Our Dermatology Online

Research Letter

A' la recherche du temps perdu: Coolants to struggle the evenience of very hot temperatures because of climate changing and desertification in the universe

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Sir,

Climate changing and desertification are overwhelming problems and concerns devastating the entire universe.

Feeling of skin discomfort and qualmishness, especially in kids and elder, is awful., both in springtime, summertime and autumn.

Effectively the skin forms a protective layer around the body against physical, chemical and thermal environmental challenges. In addition to providing a physical barrier, the skin is considered a sensory organ that allows the body to perceive harmful external stimuli and appropriate behavior or body movement can be initiated thereafter.

The peripheral nervous system governs the broadly defined sense of touch perception, communicating with the central nervous system regarding the external environment, allowing for conscious sensations of balance and coordination, pressure and vibration, pain and temperature [1]. Sensory nerves are innervated in the entire skin tissue as well as subcutaneous fat layer. Most nerve fibers and endings are found in the mid-dermis and the papillary dermis. In the epidermis, sensory nerves are linked to keratinocytes, melanocytes, Langerhans cells (LC) and Merkel cells. The epidermal nerves consist of free nerve endings or nerve organs. In the dermis, there are free sensory nerve endings such as Pinkus discs, Ruffini, Meissner, Krause and Vater-Pacini corpuscles

Peripheral sensory nerves can be classified on the basis of the degree of myelination and the velocity at which action potentials travel through afferent fibers with the fast conducting, myelinated (large) Aα fibers, Aβ fibers, Aδ fibers and the slow conducting, unmyelinated (small) C fibers. Among them, Aβ and Aδ fibers are mostly mechanical sensitive afferents (type I) localized on hairy and glabrous skin. A subpopulation of Aδ fibers on hairy skin are believed to be mechanically insensitive (type II). Aδ fibers constitute approximately 80% of primary sensory nerves sprouting from the dorsal root ganglion (DRG), whereas C fibers constitute approximately 20% of the primary afferents

C fibers are either polymodal nociceptors which can respond to chemical or mechanical stimuli and temperature changes, or more specialized perception. Among human peripheral nerves, 45% of the cutaneous afferent nerves belong to a subset of sensory nerves that are both mechano- and heat-responsive C fibers. The C fibers are the predominant nerve pathway for thermoperception of warmth. A certain subpopulation of Aδ fibers respond to gentle cooling, whereas selective C fibers become activated during noxious cold. When we lightly touch with our fingertips, the Aδ fibers respond because they are associated with a variety of cells including keratinocytes, Merkel cells and hair follicles. In addition, the C fibers are known for nociceptor action terminated at the target tissue as a free nerve ending. Similarly, specific receptor distribution and biochemical diversity of different sensory nerve subtypes exists, which is important for various perceptions.

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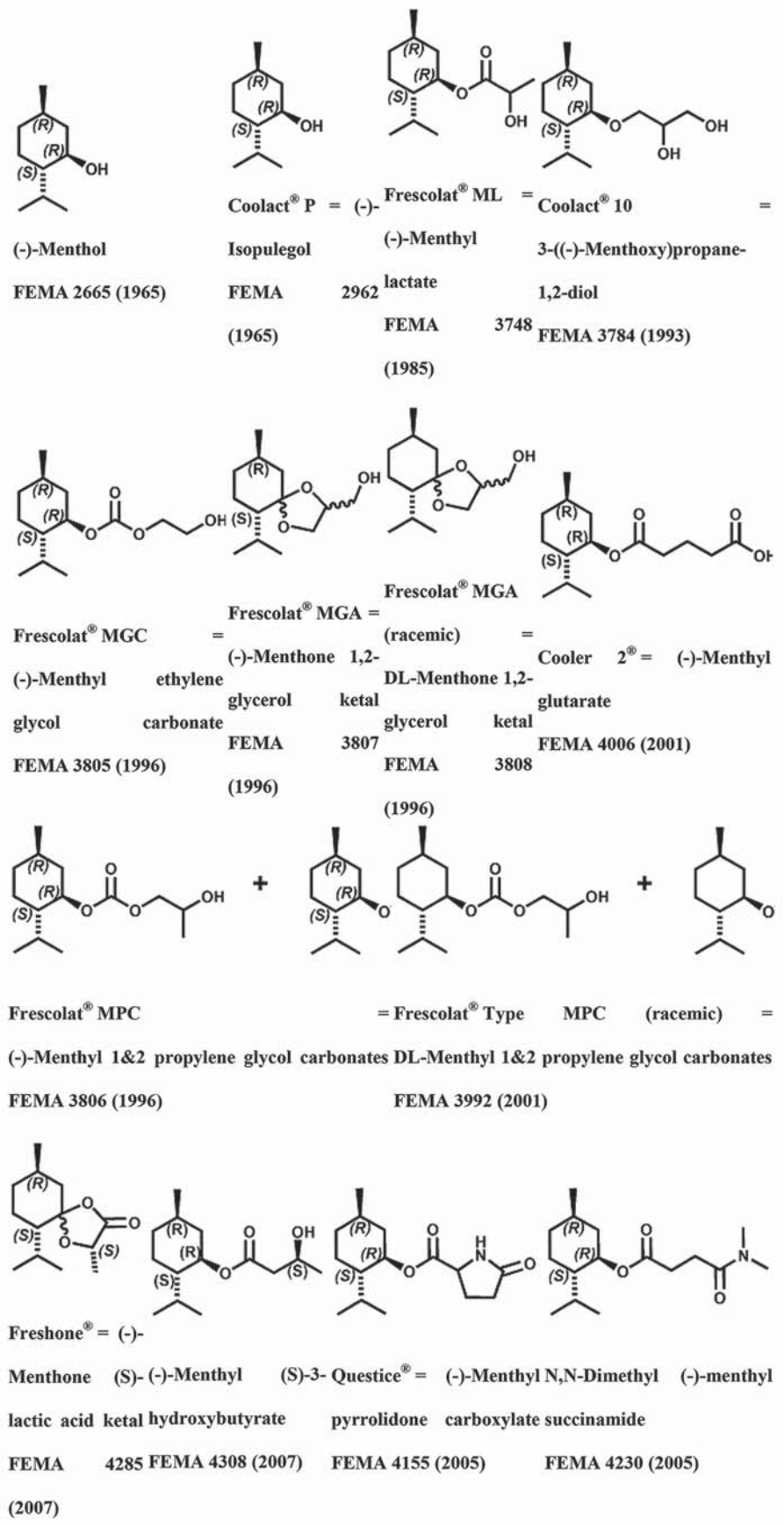

Figure 1: The most important GRAS coolants.

The information detected from the peripheral sensory nerves is transmitted to the DRG and cranial nerve ganglia such as the trigeminal ganglion. DRG are a cluster of sensory neuronal cell bodies located in the vertebral column lateral to the spinal cord. A functionally specialized zone exists at the DRG neurons that can be partitioned according to specific sensory modalities. Based on the stimulus detected, DRG neurons are functionally classified as proprioceptors, low-threshold mechanoreceptors, and cells that sense pain, itch and/or temperature. The DRG neuronal branch relays information through the dorsal horn of the spinal cord to the central nervous system to recognize the type of sensation.

Thermosensation is a sensory modality of the skin. Thermal stimuli applied to the skin induce a variable degree of sensory perception. When decreasing the stimuli temperature, the quality of sensation may change from cool to cold, from icy cold to pain. Similarly, increasing the stimuli temperature can cause a change in the sensations from warmth, to heat then to sharp or dull pain.

Sun rays are always more and more dangerous but the sensation of annoyance is the worst condition that obsesses and oppresses people living in the Mediterranean Basin and elsewhere in the world.

Cosmetic science has been trying to defeat this sensation of disconfort since decades and an avalanche of patents have been issued recently.

Over the last 30 years a considerable number of compounds have been synthesized and evaluated for the physiological sensation of "cooling".

In the 1970's Wilkinson Sword Ltd. conducted an extensive research program under the company leadership of Roy Randolph.

During this period Hugh R. Watson, David G. Rowsell and co-workers designed and evaluated about 1200 compounds for their cooling activity [1-6].

The interest in such compounds relates to cooling sensation without the minty and volatile side effects of menthol such as eye irritation from aftershave lotions, etc.

The impact of the Wilkinson-Sword research on cooling compounds and cooling receptors has recently been reviewed (John C. Leffingwell & David G. Rowsell, Wilkinson Sword Cooling Compounds: From the Beginning to Now, [7]. Of these original Wilkinson Sword compounds, eight have been successfully commercialized - WS-23, FEMA 3804; WS-3, FEMA

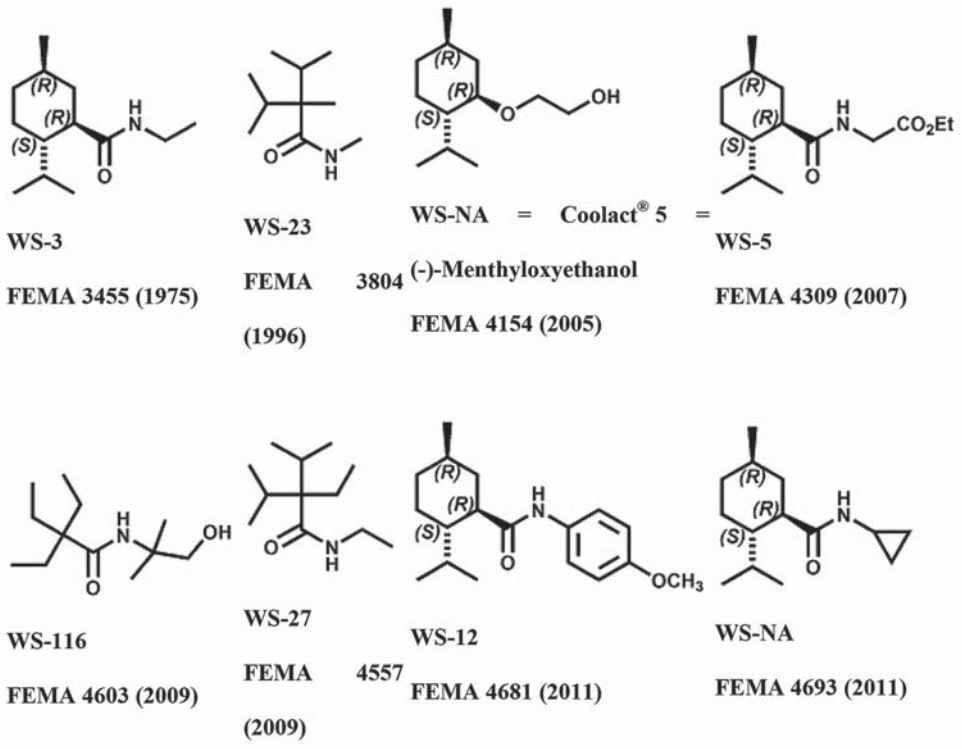

Figure 2: Wilkinson sword gras coolants.

Table 1: The cooling rating in the buccal mucosa

	Cooling Rating Relative to Control of 60				
Coolants	0 min	15 min	30 min	45 min	60 min
1500 ppm I-WS-3	53.5	36.5	27.0	20.5	15.5
1500 ppm Neo-WS-3	43.3	33.9	23.3	16.7	13.3
750 ppm Neo-WS-3 + 750 ppm I-WS-3	51.5	33.0	21.5	14.0	9.0
1500 ppm I-WS-5	53.9	40.0	26.7	17.8	13.3
1500 ppm NeoWS-5	61.9	39.3	29.3	21.4	15.7
750 ppm Neo-WS-5 + 750 ppm I-WS-5	57.0	44.0	29.0	21.5	14.0
500 ppm I-Menthyl lactate (2S)	50.0	38.0	26.5	18.5	13.5
500 ppm Neo-Menthyl lactate (2S)	62.2	43.9	33.9	27.5	16.7
1950 ppm Neo-Menthyl lactate (~2:1 S:R)	50.6	42.8	30.6	22.2	16.7
1000 ppm Neo-Menthyl pyruvate	57.8	45.0	30.6	21.1	16.1
335 ppm Neo-Menthyl lactate acetate (2S)	64.4	46.3	33.1	26.3	21.3
*Cooling Ratings on a scale of 1 - 90 vs.a control dentifrice rated at 60					

3455; WS-5, FEMA 4309; WS 1, FEMA 4681; WS-27, FEMA 4557; FEMA 4693, WS-116, FEMA 4603, FEMA 4154. FEMA 4154 was first patented by Wilkinson-Sword as a cooling agent in German Patent DE2203947 (1972) (Figs. 1 and 2).

In 2011, on FEMA GRAS List 25, the following three carboxamide cooling agents were added: FEMA 4681; FEMA 4684; and FEMA 4693.

The 2013 Japanese Flavor list (updated as of April 2015) includes 15 of the 32 FEMA GRAS cooling compounds from the FEMA lists thruough GRAS List 26. These are those with FEMA numbers 2962, 3748, 3784, 3805, 3806, 3008, 3810, 3849, 4006, 4053, 4154, 4308, 4309, 4604, 4718 and 4681.

In Table 1 was duration of sensation of freshness after application of some of the aforesaid coolants respect D-Menthyl lactate, L-menthyl lactate and other esters, as pyruvate or lactate, of menthol.(the oldest formulas apt to refresh mouth and skin).

Researchers assert that a petrolatum jelly containing 1% of one of the aforesaid cooling agents, depending on the chemical nature of the coolant, may provide a psychological effect of coolness and this is welcome in this new aggressive era.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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