

Toxins	Effects	Mechanisms	Roles of melatonin
<i>Metals</i>	/	/	/
Cd	Hepatotoxicity (19, 26)	Oxidative damage and inflammation.	Inhibition of the TXNIP-NLRP3 inflammasome pathway.
	Neurotoxicity (20)	Abnormal mitochondrial dynamics.	Blocking mitochondrial fusion and fission imbalance and enhancing TFEB-mediated autophagy.
	Carcinogenicity (28)	Oxidative and estrogenic effects.	Inhibition of ER α -mediated transcription in both ERE- and AP1-containing promoters.
	Cardiovascular toxicity (29, 30)	Promotion of systemic high blood pressure by enhancing LPO.	Reduction of LPO production.
	Immunotoxicity; Cardiac oxidative damage (22, 24)		Protection of immunotoxicity and cardiac oxidative damage.
	Reproductive toxicity (testicular injury) (23)	/	Protective effects against male reproductive toxicity.
	Destruction of chloroplast (plants) (29, 36)	/	Increases plant Cd tolerance.
Hg	Endocrine toxicity (40)	Inhibition of synthesis of antioxidant and other metabolic enzymes in the thyroid gland.	Inhibition of oxidative stress and endocrine toxicity.
	Cardiovascular toxicity (41)	Oxidative stress and increases left ventricular end-diastolic pressure.	Enhancement of antioxidant defense.
	Nephrotoxicity (42)	/	Upregulation of stress protein expression and tubule recovery.
	Genotoxicity (38)	Genotoxicity by enhancing ROS.	Inhibition of genotoxicity.
	Neurotoxicity (39)	/	Inhibition of neurotoxicity.
Mn	Neurotoxicity (52)	Mn accumulation, oxidative stress, glutathione reduction.	Increase in glutathione level and activation of Nrf2.
	Motor dysfunction (51)	Oxidative stress and dopaminergic neurodegeneration.	Antioxidant activity and preservation of the DA system.
	Mitochondrial dysfunction (46)	Mitochondrial dysfunction.	Inhibition of mitochondrial dysfunction.
Cr	Improved diabetic status in ZDF rats (Cr(III)) (62)	/	Enhancement of plasma Cr content.
	Antidepressant-like effects Cr(III) (54)	/	/
	Carcinogenicity Cr(III) (55, 63)	Production of hydroxyl radicals and 8-OH-dG.	Prevention of membrane changes.
	Cytological damage in liver (Cr(VI) (57)	Cr(VI) promotes cell necrosis/apoptosis.	Preservation of insulin and glucose levels.

	Testicular histological changes Cr(VI) (58)	Germ cell apoptosis.	Maintaining normal spermatogenesis and male fertility.
	Cytotoxicity Cr(VI) (56, 59)	/	Increase in vitamin E and C levels, CAT activity, and/or reduction of hydroxyl radical.
Pb	Toxic metal accumulation (65, 73)	Downregulation of expression of metal transporters in metal excretory organs.	Promotion of Pb excretion.
	Neurotoxicity (67)	Apoptosis.	Inhibition of oxidative stress.
	Genotoxicity (68)	/	Antioxidant capacity.
	Gonadal toxicity (75)	Oxidative stress and endocrine disturbance.	Prevention of gonadal toxicity in a dose-dependent manner.
	Nephrotoxicity (69)	Reduction of NO level and induction of oxidative stress.	Reduction of oxidative stress and nephrotoxicity without changing NO content.
	DNA damage (70)	Reduction of blood glutathione levels.	Protection of low-dose, but not high-dose of Pb toxicity.
	Memory defects (71)	/	Inhibition of oxidative stress.
	Motor deficits (67)	Increase in LPO, TBARS levels, reduction of GPx and SOD activity.	Inhibition of oxidative stress.
	Damaged plant cells (72)	/	Inhibition of the translocation of cytochrome c.
As	Genotoxicity (83)	/	Inhibition of As-induced genotoxicity.
	Carcinogenicity (79)	Promotion of ROS and oxidative stress, upregulation of ATF2 and COX-2 expression, induction of bladder cancer.	Downregulation of ATF2 and COX-2 expression.
	Neurotoxicity (85)	Oxidative and nitrosative stress in the central nervous system.	Inhibition of oxidative and nitrosative stress and proinflammatory cytokines.
	Hepatotoxicity (86)	Inhibition of SOD, GPx and CAT activity.	Upregulation of PI3K/AKT pathway to induce Nrf2 expression.
	Nephrotoxicity (80)	Mitochondrial dysfunction, TNF α -mediated cascade of inflammation and cell death, blocking glucose uptake in kidneys.	Promotion of recovery from As-induced nephrotoxicity.
	Testicular damage (81)	Oxidative stress.	Inhibition of LPO and oxidative stress.
	Breast cancer improvement (84, 88)	Apoptosis in the ER α -positive breast cancer cell line MCF-7.	Upregulation of DNA damage-inducible transcript 4 expression, inhibition of the p38/JNK pathway, and enhancement of ATO-induced apoptotic cell death.

	Bladder cancer (79, 89)	Oxidative stress, upregulation of ATF2 and COX-2 expressions promotion of ROS.	Downregulation of ATF2 expression.
<i>Non metal</i>	/	/	/
TCDD	Reduction of melatonin levels (93, 94)	Enhancement of peripheral melatonin metabolism.	/
	Cardiotoxicity (95)	Induction of ROS production.	Reduction of oxidant activity.
	Nephrotoxicity (96)	Increase in systolic blood pressure, aortic contractile response to phenylephrine and MDA in renal tissue.	Reduction of blood pressure, aortic contractile response to phenylephrine and MDA level.
FA	Neurotoxicity (98, 99)	Reduction of systemic glutathione level, melatonin concentrations in the brain, promotion of oxidative stress.	Attenuation of hippocampal neuronal death, restoration of melatonin levels in the brain, and retardation of memory decline.
	Asthma (100)	Promotion of oxidative stress and activates NF- κ B.	Inhibition of oxidative stress, pathological airway response, and NF- κ B activation.
	Neuroinflammation in asthmatic patients (101)	Increase in IL-1 β , IL-17 and NGF levels.	Reduction of IL-1 β , IL-17 and NGF levels.
	Testicular damage (102)	Oxidative damage and apoptosis in rat testes.	Inhibition of oxidative damage and apoptosis in rat testes.
	Neurotoxicity (105, 107)	Increase in hydroxyl radical and superoxide anion levels.	Reduction of mitochondrial electron leakage, LPO, superoxide anion, promotion of ATP synthesis.
Cyanide	Epilepsy (109, 110)	Induction of brain neuronal cell death.	Inhibition of free radical and LPO Formation.
	DNA damage (111)	Promotion of hydroxyl radicals.	Prevention of DNA damage.
	Neuronal damage (113-116)	Oxidative stress, inhibition of membrane-bound ATPase and creatine kinase activities, induction of neuronal apoptosis, activation of NMDAR, voltage-dependent calcium channels, and intracellular Ca(2+) stimulation of calpain.	Antiapoptotic effects, inhibition of ROS and NMDAR expression.
PCBs			