

Table 1. Immunomodulatory Glucan Extracts: Oral Animal Studies

Source	Extract	Animal	Dose/day	Duration of study	Treatment	Effects	Reference
<i>Agaricus (A. blazei) subrufescens</i>	α -1,6 and α -1,4 glucans	8-week ♀ C3H/He mice (5/group)	100 mg/kg IG every 3 days	1 month	Healthy animals	↑ #s splenic T lymphocytes (Thy1.2, CD4+ and CD8+)	[24]
	Aqueous	7-9-week ♂ Balb/cByJ mice (40/group)	1 ml 0.45N, 0.6N, or 3N aqueous extract	2 months		All doses ↑ serum IgG levels, CD3+ T cell populations and PML phagocytic activity	[22]
		7-9-week male Balb/cByJ mice (40/group)	1 ml 0.45N, 0.6N, or 3N aqueous extract	10 weeks	IP injection of OVA at 4 weeks	0.6N and 3N ↑ levels of OVA-specific serum IgG 28 days post-immunization; all doses ↑ delayed-type hypersensitivity and TNF- α secreted from splenocytes at 10 weeks; 0.6N ↑ splenocyte proliferation at 10 weeks	
		5-6 -week ♀ BALB/cHsdOla mice (8/group X 2)	One 200 μ l extract day 1, orogastric intubation	1 week	Injected IP fecal solution day 2	↓ CFU in blood of mice with severe peritonitis & improved overall survival rate in all peritonitis groups	[46]
		6-week BALB/c nu/nu mice (7/group)	2.5 mg extract days 20-41, drinking water	41 days	Injected SC Sp-2 myeloma cells day 1	↓ tumor size & weight after 21 days treatment	[65]
	Aqueous, acid treated	6-week ♀ C57BL/6 mice (10/group)	20, 100 or 500 μ g/ml, drinking water	9 days	Injected IP human ovarian cancer cells day 1	500 μ g/ml ↓ tumor weight	[66]
			20, 100 or 500 μ g/ml, drinking water	3 weeks	Injected IV murine lung cancer (3LL) cells	100 & 500 μ g/ml ↓ #s metastatic tumors	
Aqueous, with 200 ng/day β -glucan	6-week ♀ BALB/c mice (10/group)	200 ng days 5-21	3 weeks	Injected Meth A tumor cells day 1	↓ tumor size & weight	[23]	
			2 weeks	Injected Meth A tumor cells	↑ cytotoxic T lymphocyte activity & spleen cell IFN- α protein		
		300 mg	5 days	Healthy animals	↑ splenic NK cell activity		
<i>Avena</i> spp.	β -glucans (particulate)	6-7 -week ♀ C57BL/6 mice (7/group)	3 mg every 48 h, days 1-3	1 month	Oral <i>E. vermiformis</i> oocytes day 10	↓ <i>E. vermiformis</i> fecal oocyte #s; increased intestinal anti-merozoite IgA; ↓ # of IL-4-secreting MLN cells	[42]
			3 mg on alternating days, days 1-10	22 days	Injected IP <i>Eimeria vermiformis</i> day 10	↓ <i>E. vermiformis</i> fecal oocyte #s; ↑ anti-merozoite intestinal IgA	[43]

	β -glucans (soluble)	4-week ♂ CD-1 mice (24/group)	0.6 mg/ml 68% β -glucan, drinking water	1 month	Resting or exercise-stressed (days 8-10) animals administered HSV-1 IN day 10	↓ morbidity in resting and exercise-stressed animals ; ↓ mortality in exercise-stressed animals; pre-infection, ↑ M ϕ anti-viral resistance in resting and exercise-stressed animals	[38]
			~3.5 mg days 1-10, drinking water		Resting or exercise-stressed (days 5-10) animals administered HSV-1 IN day 10	Pre-infection, ↑ M ϕ antiviral resistance in resting animals	[41]
		4-week ♂ CD-1 mice (10/group)	0.6 mg/ml 68% β -glucan, drinking water	10 days	Resting animals or animals exposed to a bout of fatiguing exercise days 8-10 or moderate exercise days 5-10, injected IP with thioglycollate on day 10	↑ neutrophil mobilization in resting & moderately exercised animals; ↑ neutrophil respiratory burst activity in resting and fatiguing exercised animals	[37]
		4-week ♂ CD-1 mice (19-30/group)	0.8 mg/ml 50% β -glucan, days 1-10, drinking water	1 month	Resting or exercise-stressed (days 8-10) animals administered IN clodronate-filled liposomes to deplete M ϕ days 8 & 14 & infected IN with HSV-1 day 10	↓ morbidity, mortality, symptom severity in exercise-stressed animals, without M ϕ depletion	[40]
		4-week ♂ CD-1 mice (20/group)			Resting or exercise-stressed (days 8-10) animals administered HSV-1 IN day 10	↓ morbidity in exercise-stressed & resting animals; ↓ mortality in exercise-stressed animals	[39]
<i>Ganoderma lucidum</i>	Aqueous	7-week ♂ CD-1 mice (26/group)	5% of diet	5 months	Injected IM DMH once a week, weeks 1-10	↓ aberrant crypt foci per colon, tumor size, cell proliferation, nuclear staining of β -catenin	[69]
		4-8-week BALB/c mice (10/group)	50, 100 or 200 mg/kg, oral	10 days	Injected SD Sarcoma 180 cells	↓ of tumor weight was dose dependent: 27.7, 55.8, 66.7%, respectively	[67]
<i>Ganoderma lucidum</i> (mycelia)	Aqueous	7-week ♂ F344/Du Crj rats (16/group)	1.25% or 2.5% of diet	6 months	Injected SC AOM once a week, weeks 2-5	Both doses ↓ colonic adenocarcinoma incidence; 2.5% ↓ total tumor incidence; both doses ↓ nuclear staining of β -catenin and cell proliferation	[68]
<i>Ganoderma tsugae</i>	Aqueous	8-week ♀ BALB/cByJNarl mice (14/group)	0.2-0.4% of diet (young fungi); 0.33 or 0.66% of diet (mature fungi)	5 weeks	Injected IP OVA days 7, 14, 21; aerosolized OVA twice during week 4	In splenocytes, both doses of both extracts ↑ IL-2 and IL-2/IL-4 ratios, 0.2% young extract and 0.66% mature extract ↓ IL-4; in M ϕ , 0.66% mature extract ↑ IL-1 β , both doses of both extracts ↑ IL-6	[53]

<i>Grifola frondosa</i>	D fraction	Mice: 1) ICR, 2) C3H/HeN, 3) CDF ₁ (10/group)	1.5 mg every other day, beginning day 2	13 days	Implanted SC: 1) Sarcoma-180, 2) MM-46 carcinoma, or 3) IMC carcinoma cells	↓ tumor weight & tumor growth rate: 1) 58%, 2) 64%, and 3) 75%, respectively	[71]
		5-week ♂ BALB/c mice (10/group)	2 mg, days 15-30	45 days	Injected in the back with 3-MCA, day 1	↓ (62.5%) # of animals with tumors; ↑ H ₂ O ₂ production by plasma Mφ ; ↑ cytotoxic T cell activity	[72]
<i>Hordeum vulgare</i>	β-1,3;1,4 or β-1,3;1,6-D-glucans	Athymic nu/nu mice (4-12/group)	40 or 400 µg IG for 4 weeks	31 weeks	Mice with human xenografts (SKMel28 melanoma, A431 epidermoid carcinoma, BT474 breast carcinoma, Daudi lymphoma, or LAN-1 neuroblastoma) ± mAb (R24, 528, Herceptin, Rituximab, or 3F8, respectively) therapy twice weekly	400 µg + mAb ↓ tumor growth & ↑ survival; higher MW ↓ tumor growth rate for both doses	[75]
		Athymic BALB/c mice	4, 40, or 400 µg for 3-4 weeks	1 month	Mice with neuroblastoma (NMB7, LAN-1, or SK-N-ER) xenografts, ± 3F8 mAb therapy twice weekly	40 and 400 µg doses + mAb ↓ tumor growth; 400 µg dose ↑ survival. Serum NK cells required for effects on tumor size	[76]
	β-1,3;1,4-D-glucans	C57BL/6 WT and CR3-deficient mice (10/group)	0.4 mg for 3 weeks	100 days	Injected SC RMA-S-MUC1 lymphoma cells day 1 ± IV 14.G2a or anti-MUC1 mAb every 3rd day	± mAb ↓ tumor diameter ; ↑ survival	[73]
		♀ Fox Chase ICR immune-deficient (SCID) mice (9/group)	400 µg days 1-29	50 days	Mice with human (Daudi, EBV-BLCL, Hs445, or RPMI6666) lymphoma xenografts, ± Rituximab mAb therapy twice weekly	+mAb ↓ tumor growth and ↑ survival	[74]
<i>Laminaria digitata</i>	Laminarin	♂ ICR/HSD mice (3/group)	1 mg	1 day	Healthy animals	↑ Mφ expression of Dectin-1 in GALT cells; ↑ TLR2 expression in Peyer's patch dendritic cells	[29]
		♂ Wistar rats (7/group)	5% of diet days 1-4, 10% of diet days 5-25	26 days	Injected IP <i>E. coli</i> LPS day 25	↓ liver ALT, AST, and LDH enzyme levels; ↑ ED2-positive cells, ↓ peroxidase-positive cells in liver; ↓ serum monocytes, TNF-α, PGE2, NO ₂	[44]
<i>Lentinula edodes</i>	SME	6-week nude mice	0.1 ml water with 10% SME/10 g body weight days 1-19, 33-50	50 days	Injected SC prostate cancer (PC-3) cells day 1	↓ tumor size	[80]

β-glucans	♀ 3- and 8-week BALB/c mice (15/group)	50, 100 or 250 µg	1-2 weeks	Healthy animals	250 µg dose ↑ spleen cell IL-2 secretion	[27]	
	♀ 3- and 8-week BALB/c mice (15/group)	50, 100 or 250 µg	1-2 weeks	Injected murine mammary carcinoma (Ptas64) cells into mammary fat pads 2 weeks before treatment	↓ tumor weight		
Lentinan	6-week ♂ Wistar-Imamichi specific-pathogen free rats (10/group)	1 mg twice weekly	1-2 months	Healthy animals	↑ T cell #s, helper-cell #s & helper/suppressor ratio, ↓ suppressor cell level at 4, but not 8 weeks	[26]	
	5-6-week ♂ pre-leukemic AKR mice (10/group)	3 mg, days 1-7	3 weeks	Injected SC K36 murine lymphoma cells day 7	↓ tumor weight; ↑ tumor inhibition rate (94%)	[82]	
	5-6-week athymic mice (10/group)		5 weeks	Injected SC colon cancer (LoVo and SW48, SW480 and SW620, or SW403 and SW1116) cells day 7	↓ tumor weight, ↑ tumor inhibition rate (>90%)		
	♂ AKR mice	3 mg	1 day	Pre-leukemic mice	↑ serum IFN-α and TNF-α, peak at 4 h and then back to normal at 24 h; ↑ IL-2 and IL-1α, peak at 2 h and back to normal at 24 h; ↑ CD3+ T, CD4+ T, CD8+ T, B lymphocytes	[81]	
<i>Phellinus linteus</i>	Aqueous, alcohol-precipitated	6-7-week C57BL/6 mice (10-50/group)	200 mg/kg in drinking water	1 month	Healthy animals	↑ production and secretion of IFN-γ by con A stimulated T cells	[32]
<i>Saccharomyces cerevisiae</i>	Scleroglucan	♂ ICR/HSD mice (3/group)	1 mg one day before challenge (day 1)	6 days	IV <i>Staphylococcus aureus</i> or <i>Candida albicans</i> day 2	↑ long-term survival	[29]
	β-1,3;1,6 glucans (particulate)	3 and 8-week ♀ BALB/c mice (15/group)	50, 100 or 250 µg	1-2 weeks	Injected murine mammary carcinoma (Ptas64) cells into mammary fat pads 2 weeks before treatment	↓ tumor weight	[27]
	β-1,3-glucan				Healthy animals	All 3 doses ↑ phagocytic activity of blood monocytes & neutrophils & ↑ spleen cell IL-2 secretion	
		WT or CCD11b ^{-/-} C57BL/6 mice (2/group)	0.4 mg for 3 weeks	100 days	Injected SC RMA-S-MUC1 lymphoma cells ± 14.G2a or anti-MUC1 mAb IV injection every 3 rd day	↓ tumor diameter when included with mAb; ↑ survival with and without mAb	[73]

		C57BL/6mice (4/group)	25 mg	1 week	Healthy animals	↑ # intestinal IELs; ↑ # TCRαβ+, TCR γδ+, CD8+, CD4+, CD8αα+, CD8αβ+ T cells in IELs; ↑ IFN-γ mRNA expression in IELs and spleen	[28]
<i>Sclerotinia sclerotiorum</i>	SSG	6-8-week specific pathogen-free ♂ CDF ₁ mice (3/group)	40 or 80 mg/kg days 1-10	2 weeks	Healthy animals	10 mg dose ↑ acid phosphatase activity of peritoneal Mφ (day 14)	[30]
			40, 80 or 160 mg/kg days 2-6	35 days	Implanted SC Metha A fibrosarcoma cells day 1	80 mg dose ↓ tumor weight	
		6-8-week specific pathogen-free ♂ CDF ₁ mice (10/group)	40, 80 or 160 mg/kg days 2-11		Injected ID IMC carcinoma cells day 1		
		6-8-week specific-pathogen free ♂ mice of BDF1 and C57BL/6 mice (7/group)	0.5, 1, 2, or 4 mg days 1-10	2-3 weeks	Injected IV Lewis lung carcinoma (3LL) cells	2 mg ↓ # of 3LL surface lung nodules at 2 weeks	[83]
<i>Sclerotium rofsii</i>	Glucan phosphate	♂ ICR/HSD mice (3/group)	1 mg	1 day	Healthy animals	↑ systemic IL-6; ↑ Mφ expression of Dectin-1 in GALT cells; ↑ TLR2 expression in dendritic cells from Peyer's patches	[29]
<i>Trametes (Coriolus) versicolor</i>	PSP	6-8-week ♂ BALB/c mice (10/group)	35 µg days 5-29 in drinking water	29 days	Implanted SC Sarcoma-180 cells day 1	↓ tumor growth & vascular density	[94]