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Capsaicin in Pain Management A Spicy Solution to Chronic and Neuropathic Pain

Konrad Pilarski

Medical University of Warsaw, ul. Zwirki i Wigury 61, 02-091 Warsaw, Poland,

konradpilarski9@gmail.com

https://orcid.org/0009-0000-6730-1332

Adam Kucharski

Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland

adam.kucharski14@gmail.com

https://orcid.org/0009-0000-7210-2426

Rafał Makuch
Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland

rafalmakuch@icloud.com

https://orcid.org/0009-0001-8192-7662

Alicja Chrościcka
Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland

a.z.chroscicka@gmail.com

https://orcid.org/0009-0003-8985-890X

Kamil Gała
Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
kamilkem5@wp.pl

https://orcid.org/0009-0006-3498-6746

Andrzej Czajka
Provincial Specialized Hospital in Zgierz Parzęczewska 35, 95-100 Zgierz, Poland

andrzej.czajka0509@gmail.com

https://orcid.org/0009-0008-8888-3982

Paweł Lenard
Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland

Pawellenard@gmail.com

https://orcid.org/0009-0008-7421-3400

Sara Michalska
Medical University of Warsaw, ul. Zwirki i Wigury 61, 02-091 Warsaw, Poland

saramichalska1@gmail.com

https://orcid.org/0009-0009-4184-3366

Martyna Dewicka
Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland

m.dewicka@gmail.com

https://orcid.org/0009-0008-9282-1231

Alicja Maria Wawrzyniak
Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland

alicja.wawrzyniak@stud.umed.lodz.pl

https://orcid.org/0009-0000-5397-363X

Abstract:

Introduction and purpose:

Chronic pain, defined as pain persisting for three months or longer and neuropathic pain which is a type that arises as a result of damage or disease to the somatosensory system, including peripheral fibers (Aβ, Aδ, and C fibers) and central neurons, are serious conditions pose significant challenges for modern medicine. Addressing these challenges often necessitates a multimodal approach to analgesia, involving the use of multiple analgesic agents with different mechanisms of action. Among these agents is capsaicin, a naturally occurring compound found in hot peppers. This study will collect and analyze information

about the applications of capsaicin in pain management, its mechanisms of action, efficacy, and safety.

Brief description of the state of knowledge:

Capsaicin is a natural compound found in chili peppers. This alkaloid is a highly selective agonist of the TRPV1 vanilloid receptor. Upon activation of these receptors, skin nociceptors become less sensitive to stimuli. Incorporating capsaicin into standard chronic and neuropathic pain management may enhance, expedite, and streamline the complex process of treatment, ultimately contributing to improved quality of life for patients and communities. It also offers certain benefits in the treatment of obesity, cardiovascular and gastrointestinal pathologies, various types of cancers, neurogenic bladder, and some dermatological conditions.

Materials and Methods:

Review and summary of research studies available in databases on Google Scholar and PubMed.

Summary:

Topically applied capsaicin, especially in the form of an 8% patch is a valuable option for treating peripheral chronic and neuropathic pain, including bone and joint pain. The highest quality evidence has been presented in postherpetic neuralgia and HIV-related pain, where treatment efficacy is comparable to standard treatment.

Keywords: capsaicin; capsaicin in pain relief; capsaicin in chronic pain treatment; capsaicin in neuropathy pain treatment;

Introduction:

Chronic pain affects approximately 20% of the European population and is more prevalent among women and the elderly. While some factors are unmodifiable (e.g., gender, age), others can be modulated (e.g., pain intensity, mood). [1] Neuropathic pain affects approximately 7–10% of the general population. [2] The process of pain transmission in the nervous system is remarkably complex. However, our capacity to effectively alleviate neuropathic and chronic pain remains limited. The variety of pharmacologically distinct medications available is small, and the therapeutic outcomes achieved are often limited. It results in a reduced quality of life for patients and places an economic strain on individuals and society. [3] One of the natural substances that can be used in the therapy of these conditions is capsaicin, which is a component responsible for the spicy properties of chili peppers, which exhibits analgesic, numbing, anti-inflammatory, and thermogenic effects, making it the subject of numerous studies. Due to its spiciness, it's typically used in the form of topical preparations, such as creams, gels, and patches. These products are designed to target specific areas of pain without causing widespread discomfort, making them effective for localized pain relief. [4,5]

Capsaicin's Mechanism of Action:

Capsaicin interacts with the transient receptor potential vanilloid 1 (TRPV1) receptors, which are present on sensory nerve endings. These TRPV1 receptors, primarily located on nociceptors nerves specialized in detecting and responding to pain are heat-activated calcium channels. TRPV1 receptors also respond to high temperatures and acidic environments, explaining why capsaicin can produce sensations similar to burning or heat. When capsaicin binds to TRPV1 receptors, it triggers the opening of these ion channels, permitting an influx of calcium (Ca2+) and sodium (Na+) ions into the cell. This ion movement leads to the depolarization of the nerve cell membrane, initiating an action potential that transmits pain signals to the brain. [6,7,8] With repeated or prolonged exposure, capsaicin results in the desensitization of sensory neurons. This process makes the neurons less reactive to pain stimuli, which is advantageous for therapeutic applications. Capsaicin also stimulates the release of substance P, a neuropeptide that plays a crucial role in conveying pain and inflammatory signals within the nervous system. Continuous activation by capsaicin can eventually deplete substance P from the nerve endings, reducing the transmission of pain

signals. These effects are reversible and may last from a few hours to several months, depending on the method of administration and the concentration of the active substance. [4,9]

Tolerability and Safety:

Capsaicin, like other medications, can cause various adverse effects. When used topically, capsaicin usually presents a low risk for systemic side effects. A notable reaction is coughing, which occurs in up to 5% of users due to capsaicin's inherent pharmacological properties. On application to the skin, it frequently induces burning, redness, or stinging sensations in 40 to 70% of individuals. These effects are generally mild to moderate, transient, and self-resolving, but they can lead to treatment discontinuation in up to 30% of cases. Besides these common reactions, capsaicin has been associated with less frequent adverse effects, such as diarrhea, nausea, vomiting, high blood pressure and dizziness. [10,11,12]

Postherpetic neuralgia:

Postherpetic neuralgia (PHN) is a painful disorder that arises as a long-term complication following an episode of acute herpes zoster, commonly known as shingles. Shingles itself is caused by the reactivation of the varicella-zoster virus (VZV), which typically infects individuals during childhood as chickenpox.This condition can be extremely painful, presenting symptoms even before the characteristic rash appears, continuing throughout the rash phase, and often persisting after the visible inflammation has resolved. In many cases, the pain diminishes as the rash heals. However, when the pain continues beyond the healing period, it is identified as PHN. The likelihood of developing PHN increases with age, and managing the pain often necessitates a multi-drug approach. [13] Numerous studies have investigated the efficacy of high-concentration capsaicin patches, specifically at 8%, in treating this type of pain. Significantly more patients treated with the 8% capsaicin patch reported a ≥30% reduction in pain from baseline compared to control patients (low-concentration control patch of 0.04% capsaicin). Furthermore, the proportion of patients reporting improvement on the Patient Global Impression of Change (PGIC) scale was significantly higher among those treated with the 8% capsaicin patch compared to those receiving the control treatment [14,15]

HIV-associated distal sensory polyneuropathy (HIV-DSP):

This condition is the most frequently reported neurological complication linked to HIV infection. It can be triggered either by the HIV virus itself or as a side effect of antiretroviral medications. HIV-associated distal sensory polyneuropathy (HIV-DSP), when symptomatic, involves both small and large sensory nerve fibers. The condition manifests through painful abnormal sensations (dysesthesias), heightened sensitivity to normally non-painful stimuli (allodynia), intense burning pain, tingling, and numbness. [16,17] Utilizing the 8% capsaicin patch resulted in significant pain reduction within the first two weeks, and this relief continued consistently throughout the 12-week study duration. The percentage of patients experiencing at least a 30% reduction in pain from their initial levels was more than twice as high in those treated with the 8% capsaicin patch compared to those in the control group (low-concentration control patch of 0.04% capsaicin) [14,18,34] These studies cannot be overlooked, as there are very few effective pain relief therapies available for HIV-associated distal sensory polyneuropathy (HIV-DSP). [19]

Painful diabetic neuropathy (PDN):

PDN is a frequent and debilitating complication of diabetes, predominantly affecting the peripheral nerves, particularly in the lower extremities. This condition arises due to chronic hyperglycemia, which leads to metabolic and vascular changes that damage the nerve fibers. In PDN, patients commonly report symptoms such as burning, stabbing, or electric shock-like pain, along with tingling or numbness, primarily starting in the toes or feet and potentially spreading to the legs and hands in a "glove and stocking" distribution. These sensory disturbances can be exacerbated at night, significantly impairing sleep and overall quality of life. Additionally, patients may experience allodynia, where normal touch or pressure causes severe pain, or hyperalgesia, which is an increased sensitivity to painful stimuli. [20,21] Research has shown that using an 8% capsaicin patch, when compared to a placebo patch in the control group, provides a slight but statistically significant improvement in both pain management and sleep quality. The effectiveness of this treatment is on par with other drugs used for neuropathic pain, but it notably lacks systemic adverse effects [22,23,24]

Osteoarthritis:

Osteoarthritis is the most prevalent type of arthritis and a major contributor to pain and disability on a global scale. This chronic condition, rooted in mechanical factors, is marked by various dysfunctions. Osteoarthritis typically presents with pain, stiffness, and limitations in function and range of motion, which significantly lower the quality of life and lead to functional impairment. [25,26] Moderate effectiveness has been demonstrated for low-concentration capsaicin cream (0.025% or 0.075%) compared to placebo control groups. Recently, promising studies have also emerged regarding the intra-articular administration of capsaicin. Following a single intraarticular injection of capsaicin at doses of either 0.5 mg or 1.0 mg, or a placebo, improvements in WOMAC scores and relief from knee osteoarthritis pain were noted for up to 12 weeks in the 0.5 mg group and up to 24 weeks in the 1.0 mg group. [27,28]

Chemotherapy-induced peripheral neuropathy (CIPN):

Chemotherapy-Induced Peripheral Neuropathy, commonly referred to as CIPN, is a condition that arises as a side effect of certain cancer treatments. It occurs when chemotherapy drugs cause damage to the peripheral nerves. Patients with CIPN often experience various forms of discomfort, including tingling, burning sensations, pain, numbness, and a feeling of coldness, primarily in the hands and feet. These sensory symptoms can be quite distressing and may interfere with daily activities. The presence of CIPN can pose significant challenges for cancer patients. It not only reduces their ability to perform everyday tasks but can also necessitate changes in their cancer treatment plans. [29] It is suggested that an 8% capsaicin patch can effectively reduce pain intensity in patients with Chemotherapy-Induced Peripheral Neuropathy (CIPN). [30,31] Additionally, it may promote nerve regeneration and restore the nerve fiber phenotype, as studied through skin biopsies. [32] However, these promising results have been confirmed only in small-scale, single-center prospective studies with a limited number of participants. [30,33]

Discussion:

Numerous studies have demonstrated that high-concentration topical capsaicin is effective in treating chronic and neuropathic pain. The 8% capsaicin patch has been approved in the USA and the EU for the treatment of postherpetic neuralgia, painful neuropathy associated with HIV infection, and painful diabetic neuropathy. [35] Although studies and articles have shown promising results in various chronic and neuropathic pain conditions, they are not without limitations that must be considered when analyzing the data. Many of the

studies were conducted on a limited, small number of participants, many were single-center studies, and the results were not always consistent. Additionally, the potential for author bias cannot be ruled out. [33,35] Nevertheless, the limited range of medications available for the classic treatment of chronic and neuropathic pain compels us to seek co-analgesics that can help patients return to normal life without debilitating symptoms. In addition to pain management, capsaicin and its properties are being investigated for potential applications in various fields of medicine, including gastroenterology, diabetology, oncology, and orthopedics. [4]

Conclusions:

Overall, chronic and neuropathic pain remains a significant treatment challenge. Only a small percentage of patients achieve substantial pain relief, underscoring the importance of exploring additional therapeutic options when primary recommended treatments fail or prove inadequate. Capsaicin, despite its apparent simplicity, could potentially offer a solution.
Despite evidence supporting its efficacy, capsaicin remains underutilized in clinical practice. Integrating capsaicin into standard chronic pain management protocols could potentially enhance efficacy, expedite treatment outcomes, and alleviate the difficulties associated with managing chronic and neuropathic pain, thereby improving quality of life for patients and society as a whole.

Disclosure

Author's contribution

Conceptualization: Rafał Makuch and Adam Kucharski; Methodology: Alicja Wawrzyniak; Software: Alicja Chrościcka; Check: Andrzej Czajka and Kamil Gała; Formal analysis: Konrad Pilarski and Martyna Dewicka; Investigation: Paweł Lenard and Sara Michalska; Resources: Kamil Gała; Data curation: Alicja Chrościcka; Writing - rough preparation: Adam Kucharski and Rafał Makuch; Writing - review and editing: Alicja Wawrzyniak and Konrad Pilarski; Visualization: Martyna Dewicka; Supervision: Sara Michalska; Project administration: Rafał Makuch and Paweł Lenard; Receiving funding - no specific funding.

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Conflict of interest

The authors deny any conflict of interest.

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