Neurocosmetics

The skin is equipped with an effective communication and control system, and neurocosmetics, an emerging segment that explores topical treatments affecting this system, has only scratched the surface of advancing technological possibility.

Having treated every other aspect of the skin, cosmetic formulators have recently discovered the cutaneous nervous system. The new category that has emerged as a result, neurocosmetics, can literally affect how the brain responds to topical treatment. The subject inaugurated the 2007 program of the New York Society of Cosmetic Chemists (NYSCC)[1] and is certain to appear on many technical programs in the coming months.

Neurocosmetics targets nerve clusters sensitive to heat, cold, pain, itch and pressure. These receptors send signals through fibers in the skin to the spinal cord, which are then transmitted up to the cerebral cortex of the brain.

Physical coolants—ethanol is a common example—act through evaporation, and are a simple example of materials that create a nervous response. Lower-boiling compounds such as ether or acetaldehyde are even stronger coolants. However, evaporation as a mode of action does not qualify these materials as neuro-active.

Cosmetics have acted on neurons for many years—the cooling effect of menthol is a prime example. Menthol acts on thermoreceptors to provide the cool sensation via cold receptors, and can also create a hot or stinging pain sensation. Similarly, capsaicin can produce a hot sensation. Figure 1 shows the structure of l-menthol and capsaicin. Obviously, a great diversity of chemistry can trigger nerve impulses. A classic paper by Watson[2] and his colleagues at Wilkerson Match explained the functioning of menthol and how to create a family of chemically related cooling compounds.

Watson attributed the cooling effect of menthol to a chemical action at the nerve ending associated with the sensation of cold. The necessary chemistry included a hydrogen-bonding group, compact hydrocarbon skeleton, correct HLB and molecular weight range of 150–350. These properties correspond to a classic drug receptor interaction.

Besides cooling, menthol type chemicals are reminiscent of peppermint candy, producing a tingle and possible burning sensation. The reaction varies in different parts of the body, being very strong on typically sensitive areas. The cooling compounds must penetrate the skin in order to interact with the receptors. For a more recent account of cooling chemistry, see Erman's article[3] in *Cosmetics & Toiletries* magazine. Erman cites sources attributing the hot and cold detectors as members of the transient receptor potential superfamily. Anyone interested in the detailed science of these proteins associated with cation-selective ion channels can find a good starting point with Huang[4].

Moving past menthol, formulators are now looking at neurotrophins, a family of polypeptide growth factors. A key member is nerve growth factor (NGF), which is necessary for the survival of some classes of neurons—including some in the skin[5]. Tests show that brain-derived neurotrophic factors regulate some cutaneous mechanoreceptors. Since preservation of the neurocutaneous network is beneficial to the skin, this preservation is the logical focus of neurocosmetics.

NGF, like almost anything biochemical in nature, decreases with age. Acetylcholine, dopamine, adrenaline and serotonin are examples of neuroactive chemicals. Synthetically produced biomimetic peptides replicate a small, active amino acid sequence of neuromodulators and make them available in the dermis. Since dipeptides can be attacked by enzymes in the skin, decarboxylated dipeptides have been used to avoid enzyme destruction while maintaining biological activity similar to natural neuropeptides. The GT version has been commercialized under the INCI name "glutamylamidoethyl indole" by Exsymol S.A.M. This product is available in the United States through Biosil.

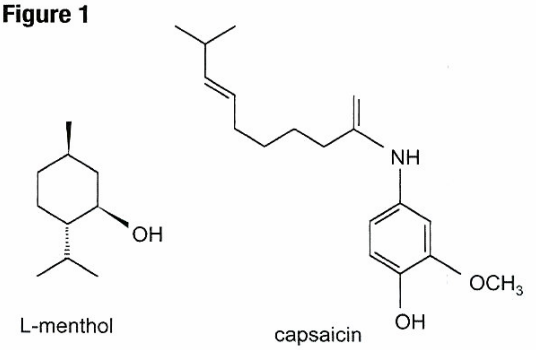
The N.V. Perricone M.D. brand utilizes Oligopeptide-17 (CLF-835 Neuropeptide). It is a 35 amino acid sequence claimed for CTFA listing to be a skin protectant. Lancôme Hydra Zen uses Acticalm, a combination of botanical and vegetal extracts. No reaction mechanisms are readily available in either of these products.

Soliance, available in the U.S. through Tri-K, markets Ocaline—a blend of seawater and pumpkin seed extract. Their Web site (*www.groupesoliance.com*) and literature proposes a mechanism of action. The pumpkin seed extract inhibits the action of neurotransmitter Substance P (as in "pain"). Under stress, Substance P is released from the nerve fibers of the skin, causing secretion of histamine from the mast cells, and leading to the typical signs of inflammation. If the activity of Substance P is inhibited, the skin becomes more resistant to attack. A simple view of this process is shown in Figure 2.

Testing dermal nerve responses with electrodes is the subject of a 2002 patent application by Cognis[6], based on research performed in France, where the patent was filed for. This study is a good place to begin an examination of the underlying science of neurocosmetics:

"The skin is equipped with a particularly effective communication and control system of which the function is to protect the organism from the environment. This

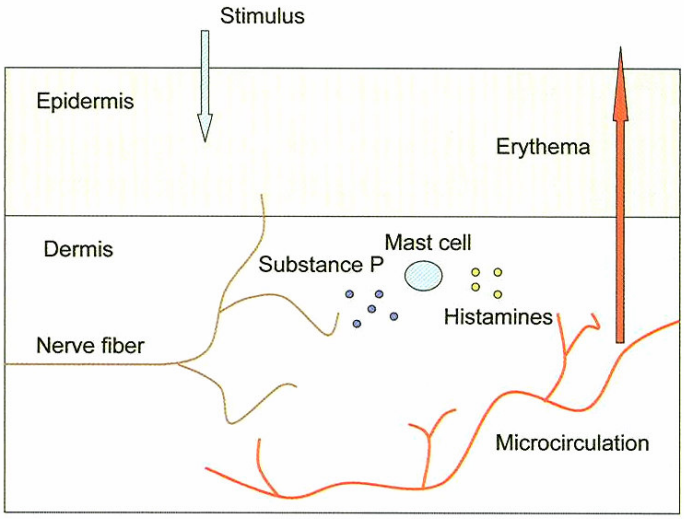
Figure 1



Menthol and capsaicin

The structure of l-menthol and capsaicin.

Figure 2



Neural inflammation

Skin becomes more resistant to attack when activity of Substance P is inhibited.

system contains a very dense system of highly specialized, outgoing autonomous nerve branches and sensory, feeder nerve branches which is distributed over all layers of the skin. The information passing through this network is processed in the central nervous system and can produce an inflammatory reaction through the antidromic propagation of impulses. The response activity of a nerve can be determined from the neuropeptides released and the receptors of the corresponding target structures."

The nervous system can easily absorb a lifetime of study. The advent of the Internet, however, makes exploration easier; simply Google search terms such as nociceptor, Aδ fiber axons, C fiber axons, mechanotransduction, thermotransduction or neurotrophins to open a world of knowledge. The challenge is not a lack of information but the ability to sort through the vast resources now available with the click of a mouse.

Neurocosmetics is clearly only a step towards the logical goal, a REACH Certified Biodegradable Green Renewable BioActive NanoNeuroCosmetic—the inevitable topic of a future Chemical Reaction column. Our industry is clearly far from the end of its quest to understand and treat aging skin, but the possibilities for new and better products seem endless.

Acknowledgments and References

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