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Neuropathic Pain: Epidemiological Trends and Herbal Intervention

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ABSTRACT :

Neuropathic pain is a complex and challenging pain syndrome that significantly impacts the quality of life. It often manifests as burning, shooting pain, numbness, and allodynia, and is notoriously difficult to manage with standard medications such as non-steroidal anti-inflammatory drugs (NSAIDs). This review explores the epidemiology, types, and mechanisms of neuropathic pain, highlighting its prevalence in women and older adults. Various forms of neuropathic pain, including post -herpetic neuralgia, diabetic neuropathy, chemotherapy-induced peripheral neuropathy, and more, are discussed. Both central and peripheral mechanisms underlying neuropathic pain involve intricate processes such as neuroinflammation, sensory processing disruptions, and interactions between the nervous and immune systems. The review also addresses the inadequacies in current treatment approaches and emphasizes the potential of herbal plants in alleviating neuropathic pain. Specifically, plants like Ocimum sanctum and Momordica charantia have shown promise in modulating biochemical pathways related to neuropathic pain, offering new avenues for effective management. Through a comprehensive understanding of these mechanisms and alternative treatments, this review aims to provide insights into improving the quality of life for individuals suffering from neuropathic pain.

Keywords: Analgesic, Antinociceptive, Chronic pain, types, mechanism, Herbal medicine for Neuropathic pain.

Introduction:

In general, neuropathic pain is recognized as a very challenging pain syndrome to treat, with frequently disappointing results. One reason for this is that neuropathy may not always be noted as a factor in pain that presents in primary care*[1]*. Additionally, there is an evidence of inadequate medication use in the treatment of neuropathic pain. Both neuropathic and inflammatory pain are painful and concerning lowering the quality of life for those who experience them, according to the International Association for the Study of Pain (IASP). Tissue injuries cause inflammatory pain, whereas somatosensory system problems cause neuropathic pain*[2]*. It often shows as burning or shooting pain, numbness, and allodynia, which is hard to explain. Neuropathic pain is difficult to treat with standard medications such as non-steroidal anti-inflammatory drugs (NSAIDs). Quick observation of neuropathic pain is important in first aid because it helps differentiate it from nociceptive pain and promotes the use of alternative analgesic methods*[3]*. A range of 10.4% to 14.3% of the population suffer chronic pain which can be moderately to severely fatal*[4]*. A complicated combination of psychosocial, genetic, biological, and clinical factors may be liable for the ranging occurrence and severity of neuropathic pain, that can affect either the peripheral or central nervous system and manifest as chronic pain in idiopathic neuropathies*[5]*. This is being studied in the 10,000-person DOLO Risk study, which is now in progress*[6]*.

2. Epidemiology:

Recurrent neuropathic pain is more common in women (8% vs. 5.7% in men) and in individuals over 50 (8.9% vs. 5.6% in those under 49). It mostly impacts the arms and legs, cervical region, upper extremities, and lumbar area*[7]*. The research that involved over 12,000 individuals with chronic pain—both nociceptive and chronic—who were sent to German pain specialists found that 40% of the participants had a variety of neuropathic pain symptoms*[8]*. Poland (mean age: 47 years), Norway (30%), and Italy were the three countries with greatest prevalence rates of chronic pain among those surveyed. Poland also showed a higher percentage of women (55%) than men with chronic pain*[9]*, and 31% reported having severe pain (Numeric Rating Scale [NRS] ≥8), though in clinical practice, only 5% of such cases were assessed by medical professionals using pain scales*[10]*. About 20% of the general population in France is affected by mild to serious chronic pain, with neuropathic pain making up about 7% of patients. 6–10% of the population overall suffering with neuropathic pain, with a rate of 8.2/1000 person-years in nations that are not European. In 15-20% of scenarios, individuals see a doctor for chronic pain; neuropathic pain individuals report more severe symptoms*[11]*. Around 29 and 86% individuals suffering multiple sclerosis (MS) report having pain, most often central neuropathic pain. In about 80% of cases with MS, spasticity also develops. In MS, pain, particularly headaches and pain in the hands and feet, usually fails to decrease with conventional methods for pain management and tends to get worse as the illness develops*[12]*.

3. Types of Neuropathic pain:

There are two types of neuropathic pain: central and peripheral.

Peripheral disorder:

Post-Herpetic Neuralgia: A frequent outcome of herpes zoster (HZ), postherpetic neuralgia (PHN) occurs within 12.5% of cases and is typically associated with immunosuppression, age, and the site of the harm after the rash disappeared[13]. This varicella zoster virus (VZV) leads to a dermatomally distributed rash and goes into latency in the trigeminal and dorsal root ganglia after primary infection. This reactivation leads to a rash that is characterized by pain that lasts for months or years and can be particularly severe when it alters the trigeminal nerve*[14]*.

Diabetic Neuropathy (DNP): Within ten years after the onset of diabetes, sensorimotor polyneuropathy—a usual complication—affects mobility badly and increases pain related to rest, impairing quality of life and sleep*[15, 16]*. The diagnosis of the disorder relies on a clinical examination that can distinguish between burning sensations and shooting or stabbing pain, with a distribution like to that of socks and gloves. Prolonged hyperglycemia is linked to the disorder's cause, being linked to elevated proteinase C and advanced glycation end products (AGEs), nerve injury and repair balance difficulties, and vascular and neuronal damage*[17]*.

Chemotherapy Induced Peripheral Neuropathy (CIPN): Chemotherapy-induced peripheral neuropathy (CIPN) is a situation in which the peripheral or autonomic nervous system has been damaged by the agents used in the treatment***[18].*** It is characterized by changed sensitive and painful paraesthesias, especially in the extremities, as well as decreased mobility and a higher likelihood of declines, especially in older adults***[19].*** The cause of this condition is elaborate and combines various factors, including medication class, dosage, patient characteristics, and drug-specific procedures such as DNA alteration and microtubule disturbances***[20].***

Post-Operative Neuropathic Pain (PONP): The nociceptive and neuropathic features of acute postoperative pain following CRS + HIPEC are affected by surgical trauma, inflammation, and thermal therapy***[21].*** Post-operative neuropathic pain is the third most common type in older adults. It can be hard to pinpoint because of its wide range of symptoms and long duration in a third of cases. Furthermore, it can be made worse by preexisting conditions such as cancer, chronic pain, surgery, and even post-operative delirium***[22].***

Complex Regional Pain Syndrome (CRPS): Clinical signs and history of CRPS are used to diagnose this illness, which is characterized by excessive regional pain with anomalies of the sensory, motor, and vasomotor systems. Trauma frequently serves as the cause of CRP***[23].*** There are uncertain links between its pathophysiology and mental disorders ***like*** anxiety and depression. It involves pro-inflammatory reactions, vasomotor defects, and brain plasticity***[24].***

Compressive Neuropathic Pain (CNP): Due to the aging of the spinal discs, which can produce ruptures or herniations, compressed nerves are common in older adults. The outcomes of scans and physical exams are used by doctors to diagnose this illness***[25]***. The main symptom, which varies depending on the damaged nerve root, is pain***[26].*** Due to various medical issues or cognitive decline, older adults may find it difficult to express their discomfort.

Post-Amputation Neuropathic Pain (PANP): A lower limb amputation is an extraction of any part of the lower limb from the body. It results in residual nerve degeneration and a reduction of sensory function, so it's hard for prosthetics to fully balance for the shortage of sensory feedback***[27].***Despite amputation has become less common, 95% of cases are known to result in chronic unease. Vascular illnesses especially over age 65, are the primary cause of lower limb amputations***[28].*** Neuromas can form at any peripheral nerve distribution site, that's because persistent pain after amputation may be due to flexion contractions, consuming or shock-like senses in phantom limb syndrome, or any one of these***[29].***

Central disorder:

Fibromyalgia: About 5% of people have fibromyalgia, which mostly strikes women between the ages of 30 and 35[30]. The etiology of fibromyalgia includes differences in excitatory neurotransmitters such as glutamate and substance P, errors in monoaminergic neurotransmission, and a decrease of serotonin and norepinephrine in the spinal cord[31].

Trigeminal Neuralgia (TN): TN is characterized by ongoing, severe, one-sided face unease that seriously affects patient well-being and regularly results in emotional pain because of how fatal it is[32]. Classical TN is primarily caused by neurovascular compression at the entry of the pons into the trigeminal nerve roots. This compression results in demyelination of the nerve fibers and abnormal firing. Dysregulated voltage-gated sodium channels, such as Nav1.3 and Nav1.7, are implicated in this process, and there is also emerging evidence of Kv7.2 dysregulation in pain related to the cold[33].

Spinal Cord Injury (SCI): Millions of people worldwide suffer from spinal cord injury (SCI), which has severe physical, psychological, and financial consequences. Developing successful treatment procedures for SCI requires a thorough understanding of its unique pathophysiology[34].The etiology of spinal cord injury comprises a series of interconnected processes that result in cytotoxic, ionic, and vasogenic edemas. These processes are increased by glutamate excitotoxicity and mitochondrial dysfunction, and ultimately lead to neuroinflammation and neuronal death[35].

Multiple Sclerosis (MS): Multiple sclerosis (MS) primarily affects young adults, leading to physical disability and cognitive impairment, with diagnosis based on clinical, radiographic, and laboratory findings[36]. Its pathogenesis involves autoimmune processes targeting the CNS, influenced by genetic predisposition, environmental factors, and human leukocyte antigen DRB1*1501[37].

Central Post-Stroke Pain Syndrome (CPSP): The complicated pathophysiology of post-stroke pain, including CPSP, makes care difficult and results in underdiagnosis and inadequate comprehension, calling for all-encompassing approaches to improve prognosis[38]. The cause of central neuropathic pain, including CPSP, is brain injury that upsets the balance between facilitatory and inhibitory influences in the thalamocortical and spinothalamic tract circuits. This results in neuronal hyperexcitability and hypersensitivity to stimuli, which are linked to denervation and a loss of inhibitory control[39].

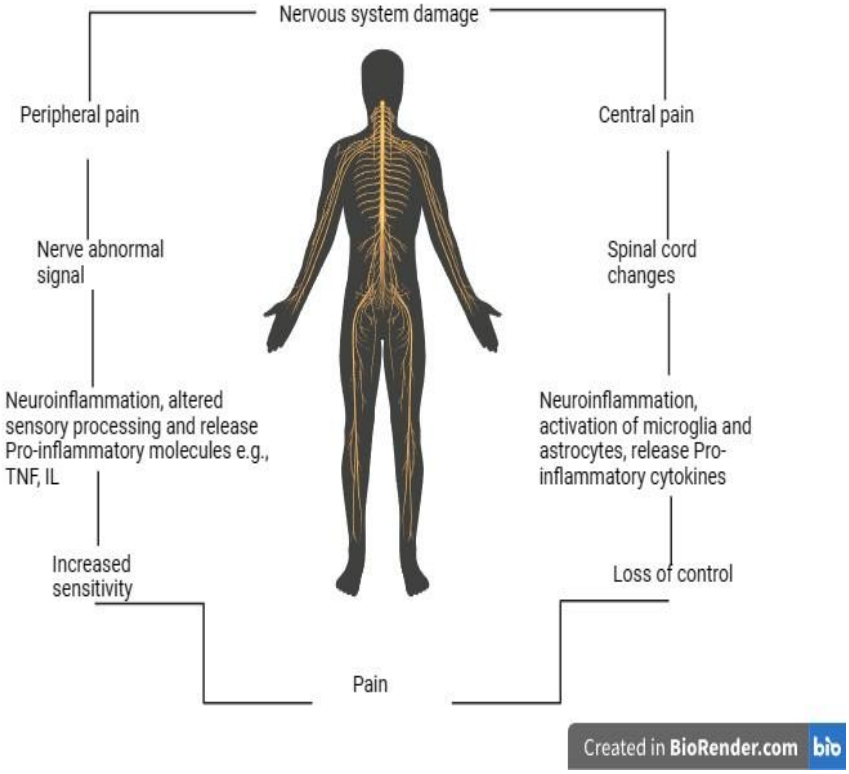
4. Mechanism of Neuropathic pain:

Nervous System Damage: Neuropathic pain can result from injury to the nerves in the body or brain. Among neuropathic pain conditions, the prevalence of evoked pain varies; peripheral nerve injury, post-herpetic neuralgia, central pain, and painful peripheral neuropathy show the highest incidence and lowest rates, respectively, of dynamic mechanical allodynia and pinprick hyperalgesia***[40].***

Peripheral Mechanisms: The neurological and immune systems interact in peripheral neuropathic pain (NP), resulting in neuroinflammation and impaired sensory processing. Ion channels and immune cell receptors may be the targets of future therapeutic approaches for the treatment of peripheral NP***[41].***

Central Mechanisms: Research indicates that as many as 80% of people with SCI go on to develop chronic neuropathic pain (CNP), with early sensory hypersensitivity and advanced age being risk factors. Because of compromised physiological processes, the therapy of CNP produces less positive results than peripheral neuropathic pain***[42].***

5. Structure



6. Herbal Plants for neuropathic plants:

Botanical name	***Family***	***Mechanism***	***Reference***
Acorus calamus	Araceae	Superoxide anion, Myeloperoxidase, tissue calcium level decrease, Malondialdehyde decrease, maintain normal protein level.	***[43]*** ***[44]***
Alstonia scholaris	Apocynaceae	Reduced glutathione, Myeloperoxidase, Total calcium.	***[45]***
Artemisia dracunculus	Asteraceae	Reduced superoxide anion levels and MPO activity, decrease in oxidative stress, reduced total calcium levels.	***[46]***
Butea monosperma	Fabaceae	Reduced glutathione (GSH) and total calcium levels	***[47]***
Citrus colocynthis	Cucurbitaceae	Decrease superoxide dismutase, malondialdehyde (MDA), catalase (CAT).	***[48]***
Crocus sativus	Iridaceae	Superoxide dismutase (SOD) and glutathione peroxidase, reduces malondialdehyde (MDA)	***[49]***
Ginkgo biloba	Ginkgoaceae	Malondialdehyde reduce Reduce NOD-like receptor protein 3 (NLRP3), (TLR4 and p-NF-κB).	***[50]*** ***[51]***
Rosmarinus officinalis	Labiatae	Decrease IL-1b, PGE-2, NO, COX-2, and MMP2.	***[52]***
Momordica charantia	Cucurbitaceae	Inhibit cytokines IL-12 and IL-1β.	***[53]***
Ocimum sanctum	Lamiaceae	Increase ascorbic acid , inhibits11βhydroxysteroid dehydrogenase type 1 ,Catechol-O-methyltransferase, decrease serotonin level	***[54]***

Conclusion:

Neuropathic pain presents a significant treatment challenge due to its complex etiology and multifaceted presentation. Standard pain medications often fall short, necessitating alternative therapeutic approaches. Epidemiological studies show a higher prevalence in women and older adults, with

conditions like diabetic neuropathy, post-herpetic neuralgia, and chemotherapy-induced peripheral neuropathy being common causes. Central mechanisms involve neuroinflammation and sensory processing disruptions, while peripheral mechanisms highlight the interaction between the nervous and immune systems. Various herbal plants, such as Ocimum sanctum and Momordica charantia, demonstrate potential in modulating biochemical pathways involved in neuropathic pain, offering hope for more effective management strategies.

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