PMMB 2025, 8, 1: a0000467. doi: 10.36877/pmmb.a000046

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Supplementary materials

Table S1: Categorization of Studies by Autophagy Type and Compound. Table categorizes the included studies details based on the type of autophagy investigated and the specific pure compound examined.

Plant name, common & scientific name, part (root/flower/leave, etc. used), country	Source	Pure compounds	Human disease (Cell lines/ animal models)	Results	Autophagy Type/Regulatory Pathway	Reference
Aloe vera, *Aloe barbadensis miller*, Serbia	Purchased from Sigma Aldrich	Aloe emodin	Brain tumours (rat C6 glioma cells and human U251 glioma cells)	Anti-glioma activities: ↑ Cytotoxicity in both glioma cells, ↑ PI-stained cells and caspase activation that induce apoptosis in both cell lines Autophagic enhancement: ↑ AO-stained acidic cytoplasmic vesicles in C6 glioma cells in both cell lines	Microautophagy	[54]
Goniothalamus species, Brazil	Chemically synthesized	Goniothalamins, styryl lactone family	Renal cancer (human 786-0 kidney cancer cells)	Anti-proliferative activities: ↑ Cell cytotoxicity and NOS activity inhibition, ↓ Bcl-2 anti-apoptotic marker and ↑ PARP cleavage that induce cell apoptosis Autophagic enhancement: ↑ LC3-II autophagic marker	Macroautophagy	[21]
Bai Shao, *Radix paeoniae alba* (root), China	Purchased from National Institute for the Control of Pharmaceutical and	Paeoniflorin	Parkinson's disease (rat PC-12 pheochromocytoma cells)	Neuroprotective activities: ↑ cell viability against MPP^+ and acidosis (pH5.0) insults, ↓ LDH release and apoptotic rate and ↓	Macroautophagy	[59]

	Biological Products of China, Beijing, China.			intracellular Ca^{2+} level in MPP^{+} and pH5.0-treat cells Autophagic enhancement: ↑ LC3-II/I ratio autophagic markers, and ↑ LAMP2a		
				Neuroprotective activities: ↑ cell viability against MPP^{+} and acidosis (pH6.0) insults in differentiated PC-12 cells. Autophagic enhancement: ↓ α-synuclein expression level, ↑ LC3-II/I ratio autophagic markers, and ↓ ASICs expression levels that lead to neuronal loss	Macroautophagy	[93]
	Purchased from Wako Pure Chemical Industries, Japan		Spinal and bulbar muscular atrophy (Neuro2A, AR24Q or AR97Q-transfected NSC34 cell, and AR24Q and AR-97Q SBMA mice	Protective effects: ↑ Nuclear factor-YA expression level to enhance proteolysis and autophagy in the mutant AR97Q-transfected NSC34 cells ↓ The onset of SBMA in mice ↑ Clearance of mutant AR protein in both SBMA cells and mice Autophagic enhancement: ↑ TFEB level, master autophagy regulator in the mutant AR97Q-transfected NSC34 cells	Signalling pathway -TFEB regulates mTOR	[94]
	Purchased from Nanjing Zelang Medical Technology		Alzheimer's disease (SH-SY5Y cells)	Neuroprotective activities: ↓ Tau hyperphosphorylation and GSK-3β activation in okadaic acid-treated SH-SY5Y cells	Signalling pathway	[95]

	company, Nanjing China			↓ Swelling and synapsis shortening, and ↑ microtubule structures of okadaic acid-treated cells ↓ Akt acitvaition and expression of calpain apoptotic marker Autophagic suppression: ↓ LC-3II/I ratio autophagic marker		
Red grape, *Vitis vinifera* (fruit skin)	Purchased from Sigma Aldrich (synthetic form) and Chromadex (natural form), US	Resveratrol	Alzheimer's disease (HEK-293 embryonic cell, mouse N2a neuroblastoma , and J20 APP transgenic mice primary neuronal cell)	Neuroprotective activities: ↑ AMPK activation and amyloidogenic activity in all cell lines *via* increasing the intracellular Ca^{2+} level. Autophagic enhancement: ↓ mTOR autophagic marker	Signalling pathway	[65]
	Source of Mega Resveratrol, rodent maintenance diet supplemented with trans-resveratrol provided by Candlewood Stars, Inc., Connecticut, United State		Amyotrophic lateral sclerosis (SOD1 mutation mice)	Neuroprotective activities: ↑ Locomotion impairment in SOD^{G93A} mice ↓ Spinal motoneuron degeneration in L4-L5 lumbar spinal cord motoneuron of SOD^{G93A} mice ↑ Survival time of SOD^{G93A} mice ↑ AMPK activation in promoting mitochondrial biogenesis Autophagic enhancement: ↑ Sirt1, Beclin-1 and LC3-II/I ratio autophagic markers	Macroautophagy and signalling pathway	[23]
	Purchased from Sigma Aldrich (R5010), China		Alzheimer's disease (rat PC-12 pheochromocytoma cells)	Neuroprotective activities: ↑ Viability of $A\beta_{25-35}$-induced neurotoxicity in differentiated PC-12 cells Autophagic enhancement:	Macroautophagy	[28]

				↑ LC3-II/I ratio, SIRT1, and PARP1, while ↓p62 autophagic markers		
	Purchased from Sigma Aldrich ,China		Traumatic brain injury (Sprague Dawley rats)	Neuroprotective activities: ↓ brain oedema, ↑ learning, memory, and motor function and ↓ hippocampal neuronal damage in TBI rats ↓TLR4 protein and NF-κB p65 neuroinflammatory marker in hippocampus of TBI rats Autophagy enhancement: ↓ LC3-II//I ratio and Beclin 1 autophagic markers in the hippocampus of TBI rats	Macroautophagy	[36]
	N/A, China		Parkinson's disease (male C57BL/6 mice)	Neuroprotective activities: ↑ Behavioural impairment of MPTP-treated mice ↑ Dopamine level and ↓ the loss nigral TH-positive neurons and striatal TH protein level in the brain of MPTP-treated mice Autophagic enhancement: ↑ SIRT1, LC3-II/I ratio and p62 autophagic markers ↓ Acetylation of LC3 level that involved in α-synuclein clearance	Macroautophagy	[30]
	Purchased from Sigma Aldrich, China		Spinal cord injury (C57BL/6 mice)	Neuroprotective activities: ↑ Tissue structural and functional recovery in post-acute SCI mice ↓ Apoptosis *via* downregulation of BAX/Bcl-2 ratio	Macroautophagy	[24]

				Autophagic enhancement: ↑ LC3-II and Beclin-1 autophagic markers		
	Purchased from Dalian Meilun, China		Spinal cord injury (female Sprague-Dawley rats)	Neuroprotective activities: ↑ motor function recovery in SCI rats ↑ Viability motor neurons and ↓ lesion size of post-SCI rats ↑ Caspase-3 activation Autophagic enhancement: ↑ SIRT1 and AMPK activation ↑ LC3-II/I ratio and ↓ p62 autophagic markers	Macroautophagy and signalling pathway	[29]
	Purchased from Abcam (ab120726), China		Subarachnoid hemorrhage (male Sprague-Dawley rats)	Neuroprotective activities: ↑ Survivability and neurological score, while ↓ subarachnoid hemorrhage grade and brain oedema ↓ Activation of caspase-3 and -9, BAX pro-apoptotic marker and ↑ Bcl-2 anti-apoptotic marker in brain tissue of SAH rats Autophagic enhancement: ↑ LC3-II/I ratio and Beclin-1, while ↓ p62 autophagic markers in both mRNA and protein levels of SAH rats	Macroautophagy	[25]
	Purchased from Sigma Aldrich (R5010), Italy		Huntington's disease (human SH-SY5Y neuroblastoma cell)	Neuroprotective activities: ↑ Viability of mutant Huntingtin expressing SH-SY5Y cells ↓ Intracellular ROS in dopamine treated SH-SY5Y cells Autophagic enhancement:	Macroautophagy and signalling pathway	[31]

				↑ Number of LC3 and LAMP1 co-stained autolysosomes in dopamine treated SH-SY5Y cells ↑ LC3-II/I and Atg4 autophagic protein markers, and ↓ p62 protein expression and mTOR activation		
	Purchased from Sigma Aldrich, China		Alzheimer's disease (PC12 cells)	Neuroprotective activities: ↑ Viability of $A\beta_{1-42}$ treated PC12 cells ↓ Number of apoptotic cells ↑ MMP level, T-SOD and CAT antioxidant enzymatic activities Autophagic enhancement: ↑ numbers of acidic vesicular organelles ↑ LC3-II/I and Beclin-1 autophagic and Parkin mitophagic markers in mRNA level	Macroautophagy	[26]
	Purchased from Calbiochem, China		Neuropathology: Endoplasmic reticulum stress (HT-22 cells)	Neuroprotective activities: ↑ Viability of Tunicamycin induced ER stress in HT22 cells ↓ Toxicity of Tunicamycin induced ER stress in HT22 cells ↓ ER stress *via* ↑ GRP78 -stained cells, preserve XBP1S mRNA levels, ↑ CHOP induction, while ↓ JNK and caspase-12 activation ↑ MnSOD and CAT antioxidant enzyme activities Autophagic enhancement: ↑ LC3-II/I ratio and Beclin-1 autophagic markers ↑ Sirt3 expression level	Macroautophagy	[27]

	Synthesized and purchased from Lallilab Inc. Durham, New York, USA		Alzheimer's disease (Male triple transgenic AD mice)	Neuroprotective activities: ↓ NF-κB, GFAP, and PARP neuroinflammatory markers level ↓ Accumulation of toxic Aβ species in brain of transgenic AD mice ↑ Expression of both BDNF and NGF neurotrophins, and Synaptophysin and PSD95 synaptic markers in brain of transgenic AD mice ↓ Activation of caspase-3, -7, and -9 apoptotic markers Autophagic suppression: ↓ LC3-I, Cathepsin B and D, LAMP2 of autophagic markers at protein level ↑ p62 and SIRT1 protein expressions	Macroautophagy and CMA	[32]
	N/A, China		Anxiety and depression (C57BL/6J mice)	Neuroprotective activities: ↓ Anxiety-like behaviour in LPS-treated mice ↓ YAP, IL-1β, Iba-1 neuroinflammatory mRNA and protein expression in the hippocampus of LPS-treated mice Autophagic enhancement: ↑ SIRT1, ULK-1 and Atg5 autophagic marker mRNA and protein expression in the microglial from hippocampus of LPS-treated mice	Macroautophagy	[96]

	Purchased from TargetMol, Poland		Sanfilippo disease (HDFa fribroblast cell line and B6.129S6-Baglu^{tm1Efn}/J mouse)	Protective activities: ↓ GAG and HS levels in MPSIIIB fibroblast cell ↓ Urinary GAG level in MPSIIIB mice ↓ Hyperactivated and anxiety-related behaviours in MPSIIIB mice Autophagic enhancement: ↑ LC3-II and LAMP-2 protein expression in the brain of MPSIIIB mice ↓ p62 protein expression in liver and brain of MPSIIIB mice	Macroautophagy and CMA	[33]
	Purchased from Sigma Aldrich, France		Oxiapoptophagy (N2a cells)	Neuroprotective activities: ↑ Viability of 7KC-treated N2a cells ↓ Plasma membrane damage in 7KC-treated N2a cells ↓ Intracellular ROS and ↑ antioxidant enzymatic activities ↑ MMP level and mitochondrial function ↓ Activated caspase-3 and PARP pro-apoptotic markers Autophagic suppression: ↓ LC3-II/I ratio autophagic markers	Macroautophagy	[37]
Berberine Chinese medicine, China	Provided by Dr. Kuan-Hau Lee	Berberine	Amyotrophic lateral sclerosis (N2a cells)	Neuroprotective activities: ↑ Viability and ↓ TDP-43 aggregation in transgenic cells Autophagic enhancement: ↑ LC3-II/I ratio and ↓ mTOR and p70S6K activation protein levels	Macroautophagy and signalling pathway	[68]

Milk thistle, *Silybum marianum* (seeds)	Silymarin	Silibin A and B, Isosilibinin A and B, silicristin and silidianin	Cerebral ischemia (male Sprague-Dawley rats)	Neuroprotective activities: ↓ Number of delayed neuronal cell death and apoptotic cells in the brain of ischemic rats Autophagic suppression: ↓ Cell death by autophagy in the brain of ischemic rats ↓ MDC staining autophagic vacuoles	Microautophagy	[55]
Whole grains	Purchased from Sigma Aldrich	Phytic acids	Alzheimer's disease (human MC-65 neuroblastoma cell and Tg2576 mice)	Neuroprotective activities: ↑ Cell viability, ↓ intracellular free radicals and Ca^{2+} levels in AβPP-C99-transfected MC-65 cell, ↓ plasma Cp activity Autophagic enhancement: ↑ Beclin-1 autophagic marker	Macroautophagy	[97]
Ginseng, *Panax ginseng* (Rhizome)	Obtained from the Ze-Long Pharmaceutical Co., Ltd., Nanjing, China	Ginsenoside Rb1	Neurological diseases (Male Sprague-Dawley rats)	Neuroprotective activities: ↓ infarction volume of the contralateral hemisphere in post-MCAO brain Autophagic enhancement: ↑ Beclin-1 and LC3 II autophagic markers in the border of infarction of post-MCAO brain tissue	Macroautophagy	[98]
	N/A	Ginsenoside Rg3	Prion protein-related neurodegenerative conditions (human SK-N-SH neuroblastoma and mice primary cortical cells)	Neuroprotective activities: ↑ Viability of PrP (106-126)-treated primary cortical cells Autophagic enhancement: ↑ LC3BII/T ratio autophagic protein marker, autophagic vacuoles, and p62/SQSTM1 mRNA expression in both cells	Macroautophagy	[99]

	Isolated from water extract	Ginsenoside Rg2	Alzheimer's disease (human HeLa cervical cancer, human HepG2 liver cancer, mouse Neuro2A neuroblastoma and rat pheochromocytoma cells, and C57BL/6JxSJL mice)	Neuroprotective activities: ↑ Cognitive function in 5XFAD mice Autophagic enhancement: ↑ LC3-II and ↓ SQSTM1 in multiple organ tissues of 5XFAD mice ↑ AMPK and ULK1 protein activation in HeLa, HepG2, Neuro2A and PC12 cells. ↑ Clearance of proteinaceous inclusions in HeLa cells and aggregate-prone proteins in 5XFAD mice	Macroautophagy and signalling pathway	[100]
	Purchased from Jilin University, Changchun, Jilin, China	Ginsenoside Rg1	Depression (primary astrocyte cells from fetal Sprague Dawley rats)	Neuroprotective activities: ↑ Cx43 protein level in CORT-treated astrocytes from prefrontal cortex and hippocampus ↓ Degradation of Cx43 protein level in CORT-treated astrocytes from prefrontal cortex and hippocampus Autophagic suppression: ↓ LC3-II/I ratio in astrocytes of prefrontal cortex	Macroautophagy	[101]
Gouteng, *Uncaria rhynchophylla* (Miq.) Jacks, Hong Kong, China	Purchased from Aktin Chemicals (APC-164)	Isorhynchophylline	Parkinson's disease (rat PC-12 pheochromocytoma cell, mouse N2a neuroblastoma, human SH-SY5Y neuroblastoma cell, DIV7 mouse primary embryonic neurons, human embryonic stem	Autophagic enhancement: ↑ LC3-II/I ratio autophagic marker in N2a, PC12, SH-SY5Y and DIV7 mouse primary embryonic neurons ↑ number of lysotracker-positive spots that reflects autophagic activity in fat body of L3 Drosophila larvae. ↑ α-synuclein clearance in N2a cells and human embryonic stem cell-transformed dopaminergic neurons	Macroautophagy	[102]

			cell-transformed dopaminergic neuronal cell and L3 Drosophila larvae)	↑ Beclin-1 autophagic marker expression level in N2a cells.		
Thunder god vine, *Tripterygium wilfordii*	Purchased from Hotmed Sciences Co. Ltd., Shanghai, China	Celastrol	Parkinson's disease (SH-SY5Y neuroblastoma cell)	Neuroprotective activities: ↑ cell viability against rotenone-induced cytotoxicity ↑ intracellular SOD and GSH, MMP levels, and ↓ cytochrome C release Autophagic enhancement: ↑ LC3 II/I ratio autophagic marker and number of autophagic vacuole ↑ α-synuclein clearance	Macroautophagy	[103]
Extra virgin olive oil, *Olea europaea* (fruit)	Synthesized *via* oleuropein deglycosylation under β-glycosidase incubation	Oleuropein aglycone	Alzheimer's disease (mouse N2a neuroblastoma, and TgCRND8 mice), Italy	Neuroprotective activities: ↑ Cognitive performance in TgCRND8 β-amyloid deposition mice model ↓ β-amyloid levels and plaque deposit, ↑ phagocytic microglial migration, ↓ astrocyte reaction in cerebral tissue analyses of TgCRND8 mice Autophagic enhancement: ↑ Beclin-1 and LC3II/I ratio, p62 autophagic markers expression in N2a cells ↑ Beclin-1 and LC3II/I autophagic markers, Cathepsin B and p62 stained autophagosome-lysosome fusion in cortex of TgCRND8 mice	Macroautophagy	[10]
				Neuroprotective activities:	Macroautophagy	[104]

				↑ animal behaviours and memory dysfunction of TgCRND8 mice ↓ Amyloid-β deposition in the brain tissue ↑ Proliferation of newborn cells in the subgranular zone of the hippocampus Autophagic enhancement: ↑ Beclin-1, LC3 and cathepsin B autophagic markers in the brain tissue		
			Alzheimer's disease (human SH-SY5Y neuroblastoma cells, and middle-aged TgCRND8 mice), Italy	Neuroprotective activities: ↑ pE3- β-amyloid clearance in the in pE3-β-amyloid-treated SH-SY5Y cell and pE3-β-amyloid-treated middle-aged TgCRND8 mice ↑ glutaminyl cyclase in the brain tissues of pE3-β-amyloid-treated middle-aged TgCRND8 mice Autophagic enhancement: ↑ Beclin-1 and LC3-II autophagic markers in both in the brain tissues of pE3-β-amyloid-treated middle-aged TgCRND8 mice	Macroautophagy	[105]
			Alzheimer's disease (human SH-SY5Y neuroblastoma cells, and TgCRND8 mice), Italy	Autophagic enhancement: ↑ Intracellular Ca^{2+}, beclin-1, autophagic vacuoles, AMPK activation in SH-SY5Y cells ↑ AMPK activation and mTOR inhibition in the cortex of TgCRND8 mice	Signalling pathway	[11]

	Purchased from Sigma Aldrich, Canada		Parkinson's disease (rat PC-12 pheochromocytoma cell)	Neuroprotective activities: ↑ Viability of 6-OHDA treated PC12 cells ↓ Superoxide production in 6-OHDA treated PC12 cells Autophagic enhancement: ↑ LC3-II/I and p62 autophagic markers in 6-OHDA treated PC12 cells	Macroautophagy	[12]
	N/A, Italy	Hydroxytyrosol	Alzheimer's disease (TgCRND8 mice)	Neuroprotective activities: ↑ Memory performance and cognitive function in treated-TgCRND8 mice ↑ Clearance of Aβ deposition in the parietal cortex and hippocampus in treated- TgCRND8 mice ↓ TNF-α expression at mRNA level ↓ SAPK/JNK activation and ↑ ERK1/2 activation at protein level Autophagic enhancement: ↑ LC3 autophagic marker	Macroautophagy	[13]
	Provided by Extrasynthase, France	Oleuropein aglycone and hydroxytyrosol	Alzheimer's disease (SH-SY5Y cells)	Neuroprotective activities: ↑ Viability of Aβ-treated SH-SY5Y cells ↑ MMP level and mitochondrial function Autophagic enhancement: ↑ Number of autophagosomes ↓ Activation of S6 ribosomal protein, while ↑ULK1 activation	Macroautophagy	[106]

				↑ LC3-II/I ratio and Beclin-1 autophagic markers, and ↓ p62 protein expression		
Turmeric, *Curcuma longa* (Rhizome)	Purchased from Sigma Aldrich	Curcumin	Genetic based Parkinson's disease (SH-SY5Y neuroblastoma cell)	Autophagic enhancement: ↑ α-synuclein clearance in A53T α-synuclein transfection of differentiated SH-SY5Y cells ↓ p-mTOR and p-p70S6K autophagic markers in A53T α-synuclein transfection of differentiated SH-SY5Y cells	Signalling pathway	[69]
	N/A		Epilepsy (male Sprague-Dawley rats)	Neuroprotective activities: ↑ Viability and ↓ apoptosis in hippocampal cells of lithium-policarpine treated static epilepsy rats ↓ MLKL and RIP-1 necroptosis markers Autophagic enhancement: ↑ Number of autophagosomes ↑ LC3-II/I ratio and Beclin-1 autophagic markers	Macroautophagy	[41]
	Purchased from Sigma Aldrich		Alzheimer's disease (N2a cells)	Neuroprotective and autophagic enhancement: ↑ Number of autophagosomes in APP695swe transfected N2a cells ↑ LC3-II autophagic marker, and ↓ p62 expression at mRNA level ↑ Beclin-1, Atg5, and Atg16L1 autophagic markers at protein level	Macroautophagy and CMA	[42]

				↑ LAMP2 lysosomal protein to induce autophagosome-lysosome binding ↑ Retrograde axonal transport molecular motor and scaffolding proteins expression (DIC, DHC1, and DLC-3)		
	N/A		Autophagic study (MN9D cells)	Neuroprotective activities: ↑ Viability and ↓ apoptosis of propofol-treated cells ↑ Tyrosine hydroxylase and dopamine secretion in propofol-treated cells Autophagic suppression: ↓ Number of autophagic vacuoles, autophagosomes and autophagosome-lysosome formation ↑ LC3-II and ↓p62 protein expressions of propofol-treated cells at both mRNA and protein levels ↑ Activation of Akt, mTOR, p70S6K of propofol-treated cells at both mRNA and protein levels	Macroautophagy and signalling pathway	[43]
Evodia rutaecarpa Bentham, Korea	Purchased from Sigma Aldrich	Evodiamine	Cerebral Ischemia (human U87-MG astrocytes)	Neuroprotective activity: ↑ TRPV-1-mediated JNK activation Autophagic enhancement: ↑ LC3II/I ratio autophagic marker, AO-stained autophagosomes in U87-MG cells. ↑ TRPV1-mediated autophagy	Macroautophagy	[107]

Nigella sativa (seed)m US	Purchased from EMD Chemicals	Thymoquinone	Brain Tumour (human T98G, U87MG and Gli36ΔEGFR glioblastoma cells)	Neuroprotective activity: ↑ Cell cytotoxicity on all glioblastoma cell lines but not on normal human astrocytes ↑ lysosome membrane permeabilization-associated cathepsin B release to induce caspase-dependent apoptosis Autophagic inhibition: ↑ LC3-II and LC3-associated protein p62 levels ↓ AO-stained cytoplasmic vacuolization that induces lysosome membrane permeabilization	Macroautophagy	[108]
Fructus arctii	Isolated from crude extract using HPLC	Arctigenin	Alzheimer's disease (HEK293-APP_{swe}, mouse BV-2 microglial cells, mouse primary cortical neurons, astrocytes and APP/PS1 mice)	Neuroprotective activity: ↑ Amyloid-β clearance in all cell lines ↑ Memory impairment in APP/PS1 AD mice ↓ Senile plaque and Amyloid-β clearance in the brain tissues of APP/PS1 AD mice Autophagic enhancement: ↓ AKT/mTOR activation that further lead to Amyloid-β clearance	Signalling pathway	[66]
	Purchased from Sigma Aldrich		Diabetic neuropathy (male Swiss albino mice)	Neuroprotective activities: ↑ histopathological and ↓pathological changes in the spinal cord of streptozotocin-treated diabetic mice ↓ Oxidative stress levels in streptozotocin-treated diabetic mice	Macroautophagy and signalling pathway	[67]

				Autophagic enhancement: ↑ AMPK activation and ↓ mTOR activation in the sciatic nerves of streptozotocin-treated diabetic mice ↑ LC3-II/I and Beclin-1 and ↓ p62 protein expression		
Green tea, *camellia sinensis* (leaves)	Provided by Shanghai U-sea Biotech Co., Ltd., Shanghai, China.	Epigallocatechin-3-gallate	Neuropathology: CUMS (Wistar rats)	Neuroprotective activities: ↑ Learning and memory impairment of Wistar mice ↓ Neuronal damage and CUMS-induced apoptotic cells in CA1 region of hippocampus Autophagic enhancement: ↑ LC3-II and ↓p62 autophagic markers in CA1 region of hippocampus	Macroautophagy	[15]
	N/A, China		Prion diseases (human SH-SY5Y neuroblastoma cell)	Neuroprotective activities: ↑ Cell viability against PrP-induced neurotoxicity ↓ Bax, cytochrome c, and activated caspase-3 levels for apoptosis Autophagic enhancement: ↑ LC3-II and Sirt1, while ↓ p62 autophagic markers	Macroautophagy	[16]
	N/A, US		Neuropathophysiology neuroinflammation (BV-2 cells)	Neuroprotective activities: ↑ Viability of LPS-treated BV-2 cells ↓ NO production and neuroinflammatory proteins in LPS-treated BV-2 cells Autophagic enhancement:	Macroautophagy (regulation of inflammatory response)	[109]

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				↑ *gm-csf* while ↓ *mif, and ccl-2* gene expression		
	Purchased from Sigma Aldrich, China	Catechin	Ischemic stroke (mouse BV-2 microglial cell)	Neuroprotective activities: ↑ Viability of hypoxia-induced BV-2 cell, ↓ intracellular ROS production and ↓ caspase-3 activation Autophagic enhancement: ↓ Akt and mTOR activation and ↑ LC3-II/I ratio autophagic marker	Macroautophagy and signalling pathway	[17]
Cereals, fruits and vegetables	Purchased from Sigma Aldrich	*p*-Coumaric acid	Neuroblastoma and solid extracranial cancer (mouse N2a neuroblastoma)	Neuroprotective activities: ↑ Cytotoxicity and ROS production ↓ GSH and MMP levels ↑ Cytochrome *c*, caspase-8 and p53 apoptotic markers Autophagic enhancement: ↑ Autophagic vacuoles, LC-3II/I ratio autophagic markers	Macroautophagy	[110]
Chinese skullcap, *Scutellaria baicalensis* (root)	Purchased from HD Biosciences Co., Ltd., Shanghai, China	Wogonin	Alzheimer's (human SH-SY5Y neuroblastoma cell and primary mouse cortical astrocyte)	Neuroprotective activities: ↑ Aβ clearance in both transgenic SH-SY5Y-APP/BACE and primary mouse cortical astrocyte ↑ GSK3β activation for tau dephosphorylation in transgenic SH-SY5Y cell Autophagic enhancement: ↑ LC3-II/I ratio autophagic marker, ↓ mTOR, P70S6K and ULK1 activation in both cell lines	Macroautophagy and signalling pathway	[18]
	N/A	Baicalein	Parkinson's disease (human SH-SY5Y	Neuroprotective activities:	Macroautophagy	[19]

			neuroblastoma cell and C57BL/6J mice)	↓ PD-related behavioural deficit in rotenone-treated mice ↑ Dopamine content, ↓ caspase-3 activation and ↑ mitochondrial integrity in both rotenone-treated SH-SY5Y cell and striatal tissue of mice Autophagic enhancement: ↑ LC3-II/I ratio autophagic markers in both rotenone-treated SH-SY5Y cell and striatal tissue of mice		
	Purchased from Sigma Aldrich		Spinal cord Injury (C57BL/6 mice)	Neuroprotective activities: ↑ Viability and functionality of motor neurons in post-SCI mice ↓ Caspase-3 and -9 activation, and Bax/Bcl-2 ratio apoptotic markers ↓ Number of TUNEL stained-apoptotic cells Autophagic enhancement: ↑ activation of PI3K, LC3-II/I ratio and ↓p62 autophagic markers	Macroautophagy	[20]
Dong quai, *Angella sinensis*	Isolated from chloroform extract, China	n-butylidenephthalide	Amyotrophic lateral sclerosis (NSC34 mouse-mouse neuroblastoma-spinal cord hybrid cell line and Tg mice)	Neuroprotective activities: ↓ LC3-II autophagic , caspase-3 apoptotic marker, and ↑ mitochondrial integrity in transformed NSC34$^{G93A\text{-}SOD1}$ cell ↑ Survival rate of transgenic Tg (SOD1^{G93A}) mice ↓ Loss of motor neuron while ↑ motor neuron performance in transgenic Tg (SOD1^{G93A}) mice	Suppress Macroautophagy	[45]

				↓ LC-3-II autophagic marker expression in the spinal cord tissues of transgenic Tg (SOD1^{G93A}) mice		
Ampelopsis grossedentata	Purchased from Zelang Medical Technological Co. Ltd., Nanjing, China	Ampelopsin/ dihyfromyricetin	Alzheimer's disease (Male Sprague Dawley rats)	Neuroprotective activities: ↑ Spatial learning and memory impairment in D-galactose induced brain aging rat ↓ Hippocampal neuron damage of D-galactose induced brain aging rat ↓ p53/p21 and miR-34a expressions in hippocampus tissue ↓ Caspase-3 activation and ↑ Bcl-2 anti-apoptotic marker in hippocampus tissue Autophagic enhancement: ↑ SIRT1, Atg7, LC3-II/I ratio and ↓ p62 autophagic markers	Macroautophagy	[111]
Rosemary, *Rosemarinus officinalis*	Purchased from Abcam, China	Carnosic acid	Alzheimer's disease (human SH-SY5Y neuroblastoma cell)	Neuroprotective activities: ↑ Viability of Aβ$_{25-35}$ treated SH-SY5Y cells ↑ Clearance of Aβ$_{25-35}$ Autophagic enhancement: ↑ LC3-II/I ratio autophagic marker and AMPK activation	Macroautophagy and signalling pathway	[70]
	Purchased from Sigma Aldrich		Neuronal starvation (human SH-SY5Y neuroblastoma cell	Neuroprotective activities: ↑ Viability against nutrient starvation in SH-SY5Y cells ↑ Akt and Erk1/2 cell survival proteins, and FoxO3a prosurvival factor activation Autophagic enhancement:	Macroautophagy and signalling pathway	[112]

				↑ Autophagic vacuoles and LC3-II protein expression		
Dioscorea nipponica	Purchased from Nanjing Zelang Medical Technology Co., Ltd., Nanjing, China	Diosgenin	Prostate cancer (human DU145 prostate cancer cell line)	Anti-proliferative activities: ↓ Viability of DU145 cells and ↑ number of apoptotic DU145 cells, ↑ caspase-9 apoptotic protein marker and ↓ Bc1-2 mRNA expression Autophagic enhancement: ↑ Autophagic vacuoles, LC3-II/I ratio autophagic protein marker, ↓ PI3K, Akt, and mTOR activation, and ↑ Beclin-1 mRNA expression	Macroautophagy and signalling pathway	[71]
Polyalthia longifolia	Isolated and provided by Dr. Yi Chen Chia from Department of Food Technology, Tajen University, Pingtung, Taiwan	16-hydroxy-cleroda-3, 13-dien-16,15-olide	Neuroblastoma (mouse N18 neuroblastoma and rat C6 glioma cells)	Antiproliferative activities: ↑ Cytotoxicity, and ROS and NO production in both cell lines ↓ GSH, SOD, GST, GPx antioxidant enzymatic activities in both cell lines ↑ p38 MAPK, ERK activation in N18 cells Autophagic enhancement: ↑ LC3-II and Beclin-1 autophagic markers	Macroautophagy	[113]
Gastrodia elata	Purchased from Shanghai Pureone Biotechnology, Shanghai, China	Gastrodin	Neuropathology: glial abnormality (mice C57BL/6 primary astrocytes)	Neuroprotective activities: ↑ Viability of lipopolysaccharides-treated primary astrocytes ↓ BAX/Bcl-2 ratio apoptotic markers ↑ Glutamine synthase enzymatic activity Autophagic enhancement: ↑ LC3-II/I ratio, p62, Beclin-1 autophagic markers	Macroautophagy	[114]

				↓ p38 activation		
Houpo, *Magnolia officinalis* Rehd. et Wilsm, Taiwan	Purchased from Sigma Aldrich	Honokiol	Neuroblastoma (Mice Neuro2A and NB41A3 neuroblastoma cells)	Antiproliferative activities: ↑ Number of apoptotic cells in both cell lines ↑ Grp78 protein expression and intracellular ROS level in both cell lines ↑ ERK1/2 activation level Autophagic enhancement: ↑ Autophagic vacuoles and LC3-II autophagic marker in both cell lines ↓ PI3K level and activation of Akt and mTOR expressions in both cell lines	Macroautophagy and signalling pathway	[115]
Rabdosia rubescens	Purchased from Chengdu Must Bio-Technology Co., Ltd. Sichuan, China	Oridonin	Neuroblastoma (human SH-SY5Y and SK-N-MC neuroblastoma cells, and female athymic (nu/nu) mice)	Antiproliferative activities: ↑ Cell death and number of apoptotic cells in Oridonin and NVPBEZ235 co-treated cells ↑ Caspase-3 and PARP activation in both cell lines ↓ Tumour tissue proliferation of athymic mice Autophagic enhancement: ↑ LC3-II and p62 autophagic marker in both cell lines	Macroautophagy	[116]
Dalbergia odorifera (heartwoods)	Isolated from ethanol extract of *D. odorifera*	Cearoin	Neuroblastoma (human SH-SY5Y neuroblastoma cells)	Antiproliferative activities: ↓ Viability, ↑ ROS and NO production of SH-SY5Y cells ↑ ERK1/2 and PARP activation	Macroautophagy	[117]

				↑ α-Spectrin and BAX pro-apoptotic markers, and ↓ Bcl-2 anti-apoptotic marker Autophagic enhancement: ↑ LC3II/I ratio autophagic marker		
Olive, Argan and hydrogenated food oils	N/A	Oleic acid, docosahexaenoic acid	Neuropathology: oxiapoptophagy (mouse BV-2 microglial cell)	Neuroprotective activities: ↓ Oxidative stress in 7KC-treated BV-2 cell ↑ Mitochondrial and plasma membrane integrity ↑ Number of apoptotic cells Autophagic enhancement: ↑ LC3II/I ratio autophagic marker	Macroautophagy	[118]
Radix puerariae (root)	N/A	Puerarin	Cerebral Ischemia (Male Sprague Dawley rats)	Neuroprotective activities: ↓ Neurological deficit score, cerebral infarct volume, brain water content in the MCAO rats Autophagic enhancement: ↓ LC3-II/I ratio autophagic marker in protein and mRNA level	Macroautophagy	[119]
	Purchased from Sigma Aldrich		Neurotoxicity study: Cadmium (male Sprague Dawley rats and primary cortical neurons)	Neuroprotective activities: ↑ Viability and ↓ neuronal injury of Cd-treated primary cells and rats Autophagic activation and modulation: ↓ LC3II and p62 protein expression in both *in vitro* and *in vivo* experiment ↓ Number of autophagosome in both *in vitro* and *in vivo* experiment	Macroautophagy	[120]

				↑ Autophagosome-lysosome formation *in vitro* and *in vivo* experiment		
Tripterygium wilfordii Hook.f.	N/A	Triptolide	Parkinson's disease (mouse MN9D dopaminergic neuronal and Sprague-Dawley rats)	Neuroprotective activities: ↑ Viability of A53T-transfected MN9D cells ↑ Clearance of α-Synuclein in A53T-transfected MN9D cells Autophagic enhancement: ↓ p62 autophagic marker	Macroautophagy	[121]
Artocarpus lakoocha	Purchased from Sigma Aldrich, Korea	Oxyresveratrol	Neuroblastoma (human SH-SY5Y and rat B103 neuroblastoma, Rat-2 and mouse NIH 3T3 fibroblast and human embryonic kidney HEK293 cell)	Antiproliferative activities: ↑ Cell death in neuroblastoma cells, but not other cell lines ↑ Apoptosis activation *via* loss of MMP in neuroblastoma ↑ Caspase-3 and -9 activation Autophagic enhancement: ↑ LC3-II/I ratio, Beclin-1, Atg5 and Atg7 autophagic markers in neuroblastoma cells ↓ mTOR, PI3K, and AKT activation, while ↑ p38 MAPK pro-apoptotic and autophagic marker	Macroautophagy and signalling pathway	[122]
			Autophagy study (Primary cortical neuron and astrocyte cells)	Autophagic enhancement: ↑ LC3 puncta and LC3-II protein expression in both chloroquine-treated cortical neuron and astrocytes ↓ p62 protein expressions in both chloroquine-treated cortical neuron and astrocytes	Macroautophagy and signalling pathway	[123]

				↑ AMPK activation and ↓ mTOR activation ↑ ULK1 and LAMP1 protein expressions in mouse cortical astrocytes		
N/A	Purchased from Sigma Aldrich	Lipoic acid	Neurotoxicity study (SH-SY5Y cells)	Neuroprotective activities: ↑ Viability and number of apoptotic cells in acrylamide-treated SH-SY5Y cells ↑ Cytochrome c release and caspase-3 activation ↓ Akt activation, ↑ MMP level, ↑ AMPK and GSK3β activation ↑ ERK activation, while ↑ JNK and p38 activation ↓ Activation p65 and IκB inflammatory markers, and translocation of NF-κB Autophagic enhancement: ↑ ND1, COX2, Sirt1 and PGC-1α mitophagy markers ↑ LC3-II/I ratio and Beclin-1 autophagic markers	Macroautophagy and signalling pathway	[124]
N/A	N/A	Polydatin	Alzheimer's disease (human SH-SY5Y and SK-N-SH neuroblastoma cells)	Neuroprotective activities: ↑ Mitochondrial integrity and ↓ Aβ-induced oxidative damage ↓ Number of apoptotic cells in Aβ-treated cells ↓ Caspase-3 and -9 activation, Cytochrome c release, PARP activation, and ↑ BAX apoptotic markers	Macroautophagy and signalling pathway	[125]

				Autophagic enhancement: ↑ LC3-II/I ratio and Beclin-1 autophagic markers ↑ AMPK activation and ↓ mTOR activation		
	Purchased from Shanghai Yuaye Biotechnology Company, Shanghai, China, and dissolved in distilled water		Parkinson's disease (SH-SY5Y cells and *Parkin-null* flies)	Neuroprotective activities: ↑ Viability of rotenone-treated SH-SY5Y cells ↓ Intracellular oxidative stress and mitochondrial dysfunction ↑ Dopaminergic mitochondrial dysfunction and phenotypes of *parkin-null* flies Autophagic suppression: ↓ Number of autophagosomes and ↑ autophagolysosomes ↑ LC3-II and Atg5 autophagic markers and ↓ p62 expression level ↓ Activation of mTOR and Ulk1/2 protein expressions ↓ PGC1β protein expression	Macroautophagy	[126]
N/A	Purchased from Sigma Aldrich	β-amyrin	Parkinson's disease (*Caenorhabditis elegans*)	Neuroprotective activities: ↑ Viability of juglone-induced oxidative stress in *C. elegans* ↓ intracellular ROS level in wild-type N2 *C. elegans* ↑ Viability of neuronal cell in 6-OHDA treated transgenic BZ555 *C. elegans* ↓ α-synuclein aggregation in transgenic NL5901 *C. elegans* Autophagic enhancement:	Mitoautophagy	[127]

				↑ LGG-1 autophagic marker in transgenic NL5901 *C. elegans*		
Rhizoma coptidis, *Radix Scutellaria* Georgi, Labiatae, *Cortex Phellodendri,* and *Fructus Gardeniae* (Chinese medicine Huang-Lian-Jie-Du-Decoction)	Purchased from Qingdao Jieshikang Biotech Co., Ltd., Qingdao, China	Berberine, baicalin and jasminoidin	Cerebral Ischemia (male Sprague Dawley rats)	Neuroprotective activities: ↑ Viability, and ↓ brain infarct volume and pathological changes in MCAO rats ↑ Mn-SOD, Cu/Zn-SOD, CAT and GPx antioxidant enzyme activation in brain tissue of MCAO rats ↑ Expressions of peroxidases and NQO-1 antioxidant markers ↓ iNOS, COX-2 proinflammatory protein markers ↓ TNF-α, IL-1β, IL-2 and IL-6 proinflammatory markers at mRNA level ↑ NF-κB and p65 activation Autophagic enhancement: ↑ LC3-II/I ratio and Beclin-1, and ↓ p62 autophagic markers ↓ mTOR activation, and ↑ expression of Atg-3, -5, -7, -12, and phosphorylated PI3K	Macroautophagy and signalling pathway	[128]
Erigerin breviscapus (Vant.) Hand-Mazz	N/A	Breviscapine	Cerebral Ischemia (male Sprague Dawley rats)	Neuroprotective activities: ↓ Neurological deficit score, infarct volume, and cerebral edema in MCAO rats Autophagic suppression: ↓ LC3-II/I ratio autophagic marker in both mRNA and protein level in both neurons and astrocytes of penumbra tissues of MCAO rats	Suppress Macroautophagy	[129]

Andrographis paniculata, China		Andrographolide	Alzheimer's disease (rat PC-12 pheochromocytoma cells)	Neuroprotective activities: ↑ Viability of $A\beta_{1-42}$-treated PC-12 cells ↓ $A\beta_{25-35}$-induced cytotoxicity, intracellular malonaldehyde and nitric oxide levels in PC-12 cells ↓ Intracellular ROS and MMP levels ↓ Cytochrome *c* release, and ↑ BAX pro-apoptotic protein level ↓ Tau protein phosphorylation ↑ Nrf2 and ↓ p21 protein expression levels Autophagic enhancement: ↑ Atg5, Atg7, and AMBRA1 autophagic markers in mRNA level ↑ Beclin-1, LC3s and reduced p62 autophagic markers in mRNA and protein levels	Macroautophagy	[130]
N/A, China	N/A	Pterostilbene	Neuropathology: Oxidative stress (rat primary spinal cord neurons)	Neuroprotective activities: ↓ Intracellular ROS level in H_2O_2-treated cells ↓ Number of apoptotic cells in H_2O_2-treated cells Autophagic enhancement: ↑ LC3-II/I ratio and Beclin-1, while ↓ p62 autophagic markers in pterostilbene-treated cells ↑ LC-3-II/I ratio autophagic marker in H_2O_2-treated cells	Macroautophagy	[131]

N/A	N/A, China	Quercetin	Autophagic-related pathogenicity (human ARPE-19 retinal pigment epithelial cell)	Autophagic enhancement: ↑ TFEB-mediated gene transcription ↑ Cellular degradation capacity ↑ LC3-II/I ratio and ↓ p62 autophagic markers ↑ Inhibition of mTOR kinase activity *via* ↓ phosphorylationg of S6 and Akt protein expressions	Macroautophagy and signalling pathway	[132]
	Purchased from Sigma Aldrich, France		Oxiapoptophagy (N2a cells)	Neuroprotective activities: ↑ Viability of 7KC-treated N2a cells ↓ Plasma membrane damage in 7KC-treated N2a cells ↓ Intracellular ROS and ↑ antioxidant enzymatic activities ↑ MMP level and mitochondrial function ↓ Activated caspase-3 and PARP pro-apoptotic markers Autophagic suppression: ↓ LC3-II/I ratio autophagic markers	Macroautophagy	[37]
	Purchased from Sigma Aldrich, India		Neurotoxicity study: Copper (SH-SY5Y cells)	Neuroprotective activities: ↑ Viability of copper-treated SH-SY5Y cells ↓ Intracellular ROS level ↓ Number of apoptotic cells and pro-apoptotic protein markers Autophagic enhancement: ↑ Number of autophagosome and autophagosome-lysosome formation ↑ LC3-II/I ratio autophagic and ↓ p62 protein expression	Macroautophagy and CMA	[60]

				↑ Hsc70, Hsc90, and LAMP-2A protein expresions		
N/A, China	Purchased from China Standard Material Center, Beijing, China.	Isoflavone	Neurotoxicity study (SH-SY5Y neuroblastoma cell)	Neuroprotective activities: ↑ Viability in Atrazine-treated SH-SY5Y cells ↑ Expression of tyrosine hydroxylase level of dopamine secretion ↓ α-synuclein accumulation level Autophagic enhancement: ↑ LC3-II/I ratio while ↓ p62 autophagic markers ↑ BEX2 autophagic marker	Macroautophagy	[119, 133]
N/A, India	Purchased from Sigma Aldrich	Geraniol	Parkinson's disease (human SK-N-SH neuroblastoma cell)	Neuroprotective activities: ↑ Viability of rotenone-induced toxicity in SK-N-SH cells ↓ Intracellular ROS and ↑ MMP levels in SK-N-SH cells ↑ Mitochondrial integrity *via* ↓ NO while ↑ ETC I and ATP ↑ TBARS, ↓ GSH and SODs antioxidant enzymatic activities ↓ Number of apoptotic cells Autophagic markers: ↑ Atg5, Atg7 and Atg12 autophagic markers while ↓ mTOR activation ↑ LC3-II/I ratio autophagic markers and clearance of α-synuclein	Macroautophagy and signalling pathway	[134]
Gentiana dinarica (roots)	Collected from Mt. Tara, western Serbia, Marcerated using Methanol	Xanthones (norswertianin and noswertianin-1-O-primeveroside)	Brain tumours (human U251 glioma cells)	Antiproliferative activities: ↓ Viability of U251 cells ↑ Intracellular ROS stress Autophagic enhancement:	Macroautophagy and signalling pathway	[135]

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	(1:2.4) (m/v) for 48 h and concentrated using rotary evaporator			↑ Number of autophagic vacuoles ↑ LC3-II/I ratio autophagic marker and ↓ p62 autophagy target ↓ p-mTOR, S6K, PRAS40, ULK1 and ERK activation		
Trillium tschonoskii (roots)	Purchased from Bellancom (14144-06-0)	Diosgenin glucoside (TTM saponin)	Neurotoxicity study (Sprague-Daley rats)	Neuroprotective activities: ↑ Memory and learning on D-galactose treated rats ↓ Hippocampal neurons damage from D-galactose treated rats ↓ Caspase-3 and BAX apoptotic markers and ↑ Bcl-2 anti-apoptotic marker at protein level Autophagic enhancement: ↑ Rheb and ↓ mTORC1 activation ↑ LC3-II/I ratio and Beclin-1 autophagic markers, while ↓ p62 protein expression	Macroautophagy	[136]
Aralia elata (Miq.) Seem. (buds)	Collected from Liaoning Province, China. The buds were extracted using 70% ethanol with reflux, size excluded, evaporated , and purified using three rounds of HPLC	Eclalbasaponin I	Neuropathology: Oxidative stress (SH-SY5Y cells)	Neuroprotective activities: ↑ Viability of H_2O_2-treated SH-SY5Y cells ↓ Number of apoptotic cells ↓ Caspase-3 activation and BAX pro-apoptotic marker, while ↑ Bcl-2 anti-apoptotic marker at protein level ↑ MMP level in H_2O_2-treated SH-SY5Y cells ↓ Intracellular ROS level, ↑ Nrf2, p-Nrf2 and HO-1 antioxidant proteins, and ↑ SOD and GSH-Px antioxidant enzyme activities Autophagic enhancement:	Macroautophagy	[137]

				↑ Number of MDC-stained autophagic cells ↑ LC3-II/I ratio and ↓ p62 autophagic markers		
Lycium babarum polysaccharides	Purchased from Beijing Solarbio Science & Technology Co. Ltd, Beijing, China	N/A	Stroke (Primary hippocampal neuron from C57BL/6 mice)	Neuroprotective activities: ↑ Viability and ↓ LDH release from oxygen glucose deprivation/reoxygenation-induced neuron ↓ Intracellular ROS level ↓ Caspase-3 activation and BAX/Bcl-2 ratio pro-apoptotic marker ↓ Number of apoptotic cells Autophagic suppression: ↓ LC3-II/I ratio and Beclin-1 autophagic markers, ↑p62 protein expression ↑ activation of Akt, mTOR protein expression	Suppress Macroautophagy and suppress signalling pathway	[48]
	Aqueous extract of dried fruits was prepared sequential decolouration and delipidation in alcohol, and boiling in distilled water, lastly, followed by freeze-dried into powder	N/A	Retinal ganglion degeneration (female Sprague Dawley rats)	Neuroprotective activities: ↓ Degeneration of retinal ganglion cells in the nasal retinas of post-PONT rats ↑ Microglia/macrophages polarization Autophagic enhancement: ↑ CD68 marker for microglia/macrophages activation ↑ LC3-II autophagic marker	Macroautophagy	[138]

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	Purchased from Yuanye Biotechnology Co. Ltd. Shanghaim China.	N/A	Parkinson's disease (Sprague Dawley juvenile rats)	Neuroprotective activities: ↓ Behavioural and locomotor dysfunction in 2,4-dichlorophenoxyacetic acid treated PD rats ↑ Viability of neuronal cells in hippocampus ↑ Microglial activation ↓ Oxidative stress and ↑ antioxidant enzyme activities in rat sera Autophagic enhancement: ↑ LC3-II/I and Beclin-1 autophagic markers mRNA expressions	Macroautophagy	[139]
Cistanche tubulosa (stem)	Purchased from Sigma Aldrich	Echinacoside	Parkinson's disease (PC12 cells and male C57BL/6 J mice)	Neuroprotective activities: ↓ Behavioural impairment and loss of nigral neurons in MPTP treated mice ↑ Clearance of α-synuclein in the brain of MPTP treated mice ↑ Viability of MPP^+ treated PC12 cells Autophagic enhancement: ↑ LC3-II and Beclin-1 autophagic markers in neuronal cell line and brain tissue ↑ Activation of PI3K and ↓ p62 expression level both in neuronal cell line and brain tissue ↑ Sirt1 and FoxO1 protein expression in PC-12 cells	Macroautophagy	[140]
Epimedium Species	Provided by Nanjing Zelang	Icariin	Aging associated pathology (male	Neuroprotective activities:	Suppress Macroautophagy	[46]

	Medical Technology Co., Ltd, Nanjing, China		SAMP8 and SAMR1 mice)	↑ Memory and learning of SAMP8 and SAMR1 mice ↓ Brain aging *via* reduction of SA-β-gal positive brain tissue of SAMP8 mice Autophagic suppression: ↓ Number of autophagosomes in the hippocampal of SAMP8 mice ↓ LC3-II autophagic marker and p62 protein expression in the hippocampal and cortex of SAMP8 mice		
	Purchased by Nanjing Zelang Medical Technology Co., Ltd, Nanjing, China		Parkinson's disease (PC12 cells and Sprague Dawley rats)	Neuroprotective activities: ↑ Viability of dopamine neurons in substantia nigra in both rotenone-treated rats amd PC-12 cells ↓ Accumulation of α-synuclein protein level in the substantia nigra ↑ Respiratory function of brain mitochondria Autophagic enhancement: ↑ LC3-II and Beclin-1 autophagic markers, and ↓ p62 expression level in both substantia nigra of rat and PC12 cells ↓ Activation of mTOR protein expression	Macroautophagy and signalling pathway	[141]
Epimedium grandiflorum	N/A	Icariside II	Cerebral ischemia (male Sprague-Dawley rats)	Neuroprotective activities: ↓ Cerebral injury in post MCAO rats ↓ Neuronal injury in oxygen-glucose deprivation and reoxygenation treated primary rat cortical neuronal	Suppress Macroautophagy	[47]

				cells from newborn Sprague Dawley rats Autophagic suppression: ↓ LC3-II/I ratio, Beclin-1, Atg5, and Atg7 autophagic markers in the penumbra tissue and primary rat cortinal neuronal cells ↑ cGMP level, PKG and PDE5 activities ↑ SQSTM1 protein expression level ↑ Activation of ser9-GSK-3β, while ↓ activation of tyr216-GSK-3β		
Dioclea violacea (seeds), Brazil	Purified using size-exclusion affinity chromatography	Lectin	Brain tumour (U87 human glioma cells)	Antiproliferative activities: ↓ Viability of both U87 wild-type and resistant subclone glioma cells ↓ Cell migration and proliferation of U87 cells ↑ MMP level distruption ↓ Activation of Akt and mTORC1, MAPK and ERK1/2 autophagy and cell death signalling proteins ↑ Phosphorylation of SAPKs, p38 MAPK and JNK1/2 protein levels Autophagic enhancement: ↑ Number of AO-stained cells ↑ LC3-II/I ratio autophagic marker	Macroautophagy and signalling pathway	[142]
N/A, Italy	Purchased from Sigma Aldrich	Trehalose	Motoneuron degeneration (NSC34 and iPSCs cells)	Neuroprotective activities: ↑ Nuclear translocation of transcription factor EB in mutant androgen receptor transgenic NSC34 cells	Macroautophagy	[143]

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				↑ Clearance of misfolded proteins in transgenic NSC34 cells and iPSCs derived from SBMA patients that differentiated into motoneuronal-like cells Autophagic enhancement: ↑ Expression of genes coding for BecN1, SQSTM1/p62, and MAP1LC3B autophagic markers		
Ginkgo biloba	Purchased from Calbiochem	Ginkgolic acid	Parkinson's disease (SH-SY5Y and embryonic cortical neurons from E18 Wistar Rattus Norvergicus embryos)	Neuroprotective activities: ↓ Clearance of α-synuclein in KC1-treated SH-SY5Y cell Autophagic enhancement: ↑ LC3-II autophagic expression level and number of autophagosomes	Macroautophagy	[144]
Stephania cepharantha	Provided by Guangzhou Jinan Biomedicine Research and Development Center, Guangdong, China	Cepharanthine	Spinal and bulbar muscular atrophy (NSC34 cells)	Neuroprotective activities: ↑ Viability of mAR51Q transgenic SBMA cells ↑ Clearance of both cytoplasmic and nuclear mAR51Q mutant protein ↓ Activation of caspase-3 pro-apoptotic marker and number of apoptotic cells ↓ Phosphorylation of AMPKα Autophagic enhancement: ↑ LC3-II/I ratio and ↓ SQSTM1/p62 autophagic markers ↓ activation of mTOR expression ↑ Number of autophagolysosomal fusion	Macroautophagy and signalling pathway	[145]

Radix sophorae flavescentis	Obtained from Tianqing Phar. Co., Chiatai, Jiangsu China.	Matrine	Multiple sclerosis (female Wistar rat)	Neuroprotective activities: ↓ Clinical severity of autoimmune encephalomyelitis rat *via* ↓ weight loss, and CNS inflammation and demyelination ↓ Apoptosis in stressed oligodendrocytes and caspase-3 activation ↓ Microglia activation, IL-1β inflammatory marker, and HSPB5 multiple sclerosis marker ↓ Cytochrome *C* protein expression in stressed oligodendrocytes of brain and spinal cord ↓ ROS production in the CNS of autoimmune encephalomyelitis rat Autophagic enhancement: ↑ Mitochondrial LC3 and Beclin-1 in stressed oligodendrocytes brain and spinal cord	Macroautophagy	[146]
Hypericum perforatum L.	Obtained from Shanghai Yuanye Biotechnology. Co., Ltd, Shanghai, China	Hyperoside	Epilepsy (male ICR mice)	Neuroprotective activities: ↑ Number of NeuN immunoreactive cells in the brain tissues of kainic acid-treated mice ↓ Epileptic behaviour scores in kainic acid-treated mice ↑ SOD1 and SOD2 antioxidant enzymatic activities ↑ Activation of PI3K, Akt, MAPK protein expressions ↓ Microglial activation and Iba-1 expression level Autophagic enhancement:	Macroautophagy	[147]

				↑ Number of autophagosomes in the hippocampal tissue ↑ LC3-II/I ratio and Beclin-1 autophagic markers		
Panax notoginseng	Purchased from Qidan Co. Ltd. Yunnan, China	Stem-leaf saponins	Sleep deprivation (male C57BL/6 mice)	Neuroprotective activities: ↑ Memory and learning functions of sleep deprived mice ↓ Neuronal injury in hippocampus of sleep deprived mice ↓ Bax/Bcl-2 ratio and activated caspase-3 apoptotic markers Autophagic suppression: ↓ Number of autophagosomes ↓ LC3-II, Beclin-1, p62 autophagic markers protein expression ↑ Activation of PI3K, Akt, mTOR at protein level	Suppress Macroautophagy	[148]
Buckwheat, teas, and apples	Purchased from Sigma Aldrich	Rutin	Huntington's disease (*C. elegans)*	Neuroprotective activities: ↓ Polyglutamine deposition in both AM141 and HA759 mutant *C. elegans* ↑ Lifespans of both AM141 and HA759 mutant *C. elegans* ↓ Intracellular ROS in both AM141 and HA759 mutant *C. elegans* ↑ Viability of juglone-induced oxidative stress in all strains	Macroautophagy	[149]
Ericaceae species	Obtained from Shanghai Yuanye Biotechnology company, Shanghai,	α-Arbutin	Parkinson's disease (SH-SY5Y cells, drosophila)	Neuroprotective activities: ↑ Viability in rotenone treated SH-SY5Y cells	Signalling pathway	[150]

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	China, and dissolved in distilled water			↓ PARP pro-apoptotic protein activation ↓ Intracellular ROS level and ↑ GSH and SOD antioxidant enzymatic activities ↑ MMP level and mitochondrial integrity ↓ Pathological phenotypes in PD drosophila Autophagic enhancement: ↓ Activation of AMPK and p62 protein expression levels		
Rhodolia rosea L.	Purchased from MedChem Express	Salidroside	Cerebral Ischemia (male C57BL/6 mice and primary spinal neurons)	Neuroprotective activities: ↓ Loss of motor neurons and motor function in the spinal cord of post SCIRI mice ↓ BAX/Bcl-2 ratio, activated caspase-3 and caspase-9 pro-apoptotic proteins in the spinal cord of post SCIRI mice and oxygen-glucose deprivation/reperfusion in primary spinal neurons from fetal mice ↓ Oxidative stress level in spinal cord tissue and primary spinal neurons ↑ GSH and SOD antioxidant enzymatic activities in spinal cord tissue ↑ MMP level and mitochondrial function Autophagic enhancement:	Macroautophagy	[151]

				↑ Number of autophagosomes and autophagosome-lysosome fusion in the mitochondria of *in vitro* and *in vivo* experiments ↑ LC3-II autophagic marker, and ↓ p62 and Tomm20 protein expressions in spinal cord tissue and primary spinal neurons ↑ Phosphorylation of Parkin and PINK1 protein expression level		
Cannabis sativa	Cultivated and collected at CREA-CIN, Rovigo, Italy, and purified under standardized and legalised method by the Ministry of Health of Italy	Cannabidiol	Parkinson's disease (Retinoic acid-differentiaed SH-SY5Y cells)	Neuroprotective activities: ↑ Viability of MPP^+ induced cell death in SH-SY5Y cell ↓ BAX, activated caspase-3 and PARP-1 pro-apoptotic protein levels ↑ Tyrosine hydroxylase dopaminergic enzyme expression level ↑ Activation of ERK and Akt cell survival protein levels Autophagic suppression: ↑ Activation of mTOR protein level ↓ LC3-II autophagic markers	Suppress Macroautophagy	[152]
	N/A		Autophagic study (*C. elegans,* SH-SY5Y cells, and primary hippocampal cells)	Autophagic enhancement: ↑ Number of autophagosomes and autophagosome-lysosome formation in aging neurons of *C. elegans* ↑ Lifespan and neuronal morphology in aging *C. elegans* with presence of *bec-1, vps-34, and sqt-1* genes ↑ Anti-aging and neuroprotective effects *via* SIRT1 and sir-2.1	Macroautophagy	[153]

				autophagic marker in both *in vitro* and *in vivo* experiments		
	Purchased from Biopurify, Chengdu, China.		Alzheimer's disease (APP/PS1 mice and C57B6/J mice)	Neuroprotective activities: ↑ Aβ clearance in APP/PS1 mice Autophagic enhancement: ↑ LC3 and Beclin-1 autophagic markers	Macroautophagy	[154]
Corn silk	Provided by Dr Maurice Snook, Russel Research Center, Athens, USA	Maysin	Parkinson's disease (SH-SY5Y cells)	Neuroprotective activities: ↑ Viability of α-synuclein treated SH-SY5Y cells ↓ α-synuclein deposition on cell surface Autophagic enhancement: ↑ Number of autophagsomes ↓ Activation ribosomal protein S6 expression level ↑ LC3-II/I ratio autophagic marker and ↓ p62 protein expression	Macroautophagy	[155]
N/A	N/A	Soybean isoflavone	Parkinson's disease (Male Sprague-Dawley rats)	Neuroprotective activities: ↓ Morphologically neuronal damage in striatal neurons from Atrazine-treated mice ↓ MDA oxidative stress protein level, and ↑ GSH antioxidant enzymatic activity ↓ TNF-α and IL-6 neuroinflammatory markers ↑ Tyrosine hydroxylase dopaminergic protein level	Macroautophagy and signalling pathway	[156]

				↓ BAX pro-apoptotic protein and ↑ Bcl-2 anti-apoptotic marker at mRNA level Autophagic enhancement: ↑ LC3-II and Beclin-1 autophagic markers, ↓ p62 protein expression ↓ Activation of mTOR protein level		
N/A	N/A		Parkinson's disease (SH-SY5Y cells)	Neuroprotective activities: ↑ Viability of Atrazine-treated SH-SY5Y cells ↑ MMP level and mitochondrial function Autophagic enhancement: ↑ Number of autophagosomes in mitochondria ↑ Tom20, BNIP3, BEX2, and NIX mitophagy marker and ↑ LC3-II autophagic marker	Macroautophagy	[157]
N/A	Purchased from Sigma Aldrich	α-linolenic acid	Alzheimer's disease (normal human astrocytes and SH-SY5Y cells)	Neuroprotective activities: ↑ Viability and secretory activity in astrocyte cells and Aβ-treated differentiated SH-SY5Y cells ↑ Synaptophysin and PSD95 synaptic markers in both cells ↑ MMP level and mitochondrial function Autophagic enhancement: ↑ PINK-1 and PARKIN mitophagy markers ↑ Atg5 and LC3II autophagic markers	Macroautophagy	[158]

Astragalus membranaceus	Provided by Jingzhu Biotechnology, Nanjing, China	Astragaloside IV	Parkinson's disease (MPTP-injected mice and primary astrocyte cell from fetal mice)	Neuroprotective activities: ↓ Behavioural deficits and loss of dopaminergic neurons in PD mice ↓ Accumulation of senescent astrocytes in PD mice and primary astrocytes cell ↑ MMP level and mitochondrial function in primary astrocytes cell Autophagic enhancement: ↑ PINK1 and Parkin autophagic marker, while ↓ Tom20 protein level in the mitochondrial of senescent primary astrocyte cells	Mitoautophagy	[159]
N/A	Purchased from Sigma Aldrich	Apigenin	Oxiapoptophagy (N2a cells)	Neuroprotective activities: ↑ Viability of 7KC-treated N2a cells ↓ Plasma membrane damage in 7KC-treated N2a cells ↓ Intracellular ROS and ↑ antioxidant enzymatic activities ↑ MMP level and mitochondrial function ↓ Activated caspase-3 and PARP pro-apoptotic markers Autophagic suppression: ↓ LC3-II/I ratio autophagic markers	Suppress Macroautophagy	[160]
N/A	Purchased from MedChem Express	Dioscin	Alzheimer's disease (HT-22 cells)	Neuroprotective activities: ↑ Viability of Aβ-treated HT22 cells ↓ Number of apoptotic cells of Aβ-treated HT22 cells ↓ Intracellular ROS level in Aβ-treated HT22 cells Autophagic enhancement:	Macroautophagy	[161]

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				↑ Number of autophagosomes and formation of autophagosome-lysosome ↑ LC3-II and Beclin-1 autophagic markers		
Lonicera Japonica	N/A	Galuteolin	Cerebral Ischemia (male Sprague Dawley rats)	Neuroprotective activities: ↓ Neuronal loss, pathological behaviour, infarct volume and brain eodema in post MCAO rats Autophagic suppression: ↓ LC3-II and Beclin-1 autophagic markers, while ↑ p62 protein expression	Suppress Macroautophagy	[162]
Cistanches Herba and *Radix Rehmanniae*	Purchased from Shanghai Yuen Ye Biotechnology, China	Acteoside	Parkinson's disease (PC-12 cells, SH-SY5Y cells, and *drosophila melanogaster*)	Neuroprotective activities: ↑ Viability of rotenone-induced PC12 cells ↑ Lifespan, pathological phenotypes and motoneuron function in PD drosophila ↓ Number of apoptotic cells and BAX/Bcl-2 ratio protein expression ↑ MMP level and ↓ intracellular ROS level Autophagic enhancement: ↑ AMPK activation in rotenone-treated PC12 cells ↑ LC3-II and ↓ p62/SQSTM1 in mitochondrial of rotenone-treated SH-SY5Y cells	Macroautophagy and signalling pathway	[163]
Walnuts, cashews, strawberries,	N/A	Ellagic acid	Parkinson's disease (SH-SY5Y cells)	Neuroprotective activities:	Macroautophagy	[164]

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raspberries and pomegranates				↑ Inhibition and disaggregation of α-synuclein amyloid fibrils formation ↑ Viability of α-synuclein-treated SH-SY5Y cells ↓ BAX/Bcl-2 ratio and p53 pro-apoptotic protein ↑ Activation of Akt protein expression Autophagic enhancement: ↑ LC3-II/I ratio and ↓ p62 autophagic markers		
	Purchased from Sigma Aldrich		Parkinson's disease (C57BL/6 mice)	Neuroprotective activities: ↓ α-synuclein accumulation in the substantia nigra of MPTP-PFF treated mice ↑ Viability of dopaminergic neurons and ↓ apoptosis in substantia nigra of MPTP-PFF treated mice Autophagic enhancement: ↑ LC3 puncta and LC3-II/I, while ↓p62 protein expression in substantia nigra of MPTP-PFF treated mice	Macroautophagy	[165]
Selaginella tamariscina, Selaginella pulvinate, Ginko biloba, Polugala sibirica	N/A	Amentoflavone	Alzheimer's disease (male Kunming mice and PC12 cells)	Neuroprotective activities: ↑ Memory and cognitive function in Aβ-treated mice ↓ GFAP and Iba-1 astrocytes and microglial activation markers in hippocampus of mice ↓ Numbers of NK and T white blood cells, while ↓ IL-6 and IL-17 neuroinflammatory markers in the blood	Macroautophagy and signalling pathway	[166]

				↓ Brain ROS level while ↑ MDA, GSH, and SOD antioxidant enzymatic activities ↓ BAX and activated caspase-3 and -9 pro-apoptotic proteins while ↑ Bcl-2 anti-apoptotic marker Autophagic enhancement: ↑ LC3-II and Beclin-1 autophagic markers, while ↓ activation of mTOR protein expression		
N/A	Provided by Prof. C. Curti, University of Pharma, Italy	Flavan-3-ols	Alzheimer's disease (SH-SY5Y cells)	Neuroprotective activities: ↑ Clearance of extracellular and intracellular Aβ levels Autophagic enhancement: ↑ LC3-II autophagic markers in both wild type and Aβ-transfected SH-SY5Y cells ↑ Number of autophagosomes in both wild type and Aβ-transfected SH-SY5Y cells	Macroautophagy	[167]
Uncaria thynchophylla	Purchased from Aktin Chemicals Inc, Chengdu, China.	Corynoxine	Parkinson's disease (C57BL/6J mice and SD rats)	Neuroprotective activities: ↑ Motoneuron functions in rotenone treated PD mice and rats ↑ Tyrozine hydroxylase dopaminergic marker level in both PD models ↓ Microglial activation in the brain, and ↓ TNF-α and IL-8 neuroinflammatory markers Autophagic enhancement:	Macroautophagy	[168]

				↑ LC3-II autophagic marker and ↓ p62, p-mTOR and p-p70 protein expressions		
Coffee	Purchased from Sigma Aldrich	Chlorogenic acid	Neurotoxicity study: Lead (zebrafish)	Neuroprotective activities: ↓ Toxicity in lead-treated zebrafish ↑ Viability of differentiated neuron in CNS in lead-treated zebrafish ↑ Locomotor function of lead-treated zebrafish ↑ *cfox* and *tuba1b* while ↓*mbp, ppary, bndf,* and dat neurodevelopment gene expression ↓ *sod1, sod2, cat, gclm,* and *gsto2* oxidative stress-related transcriptional genes Autophagic enhancmenet: ↓ *pink1, parkin, ambra1a, ulk1b,* and *ulk2* while ↑ *atg5* autophagic transcriptional genes	Macroautophagy	[169]
	N/A		Parkinson's disease (*C. elegans*)	Neuroprotective activities: ↑ motility and α-synuclein clearance in PD worm ↑ lipid content and ↓ ROS and MDA level in PD worm ↑ Dopaminergic neurons in 6-OHDA treated worm ↓ α-synuclein deposit and ROS level in 6-OHDA treated worm Autophagic enhancement: ↑ LGG-1GFP puncta in muscle of PD worm	Macroautophagy	[170]

				↑ *vps-34, Igg-1, and atg-18* mRNA expression levels		
Fusarium lateritium SSF2	Extracted from its plant using methanol solvent	4,6'-anhydrooxysporidinone	Breast Cancer (MCF-7 cells)	Antiproliferative activities: ↓ Viability of MCF-7 cells ↑ Activation of caspase-7, caspase-9, PARP and p53pro-apoptotic proteins Autophagic enhancement: ↑ Formation of LC3 puncta ↑ LC3-II/I ratio autophagic marker	Macroautophagy	[87]
N/A	N/A	Luteolin	Neurotoxicity studies: Sevoflurane (Neonatal P7 mice, and primary hippocampal cell from fetal C57BL/6J mice)	Neuroprotective activities: ↓ activated caspase-3 and PARP pro-apoptotic proteins in both *in vitro* and *in vivo* experiments ↓ NLRP-3 neuroinflammatory protein in both *in vitro* and *in vivo* experiments ↑ ↑ Cognitive and memory function of sevoflurane-treated mice Autophagic enhancement: ↑ LC3-II/I ratio, Beclin-1 and HMOX1 autophagic markers	Macroautophagy	[171]
Licorice, *Radix Glycyrrhizae* (integral part)	Purchased from ChemFaces	Licochalcone D	Pathophysiology: Oxidative stress (hBM-MSCs cells)	Neuroprotective activities: ↑ Viability of H_2O_2 treated hBM-MSCs cells ↓ p53 and activated caspase-3 pro-apoptotic proteins ↓ p53, p16, p21 cell senescent markers ↑ AMPK activation Autophagic enhancement:	Macroautophagy	[172]

				↑ LC3II and Beclin-1 autophagic markers and ↓ SQSTM1 protein level		
Magnolia officinalis	Purchased from Sigma Aldrich	Magnolol	Autophagy-associated anticancer study (HeLa and SH-SY5Y cells)	Antiproliferative activities: ↓ Viability of both cancer cell lines ↑ activated caspase-3, -9 and PARP pro-apoptotic markers ↓ MMP level in both cancer cell lines Autophagic enhancement: ↑ LC3-II autophagic marker in both cancer cell lines ↑ PINK1 and Parkin mitophagy markers	Macroautophagy	[86]
Sophora flavescens	Purchased from Beijing Zhongke quality inspection Biotechnology Co., Ltd., China)	Oxymatrine	Cerebral hypoxic ischemia (Sprague Dawley rats)	Neuroprotective activities: ↓ Neurological dysfunction, brain infarction and eodema in HIBD-treated rat ↓ Neuron pathological changes and neuronal apoptosis in hippocampus of HIBD-treated rats Autophagic suppression: ↓ Autophagosome level in hippocampus ↓ LC3 and Beclin-1 autophagic marker and ↑ p62 mRNA expression level ↑ Activation of PI3K, Akt, and mTOR protein expression levels	Suppress Macroautophagy and suppress autophagy via signalling pathway	[73]
Canavalia brasiliensis (seeds), USA	Fine powder was extracted in 160mmol/L NaCl,	ConBr lectin	Glioma (C6 glioma cells)	Neuroprotective activities: ↓ Viability and migration of C6 cells	Macroautophagy and signalling pathway	[173]

	followed by size exclusion chromatography			↑ Phosphorylation of JNK proteins, p38 MAPK protein levels ↓ Phosphorylation ERK1/2 and Akt protein levels ↑ Number of apoptotic cells and activated caspase-8 pro-apoptotic level Autophagic enhancement: ↑ Number of autophagsomes ↑ LC3-II/I ratio autophagic marker and ↓ activation of mTOR expression		
Chickpea	Purchased from Sigma Aldrich	Biochanin A	Parkinson's disease (male C57BL/6 mice)	Neuroprotective activities: ↓ Behavioural dysfunction and ↑ dopaminergic neurons in Ang-II treated mice ↑ Endophilin A2 and activation of FoxO3a Autophagic suppression: ↑ LC3-II/I ratio and Beclin-1 autophagic markers	Macroautophagy	[174]
Astragalus membranaceus	N/A	Calycosin	Parkinson's disease (*Drosophila melangoster)*	Neuroprotective activities: ↑ Viability and locomotor function in paraquat-treated flies ↑ Viability of dopaminergic neuron in paraquat-treated flies ↓ Oxidative stress level and pro-apopototic caspases activation in paraquat-treated flies ↑ MMP level and mitochondrial function in paraquat-treated flies Autophagic enhancement:	Macroautophagy	[175]

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				↑ Beclin-1 and Atg5-Atg12 autophagic proteins, and ↓ p62 protein expression ↑ activation of S6K and 4EBP1 expression level		
Originated from pomegranate fruit and walnut, produced by gut bacteria	Purchased from Selleck Chemicals	Urolithin A	Traumatic brain injury (C57BL/6J mice)	Neuroprotective activities: ↓ Brain oedema and ↑ tight junction protein and BBB function in TBI rats ↓ Number of apoptotic neurons, ↓ pro-apoptotic proteins and ↑ anti-apoptotic protein ↑ Neurological score of TBI rats Autophagic enhancement: ↑ LC3 puncta in brain of TBI rats ↑ LC3-II and ↓ p62 protein expressions ↓ Activation of Akt, mTOR, IKKα and NFκB protein expression	Macroautophagy and signalling pathway	[176]
	N/A		Early brain injury (Wistar rats)	Neuroprotective activities: ↓ Neurological deficits, BBB disruption and cerebral oedema in EBI rats ↓ Apoptotic cells and pro-apoptotic proteins in EBI rats Autophagic enhancement: ↑ LC3-II/I and Beclin-1, while ↓ p62 protein expressions ↑ AMPK activation, ↓ mTOR activation	Macroautophagy and signalling pathway	[177]
Mespillus Germanica (leaves)	Isolated from leaves using 70% ethanol, and isolated from	Kaempferol	Alzheimer's disease (male Wistar rats)	Neuroprotective activities: ↑ Memory function of Aβ-treated rats	Macroautophagy	[178]

	two-dimensional paper chromatography			↑ NRF-2 mRNA expression in the hippocampus of Aβ-treated rats Autophagic enhancement: ↑ Beclin-1 protein expression		
Cymbopogo plants	Purchased from Sigma Aldrich	Citronellol	Parkinson's disease (male Wistar rats)	Neuroprotective activities: ↓ Oxidative stress and neuroinflammatory protein levels in rotenone treated rats ↓ Microglial and astrocytes activation *via* Iba-1 and GFAP reduction ↑ Tyrosine hydroxylase dopaminergic neuron markers ↓ Accumulation of α-synuclein and ↑ pro-apoptotic protein Autophagic suppression: ↓ mTOR activation, LC3 and p62 protein expression	Suppress Macroautophagy and suppress autophagy via signalling pathway	[179]
Platycodon grandiflorus	Purchased from Cayman ChemicalcCompany	Platycodin D	Brain tumour (U87MG, U373MG cell lines, and GMB cells)	Antiproliferative activities: ↓ Viability in all cancer cell lines Autophagic suppression: ↑ LC3-II/I and p62 protein expressions ↓ Autophagosome-lysosome formation and lysosomal proteolytic activity	Suppress Macroautophagy	[89]
Garcinia mangostana Linn.	Isolated from pericarp of *G. mangostana* Linn.	α-mangostin	Parkinson's disease (PC12 cells and C57BL/6J mice)	Neuroprotective activities: ↓ Behavioural dysfunction in rotenone-treated mice	Macroautophagy and signalling pathway	[180]

				↓ Oxidative stress and ↑ antioxidant enzymatic activities in rotenone-treated mice ↑ Viability of rotenone-treated PC12 cells ↑ Tyrozine hydroxylase dopaminergic level in rotenone-treated mice Autophagic enhancement: ↑ LC3-II/I ratio, Beclin-1, activated-AMPK protein expression in both cortex and striatum in both *in vitro* and *in vivo* experiments ↓ Activation of α-synuclein level in both *in vitro* and *in vivo* experiments		
	Mixture of 0.5 mg α-mangostin and 10 mg of PEG-PLA to form nanopolyphenol		Neuropathophysiology: protein aggregation (BV-2 cells. 3x Tg mice and PD mice)	Neuroprotective activities: ↑ Viability and ↓ microglial activation in both *in vitro* and *in vivo* experiments ↑ AMPK activation in both *in vitro* and *in vivo* experiments Autophagic enhancement: ↑ Microglial phagocytosis and clearance of misfolded proteins in both *in vitro* and *in vivo* experiments ↑ LC3 and ↓ activated-mTOR protein expression in misfolded protein-treated BV-2 cells	Macroautophagy and signalling pathway	[181]
Apple, *Malus genus*	Purchased from Sigma Aldrich	Phlorizin	Aging (*C. elegans*)	Neuroprotective activities: ↓ Oxidative stress level in environmental stressed worm	Macroautophagy	[182]

				↑ Lifespan without affecting fertility in worm ↓ Aged-related motility decline in worm ↓ Worm paralysis in Aβ transgenic worm ↓ Oxidative stress related gene expression level Autophagic enhancement: ↑ *Igg-1* gene expression level		
N/A	Purchased from Sigma Aldrich	Fisetin	Pathophysiology: Oxidative stress (*C. elegans*)	Neuroprotective activities: ↑ Radical scavenging activity and ↓ cellular ROS level in worm ↑ Lifespan without affecting fertility in worm ↓ Aged-related motility decline in worm ↓ Worm paralysis in Aβ transgenic worm ↓ Dopaminergic neuronal loss in PD trasngenic worm Autophagic enhancement: ↑ *Igg-1* gene expression level	Macroautophagy	[183]
N/A	Purchased from Adamas	β-Caryophyllene	Cerebral Ischemia (HT22 cells and male C57BL/6 mice)	Neuroprotective activities: ↑ Viability and ↓ cell apoptosis in OGD/R-treated HT22 cells ↓ Neuronal injury, infarct volume in the hippocampal tissue of post MCAO mice Autophagic enhancement:	Macroautophagy	[184]

				↑ Number of autophagasomes in mitochondrial in both *in vitro* and *in vivo* experiments ↑ LC3-II/I ratio and ↓ p62 protein expression in both *in vitro* and *in vivo* experiments ↓ Tom20 and ↑ PINK1 and Parkin mitophagy markers in both *in vitro* and *in vivo* experiments		
N/A	Purchased from Sigma Aldrich		Perioperative neurocognitive disorders (male C57BL/6J mice)	Neuroprotective activities: ↑ postoperative cognitive function and CB2R expression in the hippocampus of postoperative neuroinflammation mice ↓ Neuroinflammatory marker levels in postoperative neuroinflammation mice Autophagic enhancement: ↑ LC3-II/I ratio and Beclin-1 while ↓ p62 protein expression in the hippocampus	Macroautophagy	[185]
Neptunea arthritica cumingii	N/A	YIAEDAER peptide	Parkinson's disease (Zebrafish)	Neuroprotective activities: ↓ Locomotor dysfunction in MPTP-treated zebrafish ↑ Dopaminergic neurons and blood vessels formation in MPTP-treated zebrafish ↓ α-synuclein and ROS level Autophagic regulation: ↓ pink1, parkin, beclin-1, ullk2 and ambra1a mRNA transcriptional level	Suppression of Mitophagy	[186]

Glycyrrhiza glabra	Purchased from Sigma Aldrich	Glycyrrhizin	Parkinson's disease (Zebrafish)	Neuroprotective activities: ↑ Dopaminergic neurons and blood vessels formation in MPTP-treated zebrafish ↓ Apoptotic cells and pro-apoptotic proteins in MPTP-treated zebrafish ↓ Locomotor dysfunction in MPTP-treated zebrafish Autophagic regulation: ↓ α-synuclein and atg5 while ↑ parkin, pink1 mRNA transcriptional level	Suppression of Mitophagy	[187]
Penthorum chinese Pursh.	N/A	Thonningianin A	Parkinson's disease (zebrafish and SH-SY5Y cells)	Neuroprotective activities: ↑ MMP level and ↓ cytotoxicity in -OHDA treated SH-SY5Y cells ↑ Antioxidant enzymatic activity in 6-OHDA treated SH-SY5Y cells ↓ PD pathological symptoms in 6-OHDA treated zebrafish ↓ Activation of ferroptosis pathway ↓ Keap1 protein degradation Autophagic enhancement: ↑ LC3-II, Beclin-1 and Atg7 protein expression ↑ p62 protein expression level	Macroautophagy	[188]
	Isolated from leaf, stem and flowers extract through HPLC		Alzheimer's disease (BV-2, primary microglial, PC12 cells, and APP/PS1 transgenic mice)	Neuroprotective activities: ↑ Degradation of NLRP3 inflammasome in Aβ-treated BV2 and primary microglial cells, and APP/PS1 transgenic mice	Macroautophagy and signalling pathway	[189]

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				↑ Viability and ↓ cell apoptosis in Aβ-treated PC12 and primary microglial cells Autophagic enhancement: ↑ LC3-II/I ratio and GFP-LC3 puncta in both BV-2 and primary microglial cells ↑ Atg7, activated AMPK and ULK1 protein expressions in BV-2 cells and APP/PS1 transgenic mice ↑ Phosphorylation of Raf, MEK and ERK protein expressions BV-2 cells and APP/PS1 transgenic mice		
Mediterranean sponge, *Grantia compressa*	Purified from *Eurotium chevalieri* MUT 2316 culture	Dihydroauroglaucin	Neuroblastoma (SH-SY5Y cells)	Antiproliferative activities: ↓ Cell migration of SH-SY5Y cells Autophagic activation: ↑ LC3-II/I protein expression	Macroautophagy	[190]
Artichoke	Purchased	Cynaropicrin	Neuroblastoma (SK-N-BE(2) and SH-SY5Y cells)	Antiproliferative activities: ↓ Viability and ↑ apoptosis and pro-apoptotic proteins in both neuroblastoma cells ↓ Neuroblastoma growth of SK-N-BE(2) inoculated on nude mice Autophagic activation: ↑ LC3-II/I, Beclin-1, Atg5 protein expression level ↓ Autophagic flux *via* reduction of autophagosome-lysosome formation	Macroautophagy	[191]
Corallodiscus flabellata B. L.	Isolated from the extract through HPLC	Isonuomioside A	Alzheimer's disease (Aβ treated mice)	Antiproliferative activities: ↑ Cognitive and memory functions of Aβ treated mice	Macroautophagy	[192]

				↓ Apoptosis and ROS level in the hippocampus of Aβ treated mice Autophagic activation: ↑ Autophagic vacuoles and ↓ Number of autophagosomes ↑ LC3-II, Beclin-1 and ↓ p62 protein expression in the hippocampus of Aβ treated mice		
Plumbago zeylanica L., Italy	Provided by Molnova	Plumbagin	Retinal disorder (*D. melanogaster*)	Neuroprotective activities: ↓ Visual deficit and ↑ retinal disorganization in high-sucrose diet flies ↓ Pro-apoptotic protein and oxidative stress level in retinal cells Autophagic suppression: ↓ LC3 and p62 protein expression	Suppress Macroautophagy	[193]
Citrus and grapefruit	Purchased from Gibco	Limonin	Parkinson's disease (PC12 cells, BV-2 cells and Sprague Dawley rats)	Neuroprotective activities: ↑ Motoneuron and ↓ PD pathology in 6-OHDA treated mice ↓ Neuroinflammatory response (microglial activation) in 6-OHDA treated mice ↑ Viability and ↓ pro-apoptotic markers in 6-OHDA treated PC-12 cells ↓ Neuroinflammation in BV-2 cells Autophagic suppression: ↓ LC3, p62 and Beclin-1 protein expression ↓ Atg5, Beclin-1 and ULK1 autophagy-related gene expression	Suppress Macroautophagy	[194]

Phytolacca esculenta	Provided by National Institute ofr Biological Products, Beijing, China.	Esculentoside A	Alzheimer's disease (triple transgenic AD mice)	Neuroprotective activities: ↑ Behavioural and spatial memory function in transgenic AD mice ↓ Tau phosphorylation and NFT formation in transgenic AD mice ↑ activation of Akt and GSK3β(Tyr216) protein expressions Autophagic enhancement: ↓ Activation of mTOR protein and p62/SQSTM1 levels in the hippocampus of transgenic AD mice ↑ Cathepsin protein levels in hippocampus of transgenic AD mice	Signalling pathway	[195]
Cynanchum otophyllum	Purchased from Aktin Chemicals, Inc	Caudatin	Alzheimer's disease (SCC134, CHO 7PA2, HT-22, N2A-tfLC3 cells and triple transgenic AD mice)	Neuroprotective activities: ↓ Aβ deposit and Tau phosphorylation in Aβ-treated neuronal cell lines ↑ Cognitive and memory functions of transgenic AD mice ↓ Aβ deposit and Tau phosphorylation in transgenic AD mice Autophagic enhancement: ↑ GFP-LC3 puncta, number of autophagosome and autophagosome-lysosome formation in Aβ-treated neuronal cell lines ↑ LC3B-II and LAMP-1 protein expression in Aβ-treated neuronal cell lines and transgenic AD mice	Macroautophagy	[196]

Carthamus tinctorius L.	N/A	Hydroxysafflor yellow A	Traumatic brain injury (BALB/c mice)	Neuroprotective activities: ↑ Neurological score and ↓ apoptotic cells in TBI rats ↓ Neuroinflammatory proteins and microglial activation in TBI rats Autophagic enhancement: ↓ NLRP3 inflammasome in brain of TBI rats ↑ LC3-positive cells, LC3II/I ratio and ↓ p62 protein expression level in brain of TBI rats ↑ Activation of AMPK and ↓ activation of mTOR proteins	Macroautophagy and signalling pathway	[197]
N/A	Purchased from WuXi PharmaTech, China	Cudraflavone B	Glioblastoma (U87 and U251 cells)	Antiproliferative activities: ↓ Viability and ↑ apoptosis in glioma cell lines ↑ ER stress pathway in glioma cell lines Autophagic enhancement: ↑ Autophagic vacuoles, autophagosomes in glioma cell lines ↑ LC3-II/I ratio, ↓ Activation of mTOR, p70, Akt protein expressions	Macroautophagy and signalling pathway	[198]
Nelumbinis plumula	N/A	Liensinine	Cerebral Ischemia (human cortical neurons and male Sprague Dawley rats)	Neuroprotective activities: ↑ Viability and ↓ apoptosis and cytotoxicity in OGD/R cortical neuron ↑ Neurological score and function in cerebral cortex of post MCAO rats Autophagic suppression: ↑ Activation of mTOR and p62 protein expressions	Suppress Macroautophagy	[199]

				↓ Activation of PI3K and Akt protein expressions		
Punica granatum L.	Purchased from Sigma Aldrich	Punicalagin	Parkinson's disease (male Sprague Dawley rats)	Neuroprotective activities: ↑ Motoneuron functions in $MnCl_2$ treated rats ↑ Dopamine, norepinephrine, serotonin, while ↓ Acetylcholine levels in brain of $MnCl_2$ treated rats ↓ Oxidative stress and ↑ antioxidant enzymatic activities ↓ Neuroinflammatory proteins in brain of $MnCl_2$ treated rats ↓ Apoptotic and endoplasmic stress biomarkers level Autophagic suppression: ↓ AMPK activation, Beclin-1 and SIRT-1 mRNA expression brain of $MnCl_2$ treated rats	Suppress signalling pathway	[200]
N/A	Purchased from Sigma Aldrich	Phloretin	Parkinson's disease (C57BL/6 mice and SH-SY5Y cells)	Neuroprotective activities: ↓ PD behaviour and ↑ motoneuron function in rotenone-treated mice ↑ Clearance of α-synuclein and tyrosine hydrolase dopaminergic expression in rotenone-treated mice ↓ Pro-apoptotic protein expressions in rotenone-treated mice and SH-SY5Y cells ↓ Intracellular ROS and ↑ MMP level in rotenone-treated SH-SY5Y cells Autophagic enhancement:	Macroautophagy	[201]

				↑ Atg5, Atg7 and Beclin-1 protein expressions in rotenone-treated mice and SH-SY5Y cells ↓ p62 and activated-mTOR protein expressions in rotenone-treated mice ↑ LC3-II/I ratio protein expression in rotenone-treated SH-SY5Y cells		
N/A	Purchased from MedChemExpress	Aucubin	Inflammatory pain (male C57BL/6 mice)	Protective activities: ↓ Inflammatory pain in CFA treated mice ↓ Inflammatory protein level in CFA-injected paw Autophagic enhancement: ↓ PINK1 and Parkin mitophagy protein expression in CFA-injected mice ↑ LC3B and ↓ p62 protein expression	Macroautophagy	[202]
Stephania tetrandra S. Moore	N/A	Fangchinoline	Alzheimer's disease (male C57BL/6 mice and N2A cells)	Neuroprotective activities: ↑ Viability of APP expressing transgenic AD N2A cells ↑ Cognitive and memory function of Aβ-treated mice ↓ Oxidative stress and apoptosis in Aβ-treated mice Autophagic enhancement: ↓ BACE-1 protein expression in transgenic N2A cells ↑ LC3-II/I, Beclin-1 and ↓ p62 protein expressions in transgenic N2A cells and Aβ-treated mice	Macroautophagy	[203]

Polygala tenuifolia Willd.	N/A	Tenuigenin	Spinal cord injury (male Sprague Dawley rats)	Neuroprotective activities: ↑ Locomotor function in SCI rats ↑ Viability and ↓ apoptosis in spinal neuron of SCI rats Autophagic suppression: ↓ LC3-II/I ratio and Beclin-1 proteins ↓ PTPN1, IRS1, activated-Akt and activated-mTOR protein expressions	Suppress Macroautophagy	[204]
Rhodiola rosea L.	Purchased from Chengdu Must Bio-Technology	Rosavin	Cerebral Ichemia (male C57BL/6 mice and HBMVE cells)	Neuroprotective activities: ↓ Brain infarct volume and neuronal injury in the brain of post MCAO mice ↓ Neuroinflammatory proteins and number of apoptotic cells in both post MCAO mice and OGD/R-induced HBMVE cells ↓ ERK1/2, p38, JNK1/2 protein expressions Autophagic suppression: ↓ LC3-II/I and Beclin-1 protein expressions in both experiments	Suppress Macroautophagy	[205]
Piper Longum L.	N/A	Piperine	Parkinson's disease (male Sprague Dawley rats and SH-SY5Y cells)	Neuroprotective activities: ↑ Motoneuron function and viability of dopaminergic neurons in the substantial nigra of 6-OHDA treated PD rats ↑ α-synuclein clearance in both substantial nigra and colon tissue of 6-OHDA treated PD rats Autophagic enhancement:	Macroautophagy and signalling pathway	[72]

				↑ Number of autophagosomes in substantial nigra and colon tissue of 6-OHDA treated PD rats ↑ LC3-II/I and ↓ p62 protein expression in both substantial nigra and colon tissue of 6-OHDA treated PD rats and in A53T mutant α-synuclein transgenic SH-SY5Y cells ↓ Activation of PI3K, Akt, and mTOR protein expressions in substantial nigra and colon tissue of 6-OHDA treated PD rats, and in A53T mutant α-synuclein transgenic SH-SY5Y cells		
No autophagic effect						
Green tea, *camellia sinensis* (leaves)	Provided by Shanghai U-sea Biotech Co., Ltd., Shanghai, China.	Epigallocatechin-3-gallate Catechin	Alzheimer's disease (human SH-SY5Y neuroblastoma and rat primary cortical neurons)	Show neuroprotective properties without alternation of autophagic activities in rat primary cortical neurons		[77]
Peganum harmala	Purchased from Ye Yuan Company, Shanghai, China.	Harmine	Parkinson's disease (N2a cells and primary cortical neurons from A53T-α-synuclein transgenic mice)	Neuroprotective activities: ↑ Clearance of α-synuclein in A53T-α-synuclein transgenic mice ↑ Activation of ubiquitin-proteasome system No autophagic activation: The α-synuclein clearance activity of Harmine was not disrupted by the effect of autophagy inhibitor, lysosomal inhibitor and even siRNA of autophagic genes		[83]

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N/A	N/A	Limonene (+)	Alzheimer's disease (drosophila)	Neuroprotective activities: ↓ Pathological phenotypes and cell death in AD drosophila ↓ Intracellular ROS in the eye imaginal discs of AD drosophila ↓ ERK activation in the brain of AD drosophila ↓ Number of glial cells and NO level in AD drosophila No autophagic activation: The effect of limonene (+) did not alter autophagy-related factors, and the autophagy inhibitor did not stop the protective effect of limonene (+) on viability of AD drosophila		[78]
Originated from pomegranate fruit and walnut, produced by gut bacteria	Purchased from MedChemExpress	Urolithin A	Alzheimer's disease (SH-SY5Y cell)	Minimal Neuroprotective activities: No significant result in recovering MMP level, reducing ROS level, etc. No autophagic activation: LC3-II and p62 levels unchanged		[79]

PMMB **2025**, *8*, 1; a0000467. doi: 10.36877/pmmb.a000046

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