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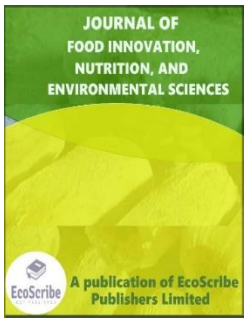

REVIEW ARTICLE

Neuroprotective Potential of Seed Oils and Selected Edible Plant Oils in Parkinson's Disease: Mechanisms, Preclinical Evidence, and Translational Perspectives

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ABSTRACT

Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder and is characterized by progressive loss of dopaminergic neurons, α-synuclein aggregation, neuroinflammation, and oxidative stress. Current treatments provide symptomatic relief but do not halt disease progression and are associated with adverse effects. This review evaluates preclinical evidence on the neuroprotective potential of seed and selected plant oils in PD and summarizes their proposed mechanisms of action.

Methods: A literature search was conducted using PubMed/MEDLINE, Web of Science, Scopus, ScienceDirect, Embase, Cochrane Library, and Google Scholar. Studies published between 2000 and 2025 investigating seed oils, plant oils, or their bioactive constituents in relation to PD were considered. Twenty-one studies met the inclusion criteria, comprising 16 preclinical studies, two human intervention studies with cognitive outcomes, and three review articles included for background information.

Results: The reviewed oils targeted multiple pathogenic pathways associated with PD. Reported effects included reduced oxidative stress through increased SOD, CAT, and GSH activities and decreased ROS and MDA levels, suppression of neuroinflammation via inhibition of NF-κB, COX-2, TNF-α, IL-1β, and IL-6, protection of dopaminergic neurons in the substantia nigra, and reduced α-synuclein aggregation in selected studies. Gut-brain axis modulation was reported only for perilla oil. Flaxseed and Nigella sativa oils demonstrated the most consistent neuroprotective effects across rotenone and 6-OHDA models, whereas evidence for perilla, sesame, marula, castor, and coconut oils remains limited. **Conclusion:** Seed and selected plant oils show promise as neuroprotective agents in PD. Further pharmacokinetic, safety, and dose optimization studies are required before clinical translation. Flaxseed and Nigella sativa oils appear to be the strongest candidates for early-phase clinical trials.

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1. INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder and the second most common neurodegenerative disorder worldwide after Alzheimer's disease, affecting approximately 10 million individuals worldwide (GBD 2016 Parkinson's Disease Collaborators, 2018). The global burden of PD has more than doubled over the past 25 years, partly attributable to ageing populations, heightened disease awareness, and improved diagnostic criteria (GBD 2016 Parkinson's Disease Collaborators, 2018). In sub-Saharan Africa, epidemiological data remain scarce, but emerging evidence suggests a non-trivial prevalence that is likely underdiagnosed (Dotchin *et al*., 2008). The prevalence of PD increases steeply with age, affecting approximately 1–3% of individuals aged 65 years and older and rising to 4–5% in those above 85 years (de Lau & Breteler, 2006; Alexander, 2004).

The hallmark pathological features of PD include the progressive loss of dopaminergic neurons within the substantia nigra pars compacta (SNpc), resulting in striatal dopamine depletion, and the intraneuronal accumulation of misfolded α-synuclein protein in the form of Lewy bodies and Lewy neurites (Spillantini *et al*., 1997; Braak *et al*., 2003). Motor manifestations such as bradykinesia, resting tremor, rigidity, and postural instability arise predominantly from nigrostriatal dopaminergic dysfunction (Rodriguez-Oroz *et al*., 2009). Non-motor symptoms, including cognitive impairment, autonomic dysfunction, sleep disturbances, anosmia, and depression, frequently antedate or accompany motor decline and significantly impair quality of life (Chaudhuri *et al*., 2006).

The aetiopathogenesis of PD is multifactorial and involves a complex interplay of genetic and environmental factors. Pathogenic mutations in genes encoding α-synuclein (SNCA), leucine-rich repeat kinase 2 (LRRK2), Parkin (PARK2), PTEN-induced kinase 1 (PINK1), and DJ-1 have been identified in familial PD cases, while environmental toxins such as rotenone, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), and paraquat recapitulate key PD features in experimental models (Schapira & Jenner, 2011; Przedborski, 2017). Core pathological mechanisms include: (i) mitochondrial dysfunction with impaired complex I activity and reduced adenosine triphosphate (ATP) production; (ii) oxidative and nitrosative stress from elevated reactive oxygen species (ROS) and reactive nitrogen species (RNS); (iii) neuroinflammation driven by activated microglia and astrocytes releasing pro-inflammatory cytokines; (iv) impairment of the ubiquitin–proteasome system and autophagy–lysosomal pathway leading to toxic protein accumulation; and (v) mitochondrial-associated apoptosis (Guo *et al*., 2018; Kouli *et al*., 2018).

Current standard-of-care pharmacotherapy for PD centres on dopamine replacement strategies, principally levodopa combined with peripheral decarboxylase inhibitors (carbidopa or benserazide), dopamine agonists (pramipexole, ropinirole, rotigotine), catechol-O-methyltransferase (COMT) inhibitors, and monoamine oxidase-B (MAO-B) inhibitors (Factor & Weiner, 2008). While these agents provide symptomatic relief, they do not arrest neurodegeneration; long-term levodopa therapy is associated with motor fluctuations and dyskinesias, and none of the approved agents has demonstrated convincing disease-modifying activity (Olanow & Schapira, 2013). This therapeutic gap motivates intense research into neuroprotective strategies that target the underlying pathophysiological processes.

Dietary bioactive compounds have attracted growing interest as candidate neuroprotective agents owing to their multi-target profiles, relative safety, low cost, and cultural acceptability across diverse populations (Balakrishnan et al., 2021). Seed oils are particularly compelling as they are rich in polyunsaturated fatty acids (PUFAs), particularly omega-3 (α-linolenic acid; ALA) and omega-6 (linoleic acid; LA) fatty acids, as well as tocopherols, phenolic compounds, lignans, phytosterols, and carotenoids, although the concentration of these minor bioactives varies considerably by oil type, cultivar, and processing method, and refined oils generally retain substantially fewer of them than cold-pressed preparations (Senila *et al*., 2020; Arbex *et al*., 2015). Several of these oils have long histories of use in traditional medicine systems in Africa and Asia, and emerging molecular studies provide plausible mechanistic underpinnings for their purported neuroprotective effects.

A synthesis of the mechanistic and preclinical evidence for seed oils specifically in PD is lacking. Previous reviews have examined omega-3 fatty acids broadly or individual oils in isolation, but a comparative, mechanism-oriented evaluation of multiple seed oils in the context of PD pathophysiology has not, to our knowledge, been undertaken; this impression is based on the search strategy described in Section 2.1 rather than on a dedicated review-of-reviews search. This narrative review addresses that gap by: (i) summarising the composition and bioactivities of key seed oils and selected non-seed plant oils considered alongside them in this literature; (ii) critically evaluating preclinical evidence from in vitro and in vivo PD models; (iii) delineating the molecular mechanisms underlying proposed neuroprotective effects; and (iv) identifying translational gaps and priorities for future clinical research. This work is intended to inform both basic researchers and clinicians exploring adjunct nutritional strategies for PD management.

2. METHODS

2.1 Search Strategy

Primary databases searched included PubMed/MEDLINE, Web of Science, Scopus, ScienceDirect, Embase, and the Cochrane Library. Additional grey literature was retrieved from Google Scholar. The search was conducted in April 2025, and re-run in July 2026 during revision to capture more

recent publications. No language restriction was applied at the search stage: records in languages other than English were screened by title and abstract alongside English-language records, but none was judged eligible at full-text review, so only English-language articles were ultimately included. For each database, search terms from three concept blocks were combined using the following Boolean structure, adapted to the field tags and controlled vocabulary (MeSH in PubMed; Emtree in Embase) of each platform: ("seed oil" OR "plant oil" OR "vegetable oil" OR "flaxseed oil" OR "linseed oil" OR "sesame oil" OR "Sesamum indicum" OR "marula oil" OR "Sclerocarya birrea" OR "Nigella sativa" OR "black seed oil" OR "thymoquinone" OR "castor oil" OR "Ricinus communis" OR "perilla seed oil" OR "Perilla frutescens" OR "coconut oil" OR "omega-3" OR "alpha-linolenic acid") AND ("Parkinson's disease" OR "parkinsonism" OR "dopaminergic neuron" OR "substantia nigra" OR "Lewy body" OR "α-synuclein") AND ("neuroprotection" OR "oxidative stress" OR "neuroinflammation" OR "dopamine" OR "antioxidant" OR "apoptosis" OR "mitochondria" OR "motor function"). For Google Scholar, results were sorted by relevance and the first 200 records were screened by title and abstract; records beyond this threshold were not reviewed, and this cut-off is stated here for reproducibility.

2.2 Study Selection Criteria

Studies were included if they: (i) investigated seed oils, selected non-seed edible plant oils, or their primary bioactive compounds (e.g., ALA, thymoquinone, sesamin, ricinoleic acid, lauric acid, rosmarinic acid) in the context of PD or relevant models; (ii) employed in vitro cell culture systems, preclinical animal models (rotenone, 6-OHDA, MPTP, manganese, malathion), or clinical/observational human studies; (iii) reported at least one PD-relevant outcome (motor behaviour, dopaminergic neuronal count, α-synuclein levels, oxidative stress markers, or inflammatory markers); and (iv) were published between January 2000 and April 2025. Studies were excluded if they: used synthetic analogues without reference to the parent seed oil; were review articles without original experimental data (retained, where cited, only for background or mechanistic context and explicitly identified as secondary sources at the point of citation — they are not counted among, and are not presented as equivalent to, the primary evidence summarised in Table 2); or were conference abstracts without peer-reviewed full-text publications, with the single exception of one conference abstract (Hashimoto *et al*., 2017) that is retained explicitly as background on human perilla oil tolerability and is labelled as a conference abstract wherever cited. See **Table 1** for complete selection criteria.

Table 1. Study Selection Criteria for This Narrative Review

Criterion	Inclusion	Exclusion
Study design	Preclinical in vivo (rodent models), in vitro cell culture, clinical/observational human studies	Conference abstracts only (except where explicitly retained as labelled background, Section 2.2); letters; non-peer-reviewed articles
Intervention	Seed oils, selected non-seed plant oils, or their characterised bioactive constituents (e.g., ALA, thymoquinone, sesaminol, ricinoleic acid, lauric acid, rosmarinic acid)	Synthetic analogues without reference to parent seed oil; multi-ingredient formulations without isolatable seed oil data
Disease model	Established PD models: 6-OHDA, rotenone, MPTP, manganese, malathion; α-synuclein overexpression cell lines; clinical PD cohorts	Non-PD neurological models unless mechanism is directly translatable
Outcomes	Motor behaviour, dopaminergic neuron count, TH immunoreactivity, α-synuclein aggregation, oxidative stress markers, inflammatory markers, mitochondrial function	Studies reporting outcomes unrelated to neuroprotection or neurodegeneration
Publication date	January 2000–April 2025	Studies published before 2000 (except highly cited foundational studies)
Language	English	Non-English studies (none identified as eligible at full-text stage)

2.3 Data Extraction and Quality Appraisal

Data were extracted independently by two authors (OOO and OPA) using a standardised form capturing: study design, biological model used, seed oil type and dose, duration of treatment, route of administration, comparator, primary outcomes, key mechanistic findings, and reference details. Discrepancies were resolved by consensus. Methodological quality of the fourteen animal and cell-based preclinical studies was appraised using a structured checklist adapted from the ARRIVE 2.0 reporting items (Percie du Sert *et al*., 2020), covering randomisation, blinding, sample-size justification, sex of animals, dose, route, and duration (**Table 2A**).

Table 2A. Structured Quality/Reporting Appraisal of Preclinical Studies (ARRIVE 2.0-Informed)

Study	Randomisation reported	Blinding reported	Sample-size justification	Sex reported	Route	Duration
Shallie *et al*. (2017a)	NR	NR	NR	Male and female	Oral	14 days
Shallie *et al*. (2017b)	NR	NR	NR	Male and female	Oral	14 days
Mahnoor *et al*. (2025)	NR	NR	NR	NR	NR	NR
Kaji *et al*. (2020)	N/A (in vitro)	NR	N/A	N/A	N/A	N/A
Ramazani *et al*. (2023)	N/A (in vitro)	NR	N/A	N/A	N/A	N/A
Sarawi *et al*. (2024)	NR	NR	NR	NR	NR (oral)	12 weeks
Alshaman *et al*. (2023)	NR	NR	NR	Male	Oral	NR
Sedaghat *et al*. (2014)	NR	NR	NR	NR	Oral	3 doses / 24 h intervals (short pre-treatment)
Haxhiu et al. (2025)	NR	NR	NR	NR	NR	NR
Faried *et al*. (2025)	NR	NR	NR	NR	NR	NR
Hosseini *et al*. (2022)	N/A (in vitro)	NR	N/A	N/A	N/A	N/A
Uzzan *et al*. (2024)	NR	NR	NR	NR	NR	Chronic (duration NR)
Yousefsani *et al*. (2024)	NR	NR	NR	NR	Oral	NR
Techaniyom *et al*. (2024)	NR	NR	NR	Male	Dietary	28 days
Ibrahim & El-Sayed (2020)	NR	NR	NR	NR	NR	NR

NR = not reported in the published source at the level of detail available to this review; N/A = not applicable (in vitro study).

3. PHYTOCHEMICAL COMPOSITION AND BIOACTIVITIES OF SEED OILS

Seed oils are complex lipidic matrices whose biological activities are determined by their fatty acid profiles, minor lipid constituents, and associated phytochemicals. Omega-3 fatty acids, particularly ALA (18:3n-3) are precursors to the longer-chain eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3), which are essential components of neuronal membranes and substrates for the biosynthesis of specialised pro-resolving lipid mediators (resolvins, protectins, maresins) that dampen neuroinflammation (Serhan, 2014). The ratio of omega-6 to omega-3 fatty acids in the Western diet has shifted markedly towards pro-inflammatory omega-6 predominance; seed oils rich in ALA in particular may help redress this imbalance, whereas oils dominated by linoleic acid (omega-6) would not be expected to do so and may in some contexts widen it further (Simopoulos, 2016). Beyond fatty acids, seed oils contain diverse phenolic antioxidants, fat-soluble vitamins, and sterols that independently modulate redox homeostasis, inflammatory signalling, and cell survival pathways relevant to neurodegeneration (**Figure 1**).

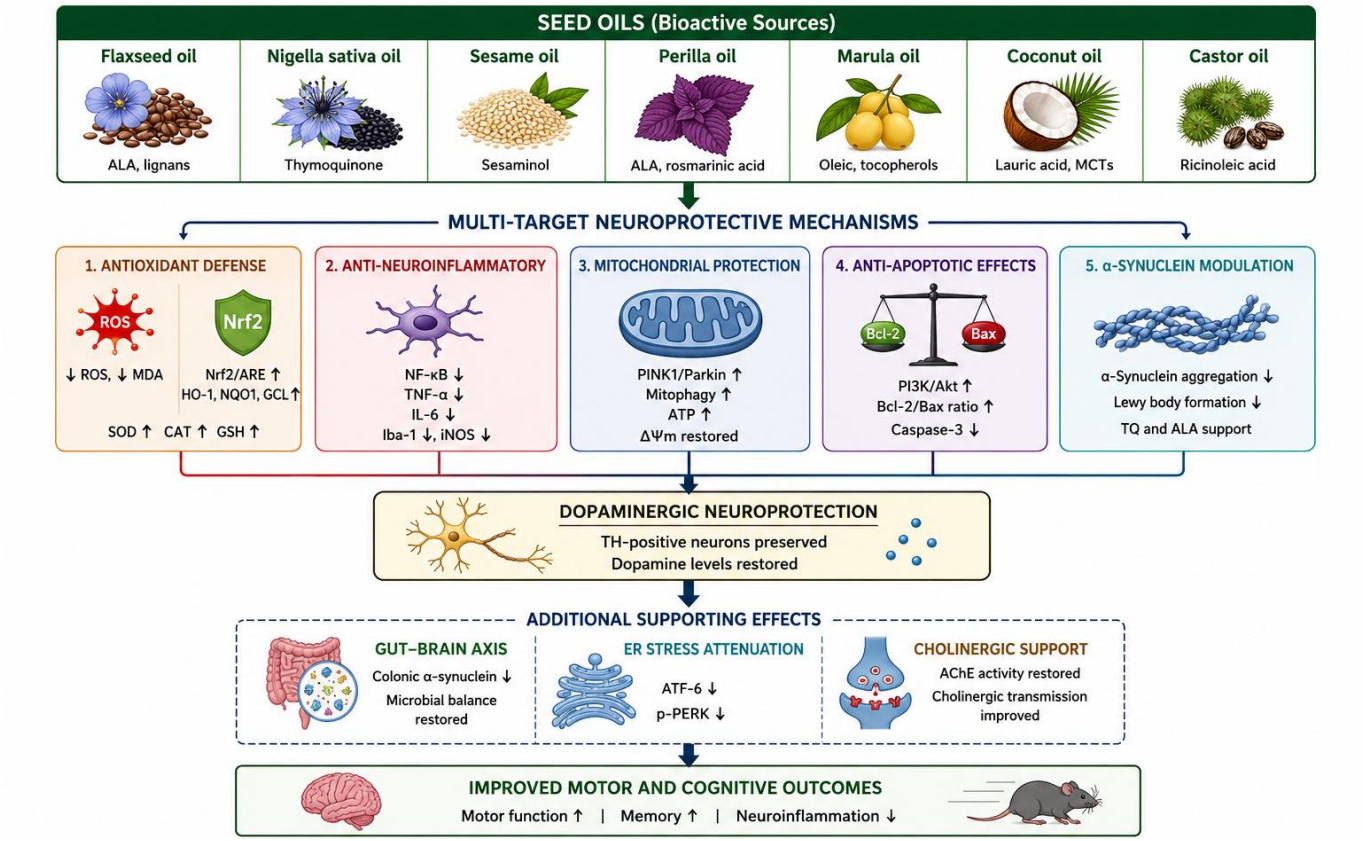

Fig. 1. Schematic overview of the molecular mechanisms by which seed oil bioactive constituents have been reported to exert neuroprotective effects in Parkinson's disease. Seed oils and their principal bioactives target multiple nodes of PD pathophysiology: oxidative stress (via Nrf2/ARE activation and direct radical scavenging), neuroinflammation (via NF-κB and COX-2 inhibition), mitochondrial dysfunction (via ketogenesis and mitophagy), apoptosis (via Bax/Bcl-2 modulation and PI3K/Akt activation), and α-synuclein aggregation. ALA, alpha-linolenic acid; TQ, thymoquinone; ARE, antioxidant response element; SOD, superoxide dismutase; GSH, glutathione; MDA, malondialdehyde; ROS, reactive oxygen species; TH, tyrosine hydroxylase; SNpc, substantia nigra pars compacta.

4. INDIVIDUAL SEED OILS: PRECLINICAL EVIDENCE AND MECHANISMS

4.1 Flaxseed Oil (Linum usitatissimum)

Flaxseed oil is derived from the seeds of *Linum usitatissimum* L. and is the richest terrestrial plant source of ALA, comprising 45–60% of total fatty acids (Mueed *et al*., 2022; Jahan *et al*., 2024). Other constituents include linoleic acid (15–18%), oleic acid (18–20%), and bioactive lignans, predominantly secoisolariciresinol diglucoside (SDG) which are converted by gut microbiota to the mammalian lignans enterodiol and enterolactone, exhibiting antioxidant and phytoestrogenic properties (Imran *et al*., 2024). Whole flaxseed, as distinct from flaxseed oil, is also a rich source of dietary fibre and plant-based protein with bioactive peptides that inhibit calmodulin-dependent neuronal nitric oxide synthase (nNOS), reducing nitric oxide overproduction implicated in neuroinflammation (Omoni & Aluko, 2006); fibre and protein are not meaningful constituents of the extracted oil itself and this distinction is maintained throughout this section.

4.1.1 Preclinical Evidence

Shallie *et al*. (2017a, 2017b) conducted two studies demonstrating the neuroprotective efficacy of flaxseed oil in rotenone-induced murine PD models. Rotenone, a mitochondrial complex I inhibitor, produces dopaminergic neurodegeneration recapitulating key PD pathology. Flaxseed oil supplementation significantly attenuated rotenone-induced neuronal derangements in both the cerebellum and striatum, with histological preservation of Purkinje cell architecture and reduced microglial activation. As with most of the preclinical literature summarised in this review (**Table 2A**), these two reports do not state whether animals were randomised or investigators blinded to treatment allocation, and this should be borne in mind when weighing their findings. More recently, Mahnoor *et al*. (2025) reported that ALA, the principal omega-3 constituent of flaxseed oil mitigated neuroinflammation and dopaminergic neuronal loss in a 6-OHDA rat model through combined in vivo and in silico approaches, including docking analysis suggestive of affinity for tyrosine hydroxylase (TH) and NF-κB regulatory nodes; as with other in silico findings discussed in this review, these docking results are computational predictions and have not been confirmed by

direct binding assays. Zanwar et al. (2023) is a general narrative review of flaxseed in disease prevention rather than a primary source of rodent neurotoxin data. In vitro, ALA and SDG have independently suppressed lipopolysaccharide (LPS)-induced microglial activation and decreased pro-inflammatory cytokine production, corroborating anti-neuroinflammatory potential (Al-Madhagy, 2023).

4.1.2 Mechanisms of Action

Flaxseed oil has been proposed to exert neuroprotective effects through several converging mechanisms. ALA and its elongated metabolites (EPA and DHA) are incorporated into neuronal membrane phospholipids, a property with plausible relevance to membrane fluidity and receptor function relevant to dopaminergic neurotransmission (Al-Madhagy, 2023). Omega-3 PUFAs have been reported to suppress NF-κB nuclear translocation, with associated downregulation of pro-inflammatory genes encoding TNF-α, IL-1β, IL-6, and inducible nitric oxide synthase (iNOS) (Imran *et al*., 2024). Flaxseed lignans are reported to activate the Nrf2/ARE (nuclear factor erythroid 2-related factor 2/antioxidant response element) pathway, with associated upregulation of cytoprotective genes including heme oxygenase-1 (HO-1), NAD(P)H quinone oxidoreductase-1 (NQO1), and glutamate–cysteine ligase (GCL) (a mechanism discussed generally for flaxseed lignans by Zanwar et al., 2023, rather than demonstrated specifically in a PD model). In whole flaxseed rather than the oil, flaxseed protein hydrolysates inhibit calmodulin, reducing nNOS-mediated nitric oxide synthesis and attenuating nitrosative stress (Omoni & Aluko, 2006). Collectively, these mechanisms would be expected to reduce oxidative and inflammatory neurotoxic burdens, though direct evidence that they do so specifically via flaxseed oil in PD models remains limited to the two Shallie *et al*. reports and the Mahnoor *et al*. study above.

4.2 Sesame Seed Oil (Sesamum indicum)

Sesame oil is extracted from the seeds of *Sesamum indicum* L. (Family: Pedaliaceae) and is among the oldest and most widely used edible oils in Asia and the Middle East. Its fatty acid composition is characterised by high levels of linoleic acid (40–50%) and oleic acid (30–43%), with the remainder comprising palmitic, stearic, and minor unsaturated acids (Jeng & Hou, 2005; Sarawi *et al*., 2024). The distinctive neuroprotective properties attributed to sesame oil are largely associated with its lignan constituents, principally sesamin, sesamolin, and sesaminol (and their triglucoside derivatives) which undergo extensive enterohepatic cycling to produce metabolites reported to have antioxidant, anti-inflammatory, and antiapoptotic activities (Kaji *et al*., 2020; Ramazani *et al*., 2023). Sesame oil also contains significant amounts of γ-tocopherol and δ-tocopherol, conferring additional antioxidant capacity.

4.2.1 Preclinical Evidence

Kaji *et al*. (2020) provided in vitro evidence that sesaminol, a major sesame lignan, protects dopaminergic PC12 cells from 6-OHDA-induced neurotoxicity by activating the Nrf2/ARE pathway. Ramazani *et al*. (2023) demonstrated that sesame seed extract and its isolated lignan fractions (sesamin and sesamolin) protect PC12 cells against 6-OHDA-induced apoptosis, reducing caspase-3 activation, cytochrome c release, and Bax/Bcl-2 ratio, markers of intrinsic apoptosis. In an in vivo model of manganese-induced parkinsonism, Sarawi *et al*. (2024) reported that daily supplementation with sesame oil for 12 weeks was associated with protection of rats from Mn-induced neurotoxicity, including improved locomotor activity, reduced oxidative stress biomarkers (MDA, protein carbonyl), enhanced antioxidant enzyme activities (SOD, CAT, GPx), decreased pro-inflammatory cytokines (TNF-α, IL-6), and suppressed endoplasmic reticulum (ER) stress markers (ATF-6, phosphorylated PERK) with restoration of the Bax/Bcl-2 balance towards the anti-apoptotic state. As with the flaxseed studies above, none of these three reports specifies randomisation or blinding (Table 2A).

4.2.2 Mechanisms of Action

Sesame oil's proposed neuroprotective mechanisms operate at multiple molecular levels. Sesaminol has been reported to scavenge superoxide, hydroxyl, and DPPH radicals in vitro, consistent with a role in reducing ROS-mediated oxidative damage to lipids, proteins, and DNA (Kaji *et al*., 2020). Nrf2 pathway activation by sesaminol is reported to upregulate antioxidant response genes (HO-1, NQO1, thioredoxin). Sesame oil has been reported to suppress microglial NF-κB activation, reducing mRNA expression of IL-6 and iNOS in LPS-activated BV2 microglia (Sarawi *et al*., 2024). The reduction in ER stress markers (ATF-6, p-PERK) indicates that sesame oil may also attenuate the unfolded protein response (UPR), which is increasingly recognised as a contributor to dopaminergic neuronal death in PD. Restoration of the Bax/Bcl-2 balance and reduced caspase-3 activity are consistent with antiapoptotic activity through the mitochondria-dependent intrinsic pathway.

4.3 Marula Oil (Sclerocarya birrea)

Marula oil is extracted from the seed kernels of *Sclerocarya birrea* (A.Rich.) Hochst. (Family: Anacardiaceae), a tree indigenous to sub-Saharan Africa with significant ethnobotanical and nutritional importance (Kamanula *et al*., 2022). The kernel oil is characterised by a high oleic acid content (70–78%), followed by stearic (5–8%) and linoleic (3–6%) acids, conferring excellent oxidative stability (Komane *et al*., 2015; Alshaman *et al*., 2023). The unsaponifiable fraction is rich in tocopherols (predominantly α-tocopherol), phytosterols, and triterpene alcohols. These oil-fraction constituents are distinct from the whole marula fruit, whose pulp and peel contain polyphenols, flavonoids, condensed tannins, and pectin with antioxidant and anti-

inflammatory activities reported by Chauke *et al*. (2025); because the fruit-extract evidence in Chauke *et al*. concerns constituents that are not present in the extracted seed kernel oil, it is presented below as separate, indirect evidence rather than as marula oil evidence. Marula oil has traditionally been used for cosmetic, skin-care, and wound-healing purposes; its potential therapeutic role in neurodegeneration has only recently been explored.

4.3.1 Preclinical Evidence

Alshaman *et al*. (2023) evaluated a formulated marula oil nanoemulsion in experimental parkinsonism. In a rotenone-induced mouse model of PD using male albino mice assigned to vehicle, PD, PD + marula oil, and PD + marula nanoemulsion groups, oral administration of marula oil or its nanoemulsion was associated with improved locomotor and motor coordination parameters (open-field, cylinder tests), reduced striatal MDA and pro-inflammatory cytokines (TNF-α, IL-1β), and elevated antioxidant markers. Exact dosing, treatment duration, and randomisation/blinding procedures were not extractable from the published abstract and summary data available to this review and are marked "not reported" in Table 2A; readers requiring these details should consult the primary source directly. Histopathological evaluation reportedly showed preserved dopaminergic neuron counts in the SNpc with maintained tyrosine hydroxylase (TH) expression. The nanoemulsion formulation was reported to enhance bioavailability compared with the crude oil. Separately, and as fruit-extract rather than seed-oil evidence, the polyphenol-rich fraction of marula fruit has demonstrated radical scavenging (DPPH, ABTS) and iron-chelating activities in cell-free assays (Chauke *et al*., 2025), which is presented here only as indirect supporting context for antioxidant plausibility and not as marula oil evidence.

4.3.2 Mechanisms of Action

Marula oil's proposed neuroprotective effects would plausibly reflect its combined antioxidant and anti-inflammatory phytochemical constituents. Tocopherols and vitamin E homologues intercept lipid peroxidation chain reactions, a mechanism consistent with reduced MDA formation reported by Alshaman *et al*. (2023). Flavonoids and oleic acid may attenuate NF-κB-mediated inflammatory gene transcription. Anti-inflammatory linoleic acid metabolites may additionally serve as competitive substrates for COX-2 and lipoxygenase pathways. The high oleic acid content may further contribute through modulation of membrane lipid microdomains and sphingolipid metabolism, with a theoretical, as yet untested, link to α-synuclein membrane association and aggregation dynamics.

4.4 Nigella sativa Oil

Nigella sativa L. (black cumin; Family: Ranunculaceae) is an annual herbaceous plant native to the Mediterranean basin, Southwest Asia, and North Africa, with centuries of use in Unani, Ayurvedic, and Islamic traditional medicine (Khazdair, 2015; Mariod, 2022). The fixed (expressed) seed oil constitutes 32–40% of seed weight and is dominated by linoleic acid (50–60%), oleic acid (20–25%), and palmitic acid (11–14%), with minor amounts of stearic, myristic, and arachidic acids; this fixed oil is distinct from the volatile (essential) oil fraction, which is present in much smaller quantity and is where thymoquinone (TQ) is concentrated. Reported ranges for TQ therefore refer to its proportion within the volatile oil (up to 30–48%), not within the fixed oil as a whole, and the two fractions should not be conflated. TQ is a benzoquinone monoterpene with extensive preclinical evidence for antioxidant, anti-inflammatory, immunomodulatory, and neuroprotective activities (Uddin *et al*., 2021; Gawas *et al*., 2023). Additional bioactives include thymohydroquinone, thymol, carvacrol, α-hederin, nigellidine, and γ-tocopherol.

4.4.1 Preclinical Evidence

Sedaghat *et al*. (2014) demonstrated TQ neuroprotection in the unilateral intrastriatal 6-OHDA rat model. Pre-treatment with TQ (5 and 10 mg/kg orally, three doses at 24-hour intervals) was associated with reduced apomorphine-induced contralateral rotations, a behavioural index of nigrostriatal denervation and fewer signs of neuronal loss in the SNpc by stereological counting. TQ pre-treatment lowered midbrain homogenate MDA and nitrite levels and was associated with partial restoration of SOD activity. Haxhiu et al. (2025) reported similar findings in an MPTP-induced mouse model, with *N. sativa* administration associated with reduced motor impairment, dopamine depletion, and neuronal degeneration in the striatum. Faried *et al*. (2025) reported, using histological and immunohistochemical analysis, that *N. sativa* oil was associated with preserved neuronal architecture in the frontal cortex and hippocampus in a rotenone-induced rat model, with maintained TH immunoreactivity. Hosseini *et al*. (2022) reported, in vitro, that *N. sativa* oil shifted LPS-induced microglial polarisation away from the M1 pro-inflammatory phenotype and toward the M2 anti-inflammatory phenotype. Uzzan *et al*. (2024) reported that chronic *N. sativa* oil treatment was associated with reduced brain inflammatory markers in a rat neuroinflammation model relevant to neuropsychiatric and neurodegenerative comorbidities, rather than a PD model specifically, and is presented here as supportive but indirect evidence.

4.4.2 Mechanisms of Action

TQ has been proposed to act through a broad mechanistic repertoire (Uddin *et al*., 2021; Gawas *et al*., 2023). As a direct antioxidant, TQ has been reported to scavenge superoxide, hydrogen peroxide, hydroxyl, and peroxynitrite radicals. It has been reported to activate the Nrf2/ARE pathway, with associated upregulation of HO-1, NQO1, glutathione peroxidase (GPx), and superoxide dismutase 2 (SOD2). TQ has been reported to inhibit COX-2 expression and suppress NF-κB translocation. Downstream, TQ has been reported to inhibit the pro-apoptotic JNK/ERK signalling cascade,

activate the PI3K/Akt–BDNF pro-survival pathway, and promote mitophagy, the selective autophagic degradation of dysfunctional mitochondria. TQ also has anticholinesterase activity reported in vitro and has been reported to inhibit β-secretase (BACE1) in preclinical models, of potential relevance to the cognitive comorbidities of PD. TQ has also been reported to reduce α-synuclein aggregation burden in preclinical models, consistent with evidence that oxidative stress promotes synuclein misfolding and Lewy body formation (Wei *et al*., 2022; Dong *et al*., 2021).

4.5 Castor Oil (Ricinus communis)

Castor oil is derived from the seeds of *Ricinus communis* L. (Family: Euphorbiaceae), a tropical shrub with broad ethnomedicinal use across Africa and Asia. The oil is unique in its extraordinarily high content of ricinoleic acid (12-hydroxy-9-octadecenoic acid; 85–90%), an 18-carbon hydroxy fatty acid not found in appreciable quantities in any other natural oil (Subramaniyan, 2020; Aslam *et al*., 2024). Ricinoleic acid has been reported to possess anti-inflammatory activity through antagonism of prostaglandin E2 and activation of specific prostanoid receptor subtypes. The remainder of castor oil comprises oleic acid (~3%), linoleic acid (~4%), stearic acid (~1%), and minor phytochemicals including flavonoids, terpenoids, and alkaloids.

4.5.1 Preclinical Evidence

Yousefsani *et al*. (2024) evaluated castor oil in malathion-induced neurobehavioural toxicity, an organophosphate model with only indirect relevance to pesticide-associated parkinsonism, rather than a standard PD model such as 6-OHDA, rotenone, or MPTP. Malathion administration elevated cerebral MDA, TNF-α, and IL-6 levels while reducing GSH and acetylcholinesterase (AChE) activity, producing spatial memory deficits and motor impairment. Oral castor oil supplementation was associated with dose-dependent reversal of these neurochemical and behavioural deficits. Javed *et al*. (2023) is a review of carvacrol, a phenolic monoterpene reported in some plant sources including castor plant tissue; carvacrol is not established as a principal constituent of castor seed oil itself at biologically meaningful concentrations, and this review does not treat carvacrol evidence as evidence for castor oil. Overall, given the indirect neurotoxin model used by Yousefsani *et al*. and the absence of a direct, PD-model-based demonstration of castor oil efficacy, castor oil is treated in this review as a preliminary candidate with the weakest supporting evidence among the seven oils considered.

4.5.2 Mechanisms of Action

Castor oil's proposed neuroprotective effects are primarily attributed to ricinoleic acid-mediated mechanisms. Ricinoleic acid has been reported to reduce oxidative stress by increasing intracellular GSH biosynthesis and decreasing MDA production. It has been reported to suppress microglial NF-κB activation, reducing TNF-α and IL-6 transcription and secretion (Yousefsani *et al*., 2024). Ricinoleic acid's hydroxyl group may confer direct radical scavenging capacity, and its structural similarity to arachidonic acid may allow competitive modulation of eicosanoid biosynthetic enzymes. Castor oil has been reported to modulate AChE activity, of potential relevance to cholinergic transmission deficits in PD (Subramaniyan, 2020), but this remains a general pharmacological observation rather than PD-specific evidence.

Table 2 provides a summary of seed oils and selected plant oils and their reported associations with neuroprotective outcomes in preclinical models of Parkinson's disease.

Table 2. Summary of Seed Oils and Selected Plant Oils and Their Reported Associations with Neuroprotective Outcomes in Preclinical Models of Parkinson's Disease

Oil	Principal Bioactive Compounds	PD Model	Key Reported Findings	Principal Proposed Mechanism(s)	Reference(s) / Evidence Type
Flaxseed oil (*Linum usitatissimum*)	ALA (45–60%), lignans (SDG), omega-6 FA	Rotenone (mice); 6-OHDA (rats, in silico)	Attenuated cerebellar/striatal derangements; reduced MDA/ROS; restored SOD/CAT/GSH (randomisation/blinding not reported)	Nrf2/ARE activation; NF-κB suppression; membrane lipid modulation	Shallie *et al*. (2017a,b); Mahnoor *et al*. (2025) — primary. Zanwar et al. (2023) — secondary/review, background only

Oil	Principal Bioactive Compounds	PD Model	Key Reported Findings	Principal Proposed Mechanism(s)	Reference(s) / Evidence Type
Sesame seed oil (*Sesamum indicum*)	Linoleic acid (40–50%), sesaminol, sesamin, sesamolin, γ-tocopherol	Mn-induced parkinsonism (rats); 6-OHDA (PC12 cells, in vitro)	Improved locomotor activity; reduced MDA, ER-stress markers; restored Bax/Bcl-2 (randomisation/blinding not reported)	Nrf2/ARE activation; ER-stress attenuation; NF-κB suppression	Sarawi *et al*. (2024); Kaji *et al*. (2020); Ramazani *et al*. (2023) — all primary
Marula oil (*Sclerocarya birrea*)	Oleic acid (70–78%), α-tocopherol, phytosterols	Rotenone (mice) — nanoemulsion formulation	Improved motor coordination; reduced striatal MDA, TNF-α, IL-1β; preserved TH-positive neurons (dose/duration not reported)	Antioxidant scavenging; NF-κB-mediated cytokine suppression	Alshaman *et al*. (2023) primary (marula seed oil). Chauke *et al*. (2025) — secondary, fruit-extract only, not oil evidence
Nigella sativa oil	Thymoquinone (TQ) in the volatile fraction; linoleic and oleic acid in the fixed oil	6-OHDA (rats); MPTP (mice); rotenone (rats)	Reduced apomorphine-induced rotations; preserved SNpc neurons; lowered MDA/nitrite; restored SOD (randomisation/blinding not reported)	Direct ROS scavenging; Nrf2/ARE induction; NF-κB/COX-2 inhibition; PI3K/Akt–BDNF activation	Sedaghat *et al*. (2014); Haxhiu et al. (2025); Faried *et al*. (2025); Hosseini *et al*. (2022); Uzzan *et al*. (2024) — all primary; Uzzan is a neuroinflammation, not PD, model
Castor oil (*Ricinus communis*)	Ricinoleic acid (85–90%)	Malathion-induced neurotoxicity (rats) — indirect PD relevance	Decreased MDA, TNF-α, IL-6; elevated GSH and AChE activity (indirect neurotoxin model, not a standard PD model)	Antioxidant GSH upregulation; NF-κB-mediated cytokine suppression	Yousefsani *et al*. (2024) — primary, indirect model. Javed *et al*. (2023), carvacrol — not treated as castor oil evidence in this review
Perilla seed oil (*Perilla frutescens*)	ALA (55–65%), rosmarinic acid, luteolin, quercetin	Rotenone (male C57BL/6 mice) — gut–brain axis assessment	Reduced colonic/cerebral α-synuclein; suppressed Iba-1 microglial activation; preserved TH neurons; 28-day dietary co-administration (randomisation/blinding not reported)	COX-2/NF-κB inhibition; gut–brain axis modulation (proposed, not established)	Techaniyom *et al*. (2024) — primary. Hashimoto *et al*. (2017, conference abstract) and (2022) — human, cognition, indirect relevance

Oil	Principal Bioactive Compounds	PD Model	Key Reported Findings	Principal Proposed Mechanism(s)	Reference(s) / Evidence Type
Coconut oil (*Cocos nucifera*), virgin — not a conventional seed oil (Section 4.7)	Lauric acid (47–52%), myristic acid (16–21%), α-tocopherol	Rotenone (rats); 6-OHDA (neuronal cell lines)	Improved motor coordination and grip strength; reduced MDA/H2O2; elevated SOD/CAT/GPx (randomisation/blinding not reported)	MCT ketogenesis (proposed bypass of complex I dysfunction); ROS scavenging	Ibrahim & El-Sayed (2020) — primary. Deepika *et al*. (2024) — secondary review, background only

4.6 Perilla Seed Oil (Perilla frutescens)

Perilla seed oil is extracted from the seeds of *Perilla frutescens* (L.) Britt. (Family: Lamiaceae), an annual herb cultivated extensively in East and Southeast Asia and used in culinary and traditional medicine contexts (Negi *et al*., 2011; Ahmed, 2018). Perilla seed oil has the highest ALA content of any commercially available vegetable oil, comprising 55–65% of total fatty acids, followed by linoleic acid (14–18%) and oleic acid (12–18%) (Kurowska *et al*., 2003). The seed also contains diverse polyphenolic compounds including rosmarinic acid, luteolin, quercetin, caffeic acid, catechin, and ferulic acid, reported to have antioxidant and anti-inflammatory bioactivities (Ahmed, 2018). Phytosterols, tocopherols, and squalene further enrich the seed's bioactive profile.

4.6.1 Preclinical Evidence

Techaniyom *et al*. (2024) conducted a comprehensive evaluation of cold-pressed perilla seed oil in a rotenone-induced murine PD model incorporating gut–brain axis assessment. Male C57BL/6 mice receiving rotenone (2 mg/kg/day subcutaneous for 28 days) and co-administered perilla seed oil at low (5%), medium (10%), or high (20%) dietary concentrations showed dose-dependent findings. High-dose perilla seed oil was associated with decreased COX-2 expression in both colonic and nigral tissue, suppressed Iba-1-positive microglial activation in the SNpc and hippocampus, reduced colonic and cerebral α-synuclein accumulation, and preserved TH-immunoreactive dopaminergic neurons in the SNpc. Motor function (rotarod, open-field, pole tests) and non-motor parameters (novel object recognition, olfactory discrimination) were reported as improved. Hashimoto *et al*. (2017), a conference abstract, and Hashimoto *et al*. (2022), a peer-reviewed randomised trial, both report cognitive outcomes of perilla oil supplementation in healthy elderly Japanese individuals; neither study involved a PD population or a PD-relevant endpoint, and both are presented here strictly as indirect human tolerability and cognition data, not as translational PD evidence. Animal studies have further reported that ALA-enriched diets are associated with reduced hippocampal neuroinflammation and cognitive deficits in ageing rodents (Lee *et al*., 2012).

4.6.2 Mechanisms of Action

The proposed neuroprotective mechanisms of perilla seed oil reflect its ALA content and polyphenolic composition. High ALA intake has been reported to elevate brain DHA levels, with a plausible role in reducing neuroinflammatory eicosanoid precursor availability and promoting the biosynthesis of resolvins and protectins (Serhan, 2014; Kurowska *et al*., 2003). ALA and its metabolites have been reported to suppress COX-2 expression. Rosmarinic acid and other perilla polyphenols have been reported to inhibit NF-κB and MAPK inflammatory signalling, with documented suppression of Iba-1 microglial activation markers in the single study available (Techaniyom *et al*., 2024). The reduction of α-synuclein accumulation in both colonic tissue and the CNS in this one study is an interesting finding, but the suggestion that perilla oil modulates prion-like α-synuclein propagation via the enteric nervous system–vagal–CNS route should be regarded as a hypothesis generated by a single study rather than an established mechanism; it awaits replication before being treated as demonstrated. Perilla polyphenols have also been reported to activate Nrf2 and SIRT1 pathways in other, non-PD contexts (Ahmed, 2018).

4.7 Coconut Oil (Cocos nucifera)

As noted in **Section 2.2**, coconut oil is not conventionally classified as a seed oil in the same sense as flaxseed, sesame, castor, perilla, or *Nigella sativa* oils. It is extracted from the flesh (copra) or the fresh kernel of *Cocos nucifera* L. (Family: Arecaceae) and is the predominant edible oil in South and Southeast Asian countries. Virgin coconut oil (VCO), obtained by cold-pressing fresh coconut meat without refining, is distinguished from refined, bleached, and deodorised (RBD) coconut oil by its intact content of phenolic antioxidants, vitamin E (predominantly α-tocopherol), and phytosterols (Ibrahim & El-Sayed, 2020). Coconut oil's fatty acid profile is predominantly saturated (>90%), with lauric acid (C12:0) constituting 47–52%, followed by myristic acid (C14:0; 16–21%) and palmitic acid (C16:0; 8–10%). Lauric and myristic acid are medium-chain fatty acids and are metabolised largely as such, conferring distinct hepatic beta-oxidation kinetics relative to long-chain saturated fatty acids; however, this description should not be over-generalised to the whole saturated fraction of coconut

oil. Palmitic acid, which makes up 8–10% of the oil, is a long-chain saturated fatty acid and does not share the rapid-oxidation, ketogenic profile of lauric and myristic acid, and myristic acid itself is intermediate in chain length and metabolic behaviour between the classic medium-chain triglycerides (C6–C10) and palmitic acid. The resulting ketone bodies (beta-hydroxybutyrate, acetoacetate) from the medium-chain fraction can cross the blood–brain barrier (BBB) and serve as alternative neuronal energy substrates, of potential relevance given the impaired mitochondrial energy metabolism reported in PD neurons (Dayrit, 2015; Deepika *et al*., 2024).

4.7.1 Preclinical Evidence

Ibrahim & El-Sayed (2020) investigated the effects of virgin coconut oil in rotenone-treated rats, reporting improvements in motor coordination (rotarod), grip strength, and locomotor activity, accompanied by reduced oxidative stress markers (MDA, H_2O_2) and elevated antioxidant enzymes (SOD, CAT, GPx). Dopaminergic neuron preservation was reported histologically with maintained TH immunostaining in the SNpc, although randomisation and blinding were not reported.

4.7.2 Mechanisms of Action

The proposed neuroprotective mechanisms of coconut oil in PD are mechanistically distinct from those of the other reviewed oils by virtue of its medium-chain, ketogenic metabolism. Lauric and myristic acid undergo comparatively rapid hepatic beta-oxidation yielding ketone bodies that can penetrate the BBB independently of glucose transporters, providing a theoretical alternative bioenergetic substrate that has been proposed to circumvent mitochondrial complex I dysfunction, the central bioenergetic lesion in PD (Deepika *et al*., 2024). Ketone body metabolism has been proposed to generate acetyl-CoA via the TCA cycle without producing the excessive superoxide that characterises impaired complex I electron transport. Beyond energetics, VCO phenolics have been reported to suppress NF-κB activation and reduce pro-inflammatory cytokines (TNF-α, IL-6), while tocopherols and polyphenols are reported to scavenge lipid peroxyl and hydroxyl radicals directly. VCO has also been reported to attenuate ceramide-mediated and Ca^{2+}-mediated apoptotic pathways in neuronal cells. Table 3 summarises the fatty acid profiles of the major oils reviewed.

Table 3. Fatty Acid Profiles of Seed Oils and Selected Plant Oils Reviewed

Oil	ALA (18:3n-3) %	LA (18:2n-6) %	OA (18:1n-9) %	Palmitic (16:0) %	Stearic (18:0) %	Source of values
Flaxseed oil	45–60	15–18	18–20	4–6	2–4	Mueed *et al*. (2022); Jahan *et al*. (2024)
Sesame seed oil	<1	40–50	30–43	8–11	4–7	Jeng & Hou (2005)
Marula oil	Trace	3–6	70–78	6–8	5–8	Komane *et al*. (2015)
Nigella sativa oil (fixed oil)	Trace	50–60	20–25	11–14	2–3	Khazdair (2015); Mariod (2022)
Castor oil	Trace	4–6	2–4	0.5–1	<1	Subramaniyan (2020)
Perilla seed oil	55–65	14–18	12–18	6–8	1–3	Kurowska *et al*. (2003)
Coconut oil (VCO)	Trace	1–2	5–8	8–10	2–4	Dayrit (2015)

ALA, alpha-linolenic acid; LA, linoleic acid; OA, oleic acid; VCO, virgin coconut oil. Values are approximate ranges. Trace = <1%

.5. DISCUSSION

This review synthesises a still-emerging body of preclinical evidence suggesting that seed oils and selected plant oils may exert neuroprotective effects relevant to PD pathophysiology across multiple experimental models and through diverse proposed molecular mechanisms. The convergence of antioxidant, anti-inflammatory, antiapoptotic, and neurorestorative actions across structurally distinct phytochemicals is notable and raises the possibility that these naturally occurring lipidic mixtures could engage with the multifactorial pathogenesis of PD more comprehensively than single-target synthetic agents, although this remains a hypothesis rather than a demonstrated clinical advantage, since no head-to-head comparison with single-target agents exists in this literature.

Among the reviewed oils, flaxseed oil and *Nigella sativa* oil have the most extensive and relatively consistent evidence across multiple experimental PD models identified in this review. The identification of ALA and TQ as principal bioactive constituents, respectively, provides tractable leads for further mechanistic dissection and dose–response characterisation, although the small number of independent research groups working on each oil, and the absence of any cross-model replication by an independent laboratory for most of the studies in Table 2, both limit how much confidence can currently be placed in these findings. The wide mechanistic repertoire reported for TQ, spanning direct antioxidant activity, Nrf2/ARE induction, NF-κB suppression, PI3K/Akt activation, mitophagy promotion, and α-synuclein modulation, is notable, and positions *N. sativa*

oil as a reasonable priority for translational investigation, though this remains a preclinical, not clinical, evidence base.

Perilla seed oil is a candidate of interest among the less extensively studied oils, given its ALA content and the single available finding of Techaniyom *et al*. (2024) implicating gut–brain axis modulation in its reported neuroprotective effects. The reduction of colonic α-synuclein accumulation alongside central dopaminergic protection is broadly consistent with the Braak staging hypothesis of PD pathology initiating in the enteric nervous system and propagating retrogradely to the CNS via vagal afferents (Braak *et al*., 2003), but this remains a single-study observation and should be described as hypothesis-generating rather than established.

Coconut oil's proposed ketogenic mechanism is mechanistically distinct from the other reviewed oils and may be relevant to the bioenergetic deficits in PD neurons, although coconut oil's inclusion in this review at all rests on the scope justification given rather than on its being a conventional seed oil. The appeal of an alternative energy substrate that bypasses complex I dysfunction is conceptually interesting, though the predominantly saturated fatty acid composition of coconut oil raises potential cardiovascular safety concerns with long-term high-dose consumption that warrant careful clinical evaluation (Dayrit, 2015). The apparently greater reported effect of VCO, enriched in polyphenols compared with refined coconut oil has been suggested to indicate that the non-lipid bioactive fraction may make a substantial contribution to neuroprotection beyond the ketogenic mechanism alone, though this comparison has not been tested directly within a single PD study in this review's evidence base.

Limitations

A critical analysis of the preclinical literature summarised in Table 2 and appraised in Table 2A reveals several methodological limitations that temper translational enthusiasm, and that are worth stating plainly rather than only in general terms. First, the majority of studies employed single neurotoxin models (6-OHDA, rotenone, MPTP, manganese, or, for castor oil, malathion, a model with only indirect PD relevance), each of which recapitulates specific but incomplete aspects of human PD pathology. None of the fourteen preclinical studies appraised in Table 2A used more than one PD model for the same oil; cross-model validation is therefore, at present, absent from this literature rather than merely limited. Second, dosing parameters across studies varied considerably and were rarely informed by pharmacokinetic data; allometric scaling to human equivalent doses was seldom performed. Third, where sex of animals was reported at all (two of fifteen preclinical studies, Table 2A), only male animals were used, whereas epidemiological evidence indicates sex differences in PD susceptibility and progression (Wooten *et al*., 2004). Fourth, most studies evaluated short-term treatment over weeks rather than months. Fifth, bioavailability and brain penetration of seed oil bioactives were rarely measured directly; the observed benefits may partly reflect systemic anti-inflammatory effects rather than direct CNS action. Sixth, none of the primary preclinical studies summarised in Table 2 reported a negative or null finding for the oil under investigation. Because published preclinical pharmacology is known to be subject to publication and selective-reporting bias, this uniformly positive pattern should be interpreted cautiously rather than as evidence that these oils are reliably effective across all conditions tested. The adoption of nanoemulsion formulation for marula oil (Alshaman *et al*., 2023) represents a promising approach to bioavailability enhancement that could reasonably be extended to other oils with limited membrane permeability.

From a clinical translational perspective, several additional considerations warrant emphasis. The complexity of seed oils as natural mixtures introduces challenges for standardisation, quality control, and dose definition that differ fundamentally from single-molecule drug development. Geographical, agricultural, and processing variations in seed oil composition mean that composition–outcome relationships established for a specific product may not generalise to commercially available preparations. Interactions between seed oil bioactives and standard PD pharmacotherapy (particularly levodopa, MAO-B inhibitors) have not, to our knowledge, been systematically characterised and would need to be before large-scale trials are undertaken, given the concurrent use of these agents in real-world patient populations. The potential for lipid-soluble bioactives to modulate cytochrome P450 enzyme activities warrants dedicated pharmacokinetic investigation. Furthermore, the safety and tolerability of chronic high-dose seed oil supplementation, including hepatic effects, gastrointestinal tolerability, and bleeding risk with high omega-3 intake requires dedicated evaluation in the target PD population, which is typically elderly with multiple comorbidities and polypharmacy.

Given these caveats, the accumulated preclinical evidence is sufficient to justify further preparatory clinical work for the most promising oils, but not yet sufficient to justify moving directly to phase II efficacy trials as previously proposed in this manuscript. A more conservative and, we believe, more defensible sequence would begin with pharmacokinetic, safety, dose-finding, and feasibility studies in small human cohorts, particularly for flaxseed oil and *Nigella sativa* oil, which have the broadest existing safety record in human populations and the most consistent preclinical signal identified in this review before biomarker-validated, placebo-controlled phase II randomised controlled trials (plasma and CSF α-synuclein, neuroimaging with DaTSCAN, MDS-UPDRS, and inflammatory biomarker panels) are considered. For oils with more preliminary or indirect evidence, including castor oil and coconut oil, we would regard even pilot dose-finding trials as premature ahead of further preclinical replication. Collaborative international consortia, drawing on institutions with existing PD cohorts and expertise in neurodegenerative clinical trials would accelerate this agenda. Figure 2 shows the proposed neuroprotective mechanisms of selected seed oil constituents

targeting dopaminergic neuronal survival pathways in Parkinson's disease.

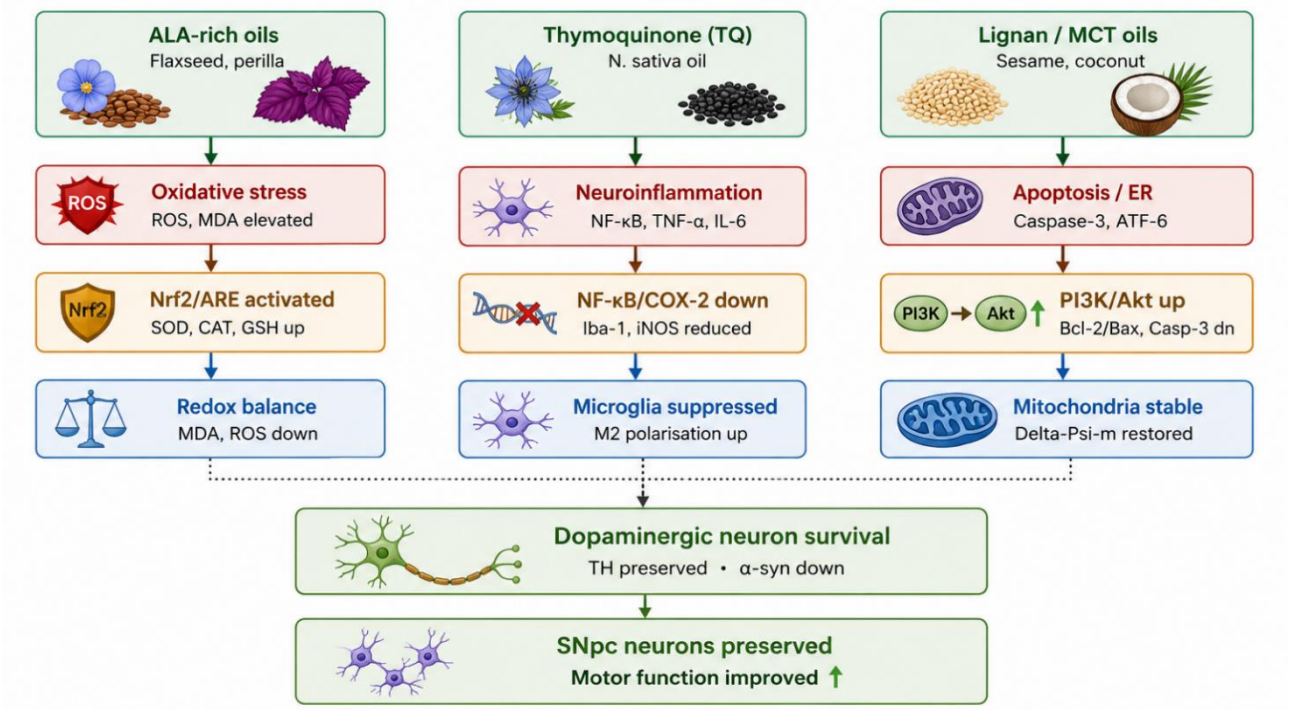

Fig. 2. Schematic representation of reported and proposed neuroprotective mechanisms of selected seed oil constituents targeting dopaminergic neuronal survival pathways in Parkinson's disease.

CONCLUSION

Seed oils and selected plant oils represent a biologically plausible and mechanistically diverse class of candidate neuroprotective agents with preclinical evidence of biological activity in experimental PD models, though this evidence is preclinical, heterogeneous in quality, and, for some oils, indirect. Flaxseed oil and *Nigella sativa* oil have the most robust and mechanistically well-characterised preclinical profiles among the oils reviewed here. Perilla seed oil's gut–brain axis finding, coconut oil's ketogenic mechanism, and sesame oil's ER-stress modulation are each supported by a small number of studies and should be regarded as promising leads rather than established mechanisms. Castor oil currently has the weakest and most indirect support of the seven oils considered and is not recommended for prioritisation ahead of the others.

The path from preliminary preclinical data to evidence-based clinical application requires addressing critical translational gaps: cross-model validation, pharmacokinetic characterisation with human bioavailability data, sex-stratified studies, standardisation of oil composition and dosing, investigation of drug interactions, and, in time, well-designed RCTs with clinically validated endpoints, preceded by the safety and dose-finding work. The relative affordability, cultural familiarity, and broad dietary safety data for several of these oils provide practical advantages over many synthetic neuroprotective candidates in the context of global PD burden.

Future research should leverage integrated omics approaches (lipidomics, transcriptomics, metabolomics) to identify molecular signatures of oil-mediated neuroprotection and patient subpopulations most likely to benefit. Network pharmacology and computational docking analyses may help accelerate the identification of key molecular targets for the most active bioactive constituents, although, such in silico findings require experimental confirmation before they are treated as established. Seed oils, used as monotherapies or as components of nutritional adjunct regimens whose efficacy remains to be established in humans, represent a candidate area for further work in developing accessible therapeutic strategies for Parkinson's disease, rather than, as previously stated, a settled or “compelling frontier”.

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Conflict of Interests

The authors declare that they have no competing interests.

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Data availability

All data generated or analysed during this review are included in the published article and its references. No additional datasets were generated.

AUTHOR CONTRIBUTIONS

CRediT roles: Conceptualisation OOO, OPA, Writing – original draft, Writing – review & editing (all authors); Data extraction and quality appraisal OOO, OPA; Methodology and revision of the search strategy (all authors); Supervision (OPA).

AI/LLM USE DISCLOSURE

Generative AI/large language model tools were not used to generate the scientific content, data, analyses, or conclusions of this manuscript. AI-based language-editing tools were used solely to check grammar and readability; the authors reviewed and take full responsibility for all content

REFERENCES

Ahmed H. M. (2018). Ethnomedicinal, Phytochemical and Pharmacological Investigations of *Perilla frutescens* (L.) Britt. *Molecules (Basel, Switzerland)*, *24*(1), 102. https://doi.org/10.3390/molecules24010102

Alexander G. E. (2004). Biology of Parkinson's disease: pathogenesis and pathophysiology of a multisystem neurodegenerative disorder. *Dialogues in clinical neuroscience*, *6*(3), 259–280. https://doi.org/10.31887/DCNS.2004.6.3/galexander

Al-Madhagy, S., Ashmawy, N. S., Mamdouh, A., Eldahshan, O. A., & Farag, M. A. (2023). A comprehensive review of the health benefits of flaxseed oil in relation to its chemical composition and comparison with other omega-3-rich oils. *European journal of medical research*, *28*(1), 240. https://doi.org/10.1186/s40001-023-01203-6

Alshaman, R., Qushawy, M., Mokhtar, H. I., Ameen, A. M., El-Sayed, R. M., Alamri, E. S., Elabbasy, L. M., Helaly, A. M. N., Elkhatib, W. F., Alyahya, E. M., & Zaitone, S. A. (2023). Marula oil nanoemulsion improves motor function in experimental parkinsonism *via* mitigation of inflammation and oxidative stress. *Frontiers in pharmacology*, *14*, 1293306. https://doi.org/10.3389/fphar.2023.1293306

Arbex, A. Bizarro, V. , Santos, J. , Araújo, L. , de Jesus, A. , Fernandes, M. , Salles, M. , Rocha, D. and Marcadenti, A. (2015) The Impact of the Essential Fatty Acids (EFA) in Human Health. *Open Journal of Endocrine and Metabolic Diseases*, **5**, 98-104. doi: 10.4236/ojemd.2015.57013.

Aslam, B., Sajid, M. R., Hussain, A., & Abbas, I. (2026). Pharmacological profiling of medicinal plants: a contemporary overview. *Natural product research*, *40*(10), 2963–2979. https://doi.org/10.1080/14786419.2024.2448853

Braak, H., Del Tredici, K., Rüb, U., de Vos, R. A., Jansen Steur, E. N., & Braak, E. (2003). Staging of brain pathology related to sporadic Parkinson's disease. *Neurobiology of aging*, *24*(2), 197–211. https://doi.org/10.1016/s0197-4580(02)00065-9

Balakrishnan, R., Azam, S., Cho, D. Y., Su-Kim, I., & Choi, D. K. (2021). Natural Phytochemicals as Novel Therapeutic Strategies to Prevent and Treat Parkinson's Disease: Current Knowledge and Future Perspectives. *Oxidative medicine and cellular longevity*, *2021*, 6680935. https://doi.org/10.1155/2021/6680935

Chaudhuri, K. R., Healy, D. G., Schapira, A. H., & National Institute for Clinical Excellence (2006). Non-motor symptoms of Parkinson's disease: diagnosis and management. *The Lancet. Neurology*, *5*(3), 235–245. https://doi.org/10.1016/S1474-4422(06)70373-8

Chauke, H., Silue, Y., Aremu, A. O., & Fawole, O. A. (2025). Nutritional values, phytochemical composition and bioactivities of Sclerocarya birrea (Marula) seeds and its potential applications: Current research and future directions. *South African Journal of Botany*, *179*, 188–197. https://doi.org/10.1016/j.sajb.2025.02.008

Dayrit, F.M. The Properties of Lauric Acid and Their Significance in Coconut Oil. *J Am Oil Chem Soc* **92**, 1–15 (2015). https://doi.org/10.1007/s11746-014-2562-7

Deepika, N. P., Kondengadan, M. S., Sweilam, S. H., Rahman, M. H., Muhasina, K. M., Ghosh, P., Bhargavi, D., Palati, D. J., Maiz, F., & Duraiswamy, B. (2024). Neuroprotective role of coconut oil for the prevention and treatment of Parkinson's disease: potential mechanisms of action. Biotechnology and Genetic Engineering Reviews, 40(4), 3346–3378. https://doi.org/10.1080/02648725.2022.2122296

de Lau, L. M., & Breteler, M. M. (2006). Epidemiology of Parkinson's disease. *The Lancet. Neurology*, *5*(6), 525–535. https://doi.org/10.1016/S1474-4422(06)70471-9

Dong, J., Zhang, X., Wang, S., Xu, C., Gao, M., Liu, S., Li, X., Cheng, N., Han, Y., Wang, X., & Han, Y. (2021). Thymoquinone Prevents Dopaminergic Neurodegeneration by Attenuating Oxidative Stress Via the Nrf2/ARE Pathway. *Frontiers in pharmacology*, *11*, 615598. https://doi.org/10.3389/fphar.2020.615598

Dotchin, C., Msuya, O., Kissima, J., Massawe, J., Mhina, A., Moshy, A., Aris, E., Jusabani, A., Whiting, D., Masuki, G., & Walker, R. (2008). The prevalence of Parkinson's disease in rural Tanzania. Movement Disorders, 23(11), 1567–1672. https://doi.org/10.1002/mds.21898

Factor, S. A., & Weiner, W. J. (2008). Parkinson's Disease: Diagnosis and Clinical Management (2nd ed.). Demos Medical Publishing.

Faried, M. A. E.-S., El-fiky, S., El-Safti, F. E.-N. A. E.-H., El-Kholy, W. B., & Zaki, N. G. (2024). The effect of Nigella sativa oil on frontal cerebral cortex and hippocampus of rotenone induced model of Parkinson's disease in the adult male albino rat: Histological and immunohistochemical study. *Egyptian Journal of Histology*. Advance online publication. https://doi.org/10.21608/ejh.2024.304554.2104

Gawas, C. G., Mathur, S., Wani, M., & Tabassum, H. (2023). *Nigella sativa* and its nano-mediated approach toward management of neurodegenerative disorders: A

review. *Ibrain*, *9*(1), 111–123. https://doi.org/10.1002/ibra.12091

GBD 2016 Parkinson's Disease Collaborators (Dorsey, E. R., Elbaz, A., Nichols, E., *et al*.). (2018). Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology, 17(11), 939–953. https://doi.org/10.1016/S1474-4422(18)30295-3

Guo, J. D., Zhao, X., Li, Y., Li, G. R., & Liu, X. L. (2018). Damage to dopaminergic neurons by oxidative stress in Parkinson's disease (Review). *International journal of molecular medicine*, *41*(4), 1817–1825. https://doi.org/10.3892/ijmm.2018.3406

Hashimoto, M., Yamashita, K., Matsuzaki, K., Kato, S., & Shido, O. (2017). Beneficial Effects Of Perilla Oil And Brain Training Intervention On Cognition In Elderly Japanese. *Innovation in Aging*, *1*(Suppl 1), 467. https://doi.org/10.1093/geroni/igx004.1665

Hashimoto, M., Matsuzaki, K., Maruyama, K., Hossain, S., Sumiyoshi, E., Wakatsuki, H., Kato, S., Ohno, M., Tanabe, Y., Kuroda, Y., Yamaguchi, S., Kajima, K., Ohizumi, Y., & Shido, O. (2022). *Perilla* seed oil in combination with nobiletin-rich ponkan powder enhances cognitive function in healthy elderly Japanese individuals: a possible supplement for brain health in the elderly. *Food & function*, *13*(5), 2768–2781. https://doi.org/10.1039/d1fo03508h

Haxhiu, H., Hoxha, M., Zela, I., & Zappacosta, B. (2025). An Overview of the Role of Medicinal Plants in Parkinson's Disease: A Semi-Systematic Review. *Biomedicines*, *13*(8), 2008. https://doi.org/10.3390/biomedicines13082008

Hosseini, A., Baradaran Rahimi, V., Rakhshandeh, H., & Askari, V. R. (2022). *Nigella sativa* Oil Reduces LPS-Induced Microglial Inflammation: An Evaluation on M_1/M_2 Balance. *Evidence-based complementary and alternative medicine : eCAM*, *2022*, 5639226. https://doi.org/10.1155/2022/5639226

Ibrahim, K. S., & El-Sayed, E. M. (2020). Beneficial effects of coconut oil in treatment of Parkinson's disease. *Neurophysiology*, *52*(2), 169–175. https://doi.org/10.1007/s11062-020-09866-1

Imran, S., Munir, S., Altemimi, A. B., Fatima, I., Rabail, R., Batool, I., Khalid, N., Abdi, G., Shabbir, M. A., & Aadil, R. M. (2024). Therapeutic implications of flaxseed peptides and bioactive components against various diseases. *Journal of Functional Foods*, 120, 106324. https://doi.org/10.1016/j.jff.2024.106324

Jahan, R., Malik, S., Shoaib, S., Alomary, M. N., Ansari, M. A., Islam, N., & Khan, S. (2024). Medicinal and nutritional importance of *Linum usitatissimum* L. in human health. In *Medicinal plants and their bioactive compounds in human health: Volume 1* (pp. 25–45). Springer Nature Singapore. https://doi.org/10.1007/978-981-97-6895-0_2

Javed, H., Mohamed Fizur, N. M., Jha, N. K., Ashraf, G. M., & Ojha, S. (2023). Neuroprotective Potential and Underlying Pharmacological Mechanism of Carvacrol for Alzheimer's and Parkinson's Diseases. *Current neuropharmacology*, *21*(6), 1421–1432. https://doi.org/10.2174/1570159X21666221223120251

Jeng, K. C. G., & Hou, R. C. W. (2005). Sesamin and sesamolin: Nature's therapeutic lignans. *Current Enzyme Inhibition*, 1(1), 11–20. https://doi.org/10.2174/1573408052952748

Kaji, H., Matsui-Yuasa, I., Matsumoto, K., Omura, A., Kiyomoto, K., & Kojima-Yuasa, A. (2020). Sesaminol prevents Parkinson's disease by activating the Nrf2-ARE signaling pathway. *Heliyon*, *6*(11), e05342. https://doi.org/10.1016/j.heliyon.2020.e05342

Kamanula, M., Munthali, C. Y., & Kamanula, J. F. (2022). Yield and physicochemical properties of marula (*Sclerocarya birrea*) seed oils among nine international provenances tested in Malawi. *International Journal of Agronomy, 2022*, Article 7145113. https://doi.org/10.1155/2022/7145113

Khazdair M. R. (2015). The Protective Effects of Nigella sativa and Its Constituents on Induced Neurotoxicity. *Journal of toxicology*, *2015*, 841823. https://doi.org/10.1155/2015/841823

Komane, B., Vermaak, I., Summers, B., & Viljoen, A. (2015). Safety and efficacy of Sclerocarya birrea (A.Rich.) Hochst (Marula) oil: A clinical perspective. *Journal of ethnopharmacology*, *176*, 327–335. https://doi.org/10.1016/j.jep.2015.10.037

Kouli A, Torsney KM, Kuan WL. Parkinson's Disease: Etiology, Neuropathology, and Pathogenesis. In: Stoker TB, Greenland JC, editors. Parkinson's Disease: Pathogenesis and Clinical Aspects [Internet]. Brisbane (AU): Codon Publications; 2018 Dec 21. Chapter 1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536722/ doi: 10.15586/codonpublications.parkinsonsdisease.2018.ch1

Kurowska, E. M., Dresser, G. K., Deutsch, L., Vachon, D., & Khalil, W. (2003). Bioavailability of omega-3 essential fatty acids from perilla seed oil. *Prostaglandins, leukotrienes, and essential fatty acids*, *68*(3), 207–212. https://doi.org/10.1016/s0952-3278(02)00271-5

Lee, J. W., Kim, Y. T., Park, J. W., Kim, J. K., Lee, B. Y., & Hwang, I. K. (2012). Antioxidation activity of oil extracts prepared from various seeds. *Food Science and Biotechnology, 21*(3), 637–643. https://doi.org/10.1007/s10068-012-0083-4

Mahnoor, Jahan, S., Elahi, L., Zakria, M., Rabia, Ikram, M., & Ullah, N. (2025). Alpha-Linolenic Acid for Mitigating Neuroinflammation and Dopaminergic Neuronal Loss in Parkinson's Disease: Insights From In Vivo and In Silico Studies. *Clinical and experimental pharmacology & physiology*, *52*(6), e70043. https://doi.org/10.1111/1440-1681.70043

Mariod, A. A. (Ed.). (2022). Biochemistry, Nutrition, and Therapeutics of Black Cumin Seed. Academic Press.

Mueed, A., Shibli, S., Korma, S. A., Madjirebaye, P., Esatbeyoglu, T., & Deng, Z. (2022). Flaxseed Bioactive Compounds: Chemical Composition, Functional Properties, Food Applications and Health Benefits-Related Gut Microbes. *Foods (Basel, Switzerland)*, *11*(20), 3307. https://doi.org/10.3390/foods11203307

Mythri, R. B., Venkateshappa, C., Harish, G., Mahadevan, A., Muthane, U. B., Yasha, T. C., Srinivas Bharath, M. M., & Shankar, S. K. (2011). Evaluation of markers of oxidative stress, antioxidant function and astrocytic

proliferation in the striatum and frontal cortex of Parkinson's disease brains. *Neurochemical research*, *36*(8), 1452–1463. https://doi.org/10.1007/s11064-011-0471-9

Negi, V. S., Rawat, L. S., Phondani, P. C., & Chandra, A. (2011). *Perilla frutescens* in transition: A medicinal and oil yielding plant need instant conservation, a case study from Central Himalaya, India. *Environment & We: An International Journal of Science & Technology, 6*, 193–200

Olanow, C. W., & Schapira, A. H. (2013). Therapeutic prospects for Parkinson disease. *Annals of neurology*, *74*(3), 337–347. https://doi.org/10.1002/ana.24011

Omoni, A. O., & Aluko, R. E. (2006). Mechanism of the inhibition of calmodulin-dependent neuronal nitric oxide synthase by flaxseed protein hydrolysates. *Journal of the American Oil Chemists' Society, 83*(4), 335–340. https://doi.org/10.1007/s11746-006-1209-8

Percie du Sert, N., Hurst, V., Ahluwalia, A., Alam, S., Avey, M. T., Baker, M., Browne, W. J., Clark, A., Cuthill, I. C., Dirnagl, U., Emerson, M., Garner, P., Holgate, S. T., Howells, D. W., Karp, N. A., Lazic, S. E., Lidster, K., MacCallum, C. J., Macleod, M., Pearl, E. J., … Würbel, H. (2020). The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *PLoS biology*, *18*(7), e3000410. https://doi.org/10.1371/journal.pbio.3000410

Perera, D. N., Hewavitharana, G. G., & Navaratne, S. B. (2020). Determination of Physicochemical and Functional Properties of Coconut Oil by Incorporating Bioactive Compounds in Selected Spices. *Journal of lipids*, *2020*, 8853940. https://doi.org/10.1155/2020/8853940

Pop, R. M., Sabin, O., Suciu, Ș., Vesa, S. C., Socaci, S. A., Chedea, V. S., Bocsan, I. C., & Buzoianu, A. D. (2020). Nigella Sativa's Anti-Inflammatory and Antioxidative Effects in Experimental Inflammation. *Antioxidants (Basel, Switzerland)*, *9*(10), 921. https://doi.org/10.3390/antiox9100921

Przedborski S. (2017). The two-century journey of Parkinson disease research. *Nature reviews. Neuroscience*, *18*(4), 251–259. https://doi.org/10.1038/nrn.2017.25

Ramazani, E., Ebrahimpour, F., Emami, S. A., Shakeri, A., Javadi, B., Sahebkar, A., & Tayarani-Najaran, Z. (2023). Neuroprotective Effects of *Sesamum indicum*, Sesamin and Sesamolin Against 6-OHDA-induced Apoptosis in PC12 Cells. *Recent advances in food, nutrition & agriculture*, *14*(2), 126–133. https://doi.org/10.2174/2772574X14666230804151124

Rodriguez-Oroz, M. C., Jahanshahi, M., Krack, P., Litvan, I., Macias, R., Bezard, E., & Obeso, J. A. (2009). Initial clinical manifestations of Parkinson's disease: features and pathophysiological mechanisms. *The Lancet. Neurology*, *8*(12), 1128–1139. https://doi.org/10.1016/S1474-4422(09)70293-5

Salem M. L. (2005). Immunomodulatory and therapeutic properties of the Nigella sativa L. seed. *International immunopharmacology*, *5*(13-14), 1749–1770. https://doi.org/10.1016/j.intimp.2005.06.008

Sarawi, W. S., Attia, H. A., Alomar, H. A., Alhaidar, R., Rihan, E., Aldurgham, N., & Ali, R. A. (2024). The protective role of sesame oil against Parkinson's-like disease induced by manganese in rats. *Behavioural brain research*, *465*, 114969. https://doi.org/10.1016/j.bbr.2024.114969

Schapira, A. H., & Jenner, P. (2011). Etiology and pathogenesis of Parkinson's disease. *Movement disorders : official journal of the Movement Disorder Society*, *26*(6), 1049–1055. https://doi.org/10.1002/mds.23732

Sedaghat, R., Roghani, M., & Khalili, M. (2014). Neuroprotective effect of thymoquinone, the nigella sativa bioactive compound, in 6-hydroxydopamine-induced hemi-parkinsonian rat model. *Iranian journal of pharmaceutical research : IJPR*, *13*(1), 227–234.

Senila, L., Neag, E., Cadar, O., Kovacs, M. H., Becze, A., & Senila, M. (2020). Chemical, nutritional and antioxidant characteristics of different food seeds. *Applied Sciences, 10*(5), Article 1589. https://doi.org/10.3390/app10051589

Serhan C. N. (2014). Pro-resolving lipid mediators are leads for resolution physiology. *Nature*, *510*(7503), 92–101. https://doi.org/10.1038/nature13479

Shallie, P. D., Talabi, D. J., Olayinka, O. O., Babatunde, B. R., Akpan, H. B., Otulana, O. J., Alese, O. O., & Shallie, O. F. (2017). Flaxseed oil as a potential neuro-protective agent on the cerebellum of rotenone mice model of Parkinson's diseases. *International Journal of Brain and Cognitive Sciences, 6*(3), 43–50. https://doi.org/10.5923/j.ijbcs.20170603.01

Shallie, P. D., Olayinka, O. O., Akpan, H. B., Otulana, O. J., Alese, O. O., Babatunde, B. R., Talabi, D. J., & Shallie, O. F. (2017). Potential neuro-therapeutic effect of flaxseed oil on the striatum of rotenone mice model of Parkinson's diseases. *Journal of Advances in Medicine and Medical Research, 22*(1), 1–9. https://doi.org/10.9734/BJMMR/2017/34207

Simopoulos A. P. (2016). An Increase in the Omega-6/Omega-3 Fatty Acid Ratio Increases the Risk for Obesity. *Nutrients*, *8*(3), 128. https://doi.org/10.3390/nu8030128

Spillantini, M. G., Schmidt, M. L., Lee, V. M., Trojanowski, J. Q., Jakes, R., & Goedert, M. (1997). Alpha-synuclein in Lewy bodies. *Nature*, *388*(6645), 839–840. https://doi.org/10.1038/42166

Subramaniyan, V. (2020). Therapeutic importance of castor seed oil. In Nuts and Seeds in Health and Disease Prevention (pp. 485–495). Academic Press.

Techaniyom, P., Korsirikoon, C., Rungruang, T., Pakaprot, N., Prombutara, P., Mukda, S., Kringkasemsee Kettawan, A., & Kettawan, A. (2024). Cold-pressed perilla seed oil: investigating its protective influence on the gut–brain axis in mice with rotenone-induced Parkinson's disease. Food Science & Nutrition, 12(9), 6259–6283. https://doi.org/10.1002/fsn3.4265

Uddin, M. N., Hoq, M. I., Jahan, I., Siddiqui, S. A., Clinton, C. D., Ibrahim, M., Islam, M. S., & Jakaria, M. (2021). The Mechanistic Role of Thymoquinone in Parkinson's Disease: Focus on Neuroprotection in Pre-Clinical Studies. *Current molecular pharmacology*, *14*(6), 1083–1092. https://doi.org/10.2174/1874467214666210105140944

Uzzan, S., Rostevanov, I.-S., Rubin, E., Benguigui, O., Marazka, S., Kaplanski, J., Agbaria, R., & Azab, A. N. (2024). Chronic treatment with *Nigella sativa* oil exerts antimanic properties and reduces brain inflammation in

rats. *International Journal of Molecular Sciences, 25*(3), Article 1823. https://doi.org/10.3390/ijms25031823

Wei, J., Wang, B., Chen, Y., Wang, Q., Ahmed, A. F., Zhang, Y., & Kang, W. (2022). The Immunomodulatory Effects of Active Ingredients From *Nigella sativa* in RAW264.7 Cells Through NF-κB/MAPK Signaling Pathways. *Frontiers in nutrition*, *9*, 899797. https://doi.org/10.3389/fnut.2022.899797

Wooten, G. F., Currie, L. J., Bovbjerg, V. E., Lee, J. K., & Patrie, J. (2004). Are men at greater risk for Parkinson's disease than women?. *Journal of neurology, neurosurgery, and psychiatry*, *75*(4), 637–639. https://doi.org/10.1136/jnnp.2003.020982

Yousefsani, B. S., Ghobadi, A., Dadmehr, M., & Shirani, K. (2024). Castor oil: a natural remedy with promising potential for Parkinson's disease prevention. Jundishapur Journal of Natural Pharmaceutical Products, 19(1), e143882. https://doi.org/10.5812/jjnpp-143882

Zanwar, A., Manimurugan, C., Sujatha, M., Rathnakumar, A., & Sandhanalakshmi, M. (2023). Role of flaxseed (Linum usitatissimum L.) in disease prevention and treatment. Asian Pacific Journal of Tropical Biomedicine, 13(7), 277–286. https://doi.org/10.4103/2221-1691.380559