

Oroxylum Indicum (L.) Kurz: Neuroprotective Phytoconstituents and Advanced Anti-Parkinson Therapeutic Potential

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ABSTRACT

The selective loss of dopaminergic neurons in the substantia nigra the hallmark of parkinson's disease (PD), a chronic, progressive neurodegenerative condition that causes crippling motor and non motor problems. Traditional medications, especially levodopa, are therefore desperately needed. Due to its abundance of bioactive flavonoids, particularly baicalein, chrysin, and oroxylin A, *Oroxylum indicum* (L.) kurz, a medicinal plant belonging to the Bignoniaceae family, has become a viable option. These phytoconstituents have strong anti-inflammatory, anti-apoptotic, and anti-oxidant qualities that directly combat the main pathologies associated with parkinson's disease. Preclinical studies verify that *O. indicum* extracts significantly protect dopaminergic neurons and restore functional motor results in well-known toxin-induced models, such as MPTP and 6-hydroxydopamine (6-OHIDA). These neuroprotective effects are mediated mechanistically by reducing oxidative stress, suppressing neuroinflammatory cascades, and precisely modifying important signaling pathways, namely NF- κ B inhibition and Nrf2 activation. Despite these encouraging results, poor water solubility and restricted blood-brain barrier permeability have historically hindered the clinical translation of *O. indicum*-derived drugs. These pharmacokinetics constraints have been successfully addressed by recent advancements in nanotechnology-based drug delivery systems, and long-term therapeutic efficacy. The neuroprotective phytoconstituents of *O. indicum*, their complex modes of action, and the importance of sophisticated formulation techniques in maximizing their anti-parkinson potential are all critically assessed in this through analysis. In the end, *O. indicum* is a very promising natural medicinal platform that merits through clinical trails to determine its safety, effectiveness, and translational feasibility in the treatment of parkinson's disease.

Keywords: Parkinson's disease, neuroprotection, flavonoids, baicalein, oxidative stress, neuroinflammation, and *Oroxylum indicum*

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INTRODUCTION

Parkinson's disease (PD) is one of the most common neurodegenerative disorders affecting the elderly population worldwide¹ It is characterized by progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to motor symptoms² further impair patient quality of life.

Current therapies mainly target dopamine deficiency and provide symptomatic relief but do not effectively address

oxidative stress, mitochondrial dysfunction, neuroinflammation, and protein aggregation³ involved in PD progression. Therefore, the development of multitarget neuroprotective therapies has gained increasing attention. Plant-derived phytochemicals, particularly flavonoids and phenolic compounds, exhibit antioxidant, anti-inflammatory, and antiapoptotic activities⁴ that help protect neuronal cells. Traditional medicinal plants are also valued

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for their safety and long-standing use in Ayurveda and Chinese medicine⁵.

Oroxylum indicum (L.) Kurz is an important medicinal plant with significant neuroprotective potential. It contains bioactive flavonoids such as baicalein, baicalin, chrysin, oroxylin A, and scutellarein,⁶ which possess strong antioxidant and anti-inflammatory properties. These compounds reduce oxidative stress, suppress NF- κ B-mediated inflammation, and activate protective pathways including Nrf2/HO-1. Experimental studies in MPTP- and 6-OHDA-induced Parkinsonian⁷ models have shown that *O. indicum* extracts improve motor function, restore striatal dopamine levels, and protect dopaminergic neurons.

Phenolic compounds, alkaloids, and tannins present in *O. indicum*⁸ further contribute to free radical scavenging, membrane stabilization, and neuronal protection. Among the major phytoconstituents, baicalein demonstrates potent antioxidant and antiapoptotic effects, while oroxylin A suppresses neuroinflammation and enhances neuronal survival. Chrysin, scutellarein, and biochanin A⁹ also exhibit significant neuroprotective activities by reducing oxidative and inflammatory damage¹⁰. Baicalin additionally shows improved bioavailability and promising neuroprotective efficacy.¹¹

Recent advances in nanotechnology-based drug delivery systems¹² have improved the bioavailability and brain targeting of *O. indicum* phytoconstituents. Owing to its multitarget mechanisms and strong preclinical evidence, *O. indicum* represents a promising natural therapeutic candidate for Parkinson's disease.

PATHOPHYSIOLOGY OF PARKINSON'S DISEASE

Parkinson's disease is characterized by progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta.¹³ Major pathogenic mechanisms include oxidative stress, mitochondrial dysfunction, α -synuclein aggregation, neuroinflammation, apoptosis¹⁴, and altered dopamine metabolism.

Loss of dopaminergic neurons decreases striatal dopamine levels, leading to tremor, rigidity, bradykinesia, and postural instability. These neurons are highly vulnerable to oxidative stress and metabolic burden. Excessive reactive oxygen species (ROS) production causes lipid peroxidation, protein oxidation, and neuronal damage¹⁵. Dopamine auto-oxidation further increases oxidative stress. Mitochondrial complex I dysfunction reduces ATP production and enhances ROS generation, accelerating neurodegeneration¹⁶.

Aggregation of α -synuclein into Lewy bodies¹⁷ disrupts neuronal homeostasis and mitochondrial function. Chronic microglial activation releases inflammatory cytokines such as TNF- α and IL-6, promoting neuronal injury. Apoptotic pathways involving caspase activation contribute to dopaminergic neuronal loss. Elevated MAO-B activity increases dopamine degradation and hydrogen peroxide

production, worsening oxidative stress and neuronal damage.

Neuroprotective Mechanisms of *Oroxylum indicum*

The neuroprotective effects of *Oroxylum indicum* are mainly attributed to its flavonoids and phenolic compounds, which act against multiple pathogenic pathways involved in Parkinson's disease (PD), including oxidative stress, neuroinflammation, mitochondrial dysfunction, apoptosis, and α -synuclein aggregation.

Oxidative stress plays a major role in dopaminergic neuronal degeneration in PD. Flavonoids such as baicalein, chrysin, and oroxylin A exhibit strong antioxidant activity by scavenging reactive oxygen species (ROS) and enhancing endogenous antioxidant enzymes including superoxide dismutase (SOD), catalase, and glutathione peroxidase. These compounds also activate the Nrf2 signaling pathway, thereby reducing oxidative damage. Neuroinflammation contributes significantly to PD progression. *O. indicum* phytoconstituents suppress microglial activation and reduce pro-inflammatory cytokines¹⁸ such as TNF- α , IL-1 β , and IL-6 through inhibition of NF- κ B signaling, thereby protecting neurons from inflammatory damage. Mitochondrial dysfunction is a key pathogenic feature of PD. Bioactive compounds from *O. indicum* help preserve mitochondrial membrane potential, improve ATP production, and reduce oxidative stress, thus enhancing neuronal survival. *O. indicum* extracts regulate apoptotic pathways by modulating Bax/Bcl-2 protein expression¹⁹ and inhibiting caspase activation, thereby reducing programmed neuronal cell death associated with PD. Baicalein and related flavonoids inhibit α -synuclein misfolding and fibril formation, reducing proteotoxic stress and neuronal degeneration in Parkinson's disease. Certain phytoconstituents of *O. indicum* inhibit monoamine oxidase-B (MAO-B), decreasing dopamine degradation and ROS generation, which helps maintain dopaminergic neurotransmission. Through combined antioxidant, anti-inflammatory, antiapoptotic, and MAO-B inhibitory actions, *O. indicum* preserves striatal dopamine levels, protects neuronal architecture, and improves motor deficits in experimental PD models, highlighting its potential as a multitarget therapeutic agent.

In Vitro Pharmacological Studies

In vitro studies demonstrate the neuroprotective potential of *O. indicum* against major pathogenic mechanisms involved in Parkinson's disease, including oxidative stress, apoptosis, mitochondrial dysfunction, and neuroinflammation.

In SH-SY5Y neuroblastoma cells,²⁰ *O. indicum* extracts and flavonoids protect against H₂O₂- and 6-OHDA-induced neurotoxicity by reducing oxidative stress and improving cell viability. Baicalein particularly decreases intracellular ROS and enhances antioxidant defenses. In PC12 cells exposed to neurotoxins,²¹ *O. indicum* extracts improve cell survival, preserve neuronal morphology, and reduce apoptotic damage through modulation of oxidative

stress pathways. Phytoconstituents of *O. indicum* effectively scavenge intracellular ROS²² and maintain mitochondrial membrane potential ($\Delta\Psi_m$), thereby preserving ATP production and cellular viability. *O. indicum* inhibits apoptosis by decreasing Bax expression, increasing Bcl-2 levels, and suppressing caspase-3 and caspase-9 activation, thereby preventing mitochondrial-mediated neuronal death. In activated microglial and macrophage models, *O. indicum* reduces the release of inflammatory cytokines such as TNF- α , IL-1 β , and IL-6 through suppression of NF- κ B signaling, thereby attenuating neuroinflammation²³.

In Vivo Experimental Studies

In vivo studies are essential for validating the neuroprotective potential of *Oroxylum indicum* in Parkinson’s disease (PD). Various neurotoxin-induced animal models²⁴ have demonstrated its ability to reduce dopaminergic neuronal loss, oxidative stress, mitochondrial dysfunction, and motor impairments.

In rotenone-induced PD models,²⁵ *O. indicum* extracts reduce oxidative stress, preserve mitochondrial function,²⁶ and protect dopaminergic neurons. Treated animals show

improved motor coordination and reduced neurological deficits compared to controls. In MPTP-induced Parkinsonism, *O. indicum* and baicalein protect dopaminergic neurons by reducing oxidative stress, suppressing microglial activation, and maintaining striatal dopamine levels. In 6-OHDA models,²⁷ *O. indicum* significantly decreases neuronal apoptosis, restores dopaminergic neurotransmission, and protects against oxidative damage through its antioxidant and antiapoptotic activities²⁸. Animal studies demonstrate that *O. indicum* improves PD-related motor deficits, including tremors, locomotor activity, grip strength, and performance in rotarod and open-field tests,²⁹ indicating restoration of nigrostriatal function. Treatment with *O. indicum* increases antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione,³⁰ while reducing lipid peroxidation markers like malondialdehyde (MDA). It also restores striatal dopamine levels. Histopathological studies³¹ further confirm reduced neuronal degeneration, preserved neuronal architecture³², and decreased glial infiltration in the substantia nigra and striatum³³.

Table1: Nanoformulation and Advanced Drug Delivery

Medicinal Plant	Active Phytoconstituent(s)	Nanoformulation Type	Particle Size (nm)	PDI/Zeta Potential	Drug Loading (%)	Delivery Route	Key Mechanism(s)	Experimental Model	Primary Outcome	References
<i>Curcuma longa</i>	Curcumin	Solid Lipid Nanoparticles (SLNs)	100–200	PDI: 0.21; ζ : -18 mV	8.4 ± 0.6	Oral, IV	BBB transcytosis, Nrf2 activation, ROS scavenging	MPTP-mice, 6-OHDA-rats	↑ Striatal DA (3.2×), ↓ α -synuclein, ↑ rotarod latency	34
<i>Ginkgo biloba</i>	Ginkgolide B, Bilobalide	PEGylated Liposomes	80–150	PDI: 0.18; ζ : -22 mV	12.1 ± 1.3	IV, Intranasal	Neurovascular protection, anti-apoptotic (Bcl-2↑)	Rotenone-induced PD rats	↓ TNF- α /IL-1 β , ↑ TH+ neurons in SNpc	35
<i>Withania somnifera</i>	Withanolide A, Withaferin A	PLGA Polymeric NPs	120–250	PDI: 0.24; ζ : -15 mV	9.8 ± 0.9	Oral	PI3K/Akt activation, caspase-3 inhibition	MPTP + probenecid mice	↓ Neuroinflammation, ↑ motor coordination	36
<i>Bacopa monnieri</i>	Bacoside A3, Bacopside II	Phytosomes (Phospholipid complex)	50–100	PDI: 0.15; ζ : -28 mV	15.3 ± 1.1	Oral	Enhanced intestinal permeability, AChE inhibition	Scopolamine-induced amnesia rats	↑ Memory retention (Morris water maze), ↑ SOD/CAT	37
<i>Camellia sinensis</i>	Epigallocatechin-3-gallate (EGCG)	Nanoemulsion (Tween 80/Captex)	20–80	PDI: 0.12; ζ : -31 mV	6.7 ± 0.5	Oral, Intranasal	Direct ROS scavenging, mitochondrial biogenesis	Paraquat + maneb PD model	↓ Oxidative stress markers, ↑ complex-I activity	38

<i>Mucuna pruriens</i>	L-DOPA + natural MAO-B inhibitors	Lipid-Core Nanocapsules	100–200	PDI: 0.20; ζ: -19 mV	18.2 ± 2.1	Oral	Sustained dopamine release, reduced peripheral decarboxylation	6-OHDA hemiparkinsonian rats	↓ Apomorphine rotations (72%), ↑ striatal DA	39
<i>Oroxylum indicum</i>	Baicalein, Oroxylin A, Chrysin	Cationic SLNs (Stearylamine)	120–180	PDI: 0.19; ζ: +24 mV	10.5 ± 0.8	Intranasal, Oral	BDNF/TrkB upregulation, Nrf2/HO-1 pathway	LPS-induced neuroinflammation + MPTP mice	↑ BDNF (8-fold), ↓ microglial activation, ↑ survival	40,41
<i>Oroxylum indicum</i>	Flavonoid-rich leaf extract	Phytosomes (Soy phosphatidylcholine)	50–100	PDI: 0.16; ζ: -26 mV	14.2 ± 1.4	Oral	Enhanced bioavailability, SOD/CAT restoration	Rotenone-induced PD zebrafish	↓ ROS (65%), ↑ TH expression, improved locomotion	42
<i>Oroxylum indicum</i>	Standardized extract (10% oroxylin A)	Intranasal Nano-carrier (Chitosan-PLGA)	<200	PDI: 0.14; ζ: +18 mV	11.3 ± 0.7	Intranasal	Direct nose-to-brain transport, bypasses P-gp efflux	MPTP-probenecid chronic model	↑ CNS bioavailability (4.1×), ↓ systemic clearance	43,44

Table 2: Comparative Toxicity Profile of Nanoformulations from Medicinal Plants

S. No	Medicinal Plant	Nanoformulation	Toxicity Type	Dose Range	Key Toxicological Findings	Safety Outcome	Reference
1	<i>Curcuma longa</i>	SLNs (Curcumin)	Acute	up to 2000 mg/kg	No mortality, mild GI irritation	Safe (LD ₅₀ >2000 mg/kg)	45
2	<i>Ginkgo biloba</i>	Liposomes	Subacute (28 days)	100–500 mg/kg	No organ toxicity, stable hematology	Safe	46,47
3	<i>Withania somnifera</i>	Polymeric nanoparticles	Chronic	90 days	Mild liver enzyme fluctuation	Acceptable safety margin	47
4	<i>Bacopa monnieri</i>	Phytosomes	Subacute	300 mg/kg	Improved antioxidant enzymes, no toxicity	Safe	48
5	<i>Camellia sinensis</i>	Nanoemulsion (EGCG)	Acute + Subacute	up to 1000 mg/kg	Dose-dependent hepatotoxicity at high dose	Moderate caution	49
6	<i>Mucuna pruriens</i>	Lipid nanoparticles	Chronic	60 days	No neurotoxicity, improved dopamine	Safe	50

CONCLUSION

Oroxylum indicum is a promising medicinal plant that contains neuroprotective flavonoids like baicalein, chrysin, and oroxylin A. These compounds have strong antioxidant, anti-inflammatory, antiapoptotic, and neuroprotective effects that help prevent the degeneration of dopaminergic neurons in Parkinson’s disease. Preclinical studies show it can reduce oxidative stress, maintain mitochondrial function, restore dopamine levels, and improve motor function. While current findings strongly support its potential for treatment, more clinical studies are needed to confirm its safety and effectiveness in humans.

CONFLICT OF INTEREST: Authors declare no conflict of interest

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