Siccanin-Related Drimane Meroterpenoids: Biological Activities and Synthesis

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Table S1. Drimane meroterpenoids with antifungal activity.

Antifungal activity			
Numb.	Compds	Species and bioactivity	Ref.
1	Siccanin	*Trichophyton interdigitale* (MIC=0.1 μg/mL) *Trichophyton asteroids* (MIC=0.1 μg/mL) *Aspergillus oryzae* (MIC=12.5 μg/mL) *Aspergillus niger* (MIC=12.5 μg/mL) *Penicillium digitatum* (MIC=12.5 μg/mL) *Gibberella fujikuroi* (MIC=5.0 μg/mL) *Macrospora bataticola* (MIC=5.0 μg/mL) *Gloeosporium kaki* (MIC=12.5 μg/mL) *Alternaria kikuchiana* (MIC=12.5 μg/mL) *Piricularia oryzae* (MIC=12.5 μg/mL) *Ophiobolus miyabeanus* (MIC=12.5 μg/mL) *Candida albicans* (MIC=25.0 μg/mL) *Saccharomyces cerevisiae* (MIC=50 μg/mL) *Zygosaccharomyces salsus* (MIC=50 μg/mL) *Torula utilis* (MIC=50 μg/mL)	1
Substituted drimane type meroterpenoids			
6	Zonarol	*Phytophthora cinnamomic* *Rhizoctonia solani* *Sclerotinia sclerotiorum* *Sclerotium rolfsii*	2
16	Macrophorin A	*Botryosphaeria berengeriana* (IC_{50}=6 μg/disc) *Gibberella fujikuroi* (IC_{50}=6 μg/disc)	3
20	Macrophorin E	*Botryosphaeria berengeriana* (IC_{50}=25 μg/disc) *Gibberella fujikuroi* (IC_{50}=12 μg/disc)	3
21	Macrophorin F	*Botryosphaeria berengeriana* (IC_{50}=6 μg/disc) *Gibberella fujikuroi* (IC_{50}=3 μg/disc)	3
22	Macrophorin G	*Botryosphaeria berengeriana* (IC_{50}=25 μg/disc) *Gibberella fujikuroi* (IC_{50}=12 μg/disc)	3
25	2',3'-epoxy-13-hydroxy-4'-oxomacrophorin A	*Aspergillus flaVus* *Fusarium Verticillioide*	4
26	Neomacrophorin I	*Cochliobolus miyabeanus*	5
27	Neomacrophorin II	*Cochliobolus miyabeanus*	5
28	Neomacrophorin III	*Cochliobolus miyabeanus*	5
41	Isozonarol	*Phytophthora cinnamomic* *Rhizoctonia solani* *Sclerotinia sclerotiorum* *Sclerotium rolfsii*	2
47	Peyssonoic acid A	*Lindra thalassiae*	6
64	Albaconol	*Sclerotinia sclerotiorum* (EC_{50}= 24.35 μM)	7
65	Neoalbaconol	*Sclerotinia sclerotiorum* (EC_{50}= 40.38 μM)	7

		Rhizoctonia solani (EC_{50}= 35.16 μM)	
66	Dictyvaric acid	*Sclerotinia sclerotiorum* (EC_{50}= 22.16 μM) *Rhizoctonia solani* (EC_{50}=22.54 μM)	7
81	Siphonodictyal B	*Aspergillus fumigatus*	8
82	Siphonodictyal B1	*Botrytis cinerea*	8
83	Siphonodictyal B2	*Botrytis cinerea*	8
Benzopyran-fused-naphthene type drimane meroterpenoid			
90	Puupehenone	*Candida albicans* (MIC= 3-3.1 μg/mL) *Trichophyton mentagrophytes* (MIC= 1.6 μg/mL *Aspergillus oryzae* *Penicillium notatum* *Saccharomyces cerevisiae* *Candida albicans* *Cryptococcus neoformans* ATCC 90113 (IC_{50}= 0.38 μg/mL) *Candida albicans* ATCC 90028 (IC_{50}= 3.02 μg/mL) *Candida Krusei* ATCC 6258 (IC_{50}= 1.49 μg/mL) *Candida glabrata* ATCC 90030 (IC_{50}= 2.67 μg/mL) *Aspergillus fumigatus ATCC 90906* (IC_{50}= 5.63 μg/mL)	9, 10,11, 12, 13
92	21-chloropuupehenone	*Aspergillus oryzae* *Penicillium notatum* *Trichophyton mentagrophytes* *Saccharomyces cerevisiae* *Candida albicans* *Cryptococcus neoformans* ATCC 90113 (IC_{50}= 5.73 μg/mL)	11, 13
93	Puupehedione	*Aspergillus oryzae* *Penicillium notatum* *Trichophyton mentagrophytes* *Saccharomyces cerevisiae* *Candida albicans*	11
94	Cyanopuupehenol	*Aspergillus oryzae* *Penicillium notatum* *Trichophyton mentagrophytes* *Saccharomyces cerevisiae* *Candida albicans*	11
97	15α-methoxypuupehenol	*Candida tropicalis*	14
162	Corallidictyal A	*Hansenula anomala* *Aspergillus fumigatus* *Botrytis cinerea* *Pythium debaryanum*	8

163	Corallidictyal B	*Hansenula anomala* *Aspergillus fumigatus* *Botrytis cinerea* *Pythium debaryanum*	8
164	Corallidictyal C	*Aspergillus fumigatus*	8
165	Corallidictyal D	*Aspergillus fumigatus*	8
Indane-fused-naphthene type drimane meroterpenoid			
199	Dasyscyphin D	*Magnaporthe grisea*	15
200	Dasyscyphin E	*Magnaporthe grisea*	15

Table S2. Drimane meroterpenoids with antibacterial activity.

Antibacterial activity			
Numb.	Compds	Species and bioactivity	Ref.
1	Siccanin	*Bacillus subtilis* (MIC=50 μg/mL) *Staphylococcus aureus 209P* (MIC=50 μg/mL) *Sarcina lutea* (MIC=50 μg/mL) *Escherichia coli* (MIC=12.5 μg/mL) *Pseudomonas aeruginosa* (MIC=50 μg/mL) *Mycobacterium tuberculosis 607* (MIC=25 μg/mL)	1
Substituted drimane type meroterpenoids			
16	Macrophorin A	*Staphylococcus aureus* (MIC=25 ppm) *Trichophyton spp.*(6.2-25 ppm)	16
25	2', 3'-epoxy-13-hydroxy-4'-oxomacrophorin A	*Staphylococcus aureus* (ATCC 259203) *Bacillus subtilis* (ATCC 6051)	4
32	Myrothecol A	*Staphylococcus aureus* (MIC= 12.5 μg/mL) *Bacillus cereus* (MIC= 25.0 μg/mL)	17
33	Myrothecol B	*Staphylococcus aureus* (MIC= 50.0 μg/mL) *Bacillus cereus* (MIC= 100.0 μg/mL)	17
34	Myrothecol C	*Staphylococcus aureus* (MIC= 50.0 μg/mL) *Bacillus cereus* (MIC= 100.0 μg/mL)	17
35	Myrothecol D	*Staphylococcus aureus* (MIC= 100.0 μg/mL) *Bacillus cereus* (MIC> 100.0 μg/mL)	17
36	Myrothecol E	*Staphylococcus aureus* (MIC= 50.0 μg/mL) *Bacillus cereus* (MIC> 100.0 μg/mL)	17
45	Siphonodictyal C	*Stuphylococcus aureus* *Bacillus subtilis* Marine bacterium *Vibrio anguillarum*	18
47	Peyssonoic acid A	*Pseudoalteromonas bacteriolytica (P. bacteriolytica)* (IC_{50} = 799 μM)	6
63	Siphonodictyal A	*Stuphylococcus aureus* *Bacillus subtilis*	19

68	Dysidphenol C	*Escherichia coli* (25922) (MIC=50 μg/mL) *Bacillus subtilis* (6633) (MIC=100 μg/mL) *Staphylococcus aureus* (25923) (MIC=100 μg/mL)	20
70	Xishaeleganin B	*Staphylococcus aureus* (*S. aureus* USA300 LAC) (MIC=1.5 μg/mL) *Streptococcus pyogenes* (*S. pyogenes* ATCC 12344) (MIC=1.5 μg/mL) *Enterococcus faecium* (*E. faecium Efm*-HS0649) (MIC=3.0 μg/mL)	21
72	Siphonodictyol H	*Stuphylococcus aureus* *Bacillus subtilis*	18
81	Siphonodictyal B	*Staphylococcus aureus* *Bacillus subtilis* *Escherichia coli* tolC	8, 19
82	Siphonodictyal B1	*Staphylococcus aureus*	8
83	Siphonodictyal B2	*Staphylococcus aureus*	8
Benzopyran-fused-naphthene type drimane meroterpenoids			
90	Puupehenone	*Staphylococcus aureu* *Streptococcus pyrogenes* *Staphylococcus aureus* *Bacillus cereus* *Staphylococcus aureus* *M. tuberculosis* (H37Rv) (MIC=12.5 μg/mL, IC_{50}= 2.0 μg/mL)	10, 12, 22, 23
91	Cyanopuupehenone	*penicillium notatum* *trichophyton mentagrophytes* *saccharomyces cerevisiae*	24
97	15α-methoxypuupehenol	*Staphylococcus aureus*	14
102	Puupehenol	*Staphylococcus aureus* *Bacillus cereus*	22
106	Hongoquercin A	*Staphylococcus aureus* (MIC= 4-8 μg/mL) *Staphylococcus haemolyticus* GC 4546 (MIC= 8 μg/mL) *Staphylococcus* Coagulase Negative GC (MIC= 4-16 μg/mL) *Enterococcus faecalis* (MIC= 8 μg/mL) *Enterococcus faecalis* (MIC= 4-8 μg/mL *Bacillus cereus* GC 4561 (MIC= 2 μg/mL) *Sarcina lutea* GC 4562 (MIC= 4 μg/mL)	25
Benzofuran-spiro-naphthene type drimane meroterpenoids			
158	Stachybotrydial	*Staphylococcus aureus*	26
162	Corallidictyal A	*Escherichia coli* tolC *Staphylococcus aureus* *Candida albicans*	8

163	Corallidictyal B	*Escherichia coli* tolC *Staphylococcus aureus* *Candida albicans*	8
164	Corallidictyal C	*Escherichia coli* tolC *Staphylococcus aureus*	8
165	Corallidictyal D	*Escherichia coli* tolC *Staphylococcus aureus*	8
168	Dysidphenol A	*Escherichia coli* (25922) (MIC=100 μg/mL) *Bacillus subtilis* (6633) (MIC=100 μg/mL) *Staphylococcus aureus* (25923) (MIC=100 μg/mL)	20
175	Stachybotrolide (Stachybotrylactone)	*Staphylococcus aureus* DHFR (IC_{50}= 41.5 μM) *Staphylococcus aureus* (IC_{50}= 32 μg/mL) Methicillin-resistant *Staphylococcus aureus CCARM3167* (IC_{50}= 32 μg/mL)	26
Indane-fused-naphthane-type drimane meroterpenoids			
198	Dasyscyphin C	MRSA (MIC=16 μg/mL) *Pseudomonas aeruginosa* (MIC=63 μg/mL) *Bacillus anthracis* (MIC=2 μg/mL)	27
201	Dasyscyphins F	MRSA (MIC=63 μg/mL) *Pseudomonas aeruginosa* (MIC=125 μg/mL) *Bacillus anthracis* (MIC=31μg/mL)	27
Others			
224	Cyclosiphonodictyol A	*Staphylococcus aureus* (MRSA) (IC_{50}= 117 μM) *Staphylococcus aureus* (MSSA) (IC_{50}= 117 μM) *Micrococcus luteus* (IC_{50}= 58 μM)	28

Table S3. Drimane meroterpenoids with antiviral activity.

Antiviral activity			
Numb.	Compds.	Species and bioactivity	Ref.
Substituted drimane type meroterpenoids			
11	Peyssonol A	HIV (IC_{50}= 1 μM) HIV-1 NL-Rluc Virus (EC_{50} = 1×10^{-6} M)	29, 30
15	Penicilliumin A	coxsackievirus B3 (CVB3) (TC_{50}=40.72 μg/mL) herpes simplex virus type I (HSV-1) (TC_{50}=133.52 μg/mL) influenza A virus subtype H5N3 (A/H5N3) (TC_{50}=43.00 μg/mL)	31
Benzopyran-fused-naphthene type drimane meroterpenoids			
90	Puupehenone	Mv l Lu/HSV II CV-l/HSV-1 BHK/VSV	11
91	Cyanopuupehenone	CV-l/HSV-1 BHK/VSV	11
92	21-	Mv l Lu/HSV II	11

	chloropuupehenone	CV-l/HSV-1 BHK/VSV	
93	Puupehedione	Mv l Lu/HSV II CV-l/HSV-1 BHK/VSV	11
94	Cyanopuupehenol	Mv l Lu/HSV II CV-l/HSV-1 BHK/VSV Herpes simplex II	11, 24
125	Chrodrimanin A	influenza A virus (H1N1) (IC_{50}= 21 μM)	32
129	Chrodrimanin E	influenza A virus (H1N1) (IC_{50}= 55 μM)	32
130	Chrodrimanin F	influenza A virus (H1N1) (IC_{50}= 57 μM)	32
135	Chrodrimanin K	influenza A virus (H1N1) (IC_{50}= 74 μM)	33
138	Chrodrimanin N	influenza A virus (H1N1) (IC_{50}= 58 μM)	33
139	3-hydroxypentacecilide A	influenza A virus (H1N1) (IC_{50}= 34 μM)	33
140	Chrodrimanin O	protein tyrosine phosphatase 1B (PTP1B) (IC_{50}= 71.6 μM)	34
143	Chrodrimanin R	protein tyrosine phosphatase 1B (PTP1B) (IC_{50}= 62.5 μM)	34
144	Chrodrimanin S	protein tyrosine phosphatase 1B (PTP1B) (IC_{50}= 63.1 μM)	34
Benzofuran-spiro-naphthene type drimane meroterpenoids			
166	F1839-I	HIV (IC_{50}=15.6 μM)	35
180	Stachybotrysin A	HIV (IC_{50}=19.6 μM) IAV (IC_{50}=12.4 μM)	35
181	Stachybotrysin B	HIV (IC_{50}=19.2 μM)	35
184	Stachybotrysin E	HIV (IC_{50}=20.5 μM) IAV (IC_{50}=45.6 μM)	35
170	Stachybotrylactone acetate	IAV (IC_{50}=18.9 μM)	35
185	Stachybotrysin F	HIV (IC_{50}=35.7 μM) IAV (IC_{50}=14.6 μM)	35
186	Stachybotrysin G	HIV (IC_{50}=18.1 μM) IAV (IC_{50}=23.4 μM)	35

Table S4. Drimane meroterpenoids with insecticidal activity.

4. Insecticidal activity			
Numb.	Compds	Species and bioactivity	Ref.
1	Siccanin	anti-trypanosomatid	36
Benzopyran-fused-naphthene type drimane meroterpenoids			
90	Puupehenone	*Trichomonas vaginalis* (MIC= 3.1μg/mL) Antimalarial activity against Chloroquine-Susceptible F32 (IC_{50}=0.6 μg/mL) and Chloroquine-Resistant FcB1	10, 14

		(IC_{50}=2.1 μg/mL) and PFB (IC_{50}=1.5 μg/mL) against *P. falciparum* Strains	
96	15-oxopuupehenol	*Plasmodium falciparum* (D6 clone) (IC_{50}=2.0 μg/mL) *Plasmodium falciparum* (W2 clone) (IC_{50}=1.3 μg/mL)	37
97	15α-methoxypuupehenol	Antimalarial activity against Chloroquine-Susceptible F32 (IC_{50}=0.4 μg/mL) and Chloroquine-Resistant FcB1 (IC_{50}=1.4μg/mL) and PFB (IC_{50}=1.2 μg/mL) against *Plasmodium falciparum* Strains	14
120	Phomoarcherin B	*Plasmodium falciparum* (IC_{50}=0.79 μg/mL)	38
124	Pentacecilide D	insecticidal activity against silkworms (LD50 = 20 μg/g)	39
126	Chrodrimanin B	third instar larva of the silkworm (LD_{50}=10 μg/g) chrodrimanin B acts as a potent, non-open-channel-blocking antagonist on B. mori RDL with an IC_{50} of 1.13 nm	40, 41
128	Chrodrimanin D	third instar larva of the silkworm (LD_{50}=20 μg/g)	39
129	Chrodrimanin E	third instar larva of the silkworm (LD_{50}=10 μg/g)	39
130	Chrodrimanin F	third instar larva of the silkworm (LD_{50}=50 μg/g)	39
Indane-fused-naphthene type drimane meroterpenoids			
191	Pelorol	brine shrimp (LC_{50}= 5-10 μg/mL)	42

Table S5. Drimane meroterpenoids with anticancer activity and cytostatic activity.

5. Anticancer activity and Cytostatic activity			
Numb.	Compds	Species and bioactivity	Ref.
Substituted drimane type meroterpenoids			
2	Tauranin	NCI-H460 (IC_{50}= 4.3 μM) MCF-7(IC_{50}= 1.5 μM) SF-268(IC_{50}= 1.8 μM) PC-3M (IC_{50}=3.5 μM) MIA Pa Ca-2 (IC_{50}= 2.8 μM)	43
6	Zonarol	L-929 (murine fibroblasts) K-562 (human leukaemia) HeLa (human cervix carcinoma)	44
9	Zonarone	L-929 (murine fibroblasts) K-562 (human leukaemia) HeLa (human cervix carcinoma)	44
10	Hyatellaquinone	KB (IC_{50}= 14 μM) HM02 (GI_{50}= 5.3 μg/mL) HepG2 (GI_{50}= 6.0 μg/mL) MCF (GI_{50}= 2.4 μg/mL) breast cancer (IC_{50}= 4.45 μg/mL) small cell lung cancer (NCI-H187) cell (IC_{50}= 10.90 μg/mL) L-929 (GI_{50}= 20.9 μM)	44, 46, 47, 48

		K-562 (GI_{50}= 8.4 μM) HeLa (CC_{50}= 72.1 μM)	
12	F-12509A	rat liver SPH kinase (IC_{50}= 18 μM.)	49
13	Purpurogemutantin	K562 (IC_{50}= 13.4 μM.) HL-60(IC_{50}=18.1 μM.) HeLa (IC_{50}= 18.9 μM.) BGC-823 (IC_{50}=33.0 μM.) MCF-7 (IC_{50}= 29.3 μM.) U937 (IC_{50}= 32.2 μM.)	45, 50
14	Purpurogemutantidin	K562 (IC_{50}= 0.93 μM.) HL-60(IC_{50}=2.48 μM.) HeLa (IC_{50}= 16.6 μM.) BGC-823 (IC_{50}=31.0 μM.) MCF-7 (IC_{50}= 26.3 μM.)	50
15	Penicilliumin A	A375 (GI_{50}= 22.88μg/mL) B16(GI_{50}=27.37 μg/mL) Hela (GI_{50}= 44.05 μg/mL)	31
16	Macrophorin A	L-5178Y (MIC=0.3 ppm) K562 (IC_{50}=2.6 μM) MCF-7 (IC_{50}=5.28 μM) Hela (IC_{50}=3.86 μM) DU145 (IC_{50}=3.29 μM) U937 (IC_{50}=1.4 μM) H1975 (IC_{50}=3.18 μM) SGC-7901 (IC_{50}=5.22 μM) A549 (IC_{50}=1.57 μM) MOLT-4 (IC_{50}=1.17 μM) HL60(IC_{50}=1.68 μM)	16, 45
24	4′-oxomacrophorin A	K562 (IC_{50}= 0.55 μM) MCF-7(IC_{50}= 0.68 μM) DU145(IC_{50}= 35.4 μM) U937(IC_{50}= 6.74 μM) H1975(IC_{50}= 0.48 μM) SGC-7901 (IC_{50}= 1.18 μM) A549 (IC_{50}=0.33 μM) MOLT-4 (IC_{50}= 0.19 μM) HL60 (IC_{50}= 0.29 μM)	45
26	Neomacrophorin I	human colon adenocarcinoma (COLO 201) cell proliferation ((IC_{50}=46 μg/mL) HL60 (IC_{50}=2.6 μM) Chymotrypshi-like (IC_{50}= 5.7 μM) Trypsin-like (IC_{50}=27.9 μM) Caspase-like (IC_{50}=5.2 μM)	5, 51
27	Neomacropho	HL60 (IC_{50}=21.6 μM)	51

	rin II	Chymotrypshi-like (IC_{50}=93.6 μM) Caspase-like (IC_{50}=87.3 μM)	
28	Neomacropho rin III	HL60 (IC_{50}=15.0 μM) Chymotrypshi-like (IC_{50}=31.9 μM) Caspase-like (IC_{50}=30.1 μM)	51
29	Neomacropho rin IV	HL60 (IC_{50}=1.3 μM) Chymotrypshi-like (IC_{50}=5.3 μM) Trypsin-like (IC_{50}=22.5 μM) Caspase-like (IC_{50}=3.9 μM)	51
30	Neomacropho rin V	HL60 (IC_{50}=25.3 μM)	51
31	Neomacropho rin VI	HL60 (IC_{50}=0.3 μM) Chymotrypshi-like (IC_{50}=26.3 μM) Trypsin-like (IC_{50}=76.1 μM) Caspase-like (IC_{50}=17.8 μM)	51
32	Myrothecol A	A549 (IC_{50}= 8.0 μM) HeLa (IC_{50}= 7.9 μM) HepG2 (IC_{50}= 15.2 μM)	17
33	Myrothecol B	A549 (IC_{50}= 39.8 μM) HeLa (IC_{50}= 29.3 μM) HepG2 (IC_{50}= 48.5 μM)	17
34	Myrothecol C	A549 (IC_{50}= 41.5 μM) HeLa (IC_{50}= 35.9 μM) HepG2 (IC_{50}= 34.2 μM)	17
35	Myrothecol D	A549 (IC_{50}= 29.4 μM) HeLa (IC_{50}= 19.2 μM) HepG2 (IC_{50}= 37.8 μM)	17
36	Myrothecol E	A549 (IC_{50}= 18.0 μM) HeLa (IC_{50}= 19.6 μM) HepG2 (IC_{50}= 27.8 μM)	17
38	Myrothecol G	A549 (IC_{50}= 46.7 μM) HeLa (IC_{50}= 15.9 μM) HepG2 (IC_{50}= 31.9 μM)	52
39	Myrothecol H	A549 (IC_{50}= 40.2 μM) HeLa (IC_{50}= 28.7 μM) HepG2 (IC_{50}= 25.7 μM)	52
41	Isozonarol	BAEC (IC_{50}= 26μM) A549 (IC_{50}= 15μM SKBR3 (IC_{50}= 11μM) L-929 (murine fibroblasts) K-562 (human leukaemia) HeLa (human cervix carcinoma)	44, 53
42	Isozonarone	L-929 (murine fibroblasts) K-562 (human leukaemia)	44

		HeLa (human cervix carcinoma)	
43	20-*O*-acetyl-21-hydroxy-ent-isozonarol	HL60 (IC_{50} = 0.37μM) MDA-MB-231 (LC_{50}=11.8 μM) A-549 (LC_{50}=11.8 μM) HT-29 (LC_{50}=14.0 μM)	55, 56
44	21-Hydroxy-*ent*-isozonarone	HL60 (IC_{50} = 0.37μM)	55
45	Siphonodictyal C	CDK4/cyclin D1 complexation (IC_{50}= 9 μg/mL)	54
47	Peyssonoic acid A	human ovarian cancer cell line (IC_{50}= 34.5 μM)	6
48	Isohyatellaquinone	breast cancer (IC_{50}= 6.69 μg/mL) small cell lung cancer (NCI-H187) cell (IC_{50}= 11.52 μg/mL)	47
49	Epoxyphomalin A	12 of a panel of 36 human tumor cell lines (IC_{50}= 0.017-11.420 μg/mL) exert their cytotoxic effect through potent inhibition of the 20S proteasome	57, 58
50	Epoxyphomalin B	12 of a panel of 36 human tumor cell lines (IC_{50}= 0.017-11.420 μg/mL) exert their cytotoxic effect through potent inhibition of the 20S proteasome	57, 58
52	Epoxyphomalin D	prostate PC3M (IC_{50}= 0.72 μM) bladder BXF 1218 L (IC_{50}= 1.43 μM) cancer cell lines	58
54	Craterellin A	Mouse HSD1 (IC_{50}= 36.3 μg/mL) Human HSD1(IC_{50}= 9.1 μg/mL) Human HSD2(IC_{50}= 1.5 μg/mL)	59
55	Craterellin B	Mouse HSD1 (IC_{50}=54.8 μg/mL) Human HSD1(IC_{50}=3.5 μg/mL) Human HSD2(IC_{50}>100μg/mL)	59
56	Craterellin C	Mouse HSD1 (IC_{50}=93.3 μg/mL) Human HSD1(IC_{50}= 14.8 μg/mL) Human HSD2(IC_{50}= 25.4 μg/mL)	59
61	Yahazunol	L-929, K-562, HeLa HM02 (GI_{50}= 4.2 μg/mL) HepG2 (GI_{50}= 7.1 μg/mL) MCF (GI_{50}= 6.0 μg/mL)	44
62	*Ent*-yahazunol	MDA-MB-231 (LC_{50}=27.7 μM) A-549 (LC_{50}=17.4 μM) HT-29 (LC_{50}=14.0 μM)	56
64	Albaconol	HepG2 (EC_{50}= 10.44 μM) MCF-7 (EC_{50}= 10.08 μM)	7
65	Neoalbaconol	downstream phosphoinositide-3 kinase (PI3-K)/Akt-	60, 61

		hexokinase 2 (HK2) pathway, and further resulted in energy depletion HepG2 (EC_{50}= 10.44 μM) MCF-7 (EC_{50}= 10.08 μM)	
69	Hippomeroterpen B	Hep-G2 MCF-7 SK-LI-1 SK-Mel-2	62
75	Spongiaquinone	L-929 (GI_{50}= 27.1 μM) K-562 (GI_{50}= 13.4 μM) HeLa (CC_{50}= 75.1 μM) L-929, K-562, HeLa HM02 (GI_{50}= 3.1 μg/mL) HepG2 (GI_{50}= 3.6 μg/mL) MCF (GI_{50}= 2.6 μg/mL)	44, 48
76	Wiedendiol B	L-929 (GI_{50}= 63.1 μM) K-562 (GI_{50}= 35.8 μM) HeLa (CC_{50}= 38.1 μM) cholesteryl ester transfer pprotein (CETP) (IC_{50}= 5 μM)	48, 64
81	Siphonodictyal B	PI3Kα (IC_{50}= 2.6 μM) *L929 mouse fibroblasts*	8, 63
82	Siphonodictyal B1	*L929 mouse fibroblasts*	8
83	Siphonodictyal B2	*L929 mouse fibroblasts*	8
Benzopyran-fused-naphthene type drimane meroterpenoids			
86	***Ent***-chromazonarol	P-338, A-549, HT-29 and MEL-28 (IC_{50}= 15.91 μM) BAEC (IC_{50}= 45 μM) A549 (IC_{50}=14 μM) H116 (IC_{50}= 14 μM) PSN1 (IC_{50}= 15 μM) SKBR3 (IC_{50}= 13 μM)	53, 65
90	Puupehenone	P388 mouse leukemia (IC_{50}= 1 μg/mL) A549 (human lung cancer cell line) (IC_{50}= 0.1-1 μg/mL) HCT-8 (human colon cancer cell line) (IC_{50}= 1-10 μg/mL) MCF-7 (human mammary cancer cell line (IC_{50}=0.1-1 μg/mL) A549(IC_{50}=0.4 μg/mL) HT-29(IC_{50}=1.2 μg/mL) P338(IC_{50}=1.3μg/mL) BAEC (IC_{50}= 10 μM) A549 (IC_{50}=7 μM)	9, 53, 64,66, 67, 68, 69

		H116 (IC_{50}= 8 μM) PSN1 (IC_{50}= 5 μM) SKBR3 (IC_{50}= 15 μM) KB (MIC=5 μg/mL) LOVO (MIC=1 μg/mL) P-388 (IC_{50}=0.25 μg/mL) A-549 (IC_{50}=0.5 μg/mL) HT-29 (IC_{50}=0.5 μg/mL) CV-1 (IC_{50}=0.5 μg/mL) DHFR (IC_{50}=5 μg/mL) TS (IC_{50}=8 μg/mL) PROT (IC_{50}=0.4 μg/mL) DNA (IC_{50}=0.3 μg/mL) RNA (IC_{50}=0.4 μg/mL) human 5-, 12-, and 15-lipoxygenases (IC_{50} = 22, 6 and 0.68 μM) A-549 HT-29 KB cells (IC_{50}=0.5μg/mL) cholesteryl ester transfer pprotein (CETP) (IC_{50}= 6 μM)	
91	Cyanopuupehenone	BAEC (IC_{50}= 11 μM) P-388 (IC_{50}=2 μg/mL) A-549(IC_{50}=2 μg/mL) HT-29 (IC_{50}=2 μg/mL) CV-1 (IC_{50}=2 μg/mL)	53,67
92	21-chloropuupehenone	KB (MIC=5 μg/mL) LOVO (MIC=1 μg/mL) P-388 (IC_{50}=0.2 μg/mL) A-549 (IC_{50}=0.5 μg/mL) HT-29 (IC_{50}=0.5 μg/mL) CV-1 (IC_{50}=0.5 μg/mL) GR (IC_{50}=6 μg/mL) DHFR (IC_{50}=5 μg/mL) TS (IC_{50}=3 μg/mL) PROT (IC_{50}=0.3 μg/mL) DNA (IC_{50}=1 μg/mL) RNA (IC_{50}>1 μg/mL) Topo II (IC_{50}=1 μg/mL) cholesteryl ester transfer pprotein (CETP) (IC_{50}= 0.3 μM)	64, 67
93	Puupehedione	*P-338, A-549 and HT-29*	70
94	15-cyanopuupehenol	*P-338, A-549 and HT-29* KB (MIC=5 μg/mL) LOVO (MIC=2 μg/mL) P-388 (IC_{50}=2 μg/mL)	24, 67, 70

		A-549 (IC_{50}=2 μg/mL) HT-29 (IC_{50}=2 μg/mL) CV-1(IC_{50}=2 μg/mL)	
97	15α-methoxypuupehenol	KB cells (IC_{50}= 6 μg/mL) Human Glioblastoma and Breast Cancer Models: the mode of action of 15a-methoxypuupehenol was that Oral gavage delivery of 15a-MP inhibited the growth of U251MG subcutaneous tumor xenografts in mice, associated with apoptosis in the treated tumor tissues.	14, 73
99	20-methoxy-9, 15-ene-puupehenol	Scavenger Receptor-Class B Type 1 HepG2 (SR-B1 HepG2) stable cell line (IC_{50}= 1.78 μM)	74
103	19-methoxy-9,15-ene-puupehenol	Scavenger Receptor-Class B Type 1 HepG2 (SR-B1 HepG2) stable cell line (IC_{50}= 3.05 μM)	74
104	BE-40644	*E. coli* TRX system (IC_{50}=0.12 μg/mL) human TRX system (IC_{50}=0.08 μg/mL) yeast GSSG reductase (IC_{50}=22 μg/mL) inhibit the human thioredoxin system as the well as the growth of several cancer cell lines.	71 72
110	Phomoarcherin C	KKU-100 (IC_{50}= 8.9 μg/mL) KKU-M139 (IC_{50}= 8.9 μg/mL) KKU-M156 (IC_{50}= 18.0 μg/mL) KKU-M213 (IC_{50}= 15.4 μg/mL) KKU-M214 (IC_{50}= 18.8 μg/mL)	38
112	Austalide L	osteoclast differentiation inhibitory activity (IC_{50}= 2.0 μg/mL)	75
113	Austalide V	osteoclast differentiation inhibitory activity (IC_{50}= 1.9 μg/mL)	75
114	Austalide W	osteoclast differentiation inhibitory activity (IC_{50}= 2.5 μg/mL)	75
115	17S-dihydroaustalide K	osteoclast differentiation inhibitory activity (IC_{50}= 2.8 μg/mL)	75
116	Kampanol A	Ras rHFPTase (IC_{50}= 13 μM) KKU-M213 (IC_{50}= 19.6 μg/mL)	38, 76
117	Kampanol B	Ras rHFPTase (IC_{50}= 7 μM)	76
119	Phomoarcherin A	KKU-M213 (IC_{50}= 16.6 μg/mL) KB (IC_{50}= 42.1 μg/mL)	38
120	Phomoarcherin B	KKU-100 (IC_{50}= 8.0 μg/mL) KKU-M139 (IC_{50}= 0.1 μg/mL) KKU-M156 (IC_{50}= 2.0 μg/mL) KKU-M214 (IC_{50}= 5.0 μg/mL)	38

		KB (IC_{50}= 9.4 μg/mL)	
121	Pentacecilide A	inhibit the synthesis of cholesteryl ester in mouse macrophage (IC_{50}= 3.65 μM) macrophages, and ACAT1- and ACAT2-CHO cells (IC_{50}=3.65, 1.09 and 0.69 μM)	77, 78
122	Pentacecilide B	inhibit the synthesis of cholesteryl ester in mouse macrophage (IC_{50}= 4.76 μM) macrophages, and ACAT1- and ACAT2-CHO cells (IC_{50}=4.76, 10.8 and 3.97 μM)	77, 78
125	Chrodrimanin A	tyrosine phosphatase 1B (PTP1B) (IC_{50}= 8.5 μM)	79
130	Chrodrimanin F	HL-60 cell (IC_{50}= 8.7 μg/mL)	80
131	Chrodrimanin G	protein tyrosine phosphatase 1B (PTP1B) (IC_{50}= 39.6 μM)	34
132	Chrodrimanin H	protein tyrosine phosphatase 1B (PTP1B) (IC_{50}= 14.9 μM)	79
145	3-acetyl-chrodrimanin F	HL-60 cell (IC_{50}= 8.1 μg/mL)	80
147	Verruculide A	protein tyrosine phosphatase 1B (PTP1B) (IC_{50}= 8.4 μM)	79
Benzofuran-spiro-naphthene type drimane meroterpenoids			
153	Stachartin A (stachybotrysin)	osteoclast differentiation in bone marrow macrophage cells via suppressing the RANKL-induced activation of p-ERK, p-JNK, pp38, c-Fos, and NFATc1	89
154	K-76	pancreatic cholesterol esterase (IC_{50}= 0.2 mM)	81
155	L-671, 776 (factor B)	*Myo*-inositol mono-phosphatase (IC_{50}= 0.4 mM) Myo-inositol 1,4,5-triphosphatase 3-kinase (IC_{50}= 3 mM) IMPase enzyme inhibitory activity (IC_{50}=460 μM)	82, 83
156	Factor A	IMPase enzyme inhibitory activity (IC_{50}=70 μM)	83
157	Factor C	IMPase enzyme inhibitory activity (IC_{50}=200 μM)	83
158	Stachybotrydial(Mer-NF5003 F)	Human Protein *Kinase CK2* (IC_{50}= 4.43 μM) pancreatic cholesterol esterase (IC_{50}= 0.06 mM) AMV-protease (IC_{50}= 7.8 μM)	81, 84, 85
159	Mer-NF5003 B	AMV-protease (IC_{50}= 16.5 μM)	85
160	Mer-NF5003 E	AMV-protease (IC_{50}= 12.8 μM) K562	85, 86
162	Corallidictyal A	protein kinase C cultured vero (African green monket kidney) cells *L929 mouse fibroblasts*	8, 87
163	Corallidictyal B	protein kinase C cultured vero (African green monket kidney) cell	87

		L929 mouse fibroblasts	
164	Corallidictyal C	*L929 mouse fibroblasts*	8
165	Corallidictyal D	*L929 mouse fibroblasts*	8
166	F1839-I	pancreatic cholesterol esterase (IC_{50}= 0.27 mM) HepG2 (IC_{50}= 18.4 μM) NCI-H460 (IC_{50}=15.8 μM) BGC823(IC_{50}= 21.9 μM)	35, 81
167	Sch 65676	CMV maturational protease (IC_{50}= 9.8 μg/ml)	88
180	Stachybotrysin A	HepG2 (IC_{50}= 24.7 μM)	35
181	Stachybotrysin B	K562, Hela and HL60 Human Protein *Kinase CK2* (IC_{50}= 13.42 μM)	84, 86
182	Stachybotrysin C	K562, Hela and HL60	86
186	Stachybotrysin G	HepG2 (IC_{50}= 24.6 μM)	35
187	Stachybotrysin H	K562, Hela and HL60	86
188	Stachybotrydial acetate	Human Protein *Kinase CK2* (IC_{50}= 0.69 μM)	84
189	Acetoxystachybotrydial acetate	Human Protein *Kinase CK2* (IC_{50}= 1.86 μM)	84
Indane-fused-naphthene type drimane meroterpenoids			
191	Pelorol	PI3Kβ (IC_{50}= 38.17μM) The compound pelorol exert cytotoxicity activity against 501Mel melanoma cells promoting apoptotic signaling and inducing changes in miRNA expression and their downstream effectors.	90, 91
195	19-*O*-methylpelorol	lung cancer PC-9 cell line (IC_{50}=9.2 μM) .	95
197	Dasyscyphin B	several human cell line	92
198	Dasyscyphin C	several human cell line MDA-MB-435 (IC_{50}= 14.1 μM) MDA-MB-231(IC_{50}= 12.2 μM) OVCAR3 (IC_{50}= 10.4 μM)	27 , 92
201	Dasyscyphin F	MDA-MB-435 (IC_{50}= 4.1 μM) MDA-MB-231(IC_{50}= 8.2 μM) OVCAR3 (IC_{50}= 16.2 μM)	27
202	Dasyscyphin	MDA-MB-435 (IC_{50}= 19.7 μM)	27

	G	MDA-MB-231(IC_{50}> 25 μM) OVCAR3 (IC_{50}>25 μM)	
204	Walsucochin A	H_2O2-induced PC12 cell damage	93
205	Walsucochin B	H_2O_2-induced PC12 cell damage	93
207	Walsucochinoid D	mouse and human 11b-HSD1 inhibitors (IC_{50}= 13.4 μM)	94
208	Walsucochinoid E	mouse and human 11b-HSD1 inhibitors (IC_{50}= 8.25 μM)	94
Bnaphthane-fused-naphthene type drimane meroterpenoids			
218	Cyclozonarone	L-929, K-562, HeLa HM02 (GI_{50}= 5.7 μg/mL) HepG2 (GI_{50}= 9.6 μg/mL) MCF (GI_{50}>10 μg/mL)	44
221	Neopetrosiquinone A	proliferation of the DLD-1 human colorectal adenocarcinoma cell line (IC_{50}= 3.7 μM) PANC-1 human pancreatic carcinoma cell line(IC_{50}= 6.1 μM) proliferation of the AsPC-1 human pancreatic carcinoma cell (IC_{50}= 6.1 μM) line	96
222	Neopetrosiquinone B	A-549 (IC_{50}= 8.3 μM) MCF-7(IC_{50}= 7.7 μM) T-48 cell (IC_{50}= 11.5 μM) proliferation of the DLD-1 human colorectal adenocarcinoma cell line (IC_{50}= 9.8 μM) PANC-1 human pancreatic carcinoma cell line(IC_{50}= 13.8 μM)	96, 97
Other drimane type meroterpenoid			
223	Bis(sulfato)-cyclosiphonodictyol	inhibits the binding of [3H]-LTB4, to intact humanneutrophils (IC_{50}= 44 μM)	98

Table S6. Drimane meroterpenoids with antioxidant activity.

3.6 Antioxidant activity			
Numb.	Compds	Species and bioactivity	Ref.
Substituted drimane type meroterpenoids			
41	Isozonarol	DPPH radical scavenging activity (EC_{50}= 71 μM)	99
42	Isozonarone	DPPH radical scavenging activity (EC_{50}= 145 μM)	99
67	Siphonodictyal A sulfate	DPPH radical-scavenging activity	100

71	13-[[2-(hexyloxy)-2,5,5,8a-tetramethyldecahydro-1-naphthalenyl](methoxy)methyl]benzenol	DPPH scavenging (IC_{50}= 1.51 mM) ABTS scavenging (IC_{50}= 1.88 mM)	101
82	Siphonodictyal B1	DPPH	8
83	Siphonodictyal B2	DPPH	8
84	Siphonodictyal B3	DPPH radical-scavenging activity	100
Benzopyran-fused-naphthene type drimane meroterpenoids			
85	Chromazonarol	DPPH radical scavenging activity (EC_{50}= 71 μM)	99
90	Puupehenone	2,2-diphenyl-1-picrylhydrazyl radical (DPPH) solution-based chemical assay and a 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) 5-HLO (IC_{50}= 0.76 μM) 15-SLLO (IC_{50}= 2.4 μM) 12-HLO (IC_{50}= 8.3 μM) 12-LOX (IC_{50} = 8.3 μM) 15-LOX (IC_{50} = 0.76 μM) NOX(IC_{50} = 1.3 μM) inhibitor of the integrated electron transfer chain 08(NADH oxidase activity 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity (IC_{50}=32 μM)	12, 22, 102, 103,104, 105
92	21-chloropuupehenone	15-HLO (IC_{50}= 0.83 μM) 15-SLLO (IC_{50}=2.4 μM) 12-HLO (IC_{50}=0.71 μM) 12-LOX (IC_{50} = 0.7 μM)	103, 104
101	Puupehanol	average Ferric Reducing Antioxidant Power (FRAP) of 2500 μM.	22
102	Puupehenol	Antioxidant	22
Indane-fused-naphthene type drimane meroterpenoids			
203	Akadisulfate A	DPPH radical-scavenging activity	100

Table S7. Drimane meroterpenoids with algicidal activity.

3.7 Algicidal activity			
Numb.	Compds	Species and bioactivity	Ref.
Substituted drimane type meroterpenoids			

6	Zonarol	*Heterosigma akashiwo*, *Chattonella antiqua*, *Heterocapsa circularisquama*	106
8	Zonaroic acid	*Heterosigma akashiwo*, *Chattonella antiqua*, *Heterocapsa circularisquama*	106
41	Isozonarol	*Heterosigma akashiwo*, *Chattonella marina*, *Chattonella antiqua*, *Heterocapsa circularisquama*	106
61	Yahazunol	*Heterosigma akashiwo*, *Chattonella marina* *Chattonella antiqua*, *Heterocapsa circularisquama*	106
74	Zonarenone	*Heterosigma akashiwo*, *Chattonella marina*, *Chattonella antiqua*, *Heterocapsa circularisquama*	106
Benzopyran-fused-naphthene type drimane meroterpenoids			
85	Chromazonarol	*Heterosigma akashiwo,* *Chattonella antiqua,* *Heterocapsa circularisquama*	106
148	Isochromazonarol	*Heterosigma akashiwo,* *Chattonella antiqua,* *Heterocapsa circularisquama*	106

Table S8. Drimane meroterpenoids with anti-inflammatory activity.

3.8 Anti-inflammatory activity			
Numb.	Compds	Species and bioactivity	Ref.
Substituted drimane type meroterpenoids			
6	Zonarol	ROS production in SOZ-stimulated granulocytes.	48
10	Hyatellaquinone	ROS production in SOZ-stimulated granulocytes.	48
41	Isozonarol	*Heterosigma akashiwo* *Chattonella marina* *Chattonella antiqua* *Heterocapsa circularisquama*	106
42	Isozonarone	3a-Hydroxysteroid dehydrogenase (3a-HSD)	48
43	20-*O*-Acetyl-21-hydroxy-ent-isozonarol	inhibited superoxide production by human neutrophils (IC_{50}= 3.0 μM)	55
44	21-Hydroxy-ent-isozonarone	inhibited superoxide production by human neutrophils (IC_{50}= 11.0 μM)	55

71	13-[[2-(hexyloxy)-2,5,5,8a-tetramethyldecahydro-1-naphthalenyl](methoxy)methyl]benzenol	COX-1 (IC_{50}= 1.72 mM) COX-2 (IC_{50}= 1.56 mM) 5-LOX (IC_{50}= 1.90 mM)	101
73	Wiedendiol A	ROS production in SOZ-stimulated granulocytes	48
75	Spongiaquinone	ROS production in SOZ-stimulated granulocytes	48
Benzopyran-fused-naphthene type drimane meroterpenoids			
88	Cyclospongiaquinone-1	cyclospongiaquinone-1 showed anti-inflammatory activity	107
Benzofuran-spiro-naphthene type drimane meroterpenoids			
175	Stachybotrolide (stachybotrylactone)	inhibiting the production of nitric oxide (NO) in RAW264.7 cells (IC_{50}= 17.9 μM)	108
182	Stachybotrysin C	inhibiting the production of nitric oxide (NO) in RAW264.7 cells (IC_{50}= 27.2μM)	108
Indane-fused-naphthene type drimane meroterpenoids			
191	Pelorol	anti-inflammatory as an in vitro activator of the inositol-5-phosphatase SHIP	109
195	19-*O*-methylpelorol	inflammatory cytokines (IL-6, IL-1β,IL-8, andPEG2) in LPS-induced THP-1 cells with IC_{50} values of 5.1–9.2 μM	95

Table S9. Other drimane meroterpenoids with anti-feedant activity

3.9 Anti-feedant activity			
Numb.	Compds	Species and bioactivity	Ref.
Substituted drimane type meroterpenoids			
6	Zonarol	young abalone *Haliotis discus hannai.* (*Ei*= 0.85)	110
9	Zonarone	young abalone Haliotis discus hannai. (*Ei*= 0.92)	110
41	Isozonarol	young abalone Haliotis discus hannai. (*Ei*= 0.78)	110
42	Isozonarone	young abalone Haliotis discus hannai. *(Ei*= 0.85)	110
Benzopyran-fused-naphthene type drimane meroterpenoids			
85	Chromazonarol	young abalone Haliotis discus hannai. (*Ei*= 0.8)	110
90	Puupehenone	shrimp, *palaemon sernus* (IC_{50}= 4.0 mg/ml)	111
Bnaphthane-fused-naphthene type drimane meroterpenoids			
218	Cyclozonarone	shrimp, *palaemon sernus* (IC_{50}= 4.0 mg/ml)	111

Table S10. Other drimane meroterpenoids with immunomodulatory activity

3.10 Immunomodulatory activity

Numb.	Compds	Species and bioactivity	Ref.
Benzopyran-fused-naphthene type drimane meroterpenoids			
90	Puupehenone	immunological response of T cells attached onto [Leu^{27}]MART-1$_{26-35}$, a modified HLA-A2-associated decapeptide identified to function as an epitope for melanoma-reactive cytotoxic T lymphocytes	37，67, 112
91	Cyanopuupehenone	immunological response of T cells	37，67,
92	21-Chloropuupehenone	immunological response of T cells	37，67,
93	Puupehedione	immunological response of T cells	37，67,
94	Cyanopuupehenol	immunological response of T cells	37，67,
96	15-Oxopuupehenol	immunological response of T cells	37, 67

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