of a vinyl group [δ 5.20 (1H, *dd*, J = 11, 1 Hz), 5.34 (1H, *dd*, J = 18, 1 Hz), 6.27 (1H, *dd*, J = 18, 11 Hz)], three methyl groups [δ 1.54, 1.57, 1.64 (each 3H, *s*) and an anomeric proton of glucopyranoside [δ 4.94 (*d*, J = 8Hz)]. In the ^{13}C NMR spectrum, 16 signals including six signals due to a glucopyranosyl moiety were observed. Enzymatic hydrolysis afforded **16a** as an aglycone and **16a** was identical to (+)-linalool by comparison of their ^{13}C NMR spectra and optical rotations [23]. Thus, the structure of linaloyl glucoside was deduced to be **16**.

The ^{1}H and ^{13}C NMR spectra of linaloyl apiosyl glucoside (**17**) were similar to those of **16**, except for signals of an apiofuranoside. The C-6 (δ 69.0) signal of the glucopyranoside was shifted downfield by 6.0 ppm compared with that of **16**. Thus, the structure of linaloyl apiosyl glucoside was ascribed to **17**.

The ^{1}H and ^{13}C NMR spectra of 9-hydroxylinaloyl glucoside (**18**) were similar to those of **16**, except for the presence of a hydroxymethyl group. In the ^{13}C NMR spectrum, the glycosylation shift (+ 6.7 ppm) was observed at C-3 as in **16** compared with that of the aglycone (**18a**) obtained from enzymatic hydrolysis suggesting that the hydroxymethyl group replaced the *trans*-methyl group (C-9) of **16**, because the signals for C-3 and C-8 were similar to those of **16** (Table 1). Furthermore, the ^{13}C NMR spectrum of **18a** agreed with that of the compound obtained by SeO_2 oxidation of linalool [24]. Thus, the structure of 9-hydroxylinaloyl glucoside was assigned to **18**.

In the ^{13}C NMR spectrum of plucheoside A (**19**), 21 carbon signals including six signals due to a glucopyranosyl moiety were observed. The ^{1}H NMR spectrum of its acetate (**19a**) obtained by acetylation after enzymatic hydrolysis exhibited the presence of a methyl group [δ 1.12 (3H, *d*, J = 7 Hz)], two vinylic methyl groups [δ 1.22 (3H, *d*, J = 1 Hz), 1.30 (3H, *d*, J = 1 Hz)] and a methine proton [δ 5.01 (1H, *dd*, J = 10, 3 Hz)] attached to a carbon bearing an acetoxyl group and the CD spectrum of **19** showed a positive Cotton effect $[\theta]_{214}$ + 145300. Thus, the acetate (**19a**) was identified as herbolide A by comparison of reported data [25]; the structure of plucheoside A was ascribed to **19**.

In the ^{13}C NMR spectrum of plucheoside B (**20**), 19 carbon signals including six signals due to a glucopyranosyl moiety, four methyl groups and four sp^2 carbons were observed. The ^{1}H NMR spectrum of an aglycone (**20a**) afforded by enzymatic hydrolysis exhibited the presence of *trans* olefinic protons [δ 5.88 (1H, *dd*, J = 18, 6 Hz, H-8), 6.34 (1H, *d*, J = 18 Hz, H-7)], three carbinyl protons [δ 4.19 (1H, *dt*, J = 13, 4 Hz, H-3), 4.32 (1H, *d*, J



$= 4$ Hz, H-4), 4.67 (1H, *qui*, $J = 6$ Hz, H-9)] and methylene protons [δ1.78 (1H, *dd*, $J = 13$, 4 Hz, H-$2_{pseud-eq}$), 2.24 (1H, *t*, $J = 13$ Hz, H-$2_{pseud-ax}$)]. The existence of an α-glycol was supported by these data and it was suggested that the two hydroxyl groups have the *cis* configuration. However, we could not determine the absolute configuration. The structure of the aglycone was deduced to be **20a** by comparison of reported data for similar compounds (β-ionone) [26] and because the C-2 (δ39.7) signal of the glycoside (**20**) was shifted upfield by 2.7 ppm compared with that of **20a**. The structure of the glycoside was **20**.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded at 89.55 and 22.5 MHz, and 399.65 MHz respectively. TMS was used as int. standard.

Plant material. Aerial parts of *P. indica* (L.) Less. were collected in Drigh Road, Karachi, Pakistan in the spring of 1988. Plants were identified by Prof. Dr S. I. Ali and Prof. Dr Muhammad Qaiser, Department of Botany, University of Karachi).

Extraction and isolation. Dried aerial parts (6 kg) were extracted twice with MeOH under reflux. The extract was concd under red. pres. and the residue suspended in H_2O. This suspension was extracted with Et_2O. The H_2O layer was passed through an Amberlite XAD-2 column and the MeOH eluate concd under red. pres. The residue (74 g) was rechromatographed on a silica gel column with $CHCl_3$–MeOH (19:1 to 9:1) and semi-prep. HPLC [ODS, H_2O–MeCN (9:1 to 7:3)] to give 28 mg **1**, 215 mg **2**, 11 mg **3**, 11 mg **4**, 32 mg **5**, 5 mg **6**, 15 mg **7**, 7 mg **8**, 4 mg **9**, 5 mg **10**, 10 mg **11**, 8 mg **12**, 13 mg **13**, 12 mg **14**, 12 mg **15**, 310 mg **16**, 19 mg **17**, 32 mg **18**, 9 mg **19** and 14 mg **20**.

Linaloyl glucoside (**16**). Colourless viscous oil. (Found: C, 58.25; H, 9.01. $C_{16}H_{28}O_6 \cdot 3/4\ H_2O$ requires: C, 58.34; H, 8.88%). $[\alpha]_D^{24}$ − 23.4° (MeOH; *c* 2.86). ^{1}H NMR (C_5D_5N): δ1.54; 1.57; 1.64 (each 3H, *s*, H_3-8/H_3-9/H_3-10), 4.94 (1H, *d*, $J = 8$ Hz, anomeric H), 5.20 (1H, *dd*, $J = 10$, 1 Hz, H-1), 5.34 (1H, *dd*, $J = 18$, 1 Hz, H-1), 6.27 (1H, *dd*, $J = 18$, 10 Hz, H-2). ^{13}C NMR: Table 1.

Linaloyl apiosyl glucoside (**17**). Colourless viscous oil. (Found: C, 54.06; H, 8.21. $C_{21}H_{36}O_{10}\ H_2O$ requires: C, 54.18; H, 8.08%). $[\alpha]_D^{23}$ − 76.2° (MeOH;*c* 1.05). ^{1}H NMR (C_5D_5N): δ1.52 (3H, *s*, Me), 1.62 (6H, *s*, Me × 2), 4.15 (2H, *s*, H_2-5 of apiose), 4.30; 4.52 (each *d*, $J = 10$ Hz, H-4 of apiose), 4.68 (1H, *d*, $J = 3$ Hz, H-2 of apiose), 4.88 (1H, *d*, $J = 8$ Hz, anomeric H of glucose), 5.20 (1H, *dd*, $J = 10$, 1 Hz, H-1), 5.36 (1H, *dd*, $J = 18$, 1 Hz, H-1), 5.70 (1H, *d*, $J = 3$ Hz, anomeric H of apiose), 6.24 (1H, *dd*, $J = 18$, 10 Hz, H-2). ^{13}C NMR: Table 1.

9-Hydroxylinaloyl glucoside (**18**). Colourless viscous oil. (Found: C, 55.56; H, 8.60. $C_{16}H_{28}O_7 \cdot 3/4\ H_2O$ requires: C, 55.43; H, 8.37%). $[\alpha]_D^{24}$ − 19.9° (MeOH; *c* 1.48). ^{1}H NMR (C_5D_5N): δ1.58/1.66 (each 3H, *s*, H_3-8/H_3-10), 4.28 (2H, *s*, H_2-9), 4.95 (1H, *d*, $J = 8$ Hz, anomeric H), 5.11 (1H, *dd*, $J = 10$, 1 Hz, H-1), 5.37 (1H, *dd*, $J = 18$, 1 Hz, H-1), 6.25 (1H, *dd*, $J = 18$, 10 Hz, H-2). ^{13}C NMR: Table 1.

Plucheoside A (**19**). Amorphous powder. FABMS *m/z* (MeOH + *m*-nitrobenzyl alcohol): 435 $[M+Na]^+$, 413 $[M+H]^+$. $[\alpha]_D^{24}$ + 21.6° (MeOH; *c* 1.16). CD (MeOH; *c* 0.011) $[\theta]$ (nm): + 145300 (214). ^{1}H NMR (C_5D_5N); δ1.14 (3H, *d*, $J = 6$ Hz, H_3-13), 1.59; 1.62 (each 3H, *br s*, H_3-14/H_3-15), 4.82 (1H, *d*, $J = 8$ Hz, anomeric H). ^{13}C NMR: Table 1.

Table 1. ^{13}C NMR spectral data of compounds **16–20**

C	16*	16a*	17*	18*	18a†	19*	19a†	20*	20a*
Aglycone moiety									
1	114.8	111.7	114.8	114.8	111.7	132.0	131.3	36.9	37.0
2	144.5	147.2	144.4	144.5	144.8	26.1	25.3	39.7	42.4
3	80.0	72.9	80.0	80.0	73.3	39.6	39.2	74.7[a]	67.1
4	42.2	43.6	42.2	42.0	41.7	140.2	140.3	68.8[b]	72.1
5	23.1	23.8	23.1	22.6	22.3	128.0	126.9	125.0	125.4
6	125.4	126.0	125.5	124.9	125.8	81.1	80.9	141.3	140.8
7	131.1	131.2	131.0	‡	134.9	51.6	51.3	127.9	127.9
8	17.8	18.2	17.7	14.0	13.5	35.4	34.2	141.3	141.0
9	25.8	28.7	25.7	68.1	68.5	83.6	80.7	68.2[b]	68.3
10	23.6	26.3	23.7	23.7	27.7	137.0	134.6	24.7	24.7
11	—	—	—	—	—	42.3	42.0	27.4[c]	27.7[d]
12	—	—	—	—	—	178.6	177.7	30.0[c]	30.2[d]
13	—	—	—	—	—	13.4	13.2	20.2	20.0
14	—	—	—	—	—	11.3	11.4	—	—
15	—	—	—	—	—	17.3	17.2	—	—
OAc	—	—	—	—	—	—	21.2	—	—
							169.8		
Sugar moiety									
Glc 1	99.7		99.6	99.7		100.0		101.6	
2	75.3		75.3	75.4		75.1		75.6[a]	
3	78.8		78.8	78.8		78.8		79.0	
4	71.8		72.1	71.9		72.1		71.7	
5	78.0		76.7	78.0		78.5		78.7	
6	63.0		69.0	63.0		63.1		62.8	
Api 1	—		111.1	—		—		—	
2	—		78.0	—		—		—	
3	—		80.4	—		—		—	
4	—		75.0	—		—		—	
5	—		65.9	—		—		—	

Run at 22.5 MHz in *C_5D_5N, †$CDCl_3$ solution.
[a–d] Assignment may be interchanged in each column.
‡ Overlapped with solvent signals.

Plucheoside B (**20**). Amorphous powder. FABMS *m/z* (MeOH + *m*-nitrobenzyl alcohol): 411 $[M+Na]^+$. $[\alpha]_D^{24}$ −69.7° (MeOH; *c* 1.32). UV λ_{max}^{MeOH} nm (log ε): 224 (3.81). ^1H NMR (C_5D_5N): δ0.96; 1.00, (each 3H, *s*, H_3-11/H_3-12), 1.50 (3H, *d*, *J* = 7 Hz, H_3-10), 2.10 (3H, *s*, H_3-13), 2.36 (1H, *t*, *J* = 13 Hz, H-$2_{pseud-ax}$), 5.25 (1H, *d*, *J* = 7 Hz, anomeric H). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **16**. A soln of **16** (50 mg) in H_2O (1 ml) was treated with cellulase (Sigma type II) (50 mg) at room temp. overnight with stirring. The reaction mixt. was dild with H_2O and extd × 5 with Et_2O. The Et_2O ext. was concd in *vacuo* to give (+)-linalool (**16a**) (23mg) as a colourless oil. $[\alpha]_D^{23}$ + 11.9° ($CHCl_3$; *c* 2.29). EIMS *m/z* (rel. int.): 154 $[M]^+$ (2), 136 (9), 121 (21). ^1H NMR ($CDCl_3$): δ1.59 (6H, *s*, Me × 2), 1.67 (3H, *s*, Me), 5.02 (1H, *dd*, *J* = 10, 1Hz, H-1), 5.09 (1H, *br t*, *J* = 6Hz, H-6), 5.18 (1H, *dd*, *J* = 18, 1Hz, H-1), 5.90 (1H, *dd*, *J* = 18, 10Hz, H-2). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **18**. **18** (14 mg) was dissolved in H_2O (1 ml) and the soln treated with cellulase (Sigma type II) (14 mg) at room temp. for 7 hr. The reaction mixt. was dild with H_2O and extracted × 3 with EtOAc. The EtOAc extract was purified by HPLC to give **18a** (0.5 mg) as a colourless oil. $[\alpha]_D^{24}$ + 20.0° (MeOH; *c* 0.05). EIMS *m/z* (rel. int.): 170 $[M]^+$ (trace), 152 (6), 137 (9), 119 (7), 84 (100). ^1H NMR ($CDCl_3$): δ1.28; 1.64 (each 3H, *s*, H_3-8/H_3-10), 1.6–2.3 (*m*), 3.93 (2H, *s*, H_2-9), 5.00 (1H, *dd*, *J* = 10, 1Hz, H-1), 5.12 (1H, *dd*, *J* = 18, 1 Hz, H-1), 5.37 (1H, *br t*, *J* = 6 Hz, H-6), 5.86 (1H, *dd*, *J* = 18, 10 Hz, H-2). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **19**. A soln of plucheoside A (**19**) (7 mg) in H_2O (1 ml) was treated with cellulase (Sigma type II) (7 mg) at room temp. for 5 hr with stirring. The reaction mixt. was dild with H_2O and extd × 3 with EtOAc. The EtOAc was evapd and the residue (2 mg) dissolved in pyridine and Ac_2O (0.2 ml of each). The reaction mixt. was left at room temp. overnight and the reagents then removed *in vacuo*. The acetate (**19a**) (2 mg) was obtained as colourless needles, mp 160–162°, after recrystallization from MeOH. EIMS *m/z* (rel. int.): 292 $[M]^+$ (3), 250 (7), 232 (100). ^1H NMR (C_6D_6): δ1.12 (3H, *d*, *J* = 7 Hz, H_3-13), 1.22 (3H, *d*, *J* = 1 Hz, H_3-14), 1.30 (3H, *d*, *J* = 1 Hz, H_3-15), 1.67 (3H, *s*, OAc), 3.96 (1H, *dd*, *J* = 9, 8 Hz, H-6), 4.15 (1H, *br d*, *J* = 9 Hz, H-5), 4.77 (1H, *br t*, *J* = 8 Hz, H-1), 5.01 (1H, *dd*, *J* = 10, 3 Hz, H-9). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **20**. **20** (10 mg) was dissolved in H_2O (1 ml) and the soln treated with cellulase (Sigma type II) (10 mg) at room temp. overnight with stirring. The reaction mixt. was dild with H_2O and extracted × 3 with EtOAc to give **20a** (2.5 mg) as an amorphous powder. $[\alpha]_D^{22}$ − 116.0° (MeOH; *c* 0.25). EIMS *m/z* (rel. int.): 226 $[M]^+$ (3), 208 (23), 193 (6), 175 (18), 84 (97), 44 (100). ^1H NMR (C_5D_5N): δ1.03; 1.13 (each 3H, *s*, H_3-11/H_3-12), 1.52 (3H, *d*, *J* = 7 Hz, H_3-10), 1.78 (1H, *dd*, *J* = 13, 4 Hz, H-

$2_{pseud-eq}$), 2.13 (3H, *s*, H_3-13), 2.24 (1H, *t*, $J = 13$ Hz, H-$2_{pseud-ax}$), 4.19 (1H, *dt*, $J = 13$, 4 Hz, H-$3_{pseud-ax}$), 4.32 (1H, *d*, $J = 4$ Hz, H-$4_{pseud-eq}$), 4.67 (1H, *qui*, $J = 6$ Hz, H-9), 5.88 (1H, *dd*, $J = 18$, 6 Hz, H-8), 6.34 (1H, *d*, $J = 18$ Hz, H-7). ^{13}C NMR: Table 1.

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