



Review of the Neuroprotective and Anti-Neuroinflammatory Potential of *Bergera koenigii* (L.)

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ABSTRACT :

Bergera koenigii (L.), commonly known as curry leaf, is an aromatic medicinal plant belonging to the family Rutaceae and is widely used as a culinary spice and traditional medicinal plant. The plant has attracted increasing scientific interest because of its diverse phytochemical composition and pharmacological properties, particularly antioxidant, anti-inflammatory and neuroprotective activities. Different parts of the plant contain structurally diverse secondary metabolites, including carbazole alkaloids, flavonoids, phenolic compounds, terpenoids, coumarins and volatile constituents. Among the different plant parts, leaves are the most extensively studied and represent the richest documented source of carbazole alkaloids such as mahanimbine, mahanine, koenimbine, girinimbine, murrayanol and related compounds. Seeds also possess considerable phytochemical diversity, including alkaloids, phenolics, flavonoids, coumarins, organic acids, lipids and amino acids, whereas stem and stem bark contain several carbazole alkaloids and other secondary metabolites. Flowers remain comparatively underexplored. Recent seed metabolomic profiling identified 102 compounds, demonstrating that phytochemical diversity is not restricted to leaves. Increasing experimental evidence suggests that *B. koenigii* may have therapeutic relevance in neuroinflammatory and neurodegenerative conditions. In particular, the leaf-derived carbazole alkaloid mahanimbine has demonstrated antioxidant, cholinergic and anti-neuroinflammatory effects in experimental models. Mahanimbine improved spatial learning and memory and reduced oxidative stress, cyclooxygenase activity and COX-2 expression in aged mice. Other investigations have demonstrated that curry leaf alkaloidal extracts can enhance antioxidant defence and modulate cholinergic transmission. These findings indicate that *B. koenigii* may provide multi-target neuroprotection through modulation of oxidative stress, neuroinflammation and cholinergic dysfunction. However, current evidence is predominantly preclinical, and important gaps remain regarding standardized extracts, compound-specific mechanisms, pharmacokinetics, blood-brain barrier penetration and clinical efficacy. Further systematic investigations are therefore required to establish *B. koenigii* as a scientifically validated therapeutic candidate for neuroinflammatory disorders.

Keywords: *Bergera koenigii*; curry leaf; neuroinflammation; neuroprotection; carbazole alkaloids; mahanimbine; oxidative stress; cognitive dysfunction.

Introduction

Neuroinflammation is an important pathological process associated with neuronal dysfunction and the progression of several neurological and neurodegenerative disorders. A controlled inflammatory response in the central nervous system contributes to protection and tissue repair; however, persistent or excessive inflammatory activation can result in the production of pro-inflammatory cytokines, reactive oxygen species and other mediators that contribute to neuronal injury. Oxidative stress and neuroinflammation are closely interconnected and can form a self-perpetuating cycle leading to neuronal dysfunction and degeneration [1,2].

The identification of natural products possessing both antioxidant and anti-inflammatory properties has therefore become an important area of neuropharmacological research. Medicinal plants contain numerous secondary metabolites that may act on multiple pathological processes simultaneously. *Bergera koenigii* (L.), commonly referred to in much of the older scientific literature as *Murraya koenigii* (L.) Spreng., is one such plant belonging to the family Rutaceae. It is commonly known as curry leaf and is extensively cultivated and consumed in South Asia. Different parts of the plant have traditionally been used for various medicinal purposes, and modern investigations have demonstrated antioxidant, anti-inflammatory, antidiabetic, antimicrobial and neuroprotective properties [3,4].

The pharmacological importance of *B. koenigii* is closely associated with its phytochemical composition. Carbazole alkaloids are particularly characteristic of the plant, together with flavonoids, phenolic compounds, terpenoids, coumarins and volatile constituents. Mahanimbine, mahanine, koenimbine, girinimbine and murrayanol are among the important carbazole alkaloids reported from different parts of the plant [3].

Among these constituents, mahanimbine has received considerable attention for its potential neuroprotective properties. Experimental studies have shown that mahanimbine can improve cognitive performance while influencing oxidative stress, cholinergic transmission, amyloid-related parameters and neuroinflammatory markers [5].

In aged mice, mahanimbine treatment improved performance in the Morris water maze and increased memory retention. The same investigation demonstrated changes in malondialdehyde, glutathione, acetylcholine, acetylcholinesterase, β -amyloid, BACE-1, total cyclooxygenase and COX-2 expression, indicating a multi-target neuroprotective effect [5].

Although leaves have received the greatest attention, other plant parts may also contain biologically important compounds. Recent LC–MS/MS profiling of seeds identified 102 metabolites, including 40 alkaloids and 35 phenolic compounds, together with organic acids, phospholipids, fatty acids, amino acids and other metabolites [6].

Therefore, comparison of the phytochemical composition of leaves, seeds, stems and flowers is important for identifying the most promising plant material for neuropharmacological research. This review specifically summarizes the plant profile, phytochemical constituents of these four plant parts and the therapeutic potential of *B. koenigii* in neuroinflammation.

2. Plant Profile of *Bergera koenigii* (L.)

Bergera koenigii is a small aromatic perennial tree or shrub belonging to the family Rutaceae. The plant is commonly known as curry leaf or curry tree and is widely distributed in the Indian subcontinent and other tropical and subtropical regions. It is valued particularly for its aromatic leaves, which are extensively used as a culinary spice.

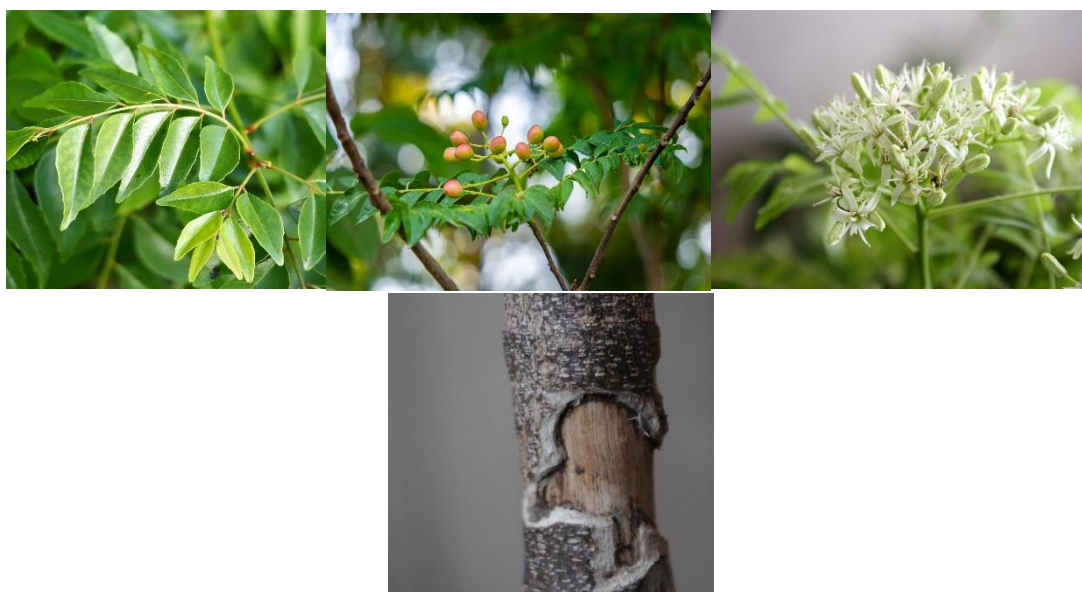


Figure1: Morphological features of *Bergera koenigii* (L.): (A) Leaf, (B) Stem, (C) Flower, and (D) Seed.

Taxonomic classification

Taxonomic rank	Classification
Kingdom	Plantae
Order	Sapindales
Family	Rutaceae
Genus	<i>Bergera</i>
Species	<i>Bergera koenigii</i> (L.)
Common name	Curry leaf / Curry tree
Common synonym in literature	<i>Murraya koenigii</i> (L.) Spreng.

The plant develops a branched stem and compound pinnate leaves containing several aromatic leaflets. The flowers are small, white and fragrant and are generally produced in inflorescences. The fruits are small and contain seeds. The characteristic aroma of the plant is associated with its volatile constituents.

Different parts of the plant have been traditionally utilized for medicinal purposes. Phytochemical investigations have identified alkaloids, flavonoids, phenolics, terpenoids, coumarins and other secondary metabolites in leaves, roots, stems, fruits and seeds [3,4].

From a pharmacological perspective, the plant is particularly notable for its carbazole alkaloids. These compounds have been associated with antioxidant, anti-inflammatory and other biological activities, making *B. koenigii* a valuable source for natural-product research [3,4].

3. Phytochemical Constituents of *Bergera koenigii*

3.1 Leaves

The leaves are the most extensively studied and best-characterized phytochemical part of *B. koenigii*. They are particularly rich in carbazole alkaloids

[3,4].

Important leaf constituents include:

- Mahanimbine
- Mahanine
- Koenimbine
- Girinimbine
- Murrayanol
- Mahanimbicine
- Bicyclomahanimbicine
- Koenigicine
- Koenigine
- Isomahanimbine
- Isomahanine
- Koenimbidine
- Euchrestine B
- Bismurrayafoline E
- Mahanimbinine
- O-methylmurrayamine A

A detailed quantitative investigation identified nine carbazole alkaloids in an alkaloid-rich leaf fraction, confirming the substantial concentration and diversity of these compounds in the leaves [7].

Leaves also contain flavonoids, phenolic compounds, terpenoids and volatile constituents. The combination of these phytochemical classes is considered responsible for many of the biological activities attributed to curry leaves.

Importantly, mahanimbine is predominantly associated with the leaves and has been extensively investigated for its cholinergic, antioxidant and neuroprotective effects [5].

3.2 Seeds

Seeds also contain considerable phytochemical diversity. Carbazole alkaloids reported from seeds include:

- Mahanine
- Mahanimbine
- Koenimbine
- Isomahanine
- Mahanimbinine
- Other carbazole derivatives

A recent UPLC-MS/MS study provided particularly strong evidence for the chemical diversity of seeds. A total of 102 compounds were identified, comprising 40 alkaloids, 35 phenolic compounds, 5 organic acids, 5 phospholipids, 3 fatty acids, 10 amino acids and several other metabolites [6].

The prominent seed carbazole alkaloids included mukoline, koenimbine, murrayanine and murrastanine A. The same study also identified numerous coumarins and flavonoid-related compounds [6].

These findings demonstrate that seeds are chemically diverse and deserve greater investigation. However, compared with leaves, direct evidence regarding the neuroprotective and anti-neuroinflammatory effects of seed-specific constituents remains limited.

3.3 Stem and Stem Bark

Stem and stem bark contain several carbazole alkaloids and other secondary metabolites. Compounds reported from these parts include:

- Mahanine
- Koenigine
- Murrayacine
- Murrayazoline
- Other carbazole alkaloids
- Coumarins
- Terpenoids
- Phenolic compounds

Mahanine has been reported from leaves, stem bark and seeds, while koenigine has been reported from leaves and stem bark [3].

The presence of carbazole alkaloids in the stem and bark indicates that these parts may also possess pharmacological potential. Nevertheless, they have received substantially less attention than leaves in neuropharmacological research. Therefore, further investigation is necessary to determine whether stem-derived compounds possess direct anti-neuroinflammatory activity.

3.4 Flowers

flowers of *B. koenigii* are comparatively underexplored in relation to phytochemical characterization. Compared with leaves and seeds, substantially fewer studies have systematically isolated and quantified individual compounds specifically from the flowers. Therefore, it is difficult to provide a reliable numerical comparison of total flower phytochemicals with those of other plant parts. The limited available information indicates the presence of secondary metabolites and volatile constituents, but comprehensive LC-MS/MS, GC-MS and NMR-based investigations of flowers are still required.

4. Comparison of Phytochemical Constituents

Plant part	Major phytochemical groups	Important examples	Current evidence
Leaves	Carbazole alkaloids, flavonoids, phenolics, terpenoids, volatile compounds	Mahanimbine, mahanine, koenimbine, girinimbine, murrayanol, euchrestine B	Very strong
Seeds	Alkaloids, phenolics, flavonoids, coumarins, organic acids, phospholipids, fatty acids, amino acids	Mukoline, koenimbine, murrayanine, murrastanine A	Strong and increasing
Stem/stem bark	Carbazole alkaloids, coumarins, phenolics, terpenoids	Mahanine, koenigine, murrayacine, murrayazoline	Moderate
Flowers	Secondary metabolites and volatile constituents	Individual constituents insufficiently characterized	Limited

Which part has more phytochemical constituents?

Based on the available literature, leaves should be described as the most extensively studied and richest documented source of carbazole alkaloids, rather than being described as unquestionably containing the greatest total number of phytochemicals. Multiple carbazole alkaloids have been isolated and characterized from leaves, and specific quantitative studies have confirmed their presence [3,7].

However, recent metabolomic analysis demonstrated that seeds can also have very high chemical diversity, with 102 compounds detected in seed/pericarp extracts, including 40 alkaloids and 35 phenolic compounds [6].

Therefore, the scientifically appropriate conclusion is:

Leaves are the most extensively characterized and particularly rich source of carbazole alkaloids, while seeds also exhibit substantial overall metabolomic diversity. Stem and stem bark contain several important alkaloids but are less investigated, whereas flowers remain comparatively undercharacterized.

5. Therapeutic Potential in Neuroinflammation

Neuroinflammation is increasingly recognized as an important component of neuronal injury and neurodegenerative disease. Persistent inflammatory responses can increase oxidative stress and contribute to neuronal dysfunction. The therapeutic relevance of *B. koenigii* is mainly supported by studies involving leaf extracts and isolated carbazole alkaloids.

5.1 Mahanimbine and neuroinflammation

Mahanimbine is one of the most extensively investigated neuroactive constituents of *B. koenigii*. Experimental studies have demonstrated that it can influence several processes associated with neurodegeneration.

In aged mice, mahanimbine administered orally for 30 days improved spatial learning and memory. The study also measured oxidative stress, cholinergic function, amyloid-related parameters and neuroinflammation. Mahanimbine reduced total cyclooxygenase activity and COX-2 expression in the brain, supporting its potential anti-neuroinflammatory action [5].

5.2 Effect against LPS-associated neuroinflammation

Evidence is particularly relevant from LPS-induced neuroinflammatory models. A review of experimental studies reported that mahanimbine treatment in LPS-challenged mice increased anti-inflammatory mediators such as TGF- β and IL-10 while reducing pro-inflammatory IL-1 β and TNF- α . It also decreased COX-2 activity and expression [8].

These findings are important because they provide evidence that a curry-leaf-derived compound can influence inflammatory responses in a model directly relevant to neuroinflammation.

5.3 Antioxidant activity

Oxidative stress is closely associated with neuroinflammatory injury. Total alkaloidal extract of curry leaves has been reported to increase antioxidant defence systems, including glutathione-related enzymes, superoxide dismutase and catalase, while reducing lipid peroxidation and nitric oxide levels in aged mice [9].

The antioxidant activity of curry leaf constituents may therefore contribute to neuroprotection by reducing oxidative stimuli that can promote inflammatory signalling.

5.4 Cholinergic neuroprotection

Cholinergic dysfunction is associated with cognitive impairment. Curry leaf alkaloidal extracts have demonstrated effects on acetylcholine and acetylcholinesterase, suggesting that modulation of cholinergic neurotransmission may contribute to their neuroprotective effects [9].

Mahanimbine has also demonstrated acetylcholinesterase-inhibitory activity. In experimental studies, increased acetylcholine levels following mahanimbine treatment were associated with improved cognitive performance [5,8].

5.5 Potential relevance to Alzheimer's disease

The neuroprotective potential of *B. koenigii* is particularly relevant to Alzheimer's disease because oxidative stress, neuroinflammation, cholinergic dysfunction and amyloid pathology are interconnected components of disease progression.

Mahanimbine improved memory performance in aged mice and affected several Alzheimer's disease-associated parameters, including acetylcholine, acetylcholinesterase, β -amyloid, BACE-1, oxidative stress and COX/COX-2-associated inflammation [5].

These findings suggest a multi-target neuroprotective effect, although they should not be interpreted as evidence that curry leaf has established clinical efficacy in Alzheimer's disease.

5.6 Potential relevance to Parkinsonian neurodegeneration

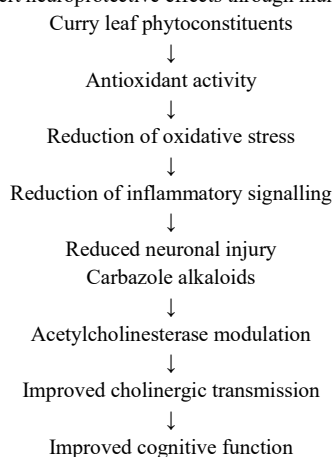
Oxidative stress, mitochondrial dysfunction and neuronal apoptosis are important features of Parkinsonian neurodegeneration. Some compounds associated with *B. koenigii*, particularly isolongifolene, have demonstrated experimental neuroprotective effects against rotenone-induced neuronal injury.

Isolongifolene attenuated oxidative stress, mitochondrial dysfunction and apoptosis in neuronal models and improved dopamine-related and motor parameters in experimental Parkinsonian models [10,11].

However, direct evidence for anti-neuroinflammatory activity of isolongifolene remains less extensive than the evidence for its antioxidant and anti-apoptotic actions. Therefore, further studies are required before attributing definitive anti-neuroinflammatory activity to this compound.

Overall therapeutic significance of *B. koenigii*

The available evidence suggests that *B. koenigii* may exert neuroprotective effects through multiple interconnected activities:



The combination of antioxidant, anti-inflammatory and cholinergic effects provides a plausible explanation for the neuroprotective effects observed in experimental models [5,8,9].

6. Conclusion

Bergera koenigii (L.) is a phytochemically diverse medicinal plant with promising neuroprotective and anti-neuroinflammatory potential. Its leaves are the most extensively studied and best-characterized plant part, particularly with respect to carbazole alkaloids such as mahanimbine, mahanine, koenimbine and girinimbine.

Seeds also demonstrate substantial phytochemical diversity, with recent LC-MS/MS analysis identifying 102 compounds, including alkaloids, phenolics, coumarins, organic acids, lipids and amino acids. Stem and stem bark contain several carbazole alkaloids, whereas flowers remain comparatively under investigated.

Among the reported constituents, mahanimbine has particularly strong experimental evidence for neuroprotective activity. It has demonstrated improvement of cognitive performance, modulation of cholinergic transmission, reduction of oxidative stress and attenuation of neuroinflammatory markers, including COX and COX-2 [5].

Overall, the available evidence supports *B. koenigii* as a promising source of natural neuroprotective compounds. However, current evidence remains predominantly preclinical. Future research should focus on comparative phytochemical profiling of leaves, seeds, stems and flowers; identification of the most active constituents; standardized extracts; blood-brain barrier penetration; pharmacokinetics; CNS-specific inflammatory pathways; and clinical validation. Such investigations are necessary to determine whether the promising anti-neuroinflammatory properties of *B. koenigii* can be translated into clinically useful therapeutic interventions.

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