**Table S1. Compounds with neuroprotective effects in neurodegenerative disease models showed inhibitory effects on microorganisms.** Asterisks (\*) mark the compounds that could inhibit the bacterial biofilm formation. ND means “not determined”.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Compounds** | **Worm models** | | **Mouse model** | | **Known effects on the microorganism** |
| **Diseases** | **Neuroprotective effects** | **Diseases** | **Neuroprotective effects** |
| Ginkgo biloba extract\* | AD | Reduce A deposit, A-induced paralysis, and chemotaxis (Wu et al., 2006) | AD | Reduce A toxicity and improves cognitive functions (Tchantchou et al., 2007) | Inhibit biofilm formation (Wu et al., 2016) |
| Caffeine\* | AD | Reduce A-induced paralysis and increase antioxidant capacity (Dostal et al., 2010) | AD | Reduce dementia (Arendash et al., 2006; Eskelinen and Kivipelto, 2010) | Inhibit bacteria growth at high dose; inhibit biofilm formation and cause biofilm dispersal (Chakraborty et al., 2020; Sandlie et al., 1980) |
| Clioquinol | AD | Reduce Aβ accumulation and enhance memory formation (Matlack et al., 2014) | AD | Reduce Aβ plaque burden and attenuate astrogliosis (Grossi et al., 2009) | Inhibit fungalbiofilm formation (You et al., 2018; You et al., 2020) |
| Curcumin\* | AD | Reduce Aβ accumulation and increase lifespan (Alavez et al., 2011; Miyasaka et al., 2016) | AD | Reduce Aβ accumulation, oxidative damage, and inflammation (Lim et al., 2001); inhibit neuronal death and iNOS expression in AD models (Begum et al., 2008) | Inhibit biofilm formation (Kali et al., 2016) and induce biofilm dispersal (Ding et al., 2017) |
| Ferulic acid\* | AD | Reduce Aβ accumulation and enhance autophagy (Wang et al., 2020) | AD | Reduce vasoconstriction of hippocampal capillaries and ameliorate Aβ plaque deposition and spatial memory deficit (Wang et al., 2021b) | Inhibit bacteria growth and inhibit biofilm formation (Borges et al., 2012; Takahashi et al., 2013); induce biofilm dispersal (Dasagrandhi et al., 2018) |
| Fluoxetine\* | AD | Reduce A-induced paralysis; enhance thermal resistance and increase lifespan (Keowkase et al., 2010b) | AD | Reduce APP cleavage and Aβ generation and neuronal apoptosis (Huang et al., 2018) | Modulate bacterial gut colonization and inhibit biofilm formation (Fung et al., 2019; Pelling et al., 2019) |
| Galanthamine | AD | Reduce A-induced paralysis; increase lifespan (Xin et al., 2013) | AD | Slow down Aplaque formation and behavioral decline (Bhattacharya et al., 2014) | ND |
| Glycitein | AD | Reduce A deposits and ROS production (Gutierrez-Zepeda et al., 2005) |  | ND | Among the antibacterial components of Doenjang extracts (Lalouckova et al., 2021) |
| JAY2-22-33 | AD | Reduce A-induced paralysis (Keowkase et al., 2010a) |  | ND | ND |
| JWB1-84-1 | AD | Reduce A-induced paralysis (Keowkase *et al.*, 2010a) | AD | Improve memory-related task accuracy (Sood et al., 2007) | ND |
| Quercetin\* | AD | Decrease Ab production (Regitz et al., 2014) | PD | Protect against DA neurodegeneration and mitochondrial dysfunction (Ay et al., 2017) | Inhibit biofilm formation (Memariani et al., 2019) |
| Rifampicin\* | AD | Reduce A-induced paralysis (Lublin et al., 2011) | AD | Inhibit Aβ oligomerization, tau hyperphosphorylation, and synapse loss and Enhance memory formation  (Umeda et al., 2018) | Antibiotic; inhibit biofilm formation (Verma et al., 2021) |
| Tannic acid\* | AD | Increase lifespan and reduce A-amyloid fibril (Lublin *et al.*, 2011) | AD | Inhibit β-secretase and prevents A-induced cognitive impairment (Takashi Mori, 2012) | Inhibit bacterial growth and biofilm formation (Dong et al., 2018); induce biofilm dispersal (Siddiquia, 2019) |
| Tetracycline\* | AD | Reduce Aβ oligomer deposition and inhibit A-induced paralysis and oxidative stress (Diomede et al., 2010) | AD | Reduce the level of Aβ oligomers and improve memory (Balducci et al., 2018) | Antibiotic; inhibit biofilm formation (Stone et al., 2002) |
| Thioflavin T\* | AD | Increase lifespan and locomotion and reduce tau toxicity (Gamir-Morralla et al., 2019) | AD | Reduce amyloid plaques and inhibit microglial activation (Sarkar et al., 2015) | Inhibit biofilm formation (Bondia et al., 2021) |
| Acetylcorynoline | AD, PD | Reduce -synuclein aggregation, DA neuron degeneration and enhance proteasome activity (Fu et al., 2014) |  | ND | ND |
| Bacitracin\* | AD, PD | Reduce Aβ-induced motor deficits and aging (Lublin *et al.*, 2011); inhibit MPP(+)-induced dopaminergic (DA) neuron loss (Lehtonen et al., 2016) | PD | Attenuate motor deficits, decrease DA neuron loss, and reduce inflammation in 6-OHDA-treated rats (Koutzoumis et al., 2020) | Antibiotic; inhibit biofilm formation (Zaidi et al., 2020) |
| EGCG\* | AD, PD | Reduce Aβ oligomer deposits and formation of lipofuscin (Abbas and Wink, 2010); reduce -synuclein-induced locomotion defects (Wang et al., 2021a) | ALS, PD, AD | Prolong symptom onset and lifespan in ALS model (Koh et al., 2006); decrease inflammation in MPTP-induced PD model (Zhou et al., 2018); restore mitochondrial function and ATP levels in AD model (Dragicevic et al., 2011) | Inhibit biofilm formation and induce biofilm dispersal (Serra et al., 2016) |
| Valproic acid | AD, PD | Reduce Aβ deposition and memory deficits (Evason et al., 2008); inhibit -synuclein-induced DA neuron loss(Kautu et al., 2013) | PD | Inhibit MPTP-induced DA neuron loss (Kidd and Schneider, 2011) | Inhibit fungal growth and fungal biofilm formation (Singh et al., 2021) |
| Acetaminophen\* | PD | Prolong lifespan (Lublin *et al.*, 2011), inhibit-synuclein-induced DA neuron loss and locomotion defects (Chen et al., 2021; Locke et al., 2008) |  | Reduce LPS-induced cognitive impairment and hippocampal damage (Zhao et al., 2017) | Inhibit biofilm formation (Abidi et al., 2019) |
| Losartan | PD | Inhibit-synuclein-induced locomotion defects (Chen *et al.*, 2021) | PD | Reduce -synuclein oligomers in PD rat neurons (Chen *et al.*, 2021) | ND |
| Rifabutin\* | PD | Inhibit -synuclein-induced locomotion defects (Chen *et al.*, 2021) | PD | Reduce -synuclein oligomers in PD rat neurons (Chen *et al.*, 2021) | Inhibit bacterial biofilm and infection (Doub et al., 2020) |
| Spermidine | AD, PD | Reduce -synuclein accumulation, improve locomotion, and activate mitophagy in PD and reduce memory loss in AD (Buttner et al., 2014; Yang et al., 2020) | FTLD | Activate autophagy, reduce TDP-43-induced neuron loss, and enhance performance in rotarod tests (Wang et al., 2012) | Promote biofilm formation (Hobley et al., 2017; Thongbhubate et al., 2021) |
| Metformin\* | AD, PD, HD | Rescue 6-OHDA-induced DA neuron loss (Saewanee et al., 2021); inhibit A-induced paralysis and improve neurotransmitter function (Ahmad and Ebert, 2017); reduce polyQ aggregation (Sanchis et al., 2019) | AD, HD, PD | Reduce behavioral defects in HD mice (Sanchis *et al.*, 2019); improve learning and memory in AD mice (Farr et al., 2019); rescue MPTP-induced neurodegeneration and increase BDNF levels (Patil et al., 2014) | Inhibit bacterial biofilm and quorum sensing (Abbas et al., 2017) |
| Icariin and its derivative icariside II\* | AD, HD | Increase tolerance to thermo and oxidative stress; delay the onset of polyQ or Aβ -induced paralysis (Cai et al., 2011) | AD | Improve cognitive function; reduce neuronal apoptosis and suppress ER stress in AD (Li et al., 2019) | Inhibit biofilm formation (Coenye et al., 2012) |
| PBT2 | AD, HD | Inhibit polyQ- and A-induced paralysis (Cherny et al., 2012; McColl et al., 2012) | AD, HD | Reduce tau accumulation and enhance cognition (Sedjahtera et al., 2018); reduces brain weight loss and enhance motor performance in HD mice (Cherny *et al.*, 2012) | Inhibit polymyxin-resistance of Gram-negative pathogens (De Oliveira et al., 2020) |
| Apomorphine | PD | Rescue MPP(+)-induced locomotion defects (Mocko et al., 2010) | AD | Reduce Aβ accumulation and tau hyperphosphorylation and enhance memory formation (Himeno et al., 2011) | ND |
| Baicalin\* | PD | Alleviate 6-OHDA-induced oxidative stress; improve locomotion and survival (Ma et al., 2021) | AD | Reduce Ab production and improve cognitive function (Zhang et al., 2013) | Antimicrobial activity; inhibit biofilm formation (Luo et al., 2017) |
| Bromocriptine | PD | Rescue MPP(+)-induced locomotion defects (Mocko *et al.*, 2010) | PD | Reduce 6-OHDA-induced DA neuron loss (Ogawa et al., 1994) | ND |
| Betulin\* | PD | Reduce -synuclein accumulation and inhibit 6-OHDA-induced DA neurodegeneration (Tsai et al., 2017) | AD | Mitigate scopolamine-induced memory deficits (Cho et al., 2016) | Inhibit biofilm formation (Viszwapriya et al., 2016) |
| Indoline and its derivative GW5074 | PD | Reduce LRRK2(G2019S)-induced DA neurodegeneration (Liu et al., 2011) | HD | Inhibit 3-Nitropropionic acid-induced neurodegeneration and behavioral deficits (Chin et al., 2004) | Inhibit gram-positive bacteria growth (Clement Opoku-Temeng, 2017) |
| Ginsenoside\* | PD | Attenuate 6-OHDA-induced DA neurodegeneration (Chalorak et al., 2021) | AD | Alleviate cognitive dysfunction and neuronal damage and decrease Ab and phosphorylated tau levels (Zhang et al., 2021) | Antibiofilm activity; induce biofilm dispersion (Cao et al., 2019) |
| Lisuride | PD | Inhibit MPP(+)-induced neurodegeneration (Braungart et al., 2004) | PD | Increase wakefulness and paradoxical sleep latency in MPTP-treated mice (Laloux et al., 2008) | ND |
| LRRK2-IN1 | PD | Reduce LRRK2 mutants-induced DA neurodegeneration (Yao et al., 2013) | PD | Inhibit LRRK2 mutants-induced DA neurodegeneration but incapable of permeating the blood-brain barrier (Chen et al., 2018) | ND |
| P7C3 | PD | Block MPP(+)-mediated DA neuron death (De Jesus-Cortes et al., 2012) | PD | Inhibits microglial activation and DA neuronal loss (Gu et al., 2018) | ND |
| Rottlerin\* | PD | Ameliorate MPP(+)-induced neurodegeneration (Braungart *et al.*, 2004) | PD | Inhibit MPTP-induced locomotor deficits and striatal depletion of dopamine (Zhang et al., 2007) | Inhibit bacterial quorum sensing and biofilm formation (Suresh et al., 2021) |
| Sorafenib and its derivative\* | PD | Inhibit LRRK2(G2019S)-induced DA neurodegeneration (Liu *et al.*, 2011) | PD | Activate PINK1-Parkin pathway (Zhang et al., 2017) | Inhibit biofilm formation (Cui et al., 2019) |
| Tauroursodeoxycholic acid | PD | Rescue the increased vulnerability to rotenone in DJ-1 knockout mutants (Ved et al., 2005) | PD | Reduce -synuclein aggregation, DA neurodegeneration and prevent glial activation, oxidation, and autophagy (Cuevas et al., 2020) | ND |
| TTT-3002 | PD | Reduce LRRK2 mutants-induced DA neurodegeneration (Yao *et al.*, 2013) |  | ND | ND |
| Celecoxib\* | HD | Delay the onset of polyQ-mediated protein aggregation and proteotoxicity(Ching et al., 2011) | PD | Reduced LPS-induced sensorimotor behavioral defects and DA neuron dysfunction (Kaizaki et al., 2013) | Inhibit biofilm formation (Tzeng et al., 2020) |
| Lithium | HD | Ameliorate polyQ-mediated neuron loss (Voisine et al., 2007) | HD | Alleviated spontaneous locomotor deficits and depressive-like behaviors in HD mice (Chiu et al., 2011) | Absorbed by biofilm polymer (Andi Kurniawan, 2013) |
| Mithramycin | HD | Ameliorate polyQ-mediated neuron loss (Voisine *et al.*, 2007) | HD | Reduce neuropathology and increase lifespan in HD mice (Ferrante et al., 2004) | Produced by bacteria (Pham et al., 2019) |
| ML346\* | HD | Activates transcription of the Hsp70 promoter and suppresses aggregation of polyQ (Calamini et al., 2010) |  | ND | Inhibit biofilm formation (Guan X, 2022) |
| Oligomycin\* | HD | Dose-dependent rescue of polyQ induced neuronal death (Varma et al., 2007) |  | ND | Antibiotic; clear established biofilm (Yamada et al., 2020) |
| Rotenone | HD | Dose-dependent rescue of polyQ induced neuronal death (Varma *et al.*, 2007) |  | Induce DA neurodegeneration at 30 mg/mL (Inden et al., 2011) | ND |
| Salidroside\* | HD | Ameliorate polyQ-mediated neuron loss, increase antioxidant capacity, and reduce paraquat-induced mortality (Xiao et al., 2014) | PD | Reduce MPTP-induced motor defects and rescue the loss of tyrosine hydroxylase (TH)-positive neurons (Zhang et al., 2016) | Inhibit biofilm formation (Coenye *et al.*, 2012) |
| Trichostatin A and other HDAC inhibitors | HD, PD | Ameliorate polyQ-mediated neuron loss (Bates et al., 2006; Voisine *et al.*, 2007) | PD | Increase the expression of TH and BDNF and protect the nigrostriatal DA neurons in MPTP-treated mice (Suo et al., 2015) | Inhibit fungalbiofilm formation (Cécile Garnaud, 2016) |
| Azaperone or isoniazid | FTDP | Reduce insoluble tau and inhibit tau-induced locomotion defects and neuronal loss (McCormick et al., 2013) | FTDP | Reduce the level of insoluble tau (Crowe et al., 2020) | ND |
| Perphenazine | FTDP | Reduce insoluble tau and inhibit tau-induced locomotion defects and neuronal loss (McCormick *et al.*, 2013) |  | ND | ND |
| Trazodone | FTDP | Reduce insoluble tau and inhibit tau-induced locomotion defects and neuronal loss (McCormick *et al.*, 2013) | FTDP | Reduced the burden of hyperphosphorylated tau (Halliday et al., 2017) | ND |
| Zotepine | FTDP | Reduce insoluble tau and inhibit tau-induced locomotion defects and neuronal loss (McCormick *et al.*, 2013) |  | ND | Inhibit fungalbiofilm formation (Siles et al., 2013) |
| Guanabenz | ALS | Reduce TDP-43-induced paralysis, neurodegeneration, oxidative stress, and ER stress response (Vaccaro et al., 2013) | ALS | Protect fibroblasts expressing SOD1(G93A) mutants during ER stress (Vieira et al., 2015) | ND |
| Propyl gallate\* | ALS | Reduce TDP-43-induced paralysis and axonal degeneration and increase lifespan (Tauffenberger et al., 2013) | AD | Inhibit Aβ aggregation (Chan et al., 2016) | Inhibit biofilm formation (Kosuru et al., 2021) |
| Salubrinal | ALS | Reduce TDP-43-induced paralysis, neurodegeneration, oxidative stress, and ER stress response (Vaccaro *et al.*, 2013) | ALS | Inhibit eIF2a dephosphorylation and reduce ER stress; ameliorate SOD1 mutants-induced disease symptoms and extend survival (Saxena et al., 2009) | ND |
| Trolox | ALS | Reduce TDP-43-induced paralysis and axonal degeneration and increase lifespan (Tauffenberger *et al.*, 2013) | ALS | Reduce cytosolic oxidative stress in SOD1 neurotoxicity (Rojas et al., 2015) | ND |
| α-methyl-α-phenylsuccinimide | ALS | Ameliorates TDP-43-induced locomotion defects and neurodegeneration (Wong et al., 2018) |  | ND | ND |
| Methylene blue\* | ALS, FTDP | Reduce detergent insoluble phospho-tau and protect against TDP-43 neurotoxicity (Fatouros et al., 2012; Vaccaro et al., 2012a; Vaccaro et al., 2012b) | FTDP | Reduce detergent insoluble phospho-tau (Hosokawa et al., 2012) | Visualize biofilm; inhibit biofilm formation; induce biofilm dispersal (Shaw et al., 2020; Wu et al., 2009) |
| PHA767491 | ALS | Reduce TDP-43 phosphorylation and prevent TDP-43-induced neurodegeneration (Liachko et al., 2013) | ALS | Ameliorate the gait ataxia and inflammatory response in TDP-43 transgenic mice (Chung et al., 2020) | ND |
| LDN-0130436 | ALS | Inhibit TDP-43 aggregation in a dose-dependent manner (Boyd et al., 2014) |  | ND | ND |

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