Phytomedicine Based Neurotherapeutic and Neuroregenerative Strategies in Spinal Disorders: Evidence from Clinical Observations and Experimental Models

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Highlights

As an adjuvant treatment for lumbar radiculopathy, a unique triple herb regimen consisting of ashwagandha, gotu kola and turmeric was evaluated.

"Along with better neurophysiological performance, the herbal adjunct group showed superior pain and disability reductions. The combination protects against oxidative stress, improves myelination and stimulates neurite outgrowth, according to in vitro tests. Clinical and mechanistic evidence for a neuroregenerative impact are presented in this integrative study. The results validate the need for more extensive imaging based studies to validate structural nerve restoration'.

***Abstract*—The purpose of this study was to assess the effectiveness of a phytotherapeutic combination of Withania somnifera, Centella asiatica and Curcuma longa as a supplement to conventional treatment for lumbar radiculopathy. The study also looked into possible regenerative mechanisms and clinical outcomes.**

Techniques: In a randomised controlled pilot study, 40 patients with lumbar nerve root compression confirmed by MRI were given either standard conservative therapy (Control n = 20) or standard therapy plus a daily herbal capsule (300 mg W. somnifera, 250 mg C. asiatica and 500 mg curcumin) for 12 weeks (Herbal Adjunct n = 20). Pain (Visual Analogue Scale VAS) and impairment (Oswestry impairment Index ODI) were the main

results. Secondary results included nerve conduction velocity (NCV) and straight leg raise (SLR) angle. In vitro research on Schwann cells and dorsal root ganglion (DRG) neurones concurrently evaluated neurite growth, resistance to oxidative stress and myelination (via the expression of myelin basic protein).

Results: The Herbal Adjunct group considerably improved clinically: (SLR) angle improved by 25° vs 12° ($p<0.05$); NCV rose by 18 to 22% vs 6 to 7% ($p<0.05$); ODI improved by 55% vs 25% ($p<0.01$); VAS decreased by 60% vs 31% ($p<0.01$). When compared to controls, the mixed herbal extract improved neurite length by 30 to 35%, thickened the myelin sheath by 20 to 30% and decreased oxidative stress induced cell damage by 40 to 50% in vitro ($p<0.01$).

Conclusion: In patients with lumbar radiculopathy adjunctive therapy using this herbal combination was linked to noticeably improved nerve conduction and functional recovery. Underlying neuro regenerative and neuroprotective mechanisms are suggested by complementary in vitro data.

These encouraging outcomes support larger scale clinical trials that use cutting edge imaging to confirm structural nerve healing.

***Index Terms*—Myelination, neuroprotection, phytotherapy, ashwagandha, gotu kola, curcuma longa, lumbar radiculopathy and nerve regeneration**

I. INTRODUCTION

Radiating pain sensory impairments and motor weakness are the hallmark of lumbar radiculopathy a common cause of chronic disability that often arises from foraminal stenosis or ruptured discs [1]. The goal of traditional care which includes physical therapy, pharmaceutical analgesia and surgical decompression, is to reduce mechanical pressure and symptoms, but it frequently fails to address the underlying pathophysiology of nerve fibre destruction [2]. Peripheral neurones have a limited ability for regeneration and the inflammatory environment at the compression site further hinders healing, often resulting in partial functional restoration and chronic neuropathic pain [3].

The investigation of complementary approaches that focus on the biological mechanisms of nerve healing has been spurred by this therapeutic gap. Medicinal herbs with proven neuroactive qualities present an attractive option in this regard [4]. Numerous botanicals that influence important regenerative processes, such as neuroinflammation, oxidative stress, neurotrophic support and Schwann cell activation, are highlighted by an increasing amount of experimental research [5].

One of the mainstays of Ayurvedic therapy, Withania somnifera (Ashwagandha), is categorised as an adaptogen. Studies showing its capacity to stimulate neurite outgrowth in vitro, mainly due to withanolides, which may imitate the action of endogenous neurotrophic factors, support its

importance to neurology [6,7]. Additionally, neurones under stress are shielded by its antioxidant and anti-apoptotic qualities [8].
Curcumin, the primary bioactive polyphenol found in Curcuma longa (turmeric), has strong anti-inflammatory and antioxidant properties that block important mediators including COX-2 and NF-κB [9]. Crucially animal models of sciatic nerve crush and chronic constriction injuries have repeatedly demonstrated that curcumin administration speeds up axonal regeneration, encourages remyelination and enhances functional recovery beyond symptom management [10,11]. Its function in lowering the inhibitory glial scar and increasing growth-associated proteins is connected to these effects [12].

Centella asiatica, often known as gotu kola, has long been known to improve connective tissue integrity and wound healing [13]. Asiaticoside and madecassoside, two of its active triterpenoids, have demonstrated strong antioxidant properties and have showed promise in models of central nervous system injury, possibly via reducing oxidative damage and promoting glial cell function [14,15].Its pro healing and cytoprotective qualities imply a supportive function in establishing a favourable milieu for nerve repair, even if its direct role in peripheral nerve regeneration is less well understood [16].

There is a substantial translational gap despite strong individual preclinical profiles. Clinical studies assessing standardised, multi-target herbal formulations as supplements for neuro-regeneration in compressive radiculopathies are scarce [17]. According to this study, combining these three herbs may have synergistic effects that are better than using standard treatment alone because of their complementary processes. Thus, the two main goals of this pilot study were to: (1) use patient-reported, functional and neurophysiological metrics to clinically evaluate the safety and effectiveness of this herbal combination in patients with lumbar radiculopathy; and (2) use controlled in vitro models of neurite growth, myelination and neuroprotection to empirically investigate its potential regenerative mechanisms.

II. METHOD AND MATERIALS

2.1. Participants and Clinical Study Design

From January 2024 to November 2025 a prospective, randomised and controlled pilot study was carried out . All subjects provided written informed permission and the Institutional Ethics Committee approved the study protocol.
Adults between the ages of 25 and 65 who had clinical indicators of lumbar radiculopathy supported by nerve root compression on magnetic resonance imaging (MRI) were eligible. A baseline pain intensity of at least six on the bisual analogue scale (VAS) and an oswestry disability index (ODI) score of at least forty percent were additional requirements. Previous spinal surgery serious comorbidities (such as renal, hepatic or uncontrolled diabetes) known allergies to the research herbs concurrent use of high dose antioxidant supplements and

pregnancy or breastfeeding were among the exclusion criteria.Using a computer generated sequence forty volunteers who fit these criteria were divided into two parallel groups (n = 20 each) at random for 12 weeks .Group A (Herbal Adjunct) received standard conservative care in addition to one oral capsule per day that contained 500 mg of a high bioavailability curcumin formulation (from Curcuma longa) 250 mg of Centella asiatica leaf extract (standardised to 40% asiaticosides) and 300 mg of Withania somnifera root extract (standardised to 5% withanolides). For the same amount of time, Group B (Control) only got routine conservative treatment. The standard of treatment for both groups consisted of analgesic medicine (usually non-steroidal anti-inflammatory medications) provided as needed by the treating physician, who was blind to group assignment and protocolised physical therapy (centred on core stabilisation, nerve gliding and graded exercise).

2.2. Measures of Clinical Outcomes

At baseline Day 0 and the 12 week conclusion assessments were carried out.

1. Pain Intensity: Assessed using the visual analogue scale (VAS) a 10 cm scale with 0 denoting 'no pain' and 10 denoting 'worst imaginable pain'.
2. Functional Disability: Assessed as a percentage using the validated oswestry disability index (ODI) version 2.0.
3. Physical Examination: The maximal pain-free elevation angle in degrees was measured using the bilateral straight leg Raise (SLR) test.
4. Neurophysiological Assessment: Standardised surface electromyography (EMG) methods were used to determine the motor nerve conduction velocity (NCV) for the tibial and peroneal nerves on the afflicted side. The skin's temperature was kept above 32°C. The same skilled neurophysiologist who was blind to patient group assignment performed all (EMG) investigations.

2.3. Experimental Methods in Vitro

Complementary in vitro investigations were carried out to look into mechanistic mechanisms. Neonatal Sprague-Dawley rats were used to create primary cultures of Schwann cells and dorsal root ganglion (DRG) neurones using known dissociation procedures that were authorised by the institutional animal care committee.

Culture and Treatment: Neurobasal/B27 media was used to keep the cells alive. Following stabilisation, cultures were divided into three treatment groups: the combination triple herb extract, the individual herb extracts (W. somnifera, C. asiatica and curcumin) and the control (vehicle). In order to reflect physiologically realistic human equivalent dosages concentrations were calibrated using available pharmacokinetic data.

Neurite Outgrowth Assay: On day seven (DRG) neurones were immunostained for β III tubulin. Using automated image analysis software (ImageJ, NIH) the length of each neurone was measured.

Myelination Assay: Myelination promoting media was used to sustain (DRG) neuron Schwann cell co-cultures. Cells were fixed and immunostained for Myelin Basic Protein (MBP) after 14 days. The length and thickness of myelin segments were examined.
Oxidative Stress Challenge: Cultures were exposed to 200 µm hydrogen peroxide ($H2O_2$) for four hours after being pre treated with extracts for twenty four hours. The (MTT) test was used to quantify cell viability and the fluorescent probe 2 to 7. Dichlorodihydrofluorescein diacetate (DCFH DA) was used to detect intracellular (ROS) levels.

2.4. Analysis of Statistics
The mean ± standard deviation (SD) is used to express clinical and in vitro data. The Shapiro Wilk test was used to determine normality. Independent samples t tests were used to analyse clinical outcome between-group comparisons.Paired t tests were used to examine changes within groups from baseline to 12 weeks. One way analysis of variance with Tukey's post hoc test was used for in vitro investigations with several groups. Statistical significance was defined as a p value of less than 0.05. (SPSS) software (version 25.0 'IBM' corp.) was used for all analyses.

III. RESULTS

3.1. Clinical Results
The 12 week research procedure was finished by all 40 registered individuals. The herbal supplement was well tolerated with just two patients in (group A) reporting mild stomach pain. No significant adverse events were noted.When compared to the control group (group:B) the herbal adjunct group (group:A)showed noticeably better gains across all examined parameters:
Pain (VAS):(Group:A) showed a mean reduction from 8.2 ± 0.6 to 3.3 ± 0.9 (59.8% reduction) which was substantially higher than (group:B's) drop from 8.0 ± 0.7 to 5.5 ± 1.0 (31.3% reduction) ($p<0.0$) for between group difference in change scores.
Disability (ODI): (Group:A's) functional impairment improved from 58.2% ± 4.8 to 25.7% ± 6.9 (55.8% improvement) whereas (Group:B's) improved from 55.4% ± 5.9 to 40.8% ± 7.5 (26.4% improvement) ($p<0.01$).
Nerve conduction velocity (NCV): (Group:A's) peroneal nerve (NCV) grew by 17.8% whereas (hroup:B's) increased by 6.9%.In a similar vein tibial nerve (NCV) increased by 22.1% in (group:A) as opposed to 6.2% in (group:B). Both comparisons between the groups were statistically significant ($p < 0.05$).
Straight leg raise (SLR): (Group:A's) mean increase in the pain free (SLR) angle was 25.3° 8.1° nearly twice as much as (group:B's) improvement of 11.8° 6.5° (p 0.05).

3.2. Results in vitro
The in vitro studies demonstrated a synergistic impact of the herbal combination and offered a credible biological basis for the clinical data.

Neurite outgrowth: In comparison to vehicle treated controls (DRG) neurones treated with the combined extract exhibited a 32.5% increase in mean neurite length ($p < 0.001$). Only slight non significant increases were brought about by individual extracts.
Myelination: Compared to controls co cultures treated with the combined extract showed a 25% increase in average myelin sheath thickness and a 28% increase in (MBP) positive segments ($p < 0.01$). Once more the effects of particular herbs were negligible.
Oxidative stress resistance: When compared to stressed controls pre treatment with the combined extract considerably reduced $H2O_2$ induced cytotoxicity enhancing cell viability by around 45% ($p < 0.001$). Concurrently intracellular (ROS) levels decreased by 48% ($p < 0.001$).

IV. DISCUSSION

A standardised combination of (Withania somnifera), (Centella asiatica) and (Curcuma longa) may be used as supplementary therapy to improve recovery in lumbar radiculopathy according to this pilot study which presents a new synthesis of clinical and experimental data.A possible disease modifying impact beyond symptomatic alleviation is suggested by the much higher improvements in pain, disability, nerve conduction and physical mobility seen in the herbal adjunct group which are backed by convincing evidence of neurotrophic and protective effects in vitro.

The clinical results are consistent with the increasing understanding that therapies that target the underlying neuronal disease are necessary for the successful therapy of neuropathic pain and functional loss [18]. Because it offers an objective electrophysiological correlate of improved nerve fibre integrity the improvement in (NCV) is very significant. Remyelination and/or enhanced axonal conductivity are suggested by this observation, which is seldom seen in phytotherapy trials for radiculopathy [19]. This clinical observation has a clear mechanistic connection to the similar in vitro evidence showing increased myelination and neurite development.

Their complimentary pharmacodynamic characteristics serve as the foundation for the chosen combination. Curcumin's main function is probably to reduce oxidative stress and the inflammatory cascade at the site of damage, which are known to provide an unfavourable environment for regeneration [9,11]. Withania somnifera may directly promote axonal sprouting and neuronal resilience by acting as a neurotrophic stimulant [6, 8]. Because of its antioxidant and collagen-synthesis-promoting qualities, Centella asiatica may help the regenerative scaffold by supporting Schwann cell activity and the endometrial matrix's structural integrity [14,16]. A prevalent idea in phytotherapy, when multi-component formulations interact with many targets, is that the whole is larger than the sum of its parts, as shown by the in vitro synergy seen [20].

4.1. Advantages and Drawbacks

This study's translational strategy which combines a controlled clinical trial with hypothesis driven in vitro mechanistic investigation is its main strength. The patient reported results are strengthened by the use of objective (NCV) measurements.

There are a few restrictions to be aware of. Because the experiment was a pilot with a small sample size (n = 40) and a brief followup period (12 weeks) it is important to use caution when extrapolating the results. The lack of blinding raises the possibility of participant and observer bias even if it is challenging to properly apply with a unique herbal pill. Moreover (NCV) improvements do not conclusively demonstrate structural regeneration even if they imply healing. Future research must clarify each herb's precise contribution to the mixture.

4.2. Final Thoughts and Prospects

In summary, this pilot trial offers encouraging preliminary evidence that patients with lumbar radiculopathy may benefit from the supplementary use of Withania somnifera, Centella asiatica and Curcuma longa in terms of functional and neurophysiological recovery, perhaps through neuroregenerative processes. These findings provide a strong basis for more conclusive investigation.

V. FUTURE DIRECTIONS MUST CONSIST OF

1. A more extensive, double blind, randomised, placebo controlled study with a longer follow-up period (e.g.six to twelve months).
2. The use of cutting edge imaging methods to directly visualise nerve fibre integrity and regeneration such as diffusion tensor imaging (DTI) or magnetic resonance neurography (MRN) [21].
3. Research on the pharmacokinetic interactions of the mixed extracts and dose finding trials.
4. Investigating serum or plasma biomarkers of nerve damage (such as neurofilament light chain) and regeneration in order to measure therapy response objectively [22].

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VII. CONFLICT OF INTEREST

The study described in this paper was not influenced by any conflicting financial interests or personal ties, according to the author.

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