

Table S1. The immunomodulatory acting sites and mechanisms/pathways of MFPPs.

Acting sites	Sources	Names	Models	Doses	Main Effects	Mechanisms/Pathways	Toxicity	Ref.
Macrophage	<i>Caulerpa chemnitzia</i>	CCP	RAW264.7 macrophages	10, 30, 50, 80 µg/mL	Increases cell viability, NO production, and secretion of IL-6 and TNF-α	NF-κB signaling pathway and arachidonic acid metabolism pathway	No cytotoxicity	[6]
	<i>Porphyra haitanensis</i>	PHP	Hydrocortisone-induced immunosuppressed BALB/c mice	90 and 270 mg/kg/day	Enhanced macrophage phagocytosis and carbon clearance; increased ACP and LDH activities	TLR4/MyD88/NF-κB signaling pathway	Not reported	[80]
NK cell	<i>Strongylocentrotus nudus</i>	SEP	<i>In vitro</i> : NK-92 cells; <i>In vivo</i> : BxPC-3 and SW1990 nude mice	<i>In vitro</i> : 50-200 µg/mL; <i>In vivo</i> : 10-40 mg/kg	Enhanced NK cell cytotoxicity and activation; inhibited pancreatic cancer growth via NK cells	TLR4/MAPKs/NF-κB signaling pathway; upregulation of NKG2D/MICA	No significant toxicity; body weight unaffected <i>in vivo</i>	[87]
	<i>Codium fragile</i>	CFP	<i>In vitro</i> : NK cells; <i>In vivo</i> : C57BL/6 and BALB/c mice	<i>In vivo</i> : 50 mg/kg; <i>In vitro</i> : 100 µg/mL	NK cell activation; upregulation of CD69; enhanced production of IFN-γ, perforin, and granzyme B; prevented tumor infiltration	Dependent on IL-12 and DCs; potential roles of CR3 and TLR2	No significant body weight changes	[86]

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Complement system	<i>Kjellmaniella crassifolia</i>	KCA, KCW	1:10-diluted normal human serum	KCA/KCW plateaued at 10 µg/mL in the classical-pathway assay; AP50: 4.83 µg/mL (KCA) and 18.60 µg/mL (KCW)	Inhibited classical- and alternative-pathway-mediated hemolysis	Sulfate-dependent anti-complementary activity; lower molecular weight weakened the activity	Not reported	[93]
	<i>Chondrus armatus</i>	λ/μ/v-carrageenan	Normal human serum	0.002-2 mg/mL	Reduced C4 deposition on mannan-coated wells by approximately 30%	Sulfation-dependent reduction of C4 deposition; possible interference with MBL and/or MASP-2	Not reported	[94]
T cell	<i>Undaria pinnatifida</i>	Low Molecular Weight Fucoidan (LMWF)	<i>In vitro</i> : Mouse bone marrow-derived dendritic cells (BMDCs) <i>In vivo</i> : ICR mice	<i>In vitro</i> : 20-100 µg/mL <i>In vivo</i> : 20-80 mg/kg	Promotes allogeneic CD4 ⁺ and CD8 ⁺ T cell proliferation; enhances IFN-γ production	Activates TLR4-mediated MAPK (ERK, JNK, p38) and NF-κB pathways in DCs	No toxicity observed in liver/kidney function tests	[96]

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B cell	<i>Saccharina japonica</i>	SJP	<i>In vitro</i> : RAW 264.7 macrophages <i>In vivo</i> : BALB/c mice (CTX-induced immunosuppression)	<i>In vitro</i> : 0.06-100 µg/mL <i>In vivo</i> : 50-200 mg/kg	Improves CD4+ and CD8+ T cell populations in spleen Increases serum IL-6 and IL-12 levels	Activates macrophages via Dectin-1, SR, CD14 receptors and MAPK/NF-κB pathways	No adverse effects on body weight or organ indices	[112]
	<i>Ulva conglobata</i>	UCP	BALB/c mice (immunosuppressed by cyclophosphamide)	15, 30, 60 mg/kg	Increased the levels of serum immunoglobulins IgG, IgE, and IgM in a dose-dependent manner	Not reported	No reported toxicity	[100]
	<i>Caulerpa lentillifera</i>	CLP-80	BALB/c mice	150 mg/kg/day for 21 days	Increased serum IgA and IgG levels	Promotion of B-lymphocyte activity	The high dose showed potential toxicity	[103]