



## Intricate role of Herbal Plants in Management of Neuropathic Pain

Shaveta Bhardwaj<sup>1</sup>, Shashidhar Mehta<sup>2</sup>, Suhasini Bhatnagar<sup>2</sup>, Puneet Sudan<sup>3</sup>, Rajesh Pandey<sup>4</sup>

1. Assistant Professor, PCTE Group of Institutes, Badowal, Ludhiana.
2. Department of Biochemistry, Mewar University, Rajasthan.
  3. Chandigarh College of Pharmacy, Landran, Punjab.
4. All Excel Inc., 135 Wood Street Suite 201 West Haven, CT 06516.

### Abstract

Among the various medical complications, neuropathic pain has emerged as the one with the most dreadful and griming which grounds serious threatening conditions by causing severe damage to the blood vessels. This damage is owed to the various alterations caused in the blood capillaries, which supply blood to the various body parts and results in the morbidity and eventually mortality. It being one of the most prevalent disorders and incurs a compelling need for its prevention and cure or treatment This review is aimed at giving an account of the various herbal plants which have till now shown successful results in their employment as a possible treatment of neuropathic pain. Some more studies need to be done for their validation so that they can not only actively substitute or be used in conjunction with the present options of treatment in order to give best results which can prevent or cure this disorder effectively but also restore the damage done to the neuropathic patient.

**Keywords:** Neuropathic Pain; morbidity; mortality; disorder; neuronal pathway

### Introduction

Pain is considered as a frequent symptom originating as a result of neurological disorder. The International Association for the Study of Pain (IASP) defines Neuropathic Pain (NP) as "pains resulting from disease or damage of the peripheral or central nervous systems, and from dysfunction of the nervous system". Originally, it was used to denote only pain related to peripheral neuropathies, and central pain (CP) was restricted to lesions of the central nervous system associated with pain. The distinction between painful conditions with or without lesions of major peripheral nerves is evidence by large amount of research that has been done in animal models of neuropathic pain, inflammatory or cancer pain This work showed a large difference in the modulatory role of the molecular, cellular and functional properties of the peripheral and central neuronal pathways involved in nociception and thus paves a way to the mechanisms that need to be highlighted in order to explore new therapeutic molecules for the benefit of mankind. The studies done showed that in animal models of partial nerve injury the site of the lesion along the peripheral course of a sensory neuron is the most important factor in the manifestations of neuropathic pain mechanisms. The various first line drugs available for neuropathic pain (such as gabapentin, pregabalin, duloxetine, tricyclic

antidepressants etc.,) are not found to be fully effective in the treatment. Henceforth, alternative treatments are being researched upon.

### **Causes of Neuropathic Pain**

A convenient classification of NP is anatomical, according to the site of initiating nervous system pathology, giving an account also the aetiological sub-classification. A mechanism-based classification is also the need of the day, but it is not yet possible to reliably link symptoms and signs to pathophysiology of the disease. The development of specific and selective treatments will depend on a mechanism-based classification. For the majority of NP sufferers, the pain will persist lifelong and the emergence of Co-morbidities (depression, impaired quality of life, employment, domestic issues etc.) also goes side by side with the onset of neuropathic pain.

### **Peripheral Causes of Neuropathic Pain**

The neuropathic pain is multifactorial in origin and thus the important factors that contribute peripherally to pain are summarized below:

- Mononeuropathies and multiple mononeuropathies conditions that cause Trauma: compression, transection, post-thoracotomy, painful scars Diabetic mononeuropathy and amyotrophy Neuralgic amyotrophy Connective tissue disease Malignant and radiation plexopathy Trench foot Borreliosis
- Polyneuropathies Metabolic/ Nutritional: Diabetic Cuban neuropathy Alcoholic Tanzanian neuropathy Pellagra Burning feet syndrome Beri-beri Strachan's (Jamaican) neuropathy
- Toxic Drugs: Isoniazid Thallium Cisplatin Arsenic Vincristine
- Clioquinol, Nitrofurantoin, Disulfiram Infective: HIV Acute inflammatory polyneuropathy
- CIDP Hereditary: Fabry's disease Dominantly inherited sensory neuropathy / HSN Malignant: Myeloma Carcinomatous Idiopathic small fibre neuropathy

### **Central Causes of Neuropathic Pain**

- Spinal Root/Dorsal Root Ganglion, Prolapsed disc, Root avulsion: Arachnoiditis Surgical rhizotomy
- Spinal Cord: Trauma including compression Syringomyelia and intrinsic tumours Multiple sclerosis
- Vascular: Myocardial infarction and other infarction, haemorrhage, AVM Spinal dysraphism Vitamin B 12 deficiency HIV Syphilis Anterolateral cordotomy Brain Stem Lateral medullary syndrome
- Multiple sclerosis Tumours: Tuberculoma Syrinx Thalamus Infarction Tumours Hemorrhage Surgical lesions Sub-cortical and Cortical Infarction Trauma AVM Tumour

### **Role of Herbal Plants in Medicines**

Plants remain the most valued source of medicines since the onset of human life. Plants provide natural biologically active molecules termed as their active chemical constituents. These molecules themselves as well as the modification of these molecules into their derivatives provide a rich source of agents with

enhanced pharmacological activity against any disease. An estimation of 400 traditional plants being useful for the treatment of neuropathic pain has been done in different studies. Thus, plants provide a spring of alternate medicinal system or a supplement to the conventional therapies of various disorders.

- ***Pinus pinaster***: *Pinus pinaster* is an evergreen tree which belongs to family Pinaceae. It is also known by the synonym Maritime Pine Tree. The tree is native to the Mediterranean regions of Europe. Pycnogenol is an extract prepared from the outer bark of this plant. Pycnogenol describes the name of a group of compounds that contain proanthocyanidins. The other constituents include taxifolin, catechin and epicatechin and acid derivatives of phenol such as p-hydroxybenzoic acid, protocatechuic acid, vanillic acid, gallic acid, cinnamic acid, p-cumaric acid, caffeic acid and ferulic acid. Along with it, the trace metals which are found in this include calcium, potassium, iron and traces of manganese, zinc and copper.
- It cause a marked accentuation in membrane integrity of the capillaries (due to the presence of procyanidins; a class of non-hydrolysable tannins, as its active constituent, which has a large affinity for binding with the proteins of the cellular membrane). Thus, it stabilizes the walls of the blood capillaries and prevents them from damaging and thus showed protective effect.
- It has potent antioxidant capability is due to its free radical scavenging activity. This contributes in lowering the amount of Reactive Oxygen Species (ROS) in the body which are responsible for the activation of advanced glycation products due to the accumulation of glycolytic metabolites. The disturbance in the equilibrium of free radicals and antioxidants contribute to number of devastations ultimately leading to neuropathic complications.
- Other components showed in this plant are pycnogenol that's responsible for decreasing the amount of advanced glycation end-products (AGEs), which are greatly responsible for the progression of neuropathic pain in patients.
- ***Anisodus tanguticus***: *Anisodus tanguticus* is a perennial flowering plant that belongs to family Solanaceae. It is also known by the name of *Scopolia tanguticus*. It is native to China where it is commonly known as Zang Qie. Apart, it is also found in Tibet. The various chemical constituents found in *Anisodus tanguticus* are tropane alkaloids such as anisodamine, anisodine (which is hydroxyhyoscine), hyoscyamine, 6-hydroxy-hyoscyamine, scopolamine, tropine, apoatropine, 3-alpha-(4,4,4-trichloro-2-phenyl-butryloxy)tropane and a non-tropane alkaloid-cusgohygrine. Out of all these, anisodamine (which is 6-beta-hydroxy-1-alpha-H, 5-alpha-H-tropane-3-alpha-ol tropane) is the most active compound of this plant.
- The presence of constituent anisodamine has fibrinolytic activity, that is responsible for the reversal of endotoxin induced vascular leakage, stabilization of lysosomes and inhibition of cathepsin, it is

known to have improvised effects on the blood circulation in the microvasculature supplying blood to various organs, thus inhibiting inflammatory responses in the capillaries.

- Anisodamine also acts as a muscarinic receptor antagonist, thus blocking the muscarinic receptor. This action leads to the rerouting of acetylcholine to alpha-7 nicotinic acetylcholine receptor, which results in the activation of cholinergic anti-inflammatory pathway. This also contributes in a wider way in response to modulatory role over the neuropathic pain.
- Anisodamine also showed cell-protective action on the cells, thus causing stabilization of the membrane, which inhibits the inflammatory action (which is responsible for the development of various kind of hemorrhages), thus preventing the hemorrhages which occur in subjects suffering with neuropathic pain.
- ***Salvia miltiorrhiza***: *Salvia miltiorrhiza* is a perennial plant that belongs to the family Lamiaceae. It is commonly known as Chinese sage or Danshen. It is natively restricted to China and Japan and was an extensively used drug in Chinese medicine. The major constituents have been identified in this plant which include diterpenes (called tanshinones), which are lipophilic in nature and polar phenolic compounds. The various compounds which come under tanshinones are tanshinone I, tanshinone IIA and cryptotanshinone. The polar phenolic compounds include phenolic acids like caffeic acid and its derivatives such as danshensu, salvianolic acid A, salvianolic acid B, rosmarinic acid and prolithospermic acid. Other compounds include baicalin, beta-sitosterol, daucosterol, flavanones, vitamin E and tannins. The lipophilic compounds are responsible for its antibacterial, antioxidant and anti-neoplastic properties whereas, the polar (hydrophilic) compounds are responsible for its antioxidant and anticoagulant properties.
- These pills showed the control in the leakage of blood and fluids which occur from the small blood capillaries supplying the blood to the various parts. These types of further micro-hemorrhages have been seen to be prevented in some patients, after the incorporation of dose of these pills in them.
- Extract also showed cell-protective action on the cells, thus causing stabilization of the membrane, which inhibits the inflammatory action.
- The magnitude of Hemorrhages and micro aneurysms was also seen to be decreased in comparison to the earlier conditions. This gave a positive result in the further usage of these pills for the treatment of neuropathic pain.

## Conclusion

Neuropathic pain is an immensely serious complication associated with morbidity and mortality, there is an urgent need to find effective treatments which could eradicate it completely. Therapy of neuropathic pain is still limited and oral treatment includes tricyclic antidepressants, gabapentin and opioids. The efficacy of carbamazepine and phenytoin is unclear and is probably overestimated. The effectiveness of sodium channel

blockers such as mexiletine or lamotrigine and of NMDA-antagonists such as dextromethorphan or memantine is of low order and the clinical use of these drugs is hampered by profound adverse effects. The various herbal drugs given in this review study aimed at giving an overview of the alternative options available which could be effectively used as a substitute to any modern medications or can be used along with them as a complementary system in order to obtain best possible results in the management of this disorder. There is further call to discover more such recourses which could help improvise the conditions prevalent in the present scenario.

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