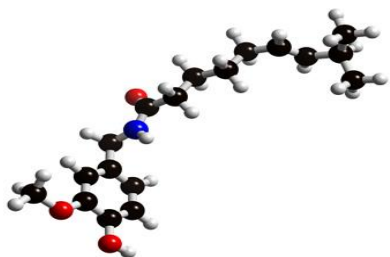


Sinol-M : Mechanism of action

Sinol-M™ nasal spray contains a mixture of natural ingredients among which capsicum - the extract from chili pepper plant is believed to be the active component that provides relief from allergy, sinus congestion and headache.

Unlike many other all-natural and homeopathic products, the chemical structure of capsicum and its mechanisms of action in animals and humans have been well characterized [1, 2]. The genes encoding their production have also been recently identified [3]. Capsaicin is a member of the vanilloid family and binds to a receptor called the vanilloid receptor subtype 1 (VR1) [4].

The burning and painful sensations associated with capsaicin result from its chemical interaction with sensory neurons. They interact with the VR1 ion channel-type receptors, which then permit cations to pass through the cell membrane and into the cell. The resulting depolarization of the neuron stimulates it to signal the brain.



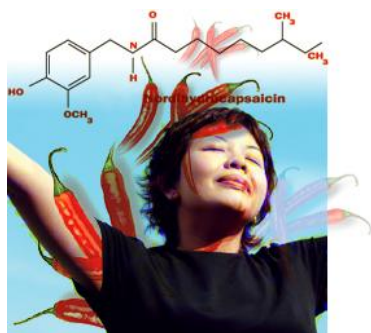
More recently, the VR1 ion channel receptor has been shown to be a member of the “superfamily” of TRP ion channels, and is now referred to as *TRPV1*. There are a number of different TRP ion channels that have been shown to be sensitive to different ranges of temperature and probably are responsible for the human range of temperature sensation. Thus, capsaicin does not actually cause a chemical burn, or indeed any damage to tissue at all; it causes only the sensation of one.

Based on this rationale, capsaicin has been proposed as a means against chronic pain. With exposure to capsaicin, neurons are overwhelmed by the ion influx and are unable to report pain for an extended period of time with a blockade of neurogenic inflammation ensuing. If capsaicin is removed, the neurons recover.

Capsaicin produces pain by selectively activating polymodal nociceptive neurons. Repetitive administrations of capsaicin produces a desensitization and an inactivation of sensory neurons. Several mechanisms are involved, including:

- receptor inactivation
- block of voltage activated calcium channels
- intracellular accumulation of ions leading to osmotic changes
- activation of proteolytic enzyme processes.

Systemic and topical capsaicin produces a reversible anti-nociceptive and anti-inflammatory action after an initial undesirable algescic effect.



Apart from use in the prevention of pain [5] capsaicin has also been used as a dietary supplement, pest repellent, in cancer treatment [6, 7] and autoimmune diabetes [8]. It is also part of standard procedure of cough threshold measurement.

A prospective clinical study of the nasal application of Sinol-M demonstrated significant symptom relief in patients with allergic rhinitis [9]. It is speculated that this effect does not depend on the duration of the contact with the mucosa, but upon triggering of local neuronal networks in the nose.

The capsaicin in Sinol-M™ nasal spray blocks C-fibre conduction, inactivates neuropeptide release from peripheral nerve endings, causes neuropeptide depletion and reduction of neurogenic inflammation and as a result, amelioration of the bothersome nasal symptoms associated with allergic rhinitis.

References

1. E. K. Nelson. The constitution of capsaicin, the pungent principle of capsicum. *J. Am. Chem. Soc.* 1919, *41*, 1115-1121.
2. S Kosuge, Y Inagaki, H Okumura (1961). Studies on the pungent principles of red pepper. Part VIII. On the chemical constitutions of the pungent principles. *Nippon Nogei Kagaku Kaishi (J. Agric. Chem. Soc.)*, *35*, 923-927; (en) *Chem. Abstr.* 1964, *60*, 9827
3. Stewart C, Kang BC, Liu K, *et al* (June 2005). "The Pun1 gene for pungency in pepper encodes a putative acyltransferase". *Plant J.* *42* (5): 675–88. Story GM, Crus-Orengo L (July-August 2007). "Feel the burn". *American Scientist* *95* (4): 326–333.
4. Caterina MJ, Julius D. The vanilloid receptor: a molecular gateway to the pain pathway. *Annu Rev Neurosci.* 2001;*24*:487-517.
5. American Association for Cancer Research (2006). "Pepper component hot enough to trigger suicide in prostate cancer cells". Retrieved on January 27, 2007.
6. Ito, K; Nakazato T, Yamato K *et al.* (February 2004). "Induction of apoptosis in leukemic cells by homovanillic acid derivative, capsaicin, through oxidative stress: implication of phosphorylation of p53 at Ser-15 residue by reactive oxygen species". *Cancer Research (American Association for Cancer Research)* *64* (3): 1071–1078.
7. Razavi R, Chan Y, Afifiyan FN, *et al* (December 2006). "TRPV1+ sensory neurons control beta cell stress and islet inflammation in autoimmune diabetes". *Cell* *127* (6): 1123–35.
8. Kaliner M, White M, Tzachev C, Efessiou C, Farrar J, Miller J, Popov T. Assessment of Two capsaicin Containing Solutions for Symptom Relief in Subjects with Persistent Allergic Rhinitis. 2009 Poster presentation at the Western Society of Allergy Asthma and Immunology 47th Annual Scientific session