

Table 1. Autophagy-inducing compounds with therapeutic potential for AD treatment

Compound	Mechanism of action	Animal model data	Clinical trial data
Rapamycin (and its derivatives)	mTOR inhibition	Reduces amyloid plaques, tauopathies, and improves cognition (Lin et al., 2013; Ozcelik et al., 2013; Spilman et al., 2010)	Down-regulates some senescence markers, and improves senescence-related physical performance (Singh et al., 2016)
Lithium	AMPK activation	Reduces tauopathies (Caccamo, Oddo, Tran & LaFerla, 2007)	Improves cognition (Matsunaga, Kishi, Annas, Basun, Hampel & Iwata, 2015)
Curcumin	mTOR inhibition	Reduces amyloid plaques, and improves cognition (Wang, Zhang, Teng, Zhang & Li, 2014)	Reduces inflammation (Salehi et al., 2019)
Resveratrol	AMPK activation	Reduces amyloid plaques (Vingtdeux et al., 2010)	Improves cognition (Kou & Chen, 2017; Turner et al., 2015)
Glucosamine	AMPK activation, mTOR inhibition	Not applied to AD animal models yet	Improves osteoarthritis (Zeng et al., 2015; Zhu, Sang, Wu, Rong & Jiang, 2018)
Metformin	AMPK activation, mTOR inhibition	Reduces amyloid plaques, tauopathies and improves cognition (DiTacchio, Heinemann & Dziewczapolski, 2015; Farr, Roesler, Niehoff, Roby, McKee & Morley, 2019; Lu et al., 2020)	Improves cognition (Koenig et al., 2017)
Oleuropein	AMPK activation, mTOR inhibition	Reduces amyloid plaques and improves cognition (Grossi et al., 2013)	Improves glucose homeostasis (Nediani, Ruzzolini, Romani & Calorini, 2019)
Memantine	Activation of autophagy in an mTOR-dependent or -independent manner	Reduces amyloid plaques, tauopathies, and improves synaptic plasticity and cognition (Martinez-Coria et al., 2010)	FDA approved for AD treatment
Carbamazepine	Activation of autophagy in an mTOR-dependent or -independent manner	Reduces amyloid plaques and improves cognition (Li et al., 2013; Zhang et al., 2017)	FDA approved for the treatment of epilepsy, trigeminal neuralgia and so on
Nilotinib	mTOR inhibition, Elevation of VPS34 complex formation	Reduces amyloid plaques and improves cognition (Lonskaya, Hebron, Desforges, Franje & Moussa, 2013)	Reduces amyloid accumulation and CSF A β (Turner et al., 2020)
Spermidine	Activation of autophagy	Not applied to AD animal models	Reduces blood pressure and

	via modulating Beclin-1	yet	cardiovascular disease risk (Eisenberg et al., 2016)
Trehalose	TFEB activation	Reduces amyloid plaques, tauopathies, and improves cognition (Du, Liang, Xu, Sun & Wang, 2013; Portbury et al., 2017; Schaeffer, Lavenir, Ozcelik, Tolnay, Winkler & Goedert, 2012)	Improves swallowing and muscle power in Oculopharyngeal Muscular Dystrophy (Khalifeh, Barreto & Sahebkar, 2019)
Nicotinamide	Mitophagy activation	Reduces amyloid plaques, tauopathies, and improves cognition (Fang et al., 2019; Gong et al., 2013; Green et al., 2008; Liu et al., 2013)	Limitedly improves cognition (Di Meco, Curtis, Lauretti & Pratico, 2020)