

FAST FACTS AND CONCEPTS #255
TOPICAL CAPSAICIN FOR NEUROPATHIC PAIN

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Background Derived from *Capsicum* chili peppers, capsaicin has been used as a topical analgesic for centuries. Available in both over-the-counter and prescription strengths, capsaicin preparations have been studied and utilized for management of neuropathic pain. This *Fast Fact* reviews use of capsaicin for topical neuropathic analgesia, including the new 8% single-dose capsaicin patch ('Qutenza').

Mechanism of Action Capsaicin is a highly selective agonist for TRPV1 receptors expressed in afferent neuronal C fibers and some A δ fibers. Local activation of TRPV1 receptors by heat, pH changes, or endogenous lipids normally leads to nerve depolarization propagated to spinal cord and brain, causing local heat, stinging, and/or itching sensations. Through intracellular enzymatic, cytoskeletal, and osmotic changes, prolonged activation of TRPV1 by capsaicin results in loss of receptor functionality, causing impaired local nociception for extended periods. At higher concentrations, topical capsaicin appears to promote temporary neurolysis, with re-innervation occurring weeks after cessation of drug therapy (1,2). Capsaicin-induced local depletion of substance P was previously thought to be its mechanism for pain relief. However, this is no longer considered to be the case (1).

Indications Topical capsaicin has shown analgesic benefits in post-herpetic neuralgia, painful polyneuropathies including diabetic and HIV-related neuropathy, and postmastectomy/surgical neuropathic syndromes (3). The 14 x 20 cm capsaicin 8% patch is FDA-approved for application of up to 4 patches at a time for post-herpetic neuralgia. Its efficacy in other neuropathies is still being investigated. Generally, these painful areas should involve a discrete area of the body such as a distal extremity or surgical scar. There is no well-defined limit to the body surface area which can be treated with capsaicin cream. Capsaicin creams have been used in children; there are no data about use of the 8% patch.

Clinical Use In addition to the patch, capsaicin is commercially available as 0.025%, 0.075%, and 0.1% creams. Creams are applied by patients or caregivers 3-4 times per day. The duration of treatment with the cream is empiric. The patch is placed on the skin for 60 minutes by a medical professional in a clinic, then removed. Because the patch application itself is painful, the area is pretreated with lidocaine cream, and residual capsaicin is cleaned afterwards with a special cleansing product. Patch placement can be repeated as often as every 3 months (4).

Effectiveness In recent systematic reviews, capsaicin 0.075% cream demonstrated statistically significant benefit in post-herpetic neuralgia, post-surgical neuropathies, and diabetic neuropathy, compared to placebo (3,4). About one person in eight who receives treatment will get good pain relief throughout 4-12 weeks of follow up, although it may take weeks of application to achieve significant benefit (4). Although studies demonstrate its effectiveness in musculoskeletal pain, capsaicin 0.025% cream has not been adequately studied for neuropathic pain. The efficacy of the single high-dose capsaicin 8% patch has been observed up to 12 weeks in published data (5). It is effective for post-herpetic neuralgia, however there have been mixed results with the patch for HIV-related neuropathy. To date, no head-to-head trials have compared the capsaicin 8% patch to capsaicin 0.075% cream.

Toxicity and Precautions Capsaicin should not be used on open wounds. Major side effects are localized and include erythema and uncomfortable burning, stinging, or itching. Over repeated applications, these burning/stinging sensations decrease, corresponding with progressive neuronal defunctionalization. Inhalation of capsaicin can cause nasopharyngeal or respiratory irritation, sneezing, and tearing. Patients are advised to use gloves while applying the cream, avoid contact with eyes and mucous membranes, and wash hands after application. Transient hypertension associated with increased local pain has been noted. Cessation of capsaicin use due to side effects appears more common with repeated low dose cream application (15% of patients) compared to the patch (1% of patients in a clinical trial setting) (5).

Cost Capsaicin 0.025%, 0.075%, 0.1% creams are available over-the-counter (approximately \$8/oz). One capsaicin 8% patch costs approximately \$900 (plus clinician fees for application). Costs for 3-month supplies of relevant neuropathic pain medications are: ~\$700 for lidocaine 5% patches, 1 a day; ~\$900 for pregabalin 100 mg 3 times a day; ~\$300 for gabapentin 600 mg 3 times a day; ~\$50 for amitriptyline 100 mg once daily (6).

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Conflicts of Interest Statement: The authors have disclosed no relevant conflicts of interest.

Version History: Originally published July 2012; Copy-re-edited August 2015 with reference #5 added and incorporated into the text and references #5 and #7 updated.

Fast Facts and Concepts are edited by Sean Marks MD (Medical College of Wisconsin) and associate editor Drew A Rosielle MD (University of Minnesota Medical School), with the generous support of a volunteer peer-review editorial board, and are made available online by the [Palliative Care Network of Wisconsin](#) (PCNOW); the authors of each individual *Fast Fact* are solely responsible for that *Fast Fact's* content. The full set of *Fast Facts* are available at [Palliative Care Network of Wisconsin](#) with contact information, and how to reference *Fast Facts*.

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