

Capsaicin

Capsaicin, the active compound in *Capsicum* species (e.g., hot peppers), is widely recognized for the spicy sensation it induces upon consumption. This compound was first isolated in the early 19th century, though its use in medicine dates back thousands of years. Today, capsaicin is primarily employed for its analgesic and anti-pruritic (anti-itch) properties. While capsaicin induces a burning sensation on initial application, this discomfort typically subsides as the compound exerts its therapeutic effects. Common over-the-counter (OTC) topical preparations include Capsagel, Salonpas-Hot, and Zostrix.

Mechanism of Action

Capsaicin exerts its effects through its interaction with the transient receptor potential cation channel subfamily V member 1 (TRPV1), which is a receptor primarily located on nociceptive neurons that detect pain and heat. Upon activation, TRPV1 receptors trigger the release of neuropeptides such as substance P and calcitonin gene-related peptide (CGRP), which are involved in pain and itch sensation. Initially, capsaicin application leads to the release of these neuropeptides, resulting in a burning or painful feeling at the site of application. However, with repeated stimulation, the neurons become desensitized, and the release of neuropeptides is depleted. This desensitization significantly reduces the sensation of pain or itch, thereby providing analgesic and anti-pruritic effects.

This neurochemical depletion mechanism underpins the efficacy of capsaicin in managing chronic neuropathic pain and pruritus, as the neurons' ability to transmit pain or itch signals is diminished over time.

Indications

Capsaicin is primarily used in dermatology for the management of localized chronic pruritus (itching) and neuropathic pain. Its most common and FDA-approved indication is the treatment of postherpetic neuralgia, a condition that often follows shingles, where nerve damage leads to chronic pain. In this context, capsaicin is used as an adjunctive therapy, alongside other medications such as anticonvulsants, tricyclic antidepressants, and opioids.

In addition to its approved use, capsaicin has numerous off-label dermatologic applications, including:

- Notalgia paresthetica (a condition causing localized itching on the back)
- Hemodialysis-associated pruritus (itching related to kidney dialysis)
- Brachioradial pruritus (itching affecting the arms and upper back)
- Reflex sympathetic dystrophy (chronic pain syndrome)

- Pain due to psoralen plus ultraviolet A (PUVA) therapy or tumor infiltration
- Erythromelalgia (a condition causing redness and burning in the extremities)
- Psoriasis (a chronic autoimmune skin disorder)
- Vulvar vestibulitis (painful condition affecting the vulva)

These off-label uses are based on capsaicin's ability to modulate pain and itching through TRPV1 receptor desensitization, which reduces the transmission of pain and itch signals in various dermatologic conditions.

Side Effects

The majority of side effects associated with capsaicin are localized to the site of application. The most common adverse effect is the initial burning or painful sensation, which occurs in approximately 80% of patients, especially during the first few days to weeks of use. This reaction is due to the activation of TRPV1 receptors and the subsequent release of neuropeptides. This discomfort often subsides as the skin becomes desensitized. The intensity of the burning sensation can be mitigated by applying topical lidocaine before using capsaicin or by storing the product in the refrigerator.

Other local side effects include:

- Pruritus (itching)
- Erythema (redness of the skin)
- Swelling (edema)
- Xerosis (skin dryness)

Though rare, systemic side effects may occur, including:

- Bradycardia or tachycardia (slow or fast heart rate)
- Hypotension or hypertension (low or high blood pressure)
- Allergic reactions, including sneezing or rash

It is important to note that capsaicin is classified as a pregnancy category C drug by the FDA, meaning that while animal studies have demonstrated potential risks to the fetus, there are insufficient human studies to determine the drug's safety during pregnancy. Pregnant women should consult their healthcare provider before using capsaicin-based treatments, as its benefits may outweigh potential risks in some cases.

Conclusion

Capsaicin remains a highly effective topical treatment for managing chronic pruritus and neuropathic pain, particularly in conditions like postherpetic neuralgia. Its mechanism of action—the depletion of neuropeptides involved in pain and itch signaling—makes it a unique therapeutic option for various dermatologic conditions. Despite its benefits, capsaicin treatment can lead to transient burning sensations and other localized side effects, though these tend to

diminish over time. It is crucial for patients to use capsaicin under medical guidance, especially when considering its off-label applications and potential interactions with other treatments.

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