

Table 2. Immunomodulatory Non-Glucan Extracts: Oral Animal Studies

Extract	Source	Animal	Oral dose/day	Duration	Treatment	Significant effects	Reference
Fucoidans	<i>Cladosiphon okamuranus Tokida</i>	8-week ♀ BALB/c mice, 10/group	0.05% w/w of diet	56 days	DSS-induced UC	↓ disease activity index and myeloperoxidase activity; ↓ # of B220-positive colonic B cells; ↓ colonic MLN IFN- γ and IL-6 and ↑ IL-10 and TGF- β ; ↓ colonic IgG; ↓ colonic epithelial cell IL-6, TNF- α , and TLR4 mRNA expression	[49]
		<i>Undaria pinnatifida</i>	5-week ♀ BALB/c mice (10-12/group)	5 mg, days 1-14 or 7-14	2 weeks	Injected HSV into cornea day 7	↓ facial herpetic lesions; ↑ survival, particularly in pre-treated animals
	10 mg		1 week	Administered 5-fluorouracil	↑ plasma NK cell activity		
	0.1 or 0.5 mg		3 weeks	Injected SC HSV	↑ cytotoxic splenic T lymphocyte activity		
	6-week ♂ ddY mice (5/group)	50, 100, 200 400 or 500 mg/kg days 1-28	3 weeks	Injected with Ehrlich carcinoma in back day 14	200-500 mg/kg ↓ tumor growth	[116]	
6-week ♂ BALB/c mice (8/group)	40 mg/kg alternating days 7-19	19 days	Injected IP Meth A fibrosarcoma day 1	↓ tumor growth			
Furanose (COLD-FX®)	<i>Panax quinquefolium</i>	Weanling ♂ SD rats (10/group)	450 or 900 mg/kg in food	1 week	Healthy animals	Both doses ↑ spleen IL-2 and IFN- γ production following ConA or LPS stimulation; ↓ proportion of total MLN and Peyer's patch CD3+ cells & activated T cells; high dose ↑ spleen cell IL-1 β production following 48 h ConA stimulation.	[33]
Galactomannan (partially hydrolyzed guar gum)	<i>Cyamopsis tetragonolobus</i>	10-week ♀ BALB/c mice, 11-15/group	5% of diet	3 weeks	DSS-induced UC at beginning of week 3	↓ disease activity index scores, ↓ colonic mucosal myeloperoxidase activity & lipid peroxidation; ↓ colonic TNF- α protein levels & mRNA expression up regulated by DSS exposure	[50]
Galactomannans (guar gum)		8-month- SD rats, 5/group	5% of diet	3 weeks	Older animals	↓ serum IgG; ↑ MLN lymphocyte IgA, IgM and IgG production	[36]
Glucomannan (KS-2)	<i>Lentinula edodes</i>	DD1 mice (10-20/group)	140 mg/kg days 2-13	50 days	Injected IP Ehrlich ascites tumor cells day 1	↑ survival	[84]

			0.1, 1, 10, or 100 mg/kg dose days 2-13	100 days	Injected Sarcoma-180 tumor cells day 1	1, 10, and 100 mg/kg doses ↑ survival	
Heteroglycan (ATOM)	<i>A. subrufescens</i>	Mice (10/group): 1) 5-week ♂ Swiss/NIH; 6 week- ♀ DS mice; 3) 8-week ♀ BALB/c nude; 4) 5-week C3H/HcN	100 or 300 mg/kg days 2-11	8 weeks	Implanted SC 1) Sarcoma-180, 2) Shionogi carcinoma 42, 3) Meth A fibrosarcoma, or 4) Ehrlich ascites carcinoma cells	Both doses ↓ Sarcoma-180 tumor size at 4 weeks & ↑ survival; 300 mg/kg ↑ peritoneal macrophage and C3-positive cells; 300 mg/kg ↓ Shionogi and Meth A tumor sizes at 4 weeks. Both doses ↑ survival of Ehrlich ascites mice	[93]
Heteroglycan (LBP _{3p})	<i>Lycium barbarum</i>	♂ Kunming mice (10/group)	5, 10 or 20 mg/kg	10 days	Injected SC Sarcoma-180 cells	5 & 10 mg/kg ↑ thymus index; all doses ↓ weight, ↓ lipid peroxidation in serum, liver and spleen & ↑ spleen lymphocyte proliferation, cytotoxic T cell activity, IL-2 mRNA	[91]
Heteroglycan (PNPS-1)	<i>Pholiota nameko</i>	SD rats (5/group)	100, 200 or 400 mg/kg days 1-8	8 days	Implanted SC cotton pellets in scapular region day 1	↓ granuloma growth positively correlated with dose: 11%, 18% and 44%, respectively	[55]
Heteroglycan (PG101)	<i>Lentinus lepideus</i>	8-10-week ♀ BALB/c mice (3/group)	10 mg	24 days	6 Gy gamma irradiation	↑ colony forming cells, granulocyte CFUs/Mφ, erythroid burst-forming units, and myeloid progenitor cells in bone marrow; induced proliferation of granulocyte progenitor cells in bone marrow; ↑ serum levels of GM-CSF, IL-6, IL-1β	[92]
Mixed polysaccharides (Ambrotose [®] or Advanced Ambrotose [®] powders)	<i>Aloe barbadensis</i> , <i>Larix</i> spp, and other plant polysaccharides	♂ SD rats (10/group)	37.7 or 377 mg/kg Ambrotose [®] powder or 57.4 or 574 mg/kg Advanced Ambrotose [®] powder	2 weeks	5% DSS in drinking water beginning day 6	574 mg/kg Advanced Ambrotose powder ↓ DAI scores; 377 mg/kg Ambrotose complex & both doses Advanced Ambrotose powder ↑ colon length and ↓ blood monocyte count	[52]
Pectin	<i>Pyrus pyrifolia</i>	6-8-week ♂ BALB/c mice (11/group)	100 µg days 1-7	22 days	Injected IP OVA day 7, provoked with OVA aerosol day 21	bronchial fluid: ↓ IFN-γ & ↑ IL-5; splenic cells: ↑ IFN-γ, ↓ IL-5; normalized pulmonary histopathological changes; ↓ serum IgE	[54]
Pectins (bupleurum 2IIc)	<i>Bupleurum falcatum</i>	6-8-week ♀ specific-pathogen-free C3H/HeJ mice	250 mg/kg	1 week	Healthy animals	↑ spleen cell proliferation	[35]
Pectins (highly methoxylated)	<i>Malus</i> spp.	8-month- SD rats (5/group)	5% of diet vs. cellulose control	3 weeks	Older animals	↑ MLN lymphocyte IgA & IgG	[36]

Pectins	Citrus spp.	5-week ♀ F344 rats (30/group)	15% of diet	34 weeks	Injected SC AOM once a week, weeks 4-14	↓ colon tumor incidence	[86]
	<i>Malus</i> spp.	5-week ♀ BALB/c mice (6/group)	5% of diet	2 weeks	Healthy animals	↑ fecal IgA and MLN CD4+/CD8+ T lymphocyte ratio & IL-2 & IFN-γ secretion by ConA-stimulated MLN lymphocytes	[51]
		5-week ♀ BALB/c mice (6/group)	5% of diet days 5- 19 vs. cellulose control	19 days	DSS-induced UC days 1-5	Significantly increased MLN lymphocytes IgA, and significantly decreased IgE; significantly decreased ConA-stimulated IL-4 and IL-10	
		4-week ♂ Donryu rats (20-21/group)	20% of diet	32 weeks	Injected SC AOM once a week, weeks 2-12	↓ colon tumor incidence	[85]
	4-week ♂ Donryu rats (19-20/group)	10 or 20% of diet	32 weeks	Injected SC AOM once a week, weeks 2-12	Both doses ↓ colon tumor incidence; 20% ↓ tumor occupied area & ↓ portal blood and distal colon PGE ₂	[90]	
Pectins (modified)	Citrus spp.	2-4-month BALB/c mice (9-10/group)	0.8 or 1.6 mg/ml drinking water, days 8-20	20 days	Injected SC with 2x2 mm section of human colon-25 tumor on day 1	Both doses ↓ tumor size	[87]
		NCR nu/nu mice (10/group)	1% (w/v) drinking water	16 weeks	Orthotopically injected human breast carcinoma cells (MDA-MB- 435) into mammary fat pad on day 7	↓ tumor growth rate & volume at 7 weeks, lung metastases at 15 weeks, # of blood vessels/tumor at 33 days post-injection	[89]
		NCR nu/nu mice (10/group)	1% (w/v) drinking water	7 weeks	Injected human colon carcinoma cells (LSLi6) into cecum on day 7	↓ tumor weights and metastases to the lymph nodes and liver	
		SD rats (7-8/group)	0.01%, 0.1% or 1.0% wt/vol of drinking water, days 4-30	1 month	Injected SC MAT- LyLu rat prostate cancer cells	0.1% and 1.0% ↓ lung metastases; 1.0% ↓ lymph node disease incidence	[88]