

Table 3. Effect of melatonin on transgenic models of AD. 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 4-month-old APP 695 transgenic mice treated with melatonin for up to 15.5 months, partial inhibition of expected elevation of β -amyloid, reduced abnormal nitration of proteins, and increased survival were seen	50 mg/kg/day p.o.	300 mg/day	(117)
In 4-month-old APP 695 transgenic mice receiving melatonin for 4 months, better learning and memory performance and preserved choline acetyltransferase activity in the frontal cortex and hippocampus were seen	10 mg/kg/day p.o.	60 mg/day	(118)
In 14-month-old transgenic (Tg 2576) mice treatment with melatonin for 4 months failed to produce anti-amyloid or antioxidant effects	3.6 mg/kg/day p.o.	20 mg/day	(119)
In 4-month-old APP 695 transgenic mice treated for 4 months melatonin prevented the increase of brain thiobarbituric acid reactive substances, the decrease in glutathione content, and the upregulation of the apoptotic-related factors	10 mg/kg/day p.o.	60 mg/day	(120)
In 5-month-old transgenic (Tg2576) mice exposed to aluminum and melatonin for 6 months a lower habituation pattern was observed in melatonin-treated animals. Aluminum-treated Tg2576 mice showed impaired learning, an effect unmodified by melatonin treatment	10 mg/kg/day p.o.	60 mg/day	(121)
In 2–2.5-month-old APP/PS1 transgenic mice receiving melatonin for 5 months, less cognitive impairment in working memory and spatial reference learning/memory was observed. Immunoreactive A β deposition was reduced in hippocampus and entorhinal cortex of melatonin treated transgenic mice	20 mg/kg/day p.o.	120 mg/day	(122)
In 5-month-old transgenic (Tg2576) mice exposed to aluminum and melatonin for 6 months the prooxidant effect of aluminum in the hippocampus was prevented	10 mg/kg/day p.o.	60 mg/day	(123)

In 9-month-old transgenic amyloid precursor protein (APP ^{SWE}) mice given melatonin for 4 wk the temporal pattern of anxiety-like behavior and time-dependent changes in basal forebrain acetylcholinesterase expression remained unmodified	1 mg/kg/day p.o.	6 mg/day	(124)
In 18-20-month-old APP/PS1 transgenic mice receiving melatonin for 1 month less mitochondrial A β levels and a near complete restoration of mitochondrial respiratory rates, membrane potential, and ATP levels were observed in hippocampus, cortex, or striatum.	20 mg/kg/day p.o.	120 mg/day	(125)
In 3.5 - 5.5 month-old APP/PS1 transgenic mice receiving melatonin or ramelteon for 5.5 months a significant reduction in hippocampal protein oxidation was observed	5 mg/kg/day p.o.	30 mg/day	(126)
In 11- 12-month-old APP ^{sw} mice treated with melatonin for 1 month a near complete restoration of brain mitochondrial function was found	100 mg/kg/day p.o.	600 mg/day	(127)
In 6-month-old 3xTg-AD mice treated with melatonin for 6 months both melatonin and physical exercise decreased soluble amyloid β oligomers, whereas only melatonin decreased hyperphosphorylated tau. Both treatments protected against cognitive impairment, brain oxidative stress, and a decrease in mitochondrial DNA whereas the combined treatment of physical exercise plus melatonin was effective to protect mitochondrial complexes	10 mg/kg/day p.o.	60 mg/day	(128)
Melatonin improved learning and spatial memory in 5-month-old transgenic (Tg2576) mice exposed for 14 months to aluminum	10 mg/kg/day p.o.	60 mg/day	(129)
In 4-month-old transgenic APP/PS1 mice administered with a curcumin/melatonin hybrid (Z-CM-I-1) 12 weeks a decreased accumulation of A β in the hippocampus and cerebral cortex and reduced inflammatory responses and oxidative stress were observed	50 mg/kg/day of Z-CM-I-1 p.o.	150 mg/day	(130)
In 10-month-old triple transgenic mice (3xTg-AD) receiving melatonin for 1 month amelioration of anxiety and depression-like behaviors were observed	10 mg/kg/day p.o.	60 mg/day	(131)

In 4-month-old transgenic (Tg2576) mice the administration of melatonin augments the glymphatic clearance of A β	100 mg/kg/day p.o.	600 mg/day	(132)
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