Scientific Research Publishing

Journal of Biosciences and Medicines, 2025, 13(10), 342-357
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Advances in Pharmacological Therapy for Spinal Cord Injury

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How to cite this paper: Zheng, Q.Y. and Xu, S.M. (2025) Advances in Pharmacological Therapy for Spinal Cord Injury. *Journal of Biosciences and Medicines*, **13**, 342-357.
https://doi.org/10.4236/jbm.2025.1310028

Received: September 19, 2025
Accepted: October 24, 2025
Published: October 27, 2025

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Abstract

Spinal cord injury (SCI) is a severe neurological disorder that can result in serious sequelae, significantly impacting patients' quality of life. Current primary treatment modalities include surgery, pharmacotherapy, and hyperbaric oxygen therapy. Pharmacological interventions play a crucial role in the management of spinal cord injury. However, there is currently no unified and highly effective pharmacological treatment strategy available. Therefore, this article reviews the current status of drugs commonly used in the clinical treatment of spinal cord injury.

Keywords

Spinal Cord Injury, Pharmacotherapy, Review

1. Introduction

Spinal cord injury (SCI) refers to a condition where damage to specific segments of the spinal cord leads to motor and sensory impairments below the level of injury, abnormal muscle tone, pathological reflexes, and other related changes [1]. It can often result in permanent disability, accompanied by numerous complications, high rates of disability and mortality, and considerable challenges in treatment. This imposes a heavy burden on individuals, families, and society. Therefore, identifying a safe and effective treatment for SCI is of great significance for improving patient prognosis. Although advancements in basic and clinical research have deepened the understanding of SCI among medical professionals, there is still no broad consensus regarding pharmacological interventions. Hence, it is necessary to systematically review and summarize the commonly used clinical drugs for treating spinal cord injury, with the aim of standardizing clinical prac-

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tice and providing new insights for drug-based therapies.

The drugs included in this review were selected based on the following criteria: 1) demonstration of potential therapeutic effects for spinal cord injury in either basic research or clinical practice; 2) support by a substantial body of literature elucidating their mechanisms or efficacy; and 3) sustained research interest in recent years. Drugs were excluded if 1) evidence was limited to isolated case reports or their mechanisms remained poorly understood, or 2) they had been clearly phased out due to insufficient safety or efficacy profiles. While we aimed for comprehensiveness, our literature search was primarily confined to Chinese and English databases, potentially introducing language bias and underrepresentation of studies published in other languages.

2. Western Medicine Treatment

2.1. Glucocorticoids

Methylprednisolone (MP), a synthetic corticosteroid, has been extensively studied for its therapeutic mechanisms in spinal cord injury. Research indicates that MP can upregulate anti-inflammatory factors, reduce inflammatory cell infiltration, alleviate neural edema, prevent intracellular potassium depletion, stabilize membrane structures, inhibit lipid peroxidation and the generation of oxygen free radicals [2], and suppress neuronal apoptosis [3]. The National Acute Spinal Cord Injury Study (NASCIS) [4] once recommended high-dose methylprednisolone pulse therapy for spinal cord injury: administration within 8 hours post-injury, with an initial dose of 30 mg/kg in the first hour, followed by 5.4 mg/kg/h over the subsequent 23 hours. This protocol was widely adopted in clinical practice, and some patients exhibited improved or restored neurological function after treatment. Subsequent animal studies by numerous researchers globally confirmed that high-dose MP could enhance motor and sensory function and promote neurological recovery in rats with spinal cord injury [5] [6].

However, in recent years, the severe side effects associated with high-dose MP have drawn significant attention and sparked debate. Some scholars, based on multiple randomized controlled trials and observational studies, have concluded that high-dose MP therapy offers no long-term benefits and may instead increase the risk of complications—such as prolonged immunosuppression, sepsis, pulmonary infections, gastrointestinal ulcers and bleeding, and adrenal insufficiency [7] [8]—thereby causing additional suffering, delaying recovery, and in severe cases, endangering patients' lives. Consequently, the 2013 edition of the "Guidelines for the Management of Acute Cervical Spine and Spinal Cord Injuries" no longer recommends high-dose MP pulse therapy as a standard treatment for acute spinal cord injury [9]. Instead, it is regarded merely as a therapeutic option rather than a routine protocol. Current clinical practice often employs medium-to-low dose methylprednisolone (e.g., a loading dose of 10 - 30 mg/kg, followed by appropriately tapered doses) in combination with other therapeutic modalities to better balance potential efficacy with safety concerns.

In light of this, recent approaches often combine MP with other treatments. For example, MP combined with mouse nerve growth factor [10] not only reduces inflammatory responses but also promotes nerve regeneration, more effectively improving neurological function and daily living activities. Similarly, MP combined with mild hypothermia therapy [11] synergistically mitigates inflammation and oxidative stress while reducing cellular metabolic demand, thereby better protecting neurons, lowering the risk of postoperative complications, and enhancing patients' quality of life. After years of research and discussion, the use of MP for spinal cord injury has been relatively well-established. However, due to its significant side effects and limited benefits at high doses, it has gradually fallen out of clinical use in recent years, with its research prospects now being considerably constrained.

2.2. Gangliosides

Gangliosides are a class of acidic glycolipid complexes that naturally occur as components of cell membranes, particularly abundant in the nerve cells of mammals. Exogenous monosialotetrahexosylganglioside (GM1) is the most commonly used ganglioside in clinical practice for treating spinal cord injury. Its pharmacological action is primarily achieved through binding to the neuronal cell membranes in the human body.

As GM1 is a natural constituent of mammalian neuronal membranes, it offers several advantages for spinal cord injury treatment, including the ability to cross the blood-brain barrier, a favorable safety profile, minimal adverse effects, and multiple routes of administration. These characteristics have made it a focus of recent research. Studies indicate that GM1 exerts neuroprotective effects through various mechanisms, such as reducing tissue edema, inhibiting neuronal apoptosis, suppressing lipid peroxidation, enhancing neuronal tolerance to hostile microenvironments, promoting synaptic remodeling, and facilitating nerve regeneration [12]-[15].

Given the limited pharmacological options currently available for promoting neural repair, GM1 has increasingly been used in recent years as an adjunct therapy for spinal cord injury. It is often combined with methylprednisolone [16], erythropoietin [17], and other agents to achieve synergistic effects. Such combinations allow for reduced dosages of individual drugs, improve therapeutic outcomes, enhance safety, and mitigate side effects associated with drugs like methylprednisolone.

However, as gangliosides cannot yet be synthetically produced, their cost remains high. The need for long-term and high-dose GM1 treatment in most spinal cord injury patients imposes a substantial financial burden on families, which to some extent limits its widespread clinical application.

2.3. Oxygen Free Radical Scavengers

Following spinal cord injury, disruption of the blood-spinal cord barrier (BSCB)

and local tissue acidosis occur. The massive generation of oxygen free radicals within the tissue induces lipid peroxidation, leading to local microvascular occlusion and spasm, which subsequently causes spinal cord ischemia, parenchymal edema, and neuronal death [18]. Therefore, it has been proposed that the use of oxygen free radical scavengers in the early stages of spinal cord injury may reduce neuronal cell death. In recent years, natural products such as curcumin and resveratrol have been widely investigated as agents to counteract oxygen free radicals after spinal cord injury.

Zhou Gongshe *et al.* [19] demonstrated through experiments on rats with spinal cord injury that curcumin significantly downregulates oxidative stress and inflammation levels and improves neurological function, primarily by inhibiting nuclear factor-kappa B (NF-κB) and Caspase-3. The regulatory effect of curcumin on oxidative stress after spinal cord injury is mainly reflected in the expression levels of antioxidant enzymes [20]. Although curcumin has been extensively studied in other central nervous system diseases, such as traumatic brain injury and Alzheimer's disease [21] [22], its antioxidant effects specifically in the context of spinal cord injury remain relatively underexplored. This indicates that the antioxidant mechanisms of curcumin in spinal cord injury require further investigation.

Resveratrol, a non-flavonoid polyphenolic organic compound, is a natural antioxidant. However, due to its poor solubility and limited ability to cross the blood-brain barrier, Li *et al.* [23] developed chitosan-modified hollow manganese dioxide nanoparticles (CM), while Zhang Yinyin *et al.* [24] designed functional selenium-doped silica nanoparticles for the delivery of resveratrol. Experimental studies have shown that carrier-mediated delivery of resveratrol enables rapid release at the injury site, directly decomposing reactive oxygen species into water and oxygen. This rapidly alleviates tissue hypoxia, suppresses oxidative stress and inflammatory responses at the lesion site, and promotes the recovery of motor function.

Currently, research on natural products for spinal cord injury is more prevalent in China than abroad. Further clinical trials are needed to confirm their efficacy and potential for clinical application.

2.4. Calcium Channel Blockers

After spinal cord injury, Ca^{2+} ions from surrounding areas flow into the injured tissue, leading to an overload of both total and intracellular Ca^{2+} levels. This results in reduced local spinal blood flow, increased oxygen free radical production, and further exacerbation of the injury. This process is recognized as a major pathway leading to neuronal death [25]. Consequently, some researchers have employed calcium channel antagonists to inhibit calcium influx and prevent the progression of secondary damage.

Nimodipine (NMD), a dihydropyridine calcium channel blocker commonly used in cerebrovascular diseases, binds to specific receptors in the central nervous system to prevent Ca^{2+} entry into cells. This reduces intracellular Ca^{2+} concentra-

tion, effectively decreasing free radical generation, attenuating neuronal death, improving spinal cord blood flow, and alleviating edema in spinal and surrounding cells, thereby exerting a neuroprotective effect.

Guo *et al.* [26] observed in experimental studies that after six weeks of NMD treatment, spinal cord-injured rats exhibited a reduction in lesion size and increased preservation of neurons around the injury site. These findings suggest that NMD treatment can mitigate the extent of damage in spinal cord injury, offering a potential therapeutic strategy.

However, the use of nimodipine may cause a decrease in mean arterial pressure and increase the risk of hypotension. Therefore, careful evaluation of the patient's condition is essential before administration. Maintaining systemic blood pressure stability and ensuring adequate local perfusion are critical to avoid adverse events.

Currently, research on nimodipine for spinal cord injury remains largely confined to animal studies, and no clinical consensus has been reached regarding its use in treating human spinal cord injury.

2.5. Other Investigational Drugs

Beyond the drugs discussed above, several other candidates are currently under investigation in preclinical or early clinical development stages. These include **Minocycline** (recognized for its anti-inflammatory and anti-apoptotic properties), **Erythropoietin** (implicated in both neuroprotection and angiogenesis), and small-molecule inhibitors targeting specific signaling pathways (such as Rho kinase inhibitors, ROCK inhibitors). These agents have demonstrated therapeutic potential in animal models but await validation in large-scale clinical trials, representing significant future directions for pharmacotherapeutic development in SCI.

3. Traditional Chinese Medicine Treatment

3.1. Single Herb Extracts

3.1.1. Ligustrazine

Chuanxiong (Ligusticum chuanxiong) is known in traditional Chinese medicine as a "blood-activating and qi-moving herb," primarily valued for its effects in promoting blood circulation, removing blood stasis, moving qi, and alleviating pain. Ligustrazine, also known as tetramethylpyrazine, is a bioactive monomer extracted from Chuanxiong and belongs to the class of amide alkaloids [27].

Using network pharmacology analysis, Qi *et al.* [28] suggested that ligustrazine exhibits significant neuroprotective effects after spinal cord injury. Through experimental studies, Liu *et al.* [29] found that ligustrazine alleviates neuronal ferroptosis by modulating the GPX4/ACSL4 axis, thereby protecting surviving neurons around the lesion, reducing glial scar formation, decreasing lesion size, improving neuronal survival, and promoting functional recovery after spinal cord injury.

To further evaluate the clinical efficacy of different dosages, Du Fangtao *et al.* [30] conducted a study involving 90 non-surgical spinal cord injury patients, who

were divided into control and observation groups. Both groups received conventional treatment, with the control group receiving 120 mg and the observation group 240 mg of ligustrazine via intravenous drip. After treatment, both groups showed increased Botsford and FIM scores compared to pre-treatment levels, with the observation group demonstrating significantly greater improvement. The study concluded that ligustrazine promotes functional recovery in spinal cord injury patients, with higher doses yielding more pronounced effects.

Although current studies have achieved certain progress in elucidating the mechanisms and clinical efficacy of ligustrazine in treating spinal cord injury, several limitations remain. For instance, most reported research—both domestic and international—is still based on animal experiments. There is no unified consensus regarding its clinical dosage and administration in spinal cord injury treatment, and further validation of its therapeutic effectiveness in clinical settings is still needed.

3.1.2. Curcumin

Curcumin, a compound isolated from the traditional Chinese herb turmeric (Curcuma longa), has attracted considerable research interest in recent years. Su Xiaochen *et al.* [31] demonstrated that curcumin can inhibit the inflammatory response following spinal cord injury by regulating the NLRP3 inflammasome, thereby promoting functional recovery in the limbs of rats. Feng Jianhao *et al.* [32] confirmed that curcumin suppresses the formation of glial scars by inhibiting the JAK/STAT3 signaling pathway, contributing to the repair of spinal cord injury. Weichao Li *et al.* [33] suggested that the therapeutic effect of curcumin on spinal cord injury may be achieved through enhanced autophagy, likely mediated by suppression of the Akt/mTOR signaling pathway.

In summary, curcumin modulates multiple signaling pathways in vivo, exerting effects such as inhibiting neuroinflammation, alleviating spinal cord edema, reducing oxidative stress, suppressing neuronal apoptosis, diminishing glial scar formation, and promoting neuronal repair and regeneration [34] [35], thereby mitigating spinal cord injury.

With its low toxicity and ability to cross the blood-brain barrier, curcumin holds promising potential for the treatment of spinal cord injury. However, its clinical application is limited by rapid hepatic metabolism and a short half-life [36], which necessitate further pharmaceutical improvements. Current research on curcumin for spinal cord injury remains constrained by certain limitations, including a lack of large-scale, multi-center clinical studies and insufficient evidence-based medical support.

3.1.3. Panax Notoginseng Saponins (PNS)

Panax notoginseng is a commonly used herb in traditional Chinese medicine for promoting blood circulation and removing blood stasis, primarily cultivated in Yunnan and Guangxi provinces of China. The primary bioactive components responsible for its medicinal effects are Panax notoginseng saponins (PNS). PNS is

known for its multiple pharmacological properties, including dissipating stasis, stopping bleeding, reducing swelling, relieving pain, tonifying qi and blood, inhibiting platelet aggregation, exerting anti-inflammatory effects, and providing antioxidant benefits [37]. Its potential in neuroprotection has increasingly become a focus of research.

Studies have demonstrated that PNS protects nerve cells through several mechanisms: inhibiting oxidative stress, promoting the release of nerve growth factors to nourish neurons, facilitating glial cell generation to reduce scar formation, and directly dilating blood vessels to improve blood flow in the injured spinal cord area [38] [39].

Current research reports indicate that PNS has certain therapeutic effects on the recovery of neurological and motor functions following spinal cord injury, showing promising potential for further investigation. However, most studies on PNS remain at the animal experiment stage in China, with limited international attention and publications on its application. Therefore, extensive clinical research is still needed to further clarify its efficacy and support its future translation into clinical practice.

3.1.4. Salvia Miltiorrhiza (Danshen)

Salvia miltiorrhiza, known as Danshen in Chinese, is traditionally used to promote blood circulation, remove blood stasis, clear heart fire, calm the mind, cool the blood, and reduce swelling [40]. Clinically, Salvia miltiorrhiza injection is commonly employed in the treatment of acute spinal cord injury (SCI). Compared to international research, domestic studies in China on its application for SCI are more extensive and in-depth.

Although Salvia miltiorrhiza cannot reverse already damaged neurons, it can protect unaffected or injured but viable nerve cells from further secondary damage, providing broad neuroprotective effects. It acts through multiple dimensions and pathways to improve neurological function in central nervous system (CNS) disorders, and is used in the prevention and treatment of various prevalent CNS conditions such as stroke, spinal cord injury, Alzheimer's disease, Parkinson's disease, and epilepsy [41].

Current research suggests that Salvia miltiorrhiza exerts its neuroprotective effects in spinal cord injury by inhibiting neuroinflammation, dilating local microcirculation, suppressing apoptosis, reducing oxidative stress, and promoting the expression of neurotrophic factors [42] [43]. However, Jiang Yiyuan *et al.* [44] found through experiments that ligustrazine outperforms tanshinone IIA (a primary active component of Danshen) in suppressing inflammatory responses and protecting neurons. As research progresses, some scholars propose that Salvia miltiorrhiza may be more effective when used in combination with other agents, producing synergistic effects for enhanced recovery after SCI. A commonly studied combination is Salvia miltiorrhiza with Chuanxiong (Ligusticum chuanxiong), both herbs known for activating blood and moving qi. Liu Gang *et al.* [45] used network pharmacology to identify 484 potential targets for the Chuanxiong-Danshen pair in SCI

treatment. Protein-protein interaction (PPI) network analysis revealed extensive interactions among these targets, with APP, PI3K, MAPK1/3, and AKT1 being the most critical proteins. Enrichment analysis indicated that the combination primarily alleviates secondary spinal cord injury by activating the PI3K/AKT signaling pathway.

Nevertheless, research on Salvia miltiorrhiza for SCI still has limitations. For instance, Salvia miltiorrhiza contains numerous active components, yet most studies focus only on tanshinone IIA. Other constituents contributing to neuroprotection remain incompletely identified and require further experimental validation, representing a promising direction for future research. Additionally, the relatively mild efficacy of Salvia miltiorrhiza and the lack of long-term clinical studies on its therapeutic outcomes have led to considerable controversy regarding its effectiveness.

3.2. Chinese Medicinal Formulas

3.2.1. Buyang Huanwu Decoction

Buyang Huanwu Decoction is composed of seven herbs: Radix Astragali (raw Huangqi), Rhizoma Chuanxiong (Chuanxiong), Radix Angelicae Sinensis (Dangguiwei), Pheretima (Dilong), Semen Persicae (Taoren), Flos Carthami (Honghua), and Radix Paeoniae Rubra (Chishao). Together, these components work to tonify qi, activate blood circulation, and unblock collaterals. It is widely used for treating hemiplegia, facial deviation, and speech difficulties resulting from stroke with qi deficiency and blood stasis syndrome [46].

In traditional Chinese medicine, spinal cord injury is viewed as an impairment of the Governor Vessel (Du Mai) with stasis obstructing the collaterals, compounded by severe depletion of primordial qi and prolonged lying, leading to further qi injury. This condition often corresponds to the pattern of qi deficiency and blood stasis. Consequently, some researchers propose the use of Buyang Huanwu Decoction for spinal cord injury, although its precise mechanisms remain incompletely elucidated.

Experimental studies by Guo Dehua *et al.* suggest that Buyang Huanwu Decoction promotes the proliferation of spinal astrocytes in rats with spinal cord injury and inhibits the formation of glial scars, thereby facilitating the recovery of motor function. Domestic research has reported multiple potential mechanisms, including activation of the PI3K/Akt/mTOR pathway [47], inhibition of the JAK2/STAT3 signaling pathway [48], promotion of neuronal regeneration through key pathways such as BDNF/TrkB [49], reduction in platelet-activating factor (PAF) content in spinal tissue [50], downregulation of malondialdehyde (MDA) levels, and upregulation of superoxide dismutase (SOD) activity to protect vascular endothelial cells from oxygen free radical damage [51]. These effects collectively contribute to inhibiting neuronal apoptosis, reducing spinal inflammation, and mitigating secondary injury.

However, the exact therapeutic mechanisms are still not fully understood. Fur-

ther research is encouraged to provide more robust theoretical foundations for the application of Buyang Huanwu Decoction in treating spinal cord injury.

3.2.2. Jisuikang

Jisuikang is an empirical formula developed by Professor Wang Jianwei, a renowned traditional Chinese medicine practitioner in Jiangsu Province. It is composed of the following herbs: raw Astragalus root (Sheng Huangqi), Chinese angelica (Danggui), Sichuan lovage (Chuanxiong), salvia root (Danshen), red peony root (Chishao), leech (Shuizhi), centipede (Wugong), prepared rhubarb (Zhi Dahuang), alismatis rhizome (Zexie), poria (Fuling), immature bitter orange (Zhishi), magnolia bark (Houpo), cistanche (Roucongrong), epimedium (Yinyanghuo), ground beetle (Dibiechong), plantain seed (Cheqianzi), and bitter cardamom (Yizhiren). The formula collectively acts to remove stasis, unblock the Governor Vessel (Du Mai), and harmonize qi and blood [52].

Jisuikang has been demonstrated to improve local microcirculation at the site of spinal cord injury, prevent secondary damage, effectively reduce the occurrence of complications, and facilitate repair and neural functional reconstruction in the injured area [53]. Recent experimental studies suggest that its mechanisms include inhibiting the activation of astrocytes [53], significantly suppressing glial scar formation and the expression of CSPG in the injured region [54], downregulating GFAP expression to control glial scar formation [55], promoting the activation of both M1 and M2 microglia [56], and inhibiting the NLRP3 inflammasome [57]. These actions collectively contribute to improving local microcirculation, controlling glial scar formation, alleviating secondary injury, and promoting the recovery of neurological function, offering a new direction for comprehensive pharmacological treatment of spinal cord injury.

A current research limitation is that studies on the mechanism of Jisuikang are largely confined to its inhibitory effects on glial scar formation, indicating a need for broader investigation into other potential pathways and systemic effects.

4. Biologics

4.1. Nerve Growth Factor (NGF)

Nerve growth factor (NGF), a member of the neurotrophin protein family, was the first neurotrophic factor to be discovered. Although present in relatively low concentrations in the central nervous system (CNS) under physiological conditions, it plays an essential role in the growth, development, and maturation of nerve cells [58] [59].

When the CNS is injured, the body upregulates the secretion of NGF to promote neuronal growth, development, and repair. However, in cases of moderate to severe injury, endogenous NGF production is insufficient to provide adequate protection and repair, and its effects are short-lived. Therefore, exogenous administration of NGF is necessary to compensate for this deficiency [60].

Extensive research has confirmed that exogenous NGF supplementation can inhibit apoptosis of spinal neurons, prevent or mitigate secondary damage, pre-

serve residual spinal function, promote axonal regeneration, and facilitate neurological recovery following spinal cord injury, thereby improving patients' quality of life. Moreover, NGF therapy is associated with minimal toxic side effects and a high safety profile, making it a promising candidate for clinical application and a focus of recent investigation [61].

However, conventional methods of NGF administration are limited by the blood-brain barrier, which restricts its therapeutic efficacy in promoting neurological recovery. Advances in stem cell therapy have led researchers to explore the induction of neural stem cells (NSCs) to stimulate neuronal differentiation in SCI models. Consequently, transplantation of genetically modified NSCs to regulate NGF delivery has garnered significant attention. For instance, Chen Mengji *et al.* [62] used adeno-associated virus (AAV) as a vector to engineer genetically modified NSCs and transplanted them into rats with spinal cord injury. They found that these NSCs not only differentiated effectively into neurons and astrocytes, promoting repair, but also enhanced NGF secretion, thereby protecting adjacent damaged neurons and reducing neuronal death.

This approach represents a promising strategy for treating SCI and offers novel therapeutic insights. Nevertheless, challenges such as technical complexity, high costs, and a lack of clinical efficacy data currently hinder its widespread clinical adoption.

4.2. Vascular Endothelial Growth Factor

Vascular endothelial growth factor (VEGF) not only demonstrates potent angiogenic capabilities but also exhibits significant potential in neuroprotection and neural repair [63]. As a pro-angiogenic factor, VEGF promotes blood vessel formation by activating endothelial cells, thereby enhancing blood supply to neurons, improving the microenvironment of neural tissues, and facilitating neural recovery following spinal cord injury [64]. Additionally, studies have shown that VEGF can promote axonal regeneration, further contributing to functional restoration after SCI [65]. However, achieving optimal therapeutic outcomes requires precise regulation of VEGF expression levels, a challenge that necessitates further in-depth investigation.

4.3. Gene Therapy

Following spinal cord injury (SCI), endogenous recovery attempts are hindered by several factors: inactivation of regenerative pathways in neurons and their stem cells; myelin debris and associated inhibitory molecules such as Nogo, myelin-associated glycoprotein (MAG), and oligodendrocyte-myelin glycoprotein (OMgp); and inhibitory extracellular matrix components [66]. In light of these barriers, cell and gene therapies have emerged as promising strategies for traumatic SCI in recent years.

Gene therapy involves modifying gene expression—for instance, through transfection of genes encoding neurotrophic factors or axonal guidance molecules—to

promote neural regeneration [67]. It offers high selectivity and specificity while potentially reducing the side effects associated with conventional pharmacological treatments. Although this approach has attracted significant research interest, it remains largely experimental and has not yet entered clinical use. Widespread clinical application will require resolving challenges such as immune rejection, economic feasibility, and long-term safety, all of which warrant further investigation.

5. Conclusions

Spinal cord injury is a severe neurological trauma often accompanied by multiple complications and potential long-term sequelae, which can result in lifelong paralysis and profoundly affect patients' physical and psychological well-being. While complete recovery remains elusive, early pharmacological intervention can help minimize secondary damage and preserve residual spinal function.

Current research indicates that spinal cord injury is not entirely irreversible, and encouraging progress has been made in drug therapy development. However, among the various agents studied, only methylprednisolone has gained widespread clinical acceptance for acute SCI management. Most other pharmacological treatments are still confined to animal studies, with efficacy and clinical protocols not yet firmly established.

As understanding of SCI deepens, it is increasingly clear that its pathological mechanisms are multifaceted. Monotherapy is often insufficient for comprehensive neural functional recovery. Traditional Chinese medicine (TCM), with its diverse interventions, notable efficacy, and favorable safety profile, has been widely applied in China, though international research remains limited. The lack of robust clinical evidence and standardized treatment protocols highlights the need for large-scale trials in the future.

In summary, effective clinical drug therapy for SCI will likely require combination treatments targeting multiple injury mechanisms synergistically to improve therapeutic outcomes.

This review is narrative in nature and did not employ systematic review methodology; consequently, the selection of drugs and literature may be subject to selection bias. Furthermore, due to language constraints, the referenced literature is predominantly in Chinese and English, potentially overlooking relevant studies published in other languages. Future research should aim to validate the efficacy and safety profiles of these pharmacological agents through systematic reviews and meta-analyses.

Funding

Our work has been funded by the Guangxi Natural Science Foundation Project (2024JJH40206).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Anjum, A., Yazid, M.D., Fauzi Daud, M., Idris, J., Ng, A.M.H., Selvi Naicker, A., *et al.* (2020) Spinal Cord Injury: Pathophysiology, Multimolecular Interactions, and Underlying Recovery Mechanisms. *International Journal of Molecular Sciences*, **21**, Article 7533. https://doi.org/10.3390/ijms21207533

[2] Zou, H., Guo, S., Zhu, L., Xu, X. and Liu, J. (2021) Methylprednisolone Induces Neuro-Protective Effects via the Inhibition of A1 Astrocyte Activation in Traumatic Spinal Cord Injury Mouse Models. *Frontiers in Neuroscience*, **15**, Article 628917. https://doi.org/10.3389/fnins.2021.628917

[3] Tang, Y., Xie, Z., Ma, M., Duan, K., Li, Y. and Ye, J. (2021) LncRNA and mRNA Expression Profiles in Methylprednisolone Stimulated Neural Stem Cells. *Frontiers in Neuroscience*, **15**, Article 669224. https://doi.org/10.3389/fnins.2021.669224

[4] Bracken, M.B., Shepard, M.J. and Holford, T.R. (1998) Administration of Methylprednisolone for 24 or 48 Hours or Tirilazad Mesylate for 48 Hours in the Treatment of Acute Spinal Cord Injury. *Journal of Neurosurgery*, **89**, 699-706.

[5] Gao, Z.Q., Yu, F.Y., Liu, C.M., *et al.* (2021) Evaluation of the Efficacy and Complications of Methylprednisolone Pulse Therapy for Spinal Cord Injury. *Shenzhen Journal of Integrated Traditional Chinese and Western Medicine*, **31**, 156-157.

[6] Wu, X.Y. and Feng, X.J. (2024) Effects of Methylprednisolone Sodium Succinate Combined with Surgical Intervention on Motor Function and Neuroinflammation in Patients with Acute Spinal Cord Injury. *Journal of Translational Medicine*, **13**, 2043-2045.

[7] Evaniew, N., Belley-Côté, E.P., Fallah, N., Noonan, V.K., Rivers, C.S. and Dvorak, M.F. (2016) Methylprednisolone for the Treatment of Patients with Acute Spinal Cord Injuries: A Systematic Review and Meta-Analysis. *Journal of Neurotrauma*, **33**, 468-481. https://doi.org/10.1089/neu.2015.4192

[8] Wang, Z., Liu, W., Muharram, A., Wu, Z. and Lin, J. (2014) Neuroprotective Effects of Autophagy Induced by Rapamycin in Rat Acute Spinal Cord Injury Model. *Neuroimmunomodulation*, **21**, 257-267. https://doi.org/10.1159/000357382

[9] Hurlbert, R.J., Hadley, M.N., Walters, B.C., Aarabi, B., Dhall, S.S., Gelb, D.E., *et al.* (2013) Pharmacological Therapy for Acute Spinal Cord Injury. *Neurosurgery*, **72**, 93-105. https://doi.org/10.1227/neu.0b013e31827765c6

[10] Tian, X.W. and Wang, X.X. (2025) Clinical Observation of Mouse Nerve Growth Factor Combined with Methylprednisolone for Injection in Acute Spinal Cord Injury. *Chinese Journal of Practical Medicine*, **52**, 93-96.

[11] Tian, X.W. and Wang, X.X. (2025) Clinical Efficacy of Murine Nerve Growth Factor Combined with Methylprednisolone for Acute Spinal Cord Injury: A Comparative Study. *Chinese Journal of Practical Medicine*, **8**, 155-157.

[12] Hu, H., Wang, H. and Liu, W. (2021) Effect of Ganglioside Combined with Chip Jiaji Electro-Acupuncture on Nogo-NgR Signal Pathway in SCI Rats. *Saudi Journal of Biological Sciences*, **28**, 4132-4136. https://doi.org/10.1016/j.sjbs.2021.02.031

[13] Torelli, A.G., Cristante, A.F., de Barros-Filho, T.E.P., dos Santos, G.B., Morena, B.C., Correia, F.F., *et al.* (2022) Effects of Ganglioside GM1 and Erythropoietin on Spinal Cord Injury in Mice: Functional and Immunohistochemical Assessments. *Clinics*, **77**, Article 100006. https://doi.org/10.1016/j.clinsp.2022.100006

[14] Jorge, D.D.M.F., Marcon, R.M., Cristante, A.F., Filho, T.E.P.B. and dos Santos, G.B. (2023) Evaluation of the Effect of Intrathecal GM1 in 24, 48, and 72 Hours after Acute Spinal Cord Injury in Rats. *Clinics*, **78**, Article 100228. https://doi.org/10.1016/j.clinsp.2023.100228

[15] Jiang, C.S., Zhang, L.F., Cheng, X.Q., *et al.* (2022) Therapeutic Value and Mechanism of Monosialotetrahexosylganglioside in acute Spinal Cord Injury. *Health World*, **14**, 13-14+16.

[16] Ren, D., Li, H. and Liu, X. (2025) Clinical Efficacy of Ganglioside Combined with Methylprednisolone in the Treatment of Spinal Cord Injury and Its Effect on Inflammatory Response and Oxidative Stress Factors. *Observational Study*, **35**, 238-241.

[17] Luo, Y.Y., Li, X.D. and Zhang, W.C. (2008) Combination Therapy with Different Doses of Methylprednisolone and Gangliosides for Experimental Spinal Cord Injury. *Chinese Journal of Rehabilitation Theory and Practice*, **8**, 701-702.

[18] Xu, B., Fang, J., Wang, J., Jin, X., Liu, S., Song, K., *et al.* (2023) Inhibition of Autophagy and RIP1/RIP3/MLKL-Mediated Necroptosis by Edaravone Attenuates Blood Spinal Cord Barrier Disruption Following Spinal Cord Injury. *Biomedicine & Pharmacotherapy*, **165**, Article 115165. https://doi.org/10.1016/j.biopha.2023.115165

[19] Zhou, G.S., Guo, H.Y., Song, Y.H., *et al.* (2023) Neuroprotective Effect and Mechanism of Curcumin in Rats with Spinal Cord Injury. *Chinese Journal of Experimental Surgery*, **40**, 1808-1811.

[20] Gu, G., Ren, J., Zhu, B., Shi, Z., Feng, S. and Wei, Z. (2023) Multiple Mechanisms of Curcumin Targeting Spinal Cord Injury. *Biomedicine & Pharmacotherapy*, **159**, Article 114224. https://doi.org/10.1016/j.biopha.2023.114224

[21] Qian, F., Han, Y., Han, Z., Zhang, D., Zhang, L., Zhao, G., *et al.* (2021) In Situ Implantable, Post-Trauma Microenvironment-Responsive, ROS Depletion Hydrogels for the Treatment of Traumatic Brain Injury. *Biomaterials*, **270**, Article 120675. https://doi.org/10.1016/j.biomaterials.2021.120675

[22] Shahbaz, S.K., Koushki, K., Sathyapalan, T., Majeed, M. and Sahebkar, A. (2022) PLGA-Based Curcumin Delivery System: An Interesting Therapeutic Approach in the Treatment of Alzheimer's Disease. *Current Neuropharmacology*, **20**, 309-323. https://doi.org/10.2174/1570159x19666210823103020

[23] Li, Y.Q., Zou, Z.R. and An, J.Y. (2022) Chitosan-Modified Hollow Manganese Dioxide Nanoparticles Loaded with Resveratrol for the Treatment of Spinal Cord Injury. *Drug Delivery*, **29**, 2498-2512. https://doi.org/10.1080/10717544.2022.2104957

[24] Zhang, Y.Y., Zhang, X.H., Dai, J., *et al.* (2024) Functional Selenium-Doped Silica Nanoparticles Loaded with Resveratrol for Spinal Cord Injury Therapy. *Journal of Jinzhou Medical University*, **45**, 8-13.

[25] Cui, X.H., Chen, X.F., Zou, P., *et al.* (2024) Effects of Nimodipine on Ca^{2+} Levels and Pyroptosis in Spinal Cord Tissue of Rats with Spinal Cord Injury. *Hainan Medical Journal*, **35**, 913-916.

[26] Guo, F., Zheng, X., He, Z., Zhang, R., Zhang, S., Wang, M., *et al.* (2021) Nimodipine Promotes Functional Recovery after Spinal Cord Injury in Rats. *Frontiers in Pharmacology*, **12**, Article 733420. https://doi.org/10.3389/fphar.2021.733420

[27] Jiang, S.Y., Deng, B.W., Xu, L., *et al.* (2022) Therapeutic Effects and Mechanisms of Ligustrazine in Spinal Cord Injury Repair. *Chinese Journal of Tissue Engineering Research*, **26**, 1799-1804.

[28] Qi, G., Li, S., Jiang, Q., Yu, Z., Peng, Z., Li, Q., *et al.* (2024) Network Pharmacology Analysis and Experimental Validation to Explore the Effect and Mechanism of Tetramethylpyrazine for Spinal Cord Injury. *Journal of Chemical Neuroanatomy*, **136**, Article 102386. https://doi.org/10.1016/j.jchemneu.2023.102386

[29] Liu, G., Deng, B., Huo, L., Fan, X., Bai, H., Zhao, Y., *et al.* (2024) Tetramethylpyrazine Alleviates Ferroptosis and Promotes Functional Recovery in Spinal Cord Injury by Regulating GPX4/ACSL4. *European Journal of Pharmacology*, **977**, Article 176710.

https://doi.org/10.1016/j.ejphar.2024.176710

[30] Du, F.T., Fang, J.F., Li, X.J., *et al*. (2019) Comparative Study on Clinical Efficacy of Different Doses of Ligustrazine in Treating Spinal Cord Injury. *China Medicine*, **14**, 1511-1514.

[31] Su, X.C., Wang, G.Q., Li, J.B., *et al*. (2022) Curcumin Attenuates Inflammatory Response after Acute Spinal Cord Injury by Regulating NLRP3 Inflammasome. *Journal of Shanxi Medical University*, **53**, 719-723.

[32] Feng, J.H. and Cheng, L.M. (2020) Research Progress on the Inhibitory Effect and Mechanism of Curcumin on Glial Scar Formation after Spinal Cord Injury. *Chinese Journal of Experimental Surgery*, **37**, 1171-1175.

[33] Li, W., Yao, S., Li, H., Meng, Z. and Sun, X. (2021) Curcumin Promotes Functional Recovery and Inhibits Neuronal Apoptosis after Spinal Cord Injury through the Modulation of Autophagy. *The Journal of Spinal Cord Medicine*, **44**, 37-45. https://doi.org/10.1080/10790268.2019.1616147

[34] Feng, J.H. and Cheng, L.M. (2023) Research Progress on the Inhibitory Effect and Mechanism of Curcumin on Glial Scar Formation after Spinal Cord Injury. *Chinese Journal of Experimental Surgery*, **40**, 1808-1811.

[35] Wu, Y.H. and Xu, J.G. (2023) Research Progress on Curcumin for Treatment of Spinal Cord Injury. *International Journal of Orthopaedics*, **44**, 173-176.

[36] Zhang, S.O., Xu, L.Y., Zhou, J.Y., *et al*. (2018) Research Progress on Curcumin Regulating Wnt Signaling Pathway for Treatment of Spinal Cord Injury. *Chinese Journal of Sports Medicine*, **37**, 88-92.

[37] Xing, N., Peng, D.H., Zhang, Z.H., *et al*. (2020) Research Progress on Effects of Processing on Chemical Constituents and Pharmacological Activities of Panax Notoginseng. *Chinese Journal of Experimental Traditional Medical Formulae*, **26**, 210-217.

[38] Luo, H.B., Zhou, M.J. and Chen, Y.X. (2022) Effects and Mechanisms of Notoginsenoside R1 on Mitochondrial Function and Neuroinflammation in Rats with Spinal Cord Injury. *Chinese Journal of Spine and Spinal Cord*, **32**, 823-833.

[39] Xie, M.K., Xu, N.R. and Huang, X.S. (2020) Effects of Panax Notoginseng Saponins on Neuronal Apoptosis and Expressions of Nrf2 and Caspase-3 in Rats with Spinal Cord Injury. *World Chinese Medicine*, **15**, 1410-1413.

[40] Hao, H.Y. (2021) Effects of *Salvia miltiorrhiza* Injection Combined with Isokinetic Muscle Strength Training on Limb Function and Cytokine Secretion in Rehabilitation Phase Spinal Cord Injury Patients. *Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine*, **21**, 41-42.

[41] Wang, L., Chen, M., Wang, F.H., *et al*. (2024) Research Progress on Tanshinone in Prevention and Treatment of Central Nervous System Diseases. *Drugs and Clinic*, **39**, 2988-2995.

[42] Rao, J.W., Liu, X.C., He, F., *et al*. (2024) Tanshinone IIA Promotes Spinal Cord Injury Repair by Regulating Phenotypic Polarization of Astrocytes. *Journal of Guizhou Medical University*, **49**, 1622-1630+1638.

[43] Liu, C.H., Aisaiti, a. and Muheremu, A. (2024) Potential Mechanisms of Tanshinone IIA in Spinal Cord Injury Repair. *Advances in Clinical Medicine*, **14**, 1610-1615.

[44] Jiang, S.Y., Deng, B.W., Liu, G., *et al*. (2023) Protective Effects and Mechanisms of Ligustrazine and Tanshinone IIA on Spinal Cord Injury. *Modern Journal of Integrated Traditional Chinese and Western Medicine*, **32**, 1176-1182.

[45] Liu, G., Pei, Z.Z., Deng, B.W., *et al*. (2023) Network Pharmacology Study and Exper-

imental Validation of Chuanxiong-Danshen Drug Pair in Treating Spinal Cord Injury. *World Chinese Medicine*, **18**, 3053-3059.

[46] Peng, T.Z., Huang, X.D., Lin, X.Z., *et al.* (2025) Effects of Kaiqiao Xingshen Acupuncture Combined with Modified Buyang Huanwu Decoction on IL-2, MMP-9, BDNF and Cerebral Blood Flow in Patients with Cerebral Hemorrhage during Recovery Phase (Qi Deficiency and Blood Stasis Syndrome). *The Journal of Practical Medicine*, **41**, 428-433.

[47] Xu, Y., Wu, C.L., Guo, D.H., *et al.* (2023) Exploring the Mechanism of Buyang Huanwu Decoction Combined with Bone Marrow Mesenchymal Stem Cell Transplantation in Treating Spinal Cord Injury via PI3K/Akt Signaling Pathway. *Chinese Journal of Experimental Traditional Medical Formulae*, **29**, 9-17.

[48] Wu, C.L., Guo, D.H., Xu, Y., *et al.* (2023) Mechanism of Buyang Huanwu Decoction Combined with Bone Marrow Mesenchymal Stem Cell Transplantation in Treating Spinal Cord Injury in Rats via JAK2/STAT3 Signaling Pathway. *Lishizhen Medicine and Materia Medica Research*, **34**, 1543-1546.

[49] Ni, L.L., Ouyang, L., Wei, L., *et al.* (2023) Mechanism of Buyang Huanwu Decoction in Treating Spinal Cord Injury via BDNF/TrkB Signaling Pathway. *Shanxi Journal of Traditional Chinese Medicine*, **39**, 52-55.

[50] Qi, Y.N., Tan, M.S., Wang, Y.L., *et al.* (2018) Effects of Buyang Huanwu Decoction on Platelet Activating Factor in Rats with Acute Upper Cervical Spinal Cord Injury. *China Journal of Orthopaedics and Traumatology*, **31**, 170-174.

[51] Wu, F.H., Liu, Y.L., Gao, Y.R., *et al.* (2021) Buyang Huanwu Decoction Alleviates Oxidative Stress Injury After Cerebral Ischemia-Reperfusion in Rats via Formyl Peptide Receptor 2. *Chinese Journal of Experimental Traditional Medical Formulae*, **27**, 9-15.

[52] Wang, G.P., Shao, Y., Wu, M., *et al.* (2023) Mechanism Research and Transcriptomics Analysis of Jisuikang in Promoting Spinal Cord Injury Repair. *Lishizhen Medicine and Materia Medica Research*, **34**, 1837-1840.

[53] Man, H., Wang, J.W., Wu, M., *et al.* (2024) Jisuikang Promotes Neurological Functional Recovery in Rats with Spinal Cord Injury by Activating YAP/PKM2 Signaling Axis in Astrocytes. *Journal of Southern Medical University*, **44**, 636-643.

[54] Zhang, S., Shao, Y., Hua, Z., *et al.* (2022) Effects of Jisuikang on Glial Scar Formation and Chondroitin Sulfate Proteoglycan Expression in Rats with Spinal Cord Injury. *Western Journal of Traditional Chinese Medicine*, **35**, 26-29.

[55] Shao, Y., Yang, J.F., Ma, Y., *et al.* (2020) Experimental Study on Traditional Chinese Medicine Compound Jisuikang Promoting Neurological Functional Recovery in Rats with Spinal Cord Injury. *Global Traditional Chinese Medicine*, **13**, 1479-1483.

[56] Wu, C.J., Guo, Y., Ma, Y., *et al.* (2021) Effects of Jisuikang on Microglial Activation and Histone Acetylation Levels in Mice with Spinal Cord Injury. *Lishizhen Medicine and Materia Medica Research*, **32**, 790-794.

[57] Zhou, Y.X., Ma, Y., Wu, C.J., *et al.* (2022) Mechanism of Jisuikang in Promoting Repair of Spinal Cord Injury in Rats via NLRP3 Inflammasome Pathway. *Chinese Journal of Traditional Chinese Medicine*, **37**, 5385-5389.

[58] Shi, S.L., Ding, T., Sun, Y., *et al.* (2021) Effects of Nerve Growth Factor on Bladder Function and Axonal Injury Repair in Rats with Traumatic Spinal Cord Injury. *Journal of Xi'an Jiaotong University* (*Medical Sciences*), **42**, 700-705.

[59] Yuan, S.G., Xie, J.J., Fan, Y.R., *et al.* (2022) Effects of Nerve Growth Factor on Bladder Function and Axonal Injury Repair in Rats with Traumatic Spinal Cord Injury. *Stroke and Nervous Diseases*, **29**, 230-235.

[60] Liu, S.H., Du, Z.Q., Yang, M., *et al.* (2025) Research Progress on Brain-Derived Neurotrophic Factor in Treatment of Spinal Cord Injury. *Journal of Traumatic Surgery*, **27**, 153-158.

[61] Zhang, H., Wu, F., Kong, X., Yang, J., Chen, H., Deng, L., *et al.* (2021) Correction To: Nerve Growth Factor Improves Functional Recovery by Inhibiting Endoplasmic Reticulum Stress-Induced Neuronal Apoptosis in Rats with Spinal Cord Injury. *Journal of Translational Medicine*, **19**, Article No. 445. https://doi.org/10.1186/s12967-021-02901-7

[62] Chen, M.J., Ye, J.H., Ying, Y.B., *et al.* (2020) Transplantation of Oxygen-Regulated Nerve Growth Factor Gene-Modified Neural Stem Cells for Acute Spinal Cord Injury. *Chinese Journal of Orthopaedics*, **40**, 669-679.

[63] Zamanian, C., Kim, G., Onyedimma, C., Ghaith, A.K., Jarrah, R., Graepel, S., *et al.* (2023) A Review of Vascular Endothelial Growth Factor and Its Potential to Improve Functional Outcomes Following Spinal Cord Injury. *Spinal Cord*, **61**, 231-237. https://doi.org/10.1038/s41393-023-00884-4

[64] Coyoy-Salgado, A., Orozco-Barrios, C., Sánchez-Torres, S., Olayo, M.G., Cruz, G.J., Morales-Corona, J., *et al.* (2023) Gene Expression and Locomotor Recovery in Adult Rats with Spinal Cord Injury and Plasma-Synthesized Polypyrrole/Iodine Application Combined with a Mixed Rehabilitation Scheme. *Frontiers in Neurology*, **14**, Article 1124245. https://doi.org/10.3389/fneur.2023.1124245

[65] Nagaoki, T., Kumagai, G., Nitobe, Y., Sasaki, A., Fujita, T., Fukutoku, T., *et al.* (2023) Comparison of the Anti-Inflammatory Effects of Mouse Adipose and Bone-Marrow-Derived Multilineage-Differentiating Stress-Enduring Cells in Acute-Phase Spinal Cord Injury. *Journal of Neurotrauma*, **40**, 2596-2609. https://doi.org/10.1089/neu.2022.0470

[66] Zavvarian, M., Toossi, A., Khazaei, M., Hong, J. and Fehlings, M. (2020) Novel Innovations in Cell and Gene Therapies for Spinal Cord Injury. *F*1000*Research*, **9**, Article 279. https://doi.org/10.12688/f1000research.21989.1

[67] Kichula, E.A., Proud, C.M., Farrar, M.A., Kwon, J.M., Saito, K., Desguerre, I., *et al.* (2021) Expert Recommendations and Clinical Considerations in the Use of Onasemnogene Abeparvovec Gene Therapy for Spinal Muscular Atrophy. *Muscle & Nerve*, **64**, 413-427. https://doi.org/10.1002/mus.27363