SUPPLEMENTARY MATERIAL

A new dihydrobenzofuran lignan and potential α -glucosidase inhibitory activity of isolated compounds from *Mitrephora teysmannii*

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Abstract

A new dihydrobenzofuran lignan, (2*R*,3*S*)-2-(3',4'-dimethoxyphenyl)-5-(3-hydroxypropyl)-7-methoxy-2,3-dihydrobenzofuran-3-methyl acetate, named as mitredrusin (**1**), was isolated from the leaves of *Mitrephora teysmannii* (Annonaceae) together with twelve known compounds including a related dihydrobenzofuran lignan: (-)-3',4-di-*O*-methylcedrusin (**2**), four polyacetylenic acids: 13(*E*)-octadecene-9,11-diynoic acid (**3**), 13(*E*),17-octadecadiene-9,11-diynoic acid (**4**), octadeca-9,11,13-triynoic acid (**5**) and octadeca-17-en-9,11,13-triynoic acid (**6**), five lignans: (-)-eudesmin (**7**), (-)-epieudesmin (**8**), (-)-phillygenin (**9**), magnone A (**10**) and forsythialan B (**11**) and two megastigmans: (3*S*,5*R*,6*S*,7*E*,9*R*)-7-megastigmene-3,6,9-triol (**12**) and annoionol A (**13**). The chemical structures of these compounds were established on the basis of their 1D and 2D NMR spectroscopic data. All compounds were evaluated for their α -glucosidase inhibitory activity. Among these isolates, polyacetylenic acids **3** and **4** showed more than 20-fold much higher activity compared with that of the antidiabetic drug acarbose.

Keywords: *Mitrephora teysmannii*; Annonaceae; Dihydrobenzofuran lignan; Mitredrusin; α -Glucosidase inhibitory activity

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Figure S1(a). ^1H NMR spectrum of mitredrusin (**1**)

Figure S1(b). ^1H NMR spectrum of mitredrusin (**1**)

Figure S1(c). ^1H NMR spectrum of mitredrusin (**1**)

Figure S2(a). ^{13}C NMR spectrum of mitredrusin (**1**)

Figure S2(b). ¹³C NMR spectrum of mitredrusin (1)

Figure S2(c). ¹³C NMR spectrum of mitredrusin (1)

Figure S3(a). COSY NMR spectrum of mitredrusin (**1**)

Figure S3(b). COSY NMR spectrum of mitredrusin (**1**)

Figure S3(c). COSY NMR spectrum of mitredrusin (**1**)

Figure S4(a). HMQC NMR spectrum of mitredrusin (**1**)

Figure S4(b). HMQC NMR spectrum of mitredrusin (**1**)

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Figure S5(a). HMBC NMR spectrum of mitredrusin (**1**)

Figure S5(b). HMBC NMR spectrum of mitredrusin (**1**)

Figure S5(c). HMBC NMR spectrum of mitredrusin (**1**)

Figure S5(d). HMBC NMR spectrum of mitredrusin (**1**)

Figure S5(e). HMBC NMR spectrum of mitredrusin (**1**)

Mass Spectrum List Report

Analysis Info

Analysis Name OSSUKR570915001.d
Method Natee20130403.m
Sample Name MM-L-H30-21-6
MM-L-H30-21-6

Acquisition Date 9/15/2014 9:23:00 AM
Operator Administrator
Instrument microTOF 72

Acquisition Parameter

Source Type ESI
Scan Range n/a
Scan Begin 50 m/z
Scan End 3000 m/z

Ion Polarity Positive
Capillary Exit 180.0 V
Hexapole RF 400.0 V
Skimmer 1 54.4 V
Hexapole 1 21.4 V

Set Corrector Fill 79 V
Set Pulsar Pull 406 V
Set Pulsar Push 388 V
Set Reflector 1300 V
Set Flight Tube 9000 V
Set Detector TOF 1910 V

#	m/z	I	I%	S/N	FWHM	Res.
1	326.1517	962	3.2	107.7	0.0394	8280
2	339.1590	1335	4.5	146.1	0.0417	8140
3	341.1405	619	2.1	67.4	0.0462	7388
4	342.1492	461	1.6	50.2	0.0401	8526
5	353.1294	644	2.2	69.5	0.0482	7321
6	355.1544	1570	5.3	169.5	0.0420	8447
7	356.1619	1055	3.6	113.7	0.0414	8612
8	357.1716	13189	44.4	1422.7	0.0420	8505
9	358.1746	2342	7.9	252.3	0.0469	7645
10	368.1534	1174	4.0	125.5	0.0448	8221
11	369.1599	502	1.7	53.5	0.0587	6288
12	370.1660	2250	7.6	240.2	0.0428	8653
13	371.1580	1033	3.5	110.1	0.0564	6582
14	385.1667	845	2.8	89.1	0.0489	7873
15	397.1649	1158	3.9	121.1	0.0498	7975
16	399.1805	767	2.6	80.0	0.0531	7513
17	425.1579	1765	5.9	180.9	0.0499	8517
18	439.1734	29693	100.0	3018.8	0.0526	8355
19	440.1771	5697	19.2	578.6	0.0525	8380
20	441.1723	984	3.3	99.6	0.0584	7553
21	455.1540	1588	5.3	159.4	0.0552	8249
22	457.1795	842	2.8	84.2	0.0522	8753
23	471.1169	930	3.1	92.2	0.0658	7160
24	481.1814	3279	11.0	323.5	0.0498	9668
25	482.1849	771	2.6	75.7	0.0502	9605
26	499.1914	1643	5.5	159.9	0.0522	9564
27	501.1463	615	2.1	59.5	0.0635	7890
28	515.1574	807	2.7	77.5	0.0522	9867
29	623.3614	791	2.7	82.6	0.0615	10129
30	739.3039	490	1.7	59.4	0.0701	10542

Figure S6. ESI-TOF-MS spectrum of mitredrusin (1)

Figure S7. Selected ^1H - ^1H COSY (thick lines) and HMBC correlation (arrows) for mitredrusin (**1**)

Table S1. α -Glucosidase inhibitory activity of **1-13**

Compounds	α -Glucosidase inhibition
	IC ₅₀ (μ M) ^a
1	NI ^b
2	NI ^b
3	53 $\pm$ 1.7
4	59 $\pm$ 1.0
5	128 $\pm$ 2.5
6	274 $\pm$ 7.3
7	NI ^b
8	NI ^b
9	NI ^b
10	NI ^b
11	NI ^b
12	NI ^b
13	NI ^b
Acarbose	1457 $\pm$ 121.8

^a IC₅₀ mean concentration required for 50% inhibition of α -glucosidase, and the values represent means $\pm$ SD ($n = 3$).

^b Inhibitory effect less than 30% at concentration of 1 mg/mL.

Experimental

Characterization of compounds 3-13

13(E)-octadecene-9,11-diynoic acid (3): a pale yellow oil. IR (neat): $\nu_{\max}$ 3445, 2949, 2850, 1696, 1645, 1463 cm^{-1} . ESI-TOF-MS m/z 275.2008 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{18}\text{H}_{27}\text{O}_2$, 275.2011).

13(E),17-octadecadiene-9,11-diynoic acid (4): a pale yellow oil. IR (neat): $\nu_{\max}$ 3440, 2921, 2849, 1692, 1644, 1460, 1273 cm^{-1} . ESI-TOF-MS m/z 271.2203 $[\text{M}-\text{H}]^+$ (calcd for $\text{C}_{18}\text{H}_{23}\text{O}_2$, 271.1698).

Octadeca-9,11,13-triynoic acid (5): a pale yellow oil. IR (neat): $\nu_{\max}$ 3444, 2956, 2930, 2865, 2219, 1696, 1467, 1432, 1410, 1090 cm^{-1} . ESI-TOF-MS m/z 273.1850 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{18}\text{H}_{25}\text{O}_2$, 273.1854).

Octadeca-17-en-9,11,13-triynoic acid (6): a pale yellow oil. IR (neat): $\nu_{\max}$ 3447, 2955, 2927, 2850, 2227, 1691, 1465 cm^{-1} . ESI-TOF-MS m/z 271.1690 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{18}\text{H}_{23}\text{O}_2$, 271.1698).

(-)-Eudesmin (7): colorless crystals. mp 96-98 °C [lit. 98-100°C]. $[\alpha]_{\text{D}}^{25}$ -51.0° (c 0.053, CHCl_3) [lit. +61.0° (c 0.4, CHCl_3)] (Iida et al. 1982). IR (neat): $\nu_{\max}$ 1613, 1596, 1517, 1460, 1263, 1147 cm^{-1} . ESI-TOF-MS m/z 409.1624 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{22}\text{H}_{26}\text{O}_6\text{Na}$, 409.1627).

(-)-Epieudesmin (8): colorless crystals. mp 126-128 °C [lit. 122-125°C]. $[\alpha]_{\text{D}}^{25}$ -112.4° (c 0.060, CHCl_3) [lit. +113.3° (c 0.38, CHCl_3)] (Iida et al. 1982). IR (neat): $\nu_{\max}$ 1613, 1596, 1517, 1460, 1260, 1162, 1147 cm^{-1} . UV (MeOH): ESI-TOF-MS m/z 409.1622 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{22}\text{H}_{26}\text{O}_6\text{Na}$, 409.1627).

(-)-Phillygenin (9): colorless crystals. mp 128-130 °C [lit. 130-131°C]. $[\alpha]_{\text{D}}^{25}$ -109.8° (c 0.051, CHCl_3) [lit. -120.0° (c 0.2, CHCl_3)] (Messiano et al. 2008). IR (neat): $\nu_{\max}$ 3573, 1610, 1596, 1510, 1460, 1275 cm^{-1} . ESI-TOF-MS m/z 395.1468 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{21}\text{H}_{24}\text{O}_6\text{Na}$, 395.1471).

Magnone A (10): colorless crystals. mp 148-150 °C [lit. 149-150°C]. $[\alpha]_{\text{D}}^{25}$ +31.4° (c 0.053, CHCl_3) [lit. +24.7° (c 0.5, MeOH)] (Jung et al. 1998). IR (neat): $\nu_{\max}$ 3465, 1662, 1595, 1584, 1518, 1465, 1435, 1422, 1265, 1155, 1024, 961, 867 cm^{-1} . ESI-TOF-MS m/z 425.1573 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{22}\text{H}_{26}\text{O}_7\text{Na}$, 425.1577).

Forsythialan B (11): colorless crystals. mp 142-144 °C. $[\alpha]_{\text{D}}^{25}$ +21.3° (c 0.055, CHCl_3) [lit. -21.5° (c 0.93, CHCl_3)] (Piao et al. 2008). IR (neat): $\nu_{\max}$ 3430, 2927, 1667, 1595, 1519, 1466, 1423, 1268, 1160, 1024, 814, 756 cm^{-1} . ESI-TOF-MS m/z 411.1416 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{21}\text{H}_{24}\text{O}_7\text{Na}$, 411.1420).

(3*S*,5*R*,6*S*,7*E*,9*R*)-7-megastigmene-3,6,9-triol (12): an orange oil. $[\alpha]_{\text{D}}^{25}$ -9.0° (c 0.055, CHCl₃) [lit. -11.4° (c 0.07, MeOH)] (Kawakami et al. 2011). IR (neat): ν_{max} 3357, 2958, 1654, 1371, 1251 cm⁻¹. ESI-TOF-MS m/z 251.1628 [M+Na]⁺ (calcd for C₁₃H₂₄O₃Na, 251.1623).

Annoionol A (13): a yellow oil. $[\alpha]_{\text{D}}^{25}$ -2.5° (c 0.058, CHCl₃) [lit. +1.45° (c 0.11, MeOH)] (Matsushige et al. 2012). IR (neat): ν_{max} 3380, 2961, 2924, 1590, 1375, 1291, 1252, 1120, 1065 cm⁻¹. ESI-TOF-MS m/z 253.1828 [M+Na]⁺ (calcd for C₁₃H₂₆O₃Na, 253.1780).

Additional reference

Iida T, Nakano M, Ito K. 1982. Hydroperoxysesquiterpene and lignan constituents of *Magnolia Kobus*. *Phytochemistry*. 21: 673-675.