Journal of
Medical and Life Sciences
AL-NAJAM An International, Peer-reviewed, Quarterly publishing, Open access, Multi-disciplinary Research Journal

SYSTEMATIC REVIEW OPEN ACCESS

Oxidative Stress, Mitochondrial Dysfunction, and Protein Misfolding Across Alzheimer's, Parkinson's, and Huntington's Disease: A Systematic Review on Biomolecular Therapeutic Interventions

Irshad Khan[1] | Asad Khalid[1] | Mujtaba Ehsan[1] | Muhammad Akram[2] | Ejaz Ehsan Khan[2*] | Khaleeq Ullah[3]

[1]Department of Biosciences, COMSATS University, Islamabad, Pakistan | [2]Department of Pathology, University of Lahore, Pakistan | [3]Department of Biology, University of Florence, Florence, Italy

***Correspondence:** Ehsan Ejaz Khan (ahspreparations512@gmail.com)

Citation: Khan I, Khalid A, Ehsan M, Akram M, Khan EE, Ullah K. Oxidative Stress, Mitochondrial Dysfunction, and Protein Misfolding Across Alzheimer's, Parkinson's, and Huntington's Disease: A Systematic Review on Biomolecular Therapeutic Interventions. Al Najam J Med Life Sci. 2026;1(1):6–11.

Received: 12 February, 2026 **Revised:** 01 March, 2026 **Accepted:** 06 March, 2026

ABSTRACT

Background: Oxidative stress, mitochondrial dysfunction, and protein misfolding are some of the key and interrelated mechanisms in major neurodegenerative disorders. The purpose of this systematic review was to assess biomolecular therapeutic interventions of these pathways in the models of Alzheimer' s disease (AD), Parkinson' s disease (PD), and Huntington' s disease (HD). **Methods:** This is a systematic review that follow PRISMA 2020 guidelines. The searches took place up to from 2020 to 2026 in PubMed, Scopus, Web of Science, and Google Scholar. Experimental in vitro, in vivo, and ex vivo studies on biomolecular interventions that examine oxidative stress, mitochondrial dysfunction, or protein misfolding were accepted and reviews, editorials, conference abstracts, and non-English articles had been excluded. Screening and data extraction were done by two independent reviewers. The risk of bias was determined with the help of SYRCLE Risk of Bias tool of animal studies and Cochrane Risk of Bias 2.0 tool of in vitro studies and certainty of evidence was measured with the help of GRADE framework. **Results:** Twelve studies that passed the inclusion criteria were included following screening and eligibility. In disease models, interventions continually lowered the level of reactive oxygen species, restored mitochondrial bioenergetics, triggered Nrf2-mediated antioxidant response, lessened pathological protein aggregation, and neurobehavioral function. The risk of bias was low to moderate. **Conclusion:** The approach of the mitochondrial redox imbalance and proteostasis is a promising cross-disease treatment of neurodegeneration. To enhance the study further, future studies are needed to concentrate on standard experimental designs and clinical validation.

Keywords: Oxidative Stress, Mitochondria, Protein Folding, Alzheimer Disease, Parkinson Disease, Huntington Disease, Neuroprotection.

Introduction

Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and Huntington's disease were progressive and characterized by irreversible neuronal loss, progressive cognitive decline and progressive motor dysfunction. They represented a large public health concern around the world due to the demographic shift to age cohorts and a lack of curative therapies (e.g., synaptic dysfunction, protein aggregation, and energy metabolism failure) [1]. A common pathological feature of these conditions was the disruption of mitochondrial integrity and redox imbalance by the excessive formation of reactive oxygen species (ROS) which compromises cellular

integrity [2]. Mitochondria were the energy-producing organelles of the cell and, consequently, the failure of this organelle leads to defective electron transport chain function, faulty autophagy-mediated removal (mitophagy), and altered calcium homeostasis, making neurons highly susceptible to oxidative injury and metabolic stress [3].

The main parameters that make up oxidative stress, mitochondrial dysfunction, and protein misfolding were the interrelated processes which lead to the progression of the disease in neurodegenerative disorders [4]. Oxidative stress occurred when a balance between oxidation and cell-based antioxidant mechanisms was upset by an increase in the formation of ROS, which lead to lipid, DNA, and protein oxidation and the subsequent, direct chain injury to neuronal function [5]. Mitochondrial dysfunction also enhanced the production of ROS and impairs the cellular bioenergetic processes which lead to deficits of synaptic transmission impairment and leads to neuronal death. These negative effects were consistently seen in many animal models of Alzheimer's disease, Parkinson's disease and Huntington's disease [6]. Protein misfolding, such as of amyloid 2 and tau in Alzheimer disease, of 2-synuclein in Parkinson disease, and of huntingtin in Huntington disease, imposed extreme stress on cellular quality-control processes. Such overloading did not only saturate the ubiquitin-proteasome system and autophagic pathways, but also carefully driven cytotoxic protein filaments, which simultaneously enhanced oxidative stress and exacerbated mitochondrial dysfunction [7].

Despite there had been extensive studies still there were no effective disease-modifying therapies which were clinically effective. Several antioxidative and mitochondria-targeted strategies had shown poor translational results and this was largely due to poor mitochondrial-engagement and insufficient mitochondrial integration into proteostasis pathways [8,9]. Moreover, although proteinopathy-based interventions, including anti-amyloid-based ones, had partial ameliorative effects in the course of Alzheimer disease, they did not fully resolve the comorbid oxidative and energetic impairments, upon which disease progression depends [10,11]. These limitations highlight the need of a systematic compilation of interventions which will e.g. deal with these biomolecular deficits in parallel in the central proteinopathies. This systematic review aims to critically discuss biomolecular treatments of oxidative stress, mitochondrial dysfunction and protein misfolding in Alzheimer, Parkinson, and Huntington diseases. The review also intended to evaluate mechanistic pathways, therapeutic effect, possible risk of bias, and general certainty of the evidence, and establish future areas of translation and recommend future directions of disease modifying strategies.

Methodology

This systematic review followed the guidelines of the PRISMA 2020 [12] as shown in Figure 1.

Inclusion and Exclusion Criteria: Studies with defined research methods and data from adult NAFLD or patients with related liver characteristics were included Studies including include reviews, editorials nor case reports in the evaluation were excluded.

Data Sources and Search String used: Eligible studies were original research investigations published as in vitro, in vivo or ex vivo studies reporting biomolecular therapeutic interventions that addressed oxidative stress, mitochondrial dysfunction or protein misfolding in the context of Alzheimer's disease, Parkinson or Huntington disease model. Studies were excluded if they were reviews, editorials, case reports, conference abstracts or non-English publications.

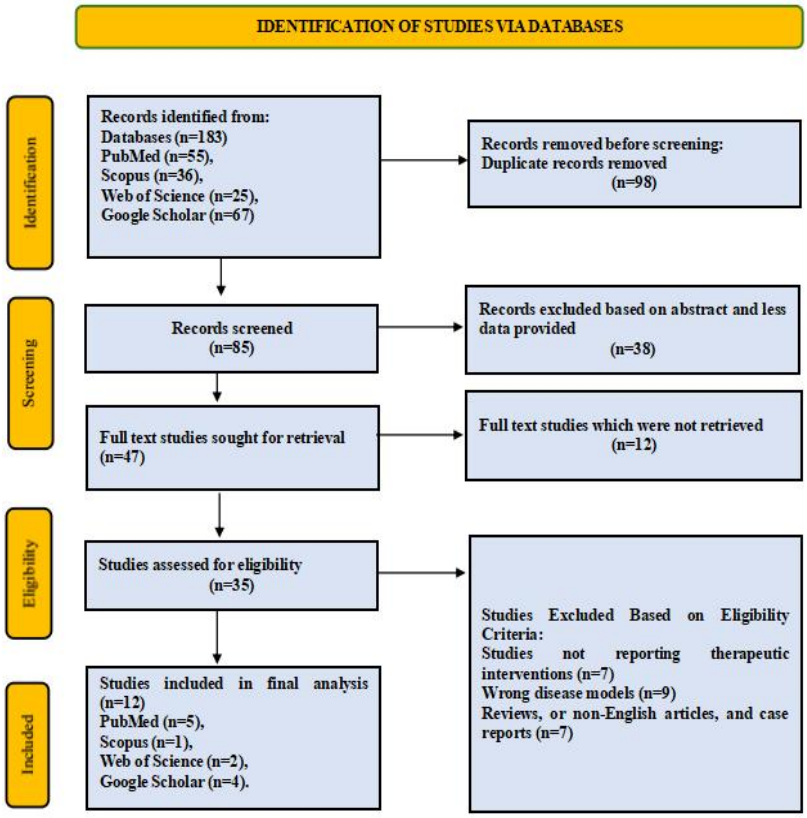

Figure 1: PRISMA Flow Diagram for Study Selection. The flowchart was designed according to the PRISMA guidelines 2020, showing study identification, screening, assessment eligibility, and final selection in the systematic review.

Study Selection and Data Extraction: Two reviewers independently done screening of title, abstract, full text and resolved any disagreement through discussion with a third reviewer. Data extraction was done using a standardised form for author, year, disease model, population characteristics, sample size, therapeutic intervention, molecular target/pathway, outcomes, and key findings. Two reviewers extracted data in separate sessions using a pre-developed data extraction form.

Primary Outcome and Quality Assessment: Risk of bias was determined by SYRCLE's Risk of Bias tool for animal studies and the Cochrane Risk of Bias 2.0 tool for in vitro studies[13,14]. The level of certainty of the evidence was determined using the GRADE framework. The primary outcome was the effectiveness of biomolecular interventions in reducing oxidative stress, improving mitochondrial function, and mitigating protein misfolding across neurodegenerative disease models. Additionally, the study evaluated changes in key molecular markers (ROS levels, mitochondrial activity, and protein aggregation) to determine the overall therapeutic impact and mechanistic efficacy of the interventions.

Results

The total number of records obtained as the result of the four database searches is 183 research articles, 55 records in PubMed, 36 records in Scopus, 25 records in Web of science, and 67 records in Google Scholar. After the removal of 98 duplicate articles, 85 different articles

were left to screen titles and abstracts. After that 38 were eliminated and at last 35 studies were eligible to assess the eligibility. Follow-up full-text evaluation led to the exclusion of 23 studies. Finally, 12 studies were included and met all inclusion were included in the systematic review. Five of these were obtained in PubMed, one in Scopus, two in Web of Science, and four in Google Scholar. Table 1 is a summary of research that explored the Biomolecular Therapeutic Interventions on Oxidative Stress, Mitochondrial Dysfunction, and Protein Misfolding Across Alzheimer's, Parkinson's, and Huntington's Disease. The table 1 summarizes the study design, disease models, population characteristics, sample size, molecular target pathway, outcomes and key points in each study.

Table 1: Characteristics of Included Studies

Author (Year)	Country	Disease model	Study design/ Sample size/ population characteristics	Molecular target pathway	Outcomes	Therapeutic Intervention
Rodriguez et al., 2024 [15]	USA	Alzheimer disease	Preclinical Experimental Study (In vivo study) n=12 mice, APP/PS1 (C57BL/6) mice in the experimental group, wild-type (C57BL/6) in control group	Mitochondrial oxidative stress and redox homeostasis, mitochondrial calcium uniporter pathway, and Aβ-mediated mitochondrial dysfunction pathway.	Improved mitochondrial redox ratio, reduced oxidative stress and Aβ burden, and modulation of mitochondrial calcium dysregulation.	SS31, Ru360, and Aβ immunodepleting.
Deng et al., 2024 [16]	China	Alzheimer's disease	Preclinical Experimental Study (In vivo) n=15 mice, experimental group (3×Tg-AD mice) and control group (C57BL/6 mice Wild-type)	KEAP1 inhibition disrupts the KEAP1–NRF2 complex	Artemisinin protected neurons from ferroptosis, reduced oxidative stress, and activated the KEAP1–NRF2–SLC7A11–GPX4 antioxidant pathway.	Artemisinin as a neuroprotective agent
Khodaei et al., 2020 [17]	Iran	Alzheimer's disease	Experimental, in vivo. n= 60 rats total Male Sprague Dawley rats.	Mitochondrial dysfunction, oxidative stress, NF-κB signaling, ROS production, sirtuin family activity.	Decreased oxidative stress markers (ROS), restored cortical ATP levels, enhanced cytochrome c oxidase activity.	Ellagic acid
Chen et al., 2025 [18]	China	Alzheimer's disease	Preclinical experimental intervention (in vitro) n=18 Double transgenic APP/PS1 mice, C57BL/6J wild-type mice	Aβ aggregation Microglial polarization Apoptosis pathway Mitochondrial function Energy metabolism	Reduced Aβ accumulation, Shift microglia to anti-inflammatory phenotype, Apoptosis decrease, increase Mitochondrial membrane potential and ATP production and neuroprotection	Photo biomodulation (PBM)
Eo et al., 2024 [19]	South Korea	Parkinson's disease	Preclinical Experimental Study (In Vivo + In Vitro) For in vitro n=64 mice C57BL/6 mouse. For in vivo neuronal cell models	Mitochondrial dysfunction, oxidative stress, neuroinflammation, and dopaminergic neuron loss.	Motor behavior, dopaminergic neuron survival, microglial activation, and pro-inflammatory cytokines improve Parkinson's.	Mitochondrial transplantation (PN-101 isolated from human mesenchymal stem cells)
Kim et al., 2022 [20]	South Korea	Parkinson's disease	Preclinical Experimental Study (In Vivo + In Vitro) For in vitro n=60 mice B6; C3-Tg, B6C3F1/slc mouse For in vivo SH-SY5Y	α-synuclein aggregation, mitochondrial dysfunction, proteostasis, and oxidative stress pathway.	Motor behavior, dopaminergic neuron loss, α-syn aggregates, microglia activation, transcriptome changes	MT101-5 Neuroprotective mitochondrial therapy
Liu M et al., 2023 [21]	India	Parkinson's disease	In vitro experimental study Human neuroblastoma SH-SY5Y cells	ROS modulation, Mitochondrial membrane potential maintenance, Apoptosis pathway,	Prdx-2 protects SH-SY5Y cells from MPP^+ toxicity by reducing oxidative stress and	Prdx-2 provides neuroprotective therapy.

				Neuron protection, and Dopaminergic neuron marker.	stabilizing mitochondria.	
El-Shamarka et al., 2023 [22]	Egypt	Parkinson's disease	In vivo experimental study n=70 mice Swiss albino mice exposed	Molecular targets: oxidative stress, dopaminergic neurons, and glial activation	Oxidative stress was reduced, glial activation decreased, and motor behavior improved.	Curcumin, Levodopa /Carbidopa, Rasagiline, Combination therapies
Jiang et al., 2025 [23]	China	Huntington's disease	Combined in vivo (mouse) and in vitro (PC12 cells) experimental study n=100 mice, C57BL/6J mice	Nrf2/HO-1 pathway, Oxidative stress (ROS), Synaptic proteins,	Oxidative and neuronal damage, NaHS protected via Nrf2 activation	NaHS (H_2S donor), ML385 (NRf2 inhibitor)
Sun X et al., 2020 [24]	China	Huntington's disease	Preclinical in vitro experimental study n=60 mice R6/2 transgenic mice, Wild-type littermate mice.	Reduction in oxidative stress, inhibits mutant huntingtin aggregation.	Reduction in mutant huntingtin aggregates and polyQ inclusions lowered ROS.	Ellagic acid
Gao et al., 2021 [25]	China	Huntington's disease	Experimental in vivo study HEK293, IMR90 Human cell lines	ROS pathways, mitochondrial bioenergetics.	Plant extracts targeted oxidative stress, protein aggregation, and protein quality control pathways	Ethanolic extracts, Acetone extracts, Quercetin
Cordeiro et al., 2021[26]	USA	Huntington's disease	In vitro experimental study 50 worms per group Transgenic *C. elegans* strains (Bristol N2, AM141, AM101, HA759, CL2070, CF1553)	ROS pathways, mitochondrial function, and neuronal metabolism.	Oxidative stress biomarkers, mitochondrial activity, and neurobehavioral measures.	Antioxidant/nutritional therapy.

ROS = Reactive oxygen species, NF-κB = Nuclear factor kappa-light-chain-enhancer of activated B cell, ATP = Adenosine triphosphate ,MMP = Mitochondrial membrane potential, ELISA = Enzyme-linked immunosorbent assay, Nrf2 = Nuclear factor erythroid 2–related factor 2, HO-1 = Heme oxygenase-1, Keap1 = Kelch-like ECH-associated protein 1, SLC7A11 = Solute carrier family 7 member 11, GPX4 = Glutathione peroxidase 4, Aβ = Amyloid-beta, Cytc = Cytochrome c, LC3II = Microtubule-associated protein 1A/1B-light chain 3-II, PKM2 = Pyruvate kinase M2, PGC1 = Peroxisome proliferator-activated receptor gamma coactivator 1-alpha, CD86 = Cluster of differentiation 86, ARG1 = Arginase 1, SH-SY5Y = Human neuroblastoma cell line, HE = Haematoxylin and eosin staining, NaHS = Sodium hydrosulfide (H_2S donor), 3BP = 3-bromopyruvate

Pharmacological and genetic treatment in transgenic and toxin-induced murine and rodent models of Alzheimer disease had the effect of reducing mitochondrial reactive oxygen species. they reestablished cellular redox balance, triggered Nrf2-dependent antioxidant signaling and ameliorated amyloid -associated mitochondrial dysplasia, leading to an increase in ATP production and reduced ferroptotic cell death. In models of Parkinson disease, therapeutic regimens reduced oxidative stress, preserved mitochondrial membrane potential, deferred the formation of alpha -synuclein aggregates, reduced neuroinflammatory responses, and produced a higher motor performance. In the studies the therapeutic agents reduced the reactive oxygen species, magnified Nrf2/HO signaling pathways, reduced mutant huntingtin aggregates, optimised mitochondrial bioenergetics, and enhanced autophagy-mediated clearance of pathogenic proteins all in the disease models of Huntington.In all the twelve studies where design-specific tools such as SYRCLE RoB for animal studies and Cochrane Risk of Bias 2.0 tool for in vitro studies were used, the overall risk of bias was low to moderate, as shown in Figure 2. Two animal model-based studies showed a high risk of bias due to lack of blinding of outcome assessment and incomplete outcome data. However, none of the studies were assessed as having critical risk of bias across all domains. Consequently, the overall GRADE certainty of the evidence was moderate.

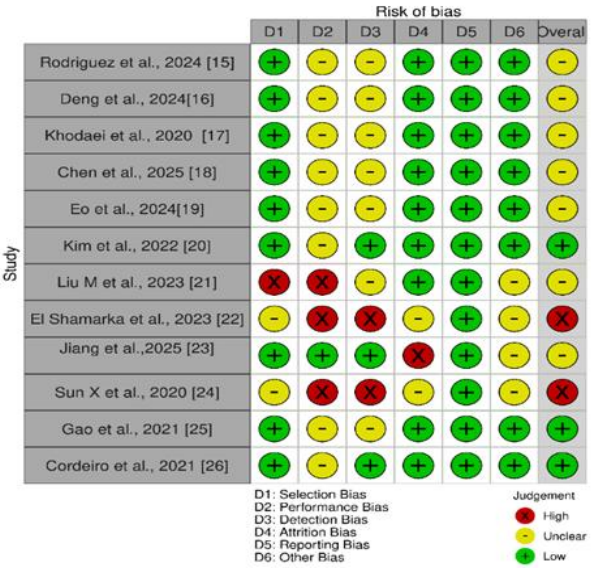

Figure 2: Traffic plots for evaluating risk of bias assessment using ROBVIS tool.

Discussion

The Neuroprotective interventions based on biomolecular therapeutic intervention approaches to oxidative stress, mitochondrial dysfunction, and protein misfolding show a consistent outcome in every experimental model of Alzheimer's disease, Parkinson's disease, and Huntington disease. In models of Alzheimer's disease, interventions led to a decrease in

the generation of reactive oxygen species by mitochondria, a reestablishment of redox homeostasis, an increase in antioxidant signaling via Nrf2, an increase in ATP production, and a decrease in the amyloid-associated mitochondrial impairment [28,39]. Convergence of mechanisms was also similar in Parkinson's disease models, where therapies maintained mitochondrial membrane potential, decreased α -synuclein aggregation, inhibited microglial activation, and enhanced motor responses especially through mitochondrial-targeted agents and mitochondrial transplantation approaches [29,34]. Activation of the Nrf2/HO -axis, decrease of mutant huntingtin aggregation, mitochondrial bioenergetic recovery, and improvement of autophagic clearance was repeatedly reported in Huntington disease models [23,27].

These findings were consistent with growing levels of translational evidence that oxidative stress and maladaptive mitochondrial quality control increase protein aggregation and neuronal susceptibility in AD, PD and HD [29,30,34]. The recent experimental and preliminary translational research highlighted the Nrf2 activation, mitophagy amplification, and ferroptosis regulation as the potential cross-disease treatment mechanisms [31]. These mechanistic pathways were supported by our results especially the key role of Nrf2-mediated antioxidant defence and mitochondrial stabilization [40]. Moreover, the behavioural improvement that was observed in transgenic models is in line with the preclinical meta-analyses indicating that mitochondrial redox system-targeting can cause eventual functional recovery [32,35]. Notably, the consistency of the results between diverse models supported the claim that multi-target biomolecular treatments can have a wider disease-modifying capability than single-pathway models [36,37]. Nonetheless, in spite of the mechanistic consistency, the variability in the dosing schedules, period of intervention and outcome measures restricts the direct comparability and the necessity of standardized preclinical frameworks [31,38].

The limitations need to be considered as various databases did not target grey literature and unpublished data in a systematic manner, which could have contributed to the bias of publication and the registration of the protocol was not conducted and this can be constraining transparency and reproducibility. Also, experimental models and result reporting were heterogeneous, and thus not able to undergo quantitative synthesis, requiring a narrative approach. Studies were mostly preclinical in vitro or animal studies and as such lack the direct clinical translatability. The sample sizes were often small and reporting on randomisation, allocation concealment, and blinding procedures was not always clear, which would pose higher chances of performance and detection bias. Cross-study comparison was further limited by variability in the models of diseases, the timing of the interventions and biomarkers. Furthermore, the long-term safety and pharmacokinetics were not adequately covered in a number of experiments, as well as dose-response relationships.

Possible improvements in future research would include standardised experimental design, transparent reporting, in accordance with ARRIVE guidelines, and multisite preclinical validation in order to enhance reproducibility [33]. It can be expected that a combination of multi-omics profiling and mitochondrial functional assessments will help understand the mechanistic pathways and finding predictive biomarkers. Translational research that would provide the gap between preclinical and early-phase clinical research is needed, especially on Nrf2 activators, mitophagy modulators and ferroptosis-targeting agents. Lastly, a more disease-modifying potential in neurodegenerative diseases could be provided by simultaneous mitochondrial dynamics, proteostasis, and oxidative stress combinational therapeutic approaches.

Conclusion

This systematic review highlights the overlapping role of the oxidative stress, mitochondrial dysfunction, and protein misfolding in Alzheimer disease, Parkinson disease, and Huntington disease as well as critically appraises biomolecular therapeutic solutions to these interrelated conditions. In preclinical in vitro and in vivo models, the interventions always decreased reactive oxygen species, recovered mitochondrial bioenergetics, triggered Nrf2-mediated antioxidant systems, enhanced the proteosome and exhibited a neuroprotective and behavioural advantage. On the whole, it is possible to assert that mitochondrial-redox modulation is a promising cross-disease treatment approach, but it needs a thorough translational research and uniform preclinical models to enhance reproducibility and bring these interventions to the clinical stage.

Acknowledgement: None
Conflict of Interest: None
Grant Support & Funding Source: None
Authors' Contribution: All authors contributed equally as per ICMJE.

References

1. Alqahtani T, Deore SL, Kide AA, Shende BA, Sharma R, Chakole RD, et al. Mitochondrial dysfunction and oxidative stress in Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis—an updated review. Mitochondrion.2023;71(6):83–92. https://doi.org/10.1016/j.mito.2023.05.007
2. Yang HM. Mitochondrial dysfunction in neurodegenerative diseases. Cells. 2025;14(4):276. https://doi.org/10.3390/cells14040276
3. Houldsworth A. Role of oxidative stress in neurodegenerative disorders: a review of reactive oxygen species and prevention by antioxidants. Brain Commun. 2024;6(1): fcad356. https://doi.org/10.1093/braincomms/fcad356
4. Zhang Y, Li XW, Zhang Y, Li X. Advances in research on mitochondrial dysfunction in neurodegenerative diseases. J Neurol. 2025;272(5):364. https://doi.org/10.1007/s00415-025-13101-4
5. Guan Y, Li L, Yang R, Lu Y, Tang J. Targeting mitochondria with natural polyphenols for treating Neurodegenerative Diseases: a comprehensive scoping review from oxidative stress perspective. J Transl Med. 2025;23(1):572. https://doi.org/10.1186/s12967-025-06605-0
6. Wong JH, Lai KO, Barron AM. Unlocking therapies for neurodegeneration: targeting mitochondrial dysfunction and oxidative stress in Alzheimer's disease. Curr Opin Physiol. 2026; 47:100874. https://doi.org/10.1016/j.cophys.2025.100874
7. Toader C, Tataru CP, Munteanu O, Serban M, Covache-Busuioc RA, Ciurea AV, et al. Decoding neurodegeneration: a review of molecular mechanisms and therapeutic advances in Alzheimer's, Parkinson's, and ALS. Int J Mol Sci. 2024;25(23):12613. https://doi.org/10.3390/ijms252312613
8. Moselhy OA, Abdel-Aziz N, El-Bahkery A, Moselhy SS, Ibrahim EA. Curcumin nanoparticles alleviate brain mitochondrial dysfunction and cellular senescence in γ-irradiated rats. Sci Rep. 2025;15(1):3857. https://doi.org/10.1038/s41598-025-87635-y

9. Islam MT. Oxidative stress and mitochondrial dysfunction-linked neurodegenerative disorders. Neurol Res. 2017;39(1):73–82. https://doi.org/10.1080/01616412.2016.1251711
10. Meng K, Jia H, Hou X, Zhu Z, Lu Y, Feng Y, et al. Mitochondrial dysfunction in neurodegenerative diseases: mechanisms and corresponding therapeutic strategies. Biomedicines. 2025;13(2):327. https://doi.org/10.3390/biomedicines13020327
11. Wadan AH, Shaaban AH, El-Sadek MZ, Mostafa SA, Moshref AS, El-Hussein A, et al. Mitochondrial-based therapies for neurodegenerative diseases: a review of the current literature. Naunyn-schmiedeberg's Arch Pharmacol. 2025;398(1):11357–11386. https://doi.org/10.1007/s00210-025-04014-0
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372(8284): n71. https://doi.org/10.1136/bmj.n71
13. Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. BMC Med Res Methodol. 2014; 14(1):43. https://doi.org/10.1186/1471-2288-14-43
14. Nejadghaderi SA, Balibegloo M, Rezaei N. The Cochrane risk of bias assessment tool 2 (RoB 2) versus the original RoB: a perspective on the pros and cons. Health Sci Rep. 2024;7(6):e2165. https://doi.org/10.1002/hsr2.2165
15. Calvo-Rodriguez M, Kharitonova EK, Snyder AC, Hou SS, Sanchez-Mico MV, Das S, et al. Real-time imaging of mitochondrial redox reveals increased mitochondrial oxidative stress associated with amyloid β aggregates in vivo in a mouse model of Alzheimer's disease. Mol Neurodegener. 2024;19(1):6. https://doi.org/10.1186/s13024-024-00702-2
16. Deng PX, Silva M, Yang N, Wang Q, Meng X, Ye KQ, et al. Artemisinin inhibits neuronal ferroptosis in Alzheimer's disease models by targeting KEAP1. Acta Pharmacol Sin. 2025;46(2):326–337. https://doi.org/10.1038/s41401-024-01378-6
17. Khodaei F, Namavar MR, Soutodeh N, Hadipour A, Asadi F, Khoshnoud MJ, et al. Mitochondrial protective effects of ellagic acid in a rat model of sporadic Alzheimer's disease induced by STZ. Sci Rep. 2026;16(1):3498. https://doi.org/10.1038/s41598-025-31867-5
18. Chen H, Li N, Liu N, Zhu H, Ma C, Ye Y, et al. Photobiomodulation modulates mitochondrial energy metabolism and ameliorates neurological damage in an APP/PS1 mouse model of Alzheimer's disease. Alz Res Ther. 2025;17(1):72. https://doi.org/10.1186/s13195-025-01714-w
19. Eo H, Yu SH, Choi Y, Kim Y, Kang YC, Lee H, et al. Mitochondrial transplantation exhibits neuroprotective effects and improves behavioral deficits in an animal model of Parkinson's disease. Neurotherapeutics. 2024;21(4): e00355. https://doi.org/10.1016/j.neurot.2024e00355
20. Kim S, Choi JG, Kim SW, Park SC, Kang Y R, Park Ds, et al. Inhibition of α synuclein aggregation by MT101 5 is neuroprotective in mouse models of Parkinson's disease. Biomed Pharmacother. 2022; 154:113637. https://doi.org/10.1016/j.biopha.2022.113637
21. Liu M, Zuo S, Guo X, Peng J, Xing Y, et al. The study of overexpression of Peroxiredoxin-2 reduces MPP+-induced toxicity in the cell model of Parkinson's disease. Neurochem Res. 2023;48(7):2129–2137. https://doi.org/10.1007/s11064-023-03880-5
22. El Shamarka ME, Abdel Salam OM, Shafee N, Zeidan HM. Curcumin modulation of L dopa and rasagiline induced neuroprotection in rotenone model of Parkinson's disease. Iran J Basic Med Sci. 2023;26(2):139–147. https://doi.org/10.22038/IJBMS.2022.61687.13650
23. Jiang Z, Liu D, Li T, Gai C, Xin D, Zhao Y, et al. Hydrogen sulfide reduces oxidative stress in Huntington's disease via Nrf2. Neural Regen Res. 2025;20(6):1776–1788. https://doi.org/10.4103/NRR.NRR D 23 01051
24. Sun X, Zhu J, Sun X, Ji M, Yu XL, Liu R. Ellagic acid rescues motor and cognitive deficits in R6/2 mouse model of Huntington's disease by lowering mutant huntingtin protein. Food Funct. 2020;11(2):1334-1348. https://doi.org/10.1039/C9FO02131K
25. Pérez Arancibia R, Ordoñez JL, Rivas A, Pihán P, Sagredo A, Ahumada U, et al. A phenolic rich extract from Ugni molinae berries reduces abnormal protein aggregation in a cellular model of Huntington's disease. PLoS One. 2021;16(7): e0254834. https://doi.org/10.1371/journal.pone.0254834
26. Cordeiro LM, Soares M, Silva A, Machado M, Obetine Baptista F, Silveira T, et al. Neuroprotective effects of rutin on ASH neurons in Caenorhabditis elegans model of Huntington's disease. Nutr Neurosci. 2022; 25(11):1–14. https://doi.org/10.1080/1028415X.2021.1956254
27. Sweeney P, Park H, Baumann M, Dunlop J, Frydman J, Kopito R, et al. Protein misfolding in neurodegenerative diseases: implications and strategies. Transl Neurodegener. 2017; 6(1):6. https://doi.org/10.1186/s40035-017-0077-5
28. Wang W, Zhao F, Ma X, Perry G, Zhu X. Mitochondria dysfunction in Alzheimer's disease. Neurosci Bull. 2020;36:220–232. https://doi.org/10.1007/s12264-019-00465-3
29. Angelova PR, Abramov AY. Role of mitochondrial ROS in the brain: from physiology to neurodegeneration. FEBS Lett. 2020;594:2370–2384. https://doi.org/10.1002/1873-3468.13714
30. Wen P, Sun Z, Gou F, Wang J, Fan Q, Zhao D, et al. Oxidative stress and mitochondrial impairment: key drivers in neurodegenerative disorders. Ageing Res Rev. 2025;104:102667. https://doi.org/10.1016/j.arr.2025.102667
31. Yusuf JA, Akanbi ST, Ijibadejo MS, Adebayo OS, Okoro CA, Bello OA, et al. A review of mitochondrial dysfunction, pathophysiology and therapeutic prospects in neurodegenerative diseases. Discov Neurosci. 2025;20(1):25. https://doi.org/10.1186/s13064-025-00223-8
32. Hou Y, Dan X, Babbar M, et al. Ageing as a risk factor for neurodegenerative disease. Nat Rev Neurol. 2023;19(1):608–624. https://doi.org/10.1038/s41582-023-00802-0
33. Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. Br J Pharmacol. 2020;177(16):3617–3624. https://doi.org/10.1111/bph.15193
34. Patel N, Satapathy T, Sahu P, Satapathy A, Bhardwaj SK, Satapathy A, et al. Molecular mechanisms of mitochondrial dysfunction in neurodegenerative diseases: pharmacological targets and therapeutic advances. J Drug Deliv Ther. 2025;15(10):272–294. https://doi.org/10.22270/jddt.v15i10.7424
35. Kallur S, Suryawanshi A, Utarade A, Kandalkar P, Morde R, Bhagwat A, et al. Oxidative stress and neurodegenerative diseases: exploring natural antioxidants for therapeutic potential. IP Int J Compr Adv Pharmacol. 2023;8(3):149–158. https://doi.org/10.18231/j.ijcaap.2023.026
36. Krsek A, Baticic L. Nanotechnology-driven therapeutic innovations in neurodegenerative disorders: a focus on Alzheimer's and Parkinson's disease. Future Pharmacol. 2024;4(2):352–379. https://doi.org/10.3390/futurepharmacol4020020
37. Chopade P, Chopade N, Zhao Z, Mitragotri S, Liao R, Chandran Suja V. Alzheimer's and Parkinson's disease therapies in the clinic. Bioeng Transl Med. 2022;8(1):e10367. https://doi.org/10.1002/btm2.10367
38. Gadhave DG, Sugandhi VV, Jha SK, Nangare SN, Gupta G, Singh SK, et al. Neurodegenerative disorders: mechanisms of degeneration and therapeutic approaches with their clinical relevance. Ageing Res Rev. 2024;99(1):102357. https://doi.org/10.1016/j.arr.2024.102357
39. Arimon M, Grimminger V, Sanz F, Lashuel HA. Hsp104 targets multiple intermediates on the amyloid pathway and suppresses the seeding capacity of fibrils and protofibrils of Aβ. J Mol Biol. 2008;384(5):1157–1173. https://doi.org/10.1016/j.jmb.2008.09.019
40. Oueslati A, Paleologou KE, Schneider BL, Aebischer P, Lashuel HA. Mimicking phosphorylation at serine 87 inhibits the aggregation of human alpha-synuclein and protects against its toxicity in a rat model of Parkinson's disease. J Neurosci. 2012;32(5):1536–1544. https://doi.org/10.1523/JNEUROSCI.3781-11.2012