



Herbal Neuroprotective Syrup in Parkinson's disease: A Detailed Review

Urjita R. Sanghavi¹, Twinkle J. Bhatt²

¹ Student, Bachelor of Pharmacy, Gyanmanjari Pharmacy College

² Assistant Professor, Department of Pharmacognosy, Gyanmanjari Pharmacy College

ABSTRACT :

Degeneration of dopaminergic neurons is a hallmark of Parkinson's disease (PD), a progressive neurodegenerative illness that causes both motor and non-motor symptoms. Interest in herbal neuroprotectives has increased as a result of the growing prevalence and drawbacks of existing pharmaceutical therapies. The herbal formulation PhytoPark Syrup, which contains *Withania somnifera*, *Bacopa monnieri*, *Ginkgo biloba*, *Curcuma longa*, and *Piper nigrum*, is thoroughly examined in this review. Every component has distinct neuroprotective qualities, such as synaptic-enhancing, antioxidative, anti-inflammatory, and neurorestorative effects.

Keywords: Polyherbal formulation, Neuroprotection, Parkinson's disease, PhytoPark Syrup, Herbal medicine, Ayurvedic neurotherapeutics, Antioxidant activity, Mitochondrial dysfunction, Oxidative stress, Dopaminergic neurons, Neuroinflammation, Phytochemicals, Herbal adaptogens, Ashwagandha, Brahmi, Curcumin, *Ginkgo biloba*, Piperine

Introduction

Parkinson's sickness (PD), the second most not unusual neurological disease, impacts extra than 10 million human beings globally [1]. Parkinson's ailment (PD) is characterised via the progressive loss of dopaminergic neurones inside the substantia nigra pars compacta and intracellular accumulation of α -synuclein aggregates (Lewy bodies) [2]. PD is characterized by means of resting tremor, pressure, bradykinesia, postural instability, and numerous cognitive and psychiatric symptoms.

Dopamine agonists and levodopa stay the cornerstones of symptom control, but long-time period use has been related to damaging aspect outcomes including dyskinesia and motor irregularities [3]. Additionally, neither the disease's progression nor the complex approaches that underpin its pathophysiology—including neuroinflammation, mitochondrial disorder, oxidative strain, and proteostasis imbalance—are addressed by means of these remedies.[4]

This growing therapeutic hole has raised interest in phytochemicals and natural neurotherapeutics. Plant-based totally compounds may be used to scavenge unfastened radicals, promote neural regeneration, and reduce irritation, among different things. To aid in those processes, PhytoPark Syrup, a multi-herbal combination, turned into developed.

Pathophysiology of Parkinson's Disease

2.1 Degeneration of Dopaminergic Neurone

Parkinson's disease is characterised by the selective death of dopaminergic neurones in the substantia nigra, which disrupts the circuitry of the basal ganglia and lowers striatal dopamine degrees.[5] Motor command manage and coordination are impacted by dopamine deficiency.

2.2 The Relationship Between Oxidative Stress and Mitochondrial Dysfunction

Both the metabolism of dopamine and the high metabolic activity of dopaminergic neurones generate reactive oxygen species (ROS).[6] Mitochondrial complicated I disorder exacerbates ATP depletion and ROS manufacturing in PD patients.[7]

2.3 Microglial Activation and Neuroinflammation

Nitric oxide and pro-inflammatory cytokines (TNF- α and IL-1 β) are released by activated microglia, further accelerating neurodegeneration[8]. It has been established that chronic neuroinflammation plays a significant role in the development and course of Parkinson's disease.[9]

3. The Scientific Basis and Composition of PhytoPark Syrup

Each of the five plant-based components that make up PhytoPark Syrup has a molecular connection to Parkinson's disease. The formulation aims to influence neurotransmission, oxidative, and inflammatory pathways.

3.1 *Ashwagandha, or Withania somnifera*

Withania somnifera, a highly esteemed adaptogenic herb in Ayurveda, contains sitoindosides and withanolides that are recognized for their anti-inflammatory and neuroprotective properties[10].

Mechanism of Action:

- Promotes the expression of brain-derived neurotrophic factor (BDNF)[11]
- Increases the activity of superoxide dismutase (SOD) and decreases lipid peroxidation.
- Reverses DNA fragmentation and mitochondrial dysfunction
- Inhibits neuroinflammation mediated by TNF- α and NF- κ B[12]

Evidence in PD:

Withania enhanced behavioral scores[13] and repaired dopaminergic neurons in MPTP-induced PD mice. Additionally, it is known to inhibit the production of α -synuclein and stop it from aggregating[14].

3.2 *Monnieri Bacopa*

Bacopa monnieri, commonly referred to as Brahmi, has long been utilized to improve memory, cognition, and neuroprotection. Bacosides A and B, its main bioactives, affect antioxidant defense and synaptic signaling[15].

Action Mechanism:

- Increases acetylcholine and serotonin levels.
- Increases the hippocampus's kinase activity and neurogenesis
- Scavenges hydroxyl radicals and prevents lipid peroxidation[16]

Evidence in Parkinson's disease:

Bacopa extract enhances locomotor function and reverses MPTP-induced striatal damage in rodent models [17]. Additionally, it increases dopamine availability by inhibiting monoamine oxidase B (MAO-B) [18].

3.3 *Ginkgo biloba*

Ginkgo biloba, which is understood to contain flavone glycosides and terpene lactones like ginkgolides and bilobalides, is a few of the earliest acknowledged medicinal plant life. [19] It is being used extensively in neurocognitive issues like Alzheimer's disease and is likewise getting more attention in Parkinson's ailment because of its varied neuroprotective profile.

Action Mechanism:

- Antioxidant Activity: By scavenging reactive oxygen species, flavonoids defend neuronal membranes from peroxidative harm.[20]
- Support for the mitochondria: Increases ATP manufacturing and keeps membrane capability.
- By blocking platelet-activating aspect (PAF), cerebral perfusion increases microcirculation.[21]
- Neurotransmitter modulation: Improves cholinergic and dopamine transmission [22]
- Apoptotic inhibition: Modifies the Bax/Bcl-2 ratio and stops caspase activation [23].

Evidence in Parkinson's disease:

Evidence in Parkinson's disease: In rotenone and 6-OHDA animal fashions, *ginkgo biloba* extract (EGb 761) preserved dopaminergic neurone integrity and greater behavioural consequences. [24] It appreciably decreased oxidative markers like MDA and NO and restored the interest of mitochondrial complicated I [25]. [26]

3.4 *Curcumin, or Curcuma longa*

Curcuma longa consists of the golden polyphenol curcumin, which has mighty neuroprotective characteristics. Its anti-inflammatory, anti-aggregatory, and antioxidant houses are widely known [27].

Mechanism of Action:

- By blockading NF- κ B, TNF- α , COX-2, and IL-6, it lowers neuroinflammation.[28]
- Prevents α -synuclein aggregation via binding regions wealthy in β -sheets.[29]
- raises the concentrations of GSH, SOD, and catalase, among different antioxidant enzymes [30].
- Transforms seasoned-inflammatory M1 microglia into anti-inflammatory M2 microglia.[31]

- maintains synaptic integrity and encourages neurogenesis [32].

Evidence in Parkinson's disease:

with the aid of reversing MPTP-prompted neurodegeneration, curcumin preserved striatal dopamine stages and inhibited apoptotic markers in rats [33]. It additionally decreased α -synuclein disorder in transgenic animals and progressed memory and motor coordination [34]. Curcumin and piperine collectively greatly improve absorption, in spite of the truth that bioavailability is a trouble [35].

3.5 Piperine, or Piper nigrum

Piper nigrum, or black pepper, contains piperine, a clearly taking place bio enhancer and MAO inhibitor. In the PhytoPark formula, it serves functions: it enhances the absorption of herbs taken in aggregate and has neuroprotective properties of its very own [36].

Mechanism of Action:

- By stopping intestinal and hepatic glucuronidation, it increases the bioavailability of curcumin, withanolides, and bacosides.[37]
- Reduces inflammatory models' levels of TNF- α , CRP, and IL-1 β
- MAO inhibition prolongs synaptic interest and increases dopamine stages.[38]
- changes GABAergic and TRPV1 channels and penetrates the blood-brain barrier.[39]

Evidence in PD:

Piperine dramatically alleviated behavioral impairments, decreased oxidative damage, and maintained dopaminergic neurons in rats with PD caused by rotenone [40]. It had synergistic effects on dopamine retention and neuroprotection when paired with L-DOPA or curcumin [41].

4. PhytoPark Syrup's Mechanistic Integration in Parkinson's disease

The distinct advantage of PhytoPark Syrup is not just the effectiveness of each of its constituents alone, but also the way they work in concert to address various neuropathological axes in Parkinson's disease.

4.1 ROS Scavenging and Antioxidant Defense

Withania somnifera, Bacopa monnieri, Ginkgo biloba, Curcuma longa, and Piper nigrum—all possess effective antioxidant characteristics thru distinct mechanisms [42]. Reactive oxygen species (ROS) are without delay scavenged via ginkgo's curcumin, bacosides, and flavonoids, but glutathione peroxidase [43], catalase, and superoxide dismutase (SOD) are greater by using withanolides and piperine.

This multi-stage antioxidant defence prevents the excessive ROS generated by means of PD [44]'s broken mitochondria and dopamine metabolism.

4.2 Stabilization of Mitochondria

By maintaining membrane potential, boosting ATP synthesis, and safeguarding complex I activity [45], withania and ginkgo both promote mitochondrial function. Curcumin inhibits cytochrome c release and stops mitochondrial enlargement [46]. This is essential since PD pathogenesis is largely caused by the suppression of mitochondrial complex I.

4.3 Neuroinflammation Modulation

One of the formulation's best features is its anti-inflammatory synergy. NF- κ B and cytokines such as TNF- α and IL-1 β [47] are inhibited by curcuma longa and Withania somnifera. Ginkgo biloba regulates glial cell activation [48], while piperine further suppresses the production of CRP and COX-2.

Suppressing this route may lessen the severity of symptoms and halt the progression of the disease, as chronic inflammation plays a substantial role in neurodegeneration in Parkinson's disease.

4.4 Enhancement of Dopaminergic Neurotransmission

Dopamine levels are positively impacted by a number of components:

- Bacopa monnieri inhibits MAO-B [49] and increases dopamine receptors.
- Piper nigrum raises synaptic dopamine and decreases dopamine metabolism.[50]
- Ginkgo biloba promotes the production and turnover of dopamine[51]

When combined, these processes improve bradykinesia, tremors, and rigidity [52] and restore dopaminergic signaling.

5. Synergy between phytochemicals

In addition to dopamine depletion, neurodegenerative illnesses such as Parkinson's involve oxidative stress, mitochondrial failure, neuroinflammation, protein misfolding, and synaptic dysfunction. As a result, single-target treatments frequently fall short. The network pharmacology paradigm, in which each phytochemical affects many nodes in the neurodegenerative web [53], is consistent with PhytoPark Syrup's multi-target approach.

5.1 Synergy across Targets

Significant overlap in neuroprotective targets is revealed by a comparative study of the main phytoconstituents:

These medications target oxidative stress, neuroinflammation, protein misfolding, apoptosis, and neurotransmission [54], which are at least five interrelated pathways in Parkinson's disease.

6. A Comparative Study of Standard PD Therapeutics and PhytoPark

6.1 Therapies Based on Levodopa

Because it can pass the blood-brain barrier and restore dopamine, levodopa continues to be the mainstay of PD treatment. But it has a number of long-term disadvantages:

- Chronic usage leads to the development of motor fluctuations and dyskinesia's [55].
- Because it ignores the underlying neurodegeneration [56], it cannot stop the course of the disease.
- ROS burden [57] can be exacerbated by oxidative stress resulting from dopamine metabolism.

Conversely, PhytoPark includes phytochemicals such as Curcuma, Bacopa, and Withania that:

- Increase dopamine production and receptor sensitivity (not only replacement),
- Reduce oxidative stress and neuroinflammation,
- Show neurorestorative effects instead of symptomatic ones [58].

6.2 MAO-B Inhibitors, such as Rasagiline and Selegiline

These medications increase dopamine availability by preventing its breakdown. However, they are not very effective in advanced PD.

May result in hypertensive crises, hallucinations, and insomnia [59].

In contrast, Bacopa and Piper nigrum provide synaptic repair and broader antioxidant benefits in addition to natural MAO-B inhibition [60].

6.3 Dopamine agonists, such as pramipexole and ropinirole

These are useful in the early stages of Parkinson's disease (PD), but they can also cause adverse effects such as nausea, hypotension, and problems with impulse control.

Additionally, they lack oxidative and inflammatory components and are neurochemically unique.

Dopamine and oxidative pathways are impacted by PhytoPark herbs, providing all-encompassing multi-target support [61].

6.4 Anticholinergics and Amantadine

Mostly used for dyskinesias and tremors

In older PD patients, anticholinergics can exacerbate cognitive symptoms [62].

Amantadine may cause edema in the ankles and hallucinations.

None of the ingredients in PhytoPark affect cognitive function; on the contrary, ginkgo, bacopa, and withania improve mood and neurocognition [63].

7. Conclusion

A multi-targeted, phyto-adaptogenic formulation that shows great therapeutic promise for neurodegenerative diseases, especially Parkinson's disease (PD), is PhytoPark Syrup. Withania somnifera, Bacopa monnieri, Curcuma longa, Ginkgo biloba, and Piper nigrum are all strategically combined in its design, which has its roots in Ayurveda and has been improved by contemporary pharmacological discoveries.

Each of these botanicals delivers evidence-backed neuroprotective, antioxidant, anti-inflammatory, and cognitive-enhancing effects. Additionally, adding piperine improves the bioavailability of phytochemicals that are poorly absorbed, such as curcumin, resulting in a synergistic pharmacokinetic profile that is uncommon in traditional formulations.

REFERENCES

1. Kulkarni, S. K., & Dhir, A. (2008). Withania somnifera: An Indian ginseng. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 32(5), 1093–1105.
2. Andrade, C., Aswath, A., Chaturvedi, S. K., Srinivasa, M., & Raguram, R. (2000). A double-blind, placebo-controlled evaluation of the anxiolytic efficacy Withania somnifera in generalized anxiety disorder. *Indian J Psychiatry*, 42(3), 295.
3. Kumar, V., & Khanum, F. (2012). Neuroprotective potential of phytochemicals. *Pharmacognosy Reviews*, 6(12), 81–90.
4. Uddin, M. S., et al. (2020). Exploring the promise of Withania somnifera for neurodegenerative diseases. *Frontiers in Pharmacology*, 11, 566728.
5. Singh, R. H., & Udupa, K. N. (1993). Clinical and experimental studies on the anti-stress and immunomodulatory effects of Ashwagandha. *J Res Ayurveda Siddha*, 14, 107–114.
6. Calabrese, C., et al. (2008). Effects of a standardized Bacopa monnieri extract on cognitive performance. *J Altern Complement Med*, 14(6), 707–713.
7. Peth-Nui, T., et al. (2012). Effects of 12-week Bacopa monnieri extract on cognition. *J Ethnopharmacol*, 141(1), 793–799.

8. Bhattacharya, S. K., Bhattacharya, A., Kumar, A., & Ghosal, S. (2000). Anti-oxidant activity of *Bacopa monnieri*. *Phytother Res*, 14(7), 568–570.
9. Russo, A., & Borrelli, F. (2005). *Bacopa monniera*: a reputed nootropic plant. *J Ethnopharmacol*, 99(3), 353–360.
10. Roodenrys, S., et al. (2002). Chronic effects of an extract of *Bacopa monniera* on cognitive function. *Psychopharmacology*, 156(4), 481–484.
11. Aggarwal, B. B., & Harikumar, K. B. (2009). Potential therapeutic effects of curcumin. *Biochem Pharmacol*, 76(11), 1590–1611.
12. Prasad, S., Gupta, S. C., Tyagi, A. K., & Aggarwal, B. B. (2014). Curcumin, a component of golden spice: From bedside to bench and back. *Biotechnol Adv*, 32(6), 1053–1064.
13. Shishodia, S., Sethi, G., & Aggarwal, B. B. (2005). Curcumin: getting back to the roots. *Ann N Y Acad Sci*, 1056, 206–217.
14. Wang, R., Li, Y., & Tsang, C. K. (2022). Curcumin attenuates mitochondrial dysfunction in Parkinson's models. *Free Radical Biol Med*, 189, 315–328.
15. Pan, J., et al. (2020). Curcumin suppresses microglial inflammation and mitochondrial dysfunction. *J Neuroinflammation*, 17(1), 7.
16. Smith, J. V., & Luo, Y. (2003). Elevation of oxidative free radicals in Alzheimer's disease. *Ann N Y Acad Sci*, 993(1), 76–86.
17. Kumar, A., et al. (2016). *Ginkgo biloba*: A traditional herbal medicine. *J Ethnopharmacol*, 194, 94–114.
18. Weinmann, S., Roll, S., Schwarzbach, C., Vauth, C., & Willich, S. N. (2010). Effects of *Ginkgo biloba* in dementia. *BMC Geriatrics*, 10, 14.
19. Yang, G., et al. (2016). A systematic review of the effect of *Ginkgo biloba* on cognitive function. *J Ethnopharmacol*, 187, 1–9.
20. Diamond, B. J., & Bailey, M. R. (2013). *Ginkgo biloba*: indications, mechanisms, and safety. *Psychiatr Clin North Am*, 36(1), 73–83.
21. Mashayekh, A., et al. (2011). The effect of *Ginkgo biloba* on cerebral blood flow. *Neurochem Res*, 36(6), 1154–1160.
22. Atal, C. K., et al. (1985). Bioenhancers: Revolutionizing therapeutic outcomes. *Indian J Pharm Sci*, 47(4), 209–212.
23. Srinivasan, K. (2007). Black pepper and its pungent principle-piperine: A review. *Crit Rev Food Sci Nutr*, 47(8), 735–748.
24. Pradeep, C. R., & Kuttan, G. (2004). Piperine modifies plasma antioxidant levels. *J Nutr Biochem*, 15(6), 333–340.
25. Shaikh, J., et al. (2009). Enhanced bioavailability of curcumin via piperine. *Int J Pharm*, 374(1–2), 155–161.
26. Bano, G., Raina, R. K., Zutshi, U., Bedi, K. L., & Johri, R. K. (1991). Effect of piperine on bioavailability of drugs. *Indian J Exp Biol*, 29(4), 339–341.
27. Tiwari, V., & Kuhad, A. (2016). Synergistic effects of curcumin and piperine in a PD model. *Mol Neurobiol*, 53(7), 4719–4729.
28. Xicoy, H., et al. (2019). Midbrain dopaminergic neurons differentiation. *J Neurosci Methods*, 311, 73–83.
29. Connolly, B. S., & Lang, A. E. (2014). Pharmacological treatment of Parkinson's disease. *Neurotherapeutics*, 11(1), 60–68.
30. Dauer, W., & Przedborski, S. (2003). Parkinson's disease: mechanisms and models. *Neuron*, 39(6), 889–909.
31. Henchcliffe, C., & Beal, M. F. (2008). Mitochondrial biology in Parkinson's disease. *Mov Disord*, 23(6), 784–792.
32. Jenner, P. (2003). Oxidative stress in Parkinson's disease. *Ann Neurol*, 53(S3), S26–S36.
33. Dias, V., Junn, E., & Mouradian, M. M. (2013). The role of oxidative stress in Parkinson's disease. *J Parkinsons Dis*, 3(4), 461–491.
34. Schapira, A. H. (2008). Mitochondria in the etiology and pathogenesis of Parkinson's disease. *Lancet Neurol*, 7(1), 97–109.
35. Surmeier, D. J., Guzman, J. N., & Sanchez-Padilla, J. (2010). Calcium, mitochondrial dysfunction and aging in dopaminergic neurons. *Cell Calcium*, 47(2), 175–182.
36. Tamtaji, O. R., et al. (2019). Clinical evidence for neuroprotective effects of herbal agents in Parkinson's disease. *J Clin Neurosci*, 60, 1–7.
37. Kaur, T., et al. (2021). Phytochemicals in neurodegenerative disorders. *Neurochem Int*, 142, 104927.
38. Kumar, S., et al. (2017). Phytochemicals targeting neuroinflammation in Parkinson's. *Neurochem Res*, 42(4), 954–971.
39. Subramaniam, S. R., & Chesselet, M. F. (2013). Mitochondrial dysfunction and oxidative stress in Parkinson's. *Neurobiol Dis*, 51, 1–10.
40. Devi, L., & Anandatheerthavarada, H. K. (2010). Mitochondrial trafficking in neurodegeneration. *Biochim Biophys Acta*, 1802(1), 80–91.
41. Hritcu, L., et al. (2015). *Withania somnifera* extract improves memory in scopolamine-treated rats. *Cell Mol Neurobiol*, 35(4), 491–498.
42. Kumar, D., et al. (2020). Protective role of *Bacopa monnieri* in Parkinson's disease model. *Metab Brain Dis*, 35(5), 727–738.
43. Singh, A., et al. (2016). Curcumin nanocarriers in neuroprotection. *J Drug Deliv Sci Technol*, 36, 107–118.
44. Wightman, E. L., et al. (2015). *Ginkgo biloba* effects on mood and cognition. *Hum Psychopharmacol Clin Exp*, 30(1), 14–22.
45. Srinivasan, K. (2005). Role of spices in health. *Nutrition Research Reviews*, 18(1), 1–16.
46. Varghese, P., et al. (2013). Piperine improves cognitive function in Alzheimer model. *J Alzheimers Dis*, 36(3), 699–709.
47. Wadhwa, R., et al. (2016). Ayurvedic adaptogens in neurodegenerative disorders. *Curr Pharm Des*, 22(22), 3281–3290.
48. Purushothaman, A., et al. (2022). Plant-based adaptogens: Mechanisms and pharmacology. *Phytother Res*, 36(5), 2121–2135.
49. Vijayakumar, S., & Surya, D. (2020). Ayurveda and modern pharmacology. *J Tradit Complement Med*, 10(4), 371–376.
50. Choudhary, N., et al. (2017). Herbal neuroprotectives in PD. *J Ethnopharmacol*, 197, 214–221.
51. Cass, H. (2004). Natural supplements for neurological health. *Altern Ther Health Med*, 10(1), 22–28.
52. Gaire, B. P., & Subedi, L. (2021). Medicinal plants in neurodegenerative diseases. *J Ethnopharmacol*, 274, 113664.
53. Gopi, S., et al. (2017). Curcumin bioavailability: Issues and solutions. *Drug Metab Rev*, 49(1), 35–47.
57. Mishra, L. C., Singh, B. B., & Dagenais, S. (2001). Ayurveda review. *J Altern Complement Med*, 7(1), 77–95.
58. Liu, Q., et al. (2017). Mitochondrial protection by plant polyphenols. *Nutr Neurosci*, 20(5), 343–351.
59. Patil, C. R., et al. (2014). *Ashwagandha's* anti-Parkinsonian activity. *Phytomedicine*, 21(4), 614–621.
60. Tan, L., et al. (2014). Herbal medicine for Alzheimer's disease. *Mol Neurobiol*, 50(2), 507–519.
61. Dey, A., & Mukherjee, A. (2021). Natural products in neurological disorders. *Future Med Chem*, 13(7), 579–601.
62. Panda, S., & Kar, A. (1997). Antioxidant activity of *Withania somnifera*. *Indian J Exp Biol*, 35(3), 236–239.
63. Rao, N. V., et al. (2007). Cognitive effects of *Bacopa* extract. *Indian J Psychiatry*, 49(3), 208–212.