Table I. *In vitro* and *in vivo* anti-HCC effects of polysaccharides.

First author/s, year	Effective substance	Source	Molecular mass, kDa	*In vivo*/*in vitro*	Model	Dose	Route of administration	Mechanism of action	Cells	(Ref.)
Zhao *et al*, 2022	Polysaccharides	*Grifola frondosa*	2,190	*In vitro*	-	0.1, 0.4, 0.8, 1.2 and 1.6 mg/ml	-	Inhibits HepG2 cell proliferation via intrinsic activation of the mitochondrial pathway and the Fas/FasL-mediated caspase-8/-3 pathway.	HepG2	(13)
Yu *et al*, 2020	Polysaccharides	*Grifola frondosa*	644.9	*In vitro*	-	12.5-800 μg/ml	-	Induces G_1/S phase cell cycle arrest, leading to suppression of proliferation and activation of apoptosis.	H22 and HepG2	(14)
Qiu *et al*, 2023	Polysaccharide	*Ulva lactuca*	-	*In vivo*	Male ICR mice, xenograft model	100, 200 and 300 mg/kg	Oral administration	Inhibits tumor cell proliferation by modulating miR-98-5p-dependent ROS signaling.	H22	(21)
Li *et al*, 2022	Polysaccharide	*Polygonatum sibiricum*	38.65	*In vitro*	-	100, 200 and 400 μg/ml	-	Triggers G_1 arrest and induces mitochondrial-dependent apoptosis via activation of caspase-9 and caspase-3 in tumor cells.	HepG2	(22)
Sang *et al*, 2023	Polysaccharide	*Hemerocallis citrina* Baroni	-	-	-	-	-	Causes G_2/M cell cycle arrest and triggers the intrinsic mitochondrial apoptotic pathway, leading to inhibition of tumor cell proliferation and induction of apoptosis.	HL-7702	(23)
Liu *et al*, 2022	Polysaccharides	*Bletilla striata* L.	23	*In vivo*	Male BALB/c mice, xenograft model	100 and 200 mg/kg/day	Oral gavage	Induces G_1 phase cell cycle arrest and apoptosis.	H22	(24)
Kong *et al*, 2024	Polysaccharides	*Brassica rapa* L.	9.906-1,090.449	*In vivo*	Male BALB/c mice, xenograft model	400 mg/kg	Oral gavage	Induces apoptosis via activation of the caspase cascade.	H22	(25)
Huang *et al*, 2016	Polysaccharides	*Astragalus membranaceus* (Fisch.) Bunge	1.61×10^3	*In vitro*		0.1, 0.5 and 1 mg/ml	-	Promotes apoptosis in human HCC cells by suppressing Notch1 expression.	H22	(26)
Wang *et al*, 2021	α-d-Glucan	*Holotrichia diomphalia* Bates	19	*In vivo*	Male BALB/c mice, xenograft model	50 mg/kg/day	i.p. injection	Inhibits aldolase activity and p-AMPKα expression, thereby suppressing tumor growth.	H22	(27)
Su *et al*, 2021	Polysaccharide	*Sipunculus nudus*	9.22	*In vivo*	Male athymic nu/nu mice, xenograft model	50, 100 and 200 mg/kg/day	Intragastric administration	Triggers the intrinsic (mitochondria-mediated) apoptotic pathway, inhibits cellular proliferation and promotes apoptosis.	HepG2	(28)
Tan *et al*, 2023	Polysaccharide	*Cordyceps sinensis*	2.1×10^3 and 21.9	*In vivo*	Male BALB/c mice, xenograft model	100 and 300 mg/kg/day	Intragastric administration	Exerts antiproliferative and pro-apoptotic effects by modulating the IL-10/STAT3/Bcl-2 axis and activating the cytochrome *c*/caspase-8/-3 cascade.	H22	(29)
Yue *et al*, 2025	Fucoidan	Brown algae (*Saccharina japonica*)	112.8	*In vivo*	Male ICR mice, xenograft model	100 mg/kg/day	Oral administration	Markedly suppresses tumor angiogenesis and downregulates pro-inflammatory cytokines, including IL-1β, IL-6 and TNF-α.	H22	(30)
Cho *et al*, 2016	Fucoidan	Brown algae (*Saccharina japonica*)	-	*In vivo*	Male BALB/c mice, splenic injection model	1 mg/ml	Oral administration	Induction of ID-1 suppression inhibits the invasive potential of HCC cells *in vitro* and *in vivo*.	Huh-7	(31)
Cho *et al*, 2016	Fucoidan	Brown algae (*Saccharina japonica*)	-	*In vitro*		0.1 mg/ml	-	NDRG-1/GAP43-dependent downregulation of ID-1 suppresses HCC invasion.	Huh-7, SNU-761 and SNU-3085	(31)
Ren *et al*, 2018	Polysaccharide	*Angelica sinensis*	-	*In vivo*	Male BALB/c mice, xenograft model	100 mg/kg/day	i.p. injection	Suppresses hepatic expression of IL-6, JAK2, p-STAT3 and p-SMAD1/5/8, indicating the involvement of the JAK/STAT and BMP-SMAD pathways in ASP-mediated hepcidin regulation.	HepG2 and H22	(32)
Feng *et al*, 2019	Polysaccharide	*Ocimum basilicum* L.	-	*In vivo*	Male BALB/c mice, xenograft model	100, 200 and 400 mg/kg/day	Oral gavage	Suppresses tumor metastasis by inhibiting HIF-1α-driven EMT.	MHCC97H and MHCC97L	(33)
Qiu *et al*, 2025	Polysaccharide	*Ulva lactuca*	-	*In vivo*	Male ICR mice, xenograft model	100 mg/kg/day	i.p. injection	Suppresses tumor cell proliferation by inhibiting miR-542-3p-mediated SLC35F6 expression.	H22 and HepG2	(34)
Li *et al*, 2025	Polysaccharides	*Antrodia cinnamomea*	-	*In vitro*		133.9 μg/ml	-	Promotes autophagic cell death in a ROS/JNK-dependent manner.	HepG2, THLE-2, HuH-7 and H22	(35)

Cheng *et al*, 2021	Polysaccharide	*Asparagus officinalis* L.	-	*In vivo*	Male BALB/c mice, xenograft model	25, 50 and 100 mg/kg/day	Intragastric administration	Inhibits the MAPK/PI3K signaling cascade, suppresses HIF-1α and VEGF expression, and impairs tumor cell migration and invasion.	SK-Hep1 and Hep-3B	(36)
Cheng *et al*, 2019	Polysaccharide	*Asparagus*	-	*In vitro*		2.5, 5 and 10 mg/ml	-	Exerts inhibitory effects on the HIF-1α/VEGF axis by suppressing AKT, mTOR and ERK phosphorylation.	SK-Hep1 and Hep-3B	(37)
You *et al*, 2023	Polysaccharide	*Lentinus edodes*	-	*In vivo*	Male C57BL/6 mice, DEN-induced primary liver cancer model	0.865, 1.73 and 3.46 mg/kg	Oral gavage	Enhances PTEN levels and inhibits PI3K/AKT signaling, resulting in apoptosis activation.	Hepa1-6	(38)
Li *et al*, 2024	Polysaccharide	*Codonopsis pilosula*	-	*In vivo*	Male BALB/c mice, xenograft model	25, 50 and 100 mg/kg/day	Oral gavage	Suppresses CDK1 activity, perturbs PDK1/β-catenin signaling, inhibits EMT, and consequently impairs tumor cell proliferation and metastasis.	Huh-7	(39)
Zhang *et al*, 2012	Sulfated glycopeptide	*Gekko swinhonis* Guenther	-	*In vitro*	-	10, 100 and 200 μg/ml	-	Blocks bFGF-mediated angiogenesis by preventing bFGF generation and extracellular release, and by competitively interfering with its binding to HSPGs.	Bel-7402 and HepG2	(40)
Zhang *et al*, 2012	Sulfated glycopeptide	*Gekko swinhonis* Guenther	-	*In vivo*	Male nu/nu nude and C57BL/6 mice, xenograft model	20 and 200 mg/kg/day	i.p. injection	Inhibits bFGF-induced angiogenesis.	Bel-7402 and HepG2	(40)
Yang *et al*, 2022	Polysaccharide	*Pholiota adiposa*	16.453	-	-	-	-	Inhibits cell cycle progression at the G_0/G_1 checkpoint, subsequently inducing apoptosis.	HepG2, Hep-3B and Huh7	(41)
Wang *et al*, 2024	Polysaccharides	Vinegar-baked Radix Bupleuri	VRP3-3, 16.05; VRP2-3, 95.35; VRP2-4, 57.90	*In vitro*	-	3.13, 6.25, 12.5, 25 and 50 μg/ml	-	Substantially improves hepatic drug accumulation by enhancing relative uptake and targeting efficiencies, resulting in superior hepatic tropism.	Huh 7, HepG2 and Bel7402	(42)
Yang *et al*, 2019	Polysaccharide	*Trametes robiniophila* Murr	55.9	*In vitro*	-	0.5 mg/ml	-	Supernatant from TPG-1-treated RAW264.7 cells exhibits time-dependent cytotoxicity against HepG2 cells, whereas supernatant from untreated cells does not.	HepG2 and SK-HEP-1	(43)
Yang *et al*, 2019	Polysaccharide	*Trametes robiniophila* Murr	55.9	*In vivo*	Male BALB/c mice, xenograft model	60 mg/kg/day	i.p. injection	Inhibits HepG2 cell proliferation and promotes leukocyte infiltration into HepG2-derived tumors in nude mice.	HepG2 and H22	(43)
Wang *et al*, 2016	Polysaccharide	*Acanthopanax senticosus* (Rupr. et Maxim.) Harms	740, 38, 45 and 23	-	-	-	-	Blocks Wnt/β-catenin signaling, resulting in G_0/G_1 phase cell cycle arrest, reduced proliferation and enhanced apoptotic cell death.	HepG2	(44)
Chen *et al*, 2019	Polysaccharides	*Grifola frondosa*	1,231.7	*In vitro*	-	100, 200 and 400 μg/ml	-	Promotes apoptotic cell death by activating the mitochondrial pathway and the caspase-8/-3 cascade, while inhibiting cellular proliferation.	HepG2	(45)
Hu *et al*, 2020	Polysaccharides	*Dictyophora* Desv.	8-14	*In vitro*	-	2.5 mg/ml	-	Promotes upregulation of Bax and cleaved caspase-3, arrests the cell cycle at the G_2/M phase, and inhibits cellular proliferation.	LM3	(46)
Ying *et al*, 2024	Polysaccharide	*Poria cocos* (Schw.) Wolf	-	*In vitro*	-	800 mg/l	-	Targets SQLE to induce NLRP3/GSDMD-mediated pyroptosis and attenuate tumor cell migration.	HepG2	(47)
Weiping *et al*, 2024	Sulfated polysaccharide	*Undaria pinnatifida*	-	*In vitro*	-	400, 800 and 1,000 mg/ml	-	Inhibits cancer cell proliferation and migration by suppressing EMT and MMP expression.	HepG2 and SMMC-7721	(48)
Cai *et al*, 2021	Polysaccharide	*Black fungus*	-	*In vitro*	-	50 and 100 μg/ml	-	Causes S-phase cell cycle arrest, exacerbates DNA damage, suppresses tumor cell proliferation, migration and invasion, and triggers apoptotic cell death.	HepG2	(49)

AMPKα, AMP-activated protein kinase α; ASP, *Angelica sinensis* polysaccharide; bFGF, Basic fibroblast growth factor; BMP, bone morphogenetic protein; GAP43, growth-associated protein 43; EMT, epithelial-mesenchymal transition; FasL, Fas ligand; GSDMD, Gasdermin D; HCC, hepatocellular carcinoma; HIF-1α, hypoxia-inducible factor-1α; HSPG, heparan sulfate proteoglycan; ICR, Institute of Cancer Research; ID-1, inhibitor of DNA binding 1; i.p., intraperitoneal; JAK, Janus kinase; miR, microRNA; NDRG-1, N-Myc downstream regulated gene 1; NLRP3, NLR family pyrin domain containing 3; p-, phosphorylated; PDK1, pyruvate dehydrogenase kinase 1; ROS, reactive oxygen species; SLC35F6, solute carrier family 35 member F6; SQLE, squalene epoxidase; TPG-1, tumor-progression-related gene 1.