Table 2. Effect of melatonin on animal models of ischemic and non-ischemic heart disease. The human equivalent dose (HED) of melatonin for a 75 kg adult is calculated by normalization of body surface area (43).

Findings	Melatonin dose	Daily HED for a 75 kg adult	Ref
In a model of rat myocardial infarction (by ligation of the left anterior descending coronary artery for 3 h before) melatonin reduced 86-87% of the area of injury and 75-80% of the number of injured myocardial areas	6 mg/kg/day p.o.	70 mg	(92)
In a rat model of isoproterenol-induced myocardial infarction, melatonin reduced cardiac damage markers, augmented cardiac antioxidant defense system and normalized the lipid profile	10 mg/kg /day i.p.	120 mg	(93)
In a rat model of severe obstructive sleep apnea, melatonin was cardioprotective by decreasing BP, oxidative stress, endothelial dysfunction, and inflammation	10 mg/kg/day i.p.	120 mg	(94)
In a rat model of myocardial infarction-induced heart failure, melatonin augmented cardiac activities of Na^+, K^+-ATPase and SERCA, content of glutathione and levels of caveolin-3, and reduced lactate dehydrogenase and creatine kinase, lysosomal enzymatic activities and cardiac malondialdehyde and myeloperoxidase	10 mg/kg/day i.p.	120 mg	(95)
In a rat model of hypoxic pulmonary hypertension with intermittent hypoxia, melatonin decreased right ventricular systolic pressures, the weight ratio RV/LV+S, pulmonary vascular structure remodeling; and several signals involved in proliferation of primary pulmonary artery smooth muscle cells	15 mg/kg/day i.p.	180 mg	(96)
In a rat model of isoproterenol-induced heart failure, melatonin decreased cardiac fibrosis, oxidative stress, insoluble and total collagen and the alteration of beta-tubulin in the left ventricle	10 mg/kg/day p.o.	120 mg	(97)
In a rat model of arterial hypertension induced by continuous light for 6 weeks, melatonin was cardioprotective by decreasing cardiac fibrosis and oxidative stress, but with no effect on left ventricle hypertrophy	10 mg/kg/day p.o.	120 mg	(106)

In a rat model of pulmonary hypertension induced by monocrotaline, melatonin exerted cardioprotection both curative and preventive by decreasing right ventricular hypertrophy, systemic oxidative stress and cardiac interstitial fibrosis	6 mg/kg/day p.o.	70 mg	(98)
In a murine model of post-infarction, cardiac remodeling and dysfunction, melatonin ameliorated cardiac dysfunction; adverse left ventricle remodeling; autophagy, apoptosis and mitochondrial dysfunction	20 mg/kg/day p.o.	120 mg	(100)
In a murine model of myocardial infarction melatonin was cardioprotective by reducing post- myocardial infarction damage, Notch1 signaling and Mfn2 expression via melatonin receptors	10 - 20 mg/kg/day i.p.	60 - 120 mg	(101)
In a murine model of myocardial infarction (ligation of the left anterior descending coronary artery for 5 days) melatonin decreased infarction damage by augmenting PGC-1α and Tom 70 expression, preserving mitochondrial integrity, and decreasing ROS production	10 - 20 mg/kg/day i.p.	60 - 120 mg -	(107)
In a murine model of pathological cardiac hypertrophy, melatonin reduced pulmonary congestion, cardiac fibrosis and the deterioration of cardiac contractile function	20 mg/kg/day p.o.	120 mg	(102)
In a model of rat diabetes mellitus, melatonin protects against streptozotocin-induced diabetic cardiomyopathy by the phosphorylation of vascular endothelial growth factor-A.	50 mg/kg/day i.p.	600 mg	(103)
In rats subjected to cardiac ischemia by coronary artery ligation for 30 min and reperfusion for 2 hr melatonin attenuated myocardial ischemia/reperfusion Injury by inhibiting autophagy via an AMPK/mTOR signaling pathway	20 mg/kg i.p.	120 mg	(108)
In a rat model of doxorubicin-induced cardiotoxicity, melatonin improves cardiac and mitochondrial function via peroxisome proliferator-activated receptor gamma coactivator 1-αand sirtuin activity	6 mg/kg/day p.o.	70 mg	(104)
In a murine model of heart failure with preserved ejection fraction melatonin improves cardiac function.	50 mg/kg/day p.o.	300 mg	(109)
In a mouse model of myocarditis infected with coxsackievirus B3 melatonin counteracted effectively myocardial injuries	14.4 mg/kg/day i.p.	88 mg	(110)

In a murine model of diabetic cardiomyopathy, melatonin activates Parkin translocation and rescues the impaired mitophagy activity of through Mst1 inhibition	20 mg/kg i.p.	120 mg	(111)
In a rat model of overload-induced ventricular hypertrophy caused by abdominal aortic constriction melatonin prevented the changes in cardio fibrosis and in gene expressions of HDAC1, HDAC2, HDAC3, HDAC4 in cardiomyocytes	10 mg/kg i.p.	60 mg	(112)
In a murine chronic pain induced by spared nerve injury model followed by myocardial ischemia-reperfusion, melatonin attenuated chronic pain related myocardial ischemic susceptibility through inhibiting RIP3-MLKL/CaMKII dependent necroptosis	20 mg/kg i.p.	120 mg	(113)
In a rat model of cardiac ischemia/reperfusion after ligation of descending coronary artery melatonin treatment maintained myocardial function and cardiomyocyte viability, and these effects were highly dependent on mitochondrial fusion/mitophagy	20 mg/kg i.p.	120 mg	(114)