

MENTHODERM[®]

MENTHOL IN AQUEOUS CREAM

The Benefits of Menthol¹

Menthol is natural cyclic terpene alcohol from plant origin and has been used since antiquity for medicinal purposes. Today Menthol can be found in both prescription and OTC medications for a range of different conditions. It is also used in Dermatology where it is frequently prescribed for its antipruritic properties.

MENTHOL - THE MECHANISM OF ACTION

Despite its widespread use the mechanism by which Menthol is able to impart a cooling sensation when applied topically to the skin remained a mystery until early 2002. Two independent studies by McKemy et al² and Peier et al³ identified a 1104 amino acid cation channel receptor - TRPM8. This receptor, cloned and characterized, could be activated by both Menthol and a thermal stimuli in the cool to cold range 8-28C. This proves that Menthol acts as an agonist for a thermally sensitive receptor. Psychophysical studies have also shown that menthol evokes a cool sensation to the skin or mucous membrane.

ANTIPRURITIC BENEFITS OF TOPICAL MENTHOL

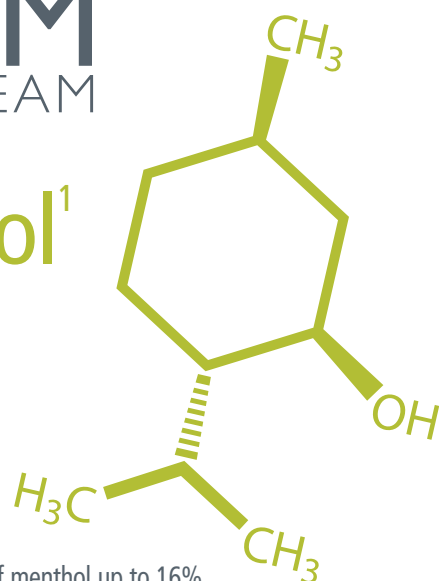
The precise mechanism by which menthol alleviates pruritus is unknown and the optimal concentration of menthol for the relief of pruritus has yet to be fully established. Different opioid receptors have contrasting effects upon pruritus. Menthol has been shown to selectively activate k-opioid receptors, and Patel et al¹ postulated that this mechanism may also possibly explain the antipruritic properties of this compound. He also noted that patients who suffer from chronic pruritic conditions, such as atopic dermatitis, uremic pruritus and psoriasis report an apparent itch reduction by taking a cold shower. Therefore, it is possible that the cooling sensation menthol imparts to the skin serves as a possible mechanism to reduce itch perception in certain patients.

LOCAL ANAESTHETIC ACTIVITY OF TOPICAL MENTHOL

In a recent study, Haeseler et al⁴ concluded that menthol blocks voltage-gated neuronal and skeletal muscle sodium channels in a concentration-dependent manner in resting and inactivated states. Furthermore, the authors suggested that this effect provided a molecular basis for the antinociceptive and local anaesthetic properties of this compound.

SAFETY PROFILE

According to Patel et al¹ Menthol is considered a safe and effective topical OTC product according to the FDA.



Concentrations of menthol up to 16% have been approved by the FDA for OTC external use, and their safety profile has been well established. Based on the large post-marketing data, the FDA panel concluded that menthol in these concentrations have an excellent safety profile. Customer complaints of 1 per 310,000 were reported by one major manufacturer, while a second manufacturer reported 1 per 950,000. No complaints of a serious nature have been filed with the FDA. Only very high concentrations of 40% Menthol has been shown to cause skin erythema and spontaneous burning.

CONCLUSION

Menthol is widely used in the UK, especially dermatology, where it is frequently part of topical antipruritic, analgesic, antiseptic, and cooling preparations, such as Menthol in a topical cream base. It has an excellent safety and toxicity profile. As highlighted by Patel et al¹ the recent discovery of the TRPM8 receptor finally provides the answer to how menthol can elicit the same cool sensation as low temperatures.

UNDECYLENIC ACID

Is an organic compound often derived from Castor Oil (ricinoleic acid) It is produced by "cracking" Castor oil under pressure. In higher strengths, can be used as a powerful antifungal agent for a variety of pathogenic fungi. Primarily undecylenic acid is the active ingredient in many medications for skin infections, which relieves itching, burning, and irritation. For example, it is used against fungal skin infections, such as athlete's foot, ringworm.

SAFETY/TOXICITY

Relatively small doses of undecylenic acid and its salts have been shown to have powerful antifungal properties, and the dosages necessary to achieve therapeutic benefit appear to be safe.

1 Patel et al., 'Menthol: A refreshing look at this ancient compound'. Journal of the American Academy of Dermatology, vol. 57, no 5, 2007, pp. 873-878.

2 McKemy et al., 'Identification of a cold receptor reveals a general role for TRP channels in thermosensation.' Nature, vol. 416, no 6876, 2002, pp. 52-58.

3 Peier A.M et al., 'A TRP channel that senses cold stimuli and menthol.' Cell, vol. 108, no 5, 2002, pp. 705-715.

4 Haeseler et al., 'Voltage-dependent block of neuronal and skeletal muscle sodium channels by thymol and menthol.' European journal of anaesthesiology, vol. 19, no 8, 2002, pp. 571-579.