

**FROM OXIDATIVE STRESS TO NEUROINFLAMMATION:
PHARMACOLOGICAL TARGETING OF THE NRF2–NF-KB–NLRP3
AXIS BY PLANT-DERIVED BIOACTIVE COMPOUNDS**

Aishwarya T. V.*

Department of Pharmacology.

Article Received on 05 Sept. 2026,

Article Revised on 25 Sept. 2026,

Article Published on 03 Oct. 2026,

<https://doi.org/10.5281/zenodo.23118735>

***Corresponding Author**

Aishwarya T. V.

Department of Pharmacology.



How to cite this Article: Aishwarya T.V.*. (2026). From Oxidative Stress To Neuroinflammation: Pharmacological Targeting of The Nrf2-Nf-Kb-Nlrp3 Axis By Plant-Derived Bioactive Compounds. World Journal of Pharmaceutical Research, 15(19), 1130–1142. This work is licensed under Creative Commons Attribution 4.0 International license.

ABSTRACT

Neurodegenerative disorders present with progressive neuronal dysfunction and loss and are increasingly recognized as conditions in which oxidative stress, mitochondrial impairment and chronic neuroinflammation interact. Reactive oxygen species can activate inflammatory signaling, while persistent activation of inflammatory pathways can further increase oxidative injury, forming a self-amplifying pathological cycle. Nuclear factor erythroid 2-related factor 2 (Nrf2), nuclear factor kappa B (NF- κB), and the nod- like receptor family pyrin domain containing 3 (NLRP3) inflammasome have emerged as interconnected pharmacological targets. Plant-derived bioactive compounds are of particular interest as many possess antioxidant and anti-inflammatory activities and may

modulate several signaling pathways simultaneously. This review examines the mechanistic relationship between oxidative stress and neuroinflammation, focusing on the Nrf2–NF-κB–NLRP3 axis, and summarizes evidence for representative phytochemicals including curcumin, quercetin, resveratrol, berberine, epigallocatechin-3-gallate, baicalein/baicalin, ginsenosides and apigenin. Evidence from cellular and experimental animal models is considered alongside pharmacokinetic limitations, bioavailability, safety, standardization and translational challenges. Particular attention is given to the potential that coordinated modulation of antioxidant and inflammatory pathways may provide a pharmacological strategy distinct from single-target approaches. Future research should prioritize well-

characterized extracts or compounds, target engagement biomarkers, rigorous pharmacokinetic studies and adequately designed clinical investigations.

KEYWORDS: *Nrf2; NF- κ B; NLRP3 inflammasome; oxidative stress; neuroinflammation; phytochemicals; neuroprotection; medicinal plants; neurodegenerative disorders; pharmacology.*

1. INTRODUCTION

Neurodegenerative disorders represent a major and growing challenge for modern pharmacology as progressive neuronal damage is frequently accompanied by complex interactions amongst oxidative stress, mitochondrial dysfunction, protein dysregulation, impaired cellular homeostasis and chronic inflammation.

Although individual diseases such as Alzheimer's disease, Parkinson's disease and other neurodegenerative conditions have distinct pathological features, several convergent molecular mechanisms are shared. Oxidative injury and persistent activation of innate immune responses are increasingly considered important contributors to neuronal dysfunction rather than merely secondary consequences of neuronal death.^[1,2]

The central nervous system is particularly vulnerable to oxidative injury due to its high oxygen consumption, abundant polyunsaturated fatty acids, relatively limited antioxidant reserves and high metabolic demand. Excessive production of reactive oxygen species (ROS) and reactive nitrogen species can damage membrane lipids, proteins, DNA and mitochondria. Mitochondrial dysfunction may then increase ROS generation, forming a feed-forward cycle of cellular injury. Importantly, oxidative stress can also function as a signaling stimulus capable of activating inflammatory pathways.^[1,2]

Neuroinflammation is another major component of this pathological network. Microglia, the resident innate immune cells of the central nervous system, respond to cellular damage and molecular danger signals. Short-term microglial activation can contribute to tissue repair and homeostasis, however sustained activation may promote the release of inflammatory mediators including cytokines, chemokines and reactive species. Astrocytes and other neural cells can also participate in inflammatory signaling. Thus, oxidative stress and neuroinflammation should not be considered completely independent processes.

Three signaling systems are particularly relevant to this interaction. Nrf2 is a major transcriptional regulator of cellular antioxidant and cytoprotective responses. Under basal conditions, Nrf2 is predominantly regulated through Keap1-mediated ubiquitination and degradation. Oxidative or electrophilic stress can disrupt this regulation, allowing Nrf2 to accumulate and activate antioxidant response element-dependent genes. In contrast, NF- κ B is a central transcriptional regulator of inflammatory responses and can stimulate expression of numerous cytokines, chemokines and inflammatory enzymes. The NLRP3 inflammasome is an intracellular innate immune complex that responds to diverse cellular stress signals and promotes activation of inflammatory caspases and maturation of interleukin-1 β and interleukin-18.^[1,3-5]

An important pharmacological question is whether these pathways can be modulated as an interconnected network. Nrf2 activation may strengthen endogenous antioxidant defenses and suppress inflammatory signaling whereas excessive NF- κ B and NLRP3 activation can perpetuate oxidative and inflammatory injury. This mechanistic convergence has generated interest in multi-target pharmacology, particularly using naturally occurring bioactive compounds. Many phytochemicals have demonstrated antioxidant, anti-inflammatory and cytoprotective effects in experimental systems, although the magnitude and clinical relevance of these effects vary considerably according to compound, formulation, dose, model and bioavailability.

Plant-derived compounds thus provide an attractive but scientifically challenging area for pharmacological investigation. Their potential advantages include chemical diversity and the ability of some compounds to influence multiple signaling pathways. However, translation from experimental neuroprotection to human therapeutic benefit is limited by poor aqueous solubility, rapid metabolism, variable systemic exposure, inconsistent botanical standardization and insufficient clinical evidence. A mechanistically focused assessment of the Nrf2–NF- κ B–NLRP3 network can help distinguish promising pharmacological hypotheses from evidence remaining preliminary.^[6-8]

The present review examines the relationship between oxidative stress and neuroinflammation focusing on the Nrf2–NF- κ B–NLRP3 axis as a pharmacological framework for understanding plant-derived neuroprotective compounds. The review also considers experimental evidence, pharmacokinetic and formulation barriers, safety considerations and key requirements for translation into clinically meaningful therapies.

2. METHODOLOGY

Findings were interpreted in relation to model type, dose, exposure, extract or compound standardization, target engagement and pharmacokinetic plausibility. Evidence from cell-free assays, cultured cells, animal models and human studies was not treated as interchangeable. The review thus emphasizes the strength and limitations of mechanistic evidence and identifies areas where additional controlled studies are required.

Studies were organized according to oxidative stress and mitochondrial dysfunction; microglial and neuroinflammatory signaling; Nrf2–Keap1–ARE regulation; NF- κ B signaling; NLRP3 inflammasome activation; Nrf2/NF- κ B/NLRP3 crosstalk; phytochemical-specific mechanisms; experimental evidence; pharmacokinetic and bioavailability limitations; safety and herb–drug interactions; and translational considerations. For each major phytochemical, emphasis was placed on the reported experimental model, principal molecular pathway, direction of pathway modulation and the distinction between direct target effects and downstream associations.

Studies were considered relevant if they addressed at least one component of the Nrf2–NF- κ B–NLRP3 network or investigated a plant-derived compound in cellular, animal or human research related to oxidative stress, neuroinflammation or neurodegenerative pathology. The information on molecular target engagement, antioxidant defense, inflammatory signaling, inflammasome activation, mitochondrial dysfunction, pharmacokinetics safety or translational limitations. Human intervention evidence was considered particularly important when discussing clinical relevance whereas preclinical studies were used to explain mechanisms and pharmacodynamic effects.

A narrative literature review design was adopted to examine the pharmacological relationship between oxidative stress, neuroinflammation and the Nrf2–NF- κ B–NLRP3 signaling axis, with particular emphasis on plant-derived bioactive compounds and their potential neuroprotective actions. The review was designed to integrate mechanistic, pharmacological, cellular, animal and translational evidence rather than to perform a quantitative meta-analysis.^[20,21]

3. Evidence Synthesis

NF- κ B-mediated inflammatory signaling and NLRP3 inflammasome activation are interconnected processes in neuroinflammatory injury. Nrf2 represents a major endogenous

antioxidant and cytoprotective mode whereas NF- κ B and NLRP3 participate in inflammatory amplification.^[22-25]

The reviewed plant-derived bioactive compounds show overlapping but non-identical mechanisms. Curcumin, quercetin, resveratrol, berberine, epigallocatechin-3-gallate (EGCG), baicalein/baicalin, ginsenosides and apigenin have been investigated for effects on oxidative stress and inflammatory signaling. Across the evidence base summarized here, reported effects include enhancement of antioxidant responses, attenuation of NF- κ B-associated inflammatory signaling and modulation of NLRP3-related inflammasome activity. These effects should be interpreted as compound model and dose-dependent rather than proof of a uniform mechanism for all phytochemicals.^[26-30]

Taken together, the evidence supports a network-based interpretation- oxidative stress can promote inflammatory signaling and inflammasome activation while inflammatory processes can further increase oxidative and mitochondrial stress. Pharmacological modulation of multiple modes may thus provide a mechanistic rationale for neuroprotective investigation. However, differences in experimental models, bioavailability, blood– brain barrier exposure, formulation, dosing and outcome measures remain important translational limitations.^[23,26,31,32]

Conceptually, the findings can be organized into three linked levels: (i) upstream redox and mitochondrial stress, (ii) signaling nodes involving Nrf2, NF- κ B and NLRP3, and (iii) downstream inflammatory mediators and neuronal injury. The framework illustrated in Figure 1 is intended as a conceptual synthesis of the mechanisms discussed in this narrative review and not as a quantitative pathway model.^[22-25]

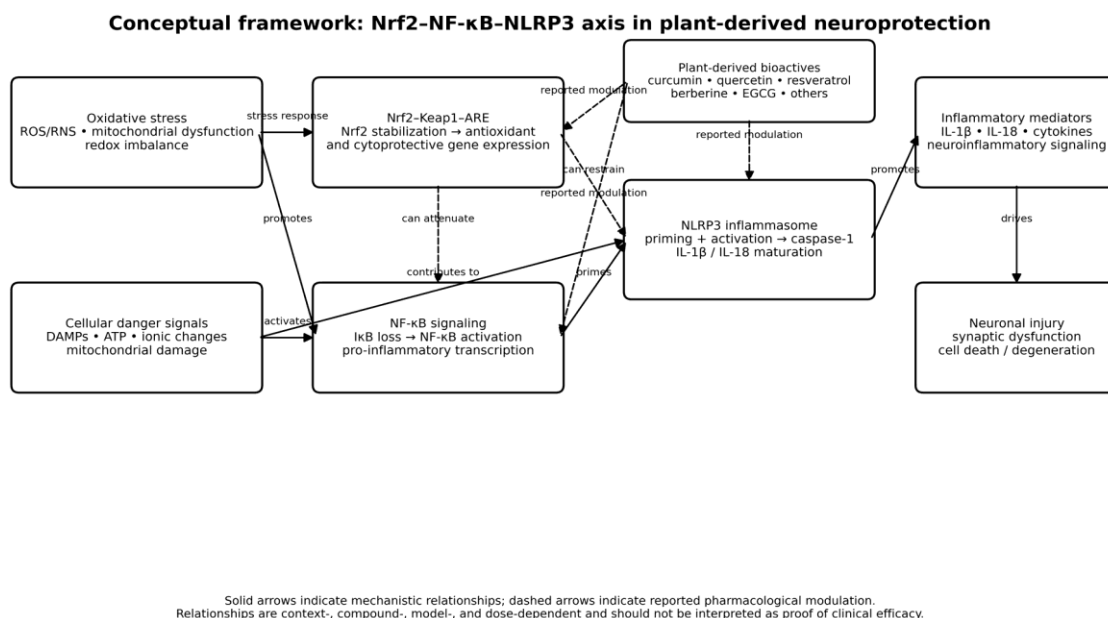


Figure 1: Conceptual framework linking oxidative stress, Nrf2, NF-κB and NLRP3 signaling in plant-derived bioactive compound- mediated neuroprotective research.

Table 1: Evidence synthesis of selected plant-derived bioactive compounds. [26-32]

Bioactive compound	Primary signaling focus	Reported neuroinflammatory/antioxidant effect	Evidence context	Translational consideration
Curcumin	Nrf2, NF-κB, NLRP3	Reported antioxidant and anti-inflammatory activity; modulation of redox-sensitive and inflammatory pathways.	Preclinical experimental models summarized in the review.	Low systemic bioavailability and formulation/BBB exposure require consideration. ^[13,14,16]
Quercetin	Nrf2, NF-κB; inflammasome-related signaling	Reported reduction of oxidative stress and inflammatory signaling in experimental systems.	Preclinical studies across neuroinflammatory models.	Pharmacokinetics, metabolism and bioavailability are important limitations. ^[15]
Resveratrol	Nrf2, NF-κB; mitochondrial/redox pathways	Reported antioxidant, anti-inflammatory and cytoprotective effects; NLRP3-related effects have also been described.	Preclinical neuroprotection literature summarized in the review.	Rapid metabolism and limited bioavailability may affect translation. ^[6]
Berberine	Nrf2, NF-κB, NLRP3-related pathways	Reported modulation of oxidative stress and inflammatory signaling, including Nrf2/HO-1-related responses in astrocytes.	Preclinical models; mechanisms vary with disease context and dose.	BBB exposure and pharmacokinetic variability need further study. ^[6]

Bioactive compound	Primary signaling focus	Reported neuroinflammatory/antioxidant effect	Evidence context	Translational consideration
EGCG	Nrf2, NF- κ B, NLRP3-related signaling	Reported antioxidant and anti-inflammatory effects with modulation of cellular stress responses.	Preclinical evidence summarized in the manuscript.	Stability, exposure and dose-response relationships require attention. ^[14]
Baicalein/baicalin	Nrf2, NF- κ B and inflammatory pathways	Reported antioxidant and anti-inflammatory actions in experimental models.	Preclinical evidence.	Bioavailability and standardization of preparations remain relevant. ^[6,14]
Ginsenosides	Nrf2, NF- κ B and stress-response pathways	Reported neuroprotective and anti-inflammatory effects across experimental models.	Preclinical evidence; effects depend on ginsenoside subtype.	Subtype-specific pharmacology and bioavailability require clarification. ^[6]
Apigenin	Nrf2, NF- κ B and inflammatory signaling	Reported attenuation of oxidative and inflammatory responses.	Preclinical evidence summarized in the manuscript.	BBB penetration, metabolism and standardized dosing need further investigation. ^[6]

Table 2: Integrated pathway-level interpretation.^[22-25]

Pathway/node	Role in the conceptual framework	Reported neuroinflammatory/antioxidant effect	Key limitation
Nrf2–ARE	Endogenous antioxidant and cytoprotective response to oxidative stress.	Reported activation or enhancement by several reviewed compounds.	Evidence is strongly dependent on model, dose and exposure. ^[1,2,3]
NF- κ B	Central transcriptional regulator of inflammatory mediators.	Several reviewed compounds are reported to attenuate NF- κ B-associated signaling.	Pathway effects may be indirect and context-dependent. ^[7,13]
NLRP3 inflammasome	Inflammasome platform linked to caspase-1 activation and IL-1 β /IL-18 maturation.	Selected compounds are reported to modulate NLRP3-related activation.	Direct versus upstream effects are not equivalent and require mechanistic validation. ^[4,5,9,10]
Nrf2–NF- κ B crosstalk	Links antioxidant and inflammatory responses.	Multi-target compounds may influence both redox and inflammatory signaling.	Network interactions are complex and not necessarily additive. ^[1,7]
Oxidative stress–inflammasome link	Mitochondrial/redox disturbances can contribute to inflammatory amplification.	Antioxidant actions may indirectly influence inflammasome signaling.	Causal relationships differ among experimental disease models. ^[5,9,10,11]

3.1 Oxidative Stress in Neurodegenerative Disorders

Oxidative stress occurs when the generation of reactive species exceeds the capacity of endogenous antioxidant systems to maintain redox homeostasis. Physiological ROS participates in cellular signaling, host defense and adaptation; pathological accumulation, however can cause oxidative modification of proteins, membrane lipids and nucleic acids. Neurons are especially susceptible due to their metabolic requirements, lipid-rich membranes and dependence on tightly regulated mitochondrial function.^[1,2,7]

3.2 Neuroinflammation and Microglial Activation

Microglia continuously survey the neural environment and respond to injury, protein aggregates, damaged cellular components and other danger-associated signals. Their activation is highly context-dependent. Beneficial responses can include phagocytosis and repair whereas prolonged inflammatory signaling can increase production of tumor necrosis factor- α , interleukin-1 β , interleukin-6, nitric oxide and other mediators. These mediators can influence neuronal survival and amplify oxidative stress.^[5,9-11]

3.3 Nrf2–Keap1–ARE Signaling

Nrf2 is a master regulator of the cellular response to oxidative and electrophilic stress. In unstressed cells, Keap1 facilitates Nrf2 proteasomal degradation. Oxidative or electrophilic modification of regulatory cysteine residues in Keap1 can alter this process, allowing Nrf2 to accumulate and translocate to the nucleus. Nrf2 then interacts with antioxidant response elements and promotes transcription of genes involved in glutathione synthesis, detoxification, redox regulation and cellular protection.^[1-3,12]

3.4 NF- κ B Signaling

NF- κ B is a central transcriptional regulator of inflammation. In its inactive state, NF- κ B family members are retained in the cytoplasm through association with inhibitory I κ B proteins. Activation of upstream signaling pathways promotes I κ B phosphorylation and degradation, permitting NF- κ B nuclear translocation and transcriptional regulation of inflammatory genes. In neurodegenerative conditions, persistent NF- κ B activity may contribute to production of cytokines and other mediators that sustain neuroinflammatory responses.^[3,7,13]

3.5 NLRP3 Inflammasome

The NLRP3 inflammasome is an intracellular multiprotein complex involved in innate immune signaling. Its activation generally requires an initial priming step followed by activation in response to cellular stress signals.

Activated NLRP3 facilitates recruitment and activation of inflammatory caspase-1, promoting maturation of interleukin-1 β and interleukin-18 and, in appropriate settings, inflammatory cell death. Oxidative stress, mitochondrial dysfunction and altered ionic homeostasis have all been investigated as contributors to NLRP3 activation.^[4,5,9,10]

3.6 Nrf2–NF- κ B–NLRP3 Molecular Crosstalk

The Nrf2, NF- κ B and NLRP3 systems form an interconnected signaling network rather than three independent pathways. Oxidative stress can influence inflammatory signaling while inflammatory activation can increase reactive species and mitochondrial stress. Nrf2-dependent cytoprotective responses may counteract this process while persistent NF- κ B activity and inflammasome activation can reinforce the inflammatory state.^[3,4,7]

3.7 Plant-Derived Bioactive Compounds as Multi-Target Modulators

Several classes of plant-derived compounds have been investigated for their ability to influence oxidative and inflammatory pathways. Curcumin, quercetin, resveratrol, berberine, epigallocatechin-3-gallate, baicalein/baicalin, ginsenosides and apigenin are among the frequently studied candidates. Their reported effects include modulation of Nrf2-related antioxidant responses, NF- κ B signaling, inflammatory cytokines, mitochondrial function and, in some models, NLRP3 inflammasome activation.^[6,7,13-16,17-19]

3.8 Evidence from Cellular and Animal Models

In vitro models provide useful mechanistic information regarding neuronal survival, oxidative stress, microglial activation and inflammatory signaling. However, simplified cellular systems may not reproduce the cellular interactions, metabolism and pharmacokinetics present in vivo. Animal models can provide information on behavioral outcomes, tissue biomarkers and pharmacodynamic responses but disease models vary in their relevance to human pathology.^[1,2,5]

3.9 Pharmacokinetic and Bioavailability Challenges

One of the major barriers to translation of phytochemical research is the discrepancy between concentrations used in experimental systems and achievable exposure in humans. Poor aqueous solubility, intestinal metabolism, rapid conjugation, hepatic metabolism and limited penetration across the blood–brain barrier can reduce effective tissue concentrations. Standardization of extracts is also essential as chemical composition can vary with plant species, cultivar, geographical origin, extraction procedure and storage.^[8,15,16]

3.10 Safety, Toxicity and Herb–Drug

Interactions Natural origin does not guarantee pharmacological safety. High-dose exposure, prolonged administration and concentrated extracts can produce effects that differ from traditional dietary exposure. Potential cytochrome P450 modulation, transporter interactions and additive pharmacodynamic effects are particularly relevant when considering phytochemicals for patients receiving conventional medicines.^[8,16]

3.11 Future Perspectives

Future studies need to transcend the antioxidant paradigm towards mechanism-based pharmacology. Key areas of priority include simultaneous measurement of Nrf2, NF-κB and NLRP3-related biomarkers; identification of active constituents; validated target-engagement assays; pharmacokinetic– pharmacodynamic relationships; standardized botanical preparations; and well-controlled clinical studies. Systems pharmacology, omics approaches and advanced delivery technologies may enable the identification of combinations of pathways that are biologically meaningful.^[1,2,8]

4. CONCLUSION

The interplay between oxidative stress and neuroinflammation forms a complex pharmacological network in which Nrf2, NF-κB and NLRP3 play critical regulatory roles. Phytochemical agents derived from plants have the potential to modulate multiple components of this network and thus represent a promising source of neuroprotective pharmacological leads. The interpretation of experimental activity should take into account dosage, exposure, target engagement, standardization and safety. The major opportunity for future research is to translate multi-pathway observations into rigorously validated pharmacological mechanisms and clinically relevant interventions.

REFERENCES

1. Suzen S, Tucci P, Profumo E, Buttari B, Saso L. A pivotal role of Nrf2 in neurodegenerative disorders: a new way for therapeutic strategies. *Pharmaceuticals (Basel)*, 2022; 15(6): 692. doi:10.3390/ph15060692.
2. Cuadrado A. Brain-protective mechanisms of transcription factor NRF2: toward a common strategy for neurodegenerative diseases. *Annu Rev Pharmacol Toxicol*, 2022; 62: 255-277. doi:10.1146/annurev-pharmtox-052220-103416.
3. Ahmed SMU, Luo L, Namani A, Wang XJ, Tang X. Nrf2 signaling pathway: pivotal roles in inflammation. *Biochim Biophys Acta Mol Basis Dis.*, 2017; 1863(2): 585-597. doi:10.1016/j.bbadis.2016.11.005.
4. Pellegrini C, Fornai M, Antonioli L, Blandizzi C, Calderone V. Phytochemicals as novel therapeutic strategies for NLRP3 inflammasome-related neurological, metabolic, and inflammatory diseases. *Int J Mol Sci.*, 2019; 20(12): 2876. doi:10.3390/ijms20122876.
5. Feng YS, Tan ZX, Wu LY, Dong F, Zhang F. The involvement of NLRP3 inflammasome in the treatment of neurodegenerative diseases. *Biomed Pharmacother*, 2021; 138: 111428. doi:10.1016/j.biopha.2021.111428.
6. Khan H, Tundis R, Ullah H, Aschner M, Belwal T, Mirzaei H, et al. Flavonoids targeting NRF2 in neurodegenerative disorders. *Food Chem Toxicol*, 2020; 146: 111817. doi:10.1016/j.fct.2020.111817.
7. Wu S, Liao X, Zhu Z, Huang R, Chen M, Huang A, et al. Antioxidant and anti-inflammation effects of dietary phytochemicals: the Nrf2/NF- κ B signalling pathway and upstream factors of Nrf2. *Phytochemistry*, 2022; 204: 113429. doi:10.1016/j.phytochem.2022.113429.
8. Clifford T, Acton JP, Cocksedge SP, Bowden Davies KA, Bailey SJ. The effect of dietary phytochemicals on nuclear factor erythroid 2-related factor 2 (Nrf2) activation: a systematic review of human intervention trials. *Mol Biol Rep.*, 2021; 48(2): 1745-1761. doi:10.1007/s11033-020-06041-x.
9. Milner MT, Maddugoda M, Götz J, Burgener SS, Schroder K. The NLRP3 inflammasome triggers sterile neuroinflammation and Alzheimer's disease. *Curr Opin Immunol*, 2021; 68: 116-124. doi:10.1016/j.coi.2020.10.011.
10. Anderson FL, Biggs KE, Rankin BE, Havrda MC. NLRP3 inflammasome in neurodegenerative disease. *Transl Res.*, 2023; 252: 21-33. doi:10.1016/j.trsl.2022.08.006.

11. Holbrook JA, Jarosz-Griffiths HH, Caseley E, Lara-Reyna S, Poulter JA, Williams-Gray CH, et al. Neurodegenerative disease and the NLRP3 inflammasome. *Front Pharmacol*, 2021; 12: 643254. doi:10.3389/fphar.2021.643254.
12. Qin S, Hou DX. Multiple regulations of Keap1/Nrf2 system by dietary phytochemicals. *Mol Nutr Food Res*, 2016; 60(8): 1731-1755. doi:10.1002/mnfr.201501017.
13. Hatami M, Abdolahi M, Soveyd N, Djalali M, Togha M, Mohammadzadeh Honarvar N. Molecular mechanisms of curcumin in neuroinflammatory disorders: a mini review of current evidences. *Endocr Metab Immune Disord Drug Targets*, 2019; 19(3): 247-258. doi:10.2174/1871530319666181129103056.
14. Olcum M, Tastan B, Ercan I, Eltutan IB, Genc S. Inhibitory effects of phytochemicals on NLRP3 inflammasome activation: a review. *Phytomedicine*, 2020; 75: 153238. doi:10.1016/j.phymed.2020.153238.
15. Suganthi N, Devi KP, Nabavi SF, Braidy N, Nabavi SM. Bioactive effects of quercetin in the central nervous system: focusing on the mechanisms of actions. *Biomed Pharmacother*, 2016; 84: 892-908. doi:10.1016/j.biopha.2016.10.011.
16. Patel SS, Acharya A, Ray RS, Agrawal R, Raghuwanshi R, Jain P. Cellular and molecular mechanisms of curcumin in prevention and treatment of disease. *Crit Rev Food Sci Nutr*, 2020; 60(6): 887-939. doi:10.1080/10408398.2018.1552244.
17. Bai X, Bian Z, Zhang M. Targeting the Nrf2 signaling pathway using phytochemical ingredients: a novel therapeutic road map to combat neurodegenerative diseases. *Phytomedicine*, 2023; 109: 154582. doi:10.1016/j.phymed.2022.154582.
18. Chen JH, Huang SM, Tan TW, Lin HY, Chen PY, Yeh WL, et al. Berberine induces heme oxygenase-1 up-regulation through phosphatidylinositol 3-kinase/AKT and NF-E2-related factor-2 signaling pathway in astrocytes. *Int Immunopharmacol*, 2012; 12(1): 94-100. doi:10.1016/j.intimp.2011.10.019.
19. Sharma K, Singla N, Kaur S, Bhatkatiya M, Vaisnav R, Gautam RK, et al. Resveratrol and the NLRP3 inflammasome: unlocking the anti-inflammatory potential of a natural compound. *Curr Pharm Des*, 2026; 32(30): 2496-2512. doi:10.2174/0113816128448299260622100931.
20. 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. *PLoS Med*, 2021; 18(3): e1003583. doi:10.1371/journal.pmed.1003583.
21. Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, Koffel JB; PRISMA-S Group. PRISMA-S: An extension to the PRISMA Statement for Reporting

- Literature Searches in Systematic Reviews. *Syst Rev.*, 2021; 10: 39. doi:10.1186/s13643-020-01542-z.
22. Cuadrado A, Manda G, Hassan A, Alcaraz MJ, Barbas C, Daiber A, et al. Transcription factor NRF2 as a therapeutic target for chronic diseases: a systems medicine approach. *Pharmacol Rev.*, 2018; 70(2): 348-383. doi:10.1124/pr.117.014753.
23. Saha RN, Pahan K. Signals for the induction of neuroinflammation in neurodegenerative diseases. *J Pharmacol Exp Ther.*, 2006; 318(2): 456-463.
24. Hennig P, Garstkiewicz M, Grossi S, Di Filippo M, French LE, Beer HD. The crosstalk between Nrf2 and inflammasomes. *Int J Mol Sci.*, 2018; 19(2): 562. doi:10.3390/ijms19020562.
25. Sivandzade F, Prasad S, Bhalerao A, Cucullo L. NRF2 and NF- κ B interplay in cerebrovascular and neurodegenerative disorders: molecular mechanisms and possible therapeutic approaches. *Redox Biol.*, 2019; 21: 101059. doi:10.1016/j.redox.2018.11.017.
26. Olcum M, Tastan B, Ercan I, Eltutan IB, Genc S. Inhibitory effects of phytochemicals on NLRP3 inflammasome activation: a review. *Phytomedicine*, 2020; 75: 153238. doi:10.1016/j.phymed.2020.153238.
27. Singh SS, Rai SN, Birla H, et al. Nrf2 modulation by natural compounds in aging, neurodegeneration, and neuropathic pain. *Pharmaceutics*, 2026; 18(1): 118. doi:10.3390/pharmaceutics18010118.
28. Nabavi SF, Russo GL, Daglia M, Nabavi SM. Role of quercetin as an alternative for the treatment of neurodegenerative disorders: a review. *J Cell Biochem*, 2015; 116(7): 1179-1185.
29. Attenuation of Nrf2/Keap1/ARE in Alzheimer's disease by plant secondary metabolites: A mechanistic review. [Review article]. [Journal name, year, volume, issue, pages/article number, DOI need to be added].
30. Recent evidence on phytochemicals in neuroinflammation supports the involvement of curcumin, EGCG, baicalein, baicalin, resveratrol, berberine, quercetin and apigenin in multiple inflammatory and oxidative-stress pathways. [Full source details need to be added].
31. Phytochemicals in Alzheimer's Disease Prevention and Management: Molecular Mechanisms, Therapeutic Potential, Translational Challenges, and Emerging Research Directions. *Int J Mol Sci.*, 2026. [Volume, article number/DOI need to be added].
32. Nrf2–Keap1 Pathway and NLRP3 Inflammasome in Parkinson's Disease: Mechanistic Crosstalk and Therapeutic Implications. *Mol Neurobiol*, 2026; 63: 91.