Structures of New Cucurbitane-Type Triterpenes and Glycosides, Karavilagenins and Karavilosides, from the Dried Fruit of *Momordica charantia* L. in Sri Lanka

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Three new cucurbitane-type triterpene called karavilagenins A, B, and C and five new cucurbitane-type triterpene glycosides called karavilosides I, II, III, IV, and V were isolated from the dried fruit of Sri Lanka *Momordica charantia* L. (Cucurbitaceae) together with two known cucurbitane-type triterpenes, 19(*R*)-methoxy-5β,19-epoxycucurbita-6,23-dien-3β,25-diol and 5,19-epoxycucurbita-6,23-diene-3,25-diol, and nine known cucurbitane-type triterpene glycosides, goyaglycosides-b, -c, and -d, and momordicosides F_1, F_2, G, I, K, and L. The structures of karavilagenins and karavilosides were elucidated on the basis of chemical and physicochemical evidence.

Key words *Momordica charantia*; karavilagenin; karaviloside; Sri Lanka; cucurbitane-type triterpene; medicinal foodstuff

The Cucurbitaceae plant *Momordica* (*M.*) *charantia* L. is cultivated in Asian countries and the fruit of this plant has been used as a bitter stomachic, a laxative, an antidiabetic, and an anthelmintic for children in Chinese, Indian Ayurvedic, and Indonesian Jamu traditional medicines. The alcoholic extract from the fruit of *M. charantia* originated in Sri Lanka was reported to inhibit the increase in serum glucose levels after glucose-loaded rats.[1)] In addition, Several cucurbitane-type triterpene glycosides were reported as chemical constituents of the fruit.[5—10)] However, chemical and pharmacological studies[1—4)] on the fruit of *M. charantia* were yet left uncharacterised. During the course of characterization studies on the bioactive constituents of medicinal foodstuffs,[11—21)] we reported the isolation and structure elucidation of eight cucurbitane-type triterpene glycosides, goyaglycosides-a, -b, -c, -d, -e, -f, -g, and -h, and three oleanane-type triterpene glycosides, goyasaponins I, II, and III, from the fresh fruit of Japanese *M. charantia*.[22)] In a continuing study of the *Momordica* plant, we have examined the constituents from the dried fruit of *M. charantia* [Sri Lankan name (Singhalese): Kariwila], which is widely cultivated in Sri Lanka and used as vegetable. From the methanol extract, three new cucurbitane-type triterpene called karavilagenins A (**1**), B (**2**), and C (**3**) and five new cucurbitane-type triterpene glycosides called karavilosides I (**4**), II (**5**), III (**6**), IV (**7**), and V (**8**) have been isolated together with two known

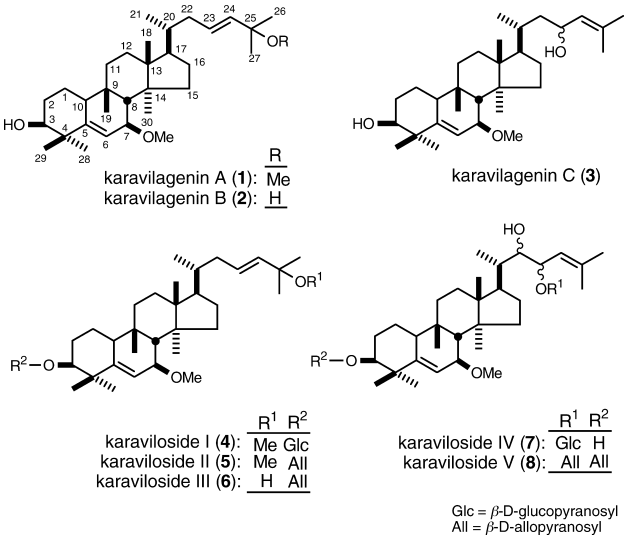

Chart 1

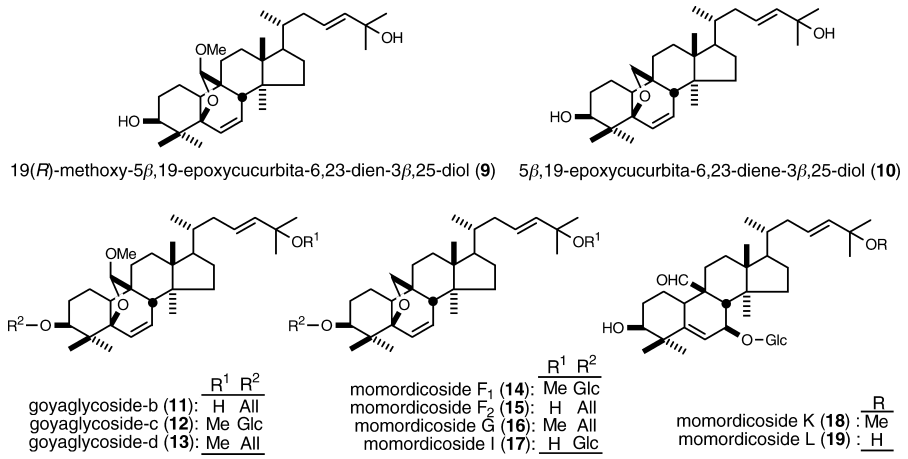

Chart 2

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cucurbitane-type triterpenes and nine known cucurbitane-type triterpene glycosides. This paper deals with the isolation and structure elucidation of karavilagenins A (**1**), B (**2**), and C (**3**) and karavilosides I (**4**), II (**5**), III (**6**), IV (**7**), and V (**8**).

The methanolic extract obtained from the dried fruit of *M. charantia*, which was cultivated in Nuwara Eliya, Sri Lanka, was subjected to normal-phase and reversed-phase silica gel column chromatography and repeated HPLC to afford karavilagenins A (**1**, 0.0030%), B (**2**, 0.0076%), and C (**3**, 0.0024%) and karavilosides I (**4**, 0.0067%), II (**5**, 0.0138%), III (**6**, 0.0033%), IV (**7**, 0.0006%), and V (**8**) together with 19(*R*)-methoxy-5β,19-epoxycucurbita-6,23-dien-3β,25-diol (**9**, 0.0019%),[23] 5β,19-epoxycucurbita-6,23-diene-3β,25-diol (**10**, 0.0036%),[23] goyaglycosides-b (**11**, 0.0003%),[22] -c (**12**, 0.0007%),[22] and -d (**13**, 0.0026%),[22] and momordicosides F_1 (**14**, 0.0083%),[7] F_2 (**15**, 0.0005%),[7] G (**16**, 0.0043%),[23] I (**17**, 0.0012%),[23] K (**18**, 0.0015%),[8] and L (**19**, 0.0011%)[8] (Charts 1, 2).

Table 1. ^{13}C-NMR Data for Karavilagenins A (**1**), B (**2**), and C (**3**) and Karavilosides I (**4**), II (**5**), III (**6**), IV (**7**), and V (**8**)

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
C-1	21.0	21.0	21.0	22.6	22.6	22.5	21.8	22.6
C-2	28.4	28.5	28.6	28.9	28.8	28.7	30.1	28.8
C-3	76.8	76.5	76.6	87.8	87.8	87.5	76.1	87.7
C-4	41.6	41.6	41.6	42.1	42.0	41.9	42.0	42.0
C-5	146.7	146.8	146.7	148.0	148.0	148.0	148.1	148.0
C-6	120.7	120.6	120.8	119.2	119.1	119.0	119.7	119.2
C-7	77.1	77.1	77.1	77.7	77.6	77.6	77.6	77.7
C-8	47.8	47.7	47.8	48.9	48.8	48.8	49.0	48.9
C-9	33.9	33.8	33.9	34.4	34.4	34.3	34.3	34.4
C-10	38.5	38.6	38.6	39.4	39.4	39.3	39.3	39.3
C-11	32.5	32.6	32.6	32.8	32.8	32.8	33.0	32.9
C-12	29.9	29.9	30.1	30.4	30.4	30.3	30.7	30.6
C-13	46.0	46.1	46.1	46.3	46.3	46.2	46.6	46.6
C-14	47.7	47.7	47.8	48.3	48.3	48.2	48.0	48.0
C-15	34.6	34.6	34.5	35.0	35.0	34.9	35.3	35.3
C-16	27.5	27.5	27.8	27.9	27.8	27.8	27.9	27.8
C-17	49.8	49.8	50.7	50.3	50.3	50.1	46.5	46.6
C-18	15.3	15.3	15.3	15.6	15.6	15.5	15.1	15.1
C-19	28.5	28.8	28.8	29.2	29.2	29.1	29.2	29.2
C-20	36.1	36.1	32.6	36.5	36.5	36.5	40.8	40.9
C-21	18.0	18.6	18.7	19.1	19.0	18.9	15.1	15.0
C-22	39.5	39.0	44.4	39.8	39.8	39.5	77.1	76.9
C-23	128.4	125.0	65.8	128.5	128.5	124.3	81.4	81.2
C-24	136.6	139.4	129.0	137.7	137.6	141.5	124.6	124.8
C-25	74.7	70.5	133.6	74.9	74.8	69.7	135.6	135.4
C-26	26.0	29.8	18.0	26.1	26.1	30.7	26.2	26.2
C-27	25.7	29.7	25.6	26.5	26.5	30.7	18.7	18.6
C-28	27.7	27.6	27.7	28.9	28.9	28.8	28.2	28.8
C-29	25.3	25.3	25.3	25.9	25.9	25.7	26.2	25.9
C-30	17.8	17.9	17.9	18.1	18.1	18.1	18.1	18.1
7-OMe	56.1	56.1	56.2	56.3	56.2	56.1		56.2
25-OMe	50.1			50.2	50.1			
C-1′				107.6	105.0	104.6	106.1	104.8
C-2′				75.2	72.1	72.0	75.9	72.1
C-3′				78.7	73.4	73.2	78.8	73.3
C-4′				71.8	69.2	69.2	71.8	69.3
C-5′				78.2	75.7	75.4	78.4	75.9
C-6′				63.2	63.3	63.3	62.8	63.4
C-1″								103.6
C-2″								73.1
C-3″								73.0
C-4″								69.1
C-5″								75.6
C-6″								63.1

125 MHz, pyridine-d_5.

Structure Elucidation of Karavilagenins A, B, and C and Karavilosides I, II, III, IV, and V Karavilagenin A (**1**) was obtained as a white powder with positive optical rotation ($[\alpha]_D^{26}$ +71.5°). The IR spectrum of **1** showed absorption bands at 3475 and 1655 cm^{-1} suggestive of hydroxy and olefin functions. In the EI-MS of **1**, a molecular ion peak was observed at *m/z* 486 [M^+], and the molecular formula $C_{32}H_{54}O_3$ was determined by high-resolution MS measurement. The ^{1}H-NMR (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra of **1**, which was assigned by various NMR experiments,[24] showed signals due to eight methyls [δ 0.70, 0.93, 0.99, 1.04, 1.21 (3H each, all s, 30, 18, 19, 28, 29-H_3), 0.90 (3H, d-like, 21-H_3), 1.25 (6H, s, 26, 27-H_3)], two methoxyl [3.14 (3H, s, 25-OCH_3), 3.34 (3H, s, 7-OCH_3)], two methines bearing an oxygen function [3.43 (1H, m, 7-H), 3.51 (1H, m, 3-H)], three olefinic protons [5.38 (1H, d, *J*=15.8 Hz, 24-H), 5.49 (1H, m, 23-H), 5.83 (1H, d, *J*=5.3 Hz, 6-H)]. The plane structure in **1** was determined by a detailed heteronuclear multiple bond correlation (HMBC) experiment. Namely, long-range correlations were observed between the following protons and carbons: 18-H_3 and 12, 13, 14, 17-C; 21-H_3 and 17, 20, 22-C; 23-H and 20, 22, 24, 25-C; 24-H and 22, 23, 25, 26, 27-C; 26, 27-H_3 and 24, 25-C; 28, 29-H_3 and 3, 4, 5-C; 30-H_3 and 8, 13, 14, 15-C; 7-OCH_3 and 7-C; 25-OCH_3 and 25-C (Fig. 1). The stereostructure of **1** was characterized by nuclear Overhauser enhancement spectroscopy (NOESY) experiment, which showed NOE correlations between the following protons and protons: 8-H and 18-H_3; 28-H_3 and 3-H, 10-H; 30-H_3 and 7-H, 10-H, 17-H (Fig. 1).[25] These findings and comparisons of ^{1}H- and ^{13}C-NMR spectra of **1** with those of known goyaglycosides[7,8,22,23] led us to formulate the structure of karavilagenin A (**1**) as 7,25-dimethoxycucurbita-5,23-dien-3β-ol.

Karavilagenin B (**2**) was obtained as a white powder with positive optical rotation ($[\alpha]_D^{26}$ +117.1°). The IR spectrum of **2** showed absorption bands at 3432 and 1655 cm^{-1} suggestive of hydroxy and olefin functions. In the EI-MS of **2**, a molecular ion peak was observed at *m/z* 472 [M^+], and the

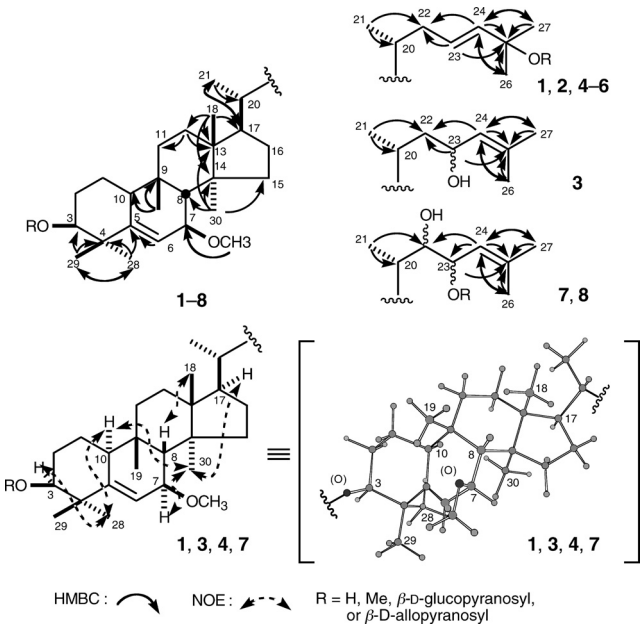

Fig. 1. Selected HMBC and NOE Correlations

molecular formula $C_{31}H_{52}O_3$ was determined by high-resolution MS measurement. The ^{1}H- (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra of **2**, which were assigned by various NMR experiments,[24] showed signals due to eight methyls [δ 0.70, 0.92, 0.99, 1.03, 1.21 (3H each, all s, 30, 18, 19, 28, 29-H_3), 0.89 (3H, d, J=4.6 Hz, 21-H_3), 1.30 (6H, s, 26, 27-H_3)], a methoxyl [3.34 (3H, s, 7-OCH_3)], two methines bearing an oxygen function [3.43 (1H, m, 7-H), 3.51 (1H, m, 3-H)], three olefinic protons [5.59 (2H, m, 23, 24-H), 5.83 (1H, d, J=4.6 Hz, 6-H)]. The ^{1}H- and ^{13}C-NMR signals due to the tetracyclic carbon skeleton structure (C-1—21, C-28—30) in **2** were superimporsable on those of **1**, whereas the signals of side chain part (C-22—27) were very similar to those of **9**—**11**, **15**, **17**, and **19** having the 25-hydroxy group. In the HMBC experiment on **2**, long-range correlations were observed between the following protons and carbons: 18-H_3 and 12, 13, 14, 17-C; 21-H_3 and 17, 20, 22-C; 23-H and 20, 22, 24, 25-C; 24-H and 22, 23, 25, 26, 27-C; 26, 27-H_3 and 24, 25-C; 28, 29-H_3 and 3, 4, 5-C; 30-H_3 and 8, 13, 14, 15-C; 7-OCH_3 and 7-C. Consequently, the structures of karavilagenin B (**2**) was determined to be 7-methoxycucurbita-5,23-dien-3β,25-diol.

Karavilagenin C (**3**) was obtained as a white powder with positive optical rotation ($[\alpha]_D^{26}$ +98.1°). The IR spectrum of **3** showed absorption bands at 3475 and 1655 cm^{-1} suggestive of hydroxy and olefin functions. In the EI-MS of **3**, a molecular ion peak was observed at m/z 472 [M^+], and the molecular formula $C_{31}H_{52}O_3$ was determined by high-resolution MS measurement. The ^{1}H- (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra of **3**, which were assigned by various NMR experiments,[24] showed signals due to eight methyls [δ 0.70, 0.95, 0.98, 1.04, 1.21, 1.68, 1.70 (3H each, all s, 30, 18, 19, 28, 29, 26, 27-H_3), 0.97 (3H, d-like, 21-H_3)], a methoxyl [3.34 (3H, s, 7-OCH_3)], three methines bearing an oxygen function [3.42 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.51 (1H, br s, 3-H), 4.46 (1H, ddd-like, 23-H)], two olefinic protons [5.20 (1H, d, J=8.3 Hz, 24-H), 5.83 (1H, d, J=5.0 Hz, 6-H)]. The ^{1}H- and ^{13}C-NMR signals due to the tetracyclic carbon skeleton structure (C-1—21, C-28—30) were superimporsable on those of **1**. In the HMBC experiment on **3**, long-range correlations were observed between the following protons and carbons: 18-H_3 and 12, 13, 14, 17-C; 21-H_3 and 17, 20, 22-C; 23-H and 20, 22, 24, 25-C; 24-H and 22, 23, 25, 26, 27-C; 26, 27-H_3 and 24, 25-C; 28, 29-H_3 and 3, 4, 5-C; 30-H_3 and 8, 13, 14, 15-C; 7-OCH_3 and 7-C. The stereostructure of **3** was characterized by NOESY experiment, in which NOE correlations were observed between the following protons and protons: 8-H and 18-H_3; 28-H_3 and 3-H, 10-H; 30-H_3 and 7-H, 10-H, 17-H (Fig. 1).[25] Consequently, the structure of karavilagenin C (**3**) was determined to be 7-methoxycucurbita-5,24-dien-3β,23ξ-diol.

Kalavilosides I (**4**) and II (**5**) were obtained as a white powder with positive optical rotation (**4**: $[\alpha]_D^{29}$ +41.1°; **5**: $[\alpha]_D^{27}$ +39.3°). **4** and **5** were found to have the same molecular formula, $C_{38}H_{64}O_8$, which was determined from the quasi-molecular ion peaks in their negative-ion FAB-MS [m/z 647 $(M-H)^-$] and positive-ion FAB-MS [m/z 671 $(M+Na)^+$, 693 $(M+2Na-H)^+$] and by high-resolution MS measurement. The IR spectra of **4** and **5** showed absorption bands suggestive of a glycosidic function (**4**: 3432, 1078, 1047 cm^{-1}; **5**: 3432, 1080, 1036 cm^{-1}). Acid hydrolysis of **4** with 5% aqueous sulfuric acid (H_2SO_4)–1,4-dioxane (1 : 1, v/v) furnished D-glucose, which was identified by GLC analysis of the thiazolidine derivative.[26,27] On the other hand, **5** furnished D-allose upon acid hydrolysis.[26,27] The ^{1}H- and ^{13}C-NMR signals due to the aglycone part of **4** and **5** were superimporsable on those of **1**. Namely, the ^{1}H- (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra[24] of **4** showed signals assignable to a β-D-glucopyranosyl moiety [δ 4.90 (1H, d, J=7.6 Hz, 1′-H)] together with a karavilagenin A moiety [δ 0.73, 0.94, 1.63 (3H each, all s, 30, 18, 29-H_3), 1.00 (3H, d, J=6.1 Hz, 21-H_3), 1.12, 1.34 (6H each, both s, 19, 28, 26, 27-H_3), 3.23, 3.32 (3H each, both s, 25-OCH_3, 7-OCH_3), 3.45 (1H, dd-like, 7-H), 3.71 (1H, br s, 3-H), 5.58 (1H, d, J=15.6 Hz, 24-H), 5.67 (1H, ddd-like, 23-H), 5.95 (1H, d, J=4.9 Hz, 6-H)]. The ^{1}H- (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra[24] of **5** showed signals assignable to a β-D-allopyranosyl moiety [δ 5.32 (1H, d, J=7.6 Hz, 1′-H)] together with a karavilagenin A part [δ 0.73, 0.93, 1.09, 1.14, 1.55 (3H each, all s, 30, 18, 28, 19, 29-H_3), 1.01 (3H, d, J=6.1 Hz, 21-H_3), 1.34 (6H, s, 26, 27-H_3), 3.22, 3.32 (3H each, both s, 25-OCH_3, 7-OCH_3), 3.44 (1H, dd-like, 7-H), 3.65 (1H, br s, 3-H), 5.57 (1H, d, J=15.8 Hz, 24-H), 5.67 (1H, ddd-like, 23-H), 5.93 (1H, d, J=4.3 Hz, 6-H)]. In the HMBC experiments on **4** and **5**, long-range correlations were observed between the following protons and carbons: 18-H_3 and 12, 13, 14, 17-C; 21-H_3 and 17, 20, 22-C; 23-H and 20, 22, 24, 25-C; 24-H and 22, 23, 25, 26, 27-C; 26, 27-H_3 and 24, 25-C; 28, 29-H_3 and 3, 4, 5-C; 30-H_3 and 8, 13, 14, 15-C; 7-OCH_3 and 7-C; 25-OCH_3 and 25-C; 1′-H and 3-C (Fig. 1). The stereostructure of the aglycone moiety in **4** was characterized by NOESY experiment, which showed NOE correlations between the following protons and protons: 8-H and 18-H_3; 28-H_3 and 3-H, 10-H; 30-H_3 and 7-H, 10-H, 17-H (Fig. 1).[25] Consequently, the structures of kalavilosides I (**4**) and II (**5**) were determined to be 7,25-dimethoxycucurbita-5,23-dien-3β-ol 3-*O*-β-D-glucopyranoside and 7,25-methoxycucurbita-5,23-dien-3β-ol 3-*O*-β-D-allopyranoside, respectively.

Karaviloside III (**6**) was obtained as a white powder with positive optical rotation ($[\alpha]_D^{28}$ +81.8°). The IR spectrum of **6** showed absorption bands at 3453, 1082, and 1036 cm^{-1} suggestive of glycosidic functions. In the negative- and positive-ion FAB-MS of **6**, quasimolecular ion peaks were observed at m/z 633 $(M-H)^-$, m/z 657 $(M+Na)^+$, and m/z 679 $(M+2Na-H)^+$ and the molecular formula $C_{37}H_{62}O_8$ was determined by high-resolution MS measurement. Acid hydrolysis of **6** with 5% aqueous H_2SO_4–1,4-dioxane (1 : 1, v/v) furnished D-allose.[26,27] The ^{1}H- and ^{13}C-NMR data due to the aglycone part in **6** were superimporsable on those of karavilagenin B (**2**). The ^{1}H- (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra[24] of **6** showed signals assignable to a β-D-allopyranosyl moiety [δ 5.28 (1H, d, J=7.9 Hz, 1′-H)] together with a karavilagenin B moiety [δ 0.70, 0.91, 1.08, 1.12 (3H each, all s, 30, 18, 28, 19-H_3), 1.00 (3H, d, J=4.6 Hz, 21-H_3), 1.54 (9H, s, 26, 27, 29-H_3), 3.32 (3H, s, 7-OCH_3), 3.44 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.65 (1H, br s, 3-H), 5.94 (3H, m, 6, 23, 24-H)]. Furthermore, in the HMBC experiment on **6**, long-range correlations were observed between the following protons and carbons: 18-H_3 and 12, 13, 14, 17-C; 21-H_3 and 17, 20, 22-C; 23-H and 20, 22, 24, 25-C; 24-H and 22, 23, 25, 26, 27-C; 26, 27-H_3 and 24, 25-C; 28, 29-H_3 and 3, 4, 5-C; 30-H_3 and 8, 13, 14, 15-C; 7-OCH_3 and 7-C; 1′-H and 3-C.

Consequently, the structures of karaviloside III (**6**) was determined to be 7-methoxycucurbita-5,23-dien-3β,25-diol 3-*O*-β-D-allopyranoside.

Karaviloside IV (**7**) was obtained as a white powder with positive optical rotation ($[\alpha]_D^{28}$ +29.8°). The IR spectrum of **7** showed absorption bands at 3432, 1078, and 1028 cm^{-1} suggestive of a glycosidic function. In the positive-ion FAB-MS of **7**, quasimolecular ion peaks were observed at *m/z* 673 $(M+Na)^+$ and the molecular formula $C_{37}H_{62}O_9$ was determined by high-resolution MS measurement. Acid hydrolysis of **7** with 5% aqueous H_2SO_4–1,4-dioxane (1 : 1, v/v) furnished D-glucose.[26,27] The ^{1}H- (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra of **7**,[24] showed signals due to a β-D-glucopyranosyl moieties [δ 5.20 (1H, d, J=7.9 Hz, 1′-H)] and an aglycone moiety [δ 0.79, 0.94, 1.13, 1.20, 1.44, 1.66, 1.92 (3H each, all s, 30, 18, 28, 19, 29, 26, 27-H_3), 1.26 (3H, d, J=6.9 Hz, 21-H_3), 3.38 (3H, s, 7-OCH_3), 3.50 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.75 (1H, br s, 3-H), 4.12 (1H, dd-like, 22-H), 4.73 (1H, t-like, 23-H), 5.56 (1H, d, J=9.9 Hz, 24-H), 6.02 (1H, d, J=5.3 Hz, 6-H)]. In the HMBC experiment on **7**, long-range correlations were observed between the following protons and carbons: 18-H_3 and 12, 13, 14, 17-C; 21-H_3 and 17, 20, 22-C; 24-H and 22, 23, 25, 26, 27-C; 26, 27-H_3 and 24, 25-C; 28, 29-H_3 and 3, 4, 5-C; 30-H_3 and 8, 13, 14, 15-C; 7-OCH_3 and 7-C; 1′-H and 23-C. The stereostructure of the aglycone moiety was characterized by NOESY experiment, in which NOE correlations were observed between the following protons and protons: 8-H and 18-H_3; 28-H_3 and 3-H, 10-H; 30-H_3 and 10-H, 17-H (Fig. 1).[25] Consequently, the structures of karaviloside IV (**7**) was determined to be 7-methoxycucurbita-5,24-dien-3β,22ξ,23ξ-triol 23-*O*-β-D-glucopyranoside.

Karaviloside V (**8**) was obtained as a white powder with negative optical rotation ($[\alpha]_D^{28}$ +18.3°). The IR spectrum of **5** showed absorption bands at 3432, 1080, and 1036 cm^{-1} suggestive of glycosidic functions. In the negative- and positive-ion FAB-MS of **8**, quasimolecular ion peaks were observed at *m/z* 811 $(M-H)^-$ and *m/z* 835 $(M+Na)^+$ together with a fragment ion peak *m/z* 649 $(M-C_6H_{11}O_5)^-$ and the molecular formula $C_{43}H_{72}O_{14}$ was determined by high-resolution MS measurement. Acid hydrolysis of **5** with 5% aqueous H_2SO_4–1,4-dioxane (1 : 1, v/v) furnished D-allose.[26,27] The ^{1}H- (pyridine-d_5) and ^{13}C-NMR (Table 1) spectra of **8**,[24] showed signals due to two β-D-allopyranosyl moieties [δ 5.26 (1H, d, J=7.9 Hz, 1′-H), 5.54 (1H, d, J=7.9 Hz, 1″-H)] and an aglycone moiety [δ 0.73, 0.90, 1.08, 1.12, 1.53, 1.64, 1.84 (3H each, all s, 30, 18, 28, 19, 29, 26, 27-H_3), 1.28 (3H, d, J=6.7 Hz, 21-H_3), 3.32 (3H, s, 7-OCH_3), 3.44 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.62 (1H, br s, 3-H), 4.06 (1H, dd, J=7.0, 9.8 Hz, 22-H), 4.65 (1H, m, 23-H), 5.26 (1H, d, J=7.9 Hz, 1′-H), 5.54 (1H, d, J=10.6 Hz, 24-H), 5.54 (1H, d, J=7.9 Hz, 1″-H), 5.93 (1H, d, J=6.9 Hz, 6-H)]. The ^{1}H- and ^{13}C-NMR signals of the aglycone moiety in **8** were superimporsable on those of **7**, except for those around the 3-position. In the HMBC experiment on **8**, long-range correlations were observed between the following protons and carbons: 18-H_3 and 12, 13, 14, 17-C; 21-H_3 and 17, 20, 22-C; 24-H and 22, 23, 25, 26, 27-C; 26, 27-H_3 and 24, 25-C; 28, 29-H_3 and 3, 4, 5-C; 30-H_3 and 8, 13, 14, 15-C; 7-OCH_3 and 7-C; 1′-H and 3-C; 1″-H and 23-C. Consequently, the structures of karaviloside V (**8**) was determined to be 23-*O*-β-D-allopyranosyl-7-methoxycucurbita-5,24-dien-3β,22ξ,23ξ-triol 3-*O*-β-D-allopyranoside.

Experimental

The following instruments were used to obtain physical data: specific rotations, Horiba SEPA-300 digital polarimeter (l=5 cm); IR spectra, Shimadzu FTIR-8100 spectrometer; EI-MS and high-resolution MS, JEOL JMS-GCMATE mass spectrometer; FAB-MS and high-resolution MS, JEOL JMS-SX 102A mass spectrometer; ^{1}H-NMR spectra, JNM-LA500 (500 MHz) spectrometer; ^{13}C-NMR spectra, JNM-LA500 (125 MHz) spectrometer with tetramethylsilane as an internal standard; and HPLC detector, Shimadzu RID-6A refractive index detector.

The following experimental conditions were used for chromatography: ordinary-phase silica gel column chromatography, Silica gel BW-200 (Fuji Silysia Chemical, Ltd., 150—350 mesh); reverse-phase silica gel column chromatography, Chromatorex ODS DM1020T (Fuji Silysia Chemical, Ltd., 100—200 mesh); TLC, precoated TLC plates with Silica gel 60F_{254} (Merck, 0.25 mm) (ordinary phase) and Silica gel RP-18 F_{254S} (Merck, 0.25 mm) (reverse phase); reverse-phase HPTLC, precoated TLC plates with Silica gel RP-18 WF_{254S} (Merck, 0.25 mm); and detection was achieved by spraying with 1% $Ce(SO_4)_2$–10% aqueous H_2SO_4 followed by heating.

Plant Material The fruit of *M. charantia* L. were cultivated in Nuwara Eliya, Sri Lanka, and identified by one of the authors (Masayuki Yoshikawa). A voucher of this plant material is on file in our laboratory.

Isolation of Karavilagenin (1—3) and Karavilosides (4—8) and Known Compounds (9—19) from the Dried Fruit of *M. charantia* L. (Karavila) The dried fruit of *M. charantia* L. (6.6 kg, cultivated in Nuwara Eliya, Sri Lanka) were cut and extracted three times with MeOH under reflux. Evaporation of the solvent under reduced pressure provided the MeOH extract (325 g, 4.9%). The MeOH extract (160 g) was subjected to normal-phase silica gel column chromatography [3 kg, $CHCl_3$–MeOH–H_2O (30 : 3 : 1, lower layer→10 : 3 : 1, lower layer, v/v)→MeOH] to give eight fractions [Fr. 1 (8.7 g), 2 (37.9 g), 3 (27.6 g), 4 (3.0 g), 5 (4.9 g), 6 (5.7 g), 7 (32.3 g), 8 (37.0 g)]. Normal-phase silica gel column chromatography [600 g, *n*-hexane–AcOEt (1 : 1→1 : 5, v/v)→MeOH] of fraction 2 (33 g) gave five fractions [Fr. 2-1 (9.9 g), 2-2 (2.7 g), 2-3 (2.3 g), 2-4 (1.9 g), 2-5 (14.6 g)]. Fraction 2-2 (2.7 g) was purified by reversed-phase silica gel column chromatography [80 g, MeOH–H_2O (90 : 10, v/v)→MeOH] and HPLC [MeOH–H_2O (95 : 5, v/v)] to give 5β,19-epoxycucurbita-6,23-diene-3β,25-diol (**10**, 102 mg, 0.0036%). Fraction 2-3 (2.3 g) was purified by reversed-phase silica gel column chromatography [60 g, MeOH–H_2O (80 : 20, v/v)→MeOH] and HPLC [MeOH–H_2O (90 : 10, v/v)] to karavilagenin A (**1**, 85 mg, 0.0030%), karavilagenin B (**2**, 214 mg, 0.0076%), karavilagenin C (**3**, 67 mg, 0.0024%). Fraction 2-4 (1.9 g) was purified by reversed-phase silica gel column chromatography [60 g, MeOH–H_2O (90 : 10, v/v)→MeOH] and HPLC [MeOH–H_2O (90 : 10, v/v)] to give 19(*R*)-methoxy-5β,19-epoxycucurbita-6,23-dien-3β,25-diol (**9**, 53 mg, 0.0019%). Fraction 3 (27.6 g) was separated by normal-phase silica gel column chromatography [500 g, $CHCl_3$–MeOH (50 : 1→50 : 3, v/v)→MeOH] to give five fractions [Fr. 3-1 (7.6 g), 3-2 (4.4 g), 3-3 (4.0 g), 3-4 (7.2 g), 3-5 (3.6 g)]. Fraction 3-2 (4.4 g) was purified by reversed-phase silica gel column chromatography [130 g, MeOH–H_2O (90 : 10, v/v)→MeOH] and HPLC [MeOH–H_2O (90 : 10, v/v)] to give karavilaside II (**5**, 448 mg, 0.0138%), goyaglycoside-d (**13**, 84 mg, 0.0026%), and momordicoside G (**16**, 140 mg, 0.0043%). Fraction 3-3 (4.0 g) was separated by reversed-phase silica gel column chromatography [120 g, MeOH–H_2O (80 : 20→90 : 10, v/v)→MeOH] to give four fractions [Fr. 3-3-1 (1.5 g), 3-3-2 (569 mg), 3-3-3 (1.2 g), 3-3-4 (509 mg)]. Fraction 3-3-2 (569 mg) was purified by HPLC [1) MeOH–H_2O (90 : 10, v/v); 2) CH_3CN–H_2O (80 : 20, v/v)] to give karaviloside III (**6**, 105 mg, 0.0033%), goyaglycoside-b (**11**, 8 mg, 0.0003%), and momordicoside F_2 (**15**, 17 mg, 0.0005%). Fraction 3-3-3 (1.2 g) was purified by HPLC [MeOH–H_2O (90 : 10, v/v)] to give karaviloside I (**4**, 219 mg, 0.0067%), goyaglycoside-c (**12**, 24 mg, 0.0007%), and momordicoside F_1 (**14**, 268 mg, 0.0083%). Fraction 3-4 (7.2 g) was purified by reversed-phase silica gel column chromatography [200 g, MeOH–H_2O (70 : 30→80 : 20→90 : 10→95 : 5, v/v)→MeOH] and HPLC [1) MeOH–H_2O (90 : 10, v/v); 2) CH_3CN–H_2O (80 : 20, v/v); 3) CH_3CN–H_2O (45 : 55, v/v)] to give momordicoside I (**17**, 39 mg, 0.0012%). Fraction 5 (4.9 g) was purified by normal-phase [150 g, $CHCl_3$–MeOH–H_2O (30 : 3 : 1, lower layer, v/v)] and reversed-phase silica gel column chromatography [100 g, MeOH–H_2O (80 : 20→90 : 10, v/v)→MeOH] and HPLC [CH_3CN–H_2O (80 : 20, v/v)] to give karavilaside IV (**7**, 19 mg, 0.0006%). Fraction 7 (22.3 g) was separated by reversed-phase silica gel column chromatography [600 g, MeOH–H_2O (70 : 30→90 : 10, v/v)→MeOH] to give

four fractions [Fr. 7-1 (11.3 g), 7-2 (3.7 g), 7-3 (640 mg), 7-4 (4.6 g)]. Fraction 7-2 (3.7 g) was purified by normal-phase silica gel column chromatography [100 g, $CHCl_3$–MeOH–H_2O (15 : 3 : 1, lower layer, v/v)→MeOH] and HPLC [1) MeOH–H_2O (90 : 10, v/v); 2) MeOH–H_2O (70 : 30, v/v); 3) MeOH–H_2O (75 : 25, v/v)] to give karaviloside V (**8**, 52 mg, 0.0023%) and momordicoside K (**18**, 33 mg, 0.0015%). Fraction 7-3 (640 mg) was purified by HPLC [MeOH–H_2O (85 : 15, v/v)] to give momordicoside L (**19**, 24 mg, 0.0011%). The known compounds (**9**—**19**) were identified by comparison of their physical data ($[\alpha]_D$, IR, ^{1}H-NMR, ^{13}C-NMR) with reported values.

Karavilagenin A (**1**): A white powder, $[\alpha]_D^{26}$ +71.5° (c=0.1, MeOH). IR (KBr): 3475, 1665 cm^{-1}. High-resolution positive-ion EI-MS: Calcd for $C_{32}H_{54}O_3$ (M^+): 486.4083. Found: 486.4073. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.70, 0.93, 0.99, 1.04, 1.21 (3H each, all s, 30, 18, 19, 28, 29-H_3), 0.90 (3H, d-like, 21-H_3), 1.25 (6H, s, 26, 27-H_3), 3.14 (3H, s, 25-OCH_3), 3.34 (3H, s, 7-OCH_3), 3.43 (1H, m, 7-H), 3.51 (1H, m, 3-H), 5.38 (1H, d, J=15.8 Hz, 24-H), 5.49 (1H, m, 23-H), 5.83 (1H, d, J=5.3 Hz, 6-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Positive-ion EI-MS: m/z 486 (M^+).

Karavilagenin B (**2**): A white powder, $[\alpha]_D^{26}$ +117.1° (c=0.1, MeOH). IR (KBr): 3432, 1655 cm^{-1}. High-resolution positive-ion EI-MS: Calcd for $C_{31}H_{52}O_3$ (M^+): 472.3916. Found: 472.3928. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.70, 0.92, 0.99, 1.03, 1.21 (3H each, all s, 30, 18, 19, 28, 29-H_3), 0.89 (3H, d, J=4.6 Hz, 21-H_3), 1.30 (6H, s, 26, 27-H_3)], 3.34 (3H, s, 7-OCH_3), 3.43 (1H, m, 7-H), 3.51 (1H, m, 3-H), 5.59 (2H, m, 23, 24-H), 5.83 (1H, d, J=4.6 Hz, 6-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Positive-ion EI-MS: m/z 472 (M^+).

Karavilagenin C (**3**): A white powder, $[\alpha]_D^{26}$ +98.1° (c=0.1, MeOH). IR (KBr): 3475, 1655 cm^{-1}. High-resolution positive-ion EI-MS: Calcd for $C_{31}H_{52}O_3$ (M^+): 472.3916. Found: 472.3909. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.70, 0.95, 0.98, 1.04, 1.21, 1.68, 1.70 (3H each, all s, 30, 18, 19, 28, 29, 26, 27-H_3), 0.97 (3H, d-like, 21-H_3), 3.34 (3H, s, 7-OCH_3), 3.42 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.51 (1H, br s, 3-H), 4.46 (1H, ddd-like, 23-H), 5.20 (1H, d, J=8.3 Hz, 24-H), 5.83 (1H, d, J=5.0 Hz, 6-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Positive-ion EI-MS: m/z 472 (M^+).

Karavilaside I (**4**): A white powder, $[\alpha]_D^{29}$ +41.1° (c=0.1, MeOH). IR (KBr): 3432, 1078, 1047 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_{38}H_{64}O_8Na$ $(M+Na)^+$: 671.4499. Found: 671.4489. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.73, 0.94, 1.63 (3H each, all s, 30, 18, 29-H_3), 1.00 (3H, d, J=6.1 Hz, 21-H_3), 1.12, 1.36 (6H each, both s, 19, 28, 26, 27-H_3), 3.23, 3.32 (3H each, both s, 25, 7-OCH_3), 3.45 (1H, dd-like, 7-H), 3.71 (1H, br s, 3-H), 4.90 (1H, d, J=7.6 Hz, 1′-H), 5.58 (1H, d, J=15.6 Hz, 24-H), 5.67 (1H, ddd-like, 23-H), 5.95 (1H, d, J=4.9 Hz, 6-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Negative-ion FAB-MS: m/z 647 $(M-H)^-$. Positive-ion FAB-MS: m/z 671 $(M+Na)^+$, 693 $(M+2Na-H)^+$.

Karavilaside II (**5**): A white powder, $[\alpha]_D^{27}$ +39.3° (c=0.1, MeOH). IR (KBr): 3432, 1080, 1036 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_{38}H_{64}O_8Na$ $(M+Na)^+$: 671.4499. Found: 671.4505. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.73, 0.93, 1.09 1.14, 1.55 (3H each, all s, 30, 18, 28, 19, 29-H_3), 1.01 (3H, d, J=6.1 Hz, 21-H_3), 1.34 (6H, s, 26, 27-H_3), 3.22, 3.32 (3H each, both s, 25, 7-OCH_3), 3.44 (1H, dd-like, 7-H), 3.65 (1H, br s, 3-H), 5.32 (1H, d, J=7.6 Hz, 1′-H), 5.57 (1H, d, J=15.8 Hz, 24-H), 5.67 (1H, ddd-like, 23-H), 5.93 (1H, d, J=4.3 Hz, 6-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Negative-ion FAB-MS: m/z 647 $(M-H)^-$. Positive-ion FAB-MS: m/z 671 $(M+Na)^+$, 693 $(M+2Na-H)^+$.

Karavilaside III (**6**): A white powder, $[\alpha]_D^{28}$ +81.8° (c=0.1, MeOH). IR (KBr): 3453, 1082, 1036 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_{37}H_{62}O_8Na$ $(M+Na)^+$: 657.4342. Found: 657.4353. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.70, 0.91, 1.08, 1.12 (3H each, all s, 30, 18, 28, 19-H_3), 1.00 (3H, d, J=4.6 Hz, 21-H_3), 1.54 (9H, s, 26, 27, 29-H_3), 3.32 (3H, s, 7-OCH_3), 3.44 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.65 (1H, br s, 3-H), 5.28 (1H, d, J=7.9 Hz, 1′-H), 5.94 (3H, m, 6, 23, 24-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Negative-ion FAB-MS: m/z 633 $(M-H)^-$. Positive-ion FAB-MS: m/z 657 $(M+Na)^+$, 679 $(M+2Na-H)^+$.

Karavilaside IV (**7**): A white powder, $[\alpha]_D^{28}$ +29.8° (c=0.1, MeOH). IR (KBr): 3432, 1078, 1028 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_{37}H_{62}O_9Na$ $(M+Na)^+$: 673.4292. Found: 673.4303. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.79, 0.94, 1.13, 1.20, 1.44, 1.66, 1.92 (3H each, all s, 30, 18, 28, 19, 29, 26, 27-H_3), 1.26 (3H, d, J=6.9 Hz, 21-H_3), 3.38 (3H, s, 7-OCH_3), 3.50 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.75 (1H, br s, 3-H), 4.12 (1H, dd-like, 22-H), 4.73 (1H, t-like, 23-H), 5.20 (1H, d, J=7.9 Hz, 1′-H), 5.56 (1H, d, J=9.9 Hz, 24-H), 6.02 (1H, d, J=5.3 Hz, 6-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Positive-ion FAB-MS: m/z 673 $(M+Na)^+$.

Karavilaside V (**8**): A white powder, $[\alpha]_D^{28}$ +18.3° (c=0.1, MeOH). IR (KBr): 3432, 1080, 1036 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_{43}H_{72}O_{14}Na$ $(M+Na)^+$: 835.4820. Found: 835.4818. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 0.73, 0.90, 1.08, 1.12, 1.53, 1.64, 1.84 (3H each, all s, 30, 18, 28, 19, 29, 26, 27-H_3), 1.28 (3H, d, J=6.7 Hz, 21-H_3), 3.32 (3H, s, 7-OCH_3), 3.44 (1H, br d, J=*ca.* 5 Hz, 7-H), 3.62 (1H, br s, 3-H), 4.06 (1H, dd, J=7.0, 9.8 Hz, 22-H), 4.65 (1H, m, 23-H), 5.26 (1H, d, J=7.9 Hz, 1′-H), 5.54 (1H, d, J=10.6 Hz, 24-H), 5.54 (1H, d, J=7.9 Hz, 1″-H), 5.93 (1H, d, J=6.9 Hz, 6-H). ^{13}C-NMR (125 MHz, pyridine-d_5) δ_C: given in Table 1. Negative-ion FAB-MS: m/z 811 $(M-H)^-$, 649 $(M-C_6H_{11}O_5)^-$. Positive-ion FAB-MS: m/z 835 $(M+Na)^+$.

Acid Hydrolysis of Kalavilosides (4—8) A solution of **4**—**8** (3 mg each) in 5% aqueous H_2SO_4–1,4-dioxane was heated under reflux for 1 h. After cooling, the reaction mixture was neutralized with Amberlite IRA-400 (OH^- form) and residue was removed by filtration. After removal of the solvent from the filtrate *in vacuo*, the residue was transferred to a Sep-Pak C18 cartridge with H_2O and MeOH. The H_2O eluate was concentrated and the residue was treated with L-cysteine methyl ester hydrochloride (4 mg) in pyridine (0.5 ml) at 60 °C for 1 h. After reaction, the solution was treated with *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (0.2 ml) at 60 °C for 1 h. The supernatant was then subjected to GLC analysis to identify the derivatives of D-glucose (i) from **4** and **7**; D-allose (ii) from **5**, **6**, and **8**; GLC conditions: column, Supeluco STB™-1, 30 m×0.25 mm (i.d.) capillary column; column temperature, 230 °C; carrier gas, N_2; t_R, (i) 17.7 min (ii) 23.2 min (iii) 24.1 min (L-allose).

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