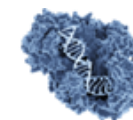
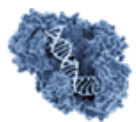


### Supplementary materials

**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.

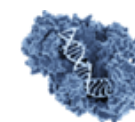
Plant name, common & scientific name, part (root/flower/leave, etc. used), country	Source	Pure compounds	Human disease (Cell lines/ animal models)	Results	Autophagy Type/Regulatory Pathway	Reference
Aloe vera, <i>Aloe barbadensis miller</i> , Serbia	Purchased from Sigma Aldrich	Aloe emodin	Brain tumours (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]
<i>Goniothalamus</i> 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, <i>Radix paeoniae alba</i> (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 <sup>+</sup> and acidosis (pH5.0) insults, ↓ LDH release and apoptotic rate and ↓	Macroautophagy	[59]

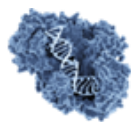




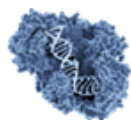
	Biological Products of China, Beijing, China.			intracellular $\text{Ca}^{2+}$ level in MPP <sup>+</sup> and pH5.0-treat cells Autophagic enhancement: ↑ LC3-II/I ratio autophagic markers, and ↑ LAMP2a		
				Neuroprotective activities: ↑ cell viability against MPP <sup>+</sup> and acidosis (pH6.0) insults in differentiated PC-12 cells. Autophagic enhancement: ↓ $\alpha$ -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-3 $\beta$ 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 activation and expression of calpain apoptotic marker Autophagic suppression: ↓ LC-3II/I ratio autophagic marker		
Red grape, <i>Vitis vinifera</i> (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 <i>via</i> increasing the intracellular Ca <sup>2+</sup> 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 <sup>G93A</sup> mice ↓ Spinal motoneuron degeneration in L4-L5 lumbar spinal cord motoneuron of SOD <sup>G93A</sup> mice ↑ Survival time of SOD <sup>G93A</sup> 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 Aβ <sub>25-35</sub> -induced neurotoxicity in differentiated PC-12 cells Autophagic enhancement:	Macroautophagy	[28]

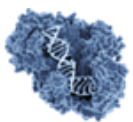




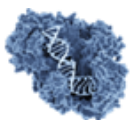
				↑ LC3-II/I ratio, SIRT1, and PARP1, while ↓ p62 autophagic markers		
	Purchased from Sigma Aldrich, China		Traumatic brain injury (Sprague Dawley rats)	Neuroprotective activities: ↓ brain oedema, ↑ learning, memory, and motor function and ↓ hippocampal neuronal damage in TBI rats ↓ TLR4 protein and NF-κB 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 <i>via</i> 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]

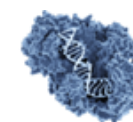


				<p>↑ Number of LC3 and LAMP1 co-stained autolysosomes in dopamine treated SH-SY5Y cells</p> <p>↑ LC3-II/I and Atg4 autophagic protein markers, and ↓ p62 protein expression and mTOR activation</p>		
	Purchased from Sigma Aldrich, China		Alzheimer's disease (PC12 cells)	<p>Neuroprotective activities:</p>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



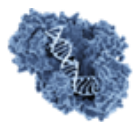
	Synthesized and purchased from Lallilab Inc. Durham, New York, USA		Alzheimer's disease (Male triple transgenic AD mice)	Neuroprotective activities: ↓ NF-κB, GFAP, and PARP neuroinflammatory markers level ↓ Accumulation of toxic Aβ species in brain of transgenic AD mice ↑ Expression of both BDNF and 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 fibroblast cell line and B6.129S6-Baglu <sup>tm1Efn</sup> /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]

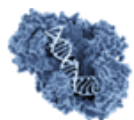




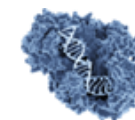
Milk thistle, <i>Silybum marianum</i> (seeds)	Silymarin	Silibin A and B, Isosilibinin A and B, silicristin and silidianin	Cerebral ischemia (male Sprague-Dawley rats)	Neuroprotective activities: ↓ Number of delayed neuronal cell death and apoptotic cells in the brain of ischemic rats Autophagic suppression: ↓ 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, <i>Panax ginseng</i> (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]

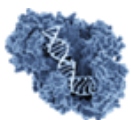


	Isolated from water extract	Ginsenoside Rg2	Alzheimer's disease (human HeLa cervical cancer, human HepG2 liver cancer, mouse Neuro2A neuroblastoma and rat pheochromocytoma cells, and C57BL/6JxSJL mice)	Neuroprotective activities: ↑ Cognitive function in 5XFAD mice Autophagic enhancement: ↑ LC3-II and ↓ 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, <i>Uncaria rhynchophylla</i> (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. ↑ $\alpha$ -synuclein clearance in N2a cells and human embryonic stem cell-transformed dopaminergic neurons	Macroautophagy	[102]

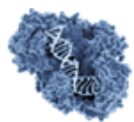


			cell-transformed dopaminergic neuronal cell and L3 Drosophila larvae)	↑ Beclin-1 autophagic marker expression level in N2a cells.		
Thunder god vine, <i>Tripterygium wilfordii</i>	Purchased from Hotmed Sciences Co. Ltd., Shanghai, China	Celastrol	Parkinson's disease (SH-SY5Y neuroblastoma cell)	Neuroprotective 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 ↑ $\alpha$ -synuclein clearance	Macroautophagy	[103]
Extra virgin olive oil, <i>Olea europaea</i> (fruit)	Synthesized via oleuropein deglycosylation under $\beta$ -glycosidase incubation	Oleuropein aglycone	Alzheimer's disease (mouse N2a neuroblastoma, and TgCRND8 mice), Italy	Neuroprotective activities: ↑ Cognitive performance in TgCRND8 $\beta$ -amyloid deposition mice model ↓ $\beta$ -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]

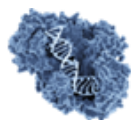




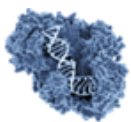
				<p>↑ animal behaviours and memory dysfunction of TgCRND8 mice</p> <p>↓ Amyloid-β deposition in the brain tissue</p> <p>↑ Proliferation of newborn cells in the subgranular zone of the hippocampus</p> <p>Autophagic enhancement:</p> <p>↑ Beclin-1, LC3 and cathepsin B autophagic markers in the brain tissue</p>		
			Alzheimer's disease (human SH-SY5Y neuroblastoma cells, and middle-aged TgCRND8 mice), Italy	<p>Neuroprotective activities:</p> <p>↑ pE3- β-amyloid clearance in the in pE3-β-amyloid-treated SH-SY5Y cell and pE3-β-amyloid-treated middle-aged TgCRND8 mice</p> <p>↑ glutaminyl cyclase in the brain tissues of pE3-β-amyloid-treated middle-aged TgCRND8 mice</p> <p>Autophagic enhancement:</p> <p>↑ Beclin-1 and LC3-II autophagic markers in both in the brain tissues of pE3-β-amyloid-treated middle-aged TgCRND8 mice</p>	Macroautophagy	[105]
			Alzheimer's disease (human SH-SY5Y neuroblastoma cells, and TgCRND8 mice), Italy	<p>Autophagic enhancement:</p> <p>↑ Intracellular Ca<sup>2+</sup>, beclin-1, autophagic vacuoles, AMPK activation in SH-SY5Y cells</p> <p>↑ AMPK activation and mTOR inhibition in the cortex of TgCRND8 mice</p>	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 A $\beta$ deposition in the parietal cortex and hippocampus in treated- TgCRND8 mice ↓ TNF- $\alpha$ 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 A $\beta$ -treated SH-SY5Y cells ↑ MMP level and mitochondrial function Autophagic enhancement: ↑ Number of autophagosomes ↓ Activation of S6 ribosomal protein, while ↑ ULK1 activation	Macroautophagy	[106]

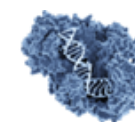


				↑ LC3-II/I ratio and Beclin-1 autophagic markers, and ↓ p62 protein expression		
Turmeric, <i>Curcuma longa</i> (Rhizome)	Purchased from Sigma Aldrich	Curcumin	Genetic based Parkinson's disease (SH-SY5Y neuroblastoma cell)	Autophagic enhancement: ↑ $\alpha$ -synuclein clearance in A53T $\alpha$ -synuclein transfection of differentiated SH-SY5Y cells ↓ p-mTOR and p-p70S6K autophagic markers in A53T $\alpha$ -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]

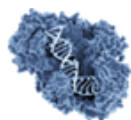


				<p>↑ LAMP2 lysosomal protein to induce autophagosome-lysosome binding</p> <p>↑ Retrograde axonal transport molecular motor and scaffolding proteins expression (DIC, DHC1, and DLC-3)</p>		
	N/A		Autophagic study (MN9D cells)	<p>Neuroprotective activities:</p> <p>↑ Viability and ↓ apoptosis of propofol-treated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

<i>Nigella sativa</i> (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]
<i>Fructus arctii</i>	Isolated from crude extract using HPLC	Arctigenin	Alzheimer's disease (HEK293-APP <sub>swe</sub> , 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]

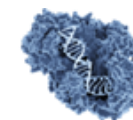


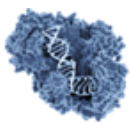




				Autophagic enhancement: ↑ AMPK activation and ↓ mTOR activation in the sciatic nerves of streptozotocin-treated diabetic mice ↑ LC3-II/I and Beclin-1 and ↓ p62 protein expression		
Green tea, <i>camellia sinensis</i> (leaves)	Provided by Shanghai U-sea Biotech Co., Ltd., Shanghai, China.	Epigallocatechin-3-gallate	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]

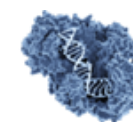
				↑ <i>gm-csf</i> while ↓ <i>mif</i> , and <i>ccl-2</i> gene expression		
	Purchased from Sigma Aldrich, China	Catechin	Ischemic stroke (mouse BV-2 microglial cell)	Neuroprotective activities: ↑ Viability of hypoxia-induced BV-2 cell, ↓ intracellular ROS production and ↓ caspase-3 activation Autophagic 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	<i>p</i> -Coumaric acid	Neuroblastoma and solid extracranial cancer (mouse N2a neuroblastoma)	Neuroprotective activities: ↑ Cytotoxicity and ROS production ↓ GSH and MMP levels ↑ Cytochrome <i>c</i> , caspase-8 and p53 apoptotic markers Autophagic enhancement: ↑ Autophagic vacuoles, LC-3II/I ratio autophagic markers	Macroautophagy	[110]
Chinese skullcap, <i>Scutellaria baicalensis</i> (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]



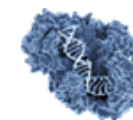


			neuroblastoma cell and C57BL/6J mice)	<p>↓ PD-related behavioural deficit in rotenone-treated mice</p> <p>↑ Dopamine content, ↓ caspase-3 activation and ↑ mitochondrial integrity in both rotenone-treated SH-SY5Y cell and striatal tissue of mice</p> <p>Autophagic enhancement:</p> <p>↑ LC3-II/I ratio autophagic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

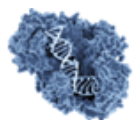
				↓ LC-3-II autophagic marker expression in the spinal cord tissues of transgenic Tg (SOD1 <sup>G93A</sup> ) mice		
<i>Ampelopsis grossedentata</i>	Purchased from Zelang Medical Technological Co. Ltd., Nanjing, China	Ampelopsin/dihyfromyricetin	Alzheimer's disease (Male Sprague Dawley rats)	Neuroprotective 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]
<i>Rosemary, Rosemarinus officinalis</i>	Purchased from Abcam, China	Carnosic acid	Alzheimer's disease (human SH-SY5Y neuroblastoma cell)	Neuroprotective activities: ↑ Viability of Aβ <sub>25-35</sub> treated SH-SY5Y cells ↑ Clearance of Aβ <sub>25-35</sub> 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]

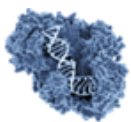


				↑ Autophagic vacuoles and LC3-II protein expression		
<i>Dioscorea nipponica</i>	Purchased from Nanjing Zelang Medical Technology Co., Ltd., Nanjing, China	Diosgenin	Prostate cancer (human DU145 prostate cancer cell line)	Anti-proliferative activities: ↓ Viability of DU145 cells and ↑ number of apoptotic DU145 cells, ↑ caspase-9 apoptotic protein marker and ↓ Bcl-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]
<i>Polyalthia longifolia</i>	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]
<i>Gastrodia elata</i>	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]

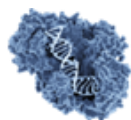


				↓ p38 activation		
Houpo, <i>Magnolia officinalis</i> Rehd. et Wilsn, Taiwan	Purchased from Sigma Aldrich	Honokiol	Neuroblastoma (Mice Neuro2A and NB41A3 neuroblastoma cells)	Antiproliferative activities: ↑ Number of apoptotic cells in both cell lines ↑ Grp78 protein expression and intracellular ROS 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]
<i>Rabdosia rubescens</i>	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]
<i>Dalbergia odorifera</i> (heartwoods)	Isolated from ethanol extract of <i>D. odorifera</i>	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]



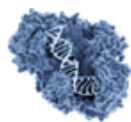


				<p>↑ <math>\alpha</math>-Spectrin and BAX pro-apoptotic markers, and ↓ Bcl-2 anti-apoptotic marker</p> <p>Autophagic enhancement:</p> <p>↑ LC3II/I ratio autophagic marker</p>		
Olive, Argan and hydrogenated food oils	N/A	Oleic acid, docosahexaenoic acid	Neuropathology: oxiaoptophagy (mouse BV-2 microglial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

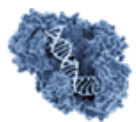


				↑ Autophagosome-lysosome formation <i>in vitro</i> and <i>in vivo</i> experiment		
<i>Tripterygium wilfordii</i> Hook.f.	N/A	Triptolide	Parkinson's disease (mouse MN9D dopaminergic neuronal and Sprague-Dawley rats)	Neuroprotective activities: ↑ Viability of A53T-transfected MN9D cells ↑ Clearance of $\alpha$ -Synuclein in A53T-transfected MN9D cells Autophagic enhancement: ↓ p62 autophagic marker	Macroautophagy	[121]
<i>Artocarpus lakoocha</i>	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 <i>via</i> 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]



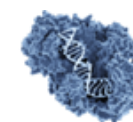


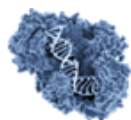
				<p>↑ AMPK activation and ↓ mTOR activation</p> <p>↑ ULK1 and LAMP1 protein expressions in mouse cortical astrocytes</p>		
N/A	Purchased from Sigma Aldrich	Lipoic acid	Neurotoxicity study (SH-SY5Y cells)	<p>Neuroprotective activities:</p> <p>↑ Viability and number of apoptotic cells in acrylamide-treated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



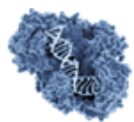
				Autophagic enhancement: ↑ LC3-II/I ratio and Beclin-1 autophagic markers ↑ AMPK activation and ↓ mTOR activation		
	Purchased from Shanghai Yuaye Biotechnology Company, Shanghai, China, and dissolved in distilled water		Parkinson's disease (SH-SY5Y cells and <i>Parkin-null</i> flies)	Neuroprotective activities: ↑ Viability of rotenone-treated SH- SY5Y cells ↓ Intracellular oxidative stress and mitochondrial dysfunction ↑ Dopaminergic mitochondrial dysfunction and phenotypes of <i>parkin-null</i> 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-amyryn	Parkinson's disease ( <i>Caenorhabditis elegans</i> )	Neuroprotective activities: ↑ Viability of juglone-induced oxidative stress in <i>C. elegans</i> ↓ intracellular ROS level in wild- type N2 <i>C. elegans</i> ↑ Viability of neuronal cell in 6- OHDA treated transgenic BZ555 <i>C. elegans</i> ↓ α-synuclein aggregation in transgenic NL5901 <i>C. elegans</i> Autophagic enhancement:	Mitoautophagy	[127]

				↑ LGG-1 autophagic marker in transgenic NL5901 <i>C. elegans</i>		
<i>Rhizoma coptidis</i> , <i>Radix Scutellaria</i> Georgi, Labiatae, <i>Cortex</i> <i>Phellodendri</i> , and <i>Fructus Gardeniae</i> (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- $\alpha$ , IL-1 $\beta$ , IL-2 and IL-6 proinflammatory markers at mRNA level ↑ NF- $\kappa$ B 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]
<i>Erigerin breviscapus</i> (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]



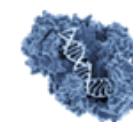


<i>Andrographis paniculata</i> , China		Andrographolide	Alzheimer's disease (rat PC-12 pheochromocytoma cells)	Neuroprotective activities: ↑ Viability of A $\beta$ <sub>1-42</sub> -treated PC-12 cells ↓ A $\beta$ <sub>25-35</sub> -induced cytotoxicity, intracellular malonaldehyde and nitric oxide levels in PC-12 cells ↓ Intracellular ROS and MMP levels ↓ Cytochrome <i>c</i> 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 <sub>2</sub> O <sub>2</sub> -treated cells ↓ Number of apoptotic cells in H <sub>2</sub> O <sub>2</sub> -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 <sub>2</sub> O <sub>2</sub> -treated cells	Macroautophagy	[131]

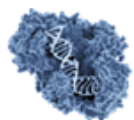


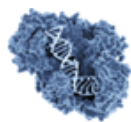
N/A	N/A, China	Quercetin	Autophagic-related pathogenicity (human ARPE-19 retinal pigment epithelial cell)	Autophagic enhancement: ↑ TFEB-mediated gene transcription ↑ Cellular degradation capacity ↑ LC3-II/I ratio and ↓ p62 autophagic markers ↑ Inhibition of mTOR kinase activity <i>via</i> ↓ phosphorylation 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 expressions		
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 ↓ $\alpha$ -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 <i>via</i> ↓ 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 $\alpha$ -synuclein	Macroautophagy and signalling pathway	[134]
<i>Gentiana dinarica</i> (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]



	(1:2.4) (m/v) for 48 h and concentrated using rotary evaporator			<p>↑ Number of autophagic vacuoles</p> <p>↑ LC3-II/I ratio autophagic marker and ↓ p62 autophagy target</p> <p>↓ p-mTOR, S6K, PRAS40, ULK1 and ERK activation</p>		
<i>Trillium tschonoskii</i> (roots)	Purchased from Bellancom (14144-06-0)	Diosgenin glucoside (TTM saponin)	Neurotoxicity study (Sprague-Daley rats)	<p>Neuroprotective activities:</p> <p>↑ Memory and learning on D-galactose treated rats</p> <p>↓ Hippocampal neurons damage from D-galactose treated rats</p> <p>↓ Caspase-3 and BAX apoptotic markers and ↑ Bcl-2 anti-apoptotic marker at protein level</p> <p>Autophagic enhancement:</p> <p>↑ Rheb and ↓ mTORC1 activation</p> <p>↑ LC3-II/I ratio and Beclin-1 autophagic markers, while ↓ p62 protein expression</p>	Macroautophagy	[136]
<i>Aralia elata</i> (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)	<p>Neuroprotective activities:</p> <p>↑ Viability of H<sub>2</sub>O<sub>2</sub>-treated SH-SY5Y cells</p> <p>↓ Number of apoptotic cells</p> <p>↓ Caspase-3 activation and BAX pro-apoptotic marker, while ↑ Bcl-2 anti-apoptotic marker at protein level</p> <p>↑ MMP level in H<sub>2</sub>O<sub>2</sub>-treated SH-SY5Y cells</p> <p>↓ Intracellular ROS level, ↑ Nrf2, p-Nrf2 and HO-1 antioxidant proteins, and ↑ SOD and GSH-Px antioxidant enzyme activities</p> <p>Autophagic enhancement:</p>	Macroautophagy	[137]

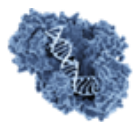


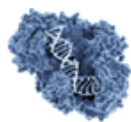


				<p>↑ Number of MDC-stained autophagic cells</p> <p>↑ LC3-II/I ratio and ↓ p62 autophagic markers</p>		
<i>Lycium barbarum</i> polysaccharides	Purchased from Beijing Solarbio Science & Technology Co. Ltd, Beijing, China	N/A	Stroke (Primary hippocampal neuron from C57BL/6 mice)	<p>Neuroprotective activities:</p> <p>↑ Viability and ↓ LDH release from oxygen glucose deprivation/reoxygenation-induced neuron</p> <p>↓ Intracellular ROS level</p> <p>↓ Caspase-3 activation and BAX/Bcl-2 ratio pro-apoptotic marker</p> <p>↓ Number of apoptotic cells</p> <p>Autophagic suppression:</p> <p>↓ LC3-II/I ratio and Beclin-1 autophagic markers, ↑p62 protein expression</p> <p>↑ activation of Akt, mTOR protein expression</p>	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)	<p>Neuroprotective activities:</p> <p>↓ Degeneration of retinal ganglion cells in the nasal retinas of post-PONT rats</p> <p>↑ Microglia/macrophages polarization</p> <p>Autophagic enhancement:</p> <p>↑ CD68 marker for microglia/macrophages activation</p> <p>↑ LC3-II autophagic marker</p>	Macroautophagy	[138]

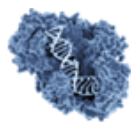


	Purchased from Yuanye Biotechnology Co. Ltd. Shanghai China.	N/A	Parkinson's disease (Sprague Dawley juvenile rats)	Neuroprotective activities: ↓ Behavioural and locomotor dysfunction in 2,4-dichlorophenoxyacetic acid treated PD rats ↑ Viability of neuronal cells in hippocampus ↑ Microglial activation ↓ Oxidative stress and ↑ antioxidant enzyme activities in rat sera Autophagic enhancement: ↑ LC3-II/I and Beclin-1 autophagic markers mRNA expressions	Macroautophagy	[139]
<i>Cistanche tubulosa</i> (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 $\alpha$ -synuclein in the brain of MPTP treated mice ↑ Viability of MPP <sup>+</sup> 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]
<i>Epimedium</i> Species	Provided by Nanjing Zelang	Icariin	Aging associated pathology (male	Neuroprotective activities:	Suppress Macroautophagy	[46]

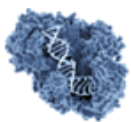




	Medical Technology Co., Ltd, Nanjing, China		SAMP8 and SAMR1 mice)	<p>↑ Memory and learning of SAMP8 and SAMR1 mice</p> <p>↓ Brain aging <i>via</i> reduction of SA-β-gal positive brain tissue of SAMP8 mice</p> <p>Autophagic suppression:</p> <p>↓ Number of autophagosomes in the hippocampal of SAMP8 mice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

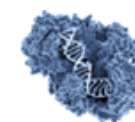


				cells from newborn Sprague Dawley rats Autophagic suppression: ↓ LC3-II/I ratio, Beclin-1, Atg5, and Atg7 autophagic markers in the penumbra tissue and primary rat cortical neuronal cells ↑ cGMP level, PKG and PDE5 activities ↑ SQSTM1 protein expression level ↑ Activation of ser9-GSK-3β, while ↓ activation of tyr216-GSK-3β		
<i>Dioclea violacea</i> (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 disruption ↓ 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]

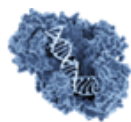


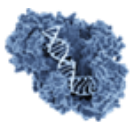
				<p>↑ Clearance of misfolded proteins in transgenic NSC34 cells and iPSCs derived from SBMA patients that differentiated into motoneuronal-like cells</p> <p>Autophagic enhancement:            ↑ Expression of genes coding for BecN1, SQSTM1/p62, and MAP1LC3B autophagic markers</p>		
<i>Ginkgo biloba</i>	Purchased from Calbiochem	Ginkgolic acid	Parkinson's disease (SH-SY5Y and embryonic cortical neurons from E18 Wistar Rattus Norvergicus embryos)	<p>Neuroprotective activities:            ↓ Clearance of <math>\alpha</math>-synuclein in KC1-treated SH-SY5Y cell</p> <p>Autophagic enhancement:            ↑ LC3-II autophagic expression level and number of autophagosomes</p>	Macroautophagy	[144]
<i>Stephania cepharantha</i>	Provided by Guangzhou Jinan Biomedicine Research and Development Center, Guangdong, China	Cepharanthine	Spinal and bulbar muscular atrophy (NSC34 cells)	<p>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 AMPK<math>\alpha</math></p> <p>Autophagic enhancement:            ↑ LC3-II/I ratio and ↓ SQSTM1/p62 autophagic markers            ↓ activation of mTOR expression            ↑ Number of autophagolysosomal fusion</p>	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 <i>via</i> ↓ 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]
<i>Hypericum perforatum</i> 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]

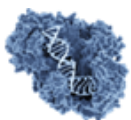


				<p>↑ Number of autophagosomes in the hippocampal tissue</p> <p>↑ LC3-II/I ratio and Beclin-1 autophagic markers</p>		
<i>Panax notoginseng</i>	Purchased from Qidan Co. Ltd. Yunnan, China	Stem-leaf saponins	Sleep deprivation (male C57BL/6 mice)	<p>Neuroprotective activities:</p> <p>↑ Memory and learning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



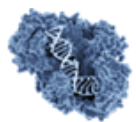


	China, and dissolved in distilled water			<p>↓ PARP pro-apoptotic protein activation</p> <p>↓ Intracellular ROS level and ↑ GSH and SOD antioxidant enzymatic activities</p> <p>↑ MMP level and mitochondrial integrity</p> <p>↓ Pathological phenotypes in PD drosophila</p> <p>Autophagic enhancement:</p>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

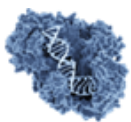


				<p>↑ Number of autophagosomes and autophagosome-lysosome fusion in the mitochondria of <i>in vitro</i> and <i>in vivo</i> experiments</p> <p>↑ LC3-II autophagic marker, and ↓ p62 and Tomm20 protein expressions in spinal cord tissue and primary spinal neurons</p> <p>↑ Phosphorylation of Parkin and PINK1 protein expression level</p>		
<i>Cannabis sativa</i>	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-differentiated SH-SY5Y cells)	<p>Neuroprotective activities:</p> <p>↑ Viability of MPP<sup>+</sup> induced cell death in SH-SY5Y cell</p> <p>↓ BAX, activated caspase-3 and PARP-1 pro-apoptotic protein levels</p> <p>↑ Tyrosine hydroxylase dopaminergic enzyme expression level</p> <p>↑ Activation of ERK and Akt cell survival protein levels</p> <p>Autophagic suppression:</p> <p>↑ Activation of mTOR protein level</p> <p>↓ LC3-II autophagic markers</p>	Suppress Macroautophagy	[152]
	N/A		Autophagic study ( <i>C. elegans</i> , SH-SY5Y cells, and primary hippocampal cells)	<p>Autophagic enhancement:</p> <p>↑ Number of autophagosomes and autophagosome-lysosome formation in aging neurons of <i>C. elegans</i></p> <p>↑ Lifespan and neuronal morphology in aging <i>C. elegans</i> with presence of <i>bec-1</i>, <i>vps-34</i>, and <i>sqt-1</i> genes</p> <p>↑ Anti-aging and neuroprotective effects via SIRT1 and sir-2.1</p>	Macroautophagy	[153]



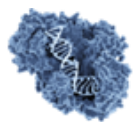


				autophagic marker in both <i>in vitro</i> and <i>in vivo</i> experiments		
	Purchased from Biopurify, Chengdu, China.		Alzheimer's disease (APP/PS1 mice and C57B6/J mice)	Neuroprotective activities: ↑ Aβ clearance in APP/PS1 mice Autophagic enhancement: ↑ LC3 and Beclin-1 autophagic markers	Macroautophagy	[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 autophagosomes ↓ 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]

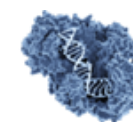


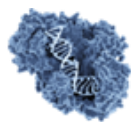
				<p>↓ BAX pro-apoptotic protein and ↑ Bcl-2 anti-apoptotic marker at mRNA level</p> <p>Autophagic enhancement:</p> <p>↑ LC3-II and Beclin-1 autophagic markers, ↓ p62 protein expression</p> <p>↓ Activation of mTOR protein level</p>		
N/A	N/A		Parkinson's disease (SH-SY5Y cells)	<p>Neuroprotective activities: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

<i>Astragalus membranaceus</i>	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 A $\beta$ -treated HT22 cells ↓ Number of apoptotic cells of A $\beta$ -treated HT22 cells ↓ Intracellular ROS level in A $\beta$ -treated HT22 cells Autophagic enhancement:	Macroautophagy	[161]

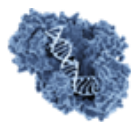


				<p>↑ Number of autophagosomes and formation of autophagosome-lysosome</p> <p>↑ LC3-II and Beclin-1 autophagic markers</p>		
<i>Lonicera Japonica</i>	N/A	Galuteolin	Cerebral Ischemia (male Sprague Dawley rats)	<p>Neuroprotective activities:</p> <p>↓ Neuronal loss, pathological behaviour, infarct volume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

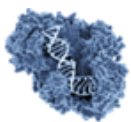




raspberries and pomegranates				<p>↑ Inhibition and disaggregation of <math>\alpha</math>-synuclein amyloid fibrils formation</p> <p>↑ Viability of <math>\alpha</math>-synuclein-treated SH-SY5Y cells</p> <p>↓ BAX/Bcl-2 ratio and p53 pro-apoptotic protein</p> <p>↑ Activation of Akt protein expression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

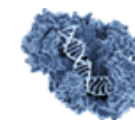


				<p>↓ Brain ROS level while ↑ MDA, GSH, and SOD antioxidant enzymatic activities</p> <p>↓ BAX and activated caspase-3 and -9 pro-apoptotic proteins while ↑ Bcl-2 anti-apoptotic marker</p> <p>Autophagic enhancement:</p> <p>↑ LC3-II and Beclin-1 autophagic markers, while ↓ activation of mTOR protein expression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



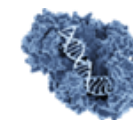
				↑ LC3-II autophagic marker and ↓ p62, p-mTOR and p-p70 protein expressions		
Coffee	Purchased from Sigma Aldrich	Chlorogenic acid	Neurotoxicity study: Lead (zebrafish)	Neuroprotective activities: ↓ Toxicity in lead-treated zebrafish ↑ Viability of differentiated neuron in CNS in lead-treated zebrafish ↑ Locomotor function of lead-treated zebrafish ↑ <i>cfox</i> and <i>tuba1b</i> while ↓ <i>mbp</i> , <i>ppary</i> , <i>bndf</i> , and <i>dat</i> neurodevelopment gene expression ↓ <i>sod1</i> , <i>sod2</i> , <i>cat</i> , <i>gclm</i> , and <i>gst02</i> oxidative stress-related transcriptional genes Autophagic enhancmenet: ↓ <i>pink1</i> , <i>parkin</i> , <i>ambra1a</i> , <i>ULK1b</i> , and <i>ULK2</i> while ↑ <i>atg5</i> autophagic transcriptional genes	Macroautophagy	[169]
	N/A		Parkinson's disease ( <i>C. elegans</i> )	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]

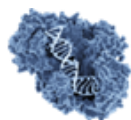
				↑ <i>vps-34</i> , <i>Igg-1</i> , and <i>atg-18</i> mRNA expression levels		
<i>Fusarium lateritium</i> SSF2	Extracted from its plant using methanol solvent	4,6'-anhydroxysporidinone	Breast Cancer (MCF-7 cells)	Antiproliferative activities: ↓ Viability of MCF-7 cells ↑ Activation of caspase-7, caspase-9, PARP and p53 pro-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 <i>in vitro</i> and <i>in vivo</i> experiments ↓ NLRP-3 neuroinflammatory protein in both <i>in vitro</i> and <i>in vivo</i> experiments ↑ Cognitive and memory function of sevoflurane-treated mice Autophagic enhancement: ↑ LC3-II/I ratio, Beclin-1 and HMOX1 autophagic markers	Macroautophagy	[171]
Licorice, <i>Radix Glycyrrhizae</i> (integral part)	Purchased from ChemFaces	Licochalcone D	Pathophysiology: Oxidative stress (hBM-MSCs cells)	Neuroprotective activities: ↑ Viability of H <sub>2</sub> O <sub>2</sub> treated hBM-MSCs cells ↓ p53 and activated caspase-3 pro-apoptotic proteins ↓ p53, p16, p21 cell senescent markers ↑ AMPK activation Autophagic enhancement:	Macroautophagy	[172]





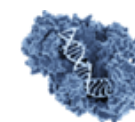
				↑ LC3II and Beclin-1 autophagic markers and ↓ SQSTM1 protein level		
<i>Magnolia officinalis</i>	Purchased from Sigma Aldrich	Magnolol	Autophagy-associated anticancer study (HeLa and SH-SY5Y cells)	Antiproliferative activities: ↓ Viability of both cancer cell lines ↑ activated caspase-3, -9 and PARP 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]
<i>Sophora flavescens</i>	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]
<i>Canavalia brasiliensis</i> (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]



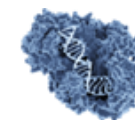


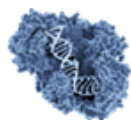
	followed by size exclusion chromatography			<p>↑ Phosphorylation of JNK proteins, p38 MAPK protein levels</p> <p>↓ Phosphorylation ERK1/2 and Akt protein levels</p> <p>↑ Number of apoptotic cells and activated caspase-8 pro-apoptotic level</p> <p>Autophagic enhancement:</p> <p>↑ Number of autophagosomes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

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

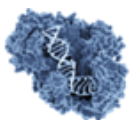


	two-dimensional paper chromatography			↑ NRF-2 mRNA expression in the hippocampus of Aβ-treated rats Autophagic enhancement: ↑ Beclin-1 protein expression		
<i>Cymbopogo</i> plants	Purchased from Sigma Aldrich	Citronellol	Parkinson's disease (male Wistar rats)	Neuroprotective activities: ↓ Oxidative stress and neuroinflammatory protein levels in rotenone treated rats ↓ Microglial and astrocytes activation <i>via</i> 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]
<i>Platycodon grandiflorus</i>	Purchased from Cayman Chemical Company	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]
<i>Garcinia mangostana</i> Linn.	Isolated from pericarp of <i>G. mangostana</i> 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]

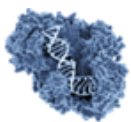




				<p>↓ Oxidative stress and ↑ antioxidant enzymatic activities in rotenone-treated mice</p> <p>↑ Viability of rotenone-treated PC12 cells</p> <p>↑ Tyrosine hydroxylase dopaminergic level in rotenone-treated mice</p> <p>Autophagic enhancement:</p> <p>↑ LC3-II/I ratio, Beclin-1, activated-AMPK protein expression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

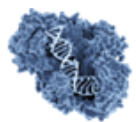


				<p>↑ Lifespan without affecting fertility in worm</p> <p>↓ Aged-related motility decline in worm</p> <p>↓ Worm paralysis in A<math>\beta</math> transgenic worm</p> <p>↓ Oxidative stress related gene expression level</p> <p>Autophagic enhancement:</p> <p>↑ <i>Igg-1</i> gene expression level</p>		
N/A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

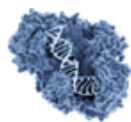


				<p>↑ Number of autophagasomes in mitochondrial in both <i>in vitro</i> and <i>in vivo</i> experiments</p> <p>↑ LC3-II/I ratio and ↓ p62 protein expression in both <i>in vitro</i> and <i>in vivo</i> experiments</p> <p>↓ Tom20 and ↑ PINK1 and Parkin mitophagy markers in both <i>in vitro</i> and <i>in vivo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

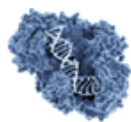
<i>Glycyrrhiza glabra</i>	Purchased from Sigma Aldrich	Glycyrrhizin	Parkinson's disease (Zebrafish)	Neuroprotective activities: ↑ Dopaminergic neurons and blood vessels formation in MPTP-treated zebrafish ↓ Apoptotic cells and pro-apoptotic proteins in MPTP-treated zebrafish ↓ Locomotor dysfunction in MPTP-treated zebrafish Autophagic regulation: ↓ $\alpha$ -synuclein and atg5 while ↑ parkin, pink1 mRNA transcriptional level	Suppression of Mitophagy	[187]
<i>Penthorum chinense</i> 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 A $\beta$ -treated BV2 and primary microglial cells, and APP/PS1 transgenic mice	Macroautophagy and signalling pathway	[189]



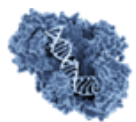




				<p>↑ Viability and ↓ cell apoptosis in Aβ-treated PC12 and primary microglial cells</p> <p>Autophagic enhancement:</p> <p>↑ LC3-II/I ratio and GFP-LC3 puncta in both BV-2 and primary microglial cells</p> <p>↑ Atg7, activated AMPK and ULK1 protein expressions in BV-2 cells and APP/PS1 transgenic mice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

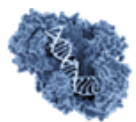


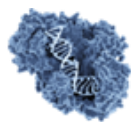
				<p>↓ Apoptosis and ROS level in the hippocampus of A<math>\beta</math> treated mice</p> <p>Autophagic activation:</p> <p>↑ Autophagic vacuoles and ↓ Number of autophagosomes</p> <p>↑ LC3-II, Beclin-1 and ↓ p62 protein expression in the hippocampus of A<math>\beta</math> treated mice</p>		
<i>Plumbago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



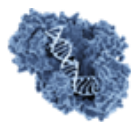
<i>Phytolacca esculenta</i>	Provided by National Institute of Biological Products, Beijing, China.	Esculentoside A	Alzheimer's disease (triple transgenic AD mice)	Neuroprotective activities: ↑ Behavioural and spatial memory function in transgenic AD mice ↓ Tau phosphorylation and NFT formation in transgenic 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]
<i>Cynanchum rotophyllum</i>	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]

<i>Carthamus tinctorius</i> 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]
<i>Nelumbinis plumula</i>	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]



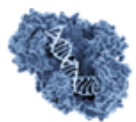


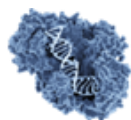
				↓ Activation of PI3K and Akt protein expressions		
<i>Punica granatum</i> L.	Purchased from Sigma Aldrich	Punicalagin	Parkinson's disease (male Sprague Dawley rats)	Neuroprotective activities: ↑ Motoneuron functions in MnCl <sub>2</sub> treated rats ↑ Dopamine, norepinephrine, serotonin, while ↓ Acetylcholine levels in brain of MnCl <sub>2</sub> treated rats ↓ Oxidative stress and ↑ antioxidant enzymatic activities ↓ Neuroinflammatory proteins in brain of MnCl <sub>2</sub> treated rats ↓ Apoptotic and endoplasmic stress biomarkers level Autophagic suppression: ↓ AMPK activation, Beclin-1 and SIRT-1 mRNA expression brain of MnCl <sub>2</sub> 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]



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

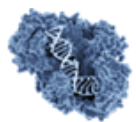
<i>Polygala tenuifolia</i> Willd.	N/A	Tenuigenin	Spinal cord injury (male Sprague Dawley rats)	Neuroprotective activities: ↑ Locomotor function in SCI rats ↑ Viability and ↓ apoptosis in spinal neuron of SCI rats Autophagic suppression: ↓ LC3-II/I ratio and Beclin-1 proteins ↓ PTPN1, IRS1, activated-Akt and activated-mTOR protein expressions	Suppress Macroautophagy	[204]
<i>Rhodiola rosea</i> L.	Purchased from Chengdu Must Bio-Technology	Rosavin	Cerebral Ischemia (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]
<i>Piper Longum</i> 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 substantia nigra of 6-OHDA treated PD rats ↑ $\alpha$ -synuclein clearance in both substantia nigra and colon tissue of 6-OHDA treated PD rats Autophagic enhancement:	Macroautophagy and signalling pathway	[72]





				<p>↑ Number of autophagosomes in substantial nigra and colon tissue of 6-OHDA treated PD rats</p> <p>↑ LC3-II/I and ↓ p62 protein expression in both substantial nigra and colon tissue of 6-OHDA treated PD rats and in A53T mutant <math>\alpha</math>-synuclein transgenic SH-SY5Y cells</p> <p>↓ Activation of PI3K, Akt, and mTOR protein expressions in substantial nigra and colon tissue of 6-OHDA treated PD rats, and in A53T mutant <math>\alpha</math>-synuclein transgenic SH-SY5Y cells</p>		
No autophagic effect						
Green tea, <i>camellia sinensis</i> (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]
<i>Peganum harmala</i>	Purchased from Ye Yuan Company, Shanghai, China.	Harmine	Parkinson's disease (N2a cells and primary cortical neurons from A53T- $\alpha$ -synuclein transgenic mice)	<p>Neuroprotective activities:</p> <p>↑ Clearance of <math>\alpha</math>-synuclein in A53T-<math>\alpha</math>-synuclein transgenic mice</p> <p>↑ Activation of ubiquitin-proteasome system</p> <p>No autophagic activation:</p> <p>The <math>\alpha</math>-synuclein clearance activity of Harmine was not disrupted by the effect of autophagy inhibitor, lysosomal inhibitor and even siRNA of autophagic genes</p>		[83]





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]