

Supplementary Table S1: Toxins from dinoflagellate and their different potential therapeutic applications

Sl. No.	Toxin name	Source	Therapeutic action	References
1	Saxitoxin (STXs)	<i>Alexandrium minutum</i> , <i>Alexandrium tamarense</i> , <i>Alexandrium catenella</i> , <i>Gymnodinium. catenatum</i> , and <i>Pyrodinium bahamense</i> ,	Displayed <i>in vitro</i> antifungal, antibacterial, antialgal and antiprotozoal activity	[88]
2	Gonyautoxins (GTX)	<i>Amphydinium</i>	Used as a pain reliever	[73]
	GTX2 and GTX3	<i>Amphydinium</i>	Chronic tension-type headaches	[74]
3	Tetrodotoxin (TTX)	<i>Alexandrium tamarense</i>	Reduce narcotic cravings in laboratory animals and is being employed in drug addiction. Treatment of heroin addiction withdrawal	[122]
4	Okadaic acid (OA)	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum belezeanum</i> , <i>Porocentrum mascul</i>	Cytotoxic effects in numerous cell types, including intestinal cells, blood cells, brain cells, lung cells, and hepatic cells,	[43]
4	Okadaic acid (OA)	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Act as anti-tumor agents on breast cancer cells as it inhibits protein phosphatase 2A	[42]
5	Okadaic acid (OA)	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Act as typical antipsychotic medications in the treatment of cognitive impairment and neuropathological alterations in schizophrenia and other neurodegenerative illnesses because of its tumor-promoting and cytotoxic actions	[75]
6	Okadaic acid (OA)	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Alzheimer's disease and other neurodegenerative illnesses linked to memory loss	[68]
7	Okadaic acid (OA)	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Diabetes, AIDS, and cancer to reveal numerous pathways related to these diseases	[76]
8	Okadaic acid (OA)	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Immunoregulatory potential, since it causes T-cell receptor expression to be	[128]

				downregulated, affecting T-cell responsiveness and, as a result, immunological response	
9	Okadaic acid (OA)	acid	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Triggers an inflammatory response in HL-60 human cells by significantly increasing interleukin 8 (IL-8) levels	[44]
10	Okadaic acid (OA)	acid	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Increase the activity of hypoxia-inducible factor-1 (HIF-1) a protein closely linked to vascular endothelial growth factor in human endothelial cells	[45]
11	Okadaic acid (OA)	acid	<i>Porocentrum lima</i> , <i>Porocentrum cuncavum</i> , <i>Porocentrum</i>	Fungicidal properties, specifically the capacity to suppress <i>Candida albicans</i> growth	[79]
12	Amphidinolides and colopsinols		<i>Amphidinium</i>	Exhibit powerful anticancer effects via inhibition of cancer cell lines	[129]
13	Amphidinolides and colopsinols		<i>Amphidinium</i>	Showed high cytotoxicity against murine lymphoma L1210 and human epidermoid carcinoma KB cells	[46]
14	Caribenolide I		<i>Amphidinium</i>	Showed high cytotoxicity in human colon tumor cell line HCT 116 and its drug-resistant variation HCT 116/VM 46	[47]
15	Caribenolide I		<i>Amphidinium</i>	Showed efficacious <i>in vivo</i> against the mouse tumor P388	[48]
16	Gonyautoxins		<i>Amphidinium</i>	It has been employed in clinical practice for anal sphincter infiltrations	[73]
17	Goniodomin-A		<i>Goniodoma pseudogoniaulax</i>	Prevent angiogenesis by decreasing endothelial cell migration and tube formation caused by basic fibroblast growth factor (bFGF)	[124]
18	Gymnocin-A		<i>Gymnodinium mikimotoi</i>	Displayed cytotoxic to P388 murine leukemia cells	[49]
19	Yessotoxins (YTXs)		<i>Protoceratium reticulatum</i> , <i>Lingulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Impair the E-cadherin–catenin system selectively in epithelial cells, thus jeopardizing Ecadherin's tumor-suppressive effects	[50]

20	Yessotoxins (YTXs)	<i>Protoceratium cf. reticulatum</i>	Displayed significant cytotoxic effects	[120]
21	Protoceratins I, II, III, and IV	<i>Protoceratium cf. reticulatum</i>	Displayed cytotoxicity selectively against human cancer cell lines with mean IC ₅₀ values of less than 0.0005 M	[53]
22	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Displayed multiple biological apoptotic pathways	[131]
23	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	In BC3H1 myoblast cells, primary cortical neurons, and glioma cells, it also causes non-apoptotic cell death	[51]
24	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Modulates caspase protein activation via permeability transition through mitochondria and alteration of cytoskeleton (viz. selective disruption of F-actin microfilaments)	[133,134]
25	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Inhibits the growth of melanoma tumor cells in mice cells <i>in vivo</i> , with minimal damage	[52]
26	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Impair immunological function by reducing phagocytic activity in the J774 cell line and increasing cytokine expression in J774 phagocyte mammalian cells	[133]
27	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Control the immunological impact on T-lymphocyte EL-4 cells via reversible T-cell receptor complex down-regulation	[128]
28	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Used to treat Alzheimer's disease by lowering the levels of t- and β -amyloid, two insoluble formations found in the brain that are responsible for the illness's onset	[69]
29	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Lin-gulodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Treatment/prevention of lipid and glucose metabolism-related disorders in glioma cells, as well as pancreatic and liver transcriptional abnormalities	[135]

30	YTX and its analogues	<i>Protoceratium reticulatum</i> , <i>Leptodinium polyedra</i> , and <i>Gonyaulax spinifera</i>	Minor role as anti-allergenic and -asthmatic drug	[83]
31	Pectenotoxin (PTX)	<i>D. fortii</i> , <i>D. acuta</i> , <i>D. tripus</i> , <i>D. acuminata</i> , <i>D. caudate</i> , <i>D. rotundata</i> , and <i>D. norvegica</i>	Strong cytotoxic against various human cancer cell lines such as lung, colon, and breast cancer cells	[54]
32	Pectenotoxin (PTX)	<i>D. fortii</i> , <i>D. acuta</i> , <i>D. tripus</i> , <i>D. acuminata</i> , <i>D. caudate</i> , <i>D. rotundata</i> , and <i>D. norvegica</i>	Act as potential chemotherapeutic treatment for p53-deficient malignancies	[138]
33	Ciguatoxin (CTX)	<i>Gambierdiscus toxicus</i>	Increased muscular contraction, particularly in cardiac tissue, and excessive fluid secretion by gastrointestinal cells	[55,56]
34	Maitotoxin (MTX)	<i>Gambierdiscus toxicus</i> , <i>G. australes</i> , and <i>Gambierdiscus pacificus</i>	Displayed innate immune responses and inflammation	[144,150]
35	Maitotoxin (MTX)	<i>Gambierdiscus toxicus</i> , <i>G. australes</i> , and <i>Gambierdiscus pacificus</i>	Promotes the synthesis and secretion of nerve growth factor by activating voltage-insensitive Ca ²⁺ channels in C6-BU-1 glioma cells	[151]
36	Brevetoxin (BTX)	<i>Karenia brevis</i> (formerly known as <i>Gymnodinium breve</i> or <i>Ptychodiscus brevis</i>)	Reduces respiratory irritation symptoms such as cough, irritability of the nose, congestion, bronchoconstriction, and/or asthma attacks in people	[156]
37	Brevetoxin (BTX)	<i>Karenia brevis</i> (formerly known as <i>Gymnodinium breve</i> or <i>Ptychodiscus brevis</i>)	Alters immunological response in alveolar macrophage cells by increasing cytokines (such as TNF- and IL-2) involved in immune cell activation, which reduces phagocytosis activity and plays a key role in allergic inflammation in pulmonary tissue	[57,157,158]
38	Brevetoxin (BTX)	<i>Karenia brevis</i> (formerly known as <i>Gymnodinium breve</i> or <i>Ptychodiscus brevis</i>)	Displayed a dose-dependent effect on cell growth, causes cell death via an apoptotic mechanism, and has genotoxic properties	[57,58]
39	BTX-2	<i>Karenia brevis</i> (formerly known as <i>Gymnodinium breve</i> or <i>Ptychodiscus brevis</i>)	It can improve neuronal plasticity and treatments for restoring brain function	[84]

			following a stroke or other traumatic brain damage	
40	Zooxanthella-toxins (ZTs) A, B, and C	<i>Symbiodinium</i> sp.	Vasoconstrictive activity	[161]
41	Symbioimine	<i>Symbiodinium</i> sp.	Displayed an antiresorptive medication that could be used to prevent and treat osteoporosis in postmenopausal women	[85]
42	Symbioimine	<i>Symbiodinium</i> sp.	May also be useful in the development of new nonsteroid anti-inflammatory medicines for the treatment of cyclooxygenase-2-related disorders	[86]
43	Palytoxin (PLTX)	<i>Ostreopsis siamensis</i> , <i>Ostreopsis mascarenensis</i> , <i>Ostreopsis lenticularis</i> , <i>Ostreopsis ovata</i> , <i>Ostreopsis fattorussoi</i>	Remarkable biological activity including a wide spectrum of pharmacological effects	[162,163]
44	Ostreocin-D	<i>Ostreopsis siamensis</i> , <i>Ostreopsis mascarenensis</i> , <i>Ostreopsis lenticularis</i> , <i>Ostreopsis ovata</i> , <i>Ostreopsis fattorussoi</i>	Modulates neurotransmitters (norepinephrine and/or acetylcholine), and activates pro-inflammatory signaling cascades such as release of histamine and prostaglandin-E2	[164]
45	PLTX and Ostreocin-D	<i>Ostreopsis siamensis</i> , <i>Ostreopsis mascarenensis</i> , <i>Ostreopsis lenticularis</i> , <i>Ostreopsis ovata</i> , <i>Ostreopsis fattorussoi</i>	Modulates cytoskeleton distortion and dynamics in intestinal and neuroblastoma cells and also can significantly reduce cytotoxicity	[60,61]
46	PLTX	<i>Palythoa clavata</i> polyps	Suitable for therapeutic use against lymphoblastic or myelogenous leukemia	[59]
47	Gambierol	<i>Gambierdiscus toxicus</i>	Beneficial to patients of brain injury	[87]
48	Gambierol	<i>Gambierdiscus toxicus</i>	T-cell-mediated autoimmune disorders	[77,78]
49	Gambierol	<i>Gambierdiscus toxicus</i>	Used against multiple sclerosis, type 1 diabetes, and rheumatoid arthritis	[77,78]
50	Gambierol	<i>Gambierdiscus toxicus</i>	Reducing β -amyloid and/or tau hyperphosphorylation in Alzheimer's disease both <i>in vitro</i> and <i>in vivo</i>	[70]

51	Azaspiracid (AZA)	<i>Azadinium spinosum</i> , <i>Azadinium poporum</i> , and <i>Azadinium dexteroporum</i>	Cytotoxicity against a variety of human cell types, as well as the capacity to modify cell shape and cytoskeleton structure, particularly in the E-cadherin system	[136,175,176]
52	Azaspiracid (AZA)	<i>Azadinium spinosum</i> , <i>Azadinium poporum</i> , and <i>Azadinium dexteroporum</i>	Effective modulator of intracellular cAMP and calcium levels, as well as a potent activator of c-Jun-N-terminal kinase (JNK) and caspases, both of which are involved in stress-signaling pathways such as cell damage, apoptosis, and cytoskeleton regulation	[177-179]
53	Azaspiracid (AZA)	<i>Azadinium spinosum</i> , <i>Azadinium poporum</i> , and <i>Azadinium dexteroporum</i>	Lowers cell cholesterol levels, especially in T-lymphocyte cells	[62,63]
54	Gymnocin-A (GYMA)	<i>Gymnodinium mikimotoi</i>	Extremely toxic to P388 murine leukemia cells.	[64]
55	Karlotoxin (KmTx)	<i>Karlodinium veneficum</i>	Displayed variety of actions, including haemolytic, cytotoxic, ichthyotoxic, and antifungal	[65,80-82]
56	Karlotoxin (KmTx)	<i>Karlodinium veneficum</i>	Used to treat a variety of human diseases, including coronary heart disease (CHD)	[65,66]
57	Karlotoxin (KmTx)	<i>Karlodinium veneficum</i>	Used as new chemotherapeutic drug to control cancer in various solid tumor lines, such as breast and prostate cancer cells, by inducing cell death through cholesterol depletion	[65,66]
58	Spirolide (SPX)	<i>Alexandrium ostenfeldii</i> /peruvianum and <i>Karenia selliformes</i>	Cytotoxic effects	[186]
59	Combination of GYM and OA		Employed therapeutically to boost anti-cancer effects by inducing tumor cell toxicity and acting as chemotherapeutic drugs	[67]
60	GYM		More sensitive to apoptotic stimuli. Neuro2a neuroblastoma cell line	[67]

61	GYM	Lowering β -amyloid levels and tau phosphorylation, which could help with the treatment of degenerative illnesses	[71]
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