

NATURAL PHYTOCHEMICALS IN NEUROPROTECTION AND PERIPHERAL NERVE REGENERATION: A COMPREHENSIVE REVIEW

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Abstract

Peripheral nerve injuries often lead to functional loss and slow recovery due to limited natural regeneration. Recent research highlights the potential of phytochemical bioactive compounds derived from plants in promoting nerve repair through antioxidant, anti-inflammatory, and neurotrophic mechanisms. Compounds such as quercetin, berberine, ginsenoside Rg1, salidroside, glycyrrhizin, and asiatic acid have shown the ability to enhance Schwann cell proliferation, modulate growth factors like BDNF, NGF, and GDNF, and support axonal regeneration in experimental models. Several plant extracts, including *Hericium erinaceus*, *Alpinia oxyphylla*, *Centella asiatica*, *Lycium barbarum*, and *Radix Hedysari*, have demonstrated complementary benefits

by improving nerve function and promoting structural recovery. Despite these encouraging findings, challenges such as poor bioavailability, limited dosage standardization, and lack of extensive clinical data restrict their therapeutic use. Continued research focusing on molecular pathways, toxicity profiles, and controlled clinical trials may enable the translation of these naturally derived compounds into effective treatments for peripheral nerve injuries.

INTRODUCTION

The nervous system constitutes an intricate communication network that regulates and integrates almost all physiological processes through the transmission of electrochemical signals between the brain, spinal cord, and peripheral organs [1]. Peripheral nerve fibers represent some of the most delicate and vulnerable components of the human body, making them highly susceptible to injury from compression, stretching, or traumatic impact. Damage to these fibers disrupts normal communication between the brain, spinal cord, and target organs or muscles, resulting in impaired neuromuscular function [2]. Peripheral nerve injuries (PNIs) are considered a major clinical concern

due to their relatively high incidence and significant impact on patient quality of life. Such injuries often lead to partial or complete loss of motor control and sensory perception in the affected region [3].

Peripheral nerve injuries (PNIs) trigger a series of biological reactions that exacerbate the damage and impede the recovery of nerve function. Factors such as cell death, the build-up of tissue debris, and changes in the surrounding environment all play a part in making the injury more severe [4]. The growth of new nerve fibers happens very slowly, and so far, there is no treatment available in clinics that can speed up this process [5].

Various surgical techniques, including direct nerve repair, nerve conduits, and nerve grafting, have been developed to address the challenges associated with peripheral nerve repair. However, these approaches are often limited in their effectiveness, prompting researchers to explore alternative therapeutic strategies for peripheral nerve injuries (PNIs). In this context, dietary biomolecules, particularly phytochemicals, have emerged as promising agents due to their potential to support nerve regeneration and protect against cellular damage. The concept of using food-derived compounds for healing is not new, as several naturally occurring food constituents exhibit therapeutic properties. Such bioactive components include dietary fibers, carotenoids, fatty acids, isothiocyanates, flavonoids, phenolic acids, plant sterols, prebiotics, probiotics, phytoestrogens, vitamins, and minerals [6]. These molecules may play a significant role in modulating oxidative stress, inflammation, and cellular repair mechanisms, thereby contributing to nerve recovery.

Researchers have increasingly focused on identifying natural compounds in foods that may help to lower the risk of many diseases [7]. In particular, plant-based foods have gained attention because their natural components appear to slow down or prevent the development of several health problems. Studies have shown that people who eat more fruits and vegetables, rich sources of phytochemicals, tend to enjoy better overall health. These plant compounds, which act as dietary biomolecules, may help protect the body by reducing the harmful effects of reactive

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oxygen species (ROS), one of the main causes of nerve damage and other degenerative conditions [8].

More than 80,000 plant species worldwide are utilized for medicinal purposes [9], and approximately 80% of the global population relies on plant-derived compounds as a primary source of healthcare [10, 11]. Various plant-derived compounds reported to accelerate regeneration after peripheral nerve injury (PNI) are summarized in the following section.

1. Ursolic acid

Ursolic acid (UA) is a pentacyclic triterpenoid commonly found in the leaves, flowers, and fruits of various herbs. It is known for its wide range of beneficial effects, including antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, cardioprotective, antihyperlipidemic, and hypoglycemic activities [12]. In addition, studies have shown that UA supports nerve regeneration. Research using a mouse model demonstrated that ursolic acid can promote the regeneration of an injured sciatic nerve, suggesting its potential as a therapeutic agent for nerve repair [13].

2. Quercetin

Quercetin is a widely distributed flavonoid found abundantly in apples, honey, raspberries, onions, red grapes, cherries, citrus fruits, and leafy green vegetables. It exhibits multiple pharmacological properties, including antioxidant, anti-angiogenic, anti-inflammatory, neuroprotective, and anti-apoptotic effects [14, 15]. Experimental studies have demonstrated that quercetin enhances nerve regeneration by modulating several key molecular pathways. It upregulates pro-regenerative markers such as Bcl-2-associated X protein, caspase-3, caspase-9, and p53 mRNA, thereby promoting neuronal repair following sciatic nerve crush injury in rats. Quercetin also reduces the release of pro-inflammatory cytokines, including TNF- α and IL-1 β (Ji et al., 2017), and inhibits TLR and NF- κ B signaling via activation of transforming growth factor- β -activated kinase-1, a critical modulator in the pathogenesis of neuropathic pain [16].

Furthermore, quercetin suppresses glial fibrillary acidic protein (GFAP) expression in satellite glial cells, downregulating oxidative stress and inflammatory markers, including nitric oxide, lipid

peroxidation, TNF- α , IL-1 β , and IL-6. These effects collectively attenuate mechanical allodynia and thermal hyperalgesia in models of partial sciatic nerve ligation [17]. Interestingly, its derivative, isoquercetin, has also been shown to enhance motor recovery, nerve regeneration, and myelination by downregulating Nox4 and Duox1 while upregulating Nrf2 and SOD2 expression [18]. In addition, quercetin protects neurons against oxidative stress-induced neurotoxicity in Alzheimer's disease models [19].

3. Curcumin

Curcumin is a yellow pigment derived from the *Curcuma longa* plant and is widely used as a natural food coloring and spice. Its potential therapeutic value is mainly linked to its strong anti-inflammatory and antioxidant effects, which make it beneficial in managing conditions such as metabolic syndrome, arthritis, anxiety, and hyperlipidemia [20]. Research has shown that curcumin enhances the number and size of myelinated axons in the sciatic nerve by inducing autophagy, which protects Schwann cells from apoptosis [21]. It also promotes sciatic nerve repair by stimulating nerve growth factor (NGF), which activates survival signaling pathways such as phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) and tropomyosin receptor kinase- A [22]. The anti-inflammatory effects of curcumin are attributed to its interaction with cytokines and inflammatory mediators, including TNF- α , IL-1 β , and IL-6, as well as macrophages [23]. Moreover, curcumin inhibits the JAK-STAT signaling pathway and reduces inflammation in brain glial cells [24]. It also alleviates neuropathic pain by downregulating IL-1 β through suppression of the NALP1 inflammasome and JAK2-STAT3 signaling in astrocytes [25].

Overall, curcumin demonstrates significant neuroprotective potential by reducing damage caused by peripheral nerve injury (PNI) [26]. Further studies are needed to explore its possible use as a treatment for PNI and peripheral neurotoxicity.

4. Huperzine

Huperzine-A (Hup A) is a naturally occurring sesquiterpene alkaloid found in *Huperzia serrata* and other firmoss species. It has been widely studied for its ability to enhance cognitive function,

particularly in Alzheimer's disease [27]. Because Hup A can readily cross the blood–brain barrier (BBB), it exhibits a range of neuroprotective effects. It functions as a potent acetylcholinesterase (AChE) inhibitor [28] and as an antagonist of the N-methyl-D-aspartate (NMDA) receptor [29]. Notably, NMDA receptor inhibition has been shown to reduce neuronal demyelination and immune cell infiltration in ischemia-induced sciatic nerve injury [30].

Hup A also promotes neuroprotection by stimulating the production of key neurotrophic factors, including brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and glial cell line-derived neurotrophic factor (GDNF). BDNF is crucial for neuronal survival, differentiation, axonal sprouting, and synaptic plasticity processes essential for learning and memory [31]. Reduced levels of BDNF have been observed in patients with Alzheimer's disease, highlighting its importance in maintaining neuronal health [32]. Similarly, NGF supports the survival and function of cholinergic neurons and contributes to cognitive function and synaptic integrity [33]. Overall, Hup A enhances neuronal survival and axonal regeneration by increasing the expression of neurotrophic factors and mitigating glutamate-induced excitotoxicity, which in turn helps prevent synaptic loss and neuronal death [34].

5. Berberine

Berberine (BBR) is an isoquinoline alkaloid naturally present in several edible and medicinal plants, including goldenseal, *Phellodendron*, tree turmeric, and European barberry. It possesses multiple pharmacological properties, such as anti-inflammatory [35], antioxidant [36], and antitumor activities [37]. Berberine has been reported to enhance neurogenesis, improve short-term memory, and promote motor coordination by inhibiting neuronal apoptosis [38].

In models of peripheral nerve injury, berberine facilitates axonal regeneration and improves functional recovery, as demonstrated in sciatic nerve injury studies [39]. It also alleviates neuropathic pain in rats with partial sciatic nerve ligation [40]. The compound appears to support peripheral nerve repair by stimulating Schwann cell proliferation and activity [41]. Furthermore, berberine suppresses neuroinflammation by downregulating pro-inflammatory cytokines such as

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IL-6, IL-1 β , and TNF- α [42]. Despite its neuroprotective potential, berberine exhibits dose-dependent neurotoxicity. Concentrations between 10–30 μ M have been shown to inhibit dopamine synthesis and exert harmful effects on neurons [43]. Therefore, future research should focus on understanding and minimizing berberine's neurotoxic effects while exploring its therapeutic potential in the treatment of peripheral nerve injuries through well-designed preclinical and clinical studies.

6. *Alstonia scholaris*

Vinorine is a naturally occurring monoterpenoid indole alkaloid found in *Alstonia scholaris*, recognized for its diverse pharmacological properties, including antibacterial, antitumor, and anti-inflammatory activities. It has been reported to improve motor and sensory function following sciatic nerve injury by regulating the expression of nerve growth factor (NGF) and extracellular signal-regulated kinase (ERK) (Guo et al., 2018). In addition, vinorine exhibits acetylcholinesterase inhibitory activity, which may contribute to its neuroprotective effects [44].

7. *Alpinia oxyphylla* Miq

Alpinia oxyphylla Miq. (AOF) is an edible and medicinal herb traditionally used to treat conditions such as diarrhea, hypertension, dementia, tumors, and cardiovascular disorders [45]. Extracts of AOF have demonstrated neuroprotective effects, particularly against oxidative stress and neurotoxicity [46]. Protocatechuic acid (PCA), a major bioactive compound found in AOF seeds [47], possesses strong antioxidant, anti-inflammatory, and anti-apoptotic properties [48]. In vitro studies have shown that PCA enhances Schwann cell (RSC96) regeneration and migration by activating the ERK1/2, JNK1/2, and p38 MAPK signaling pathways [49]. Additionally, AOF extracts promote Schwann cell proliferation and survival by upregulating the IGF-1-mediated PI3K/Akt pathway and modulating cell cycle regulatory proteins [50].

8. Baicalin

Baicalin is a flavonoid commonly found in apples, citrus fruits, tea, wine, and dark chocolate. It enhances Schwann cell (SC) metabolic activity by regulating the production of key neurotrophic

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factors, including glial cell line-derived neurotrophic factor (GDNF), brain-derived neurotrophic factor (BDNF), and ciliary neurotrophic factor (CNTF) [51]. Furthermore, baicalin supports nerve repair by increasing Schwann cell vitality and differentiation through the upregulation of S100 protein expression, thereby facilitating the regeneration of damaged nerve fibers [52].

9. Salidroside

Salidroside (SDS), a bioactive compound derived from *Rhodiola rosea L.*, is known for its wide range of pharmacological activities, including antiviral, anticancer, hepatoprotective, antidiabetic, and antioxidant effects [53]. It supports Schwann cell (SC) survival and proliferation by enhancing the secretion of key neurotrophic factors such as GDNF, BDNF, and CDFN [54]. Additionally, salidroside reduces inflammation by suppressing STAT3 phosphorylation, thereby decreasing IL-6 expression and inhibiting inflammatory cell infiltration [55].

Salidroside also helps counteract oxidative stress and prevents muscle atrophy in denervation-induced skeletal muscle models [56]. Moreover, studies in rat models have shown that treatment with salidroside, particularly when combined with an epimysium conduit and Schwann cells, enhances sciatic nerve regeneration and significantly improves motor functional recovery following peripheral nerve injury [57].

10. Myricetin

Myricetin is a naturally occurring flavonoid found in a wide range of fruits, vegetables, nuts, and red wine. It possesses strong antioxidant properties. Studies have shown that myricetin promotes functional recovery and enhances nerve regeneration after peripheral nerve injury by activating the PI3K/AKT/mTORC1/GSK3 β signaling pathways [58]. Additionally, myricetin provides neuroprotection against ischemic brain injury through mechanisms involving the p38 MAPK, NF- κ B/p65, and AKT pathways. Furthermore, myricetin contributes to cellular homeostasis in neurodegenerative conditions by facilitating the removal of misfolded or abnormal proteins through the modulation of Hsp70 chaperone and E3 ubiquitin ligase expression [59].

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11. Glycyrrhizin

Glycyrrhizin, a major bioactive compound extracted from *Glycyrrhiza glabra* (licorice root), is responsible for its characteristic sweetness and a wide range of pharmacological effects. It exhibits antibacterial, anti-inflammatory, antiviral, and anti-ulcer activities, along with strong free radical scavenging properties [60]. Studies have shown that glycyrrhizin supports sciatic nerve regeneration and functional recovery by downregulating the p75 neurotrophin receptor (p75^{NTR}) [61]. This downregulation is associated with improved myelination, neuronal regeneration, and enhanced recovery of sciatic nerve function. Moreover, glycyrrhizin administered as diammonium glycyrrhizinate has been reported to aid nerve repair in rat models of severe traumatic brain injury (STBI) by stimulating nerve cell regeneration, proliferation, and differentiation. These effects are associated with activation of the Wnt/ β -catenin signaling pathway, which contributes to hippocampal nerve tissue reconstruction [62].

Table 1. Summary of selected phytochemicals with their common names, recommended daily intake, therapeutic doses, and references supporting their neuroregenerative potential.

Bioactive Compounds	functions	daily intake (body weight)	references
Ursolic acid	Shows immune-modulating, antimicrobial, anticancer, antioxidant, cardioprotective, liver-protective, anti-inflammatory, chemopreventive, lipid-lowering, and hypoglycemic properties.	5 mg/kg	[13], [63]

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Quercetin	Anti-inflammatory, antioxidant & neuroprotective.	15.5 mg	[67, 68]
Curcumin	Boosting S100 protein expression. It reduces oxidative stress, inflammation, anxiety, arthritis, and metabolic imbalances.	3 mg/kg	[69]
Huperzine A	Enhances neuronal survival and axonal regeneration by increasing the expression of neurotrophic factors	50– 400 mg	[34]
Berberine	Enhance neurogenesis, improve short-term memory, and promote motor coordination by inhibiting neuronal apoptosis, support peripheral nerve repair by stimulating Schwann cell proliferation and activity.	500– 1,500 mg	[38,41]
Alstonia scholaris	Antibacterial, antitumor, anti-inflammatory, and	7.5–30 mg/kg	[44]

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improve motor and sensory functions.

Alpinia oxyphylla Miq	AOF extracts promote Schwann cell proliferation and survival by upregulating the IGF-1-mediated PI3K/Akt pathway and modulating cell cycle regulatory proteins.	20-200 µg/mL	[50]
Baicalin	Facilitates the regeneration of damaged nerve fibers, supports nerve repair by increasing Schwann cell vitality and differentiation through the upregulation of S100 protein expression.	200– 800 mg	[66]
Salidroside	Antiviral, anticancer, hepatoprotective, antidiabetic, and antioxidant.	12– 24 mg/kg	[53, 57]
Myricetin	Myricetin promotes functional recovery and	10 mg/kg	[58]

	enhances nerve regeneration by activating the PI3K/AKT/mTORC1/GSK3β signaling pathways.		
Glycyrrhizin	Supports sciatic nerve regeneration and functional recovery by downregulating the p75 neurotrophin receptor (p75 ^{NTR}).	0.015–0.229mg/kg	[61]
Ginsenoside	In Schwann cells (RSC96), GsRg1 has been found to promote proliferation and migration by activating the ERK1/2, JNK1/2, and MAPK signaling pathways.	50.2– 64.7 mg	[67]
Triptolide	Enhances nerve regeneration and promotes functional recovery following brain and spinal cord injuries, primarily through its ability to suppress inflammation and gliosis.	1.5 mg/kg daily	[68,70]

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Hericium erinaceus	Enhance the synthesis of nerve growth factor (NGF) and stimulate NGF-induced neurite outgrowth in various cell types, contributing to neuronal repair and recovery.	0.05– 0.1 mg	[84]
Red Propolis	Enhanced regenerative responses and promoted faster functional recovery following sciatic nerve crush injury.	10 mg/kg	[11]
Lycium babarum	Strong antioxidant activity, significantly enhances nerve repair and regeneration, indicating their potential as a therapeutic agent for promoting nerve recovery after injury.	10 mg/kg	[87,88]
Daphne odora	known for its antimutagenic, immune-modulating, antiviral, anticancer, and cytotoxic activities. supports nerve	2.5 mg/kg	[10,90]

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	regeneration and functional recovery.		
Centella asiatica	Accelerate functional recovery and enhance axonal regrowth following nerve injury.	300–330 mg/kg	[93]
Radix Hedysari	Stimulate the growth of lateral buds in the proximal nerve stump and amplify regenerative effects during peripheral nerve repair.	0.25 g/mL	[98]

Collectively, glycyrrhizin shows strong potential as a neuroprotective and neuroregenerative agent. However, further studies are required to clarify its mechanisms and optimize its therapeutic applications for nerve injury repair.

12. Ginsenoside and ginseng

Ginsenoside Rg1 (GsRg1), a major active component found in the edible berries and roots of *Panax ginseng*, exhibits strong neuroprotective and neurotrophic properties [71]. In experimental models of sciatic nerve injury, GsRg1 has been shown to promote nerve repair and regeneration, restore motor fiber conductivity, and prevent skeletal muscle atrophy associated with nerve damage. These effects are largely attributed to its antioxidant potential [72]. Further studies revealed that GsRg1 reduces oxidative stress by lowering malondialdehyde (MDA) levels and enhancing the activities of key antioxidant enzymes such as superoxide dismutase (SOD) and glutathione (GSH). It also modulates apoptotic signaling by decreasing XIAP protein levels and increasing caspase-3 expression in the spinal cord, suggesting that its neuroprotective role

involves both antioxidant and anti-apoptotic pathways [73]. In Schwann cells (RSC96), GsRg1 has been found to promote proliferation and migration by activating the ERK1/2, JNK1/2, and MAPK signaling pathways [74]. It also enhances the IGF-I and FGF-2–uPA–MMP9 pathways, which contribute to cell growth and migration, key processes in nerve regeneration [75]. Moreover, in a rat model of spinal cord injury, administration of GsRg1 increased the secretion of neurotrophic factors and cell adhesion molecules from astrocytes via activation of the PI3K/Akt pathway. It also reduced the expression of GFAP and CSPGs, thereby suppressing glial scar formation and limiting astrogliosis [76]. Overall, GsRg1 demonstrates promising therapeutic potential for promoting neuronal regeneration and repair. However, further studies are required to fully elucidate its cellular and molecular mechanisms before its use can be translated into clinical applications.

13. Triptolide

Triptolide, the principal bioactive compound derived from the edible Chinese herb *Tripterygium wilfordii* Hook F., has shown significant neuroprotective potential. Several studies have demonstrated that triptolide enhances nerve regeneration and promotes functional recovery following brain and spinal cord injuries, primarily through its ability to suppress inflammation and gliosis [77, 78].

The compound exerts its anti-inflammatory effects by downregulating key signaling pathways, including NF- κ B and MAPK (p38, ERK1/2), thereby reducing neuroinflammation [78,79]. It decreases the expression of pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6, and inhibits the release of these mediators from non-neuronal cells, including Schwann cells and macrophages [80]. By blocking CXCR2 activity, triptolide protects neuronal cells from secondary inflammatory damage.

In both in vitro and in vivo studies, triptolide has been shown to inhibit astrocyte activation by suppressing the JAK2/STAT3 signaling pathway, thereby reducing astrocyte gliosis and glial scar formation in injured spinal cords. Treatment with triptolide also leads to a decrease in ED-1

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and CD11b-positive inflammatory cells at lesion sites and significantly enhances axonal regeneration and functional recovery [81,82].

Additionally, triptolide, a diterpenoid compound, is recognized as a modulator of autophagy. It promotes neuroprotection by upregulating Beclin-1 and Mcl-1, while downregulating Bcl-2 and caspase-3, which are key regulators of apoptosis [83]. Beclin-1 is essential for autophagy processes, whereas Bcl-2 functions as an anti-apoptotic protein. Through this balance between autophagy and apoptosis, triptolide contributes to neuronal survival and repair following injury.

14. Erinacine

Hericium erinaceus, an edible and medicinal mushroom, contains erinacines, a group of cyathane-type diterpenoids with strong neuroprotective and neurotrophic activities. These compounds are known to enhance the synthesis of nerve growth factor (NGF) and stimulate NGF-induced neurite outgrowth in various cell types, contributing to neuronal repair and recovery [84]. Importantly, erinacines can cross the blood–brain barrier and upregulate NGF mRNA expression, further supporting neural survival and regeneration.

Preclinical studies have shown that erinacine A protects neurons by reducing oxidative and endoplasmic reticulum stress and by modulating several key signaling pathways, including TRAF2–IRE1–GADD45 and PAK1/AKT/LIMK2 [85]. These mechanisms help limit the accumulation of toxic substances in the nervous system and promote neuronal endurance. In animal models of peripheral nerve injury, extracts of *H. erinaceus* have been found to delay neuronal cell death, enhance functional recovery, and accelerate nerve regeneration [86].

Collectively, *H. erinaceus* mycelium enriched with erinacine shows promise as a natural therapeutic candidate for promoting nerve regeneration and protecting against neurodegenerative conditions.

15. Red Propolis

Red propolis is recognized for its strong anti-inflammatory and antioxidant activities. In a study using a rat model of sciatic nerve axonotmesis, a hydroalcoholic extract of red propolis was

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administered orally for one month. Behavioral and morphometric assessments were performed to evaluate the extent of nerve repair [11]. The results demonstrated that treatment with red propolis extract enhanced regenerative responses and promoted faster functional recovery following sciatic nerve crush injury. Therefore, red propolis may represent a valuable complementary approach for supporting nerve regeneration and functional restoration [11].

16. *Lycium barbarum*

A traditional medicinal herb and dietary supplement has been used in China for over two millennia. It is a rich source of several bioactive compounds, including betaine, phenolics, carotenoids, cerebrosides, 2-O- β -d-glucopyranosyl-l-ascorbic acid (AA-2 β G), β -sitosterol, flavonoids, and essential vitamins such as riboflavin, thiamine, and ascorbic acid [87]. Among these, *Lycium barbarum* polysaccharides (LBPs) are the major active constituents known for their strong antioxidant activity [88]. Studies have shown that oral administration of LBPs significantly enhances nerve repair and regeneration, indicating their potential as a therapeutic agent for promoting nerve recovery after injury [89].

17. *Daphne odora*

It is a plant that belongs to the Thymelaeaceae family, and it contains the phytochemical 7,8-dihydroxycoumarin, a naturally occurring polyphenolic compound known for its antimutagenic, immune-modulating, antiviral, anticancer, and cytotoxic activities [10]. In a mouse model of sciatic nerve injury, intraperitoneal administration of 7,8-dihydroxycoumarin was shown to enhance nerve repair. This effect was associated with the upregulation of growth-associated protein-43 expression in the spinal cord segments linked to the injured sciatic nerve, suggesting that the compound supports nerve regeneration and functional recovery [90].

18. *Centella asiatica*

It is also known as *Hydrocotyle asiatica* L., a well-known medicinal herb that has been used in Ayurvedic medicine for centuries as a nerve tonic [65]. Studies have shown that the ethanolic extract of *C. asiatica* (100 μ g/mL) significantly enhances neurite outgrowth in human SH-SY5Y cells

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when combined with nerve growth factor (NGF). Asiatic acid (AA), a triterpenoid compound present in the extract, has been identified as a key bioactive component responsible for promoting neurite extension and supporting nerve regeneration [92]. Furthermore, *C. asiatica* has been found to accelerate functional recovery and enhance axonal regrowth following nerve injury, suggesting that its ethanolic extract could serve as a promising natural agent for promoting nerve repair [93].

19. Radix Hedysari

Radix Hedysari, a traditional Chinese medicinal herb, has long been recognized for its therapeutic effects in promoting nerve repair. Studies have demonstrated that both the aqueous and modified extracts of Radix Hedysari enhance the regeneration of injured peripheral nerves [94]. The main bioactive component, Hedysari polysaccharides (HPS), has shown significant potential in improving nerve recovery following injury in adult animal models. Oral administration of HPS solution (2 ml daily, 0.25 g/ml) resulted in marked improvements in the tibial, sciatic, and peroneal nerve function indices, along with enhanced conduction velocity and increased numbers of regenerating nerve fibers, highlighting its possible clinical value for treating peripheral nerve injuries [95,96,97].

Furthermore, Hedysari extract has been reported to stimulate the growth of lateral buds in the proximal nerve stump and amplify regenerative effects during peripheral nerve repair [98]. Overall, these findings suggest that Radix Hedysari and its active compounds hold considerable promise as natural agents for enhancing functional nerve recovery. However, further preclinical and clinical investigations, including dose-dependent and toxicity studies, are essential to establish their safety, efficacy, and the molecular pathways involved.

Conclusions

Phytochemicals derived from medicinal plants and natural sources have shown remarkable promise in supporting nerve regeneration and functional recovery after injury. Through various biological mechanisms, including antioxidant activity, modulation of inflammatory responses, and stimulation of neurotrophic factors, these compounds help protect neurons, promote axonal

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growth, and enhance remyelination. Evidence from experimental studies suggests that phytochemicals such as salidroside, glycyrrhizin, ginsenoside Rg1, triptolide, erinacine, and others can improve both structural and functional aspects of nerve repair.

Despite these encouraging findings, most research remains at the preclinical stage, and translation into clinical practice requires further exploration. Future studies should focus on optimizing dosage, improving bioavailability, and identifying precise molecular targets to ensure safety and efficacy. Combining traditional knowledge with modern experimental approaches may open new pathways for developing plant-based therapeutic agents for peripheral nerve injuries and related neuropathies. Overall, phytochemicals represent a valuable and largely untapped resource for regenerative medicine. With continued research and well-designed clinical trials, they could eventually complement or even replace certain conventional treatments, offering safer and more natural alternatives for nerve repair and recovery.

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