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Review Article

A Review article on Mechanistic Insight into Neuroprotection by Natural Antioxidants in Parkinson's Disease

Tamanna Khokher*, Parveen Kumar

Department. of Pharmacy, Jagannath University, Jaipur, India

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ABSTRACT

Parkinson's Disease (PD) is a neurodegenerative disorder characterized by progressive loss of dopaminergic neurons and decreased dopamine levels in the brain. The main contributing causes of the disease are oxidative stress, mitochondrial dysfunction, neuro-inflammation, α-synuclein accumulation and apoptosis. Treatments like Levodopa relieve the symptoms but do not prevent neuronal degeneration. Natural antioxidants obtained from food and herbal plants are important due to their antioxidant, anti-inflammatory, anti-apoptotic, and neuroprotective effects. There are compounds that have neuroprotective effects in laboratory models by decreasing oxidative stress and improving antioxidant defense. Examples include Curcumin, Resveratrol, Quercetin, EGCG, Vitamin C, and Vitamin E. However, their clinical use is limited due to poor bioavailability and inability to cross the blood brain barrier. Advanced delivery techniques may be used in future approaches

INTRODUCTION

Parkinson's disease (PD) is a progressive neurological disorder resulting from the death of dopamine-producing cells and decreased dopamine production within the brain. PD causes various motor symptoms like tremors, rigidity, slow movements, and postural imbalance, along with non-motor manifestations including mood disorders, sleep disorders, fatigue, and cognitive decline. Various factors like oxidative stress, mitochondrial defects, neuroinflammation, alpha-synuclein protein accumulation, and apoptosis contribute significantly to the progression of Parkinson's disease. Existing treatment methods like Levodopa can only provide temporary relief and are incapable of preventing nerve cell death. Therefore, natural antioxidants found in food sources and plants have been extensively researched to assess their neuroprotective, antioxidant, anti-inflammatory, and mitochondrial-preserving activities in managing PD. Various natural antioxidants like curcumin, resveratrol, quercetin, EGCG, vitamin C, and

***Corresponding Author:** Tamanna Khokher
Address: *Department. of Pharmacy, Jagannath University, Jaipur, India*
Email : tamannakhokher8386@gmail.com

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vitamin E have exhibited considerable neuroprotective properties in experimental research studies. They aid in mitigating oxidative stress, enhancing mitochondrial functionality, controlling inflammation, and safeguarding nerve cells from damage. Natural antioxidants have emerged as potent therapeutic support agents in the management of Parkinson's disease.

2. PATHOPHYSIOLOGY OF PARKINSON'S DISEASE

- The pathophysiology of Parkinson's disease is complex and involves multiple interrelated processes that result in neuronal degeneration
- **Oxidative Stress:** Too much production of reactive oxygen species (ROS) leads to damage of lipids, proteins, DNA and mitochondria. Dopamine metabolism produces free radicals, and dopaminergic neurons are highly vulnerable.
- **Mitochondrial Dysfunction:** Mitochondria dysfunction leads to reduced ATP synthesis and increased ROS formation, thus causing neuronal injury and cell death.
- **Neuroinflammation:** Inflammatory cytokines are released by activated microglia, including TNF-α, IL-1β, and IL-6, which can promote inflammation and accelerate the degeneration of neurons. All of these activities work together to support the development of Parkinson's disease.

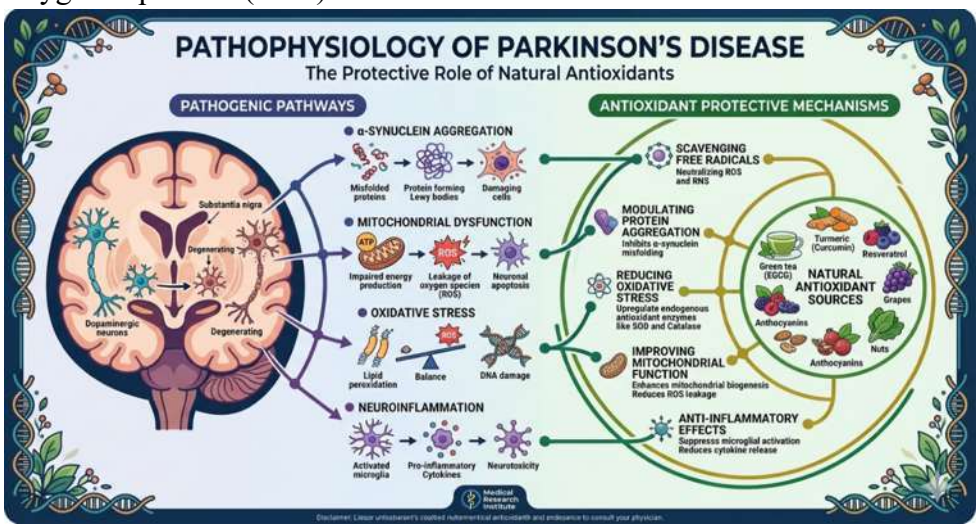

Figure 1. pathophysiology of Parkison's disease

3. NATURAL ANTIOXIDANTS

a. Resveratrol

- Found in grapes
- Activates SIRT1 pathway
- Reduces oxidative stress Quercetin
- Strong antioxidant and anti-inflammatory properties

b. Epigallocatechin Gallate (EGCG)

- Found in green tea
- Reduces neuroinflammation and oxidative damage

c. Vitamin E

- Lipid-soluble antioxidant
- Prevents lipid peroxidation

4. MECHANISMS OF NEUROPROTECTION BY NATURAL ANTIOXIDANTS

a. Free Radical Scavenging

- Natural antioxidants neutralize ROS and reduce oxidative stress.

b. Activation of Nrf2 Pathway

- Enhances antioxidant enzyme production
- Protects neurons from oxidative damage

c. Inhibition of NF-κB Pathway

- Reduces inflammation
- Suppresses cytokine release

d. Mitochondrial Protection

- Maintains mitochondrial integrity
- Improves ATP production

e. Anti-apoptotic Effects

- Prevents neuronal cell death
- Regulates Bcl-2 and caspase pathways

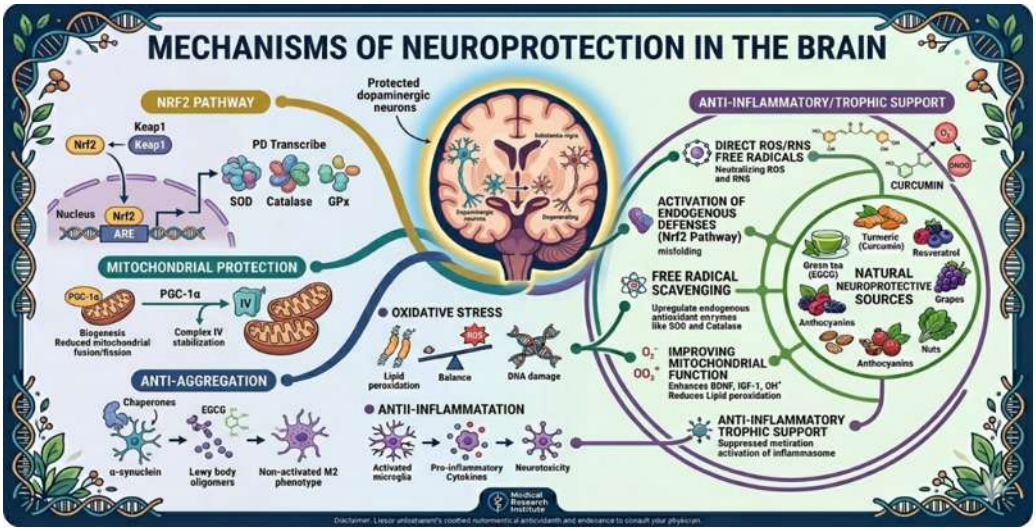

Figure 2. mechanism of neuroprotection in brain

5. EXPERIMENTAL AND CLINICAL EVIDENCE

a. Experimental Evidence

Experimental studies show that natural antioxidants such as resveratrol, quercetin, and EGCG protect neurons by reducing oxidative stress, inhibiting α-synuclein aggregation, and improving motor function in animal models. Their action includes free radical scavenging, Nrf2 activation, and anti-inflammatory effects..

b. Clinical Evidence

Clinical evidence is limited, but it suggests that Vitamin E, green tea (EGCG), and resveratrol may help lower disease risk and slow progression.

6. CONCLUSION

Natural antioxidants have shown significant potential in neuroprotection in Parkinson's disease via targeting multiple pathological mechanisms such as oxidative stress, mitochondrial dysfunction, and neuroinflammation. They include compounds such as resveratrol, quercetin, EGCG, and vitamin E, which help in reducing neuronal damage and improving cellular defense

systems. There is overwhelming experimental evidence in support of their effectiveness, and although the clinical evidence is limited, it is positive. These antioxidants act through pathways like free radical scavenging and induction of endogenous antioxidant systems. Poor bioavailability, and lack of large-scale clinical trials, among other factors, are still issues despite the encouraging results. Therefore, further researches are required to validate their therapeutic potential. Besides, enhanced drug delivery systems and formulation mechanisms may improve on the potency of these natural compounds. This approach of natural antioxidants, in combination with conventional therapies, could act synergistically to slow down the disease progression. Also, future studies should focus on personalized treatment approaches based on biomarkers. Overall, natural antioxidants may work well as adjuncts in the management of Parkinson's disease.

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