

Table 6. Safety of Immunomodulatory Polysaccharide Products Following Oral Intake

Category	Source	Test group	Test	Design	Results	Equivalent human dose*	Reference
Arabinogalactans	<i>Argemone mexicana</i> (arabinogalactan protein)	Pregnant rats	Developmental toxicity	250, 500, or 1,00 mg/kg, gestational days 5-19	No developmental toxicity: NOAEL = 1 g/kg	68 g	[151]
		♀ and ♂ rats	Fertility	250, 500, or 1,00 mg/kg, 1 month	No effects on reproduction: NOAEL = 1 g/kg		
Fucoidans	<i>Undaria pinnatifida</i>	Rats	Subchronic toxicity	1.35 g/kg, 1 month	No evidence of toxicity	91.8 g	[152]
Galactomannans	<i>Cyamopsis tetragonolobus</i>	Adolescent and adult ♂ rats	Subchronic and chronic toxicity	8% of diet, 6-67 weeks	No evidence of toxicity	8% of diet	[153]
		Rats	Acute toxicity	One 7.06 g/kg dose: observed 2 weeks	LD ₅₀ = 7.06 g/kg	480 g	[96]
			Subchronic and chronic toxicity	1, 2, 4, 7.5 or 15% of diet, 3 months	All doses ↓ ♀ BW; 7.5-15% ↓ ♂ BW; 15% ↓ bone marrow cellularity; ↓ kidney and liver weights	1-15% of diet	
		19 adults with hypercholesterolemia		18 g/day, 1 year	Short-term gastric bloating/loose stools, in 8 subjects, resolved in 7-10 days; 2 withdrew because of diarrhea. No toxicity for 13 subjects completing study	18 g	[154]
		16 Type II diabetics		26.4-39.6 g/day, 6 months	No effects on hematologic, hepatic, or renal function	39.9 g	[155]
		18 Type II diabetics		30 g/day, 4 months		30 g	
		Mice & rats	Acute toxicity	One 6 g/kg dose; observed 2 weeks	LD ₅₀ > 6 g/kg	>408 g	[156]
		Rats	Subchronic toxicity	0.2, 1.0 or 5% of diet, 13 weeks	No evidence of toxicity	5 % of diet	
		0.5 or 2.5 g/kg, 1 month	NOAEL > 2.5 g/kg	>170 g	[157]		
	<i>S. typhimurium</i>		Mutagenicity	Ames test	Not mutagenic	NA	
Glucans	<i>Agaricus subrufescens</i>	Rats	Subchronic toxicity	0.63, 1.25, 2.5 or 5% of diet, 3 months	NOAEL = 5% of diet	5% of diet	[158]

	(aqueous extract)	3 women with advanced cancers	Case reports	Specific identity of products, doses, and durations of intake unknown	Severe hepatotoxicity; two patients died	NA	[97]
	<i>Agaricus subrufescens</i> (freeze dried powder)	24 normal adults and 24 adults with liver problems	Subchronic toxicity	3 g, 4 months	No evidence of toxicity	3 g	[159]
	<i>Ganoderma lucidum</i> (supplement)	Elderly woman	Case report	1 year <i>G. lucidum</i> (and another unidentified product, initiated one month previous)	Elevated liver enzymes and liver tissue damage	NA	[98]
	<i>Grifola frondosa</i> (powder)	Rats	Acute toxicity	One 2 g/kg dose	No evidence of toxicity	136 g	[160]
	<i>Lentinula edodes</i> (powder)	10 adults	Safety	4 g/day for 10 weeks; repeated 3-6 months later	50% of subjects experienced blood eosinophilia, ↑ eosinophil granule proteins in serum and stool, ↑GI symptoms	4 g	[99]
	<i>Lentinula edodes</i> (SME)	Nude mice	Safety	10% of diet days 1-18, 33-50	No adverse events	10% of diet	[80]
		61 men with prostate cancer		0.1 g/kg, 6 months	No adverse events	6.8 g	
	<i>Lentinus lepideus</i> (PG101)	Female mice	Subchronic toxicity	0.5 g/kg, 24 days	No evidence of toxicity	34 g	[92]
	<i>Phellinus linteus</i> (crude extract)	Rats	Acute toxicity	One 5 g/kg dose; observed 2 weeks	LD ₅₀ > 5 g/kg	349 g	[161]
	<i>Pleurotus ostreatus</i> (aqueous extract)	Mice	Acute toxicity	One 3 g/kg dose; observed 1 day	LD ₅₀ > 3 g/kg	>204.g	[100]
			Subacute toxicity	319 mg/kg, 1 month	Hemorrhages in intestine, liver, lung, kidney; inflammation and microabscesses in liver	21.7 g	
	<i>Saccharomyces cerevisiae</i> (particulate glucan [WGP])	Rats	Acute toxicity	One 2 g/kg, observed 2 weeks	LD ₅₀ > 2 g/kg	>136 g	[144]
			Subchronic toxicity	2, 33.3 or 100 mg/kg, 3 months	NOAEL = 100 mg/kg	6.80 g	
Heteroglycans	<i>Trametes versicolor</i> (PSP)	Rats	Subchronic toxicity	1.5, 3.0 or 6.0 mg/kg, 2 months	No evidence of toxicity	408 mg	[162]
		Rats & monkeys	Subchronic and chronic toxicity	100-200X equivalent human dose, 6 months	No evidence of toxicity	NA	

	<i>Trametes versicolor</i> (PSK)	Humans with colon cancer	Safety	3 g/day, up to 7 years	No significant adverse events	3 g	[57]
		Humans with colorectal cancer		3 g/day, 2 years		3 g	[58]
Mannans	<i>Aloe vera</i> gel	Dogs	Acute toxicity	Fed one 32 g/kg; observed 2 weeks	LD50 > 32 g/kg	>2,176 g	Bill Pine, personal communication
		Rats		One 21.5 g/kg; observed 2 weeks	LD50 > 10 g/kg	>680 g	

*150 lb adult