

Supplementary Materials for

## **Research Progress of Natural Active Substances with Immunosuppressive Activity**

Fei Shao <sup>1</sup>, Qiying Shen <sup>1</sup>, Zhengfei Yang <sup>3</sup>, Wenqian Yang <sup>1</sup>, Zixiang Lu <sup>1</sup>, Jie Zheng <sup>1</sup>,

Liming Zhang <sup>1,\*</sup> and Hangying Li <sup>1,2,\*</sup>

<sup>1</sup> School of Pharmacy, Ningxia Medical University, Yinchuan 750004, China

<sup>2</sup> Key Laboratory of Craniocerebral Diseases of Ningxia Medical University, Yinchuan 750004, China

<sup>3</sup> School of Traditional Chinese Medicine, Ningxia Medical University, Yinchuan 750004, China

\* Correspondence: nyzlm@163.com (L.Z.); lihy17@lzu.edu.cn (H.L.)

## List of Supplementary Materials

<b>Table S1.</b> Compounds <b>1–36</b> with Immunosuppressive Effects.....	3
<b>Table S2.</b> Compounds <b>37–115</b> with Immunosuppressive Effects.....	6
<b>Table S3.</b> Compounds <b>116–136</b> with Immunosuppressive Effects.....	10
<b>Table S4.</b> Compounds <b>137–149</b> with Immunosuppressive Effects.....	12
<b>Table S5.</b> Compounds <b>150–176</b> with Immunosuppressive Effects.....	13
<b>Table S6.</b> Compounds <b>177–234</b> with Immunosuppressive Effects.....	15
<b>Table S7.</b> Compounds <b>235–262</b> with Immunosuppressive Effects.....	19
<b>Table S8.</b> Compounds <b>263–270</b> with Immunosuppressive Effects.....	22
<b>Table S9.</b> Compounds <b>271–324</b> with Immunosuppressive Effects.....	23

**Table S1.** Compounds 1–36 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities	Model 2	Activities	Reference
					IC <sub>50</sub>		IC <sub>50</sub>	
1	Argyrolide G				5.3 $\mu$ M		/	
2	8 $\alpha$ -acetoxy-3 $\beta$ -chloro-1 $\alpha$ ,4 $\alpha$ -dihydroxyguai-9,11(13)-dien-6 $\alpha$ ,12-olide				3.2 $\mu$ M		/	
3	8 $\alpha$ -acetoxy-3 $\alpha$ -chloro-1 $\alpha$ ,4 $\beta$ -dihydroxyguai-9,11(13)-dien-6 $\alpha$ ,12-olide				6.9 $\mu$ M		/	
4	8 $\alpha$ -acetoxy-3 $\beta$ -chloro-1 $\alpha$ ,4 $\alpha$ -dihydroxyguai-10(14),11(13)-dien-6 $\alpha$ ,12-olide	Plant	<i>Artemisia argyi</i>	LPS stimulated in BV-2 microglial cells	4.2 $\mu$ M	/	/	[28]
5	8 $\alpha$ -acetoxy-3 $\alpha$ -chloro-1 $\beta$ ,2 $\beta$ -epoxy-4 $\beta$ ,10 $\alpha$ -dihydroxy-5 $\alpha$ ,7 $\alpha$ H-guai-11(13)-en-12,6 $\alpha$ -olide				22.2 $\mu$ M		/	
6	3 $\beta$ -chloro-1 $\alpha$ ,2 $\alpha$ -epoxy-4 $\alpha$ ,10 $\alpha$ -dihydroxy-5 $\alpha$ ,7 $\alpha$ H-guai-11(13)-en-12,6 $\alpha$ -olide				6.4 $\mu$ M		/	
7	Tremutin A	Fungi	<i>Irpex lacteus</i>	ConA-induced T-cell proliferation	/	LPS-induced B-cells proliferation	22.4 $\mu$ M	[29]
8	Tremutin B				16.7 $\mu$ M		13.6 $\mu$ M	

9	Canin				2.7 $\mu\text{M}$	/	/	
10	<i>seco</i> -tanapartholide B				1.0 $\mu\text{M}$	/	/	
11	<i>seco</i> -tanapartholide A	Plant	<i>A. argyi</i>	anti-CD3/anti-CD28 stimulated spleen cells	1.2 $\mu\text{M}$	/	/	[28]
12	Arteglasin A				1.9 $\mu\text{M}$	/	/	
13	8-acetylarteminolide				3.2 $\mu\text{M}$	/	/	
14	Maydispenoid A				5.28 $\mu\text{M}$	/	/	
15	Maydispenoid B	Fungi	<i>Bipolaris maydis</i>	anti-CD3/anti-CD28 stimulated spleen cells	9.38 $\mu\text{M}$	/	/	[30]
16	Antroxazole A	Fungi	<i>Antrodiella albocinnamo mea</i>	/	/	LPS-induced B-cells proliferation	16.3 $\mu\text{M}$	[14]
17	(+)-aspersydowin A	Fungi	<i>Aspergillus sydowii</i>	anti-CD3/anti-CD28 stimulated spleen cells	>40 $\mu\text{M}$	LPS-induced B-cells proliferation	10.9 $\mu\text{M}$	[31]
18	(+)-aspersydowin B				>40 $\mu\text{M}$		17.6 $\mu\text{M}$	
19	(7S)-(+)-7-O-methylsydono				>40 $\mu\text{M}$		13.4 $\mu\text{M}$	
20	Parasubolide D	Plant	<i>Parasenecio albus</i>	LPS-induced spleen-cell proliferation	23.1 $\mu\text{M}$	/	/	[32]
21	Parasubolide E				33.8 $\mu\text{M}$	/	/	
22	Parasubolide L				26.6 $\mu\text{M}$	/	/	
23	Steccherin A	Fungi	<i>Steccherinum ochraceum</i>	ConA-induced T-cell proliferation	>40 $\mu\text{M}$	LPS-induced B-cells proliferation	26.3 $\mu\text{M}$	[33]
24	Steccherin B				>40 $\mu\text{M}$		>40 $\mu\text{M}$	
25	Steccherin C				37.8 $\mu\text{M}$		6.2 $\mu\text{M}$	
26	Steccherin D				>40 $\mu\text{M}$		16.1 $\mu\text{M}$	
27	Soltorvum A	Plant	<i>Solanum torvum.</i>	ConA-induced T-cell proliferation	27.0 $\mu\text{M}$	/	/	[34]
28	Soltorvum B				18.0 $\mu\text{M}$	/	/	

29	Craterodoratin C			/		12.62 $\mu$ M		
30	Craterodoratin J			/		19.4 $\mu$ M		
31	Craterodoratin L			/		13.7 $\mu$ M		
32	Craterodoratin M	Fungi	<i>Craterellus odoratus</i>	ConA-induced T-cell proliferation	/	LPS-induced B-cells proliferation	15.4 $\mu$ M	
33	Craterodoratin N							13.2 $\mu$ M
34	Craterodoratin O							17.1 $\mu$ M
35	Craterodoratin Q							31.5 $\mu$ M
36	Craterodoratin S							/

[35]

**Table S2.** Compounds 37–115 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
37	Ineleganolide	Coral	<i>Simularia scabra</i> and <i>Simularia polydactyla</i>	ConA-induced	>50 $\mu$ M	LPS-induced	>50 $\mu$ M	[36]
38	Yonarolide			T-cell proliferation	>50 $\mu$ M	B-cells	>50 $\mu$ M	
39	Scabrolide A			T-cell proliferation	>50 $\mu$ M	proliferation	>50 $\mu$ M	
40	Cinnacassiol G	Plant	<i>Cinnamomum cassia</i>	ConA-induced	/	/	/	[37]
41	Cinnacasol			T-cell proliferation	/	/	/	
42	3,5,10-O triacetyl-8-O-isobutanoyl-14-O-benzoylcyclomy rsinol	Plant	<i>Euphorbia</i> <i>kopetdaghi</i> Prokh	PHA-activated T-Cell proliferation	1.83 mg /mL	/	/	[38]
43	Xylarilongipin A	Fungi	<i>Xylaria longipes</i> HFG1018	ConA-induced T-cell proliferation	22.4 $\mu$ M	LPS-induced B-cells proliferation	22.4 $\mu$ M	[39]
44	Tripterifordin	Plant	<i>Ligularia fischeri</i>	human B	56.3 $\mu$ M	/	/	[40]
45	16 $\alpha$ ,17-dihydroxy-ent-kaur-20-al.			lymphoblast	13.3 $\mu$ M	/	/	
46	ent-2 $\beta$ -hydroxymanool			HMy2.CIR cells	31.4 $\mu$ M	/	/	
47	Koilodenoid D	Plant	<i>Koilodepas</i> <i>hainanense</i>	ConA-induced T-cell proliferation	23.8 $\mu$ M	LPS-induced B-cells proliferation	10.2 $\mu$ M	[41]
48	Koilodenoid G				3.1 $\mu$ M		2.2 $\mu$ M	
49	ent-5 $\alpha$ ,2,15-dioxodolabr-3-ene-3,16-diol				0.8 $\mu$ M		0.3 $\mu$ M	
50	ent-5 $\alpha$ ,3,15-dioxodolabr-1,4(18)-diene-2,16-diol				30.5 $\mu$ M		4.7 $\mu$ M	
51	ent-16-nor-5 $\alpha$ ,13 $\alpha$ (methyl)-2-oxodolabra-3-en-3 -ol-15-oicacid				3.4 $\mu$ M		3.1 $\mu$ M	

52	Xylarinorditerpene B	Fungi	<i>Xylaria longipes</i> HFG1018	ConA-induced T-cell proliferation	11.1 $\mu$ M	LPS-induced B-cells proliferation	35.1 $\mu$ M	[42]
53	Xylarinorditerpene C				6.6 $\mu$ M		38.2 $\mu$ M	
54	Xylarinorditerpene D				21.1 $\mu$ M		51.8 $\mu$ M	
55	Xylarinorditerpene E				14.9 $\mu$ M		49.4 $\mu$ M	
56	Xylarinorditerpene I				1.0 $\mu$ M		16.1 $\mu$ M	
57	Xylarinorditerpene N				4.0 $\mu$ M		46 $\mu$ M	
58	14 $\alpha$ ,16-epoxy-18-norisopimar-7-en-4 $\alpha$ -ol				27.2 $\mu$ M		40 $\mu$ M	
59	Agatadiol				15.6 $\mu$ M		47.2 $\mu$ M	
60	Robustaditerpenes C	Fungi	<i>Ilyonectria robusta</i>	ConA-induced T-cell proliferation	/	LPS-induced B-cells proliferation	17.42 $\mu$ M	[43]
61	Robustaditerpenes E				75.22 $\mu$ M		/	
62	Scopariusicid I	Plant	<i>Isodon scoparius</i>	ConA-induced T-cell proliferation	10.1 $\mu$ M	/	/	[44]
63	Scopariusicid J				9.4 $\mu$ M	/	/	
64	Scopariusicid L				16.3 $\mu$ M	/	/	
65	Scopariusic Acid	Plant	<i>Isodon scoparius</i>	ConA-induced T-cell proliferation	2.6 $\mu$ M	/	/	[46]
66	Ceforloid F	Plant	<i>Cephalotaxus fortunei</i> var. <i>alpina</i> and <i>C.</i> <i>sinensis</i>	ConA-induced T-cell proliferation	1.93 $\mu$ M	/	/	[45]
67	Xiguscabrolide H	Coral	<i>S. scabra</i> and <i>S.</i> <i>polydactyla</i>	ConA-induced T-cell proliferation	45.7 $\mu$ M	LPS-induced B-cells proliferation	44.1 $\mu$ M	[36]
68	10-epi-gyrosanolide E				>50 $\mu$ M		>50 $\mu$ M	
69	5-Epi-sinuleptolide				39.6 $\mu$ M		>50 $\mu$ M	
70	Norcembrene 5				>50 $\mu$ M		>50 $\mu$ M	
71	Scabrolide D				>50 $\mu$ M		>50 $\mu$ M	

72	Scabrolide G	Coral	<i>scabra</i> and <i>S. polydactyla</i>	ConA-induced T-cell proliferation	23.7 $\mu\text{M}$	LPS-induced B-cells proliferation	20.5 $\mu\text{M}$	[36]
73	Sinularcasbane O				>50 $\mu\text{M}$		>50 $\mu\text{M}$	
74	Gyrosanolide F				29.1 $\mu\text{M}$		>100 $\mu\text{M}$	
75	Sinuleptolide				8.5 $\mu\text{M}$		21.7 $\mu\text{M}$	
76	Xiguscabrate A				>50 $\mu\text{M}$		46.5 $\mu\text{M}$	
77	Xiguscabrate B	8.4 $\mu\text{M}$	25.6 $\mu\text{M}$					
78	Xiguscabral A	15.8 $\mu\text{M}$	44 $\mu\text{M}$					
79	Xiguscabrol A	5.5 $\mu\text{M}$	>50 $\mu\text{M}$					
80	Xiguscabrol B	3.9 $\mu\text{M}$	44.8 $\mu\text{M}$					
81	8- <i>epi</i> -xiguscabrol B	2.3 $\mu\text{M}$	34.9 $\mu\text{M}$					
82	(1 <i>Z</i> ,5 <i>E</i> ,7 <i>E</i> ,11 <i>E</i> )-8-isopropyl-5,11-dimethylcyclo tetradeca-	>50 $\mu\text{M}$	>50 $\mu\text{M}$					
83	11 <i>S</i> ,12 <i>S</i> -epoxy-11,12-dihydrocembrene-C	39.2 $\mu\text{M}$	14 $\mu\text{M}$					
84	Sinulariol C	Plant	<i>S. scabra</i>	ConA-induced T-cell proliferation	4.5 $\mu\text{M}$	LPS-induced B-cell proliferation	46.8 $\mu\text{M}$	[47]
85	Cembrene-A				44.3 $\mu\text{M}$		16.7 $\mu\text{M}$	
86	Pentaene-cembrene				>50 $\mu\text{M}$		39.3 $\mu\text{M}$	
87	(1 <i>S</i> )-isoscaphytol-A				27.1 $\mu\text{M}$		44.1 $\mu\text{M}$	
88	(1 <i>E</i> ,3 <i>E</i> ,7 <i>E</i> ,11 <i>E</i> )-( 14 <i>R</i> )-cembra-1,3,7,11-tetraen- 14-ol				19.6 $\mu\text{M}$		>50 $\mu\text{M}$	
89	(1 <i>S</i> ,2 <i>E</i> , 4 <i>S</i> ,7 <i>E</i> ,11 <i>E</i> ) -2,7,11-cembratriene-4-ol				>50 $\mu\text{M}$		49.8 $\mu\text{M}$	
90	Nephtenol				10.7 $\mu\text{M}$		38.6 $\mu\text{M}$	
91	(3 <i>E</i> ,11 <i>E</i> )-cembra-3,8(19),11,15-tetraene-7-ol				48.9 $\mu\text{M}$		42.5 $\mu\text{M}$	
92	Sarcophytol T				40.4 $\mu\text{M}$		32.1 $\mu\text{M}$	
93	Gibberosene B				33.5 $\mu\text{M}$		>50 $\mu\text{M}$	

94	(1 <i>E</i> ,3 <i>E</i> ,7 <i>E</i> ,11 <i>R</i> *12 <i>R</i> *)-15-(acetoxymethyl)cembra-11,12-epoxy-1,3,7-triene				>50 $\mu$ M		10.3 $\mu$ M	
95	(1 <i>R</i> ,3 <i>S</i> ,4 <i>S</i> ,7 <i>E</i> ,11 <i>E</i> )-3,4-epoxycembra-7,11,15-triene				>50 $\mu$ M		>50 $\mu$ M	
96	Lobocrassin C				23.1 $\mu$ M		>50 $\mu$ M	
97	Pseudoplexauric acid methyl ester				>50 $\mu$ M		>50 $\mu$ M	
98	(1 <i>E</i> ,3 <i>E</i> ,7 <i>R</i> ,8 <i>R</i> ,11 <i>E</i> ,14 <i>R</i> )-3,4-epoxy-14-acetatecembra-1,3,11-trien-14-ol				11.9 $\mu$ M		40.1 $\mu$ M	
99	(2 <i>R</i> ,11 <i>S</i> ,12 <i>S</i> )-is sarcophytoxide				>50 $\mu$ M	LPS-induced	4.4 $\mu$ M	
100	Sarcophytoxide	Plant	<i>S. Scabra</i>	ConA-induced	>50 $\mu$ M	B-cell	>50 $\mu$ M	
101	Is sarcophine			T-cell proliferation	47.8 $\mu$ M	proliferation	>50 $\mu$ M	[47]
102	(+)-marasol				27.4 $\mu$ M		>50 $\mu$ M	
103	Sarcophytol W				>50 $\mu$ M		>50 $\mu$ M	
104	Sinulariol Z				>50 $\mu$ M		>50 $\mu$ M	
105	Sinulariol Z				6.1 $\mu$ M		52.9 $\mu$ M	
106	Sinuflexibilin D				39.4 $\mu$ M		34.5 $\mu$ M	
107	Sinulariolide				19.5 $\mu$ M		9.2 $\mu$ M	
108	Sinuladiterpene G				>50 $\mu$ M		>50 $\mu$ M	
109	Sarcomililate 1a				49.8 $\mu$ M		20.2 $\mu$ M	
110	Sarcomililate 1b				38.9 $\mu$ M		22.1 $\mu$ M	
111	Sarcomililatol B		the Hainan Soft Coral		>50 $\mu$ M	LPS-induced	>50 $\mu$ M	
112	Sarcomililatols 2a	Coral	<i>Sarcophyton mililatensis</i>	ConA-induced	44.5 $\mu$ M	B-cell	18.7 $\mu$ M	[48]
113	Sarcomililatols 3a			T-cell proliferation	>50 $\mu$ M	proliferation	49.5 $\mu$ M	
114	Yalongene A				>50 $\mu$ M		4.8 $\mu$ M	
115	Sarcophytol M				11.4 $\mu$ M		4.9 $\mu$ M	

**Table S3.** Compounds 116–136 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
116	Munronoid P	Plant	<i>Munronia pinnata</i>	ConA-induced T-cell proliferation	2.73 $\mu$ M	LPS-induced B-cell proliferation	34.88 $\mu$ M	[49]
117	Triterhyper A	Plant	<i>Hypericum longistylum</i>	anti-CD3/anti-CD28 stimulated spleen cells	4.5 $\mu$ M	/	/	[50]
118	Lupeol				18.3 $\mu$ M		/	
119	3b-hydroxyoleane-6b-oxethyl-12-en-28-oicacid-3-O-b-D-glucuronic	Plant	<i>Epigynum griffithianum</i>	proliferation of mice splenocyte	2.5 $\mu$ M	/	/	[14]
120	Schincarin C	Plant	<i>Schisandra</i>	LPS-induced B-cell proliferation	10.2 $\mu$ M	/	/	[51]
121	BC-1	Plant	<i>Beesia calthaefolia</i>	anti-CD3/anti-CD28 stimulated spleen cells	9.5 $\mu$ M	/	/	[52]
122	Dictabretol A	Plant	<i>Dictamnus dasycarpus</i>	ConA-induced T-cell proliferation	1.5 $\mu$ M	/	/	[53]
123	Dictabretol B				>20 $\mu$ M		/	
124	Dictabretol C				1.8 $\mu$ M		/	
125	Dictabretol D				1.5 $\mu$ M		/	
126	Schincalactones A				Plant		<i>Schisandra</i>	
127	Phainanolid A	Plant	<i>Phyllanthus hainanensis</i>	ConA-induced T-cell proliferation	364.75 $\mu$ M	LPS-induced B-cell proliferation	245.47 $\mu$ M	[55]
128	Phainanoid G				566.83 $\mu$ M		456.63 $\mu$ M	
129	Phainanoid H				16.15 $\mu$ M		8.24 $\mu$ M	
130	Phainanoid I				218.14 $\mu$ M		305.38 $\mu$ M	

131	Phainanoid A				184.9 $\mu\text{M}$		122.28 $\mu\text{M}$	
132	Phainanoid B				192.8 $\mu\text{M}$		249.49 $\mu\text{M}$	
133	Phainanoid C	Plant	<i>Phylanthus hainanensis</i>	ConA-induced T-cell proliferation	6.24 $\mu\text{M}$	LPS-induced B-cell proliferation	2.35 $\mu\text{M}$	[56]
134	Phainanoid D				8.28 $\mu\text{M}$		17.04 $\mu\text{M}$	
135	Phainanoid E				43.26 $\mu\text{M}$		4.38 $\mu\text{M}$	
136	Phainanoid F				2.04 $\mu\text{M}$		<1.60 $\mu\text{M}$	

**Table S4.** Compounds 137–149 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
137	Peniandranoid A	Fungi	<i>Penicillium</i> sp	ConA-induced T cell proliferation(EC <sub>50</sub> )	19 $\mu$ M	LPS-induced B-cells proliferation(EC <sub>50</sub> )	/	[56]
138	Peniandranoid B				/		50 $\mu$ M	
139	Peniandranoid C				4.3 $\mu$ M		11 $\mu$ M	
140	Peniandranoid D				11 $\mu$ M		8.8 $\mu$ M	
141	Peniandranoid E				27 $\mu$ M		12 $\mu$ M	
142	Isopenicin C				23 $\mu$ M		23 $\mu$ M	
143	Isopenicin A				8.5 $\mu$ M		8.5 $\mu$ M	
144	Isopenicin B				23 $\mu$ M		7.5 $\mu$ M	
145	Nitidasin	Plant	<i>Gentianella turkestanorum</i>	anti-CD3/anti-CD28 stimulated spleen cells	12.31 $\mu$ M	IFN- $\gamma$ production	16.5 $\mu$ M	[57]
146	Gentianelloid F				13.68 $\mu$ M		14.66 $\mu$ M	
147	Alborosin				14.31 $\mu$ M		12.4 $\mu$ M	
148	Colquhounoid D	Plant	Colquhounia coccinea var. mollis	induced by anti-CD3/CD4 monoclonal antibodies	8.38 $\mu$ M	/	/	[58]
149	14- <i>epi</i> -colquhounoid D				5.79 $\mu$ M	/	/	

**Table S5.** Compounds 150–176 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
150	Wilfordatin E		<i>Tripterygium</i>		8.75 $\mu$ M		/	
151	Tripfordine A	Plant	<i>wilfordii</i> Hook.	HEK293 cells induced by LPS	0.74 $\mu$ M	/	/	[60]
152	Wilforine		f.		15.66 $\mu$ M		/	
153	Alopecine A				>100 $\mu$ M		69.6 $\mu$ M	
154	Alopecine B				>100 $\mu$ M		96.8 $\mu$ M	
155	Alopecine C	Plant	<i>Sophora</i>	ConA-induced T cell proliferation	>100 $\mu$ M	LPS-induced B-cells proliferation	59.5 $\mu$ M	[61]
156	Alopecine D		<i>alopecuroides</i>		3.9 $\mu$ M		3.7 $\mu$ M	
157	Alopecine E				58.7 $\mu$ M		9.4 $\mu$ M	
158	Albifpyrrol B	Fungi	<i>Albifmbria viridis</i>	ConA-induced T-cell proliferation	/	LPS-induced B-cell proliferation	16.16 $\mu$ M	[62]
159	Fumiquinazoline J		<i>Aspergillus</i>		29.38 $\mu$ M		162.58 $\mu$ M	
160	Fumigaclavine C	Fungi	<i>fumigatus</i> HQD24.	ConA-induced T-cell proliferation	52.13 $\mu$ M	LPS-induced B-cell proliferation	/	[63]
161	12-Methoxychanofruticosinic acid				27.8 $\mu$ M			
162	N(4)-methylkopsinate	Plant	<i>Kopsia officinalis</i>	human T cell proliferation (PBMCs)	21.6 $\mu$ M	/	/	[64]
163	Demethoxycarbonylkopsin				25.4 $\mu$ M			
164	Rhazinilam				1.0 $\mu$ M			

165	Gentianelloid A	Plant	<i>Gentianella turkestanorum</i>	anti-CD3/CD28 mAbs induced	5.64 $\mu$ M		/	[65]
166	Gentianelloid B			murine T lymphocytes proliferation	3.93 $\mu$ M	/	/	
167	Eurysoloids A	Plant	Eurysolen gracilis	anti-CD3/CD28 mAbs induced	17.4 $\mu$ M		/	[66]
168	Eurysoloids B			murine T lymphocytes proliferation	15.94 $\mu$ M	/	/	
169	Rhazinilam	Plant	<i>Pausinystalia yohimbe</i>	ConA-induced T-cell proliferation	16.8 $\mu$ M	LPS-induced B-cell proliferation	13.5 $\mu$ M	[65]
170	Ophiorrhine C	Plant	<i>Ophiorrhiza cantoniensis</i>	ConA-induced T cell proliferation	23.6 $\mu$ M	LPS-induced B-cell proliferation	8.7 $\mu$ M	[66]
171	Ophiorrhine D				17.9 $\mu$ M		68.5 $\mu$ M	
172	Ophiorrhine E				>200 $\mu$ M		116.2 $\mu$ M	
173	Ophiorrhine F	Plant	<i>Ophiorrhiza japonica</i>	ConA-induced T cell proliferation	>200 $\mu$ M	LPS-induced B-cells proliferation	<0.4 $\mu$ M	[67]
174	Ophiorrhine G				>201 $\mu$ M		47.3 $\mu$ M	
175	Reserpine	Plant	<i>Rauvolfia yunnanensis</i>	human T cell	5.0 $\mu$ M			[68]
176	11-hydroxyburnamine				<i>Tsiang</i>	5.9 $\mu$ M	/	

**Table S6.** Compounds 177–234 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
177	Hyaluron A	Plant	<i>Hypericum patulum</i>	LPS-induced B-cell proliferation	6.8 $\mu$ M	/	/	[72]
178	Eucalyptin A	Plant	<i>Eucalyptus globulus.</i>	ConA-induced T-cell proliferation	18.2 $\mu$ M	/	/	[73]
179	Eucalyptin B				19.1 $\mu$ M		/	
180	Eucalyptin C				11.8 $\mu$ M		/	
181	Eucalyptin D				10.2 $\mu$ M		/	
182	Eucalyptin E				35.8 $\mu$ M		/	
183	Eucalyptin F				26.3 $\mu$ M		/	
184	Eucalyptin G				35.3 $\mu$ M		/	
185	Macrocarpal A				20.4 $\mu$ M		/	
186	Macrocarpal B				31.2 $\mu$ M		/	
187	Macrocarpal C				69.6 $\mu$ M		/	
188	Macrocarpal D				41.2 $\mu$ M		/	
189	Macrocarpal E				42.4 $\mu$ M		/	
190	Macrocarpal Q				52.3 $\mu$ M		/	
191	Eucarobustol E				68.4 $\mu$ M		/	
192	Euglobal-V	69.3 $\mu$ M	/					
193	Euglobal-III	129.3 $\mu$ M	/					
194	1-(2,6-dihydroxy-4-methoxy-3,5-dimethylphenyl)-2-methylbutan-1-one				70.2 $\mu$ M		/	

195	1-(2,4-dihydroxy-6-methoxy-3,5-dimethylphenyl)-3-methylbutan-1-one	Plant	<i>Eucalyptus globulus</i> .	ConA-induced T-cell proliferation	132.9 $\mu$ M	/	/	[72]
196	Prenyllongnol A	Plant	<i>Hypericum longistylum</i>	ConA-induced T cell proliferation	3.44 $\mu$ M	/	/	[74]
197	Prenyllongnol B				2.98 $\mu$ M	/	/	
198	Prenyllongnol C				5.31 $\mu$ M	/	/	
199	Prenyllongnol D				6.34 $\mu$ M	/	/	
200	Dendrophenene A	Plant	<i>Dendrobium devonianum</i>	ConA-induced T cell proliferation	0.17 $\mu$ M	LPS-induced B cell proliferation	28.3 $\mu$ M	[75]
201	Dendrophenene B				2.47 $\mu$ M		52.6 $\mu$ M	
202	Tyrosol	Plant	<i>H. abyssinica</i>	PMNs and MNCs	/	/	/	[76]
203	3,4-dihydroxy-ethyl ester				/	/	/	
204	Daldiniols A	Plant	<i>Anoectochilus roxburghii</i>	LPS-induced B-cell proliferation	0.06 $\mu$ M	/	/	[77]
205	2-phenylpropanoate-2-O- $\beta$ -D-apiofuranosyl-(1 $\rightarrow$ 6)-O- $\beta$ -D-glucopyranoside	Plant	<i>Cinnamomum cassia</i>	ConA-induced murine T cells	>200 $\mu$ M	/	/	[72]
206	3,4,5-trimethoxyphenol- $\beta$ -D-apiofuranosyl-(1 $\rightarrow$ 6)-O- $\beta$ -D-glucopyranoside				12.5 $\mu$ M	/	/	
207	(+)-Hyperzewalsin B	Plant	<i>hypericum przewalskii maxim</i>	LPS-induced B-cell proliferation	7.36 $\mu$ M	/	/	[78]
208	(-)-hyperzewalsin B				7.14 $\mu$ M	/	/	
209	Hyperzewalsin E				7.2 $\mu$ M	/	/	
210	Lupulone D				6.61 $\mu$ M	/	/	

211	8- <i>O</i> -methyl mycophenolic acid			/		4.21 $\mu$ M	
212	3-hydroxy mycophenolic acid			/		1.23 $\mu$ M	
213	6-(5-carboxy-3-methylpent-2-enyl)-7-hydroxy-3,5-dimethoxy-4-methylphthalan-1-one			/		2.76 $\mu$ M	
214	6-(5-methoxycarbonyl-3-methylpent-2-enyl)-3,7-dihydroxy-5-methoxy-4-methylphthalan-1-one	Fungi	<i>Penicillium bialowiezense</i>	/		9.12 $\mu$ M	
215	6-(3-carboxybutyl)-7-hydroxy-5-methoxy-4-methylphthalan-1-one			/		>40 $\mu$ M	
216	6-[5-(2,3-dihydroxy-1-carboxyglyceride)-3-methylpent-2-enyl]-7-hydroxy-5-methoxy-4-methylphthalan-1-one			/		19.65 $\mu$ M	[79]
217	6-[5-(1-carboxy-4- <i>N</i> -carboxylate)-3-methylpent-2-enyl]-7-hydroxy-5-methoxy-4-methylphthalan-1-one	Fungi	<i>Penicillium bialowiezense</i>	/		24.58 $\mu$ M	
218	<i>N</i> -mycophenoyl-L-valine			/		30.56 $\mu$ M	
219	<i>N</i> -mycophenoyl-L-phenylalanine			/		>40 $\mu$ M	
220	<i>N</i> -mycophenoyl-L-alanine			/		>40 $\mu$ M	

221	Hyperformitin A				9.7 $\mu$ M		/	
222	Hyperformitin B				>10 $\mu$ M		/	
223	Hyperformitin C				4.3 $\mu$ M		/	
224	Hyperformitin D				9.3 $\mu$ M		/	
225	Hyperformitin E	Plant	<i>Hypericum perforatum</i>	LPS-Induced Murine B Cell Proliferation	4.1 $\mu$ M	/	/	[80]
226	Hyperformitin G				9.2 $\mu$ M		/	
227	Hyperformitin H				>10 $\mu$ M		/	
228	Hyperformitin J				>10 $\mu$ M		/	
229	Hyperformitin K				8.8 $\mu$ M		/	
230	Hyperformitin L				>10 $\mu$ M		/	
231	Hyperformitin M				>10 $\mu$ M		/	
232	Przewalcyrone C	Plant	<i>Hypericum przewalskii</i> Maxim	anti-CD3/anti-CD28 stimulated spleen cells	5.01 $\mu$ M	/	/	[81]
233	Przewalcyrone D				5.26 $\mu$ M		/	
234	Cumilcinol E	Plant	<i>Hypericum wilsonii</i>	ConA-induced T-cell proliferation	4.803 $\mu$ M	/	/	[82]

**Table S7.** Compounds 235–262 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
235	Jaceosidin	Plant	<i>Artemisia argyi</i>	LPS stimulated in BV-2 microglial cells	1.9 $\mu$ M	/	/	[83]
236	Eupatilin				4 $\mu$ M	/	/	
237	Tsaokonol A	Plant	<i>Amomum tsao-ko</i>	against LPS-induced RAW 264.7 macrophages	16.2 $\mu$ M	/	/	[28]
238	Tsaokonol B				14 $\mu$ M		/	
239	Tsaokonol C				10.6 $\mu$ M		/	
240	Tsaokonol D				13.5 $\mu$ M		/	
241	Tsaokonol E				41.5 $\mu$ M		/	
242	Tsaokonol F				39.2 $\mu$ M		/	
243	Tsaokonol G				26.1 $\mu$ M		/	
244	Tsaokonol H				28.7 $\mu$ M		/	
245	Tsaokonol I				30.6 $\mu$ M		/	
246	Tsaokonol J				13.5 $\mu$ M		/	
247	4',5'-dihydroxy-5,7-dimethoxy-6-(3-methylbut-2-enyl)-coumaronochromone	Plant	<i>Campylotropis hirtella</i>	ConA-induced T-cell proliferation	0.28 $\mu$ M	LPS-induced B-cell proliferation	1.55 $\mu$ M	[84]
248	6,3'-di(3-hydroxy-3-methylbutyl)-5,7,2'-4'-tetrahydroxyisoflavanone				79.13 $\mu$ M		29.12 $\mu$ M	
249	3(R)-6,3'-di(3-hydroxy-3-methylbutyl)-2'-methoxyl-5,7,4'-trihydroxyisoflavanone				18.12 $\mu$ M		6.66 $\mu$ M	
250	Hydroisoflavone C				53.16 $\mu$ M		25.76 $\mu$ M	

251	3-(1',4'-dihydroxycyclohexyl)-6-geranyl-5,7,-dihydroxyisoflavone				3.25 $\mu\text{M}$		2.68 $\mu\text{M}$	
252	5,7,4'-trihydroxy-3'-[6,7-dihydroxy-3,7-dimethyl-2( <i>E</i> )-octenyl] isoflavone	Plant	<i>Campylotropis hirtella</i>	ConA-induced T-cell proliferation	4.52 $\mu\text{M}$	LPS-induced B-cell proliferation	2.38 $\mu\text{M}$	[84]
253	2R,3R-3'-[7-hydroxy-3,7-dimethyl-2( <i>E</i> )-octenyl]-2,3-trans-5,7,4'-trihydroxy-flavonol				4.34 $\mu\text{M}$		4.82 $\mu\text{M}$	
254	3''',4',4''',7-tetrahydroxy-3''',5-dimethoxy-3- <i>O</i> - $\beta$ -D-glucopyranosyl-8-isopentenol-8'''-prenyl-(3'→7'')-biflavonoid				16.83 $\mu\text{M}$		/	
255	3''',4'''-dihydroxy-5-methoxy-3- <i>O</i> - $\beta$ -D-glucopyranosyl-7,8-(12,13-dimethylchromene)-9'''-isopropyl-(3'→7'')-biflavonoid	Plant	<i>Citrus medica L. var.</i>	ConA-induced T-cell proliferation	18.95 $\mu\text{M}$	/	/	[85]
256	3''',4'''-dihydroxy-3''',5,5'''-trimethoxy-3- <i>O</i> - $\beta$ -D-glucopyranosyl-7,8-isopropylpenentenone-9'''-carbonyl-(3'→7'')-biflavonoid				20.28 $\mu\text{M}$		/	
257	Amentoflavone 7''- <i>O</i> - $\beta$ -D-glucopyranoside				50.90 $\mu\text{M}$		/	

258	2-(4'-hydroxy-3'-methoxyphenyl)-3-hydroxy-12,13-dimethylchromene-3",4",5"-129-trimethoxyphenyl-8"-(4",5"-dimethylallyl)-dipyrano-xanthene-4,9"-dione			41.82 $\mu$ M	/		
259	2-(4'-hydroxy-3'-methoxyphenyl)-3-hydroxy-7,8-furan-10-isopropanol-1",5"-144 isopropylpentenone-pyranochromene-2",4,6"-trione	Plant	<i>Hippophae rhamnoides</i> L.	ConA-induced T-cell proliferation	19.42 $\mu$ M	/	[86]
260	2-(4'-hydroxy-3',5'-dimethoxyphenyl)-3-hydroxy-12,13-dimethylchromene-1491",5"-isopropylpentenone-pyranochromene-2",4,6"-trione				20.19 $\mu$ M	/	
261	Cinchonain A				48.05 $\mu$ M	/	
262	Cinchonain B				46.91 $\mu$ M	/	

**Table S8.** Compounds 263–270 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
263	Quadristerol B				7.43 $\mu$ M		/	
264	Quadristerol C	Fungi	<i>Aspergillus quadrilineata</i>	ConA-induced T-cell proliferation	3.95 $\mu$ M	LPS-induced B-cell proliferation	/	[87]
265	Quadristerol D				/		10.96 $\mu$ M	
266	Quadristerol E				/		7.47 $\mu$ M	
267	Atracynoside A	Plant	<i>Cynanchum atratum</i>	ConA-induced T-cell proliferation	3.3 $\mu$ M	/	/	[88]
268	Atracynoside B				7 $\mu$ M		/	
269	Atracynoside C				6.7 $\mu$ M		/	
270	Atracynoside E				59.3 $\mu$ M		/	

**Table S9.** Compounds 271–324 with Immunosuppressive Effects.

Number	Compounds	Type	Source	Model 1	Activities IC <sub>50</sub>	Model 2	Activities IC <sub>50</sub>	Reference
271	(+)-Adprepyrone B	Fungi	<i>Talaromyces adpressu</i>	ConA-induced T-cell proliferation	11.6 $\mu$ M	/	/	[89]
272	(+)-Adprepyrone D				8.9 $\mu$ M		/	
273	(–)-Adprepyrone D				9.6 $\mu$ M		/	
274	(+)-Adprepyrone E				16.8 $\mu$ M		/	
275	(–)-Adprepyrone E				16.8 $\mu$ M		/	
276	6-[( <i>E</i> )-3-Hydroxyprop-1-enyl]-4-methoxy-5-methyl-2-pyrone				19.8 $\mu$ M		/	
277	Pinoresinol	Plant	<i>Epigynum cochinchinensis</i>	ConA-induced T-cell proliferation	12.5 $\mu$ M	/	/	[90]
278	Syringaresinol				50 $\mu$ M		/	
279	Sydoxanthone B	Fungi	<i>Aspergillus sydowii</i>	ConA-induced T-cell proliferation	22.53 $\mu$ M	LPS-induced B-cells proliferation	15.3 $\mu$ M	[91]
280	13- <i>O</i> -acetylsydowinin B				172.7 $\mu$ M		/	
281	Diaporchromone A	Plant	<i>Rhizophora mangle</i>	ConA-induced T-cell proliferation	34 $\mu$ M	LPS-induced B-cells proliferation	117 $\mu$ M	[92]
282	Peniphenone	Fungi	<i>Penicillium sp.</i> ZJ-SY2	ConA-induced T-cell proliferation	8.1 $\mu$ M	LPS-induced B-cells proliferation	9.3 $\mu$ M	[93]

283	Methyl peniphenone				17.5 $\mu$ M		23.7 $\mu$ M	
284	Conioxanthone A				8.2 $\mu$ M		7.5 $\mu$ M	
285	Methyl-8-hydroxy-6-methyl-9-oxo-9H-xanthene -1-carboxylate				25.7 $\mu$ M		26.4 $\mu$ M	
286	Pinselín	Fungi	<i>Penicillium sp.</i> ZJ-SY2	ConA-induced T-cell proliferation	5.9 $\mu$ M	B-cells proliferation	7.5 $\mu$ M	[93]
287	Sydowinin B				19.2 $\mu$ M		20.8 $\mu$ M	
288	Sydowinin A				6.5 $\mu$ M		7.1 $\mu$ M	
289	Remisporine B				30.1 $\mu$ M		32.4 $\mu$ M	
290	Epiremispörine B				30.8 $\mu$ M		31.2 $\mu$ M	
291	Pestaphilone A				9.36 $\mu$ M		/	
292	Pestaphilone B				21.78 $\mu$ M		/	
293	Pestaphilone C	Fungi	<i>Pestalotiopsis</i> <i>oxyanthi</i>	murine T lymphocyte proliferation stimulated by Con A	17.94 $\mu$ M	/	/	[94]
294	Pestaphilone D				19.72 $\mu$ M		/	
295	Pestaphilone E				25.64 $\mu$ M		/	
296	Pestaphilone F				35.21 $\mu$ M		/	
297	Podospin A				10.6 $\mu$ M		10.3 $\mu$ M	
298	Podospin E				25.1 $\mu$ M		27.7 $\mu$ M	
299	Podospin J				18.8 $\mu$ M		21.9 $\mu$ M	
300	Podospin L				16.5 $\mu$ M		14.6 $\mu$ M	
301	LL-Z1640-1	Fungi	<i>Podospora sp</i>	ConA-induced T cell proliferation	7.4 $\mu$ M	LPS-induced B cell proliferation	6.4 $\mu$ M	[95]
302	(5E)-7-oxozeaenol				6.0 $\mu$ M		6.2 $\mu$ M	
303	Cochliomycin D				11.4 $\mu$ M		6.8 $\mu$ M	
304	Cochliomycin E				24.1 $\mu$ M		29.1 $\mu$ M	
305	Cochliomycin F				15.2 $\mu$ M		11.8 $\mu$ M	

306	Dihydrohypothenycin	Fungi	<i>Podospora</i> sp	ConA-induced T cell proliferation	8.1 $\mu$ M		8.5 $\mu$ M	[95]
307	Aigialomycin D				16.3 $\mu$ M		18.4 $\mu$ M	
308	1-naphthaleneheptanoic acid				16.51 $\mu$ M	/	/	
309	Monacolin K	Fungi	<i>Tripterygium wilfordii</i> .	anti-CD3/anti-CD28 stimulated spleen cells	8.75 $\mu$ M		/	[96]
310	Monacolin L				5.3 $\mu$ M		/	
311	Monacolin J				6.74 $\mu$ M		/	
312	Curtachalasin F				70.9 $\mu$ M		2.4 $\mu$ M	
313	Curtachalasin H				28.5 $\mu$ M		72.6 $\mu$ M	
314	Curtachalasin I				13.3 $\mu$ M		72.6 $\mu$ M	
315	Curtachalasin J				21.0 $\mu$ M		/	
316	Curtachalasin M	Fungi	<i>Xylaria cf. curta</i>	ConA-induced T-cell proliferation	31.1 $\mu$ M	LPS-induced B-cell proliferation	/	[75]
317	Curtachalasin N				62.5 $\mu$ M		/	
318	Curtachalasin O				12.6 $\mu$ M		/	
319	Curtachalasin P				16.5 $\mu$ M		72.3 $\mu$ M	
320	urtachalasins A				29.0 $\mu$ M		/	
321	Curtachalasins B				39.7 $\mu$ M		35.4 $\mu$ M	
322	Curtachalasins E				22.4 $\mu$ M		88.0 $\mu$ M	
323	Ivorenolide B	Plant	<i>Khaya ivorensis</i>	LPS-induced B-cell proliferation	7.2 $\mu$ M	/	/	[97]
324	Efophylin B	Fungi	<i>Streptomyces malaysiensis</i>	ConA-induced T-cell proliferation	24.6 $\mu$ M	/	/	[98]