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Supplementary Information

Plant Secondary Metabolites as Modulators of Mitochondrial Health: An Overview of Their Antioxidant, Anti-Apoptotic, and Mitophagic Mechanisms

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Table S1. Concentrations and solvents of plant secondary metabolites investigated as experimental modulators of mitochondrial health. Abbreviations: AD, Alzheimer's disease; PD, Parkinson's disease; HD, Huntington's disease.

Type of compound	Active substance	Sources	Concentrations and experimental models	Solvent used in experimental models	Mechanism of action	Condition	Solubility
Alkaloids	Berberine **(BBR)**	*Phellodendron, Coptis chinensis, Berberis vulgaris, Berberis aristata, Berberis petiolaris, Rhizoma coptidis, Rhizoma cyperus, Rhizoma rhei*	Cell line: 5, 10, 20, 40, 60, 80, 100 μM; for 3, 6, 24 h [1]	-	Induction of mitochondrial biogenesis; Activation of mitophagy [1]	-	Water: 2.1 mg/ml [2] Ethanol: 2.75 mg/ml [2] DMF: 0.5 mg/ml [3] DMSO: 25 mg/ml [3]
			Cell line: 1 μM; for 24 h; Mice: 100 mg/kg/d; orally; for 30 days [4]	PBS [4]	Improvement of mitochondrial functions; Promotion of mitophagy [4]	AD	

			Cell line: 2, 4, 8, 16, 32 μM; for 6 h [5]	DMSO [5]	Regulation of mitophagy [5]	PD	
			Rats: 150 mg/kg b.w.; intragastrically; for 21 days [6]	Saline [6]	Increase in the activity of mitochondrial complexes [6]	Acetampirid toxicity	
			Rats: 200 mg/kg b.w.; orally; for 42 weeks [7]	0.9% saline [7]	Reduction of oxidative stress; Increase in the activity of mitochondrial complexes [7]	Aging	
			Rats: 30, 100 mg/kg; orally; for 21 days [8]	Double-distilled water [8]	Reduction of oxidative stress [8]	PD	
	Caffeine (**Cof**)	*Coffea*, Tea, Cocoa	*C. elegans*: 10 mM; for 3 days [9]	Nematode growth medium [9]	Regulation of ΔΨm and oxidative stress; Improvement of mitochondrial morphology [9]	Aging	Water: 27.1 mg/ml [10] Ethanol: worse than in water [11] DMSO: better than in water [11]
			Cell line: 256, 512 μM; for 1, 24 h [12]	-	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway [12]	UV irradiation	

	Capsaicin (**CS**)	Chili peppers	Cell lines: 20, 50, 100 μM; for 1 h [13]	DMSO [13]	Decrease in mitochondrial respiration and ATP production [13]	Lung cancer	Water: poor solubility [14] Ethanol: 61 mg/ml [14] DMSO: 61 mg/ml [14]
			Cells: 5, 10, 20, 40, 80 μM; for 12 h [15]	-	Reduction of oxidative stress; Regulation of mitochondrial respiration [15]	LPS-induced sepsis	
	Piperine (**PIP**)	*Piper longum*	Cell line: 10, 20, 40 mg/l; for 24 h [16]	Medium [16]	Induction of oxidative stress; Induction of mitochondrial apoptosis pathway [16]	Gastric cancer	Water: 40 mg/l [17] Ethanol: 66.6 mg/ml [17] DMSO: high solubility [17]
			Rats: 10 mg/kg; orally; for 15 days [18]	-	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway [18]	Ischemic stroke	
Phenols	L-DOPA	*Mucuna pruriens var. Utilize* (leaves, seeds)	Rats: 50 mg/kg/d; intraperitoneally; for 7, 14 days [19]	Saline [19]	Stabilisation of ΔΨm and mitochondrial structure [19]	Cerebral ischemia/ reperfusion injury	Water: 10 mg/ml [20] Ethanol: better solubility than in water [20] DMSO: high solubility [20]
Terpenoids	Perillaldehyde (**PAE**)	*Perilla frutescens*	*C. elegans*: 50, 100 μM [21]	DMSO [21]	Preservation of mitochondrial network [21]	HD	Data is not directly available; Water: limited solubility [22] Ethanol: high solubility [22] DMSO: high solubility [22]

	Asiatic acid (**AA**)	*Centella asiatica*	Mice: 0.05% AA = 5 mg AA in 1kg diet; 0.5% AA = 50 mg AA in 1 kg diet; 1% AA = 1000 mg AA in 1 kg diet [23]	-	Increase in basal mitochondrial respiration [23]	AD	Data is not directly available; Water: poor solubility [24,25] Ethanol: better solubility than in water [24,25] DMSO: better solubility than in water [24,25]
			Mice: 100 mg/kg/d; intragastrically; for 7 days [26]	DMSO, saline [26]	Reduction of oxidative stress; Maintenance of mitochondrial morphology [26]	Myocardial ischemia/ reperfusion injury	
			Rats: 10, 50 mg/kg; intraperitoneally; for 30 min [27]	1% DMSO [27]	Improvement of mitochondrial functions [27]	Epilepsy	
	α-bisabolol (**BSB**) = levomenol	*Salvia runcinate, Myoporum crassifolium, Matricaria chamomilla, Ereman thusery-thropappus, Siparuna guianensis*	Rats: 50 mg/kg b.w./d; intraperitoneally; for 28 days [28]	Sunflower oil [28]	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway [28]	PD	Data is not directly available; Water: poor solubility [29] Ethanol: better solubility than in water [29] DMSO: better solubility than in water [29]

	Astaxanthin (**AST**)	Microalgae	Cell line: 20 μM; for 24 h [30]	DMSO [30]	Inhibition of mitochondrial apoptosis pathway; Protection of ΔΨm and ETC proteins [30]	Oxidative stress in neuronal cells	Data is not directly available; Water: poor solubility [31] Ethanol: moderate solubility [31] DMSO: high solubility [31]
		Algae	Cell line: 80 μg/l; for 24 h [32]	-	Reduction of mitophagy [32]	Oxidative stress in neuronal cells	
	Forskolin (**FSK**)	*Coleus forskohlii*	Rats: 15, 30, 45 mg/kg; orally; for 21 days [33]	2% ethanol in water [33]	Reduction of oxidative stress; Increase in the activity of mitochondrial complexes [33]	PD	Data is not directly available; Water: poor solubility [34] Ethanol: moderate solubility [34] DMSO: high solubility [34]
	Carvacrol (**CARV**)	*Lamiaceae*	Rats: 25, 50, 100 mg/kg/d; orally; for 40 days [35]	-	Reduction of oxidative stress; Protection of ΔΨm [35]	Lead toxicity	Water: 0.83 g/l [36] Ethanol: high solubility [37] DMSO: high solubility [38]
			Cell line: 100 μM; for 1, 24 h [39]	Medium [39]	Reduction of oxidative stress; Protection of ΔΨm [39]	Oxidative stress in neuronal cells	

	Carnosic acid (**CA**)	*Rosmarinus officinalis*, *Salvia officinalis*	Mice: 30, 60 mg/kg b.w.; orally; for 14 days [40]	1% DMSO [40]	Reduction of oxidative stress [40]	Chlorpyrifos (CPF) toxicity	Data is not directly available; Water: poor solubility [41] Ethanol: better solubility than in water [42] DMSO: better solubility than in water [40,43]
			Cell line: 1 μM; for 0.5, 1, 3,18, 24 h [43]	DMSO [43]	Enhancement of mitochondrial fusion; Inhibition of mitochondrial apoptosis pathway [43]	PD	
			Cell line: 1 μM; for 18 h [44]	DMSO [44]	Induction of mitochondrial biogenesis [44]	PD	
	Linalool (**LIN**)	Jasmine, basil, rosewood, lavender, thyme	Cells: 10, 25, 50 mM; for 4 h [45]	0.05% DMSO [45]	Reduction of oxidative stress; Regulation of $\Delta\Psi m$ [45]	Benzene toxicity	Water: 683.7 mg/L [46] Ethanol: moderate solubility [47] DMSO: high solubility [48]
	Genipin	(poly)phenol-enriched fraction (PEF) of *Corema album* leaf extract	Cells: 10 μM; for 24 h [49]	H_2O, acetonitrile with 0.1% formic acid [49]	Modulation of oxidative phosphorylation [49]	PD	Water: less than 1mg/ml [50] Ethanol: moderate solubility [51] DMSO: potential solubility [52]

		Gardenia jasminoides (fruit)	Mice: 10 mmol/l = 0.4 µl/eye; intraocularly; Cell line: to 1 µmol/l; for 1-14 days [53]	Penicillin-streptomycin solution (PBS) [53]	Reduction of oxidative stress [53]	Diabetic retinopathy	
Terpenoids (saponins)	*P. grandiflorum* crude saponin (**PGS**)	*Platycodon grandiflorum* (roots)	Cell line: 5, 10, 20 µg/ml; for 24 h [54]	Ethanol, distilled water [54]	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway [54]	AD	Data is not directly available; Water: poor solubility [55] Ethanol: high solubility [55] DMSO: potential solubility [55]
	P. japonicus saponins (**SPJ**)	*Panax japonicus* (roots)	Rats: 10, 30 mg/kg/d; orally; for 4 months; Cell line: 25, 50 µg/ml; for 12 + 48 h [56]	Water [56]	Improvement of mitochondrial morphology; Regulation of mitochondrial dynamics; Reduction of oxidative stress [56]	Aging	Data is not directly available; Water: high solubility [57] Ethanol: high solubility [57] DMSO: potential solubility [55]
	Marsdenia Tenacissima saponins (**SMT**)	*Marsdenia Tenacissima*	Cell line: 125, 250, 500 µg/ml; for 24 h [58]	PBS [58]	Destruction of mitochondrial morphology; Induction of mitochondrial apoptosis pathway [58]	Liver cancer	Data is not directly available; Water: high solubility [59] Ethanol: high solubility [60] DMSO: potential solubility [55]

	Deoxytrillenoside CA (**DTCA**), Epitrillenoside CA (**ETCA**)	*Trillium tschonoskii*	<u>*C. elegans*</u>: 25, 50, 100, 200 μM; for 24, 48, 72 h [61]	-	Reduction of oxidative stress; Induction of mitophagy [62] Promotion of mitochondrial biogenesis [61]	HD	Data is not directly available; Water: poor solubility [62] Ethanol: potential solubility [63] DMSO: high solubility [55]
	Ginsenoside Rb1	*Panax ginseng*	<u>Cells</u>: 0.1, 1, 10 μM; for 4 h [64]	Saline [64]	Reduction of oxidative stress; Inhibition of complex I activity [64]	Brain ischemia	Data is not directly available; Water: limited solubility [65] Ethanol: moderate solubility [66] DMSO: high solubility [66]
			<u>Cells</u>: 10 μM; for 1 h, for 15 min; <u>Mice</u>: 50 mg/kg; Intraperitoneally; for 14, 28 days [67]	-	Reduction of oxidative stress; Stabilisation of mPTP and ΔΨm; Inhibition of mitochondrial apoptosis pathway [67]	Ischemia/ reperfusion injury	
	Astragaloside IV (**AS-IV**)	*Astragalus membranaceus*, *Astragalus mongholicus*	<u>Mice</u>: 100 mg/kg; intraperitoneally; for 5 weeks [68]	Saline [68]	Reduction of oxidative stress; Promotion of mitophagy [68]	PD	Water: < 1 mg/ml [69] Ethanol: moderate solubility [70] DMSO: high solubility [71]

			Rats: 40, 80 mg/kg/d; by gavage; for 28 days [72]	Saline [72]	Improvement of mitochondrial ultrastructure; Promotion of mitophagy; Inhibition of mitochondrial apoptosis pathway [72]	Myasthenia gravis	
			Mice: 20 mg/kg/d; for 6 weeks; Cell line: 50, 100 μM; for 24 h [73]	-	Reduction of oxidative stress; Improvement of mitochondrial morphology; Enhanced mitochondrial biogenesis [73]	Diabetic nephropathy	
			Rats: 30, 90 mg/kg/d; intraperitoneally; for 16-20 months [74]	1% sodium carboxyl methyl-cellulose [74]	Increase in activities of complexes I, II, III, and IV [74]	Aging	
			Rats: 60 mg/kg/d; intragastrically; for 12 weeks [75]	Saline [75]	Improvement of mitochondria morphology; Reduction of oxidative stress; Increase in activities of complexes I, II, III and IV [75]	Diabetic peripheral neuropathy	

	Cycloastragenol (**CAG**)	*Astragalus radix*	Mice: 20 mg/kg/d; for 6 weeks [76]	5% DMSO, 2% Tween-20 in PBS [76]	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway [76]	AD	Data is not directly available; Water: poor solubility [77] Ethanol: moderate solubility [78] DMSO: high solubility [71]
			Mice: 5, 10, 20 mg/kg; intraperitoneally; for 3 days [79]	DMSO, 2% Tween-20 in PBS [79]	Inhibition of mitochondrial apoptosis pathway [79]	Ischemic stroke	
Polyphenols (extra-virgin olive oil (EVOO))	Oleuropein aglycone (**OleA**), Oleuropein (**Ole**), Hydroxytyrosol (**HT**)	Olive leaves and drupes	Cell line: 75 μM EVOO; (2/1, 1/1, 1/2) OleA/HT molar ratios; for 24 h [80]	OleA - DMSO; HT – water [80]	Reduction of oxidative stress [80]	AD	Data is not directly available; Water: poor solubility [81] Ethanol: moderate solubility [82] DMSO: likely high solubility [83]
Polyphenols (flavonoids)	Quercetin	Common fruits and vegetables (e.g., onions, broccoli, apples, capers, gigs, cranberries)	Rats: 50 mg/kg; orally; for 14 days [84]	Saline [84]	Reduction of oxidative stress [84]	PD	Water: 10 mg/l [85] Ethanol: high solubility [86] DMSO: > 100 mg/ml [87]
			Cell line: 1, 10, 20, 50, 100 μM; for 4 + 24 h; Rats: 30 mg/kg; for 14 days [88]	DMSO [88]	Reduction of oxidative stress; Improvement of mitochondrial structure; Induction of mitophagy [88]	PD	

			Cell line: 20, 40, 80 μM; for 24 h [89]	-	Reduction of oxidative stress; Regulation of mitochondrial dynamics [89]	Alcoholic liver disease	
	Naringenin (**NAR**)	Citrus fruits (grapefruit, oranges, bergamot), tomatoes, a few varieties of figs	Cell line: 12.5, 20, 25 μM; for 24 h; *Danio rerio*: 10, 20, 40 μM; for 72 h [90]	DMSO [90]	Cell line: reduction of oxidative stress; *Danio rerio*: regulation of PD-related genes [90]	PD	Water: 500 mg/l [85] Ethanol: 4.38 μg/ml [91] DMSO: higher solubility than in water [92]
			Cell line: 20, 40, 60, 80, 100 μM; for 24 h; Rats: 40 mg/kg b.w.; orally; for 21 days [93]	Saline [93]	Reduction of oxidative stress [93]	PD	
			Cell line: 100, 200, 400, 800 μM; for 24, 48, 72 h [94]	-	Promotion of mitochondrial apoptosis pathway [94]	Lung cancer	
			Mice: 100 mg/kg/d; orally; for 10 months [95]	Carbox-ymethyl-cellulose sodium solution [95]	Regulation of mitochondrial dynamics [95]	Aging	

	Fisetin, quercetin, apigenin, chrysin, naringenin	Fruits, vegetables	<u>*C. elegans*</u>: 100 μM; for 15 days [96]	DMSO [96]	Mitochondrial uncoupling [96]	Aging	
	Sterubin, fisetin	Sterubin – *Eriodictyon californicum;* Fisetin – strawberries;	<u>Cell line</u>: sterubin – 2.5 μM; fisetin – 5 μM; for 16 h (overnight) [97]	0.2% ethanol	Reduction of oxidative stress; Regulation of mitochondrial dynamics; Enhancement in mitochondrial bioenergetics [97]	Ferroptosis	
	Gossypitrin (**Gos**)	*Taliparititi elatum*	<u>Cell line, cells</u>: 0.01, 1, 10, 20, 25, 30, 40, 50, 60, 80, 100 μM; for 2, 24 h [98]	DMSO [98]	Reduction of oxidative stress; Preservation of mitochondrial morphology [98]	Iron toxicity	Data is not directly available; Water: moderate solubility [99] Ethanol: moderate solubility [99] DMSO: moderate solubility [98]

	Diosmin (**DSM**)	Pericarp of citrus fruits (*Rutaceae*)	Rats: 50, 100 mg/kg; intraperitoneally; for 21 days [100]	0.5% DMSO, normal saline [100]	Reduction of oxidative stress; Enhancement of complex I/II activity [100]	Neurodegeneration	Data is not directly available; Water: poor solubility [101] Ethanol: moderate solubility [101] DMSO: better solubility than in ethanol [102]
	Silibinin (**SIL**)	*Silybum marianumis* (fruit), *Silybum marianum* (seeds)	Mice: 70, 140, 280 mg/kg; orally; for 7 days [103]	0.5% sodium carboxymethyl cellulose [103]	Reduction of oxidative stress; Promotion of mitophagy [103]	PD	Water: 0.4 mg/100 ml [104] Ethanol: poor solubility [105] DMSO: high solubility [105]
			Mice: 70, 140, 280 mg/kg/d; intragastrically; for 24 days [106]	0.5% sodium carboxymethyl cellulose [106]	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway; Regulation of mitochondrial dynamics and morphology [106]	PD	
			Cell line: 1, 5, 10 μM; for 12 h [107]	Medium [107]	Reduction of oxidative stress; Regulation of mitochondrial dynamics and morphology [107]	Oxidative stress in neuronal cells	

			Cell line: 50, 100 μM; for 24 h [108]	DMSO [108]	Inhibition of mitochondrial rupturing [108]	AD	
			Cell line: 50, 100 μM; for 24 h [109]	0.1% DMSO [109]	Induction of mitochondrial apoptosis pathway [109]	Oral cancer	
	Luteolin (**LUT**)	Vegetables, fruits, herbs, *Ajuga decumbens thumb*	Cell line: 1, 2.5, 5 μM; for 6, 24 h [110]	DMSO [110]	Enhancement of mitochondrial complexes I and II activities; Increase in the number of contacts between mitochondria and ER [110]	-	Water: 0.4 mg/l [85] Ethanol: moderate solubility [111] DMSO: high solubility [85]
			Cells: 1, 10, 50 μM; for 24 h [112]	DMSO [112]	Decrease in apoptosis; Promotion of mitochondrial autophagy [112]	Cardiotoxicity	
			Cell line: 10, 20, 30, 40, 50, 60, 70, 80 μM; for 24, 48 h [113]	DMSO, complete medium [113]	Promotion of mitochondrial apoptosis pathway; Disruption of mitochondrial functions [113]	Gastric cancer	
			Cells: 0.5 μg/ml; for 12 + 24 h [114]	Medium [114]	Regulation of ATP production and mitochondrial dynamics [114]	Ammonia poisoning	

Polyphenols (flavonoid-rich extract)	Mandarin juice extract (MJe)	*Citrus reticulata*	Cell line: 0.1, 0.5 mg/ml; for 1, 24 h [115]	DMSO [115]	Reduction of oxidative stress; Downregulation of PD-related genes; Inhibition of mitochondrial apoptosis pathway [115]	PD	Data is not directly available; Water: high solubility [116] Ethanol: high solubility [116] DMSO: moderate solubility [115]
Polyphenols (flavonoids)	Hesperidin (**Hsd**)	Citrus fruits (e.g., oranges, grapefruit, lemons, tangerines)	Mice: 50 mg/kg/d; orally; for 28 days [117]	Saline [117]	Increase in mitochondrial enzymes activity; Inhibition of mitochondrial apoptosis pathway [117]	PD	Water: 4.93 μg/ml [118] Ethanol: high solubility [119] DMSO: high solubility [119]
	Hesperetin (**Hst**)		Cell lines: 25, 50,100, 200, 300, 400, 600, 800 μM; for 24, 48 h [120]	DMSO [120]	Enhancement of oxidative stress; Induction of mitochondrial apoptosis pathway [120]	Bladder cancer	Water: 4.5 μmol/l [121] Ethanol: 87 mmol/l [121] DMSO: 5 mg/ml [122]
			Cell line: 20, 40 μM; for 4, 24 h [123]	0.1% DMSO [123]	Improvement of mitochondrial functions; Promotion of mitophagy [123]	Nonalcoholic fatty liver disease	

	Epigallocatechin gallate (**EGCG**), gallocatechin gallate (**GCG**), gallocatechin (**GC**), epicatechin gallate (**ECG**), epicatechin (**EC**)	Green tea (young leaves) extract of Camellia (*Camellia sinensis*)	Cell line: Catechins: 3.15, 6.25, 12.5, 25, 50, 100, 200 μM; GCG: 50, 100 μM [124]	DMSO [124]	Reduction of oxidative stress [124]	Oxidative stress in neuronal cells	Data is not directly available; Water: partial solubility [125] Ethanol: high solubility [125] DMSO: high solubility [124]
	Icariin (**ICA**)	*Epimedium brevicornu*, *E. wushanense*, *E. sagittatum*, *E. pubescens*	Cell line: 5 μmol/l for 24 h + 5 μmol/l for 48 h [126]	DMSO [126]	Inhibition of mitochondria-related autophagy [126]	Neuronal injury	Water: 15 μg/ml [127] Ethanol: 188 mg/l [128] DMSO: high solubility [126,129]
			Cells: 0.1, 1, 10 μM; for 24 h [130]	Medium [130]	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway [130]	Intervertebral disc degeneration	
			Cell line: 10, 20 μM; for 24 h [129];	DMSO, medium [129]	Promotion of mitochondrial apoptosis pathway; Induction of oxidative stress [129]	Breast cancer	

Polyphenols (phenylpropanoid + flavonoid)	β-Asarone + ICA	β-Asarone - *Acorus tatarinowii*; ICA - *Epimedium*	Cell line: β-asarone: 36 μM; ICA: 6 μM; for 12 h; Mice: β-asarone: 15 mg/kg/d; ICA: 20 mg/kg/d; for 4 weeks [131]	-	Induction of mitophagy [131]; β-Asarone: Ability to cross the blood-brain barrier [132]	AD	β-Asarone : Data is not directly available; Water: poor solubility [133] Ethanol: better solubility than in water [133] DMSO: better solubility than in water [134]
Polyphenols (nonflavonoid polyphenols)	Magnolol (**MGN**)	*Magnolia officinalis*, *Magnolia grandiflora*	*C. elegans*: 2.5, 5, 10, 25, 50 μM; for different time periods [135]	DMSO, *E.coli* OP50 [135]	Reduction of oxidative stress; Preservation of mitochondrial morphology [135]	Aging	Water: 12.5 μg/ml [136] Ethanol: better solubility than in water [137] DMSO: better solubility than in water [135]
			Cells: 4 μM; for 12 h [138]	-	Reduction of oxidative stress; Elevation of mitochondrial mass and ΔΨm [138]	Osteoarthritis	
	Mito-magnolol (**Mito-MGN**)	Semisyntetic	Cell line: 0.01, 0.03, 0.1, 0.2, 0.3, 0.4, 0.5, 0.75, 1, 3, 10 μM; for 24, 48 h [139]	20% ethanol in PBS [139]	Inhibition of complex I activity; Induction of mitophagy; Decrease of ΔΨm [139];	Melanoma	Data is not directly available; Water : poor solubility [136] Ethanol: moderate solubility [140] DMSO: moderate solubility [140]

	CT1-3 (MGN-SFN hybrid)	Syntetic	Cell line: 7.5, 10 μM; for 8, 24 h [141]	-	Induction of mitochondrial apoptosis pathway [141]	Cancer	Data is not directly available; Nanocarrier systems and optimizing solvent compositions can significantly enhance solubility [142]
	Tannic acid (**TA**)	Many fruits and vegetables (e.g., grapes), black tea, nuts, sorghums	Rats: 50 mg/kg b.w.; orally; for 28 days [143]	Water [143]	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway [143]	PD	Water: 300 g/l [144]
			Rats: 50 mg/kg b.w.; intraperitoneally; 30 min before and 6 and 18 h after post-TBI [145]	0.9% sterile normal saline [145]	Reduction of oxidative stress; Inhibition of apoptosis pathway; Enhancement of mitochondrial biogenesis [145]	Traumatic brain injury	
			Cell line: 25, 50, 100, 200 μM; for 24 h [146]	Medium [146]	Induction of mitochondrial apoptosis pathway [146]	Bladder cancer	
	Resveratrol (**RSV**)	Grapes, berries, peanuts, herbs	Rats: 10, 30, 50 mg/kg; for 24 h; Cell line: 1, 10, 25, 50, 75, 100 M; for 1 h [147]	DMSO, 0.9% saline [147]	Reduction of oxidative stress; Improvement of mitochondrial morphology and functions [147]	Sepsis-induced cardiomyopathy	Water: 0.05 mg/ml [148] Ethanol: 50 mg/ml [148] DMSO: 16 mg/ml [148]

			Cells: 5, 20 μM; for 24 h [149]	DMSO [149]	Reduction of oxidative stress; Elevation of mitochondrial content; Promotion of mitophagy [149]	Myocardial ischemia/ reperfusion injury	
			Carassius gibelio: 500 mg/kg; 3 times/day; for 8 weeks [150]	-	Reduction of oxidative stress; Regulation of mitochondrial dynamics [150]	Lipopolysaccharide (LPS)-induced liver injury	
			Cell line: 20 μM; for 2 h; Rats: 200 mg/kg b.w./d; by gavage; for 50 days [151]	Water [151]	Enhancement of mitochondrial biogenesis; Improvement of mitochondrial morphology [151]	Spontaneous intracerebral hemorrhage	
			Drosophila melanogaster: 15, 30, 60 mg/kg diet; for 10 days [152]	2% ethanol [152]	Reduction of oxidative stress; Elevation of mitochondrial content [152]	PD	
			Cell line: 6, 12 μg/ml; for 48 h [153]	DMSO [153]	Reduction of oxidative stress; Activation of mitochondrial apoptosis pathway [153]	Colorectal cancer	

	Pterostilbene (**PTE**)	Blueberry, grapes	Rats: 25 mg/kg/d; orally; for 30 days [154]	-	Reduction of oxidative stress [154]	Cerebral ischemia/ reperfusion injury	Water: 21 mg/l [155] Ethanol: 50 g/l [155] DMSO: 16 g/l [155]
			Mice: 10 mg/kg; for 72h; Cell line: 5 μM; for 4 + 24 h [156]	DMSO, saline [156]	Mice: Inhibition of mitochondrial apoptosis pathway; Cell line: Regulation of mitochondrial dynamics and morphology [156]	Secondary brain injury after intracerebral hemorrhage	
			Cell line: 20, 40, 80,100 μM; for 24, 48, 72 h [157]	DMSO [157]	Induction of oxidative stress; Promotion of mitochondrial apoptosis pathway [157]	Glioma	
	Mangiferin (**MGF**)	*Gentianaceae, Mangifera indica, Anemarrhena asphodeloides, Iris unguicularis, Arrabidaea patellifera,* [illegible]	Cell line: 10, 25, 50 μM; for 4 h [158]	DMSO [158]	Inhibition of mitochondrial apoptosis pathway; Regulation of mitochondrial dynamics [158];	Fluoride toxicity	Water: 0.111 mg/ml [159] Ethanol: poor solubility [160] DMSO: high solubility [161]
			Cell line: 20 μM; for 1 + 24 h [162]	DMSO [162]	Inhibition of mitochondrial apoptosis pathway; Reduction of oxidative stress [162]	Oxidative stress	

			Mice: 10, 20, 40 mg/kg b.w.; intraperitoneally; twice/day for 7 days + once/day for 5 days [163]	2% Tween-80 in saline [163]	Regulation of mitochondrial morphology, dynamics and functions; Induction of mitophagy [163]	PD	
			Cells: 100, 500 μM/ml; for 24, 48 h [164]	PBS [164]	Improvement of mitochondrial morphology and functions; Inhibition of mitochondrial apoptosis pathway [164]	Intervertebral disc degeneration	
Polyphenols (ellagitannins)	Urolithin A (**UA**)	Pomegranate, nuts, strawberries, berries	Cell line: 1, 10 μM; for 24 h [165]	DMSO [165]	Enhancement of OXPHOS and mitochondrial biogenesis [165]	AD	Data is not directly available; Water: poor solubility [166] Ethanol: high solubility [166] DMSO: high solubility [166]
			Cell line: 2, 10, 20, 30 μM; for 2, 24 h; Tissues: 30 μM; for 2 h [167]	-	Induction of mitophagy; Restoration of ΔΨm [167]	Aging	
			Cells: 6.25, 12 μM; for 24 h [168]	DMSO [168]	Enhancement of respiration; Induction of mitophagy [168]	Osteoarthritis	

			Humans: 500, 1000 mg/d; orally; for 120 days [169]	-	Induction of mitophagy; Stimulation of ETC enzymes activity [169]	Aging	
	UA + EGCG	UA: pomegranates; EGCG: green tea	Mice: UA: 2.5 mg/kg b.w.; EGCG: 25 mg/kg b.w.; intraperitoneally; 3 times/week for 4 months [170]	UA – DMSO EGCG – H_2O [170]	Reduction of oxidative stress; Improvement of mitochondrial dynamics and functions [170]	AD	Data is not directly available
Glucosinolates	Sulforaphane (**SFN**)	Cruciferous plants (e.g., broccoli, cauliflower, cabbage, kale)	Cell line: 0.5, 1, 2, 5 μM; for 6 – 24 h [171]	DMSO [171]	Reduction of oxidative stress; Inhibition of mitochondrial apoptosis pathway; Increase in mitochondrial enzymes activity [171]	CPF and LPS cytotoxicity	Water: 2.55 mg/ml [172] Ethanol: 20 mg/ml [172] DMSO: high solubility [171]
			Rats: 5 mg/kg/dose; intraperitoneally; 2 doses; 24, 48 h [173]	DMSO, PBS [173]	Reduction of oxidative stress [173]	Epilepsy	
			Cells: 5 μM; for 72 h [174]	0.01% DMSO [174]	Enhancement of coupling efficiency [174]	Fragile X-Associated Tremor/Ataxia Syndrome	

Leaves extract	Ethanolic extract of *Mentha piperita* **(EthMP)**	*Mentha piperita*	Mice: 200 mg/kg/d; orally; for 21 days [175]	2.5% DMSO [175]	Reduction of oxidative stress [175]	PD	Data is not directly available; Water: limited solubility [176] Ethanol: high solubility [176] DMSO: high solubility [175]
Phytocannabinoids	Cannabinol **(CBN)**	*Cannabis sativa*	Cell line: 5, 10 μM; for 1 h + 16 h [177]	0.2% ethanol [177]	Reduction of oxidative stress; Promotion of mitochondrial biogenesis; Regulation of mitochondrial dynamics [177]	Ferroptosis	Data is not directly available; Water: poor solubility [178] Ethanol: high solubility [178] DMSO: high solubility [178]

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