

Supplementary file for Marine-Derived Bioactive Metabolites as a Potential Therapeutic Intervention in Managing Viral Diseases: Insights from the SARS-CoV-2 In Silico and Pre-Clinical Studies

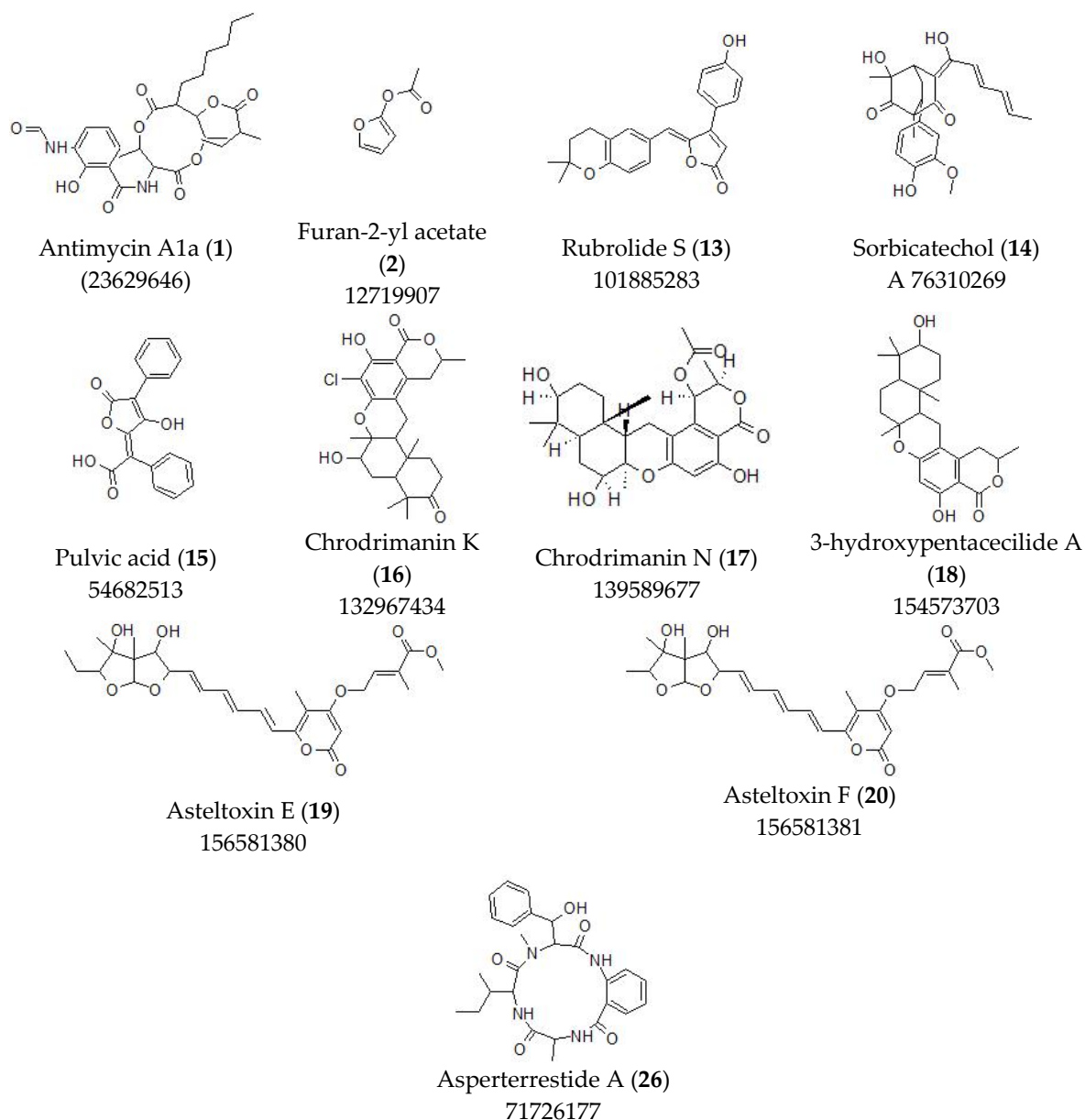


Figure S1. Chemical structures of identified compounds from marine microorganisms (Bacteria and fungi) that inhibit viruses.

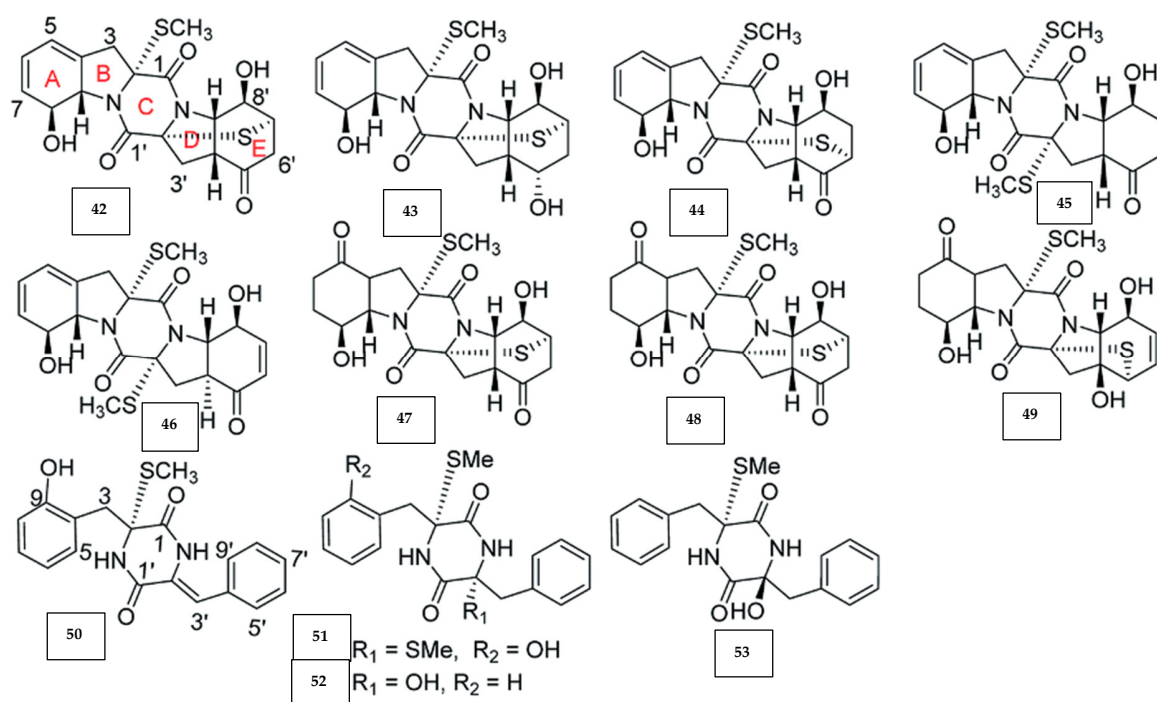
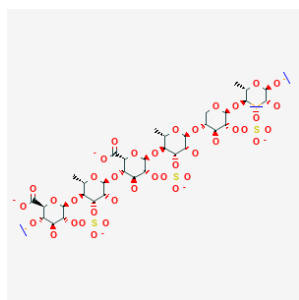
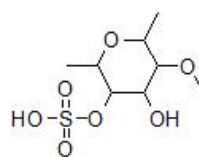


Figure S2. Eutypellazines A-L 42-53 found in deep sea sediment collected from the south Atlantic Ocean [1].

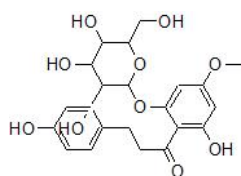


Ulvan (84)
405234592



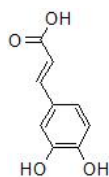
Fucoidan (85)
129532628

Figure S3. Chemical structures of identified compounds from marine microorganisms (marine algae) that inhibit viruses.



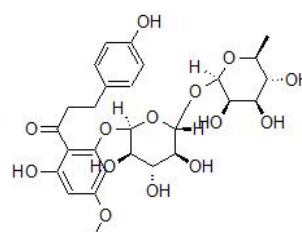
Asebotin (84)

11190157

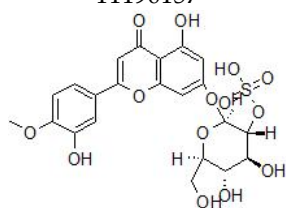


Trans-cafeic acid (88)

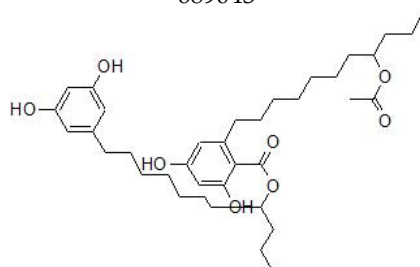
689043



Thalassodendrone (90)

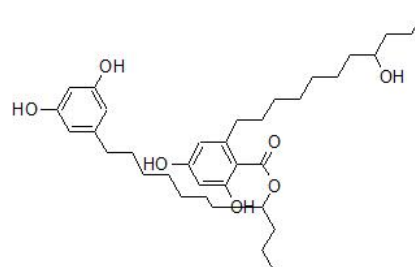


Thalassiolin D (91)



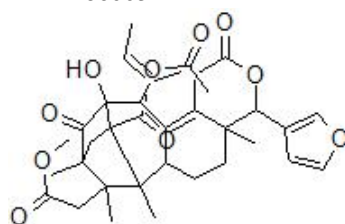
Integracin A (92)

486005



Integracin B (93)

70678748



Thaixylomolin I (94)

355351742

Figure S4. Chemical structures of identified compounds from marine plants that inhibit viruses.

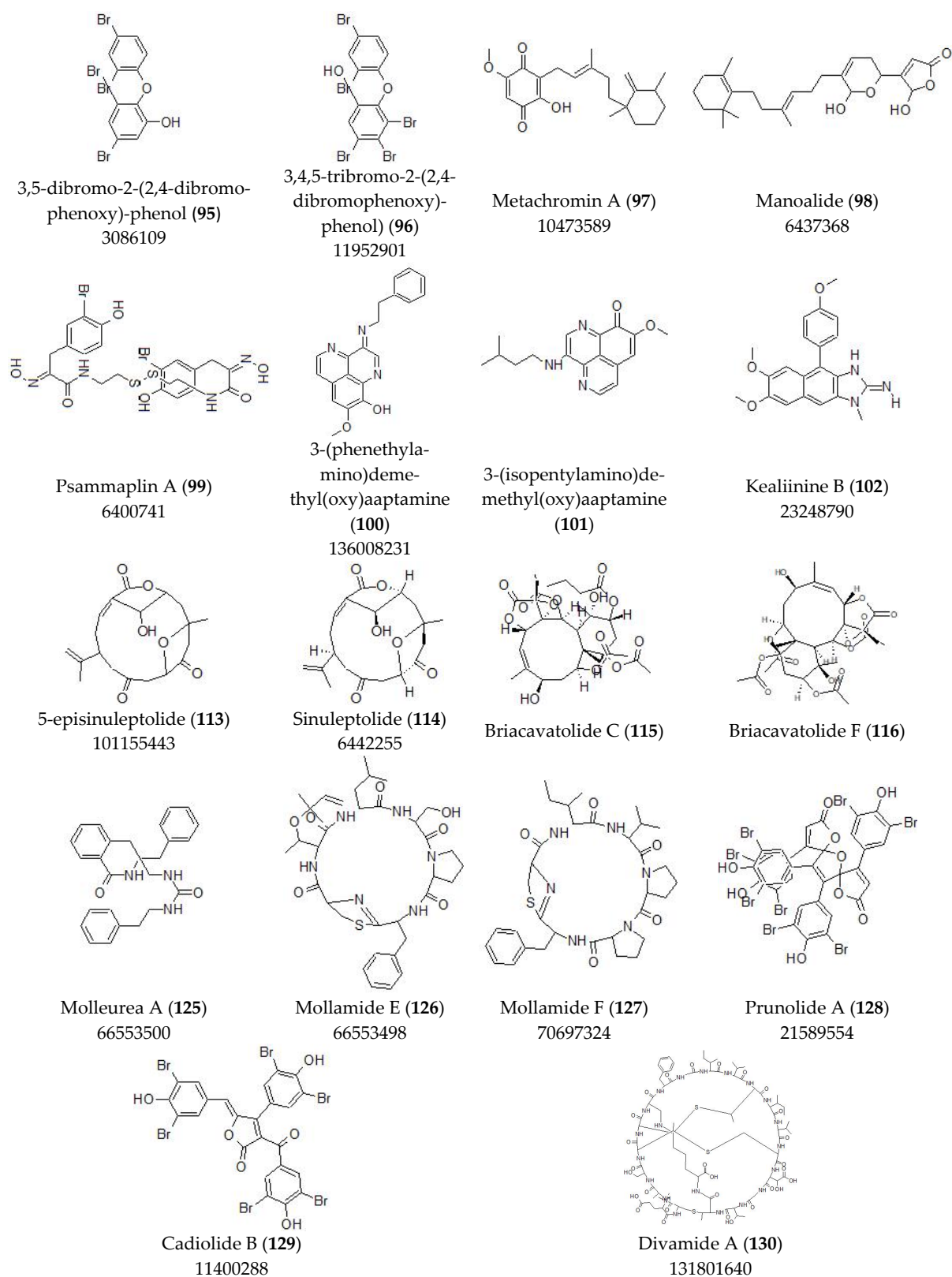


Figure S5. Chemical structures of identified compounds from marine macro-organisms (invertebrates) that inhibit viruses.

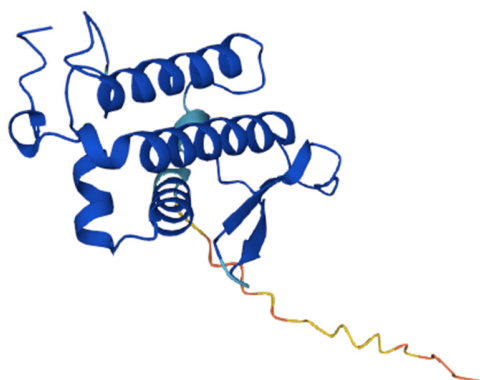


Figure S6. Phospholipase A2 (AP-PLA-2) (**132**) from Echinoderm (starfish) found in Moluccas Islands, eastern Indonesia [3].

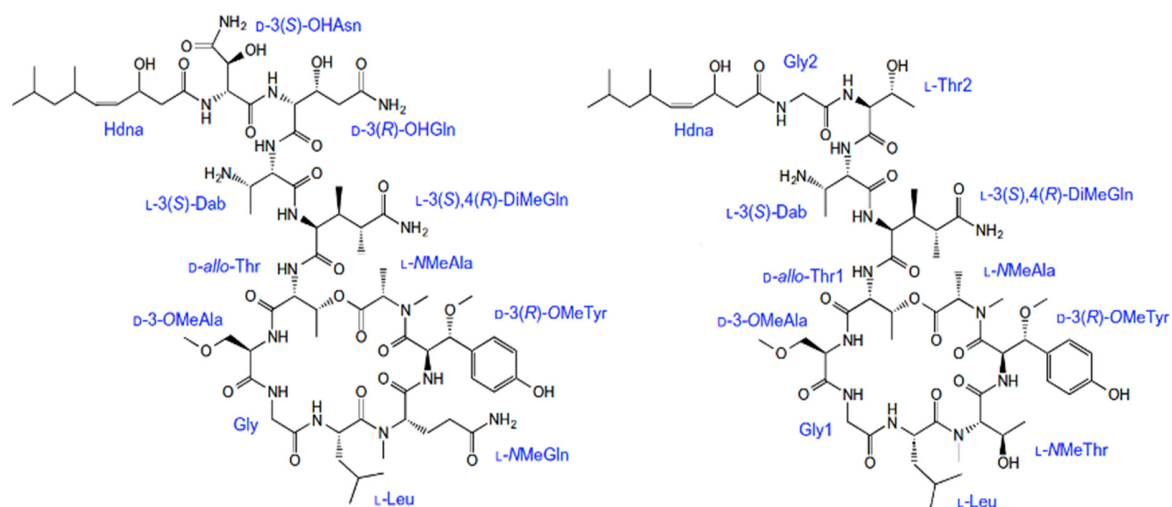
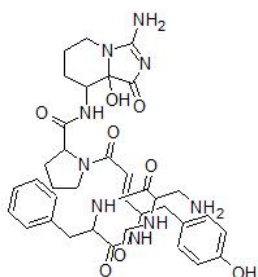
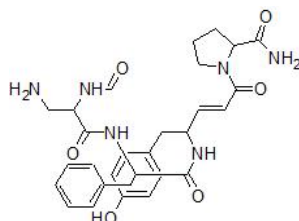


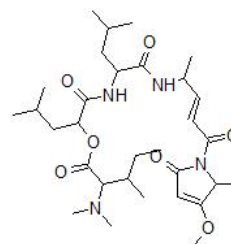
Figure S7. Stellattapeptins A (134) and B (135) isolated from *Stellatta* sp. found in North-western Australia [2].



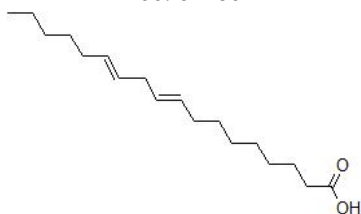
Pseudotheonamide C (171)
100964480



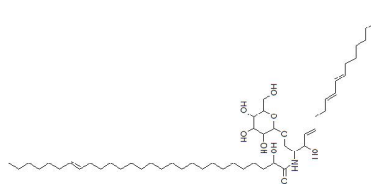
Pseudotheonamide D (172)
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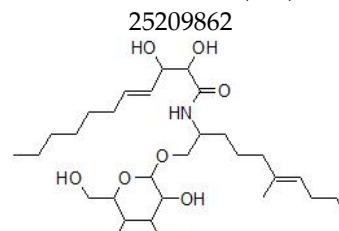
Gallinamide A (173)
25209862



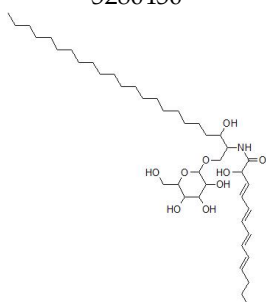
Linoleic acid (179)
5280450



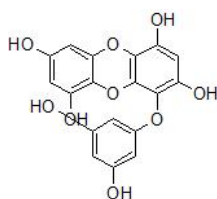
Renieroside A1 (182)
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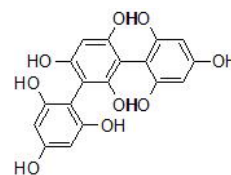
Penicilloside B (184)
156581282



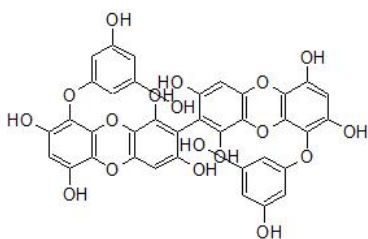
Asperiamide B (185)
139587498



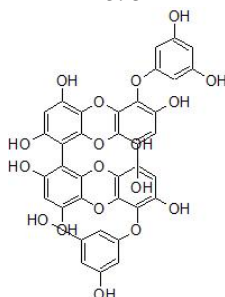
Eckol (186)
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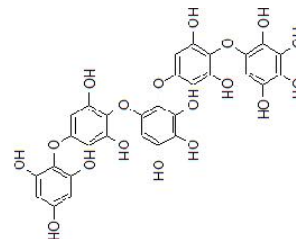
Trifucol (188)
71401226



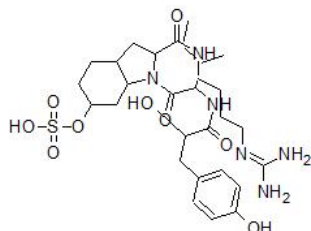
8,8-bieckol (188)
3008867



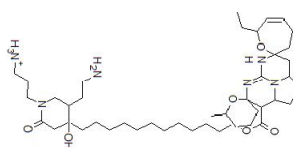
6,6-bieckol (189)
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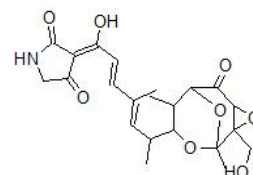
Hydroxypentafuhalol A
(194) 102274236



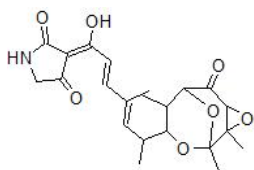
Aeruginosin 98B (196)
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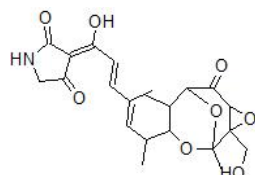
Crambesidin 786 (204)
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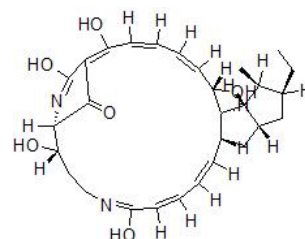
Isotirandamycin B (206)
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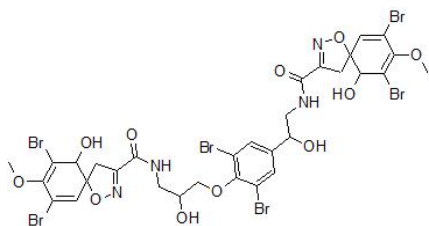
Tirandamycin A (207)
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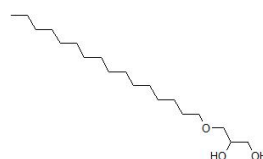
Tirandamycin B (208)
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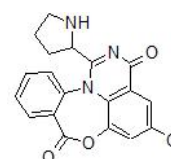
Alteramide A (209)
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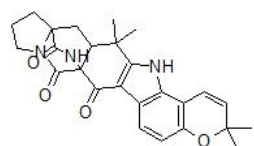
Isofistularin-3 (210)
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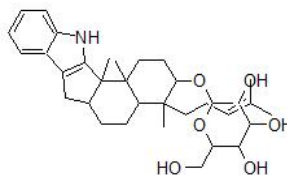
Chimyl alcohol (211)
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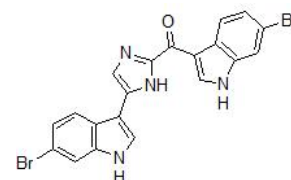
Aspergicin (212)
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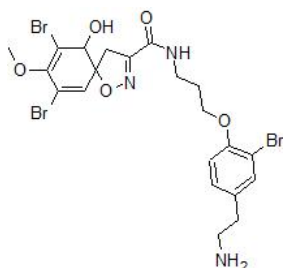
Notoamide I (215)
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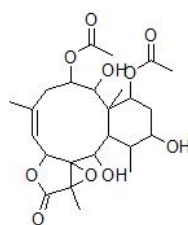
Emindole SB beta-mannoside (216)
76317959



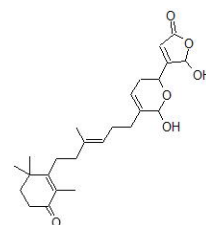
Dibromodeoxytypsentin (218) 11363725



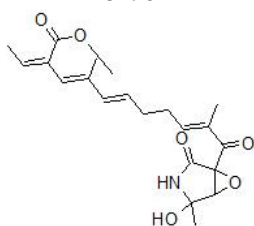
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131984



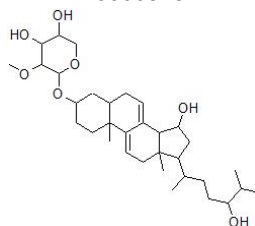
Excavatolide M (226)
10600828



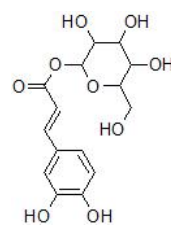
Fasciospongide A (228)



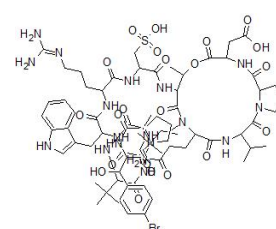
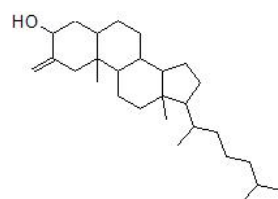
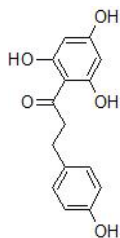
Epolactaene (229)
6442272



Moniloside A (230)
44575900



Caffeic acid hexoside (231)
6124135



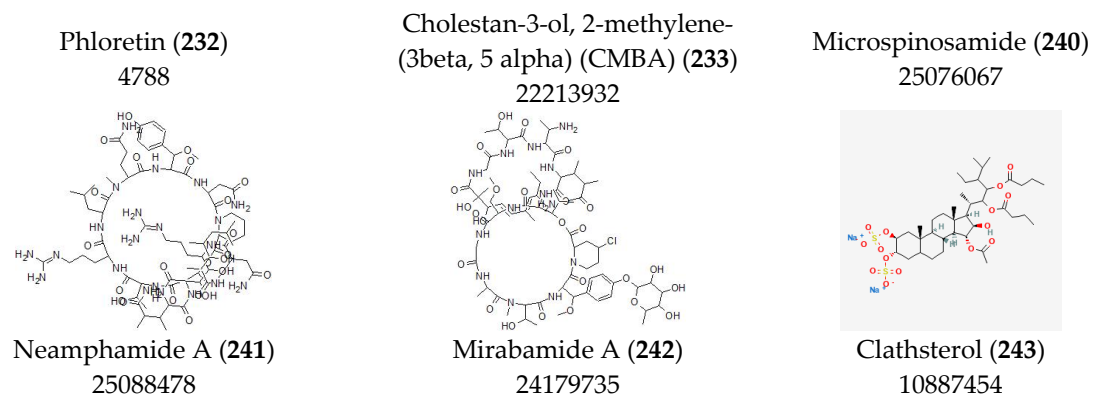
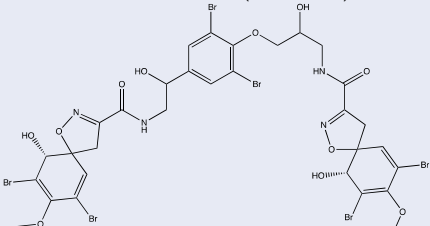
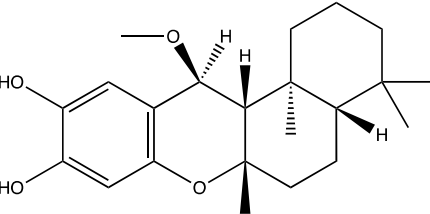
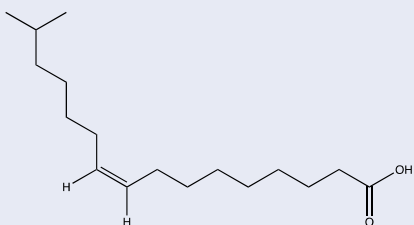
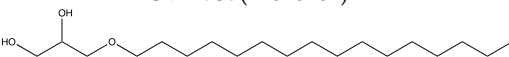
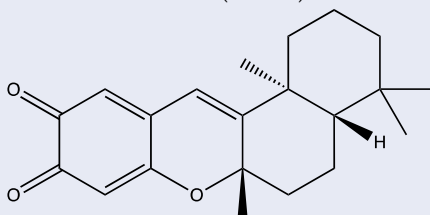
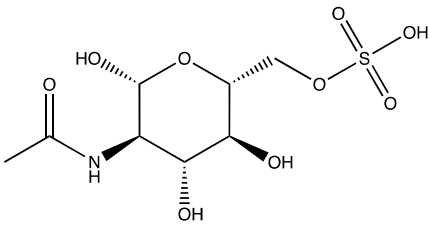
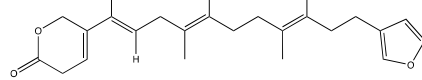
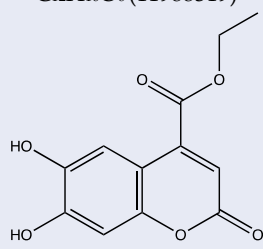
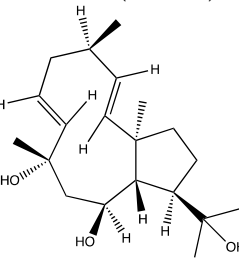
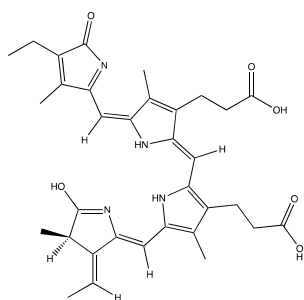


Figure S8. Chemical structures of identified compounds from marine organisms with inhibitory properties against SARS-CoV-2.

Table S1. Selected marine compounds with potential inhibitory properties against SARS-CoV-2 in silico.

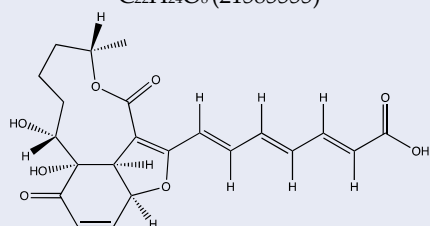
Compound and structural formula. (PUBCHEMID)	Class of compound	Source	Target site	Binding Energy ΔG_B (kcal/mo)	Refs.
Fistularin-3/11-epi-fistularin-3 (245) C₃₁H₃₀Br₆N₄O₁₁ (11170714) 	Alkaloid	Marine sponge Fam- ily Aplysinidae	Mpro	-7.8	[4]
15-α-methoxypuupehenol (246) C₂₂H₃₂O₄ (21591485) 	Phenol	Marine sponge <i>Petro- sia strongy- lophora</i> sp.	Mpro	-7.2	[4]
Palmitoleic Acid acid (247) C₁₆H₃₀O₂ (445638) 	Lipid	Soft coral <i>Pterogorgia citrina</i>	Mpro	-7.5	[4]
(Hexadecyloxy) propane,1,2-diol (248) C₁₉H₄₀O₃ (21646261) 	Lipid	Marine sponge Fam- ily Aplysinidae	Mpro	-7.5	[4]
Puuphedione (249) C₂₁H₂₆O₃ (460087) 	Terpene	Marine sponge <i>Petro- sia strongy- lophora</i> sp	Mpro	-7.2	[4]
Glycosaminoglycan (250) C₈H₁₅NO₉S (10053416)	Sulfonated poly- saccharides	Marine Bac- teria <i>Pseudomonas</i> sp.	Mpro	-7.9	[5]

					
Polyacetylenetriol (251) $C_{29}H_{30}O_3$ (6474656)		Marine Sponge <i>Petrosia</i> sp.,	Mpro	-7.4	[5,6]
	Furanoterpene	Marine Sponge <i>Lendenfeldia</i> sp.	Mpro	-6.2	[5]
Esculetin ethyl ester (203) $C_{12}H_{10}O_6$ (11988319)	Polyketide	Marine Sponge <i>Axinella</i> cf. <i>corugata</i>	Mpro	-8.4	[5,7]
					
Dolabelladienetriol (253) $C_{20}H_{34}O_3$ (6477027)	Terpenoid	Marine alga <i>Dictyota</i> <i>pfaffii</i>	Mpro	-7.6	[5]
					
Hamigeran b (227) $C_{18}H_{21}BrO_3$ (9976066)	Diterpene	Marine sponge <i>Hamigera</i> <i>tarangaensis</i>	Mpro	-7.9	[5]
Phycocyanobilin (174) $C_{33}H_{38}N_4O_6$ (5288007)	Phycobilin pigment	Cyanobacteria <i>Arthrospira</i> spp	Mpro RdRp PLpro	-8.6 -9.3 -9.8	[8–10]



Dictyosphaeric acid A (225)

$C_{22}H_{24}O_8$ (21585555)



Polyketide
decalactone

Green algae
*Dicty-
osphaeria ver-
sluyii*

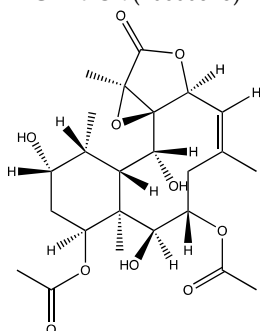
TMPRSS
2

-14.0

[11]

Excavatulide M (226)

$C_{24}H_{34}O_{10}$ (10600828)



Diterpene

Soft coral
*Briareum
excavatum*

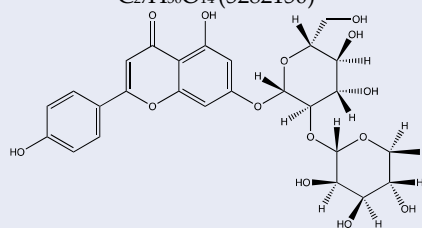
TMPRSS
2-S, PPIs,
hACE2-S

-14.3

[11]

Apigenin-7-O-neohesperidoside (200)

$C_{27}H_{30}O_{14}$ (5282150)



Flavonoid

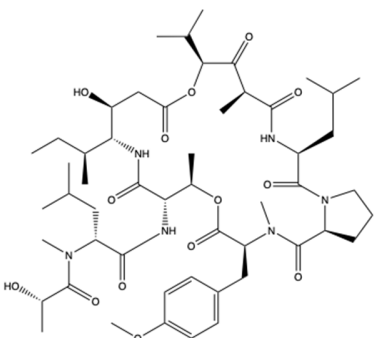
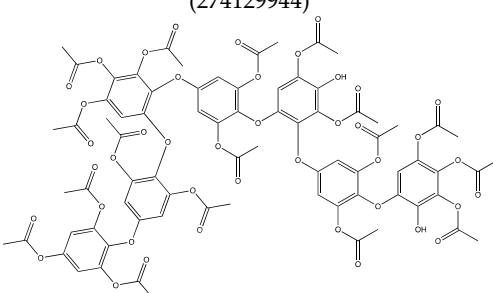
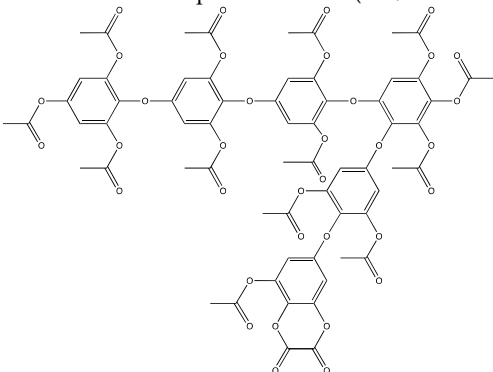
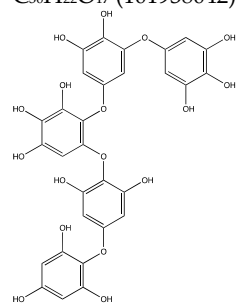
Brown algae
*Sargassum
spinuligerum*

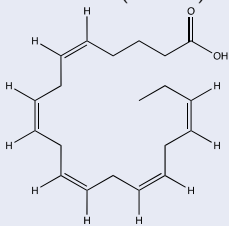
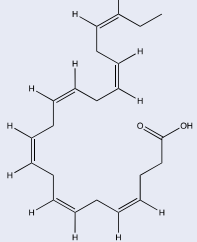
Mpro

-12.4

[12]

Luteolin-7-rutinoside (201) $C_{27}H_{30}O_{15}$ (10461109)					
Flavonoid	Brown algae <i>Sargassum spinuligerum</i>	Mpro	12.1	[12]	
Resinoside B (197) $C_{31}H_{34}O_{13}$ (10053416)					
Flavonoid	Brown algae <i>Sargassum spinuligerum</i>	Mpro	-12.2	[12]	
Didemnins A (168) $C_{49}H_{78}N_6O_{12}$ (123844)					
			-11.8		
Didemnins B (169) $C_{57}H_{89}N_7O_{15}$ (122651)					
Depsipeptide	Tunicate <i>Trididemnum solidum</i>	Mpro	-10.2	[13]	
Didemnins C (170) $C_{52}H_{82}N_6O_{14}$ (9963211)					

						-9.2
Heptafuhalol A (190) (274129944)						
						-14.6
Phlorethopentafuhalol B (192)						
	Phlorotannin	Brown algae <i>Sargassum spinuligerum</i>	Mpro	-14,2	[12]	
Pseudopentafuhalol C (193) $C_{30}H_{22}O_{17}$ (101938042)						
						-14,2

Eicosapentaenoic acid (181) $C_{20}H_{30}O_2$ (446284) 					-120.1
Docosahexaenoic acid (180) $C_{22}H_{32}O_2$ (445580) 	Lipids (ω -6 PUFA)	Fish, other seafoods and algae	S-protein via binding to the FABP	[14]	-110.8

ID₅₀ is ineffective dose, EC₅₀ is Half maximal effective concentration, IC₅₀ is Half maximal inhibitory concentration, FABP is fatty acid-binding pocket.

References

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