Author: Tim Baron

Product Efficacy and Ingredient Essay

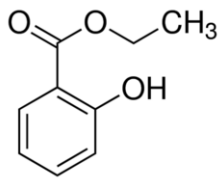
Methyl Salicylate (focusing on NSAID/anti-inflammatory)

Methyl salicylate, also called wintergreen oil, is an organic substance naturally produced by many species of plants, particularly wintergreens. Methyl salicylate is frequently used as a topical pain remedy applied directly to the skin. It has both analgesic and anti-inflammatory properties.

The mechanism of action of methyl salicylate is theorized to be mediated by the inhibition of prostaglandin synthesis. Salicylate inhibits the synthesis of prostaglandins by irreversibly acetylating and inactivating cyclooxygenase.[1]

The efficacy of methyl salicylate has been studied in clinical trials. A 2010 study looked at the efficacy of a topical methyl salicylate and menthol patch when used on adult patients. The study concluded that a single, 8-hour application of a patch containing methyl salicylate and l-menthol provided noticeable pain relief for mild to moderate muscle strain in adult patients who received the patch compared to patients receiving a placebo patch.[2]

Evidence from randomized, double blind, controlled trials on the efficacy and safety of topically applied NSAIDs for acute pain indicates that topical NSAIDs can provide pain relief for the treatment of acute musculoskeletal conditions. Topical NSAIDs do not have the negative side effects associated with oral NSAIDs. [3]



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[1] Department of Health and Human Services, "Public Health Service Food and Drug Administration Center for Drug Evaluation and Research", Vol 1 (February 2006), 7-27 of 155.
http://www.accessdata.fda.gov/drugsatfda_docs/nda/2008/022029s000pharmr.pdf

[2] Higashi Y., Kiuchi T., Furuta K., "Efficacy and safety profile of a topical methyl salicylate and menthol patch in adult patients with mild to moderate muscle strain: a randomized, double-blind, parallel-group, placebo-controlled, multicenter study", *Clinical Therapeutics*, 32(1) (January 2010): 34-43,
doi: 10.1016/j.clinthera.2010.01.016.

[3] Massey T., Derry S., Moore R.A., McQuay H.J., "Topical NSAIDs for acute pain in adults", *The Cochrane Database of Systematic Reviews*, no. 6 (June 2010),
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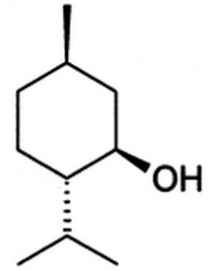
Menthol

Menthol is an organic compound that can be synthesized or procured from mint oils. It is a waxy, crystalline substance that is clear or white in color. Menthol can be used as a local anesthetic and acts as a weak kappa opioid receptor agonist.

Menthol produces a cool sensation via the activation of the TRPM8 channel. Although the mechanism of action is unknown, a hypothesis has been tested regarding the possibility that menthol may block voltage-gated Na(+) channels in dorsal root ganglion (DRG) neurons. The study concluded that menthol is a state-selective blocker of Nav1.8, Nav1.9, and TTX-sensitive Na(+) channels.[4]

A 2012 study compared the usage of ice and menthol for pain reduction. Sixteen subjects were randomly given a topical gel containing 3.5% menthol or a topical application of ice to the non-dominant elbow flexors two days after the subjects performed an exercise designed to induce muscle soreness. The study found that the efficacy of menthol was significant. Menthol reduced perceived pain and allowed for increased muscle usage.[5]



[4] Gaudioso C., Hao J., Martin-Eauclaire M.F., Gabriac M., Delmas P., "Menthol pain relief through cumulative inactivation of voltage-gated sodium channels", *Pain*, 153(2) (February 2012): 473-84, doi: 10.1016/j.pain.2011.11.014.
[5] Johar P., Grover V., Topp R., Behm D.G., "A comparison of topical menthol to ice on pain, evoked tetanic and voluntary force during delayed onset muscle soreness", *International Journal of Sports Physical Therapy*, 7(3) (June 2012): 314–322.

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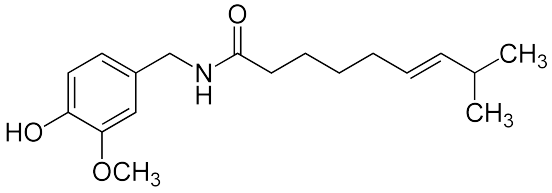
Capsaicin

Capsaicin is an active component of chili peppers, which belong to the genus Capsicum. Capsaicin is used as an analgesic in topical ointments and produces a burning sensation. Generally, therapeutic concentrations of capsaicin are between 0.025% and 0.25%. However, a high-concentration 8 % capsaicin patch is approved in the EU and the US.[6]

The mechanism of action of capsaicin results from its chemical interaction with sensory neurons. Capsaicin binds to a receptor called the vanilloid receptor subtype 1 (TRPV1).[7] When binding to the TRPV1 receptor, the capsaicin molecule produces sensations of heat. It does not cause a burn, but inflammation from capsaicin is likely the result of the body's reaction to nerve excitement.

Evidence suggests that the utility of topical capsaicin may extend beyond painful peripheral neuropathies. A meta-analysis of numerous studies indicates that daily self-administered applications of low-concentration capsaicin formulations are safe and show modest efficacy.[8]



[6] Anand P., Bley K., "Topical capsaicin for pain management: therapeutic potential and mechanisms of action of the new high-concentration capsaicin 8% patch", *British Journal of Anesthesiology*, 107(4) (October 2011): 490-502, doi: 10.1093/bja/aer260.

[7] Story G.M., Crus-Orengo L., "Feel the burn", *American Scientist*, 95(4) (July–August 2007): 326–333, doi: 10.1511/2007.66.326.

[8] Anand et al.

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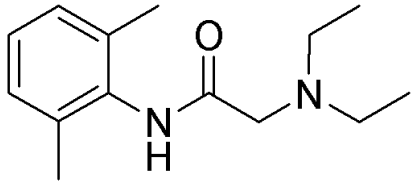
Lidocaine

Lidocaine is a local anesthetic and class-1b antiarrhythmic drug. It is commonly used topically to relieve itching, burning, and pain. It is on the WHO List of Essential Medicines for basic healthcare.

The mechanism of action of lidocaine is believed to be voltage-gated sodium channels, which are important in the generation and propagation of action potentials in neurons and muscle cells.[9] A 2007 study identifies important components of the molecular mechanism underlying the use-dependent block of sodium channels by lidocaine.[10]

The efficacy of lidocaine patches has been studied in the treatment of neuropathic pain syndromes. A randomized, double blind, placebo-controlled study concluded that, as an add-on therapy, a lidocaine patch (5%) was effective in reducing ongoing pain and allodynia during the first 8 hours after application. The patches also worked well over a 7-day period.[11]



[9] Theodore R. C., "Setting up for the block: the mechanism underlying lidocaine's use-dependent inhibition of sodium channels", *The Journal of Physiology*, 582 (pt.1) (July 2007): 11, doi: 10.1113/jphysiol.2007.136671.
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