Additional Table 1 Characteristics of the major studies.

Study	Animal	SCI Model	Experimental groups	Control groups	Time of study	Treatment (MT)	Biochemical outcomes	Behavioral outcomes	Major findings and conclusions
Shen et al. (2017)	Female Sprague–Dawley rats 180–220 g	$T_{9–10}$ Weight-drop	SCI + MT 12.5 mg/kg, i.p.	1. Sham 2. SCI + vehicle	0, 1, 3, 7, 14, 21, and 28 d	Each day for 3 d	Bax, caspase-3 Bcl-2	BBB	MT decreased SCI through activation of the Wnt/β catenin signaling pathway.
Yuan et al. (2016)	Male C57BL/B6 mice Eight-week-old	T_{10} Weight-drop	SCI + MT 10 mg/kg 25 mg/kg 50 mg/kg i.p.	1. Sham 2. SCI + vehicle	24 h, 48 h, 72 h, 7 d	30 min after SCI	MDA, GSH, GSSG and MPO	No	MT treatment plays a role in protecting the testes of SCI animals by preventing oxidative stress damage.
Krityakiarana et al. (2016)	Female mice 3 months old	T_{12} Compression	SCI + MT (single dose) SCI + MT14 (14 d' treatment) 10 mg/kg i.p.	1. Sham 2. SCI + vehicle	1, 3, 5, 7, 10 and 14 d	10 min after lesion, daily for 14 d	IL-1β and NG-2	BMS	MT prevented scar formation through reducing inflammatory cytokines after SCI.
Jing et al. (2017)	Female Sprague-Dawley rats 180–220 g	T_{10} Weight-drop	SCI + MT 10 mg/kg i.p.	1. Sham 2. SCI + vehicle	7 d	30 min after SCI for 7 d twice daily	BSCB, BDNF, Synapsin-I, or GAP-43	No	Improvement of microcirculation and decrease of neurological impairment may contribute to the

									neuroprotective effects of melatonin.
Paterniti et al. (2017)	C57BL/6N 20–22 g 4–5 weeks old	$T_{5–8}$ Compressed	SCI + MT 30 mg/kg i.p.	1. Sham 2. SCI + vehicle	1–20 d	1, 6, and 12 h after SCI	Neutrophil infiltration, NF-κB, iNOS	BMS	The anti-inflammatory activity of MT is related to PPAR-α in SCI.
Gao et al. (2016)	Male Kunming white mice 40–45 g 8 weeks old	$T_{6–10}$ Weight-drop	SCI + AEC (amniotic epithelial cells) treated by MT (0.01, 0.1, 1, 10 or 100 μM)	1. Sham 2. SCI + PBS 3. SCI + neural cells	1-42 delivery day post-injury	Transplantation surgeries were performed at 6 d after surgery	Differentiation into neural cells Tubb3 and GFAP	BBB	Co-treatment of MT and Wnt-4 improved the recovery of SCI and neural cell differentiation in bovine amniotic epithelial cells.
Aydemir et al. (2016)	Wistar albino rats	L_3 Clamping	SCI + MT 50 mg/kg i.p.	1. Sham 2. Sham + MT 3. SCI+vehicle	48 h	10 min before the aorta was clamped	MDA,GSH, caspase-3	No	MT played a protection role after ischemia in rats.
Liu et al. (2015)	Male Sprague–Dawley rats 205–225 g	T_{12} Compression	SCI + MT 100 mg/kg i.p.	1. Sham 2. SCI + vehicle	12, 24, 48 and 72 h	immediately after injury and then daily for 2 d	AQP4 , GFAP	No	MT may eliminate astrocytic swelling and anti-edema after acute SCI.
Haddadi and Fardid (2015)	Male Wistar rats 180–220 g	C_1-T_2 Irradiation	SCI + MT 100 mg/kg, 5 mg/kg	1.Sham + vehicle 2. Sham + MT 3. SCI + vehicle	3 w after irradiation	100 mg/kg oral administration. 30 min later	TNF-α, MDA	No	Administration of MT can inhibit TNF-α expression and prevent radiation-induced

						exposed to radiation, 5 mg/kg of melatonin daily for 3 w			SCI.
Wu et al. (2014)	Male C57BL/B6 mice 20–25 g	T_{10} Weight-drop	SCI + MT 5, 10, 25, 50 100 mg/kg/day i.p.	1. Sham 2. SCI + vehicle	48 h	immediately after SCI	BSCB permeability MMP3, AQP4, HIF-1α, VEGF, VEGFR2	No	MT may stabilize the function of microvascular barrier and microcirculation of SCI by promoting recovery of damaged BSCB.
Tavukçu Hasan et al. (2014)	Male Wistar albino rats 250–300 g	$T_{7–10}$ Weight-drop:	SCI + MT (10 mg/kg, i.p.), SCI + MT (10 mg/kg, i.p.) + tadalafil (10 mg/kg, p.o.)	1.Sham + vehicle 2. SCI + vehicle 3. SCI + tadalafil (10 mg/kg, p.o.)	7 d	Post-SCI for 7 d	Restored ED, caspase 3, NOS, MPO, SOD cGMP, NGF, GSH	No	The anti-oxidant effects of MT prevented the destroy of cavernosal tissues and promoted the recovery of ED.
Piao et al. (2014)	Female Sprague–Dawley rats 250–300 g 8 weeks old	T_{8-9} Photo-thrombotic injury	SCI + MT 50 mg/kg i.p.	1. Sham 2. SCI + vehicle	3 d after SCI and then once/week for 4 w	starting 1 h after injury and at 12 h intervals for 7 d	MMP-2, MMP-9	BBB	MT improved function by reducing the expression of MMP-9.
Lee et al. (2014)	Male Sprague–Dawley rats	T_{9-10} Weight-drop	SCI + MT 10 mg/kg SCI + MT +	1.Sham + vehicle 2. SCI + vehicle	1, 3, 7, 14, 21 d	Twice daily for 3 w	eNSPCs, MAP2, GFAP	BBB	Cotreatment with MT and exercise might promote

	250–270g		Ex s.c.						regeneration of endogenous neural stem/progenitor cells after SCI.
Jing et al. (2014)	Male C57BL/6 18–22 g	T_{10} Weight-drop	SCI + MT 10 mg/kg i.p.	1. Sham 2. SCI + vehicle	2, 7, 10, 14 d	Twice daily for 2 w	BSCB permeability AQP4, Ang1, ICAM-1, Bcl-2, and Bax	BMS	MT improved the disruption of BSCB and blood vessels by increasing of pericyte coverage.
Akakin et al. (2013)	Male Wistar albino rats 250–300 g	$T_{7\text{-}10}$ Weight drop	SCI + MT 10 mg/kg/day	1. Sham 2. SCI + vehicle	7 d	Once daily for 7 d	MDA,GSH, oxidative stress in the rat kidney	No	MT decreased oxidative stress of kidney after SCI.
Haddadi et al. (2013)	Male Wistar rats 180–220 g	C_1-T_2 Radiation	SCI + MT 100 mg/kg 5 mg/kg i.p.	1.Sham + vehicle 2. Sham + MT 3. SCI	1, 3, 8, 16, 20 and 22 w after radiation treatment.	100 mg/kg, 5 mg/kg daily for 22 w	VEGF	No	MT modulates the expression of VEGF and promotes survival of irradiated SCI animals.
Erşahin et al. (2012)	Wistar albino rats 250–300 g	$T_{7\text{-}10}$ Weight drop	SCI + MT 10 mg/kg/day, i.p.	1. Sham 2. SCI + vehicle	7 d	15 min post-injury daily for 1 w	MDA, GSH, NGF, caspase-3	Motor function scores	MT reduced tissue injury and improved the bladder function by reducing oxidative stress and affecting the expression of

									NGF.
Park et al. (2012)	Male Sprague–Dawley rats 250–260 g	T_{9-10} Weight drop	SCI + MT 10 mg/kg s.c.	1. Sham 2. SCI + vehicle	1, 3, 7, 14, 21, 28 d	Twice daily for 28 d	iNOS, GFAP, MAFbx, MuRF1	BBB	MT could prevent acute inflammation and skeletal muscle atrophy.
Park et al. (2010)	Male Sprague–Dawley rats 230–270 g 8 w old	T_{10} Weight drop	SCI + Ex + MT 10 mg/kg s.c.	1. SCI 2. SCI + Ex	1, 3, 7, 14, 21, 28 d after injury	twice daily for 4 w	iNOS, Beclin-1, LC3, p53, IKKα	BBB	Cotreatment with MT and exercise decreased the secondary damage of SCI rats. Combined therapy may reduce the side effects including fatigue induced by exercise.
Nesic et al. (2008)	Male Sprague–Dawley rats 225–250 g	T_{10} Weight drop	SCI + MT 10 mg/kg i.p.	1. Sham 2. SCI + vehicle	1–35 d	Once daily for 35 d	AQP1	BBB	MT treatment is related to the decreased AQP4 level and reduced mechanical allodynia in SCI animals.
Genovese et al. (2007)	Mice	$T_{6–7}$ Compression	1.SCI + MT 2.SCI + MT + dexamethasone MT: 10 mg/kg dexamethason	1. SCI + vehicle 2. SCI + dexamethasone 3. Sham + vehicle 4. Sham + MT	Once daily for 10 d after injury.	dexametha sone + melatonin 1 h and 4 h after SCI, and daily	Bax, Bcl-2, TNF-α, iNOS Fas Ligand	BBB	Cotreatment MT with dexamethasone decreased secondary damage of SCI mice and

			e: 0.025 mg/kg i.p.	+ dexamethasone		until day 9			MT reduced the side effects of steroids.
Erol et al. (2008)	Male Wistar rats 200–250g	$T_{4–5}$ Compression	SCI + MT 7.5 mg/kg i.p.	1. Sham 2. SCI + saline 3. SCI + octreotide	1, 10 d	each day for 10 d	MDA, SOD, GSH-Px	No	MT is more effective than octreotide in preventing secondary damage of SCI animals
Cayli et al. (2004)	Female albino rats 200–250g	$T_{7–10}$ Weight drop	SCI + MT 10 mg/kg i.p	1. Sham 2. SCI + vehicle	1–10 d	4 h, 24 h, 10 d	MDA	Motor function scale	MP, MT, used either alone or in combination, exerted similar effects in promoting functional recovery.

T: Thoracic vertebrae; C: cervical spine; L: lumbar vertebrae; SCI: spinal cord injury; MT: melatonin; i.p.: intraperitoneal; s.c.: subcutaneous; Bax: Bcl-2 associated X protein; Bcl-2: B-cell lymphoma-2; MDA: malondialdehyde; GSH: glutathione; BBB: Basso: Beattie: and Bresnahan; BMS: Basso Mouse Scale ;GSSG: glutathione (oxidized form); MPO: myeloperoxidase; IL-1β: interleukin-1β; NG-2: neural/glial antigen 2; BSCB: blood-spinal cord barrier; BDNF: brain-derived neurotrophic factor; NF-κB: nuclear factor κB; iNOS: inducible nitric oxide synthase; GAP-43: growth-associated protein-43; Tubb3 tubulin beta3 class III; GFAP: glial fibrillary acidic protein; TNF-α: tumor necrosis factor α; AQP4: Aquaporin 4; GFAP: glial fibrillary acidic protein; MMP3: matrix metalloproteinase-3; HIF-1α: hypoxia inducible factor α; VEGF: vascular endothelial growth factor; VEGFR2: vascular endothelial growth factor receptor 2; eNSPCs: endogenous neural stem/progenitor cells; MAP2: microtubule-associated protein 2; MPO: myeloperoxidase; SOD: superoxide dismutase; NGF: nerve growth factor; GSH: L-glutathione; Ang1: angiopoietin 1; ICAM-1: intercellular adhesion molecule 1; MAFbx: including muscle atrophy F-box; MuRF1: muscle-specific ring-finger protein 1; IKKα: inhibitor of nuclear factor kappa-B; d day(s); h: hours; min: minutes; w: week(s).