Table SI. Curcumin-based metabolites.

Metabolites	Molecular weight (g/mol)	Molecular formula	PubChem CID
Curcumin	368.4	$C_{21}H_{20}O_6$	969516
Tetrahydrocurcumin	372.4	$C_{21}H_{24}O_6$	124072
Demethoxycurcumin	338.4	$C_{20}H_{18}O_5$	5469424
Bisdemethoxycurcumin	308.3	$C_{19}H_{16}O_4$	5315472
(1E,4Z,6E)-5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,4,6-tried-3-one	368.4	$C_{21}H_{20}O_6$	5281767
Monodemethylcurcumin	354.4	$C_{20}H_{18}O_6$	5469426
Curcumin sulfate	448.4	$C_{21}H_{20}O_9S$	66645351
Curcumin glucuronide	544.5	$C_{27}H_{28}O_{12}$	71315012
Curcumin diglucoside	544.5	$C_{33}H_{40}O_{16}$	46173989
Curcumin monoglucoside	692.7	$C_{33}H_{40}O_{16}$	11526601
Curcumin 4'-O-beta-D-gentiobioside	530.5	$C_{27}H_{30}O_{11}$	46926100
Curcumin dimer 1	692.7	$C_{33}H_{40}O_{16}$	100972288
Curcumin dimer 3	734.7	$C_{42}H_{38}O_{12}$	131752651

Table SII. Curcumin and its therapeutic effects in various disease models.

Activity	Disease model	*In vitro* and concentration	*In vivo* and dose	Effects	(Refs.)[a]
Anti-inflammatory	Inflammatory diseases	RAW 264.7 macrophages (1 to 10 μM)	C57BL/6 mice	Curcumin analogs produced from β-ionone have potential applications as anti-inflammatory medicines.	(63)
	Acute lung injury	HUVECs, RAW 264.7 (1 to 10 μM)	C57BL/6 (10 mg/kg) and Sprague-Dawley rats (20 mg/kg)	Analogs of curcumin may be used to treat inflammatory conditions.	(62)
	Sepsis	Mouse macrophages RAW 264.7 (10, 20, or 40 μM)	Not performed	Because FM0807 exhibits anti-inflammatory properties in vitro, there may be a clinical application for it in sepsis.	(63)
	LPS-induced sepsis	Human THP-1 (0.25 to 4 μM)	C57BL/6 mice (1, 3, or 10 mg/kg)	NLRP3 inflammasome-driven disorders, such as sepsis, may benefit from the use of I-44 as a potential treatment.	(64)
	Sepsis	RAW 264.7 macrophages (5μM CLEN)	Balb/c mice (50 mg/kg *C. longa*-extract loaded nanoemulsion (CLEN))	Treatment for endotoxemia may benefit from C. longa's ability to inhibit the synthesis of HMGB1.	(65)
	Inflammation-related diseases	RAW 264.7 macrophages	C57BL/6 mice (20 mg/kg)	Curcumin can reduce inflammation brought on by LPS.	(95)

	(sepsis)	(5, 10, and 15 μM)			
	Acute liver failure	Hepatic stellate cells (0.5 to 2 μM)	C57BL/6 mice (20,40, and 80 mg/kg)	In therapeutic settings, curcumin may be utilized to treat inflammatory diseases like sepsis.	(66)
Immunomodulatory	Sepsis and leukemia	THP-1, HL-60, MCF-7, and MDA-MB-231 (1-10 μM for THP-1 cells and 1-100 μM for other cells)	Swiss albino mice (30, 100, and 300 mg/kg)	Sepsis can be efficiently treated with curcumin because it regulates the immune response.	(67)
	CLP-induced sepsis	U937 cells	ICR mice (1 and 10 mg/kg)	The effectiveness of curcumin analog BHMC in avoiding death after deadly sepsis may be attributed to its increased potency to inhibit p38.	(68)
	Microvascular dysfunction	Not performed	C57BL/6 mice (100 mg/kg)	In CLP, curcumin reduces immune system dysfunction	(96)
	Acute lung injury (ALI)	Human pulmonary epithelial cells (1, 5, and 10 μM)	Sprague-Dawley rats (20 mg/kg/day)	Curcumin analog (c26) protects septic mice against LPS-induced ALI in a potent manner.	(69)
	Septic shock and NLRP3 inflammasome-	J774A.1 cells (50 μM)	C57BL/6 mice (2mg)	Curcumin has the potential to treat septic shock because it prevents the NLRP3 inflammasome from activating.	(70)

	driven diseases				
	Sepsis	Mouse primary peritoneal macrophage (2.5 to 20 μg/ml)	C57BL/6 mice (10 mg/kg)	A curcumin analog might be created as a possible mediator for the management of sepsis.	(71)
	Gram-negative sepsis	J774 macrophages, HepG2 (0-3 mg/l)	Balb/c mice (10 and 20 mg/ kg)	Curcumin may be a suitable interventional strategy for the management of sepsis and related excessive-inflammatory conditions.	(72)
Antioxidant	Sepsis	RAW 264.7, HepG2, HEK-2936 (1.5 and 3 mg/l)	Sprague-Dawley rats (10 mg/kg)	Curcumin may lessen tissue oxidative damage.	(73)
	Acute inflammatory diseases	Mouse macrophages and HL-7702 cells (1 to 5 μM)	C57BL/6 mice (10 mg/kg)	Curcumin analogues are beneficial in treating inflammatory illnesses.	(74)
	LPS-induced sepsis	RAW 264.7 (1 to 10 μM)	C57BL/6 mice (20 mg/kg)	Curcumin analogues are anti-inflammatory drugs.	(75)

[a]Refernece citations pertain to the reference list in the main manuscript. LPS, lipopolysaccharide; ALI, acute lung injury.

Table SIII. Effects of curcumin on Gram-negative and Gram-positive bacteria.

Bacteria	Concentration used	Main findings	Techniques used (disc diffusion/well diffusion/broth dilution)	(Refs.)[a]
S. aureus; E. coli; Enterococcus faecalis; Pseudomonas aeruginosa	25 μM, 50 μM, and 100 μM	Demonstrated antibacterial activity by damaging the membrane.	Brain heart infusion (BHI) broth dilution method	(81)
Streptococcus mutants	5 mg/ml	Reduced adhesion of *S. mutants* to dental surfaces, including extracellular matrix proteins	Brain heart infusion (BHI) broth dilution method	(82)
Acinetobacter baumannii	256-0.5 μg/ml	Curcumin in combination with epigallocatechin gallate (EGCG) showed antimicrobial activity against MDR *A. baumannii*.	Standard broth microdilution method	(83)
MRSA	125 to 250 g/ml	Curcumin demonstrated antibacterial activity against MRSA by lowering the MICs of tested drugs, including ampicillin, ciprofloxacin, norfloxacin and oxacillin.	Standard broth microdilution method	(84)

Porphyromonas gingivalis, *S. gordonii*	100 µg/ml	Curcumin demonstrated antibacterial activity by inhibiting the biofilm formation of *Porphyromonas gingivalis* and *S. gordonii*.	Broth microdilution method	(85)
S. aureus	2 to 16 µg/ml	Curcumin protected mice infected with MRSA (methicillin-resistant strains) by inhibiting the pore-forming action of α-hemolysin.	Broth microdilution method	(86)
Helicobacter pylori	5 g/ml to 50 g/ml	Curcumin blocked the growth of *H. pylori* and ameliorated the *H. pylori*-induced gastric damage.	Brain heart infusion (BHI) broth dilution method	(87)
E. coli	12 µg/ml	Curcumin restrained the growth of *E. coli* by displaying apoptotic markers, including ROS, membrane depolarization, and Ca^{2+} influx.	Broth microdilution method	(88)
P. aeruginosa	1 mg/ml	Curcumin in combination with gentamicin and azithromycin showed synergistic effects against *P. aeruginosa* quorum-sensing systems.	Broth microdilution method	(29)

Salmonella typhimurium	20 μM	Curcumin demonstrated antibacterial activity by adhering and making it prone to breaking into smaller fragments in *S. typhimurium*.	Broth microdilution method	(89)
E. coli	>16 g/ml	Levofloxacin-induced SOS reaction in *E. coli* is inhibited by curcumin.	Well diffusion method	(90)
[a]Refernece citations pertain to the reference list in the main manuscript.				

Table SIV. Organ-protective potential effects of curcumin.

Activity	Disease model	*In vitro;* *In vivo* (dose and type of administration)	Duration of study	Main findings	(Refs.)[a]
Lung protection	Acute lung injury	EA. hy926 (10 and 30 μM); C57BL/6J mice (30 mg/kg, i.p.)	2 h before LPS injection. 15 min/day for cell	Lung damage caused by sepsis may benefit from the use of curcumin and its derivatives.	(110)
	Acute lung injury	Balb/c mice (10 mg/kg, i.n.)	Single dose After 24 h of intranasal LPS	Curcumin offered protection from sudden acute lung damage.	(111)
	Acute lung injury	Sprague-Dawley (SD) rats (42 mg/kg, i.p.)	Single dose, 4 and 12 h after CLP	Curcumin can alleviate acute lung injury and enhance survival	(112)
	Acute lung injury	SD rats (50 or 200 mg/kg, i.p.)	At 2 h post-CLP	Curcumin can guard against ALI brought on by CLP.	(124)
	Acute lung injury	SD rats (200 mg/kg/day, i.p.)	24 h after	Curcumin protected ALI brought on by sepsis.	(59)
	Lung injury, ARDS	Swiss albino mice (20 mg/kg, i.p., and 10 mg/kg, i.n.)	Single dose, 1, 6, 24, and 72 h	Early in the course of endotoxemia, curcumin can be utilized as a supplementary intervention.	(97)

	Chronic lung injury	Male albino rats (50 and 100 mg/kg bwt, orally)	Consecutive 45 days	Curcumin exhibits therapeutic properties against CLP-induced CLI.	(98)
	Septic lung injury	Bone marrow-derived macrophages (BMDM) (10 μM); C57BL/6J mice (200 mg/kg, i.p.)	Single Dose for 4hr (*in vitro*)	Septic lung damage and other inflammatory diseases are inhibited by curcumin.	(113)
Cardioprotective	Vascular dysfunction	ICR mice (50 or 100 mg/kg)	3 hr before LPS administration; for 15 h	Curcumin has demonstrated efficacy in treating vascular dysfunction in mice exhibiting endotoxemia induced by LPS	(114)
	Vasoconstrictive dysfunction	SD rats (10 or 20 mg/kg, i.p.)	24 h	Curcumin relieved aortic media and intima damage and restored vasoconstrictive function.	(115)
	Myocardial injury	SD rats (200 mg/kg/d, i.p.)	3 Days	Curcumin improves fractional shortening, ejection fraction and cardiac function.	(107)
	Sepsis-induced acute organ dysfunction/inflammatory tissue injury	Balb/c mice (50, 100, and 200 mg/kg)	12 h after CLP	Curcumin inhibits TNF-α and IL-6 in septic mice and improves survival after CLP.	(116)

	Hypoglycaemia and hypovolemia	Wistar rats (100 mg/kg, p.o.)	7 days before CLP and 2 h after surgery	The dosage of curcumin dispersion reduced sepsis complications.	(117)
	Lipopolysaccharide-induced sepsis	IL-1b transgenic mice (30 mg/kg, i.p.)	30 min before LPS	Curcumin loaded lipid nanoparticles have the potential to be a safe and effective therapeutic agent for the treatment of sepsis.	(44)
Hepatoprotective	Hepatocyte injury	Wistar rats (50 and 100 mg/kg, i.p.)	Single dose for 7 days	Liver function was shielded by curcumin.	(118)
	Acute liver failure (ALF)	Hepatic stellate cells (HSCs) (0.5, 1 and 2 mM); C57BL/6 mice (20, 40 and 80 mg/kg, orally)	After 24 h for 4 weeks	Curcumin alleviates liver injury.	(66)
	Acute liver injury	Balb/c mice (100 mg/kg, i.p.)	3 hr before LPS/GalN	Curcumin attenuates LPS-induced hepatic injury.	(119)
	Hepatorenal oxidative injury	Wistar Albino rats (200 mg/kg, i.p.)	After perforation and 12 h post-perforation	Curcumin has potent anti-inflammatory and antioxidant properties.	(125)
Renoprotective	Chronic inflammatory diseases	293 (0 to 10 μM)	1 h before stimulation with LPS	Curcumin, a novel inhibitor that selectively binds to MD2, is and	(120)

				potential therapy for bacterial infections.	
	Disseminated intravascular coagulation and renal injury	SD rats (60 mg/kg bwt, i.p.)	Single dose, 3 hr before LPS infusion	Curcumin prevents fibrin deposition in the glomeruli of the kidney.	(121)
	Septic acute kidney injury (SAKI)	C57BL/6 mice (50, 100, 200 mg/kg)	Before LPS injection, i.p., for 24 h	Curcumin reduces kidney damage and levels of creatinine, cystatin C, and blood urea nitrogen in serum, and attenuates PVT1 expression in mice.	(93)
	Septic acute kidney injury	Human kidney-2 cells (0, 5, 10 and 20 μmol/l); C57 mice (100 and 200 mg/kg, i.p.)	12 hr for cells; 24 h for mice	Curcumin attenuates SAKI by blocking NF-κB and JAK2/STAT3 signaling pathways.	(122)
	Septic acute kidney injury	Male SD rats (100 mg/kg, i.p.)	12 hr and 24 h (single dose immediately after surgery)	Curcumin reduces AKI in rats by improving renal microcirculatory perfusion.	(123)
	Acute tubular necrosis	Albino Wistar rats (1.2 g/kg, i.p.)	7 Days	Curcumin helps in treating organ failure in sepsis.	(99)

Neuroprotective	Cerebral mitochondrial dysfunction or septic brain injury	C57BL/6J mice (100 mg/kg, i.p.)	Single dose, 3, 12, and 24 h after surgery	Curcumin enhances survival rate, reduces brain edema, increases BBB integrity, reduces apoptosis and mitochondrial dysfunction.	(105)
[a]Refernece citations pertain to the reference list in the main manuscript. LPS, lipopolysaccharide; CLP, cecal ligation/puncture; ARDS, acute respiratory distress syndrome; CLI, chronic lung injury; AKI, acute kidney injury.					