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A Systematic Review on The Role of Plant Secondary Metabolites in Combating Neurodegenerative Disorders

Rakesh Sahebrao Jadhav[1*], Kalpana Krishnarao Jadhav[1], Milind Mohan Godbole[1]

[1]Yashwant Ayurvedic College, PGT & RC Kodoli, Tal Panhala, Dist. Kolhapur, Maharashtra, India

***Corresponding Author E-mail: drrakeshsj@gmail.com**

ABSTRACT

Neurodegenerative disorders, Alzheimer, Parkinson, Huntington, among others form an array of conditions characterized by loss of neurons, cognitive impairment and motor loss, and are progressive conditions associated with a grave social, economic, and healthcare burden to society. The existing pharmacological treatment affects the progress of the disease much less as it is mainly symptomatic; it causes some interest in alternative treatment methods. Flavonoid, alkaloid, terpenoid, and phenolic compounds, which represent plant secondary metabolites (PSMs) neuroprotective potential, have demonstrated significant neuroprotective effects in preclinical animal models through targeting several pathological mechanisms. These substances reduce oxidative stress by potentiating endogenous antioxidant protection, inhibit neuroinflammation via cytokine and microglial adjustment and prevent toxic protein formation, augment neurotransmitter channels, which maintain the neurotransmitter balance in the neurons further enhancing cognitive and motor functions. The translation of preclinical evidence to a direct clinical application is hampered, however, by limitations in bioavailability, blood-brain barrier penetration, heterogeneity of experiments, and lack of long-term studies, despite the promising results evident in past studies. Delivery optimization, animal models routines, and examination of chronic or combinatorial intervention are critical to bring PSMs to safe and viable therapeutic use in human NDs.

Key Words:

Neurodegenerative disorders, Plant secondary metabolites, Flavonoids, Alkaloids, Terpenoids, Phenolic compounds, Neuroprotection

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1. INTRODUCTION

The importance of animal models in neurodegenerative disorders (NDs) is immense in terms of pathophysiology and the potential benefits of compounds in therapeutic situations. Rodent models, which consist of transgenic mice and chemically induced lesions, reproduce the major characteristics of the pathology, e.g. amyloid-beta deposition, dopaminergic neuronal degeneration and striatal atrophy, enabling the investigation of the nature of the disease in controlled conditions[1]. These models allow assessing behavioral, biochemical, and molecular outcomes, giving information about cognitive and motor deficiencies and the mechanisms behind these deficiencies in the cells. Animal models allow testing the effects of new interventions, such as plant secondary metabolites (PSMs) in a systematic way before translating them to clinical research.

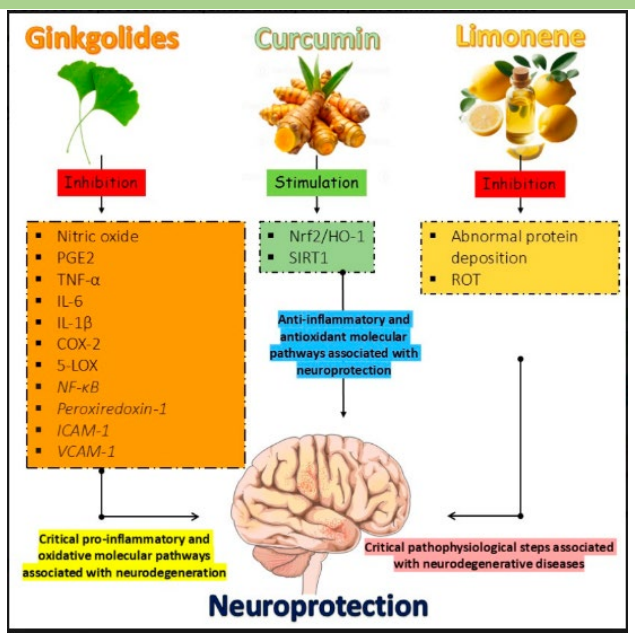

Figure 1: Neuroprotective Roles of Ginkgolides, Curcumin, and Limonene Against Neurodegeneration[2]

The mechanistic studies in the study of animal models are also more readily achievable due to the specificity of dosing regimens, administration routes, and timing which are achievable in a controlled animal setting immeasurably more than they are in humans. In addition, the models assist in the pharmacokinetics, bioavailability, and toxicity of neuroprotective compounds which play a pivotal role in determining whether a candidate is therapeutically promising. In sum, these animal-based studies become the keys to bring preclinical findings into successful and safe methods of neurodegenerative disorders control[3].

1.1 Background Information and Context

Neurodegenerative diseases (NDs) such as Alzheimer disease (AD), Parkinson disease (PD) and Huntington disease (HD) are a progressive disorder defined by the degeneration of neurons, cognitive impairments and disorders of motor dysfunctions. These conditions are very costly in terms of social, economic, and healthcare expenses in the global scenario. Modern pharmacotherapies are based mainly on the alleviation of symptoms and fail to stop or regress disease progression. The constraints have led to increased research with respect to alternative therapeutic initiatives, most notably those that are natural materials that are multi-targeted neuroprotective[4]. Plant secondary metabolites (PSMs)-flavonoids, alkaloids, terpenoids, saponins, and phenolic acids, have received particular interest in mitigating the oxidative stress, inflammation, apoptosis, and protein aggregation that are major pathological mechanisms of NDs.

1.2 Objectives of the Review

The primary objective of this review is:

- To systematically evaluate the neuroprotective effects of plant secondary metabolites (PSMs) in animal models of Alzheimer's, Parkinson's, and Huntington's diseases.
- To analyze the mechanisms of action of PSMs, including antioxidant, anti-inflammatory, anti-apoptotic, protein-aggregation modulation, and neurotransmitter regulation.
- To examine the pharmacokinetics, bioavailability, and optimal administration routes of PSMs in preclinical animal studies.

- To critically assess the strengths, limitations, and translational relevance of animal-based studies on PSMs in neurodegenerative disorders.
- To identify research gaps and propose future directions for enhancing the clinical applicability of PSM-based neuroprotective strategies.

1.3 Importance of the Topic

Translation gap between preclinical research and clinical application is very important to understand effects of PSMs in controlled animal models. Identifying deficiency in research, limitations, and future possibilities, this review is aimed to serve as a guide when developing safe and effective interventions in the treatment of neurodegenerative conditions based on PSM[5].

2. ANIMAL MODELS AND PRECLINICAL EVALUATION OF NEUROPROTECTIVE PLANT SECONDARY METABOLITES

The animal model is critical in the process of researching on the neurodegenerative diseases and in this case, the controlled advantages of the plant secondary metabolites (PSMs), including flavonoids, alkaloids, terpenoids and phenolic compounds, will be examined[6]. Neuroprotective effects of these metabolites are discussed as antioxidant, anti-inflammatory, anti-apoptotic, and protein-aggregation-modulating activities useful in enhancing cognitive and motor functions in AD, PD, and HD models. Behavioral, biochemical, or molecular measurements present the best information but their disadvantages are experimental variability, inadequate bioavailability of PSMs, low long-term investigations, and animal/human pathology dissimilarities that influence translation application.

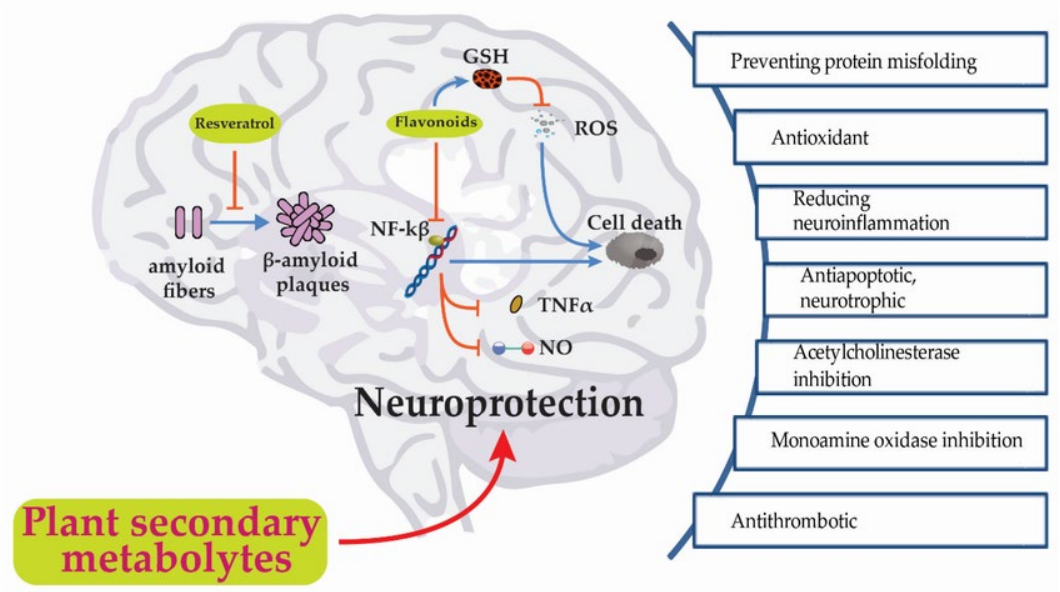

Figure 2: Mechanisms of Neuroprotection by Plant Secondary Metabolites: Role of Flavonoids and Resveratrol[7]

2.1 Methodologies in Animal-Based Studies

Animal models have become an indispensable part of research on neurodegenerative diseases (ND) and help reveal the key aspects of the progression of the disease, its pathophysiology, and the effects of introducing treatment measures. Such models can recapitulate some of the main pathological characteristics of human diseases and thereby allow a preclinical assessment of the plant secondary metabolite (PSMs)[8].

- **Alzheimer Disease (AD) Models:** Much effort has been invested in the development of transgenic mouse models that overexpress human analogs of the protein amyloid precursor protein (APP) or presenilin mutations, which result in amyloid-b accumulation and deficits in cognition. Alternatively, acute models of therapeutic testing are intracerebral injections of 2-amyloid peptides, which cause local plaque and local neuroinflammation.
- **Parkinson?s Disease (PD) Models:** The models used to induce degeneration of dopaminergic neurons include; 6-hydroxydopamine (6-OHDA) lesions in the nigro-striatal pathway or secondarily, administration of MPTP, which selectively destroys dopaminergic neurons. These models recapitulate motor defects and biochemical defects of PD.
- **The Models of Huntington Disease (HD):** Transgenic animals that produce mutant huntingtin protein recapitulate striatal neurodegeneration, motor deficits, and behavior irregularities; chemically mimicked lesions such as quinolinic acid (to mimic excitotoxicity-related neuronal loss) are also used[9].

Oral gavage, intraperitoneal administration and dietary supplement are used to deliver PSMs, and dosages are adjusted at the optimum according to pharmacokinetics and toxicity. The presence of neuroprotective effects is measured using a battery of behavioral (e.g., Morris water maze to detect spatial memory, rotarod to assess motor coordination and the open-field test to assess locomotion activity), histopathological (e.g., neuronal counts, staining of amyloid plaques), biochemical (oxidative stress indicators, cytokines of inflammation, and neurotransmitter levels), and molecular (Western blot, RT-PCR to measure changes in protein and gene expression). The given multi level strategy will provide an opportunity of a complex assessment of PSM impact on neuronal health[10].

2.2 Key Findings from Research Studies

Flavonoids

Comapared to other polyphenolic compounds, flavonoids have been intensively studied in terms of their neuroprotective effects, in AD and PD models. Others like quercetin, kaempferol and luteolin show cognitive and cellular effect. A case in point, the administration of quercetin in the APP/PS1 mice enhanced spatial memory and minimized the fibril deposition of amyloid-beta. Mechanically, flavonoids confer their antioxidant properties by increasing superoxide dismutase (SOD), and catalase (CAT), antihypoxic effects by inhibiting cytokines, e.g., IL-1b and TNF-a, andowych the apoptotic properties by regulating bcl-2/bax pathways, which finally lead to neuronal survival[11].

Alkaloids

Alkaloids such as berberine and galantamine exhibit potent neuroprotective properties via the modulation of oxidative stress, inflammation and neurotransmission. In the case of MPTP rodent models, berberine effectively inhibited the loss of dopaminergic neurons, probably through the alleviation of the oxidative stress and inflammatory activation of microglia[12]. The increased cognitive performance of AD models following Galantamine, given that it is an acetylcholinesterase inhibitor, has been attributed to the enhancement of cholinergic signalling and neuronal degeneration inhibition. These results reinforce the multi-modal alkaloid in NDs mechanisms.

Terpenoids

Various terpenoids especially ginkgolides and curcuminoids have been found to show profound neuroprotection levels in several ND models. Curcumin minimized amyloid plaque formation, alleviated neuroinflammation, and induced neurogenesis in the models of AD. Ginkgolide B

inhibited mitochondrial dysfunction and oxidative injury in the PD models via a combination of enhancing mitochondrial metabolism and decreasing apoptosis. The efficacy brings out the potentiality of terpenoids as mitochondrion targeting agents of neuroprotective agents[13].

- **Phenolic Compounds**

Neuroprotection Caffeic acid and rosmarinic acid phenolic acids protect against neurons (with mechanisms incorporating both oxidative stress and acetylcholinesterase activity inhibition and inflammatory signaling). These compounds have neuroprotective and cognitive-enhancing effects and showed broad-spectrum advantages in HD and AD models, including all of the following: neuronal damage reduction, including neuroinflammation and neuroprotection, improved behavioral outcomes, and neuroinflammation and neuroprotection[14].

2.3 Critical Evaluation of Strengths and Limitations

- **Strengths**

Animal models are useful to provide mechanistic understanding and to allow controlled assessment of the impact of plant secondary metabolites (PSMs) on neurodegenerative conditions. The neuroprotective effects of PSMs are multi-targeted and differ substantially due to the fact that they concurrently regulate oxidative stress, neuroinflammation, protein aggregation as well as apoptotic mechanisms[15]. These humane endpoints that include behavioral, biochemical and molecular endpoint will permit an effective evaluate of their therapeutic value that will involve functional, cellular and molecular effects.

- **Limitations**

Notwithstanding these positive aspects, there are quite a few drawbacks of using animal models in the assessment of the plant secondary metabolites (PSMs). Reproducibility can be decreased by experimental heterogeneity due to the use of different species, strains, age, dosing and administration routes, which are potential barriers to translational relevance. Also, a significant portion of PSMs have low bioavailability, posing a problem to their efficacy in vivo and making it difficult to use in clinical practice[16]. Safety, efficacy long-term studies are not available, and any combinatorial treatment approaches are sparse. Moreover, the fact that the rodent models are dissimilar to human pathology can limit the straightforward extrapolation of findings, which further highlights the presence of required caution and validation in the top-of-the-line models or even at the clinical level itself.

3. MECHANISMS OF NEUROPROTECTION BY PLANT SECONDARY METABOLITES IN NEURODEGENERATIVE DISEASES

Multiple mechanisms have been identified by which plant secondary metabolites (PSMs), exert protective effects against neurodegenerative diseases, such as antioxidant efficacy that lowers reactive oxygen species levels and increases native defense mechanisms, anti-inflammatory and immune-modulatory properties that reduce microglia activation and cytokines release, protein aggregation modulation which prevents amyloid-β and alpha-synuclein toxicity, and modulation of neurotransmitter systems to enhance cognitive and motor abilities. Collectively, these neuronal-specific effects protect the integrity of neurons, the synaptic communication process and the brain as a whole in AD, PD and HD models[17].

3.1 Neuroprotection through Antioxidant Mechanisms

Secondary metabolites of plants (PSMs) are essential in the relief of oxidative stress, which is a significant pathogenesis of neurodegenerative diseases (NDs). They limit the formation of reactive oxygen species (ROS) and the activation of endogenous antioxidant defense, such as superoxide

dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), etc[18]. Inhibition of ROS generation, disruption of lipid peroxidation, damage of DNA, and oxidation of proteins may cause oxidative damage to neurons resulting in disrupted cellular homeostasis and reduced survival of AD, PD, and HD models, which are prevented by PSMs, protecting the neurons against damage caused by oxidative stresses as shown by cellular homeostasis and enhancing the life of neurons.

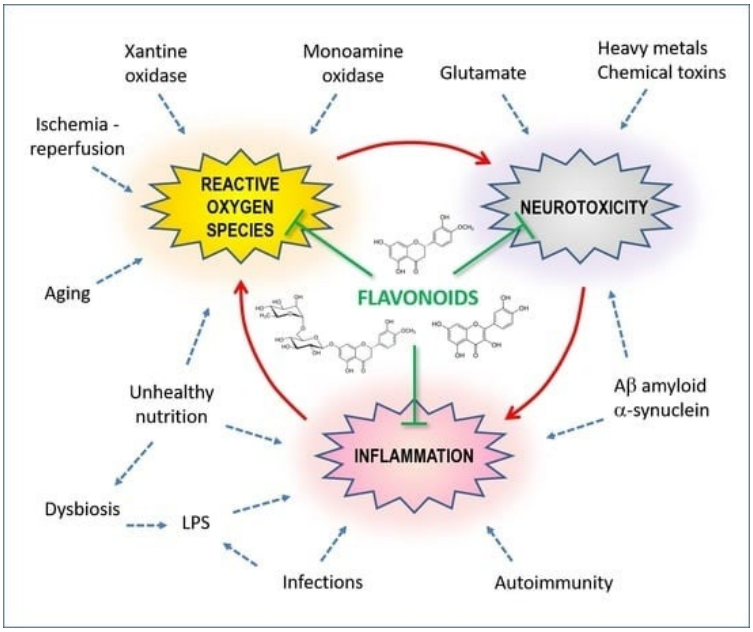

Figure 3: Antioxidant Role of Flavonoids in Modulating Neurotoxicity, Inflammation, and Oxidative Stress[19]

3.2 Anti-Inflammatory and Immunomodulatory Effects

A specific feature of NDs is neuroinflammation, the activation of microglia, and the secretion of pro-inflammatory cytokines IL-1b, TNF-a, and IL-6. PSMs, more specifically flavonoids, alkaloids, and terpenoids have strong anti-inflammatory and immunomodulatory activity due in part to their ability to dampen microglial activation and cytokine production. This regulation of the inflammatory process decreases neuron damage and linearly slows the progression of the disease. Moreover, there are certain PSMs modulating signalling pathways, including NF-lkB and MAPK, and further regulating cascades of inflammation and neuroimmune balance[20].

3.3 Modulation of Protein Aggregation

The accumulation of misfolded proteins such as amyloid-B in AD and 1-synuclein in PD interferes with the functioning of neurons and induction of apoptosis. PSMs disrupt these aggregation processes by stabilizing protein structure, stimulating clearance of oligomers and inhibition of toxic oligomer formation. The neuronal networks are maintained and synapses remained intact through the regulation of protein accumulation by PSMs, thereby alleviating neurotoxicity, which is paramount to preservation of cognitive and motor abilities[21].

3.4 Neurotransmitter Regulation

Dysfunctional changes in neurotransmitter systems can be related to the cognitive and motor impairments in NDs. Some alkaloids, as well as phenolic compounds, promote cholinergic, dopaminergic, and glutamatergic transmission. As an example, galantamine has positive effects on acetylcholine levels which enhance cognition in the AD models and berberine prevents the loss of the dopaminergic cells in the PD models. PMs alleviate neurotransmitter imbalances and

enhance synptotic communications, motor coordination, and memory and learning initiation, as well as, structural neuroprotection, with apparent functional advantages associated with neurotransmitter balancing genomically to neuroactive and substrates[22].

4. PHARMACOKINETICS AND BIOAVAILABILITY OF PLANT SECONDARY METABOLITES IN ANIMAL MODELS

Neuroprotective potential of plant secondary metabolites (PSMs) must be understood and their pharmacokinetics (PK) and bioavailability found to translate their true potential into effective clinical interventions. Pharmacokinetics is the absorption, distribution, metabolism and excretion (ADME) of compounds and bioavailability is the fraction of an administered units dose that reaches the systemic circulation in an active form. These parameters have been shown to play an essential role in establishing exemplary dosing sources, routes of administration and estimated therapeutic effect in animal model studies[23].

Table 1: Summary of Key Literature on Natural Products, Herbal Interventions, and Dietary Neuroprotection[24]

Author(s)	Study	Focus Area	Methodology	Key Finding
Mohd Sairazi et al. (2020)[25]	Natural products and their bioactive compounds: neuroprotective potentials against neurodegenerative diseases	Neuroprotective effects of phytochemicals	Literature review of bioactive compounds in experimental models	Flavonoids, alkaloids, and terpenoids showed antioxidant, anti-inflammatory, and anti-apoptotic activities, contributing to neuronal protection and slowing disease progression
Neto et al. (2024)[26]	Investigating the neuroprotective and cognitive-enhancing effects of Bacopa monnieri	Cognitive enhancement and neuroprotection via Bacopa monnieri	Systematic review of preclinical and clinical studies	Bacopa monnieri improved memory, learning, and cognitive function by reducing inflammation, oxidative stress, mitochondrial dysfunction, and apoptosis
Pagotto et al. (2024)[27]	Ginkgo biloba: a leaf of hope in the fight against Alzheimer's dementia	Clinical effects of Ginkgo biloba in Alzheimer's disease	Systematic review of clinical trials	Ginkgo biloba modestly improved cognitive performance, attention, and daily functioning and was safe as a complementary therapy

Pogačnik et al. (2020)[28]	An overview of crucial dietary substances and their modes of action for prevention of neurodegenerative diseases	Role of dietary substances in neuroprotection	Literature review on essential nutrients	Polyphenols, vitamins, and omega-3 fatty acids demonstrated neuroprotective effects, supporting dietary interventions to reduce risk and progression of neurodegenerative disorders

Absorption

In animal models, PSMs can be orally administered, added to the peritoneum or enriched as a part of the diet. Oral preparations are frequently used but can be restricted by insufficient solubility, GI instability, or first-pass elimination, thus the fraction of active compound gaining access to the circulation. Specific flavonoids and phenolic acids, such as those that are highly metabolized by the gut and liver, which form conjugates which may derivatively exhibit decreased or altered bioactivity[29].

Distribution

After absorption, the PSMs disperse to a number of different parts of the body such as brain, which applies specifically in the case of neurodegenerative disease models. The capability of PSMs to penetrate the blood Brain barrier (BBB) is essential to reaching neuroprotective effects. Lipophilic substances like curcumin and ginkgolides have greater BBB transit and highly polar ones could need the specific delivery structures to achieve efficient levels in the CNS.

Metabolism

The PSMs are mainly metabolized within the liverby the action of phase I (oxidative or reductive alteration, hydrolysis) and phase II (glucuronidation, sulfation, methylation). Bioactivity can be gained, released or even be maintained by metabolites. As an example, quercetin is largely converted to glucuronides and sulfates, which can elicit different antioxidant/anti-inflammatory activity than the parent compound. Knowledge of metabolic pathways can be used to predict efficacy, the risk of toxicity, drug/compound interactions[30].

Excretion

PSMs and its metabolites are excreted mainly in urine and feces. Such clearance rates may differ on molecular size, polarity and binding to the plasma proteins. This potentially leads to a short clearance time which can limit therapeutic efficacy hence requiring repeated or prolonged dosing schemes[31].

Bioavailability Challenges

Lack of BBB penetrability, unstable in digestive fluids, undergoing rapid metabolism, and poor solubility in the majority of PSMs explain the low bioavailability of these drugs due to inadequate oral absorption. These limitations may limit their in vivo neuroprotective potential even though they have a potent in vitro activity. Among the relevant approaches adopted by researchers to deal

with this fact, there are nanoparticle encapsulation, prodrug, liposomal delivery, co-administration with absorption enhancer, and so on, which increase the systemic and brain bioavailability[32].

Relevance in Animal Models

In animal models, the parameters of the PK can be accurately measured with the help of blood sampling, along with the distribution of it in taser systems as well as metabolite analysis. Such studies inform the identification of effective doses, dose frequency, and routes of administration and thus inform translational studies with potential clinical applications. The association of PK and bioavailability responses with behavioral and molecular endpoints allows the investigator to relate systemic exposure to therapeutic response, thereby enabling the preclinical data to be more reliable.

5. DISCUSSION

This survey has revealed that plant secondary metabolites (PSMs) have a potent neuroprotective effect on animal models of neurodegenerative diseases with multi-targeted mechanisms, including antioxidant, anti-inflammatory, anti-apoptotic and neurotransmitter-regulating effects[33]. These outcomes enhance both motor and cognitive capabilities, which establishes the therapeutic potential of PSMs to act as alternatives or adjuvants to the existing forms of treatment. Nevertheless, the problems like a high degree of experimental variability, inadequate bioavailability, low penetration of the blood-brain barrier, and lack of long-term studies limit clinical translation. Future work needs to uniformize models, maximize delivery systems and test chronic and combinatorial interventions in an attempt to increase the translational applicability in the future[34].

5.1 Interpretation and Analysis of Findings

This review describes that plant secondary metabolites (PSMs) have considerable neuroprotective potential in models of neurodegenerative disorders (NDs) in animals. Flavonoids, alkaloids, terpenoids, and phenolic compounds were repeatedly reported to exert a multi-targeted effect, which includes antioxidant activity, anti-inflammatory and immunomodulatory effects, protein aggregation, and neurotransmitter systems[35]. The combined effect of these mechanisms is to maintain neuronal health, promote synaptic functional traits, and of enhancing cognitive and motor performance in Alzheimer disease (AD), Parkinson disease (PD), and Huntington disease (HD) models. Animal studies offer the possibility of controlling experimental conditions to an extent that they allow mechanistic analysis of the manner in which PSMs interfere with pathological pathways of NDs[36].

5.2 Implications and Significance

The results provide evidence of the therapeutic significance of PSMs as the alternative or complementary treatment of NDs in comparison to the traditional pharmacological interventions. Their multi-modalities enable them to concurrently hit oxidative stresses, neuroinflammation, protein misfolding, neurotransmitter imbalance, with these features being essential markers of neurodegeneration[37]. Moreover, behavioral, biochemical, and molecular evaluations align animal models to strengthen the preclinical data to a translation context. Pharmacokinetic and bioavailability data emphasize the significance of dose optimization dosage route, and drug delivery system to increase efficacy in vivo especially in drugs with low oral bioavailability or poor blood-brain barrier permeation[38].

5.3 Research Gaps and Future Directions

Regardless of good preclinical results, there are gaps that need to be filled. Experimental heterogeneity, such as the different species, strains, age, and dosing schedules restricts reproducibility and extrapolation of the results to humans[39]. There is a paucity of long-term efficacy and safety studies, and the interaction of a combination or synergistic effects of multiple PSM remain understudied. Moreover, there is poor bioavailability and little blood-brain barrier penetration, which are problems with clinical translation. Developed animal models should be standardized and delivery systems (e.g. nanoparticles, liposomes, or prodrugs) optimized in future studies on chronic intervention trials to study long-term neuroprotective effects. Closing such gaps will be important in addressing how PSMs can be used to develop effective therapeutic approaches to human neurodegenerative disorders[40].

6. CONCLUSION

This systematic review points toward the high promise of neuroprotection of plant secondary metabolites (PSMs) in animal models of neurodegenerative conditions, namely Alzheimer, Parkinson, and Huntington diseases. Anti-oxidant, neuroinflammation, protein aggregation, and neurotransmitter modulatory effects in flavonoids, alkaloids, terpenoids, and phenolics provide complex therapies in preventing disruptions in neurotransmitter and protein aggregation and stabilization of neurons, thereby improving cognition and motor-related functioning. Although preclinical evidence supports their therapeutic potential as alternatives or adjunct to conventional therapies, clinical translation is limited by low bioavailability, lack of blood brain barrier distribution ability, inter-experiment variability and a lack of studies over a long period of time. To overcome these shortcomings and forge ahead to clinical practice of PSMs in human neurodegenerative disorders, future studies with emphasis on standardized animal models, ideal delivery approaches, and chronic or combinatorial deliveries will be important.

REFERENCES

1. Abd Rashed, A., Abd Rahman, A. Z., & Rathi, D. N. G. (2021). Essential oils as a potential neuroprotective remedy for age-related neurodegenerative diseases: A review. Molecules, 26(4), 1107.
2. Abdulwanis Mohamed, Z., Mohamed Eliaser, E., Mazzon, E., Rollin, P., Cheng Lian Ee, G., & Abdull Razis, A. F. (2019). Neuroprotective potential of secondary metabolites from Melicope lunu-ankenda (Rutaceae). Molecules, 24(17), 3109.
3. Alvi, S. S., Ahmad, P., Ishrat, M., Iqbal, D., & Khan, M. S. (2019). Secondary metabolites from rosemary (Rosmarinus officinalis L.): Structure, biochemistry and therapeutic implications against neurodegenerative diseases. In Natural Bio-active Compounds: Volume 2: Chemistry, Pharmacology and Health Care Practices (pp. 1-24). Singapore: Springer Singapore.
4. Aryal, B., Raut, B. K., Bhattarai, S., Bhandari, S., Tandan, P., Gyawali, K., ... & Parajuli, N. (2022). Potential therapeutic applications of plant-derived alkaloids against inflammatory and neurodegenerative diseases. Evidence-Based Complementary and Alternative Medicine, 2022(1), 7299778.
5. Ayaz, M., Ullah, F., Sadiq, A., Kim, M. O., & Ali, T. (2019). Natural products-based drugs: potential therapeutics against Alzheimer's disease and other neurological disorders. Frontiers in pharmacology, 10, 1417.
6. Bansal, R., & Singh, R. (2018). Exploring the potential of natural and synthetic neuroprotective steroids against neurodegenerative disorders: A literature review. Medicinal research reviews, 38(4), 1126-1158.

7. Bose, B., Tripathy, D., Chatterjee, A., Tandon, P., & Kumaria, S. (2019). Secondary metabolite profiling, cytotoxicity, anti-inflammatory potential and in vitro inhibitory activities of Nardostachys jatamansi on key enzymes linked to hyperglycemia, hypertension and cognitive disorders. Phytomedicine, 55, 58-69.
8. de Andrade Teles, R. B., Diniz, T. C., Costa Pinto, T. C., de Oliveira Junior, R. G., Gama e Silva, M., de Lavor, É. M., ... & da Silva Almeida, J. R. G. (2018). Flavonoids as therapeutic agents in Alzheimer's and Parkinson's diseases: a systematic review of preclinical evidences. Oxidative medicine and cellular longevity, 2018(1), 7043213.
9. de Oliveira, N. K., Almeida, M. R. S., Pontes, F. M. M., Barcelos, M. P., de Paula da Silva, C. H. T., Rosa, J. M. C., ... & da Silva Hage-Melim, L. I. (2019). Antioxidant effect of flavonoids present in Euterpe oleracea Martius and neurodegenerative diseases: A literature review. Central Nervous System Agents in Medicinal ChemistryChemistry-Central Nervous System Agents), 19(2), 75-99.
10. Fakhri, S., Abdian, S., Zarneshan, S. N., Akkol, E. K., Farzaei, M. H., & Sobarzo-Sánchez, E. (2021). Targeting mitochondria by plant secondary metabolites: a promising strategy in combating Parkinson's disease. International journal of molecular sciences, 22(22), 12570.
11. Fakhri, S., Pesce, M., Patruno, A., Moradi, S. Z., Iranpanah, A., Farzaei, M. H., & Sobarzo-Sánchez, E. (2020). Attenuation of Nrf2/Keap1/ARE in Alzheimer's disease by plant secondary metabolites: A mechanistic review. Molecules, 25(21), 4926.
12. Gomes, T. M., Sousa, P., Campos, C., Perestrelo, R., & Câmara, J. S. (2024). Secondary bioactive metabolites from foods of plant origin as theravention agents against neurodegenerative disorders. Foods, 13(14), 2289.
13. Hamsalakshmi, Alex, A. M., Arehally Marappa, M., Joghee, S., & Chidambaram, S. B. (2022). Therapeutic benefits of flavonoids against neuroinflammation: a systematic review. Inflammopharmacology, 30(1), 111-136.
14. Hussain, G., Huang, J., Rasul, A., Anwar, H., Imran, A., Maqbool, J., ... & Sun, T. (2019). Putative roles of plant-derived tannins in neurodegenerative and neuropsychiatry disorders: An updated review. Molecules, 24(12), 2213.
15. Hussain, G., Rasul, A., Anwar, H., Aziz, N., Razzaq, A., Wei, W., ... & Li, X. (2018). Role of plant derived alkaloids and their mechanism in neurodegenerative disorders. International journal of biological sciences, 14(3), 341.
16. Hussain, G., Zhang, L., Rasul, A., Anwar, H., Sohail, M. U., Razzaq, A., ... & Sun, T. (2018). Role of plant-derived flavonoids and their mechanism in attenuation of Alzheimer's and Parkinson's diseases: An update of recent data. Molecules, 23(4), 814.
17. Jaafaru, M. S., Abd Karim, N. A., Enas, M. E., Rollin, P., Mazzon, E., & Abdull Razis, A. F. (2018). Protective effect of glucosinolates hydrolytic products in neurodegenerative diseases (NDDs). Nutrients, 10(5), 580.
18. Kamran, M., Kousar, R., Ullah, S., Khan, S., Umer, M. F., Rashid, H. U., ... & Rehman, M. U. (2020). Taxonomic distribution of medicinal plants for Alzheimer's Disease: a cue to novel drugs. International Journal of Alzheimer's disease, 2020(1), 7603015.
19. Kaur, N., Chugh, H., Sakharkar, M. K., Dhawan, U., Chidambaram, S. B., & Chandra, R. (2020). Neuroinflammation mechanisms and phytotherapeutic intervention: a systematic review. ACS chemical neuroscience, 11(22), 3707-3731.
20. Khan, A., Ikram, M., Hahm, J. R., & Kim, M. O. (2020). Antioxidant and anti-inflammatory effects of citrus flavonoid hesperetin: Special focus on neurological disorders. Antioxidants, 9(7), 609.
21. Kong, Y. R., Tay, K. C., Su, Y. X., Wong, C. K., Tan, W. N., & Khaw, K. Y. (2021). Potential of naturally derived alkaloids as multi-targeted therapeutic agents for neurodegenerative diseases. Molecules, 26(3), 728.

22. Leuci, R., Brunetti, L., Poliseno, V., Laghezza, A., Loiodice, F., Tortorella, P., & Piemontese, L. (2020). Natural compounds for the prevention and treatment of cardiovascular and neurodegenerative diseases. Foods, 10(1), 29.
23. Luthra, R., & Roy, A. (2022). Role of medicinal plants against neurodegenerative diseases. Current pharmaceutical biotechnology, 23(1), 123-139.
24. Maurya, P. K. (2022). Health benefits of quercetin in age-related diseases. Molecules, 27(8), 2498.
25. Mohd Sairazi, N. S., & Sirajudeen, K. N. S. (2020). Natural products and their bioactive compounds: neuroprotective potentials against neurodegenerative diseases. Evidence-Based Complementary and Alternative Medicine, 2020(1), 6565396.
26. Neto, L. J. V., de Araujo, M. R., Junior, R. C. M., Machado, N. M., Joshi, R. K., dos Santos Buglio, D., ... & Barbalho, S. M. (2024). Investigating the neuroprotective and cognitive-enhancing effects of Bacopa monnieri: a systematic review focused on inflammation, oxidative stress, mitochondrial dysfunction, and apoptosis. Antioxidants, 13(4), 393.
27. Pagotto, G. L. D. O., Santos, L. M. O. D., Osman, N., Lamas, C. B., Laurindo, L. F., Pomini, K. T., ... & Barbalho, S. M. (2024). Ginkgo biloba: a leaf of hope in the fight against Alzheimer's dementia: clinical trial systematic review. Antioxidants, 13(6), 651.
28. Pogačnik, L., Ota, A., & Poklar Ulrih, N. (2020). An overview of crucial dietary substances and their modes of action for prevention of neurodegenerative diseases. Cells, 9(3), 576.
29. Pohl, F., & Kong Thoo Lin, P. (2018). The potential use of plant natural products and plant extracts with antioxidant properties for the prevention/treatment of neurodegenerative diseases: in vitro, in vivo and clinical trials. Molecules, 23(12), 3283.
30. Puri, V., Kanojia, N., Sharma, A., Huanbutta, K., Dheer, D., & Sangnim, T. (2022). Natural product-based pharmacological studies for neurological disorders. Frontiers in pharmacology, 13, 1011740.
31. Rahman, M. H., Bajgai, J., Fadriquela, A., Sharma, S., Trinh, T. T., Akter, R., ... & Lee, K. J. (2021). Therapeutic potential of natural products in treating neurodegenerative disorders and their future prospects and challenges. Molecules, 26(17), 5327.
32. Riaz, M., Khalid, R., Afzal, M., Anjum, F., Fatima, H., Zia, S., ... & Aslam, M. A. (2023). Phytobioactive compounds as therapeutic agents for human diseases: A review. Food science & nutrition, 11(6), 2500-2529.\
33. Sharifi-Rad, M., Lankatillake, C., Dias, D. A., Docea, A. O., Mahomoodally, M. F., Lobine, D., ... & Sharifi-Rad, J. (2020). Impact of natural compounds on neurodegenerative disorders: from preclinical to pharmacotherapeutics. Journal of Clinical Medicine, 9(4), 1061.
34. Srivastava, A., Srivastava, P., Pandey, A., Khanna, V. K., & Pant, A. B. (2019). Phytomedicine: A potential alternative medicine in controlling neurological disorders. In New look to phytomedicine (pp. 625-655). Academic Press.
35. Valotto Neto, L. J., Reverete de Araujo, M., Moretti Junior, R. C., Mendes Machado, N., Joshi, R. K., dos Santos Buglio, D., ... & Barbalho, S. M. (2024). Investigating the neuroprotective and cognitive-enhancing effects of Bacopa monnieri: a systematic review focused on inflammation, oxidative stress, mitochondrial dysfunction, and apoptosis. Antioxidants, 13(4), 393.
36. Velu, G., Palanichamy, V., & Rajan, A. P. (2018). Phytochemical and pharmacological importance of plant secondary metabolites in modern medicine. In Bioorganic phase in natural food: an overview (pp. 135-156). Cham: Springer international publishing.
37. Venditti, A., & Bianco, A. (2020). Sulfur-containing secondary metabolites as neuroprotective agents. Current medicinal chemistry, 27(26), 4421-4436.

38. Wahid, M., Ali, A., Saqib, F., Aleem, A., Bibi, S., Afzal, K., ... & Bin Asad, M. H. H. (2020). Pharmacological exploration of traditional plants for the treatment of neurodegenerative disorders. Phytotherapy research, 34(12), 3089-3112.
39. Wojtunik-Kulesza, K., Rudkowska, M., Kasprzak-Drozd, K., Oniszczuk, A., & Borowicz-Reutt, K. (2021). Activity of selected group of monoterpenes in alzheimer's disease symptoms in experimental model studies—A non-systematic review. International Journal of Molecular Sciences, 22(14), 7366.
40. Zhang, Y., Yu, W., Zhang, L., Wang, M., & Chang, W. (2022). The interaction of polyphenols and the gut microbiota in neurodegenerative diseases. Nutrients, 14(24), 5373.