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PERFUMER & FLAVORIST

The chemistry of F&F

Physiological Coolants

New materials and emerging applications

Steve Pringle and David Brassington, Oxford Chemicals Ltd.

Physiological cooling agents act in a number of ways. In a flavor or fragrance they can be the first impact, leaving a cool sensation on the palate or skin prior to the main aroma being imparted. Similarly, the main aroma may be the first thing one tastes, while a cooling sensation gradually builds up. Finally, there is the coolant that coats the mouth or skin, leaving one with a refreshed feeling.

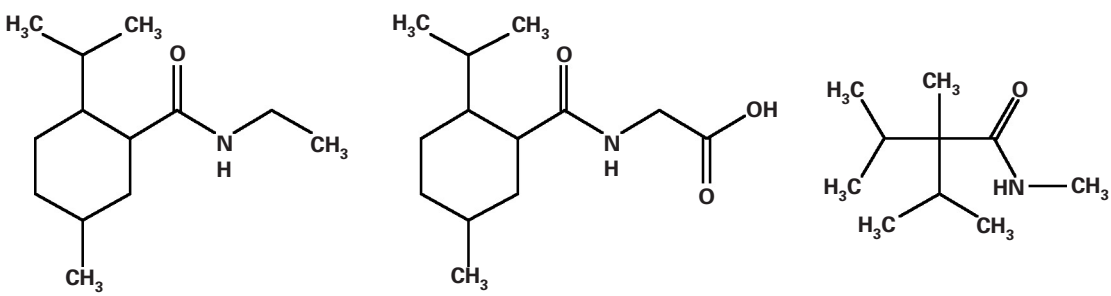
The longevity of the feeling of refreshment from an oral coolant in a toothpaste or mouthwash can be as important to the user as the initial taste and experience.

In the past 30 years, a tremendous amount of research has taken place in the development of compounds that have a cooling effect. Wilkinson Sword was probably the most prolific in the early days, evaluating more than 1,200 compounds for a cooling sensation. To this day, three of these compounds are still successful commercial products (F-1). The synthesis of one of these materials, N-ethyl-p-menthane-3-carboxamide, is shown in F- 2.

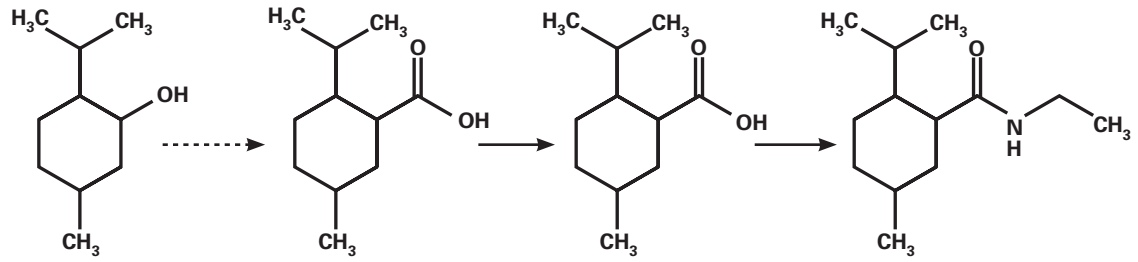
All of these materials are solids, which potentially can make formulations more difficult due to possible solubility problems. Although flavorists and perfumers have been able to formulate around these potential issues, it is clear that new materials are always welcome in order to avoid such problems. In addition, under Japanese legislation, they cannot be added to foodstuff because amides are not permitted in foodstuffs (see *www.jetro.go.jp/en/market/regulations/pdf/flavor2003aug-e.pdf*).

More recent developments include menthone glycerol ketal and menthyl lactate, but, again, these are solids and could pose problems, as highlighted previously. In 2005, a number of menthyl ester derivatives were patented, of which N,N-dimethyl menthyl succinamide received GRAS status. At the same time, a range of liquid cooling agents that are blends of 2-2-isopropyl-N,2,3-trimethylbutyramide and N-Ethyl-p-menthane-3-carboxamide also has been released.

Commercially successful Wilkinson Sword compounds N-ethyl-p-menthane-3-carboxamide, ethyl 3-(p-menthane-3-carboxamido)acetate and 2-2-isopropyl-N,2,3-trimethylbutyramide **F-1**



Synthesis of N-ethyl-p-menthane-3-carboxamide **F-2**

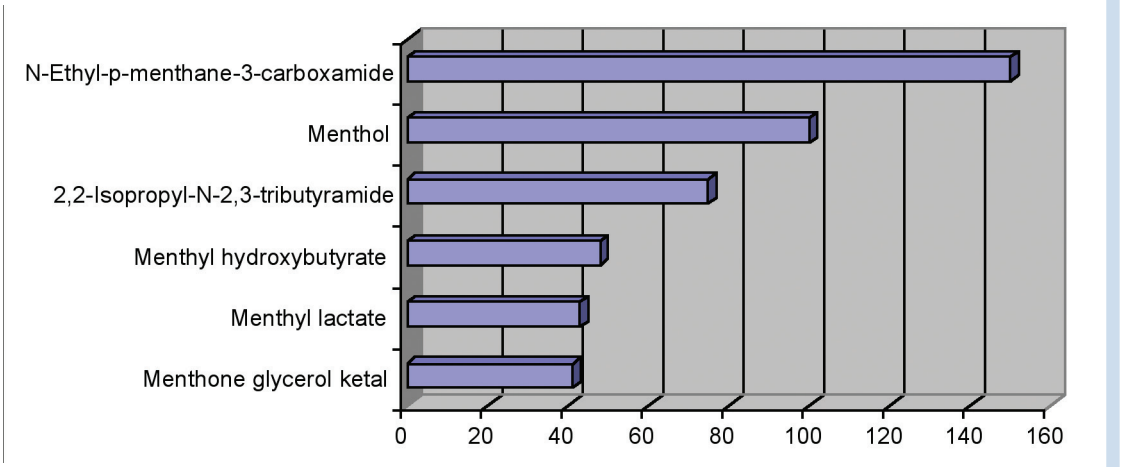


An even more recent development in this area is menthyl 3-hydroxyl butyrate. This material has been developed by Oxford Chemicals Ltd. in collaboration with Japan's San-Ei Gen FFI Inc. (Flavor and Extract Manufacturers Association status pending). The material is a liquid coolant that has almost no detectable odor and a cooling effect that is slightly stronger than that of menthyl lactate (F-3).

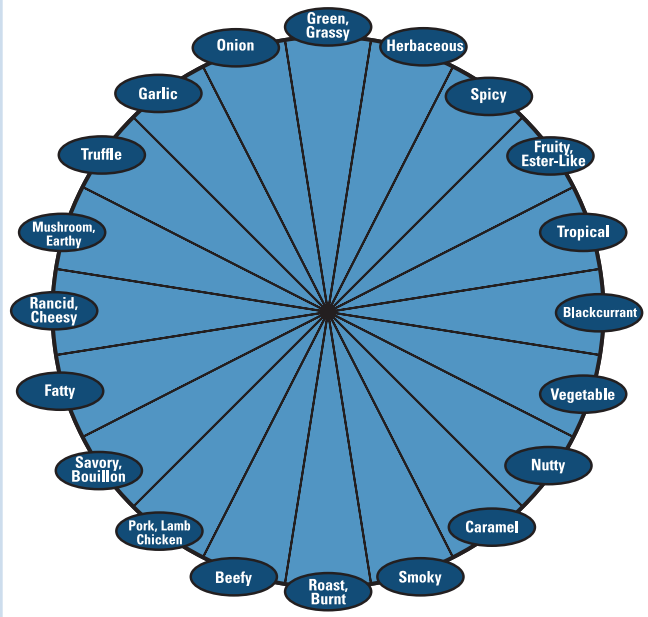
Formulation Challenges

In all of the uses described in subsequent sections, the ingredients used by the perfumer or flavorist must meet ever-stringent and difficult criteria. As the consumer becomes better informed—and, in some ways, more difficult to please—the flavorist's and perfumer's jobs become

Approximate relative cooling strengths vs. menthol (Source: *leffingwell.com*) **F-3**



A flavor wheel, such as the one that appears here, can be a useful tool for the flavorist and perfumer, linking chemical structure to organoleptic properties **F-4**



Flavor market growth by application **T-1**

Segment	Average growth rate 2001–2005 (%)
Beverages	4.2
Dairy	2.3
Bakery	1.9
Confectionery	2.0
Savory/convenience	4.4
Snacks	3.3
Meat	3.7
Oral hygiene/pharmaceutical	2.6
Others	3.3
Overall average	**3.3**

Global oral hygiene market sales: $billion, 2003–2008 **T-2**

Year	$ billion	$ billion	% Growth
2003	17.7	17.7	3.8
2004	18.3	18.3	3.4
2005	19.0	19.0	3.9
2006	19.8	19.8	4.0
2007	20.5	20.5	3.8
2008	21.3	21.3	4.0

Compound annual growth rate, 2003–2008: 3.8%;
Source: Data Monitor (2004)

increasingly more difficult. The desired flavor or aroma characteristics may be attainable through the skill of the perfumer and flavorist, but products are expected to have some form of longevity in order to meet consumer expectations *and* reach the consumer in the first place. This is where the formulation sometimes can fail. Factors of solubility, stability and others also must be examined. Also, don't forget that delivery methods to the consumer may differ for different geographical markets—solids in one country may need to be replaced by liquids or pastes in another.

Commercial Aspects of Oral Coolants

A flavor wheel, such as the one that appears in F-4, can be a useful tool for the flavorist and perfumer, linking chemical structure to organoleptic properties. However, some compounds for use in flavor and fragrance applications do not fit into this category. These materials have properties that arouse other senses and, as such, can affect the end user in different ways. One group of such materials are c ooling compounds. It is the use of such physiological cooling materials to arouse, enhance and improve the experience of the user/consumer, which leads this particular group of materials to be of great interest to perfumers, flavorists and marketers alike. One could ask how the senses affect the experience of a product and, in the case of the flavorist and perfumer, how the other senses can be utilized to enhance the experience created by using aromas.

Fragrance and Perfumery Applications

Cooling agents are used widely in fragrance and perfume applications. This is not just limited to skin creams in which a cooling effect experienced by touch is desirable, but also can involve fragrances in which a fresh aroma can be supplemented by a light cooling effect on the skin. (In the case of skin creams, a cooling effect additionally can serve to signal efficacy to the user; the cooling sensation says, "This product is actively working.") The addition of cooling agents to fine fragrance and other applications, where traditionally the main sensation has been formed by the creation of an aroma, can enhance the consumer experience significantly. The challenge here for the perfumer is to stimulate both senses of smell and touch in such a way that one is not detrimental to the other. For example, if the perfumer wishes to arouse the sense of smell initially and add to this by stimulating the skin with a physiological coolant, this task can be difficult using more traditional cooling materials. What is necessary is a material that first allows the aroma to be experienced and promotes a cool feeling as the cooling sensation builds on the skin.

Flavor Applications

Looking at T-1, one can see the flavor market broken down into application segments, along with average growth rates of these flavor segments.

European oral hygiene market sales; segmentation by usage **T-3**

Market segment	% Share
Toothpaste	54.8
Toothbrushes	25.8
Denture care	9.3
Mouthwashes and fresheners	7.7
Dental floss	2.4
Total	100.0

Source: Data Monitor (2004)

Here you can see that "beverages" and "convenience/ snack foods" show the highest growth rates throughout the past five years. This growth is reflected in the number of new products and new flavor and brand extensions of current products that consumers are seeing on store shelves. The challenge for the marketer, as well as the perfumer and flavorist, is to develop a product that will satisfy consumer needs—physiological coolants have the potential to open up a whole new area in flavor development.

Oral Hygiene

Oral hygiene markets have seen steady growth (T-2), with applications such as toothpaste and mouthwash (T-3) using physiological coolants to excellent effect. The use of oral coolants in toothpaste is a clear example of an application in which these materials impart an effect on the consumer, in addition to flavor. The longevity of the feeling of refreshment from an oral coolant in a toothpaste or mouthwash can be as important to the user as the initial taste and experience. To this end, the use of a combination of coolants that give an initial cooling sensation, such as 2-isopropyl-N,2,3-trimethylbutyramide, with those that take some time to build but have a greater longevity, such as menthyl 3-hydroxybutyrate, possibly could produce the desired effect.

Food and Flavor Applications

Away from oral hygiene areas, traditional applications in the flavor field generally are concentrated on such uses in which the cooling effect of the ingredient acts as an oral freshener. Applications such as chewing gums and hard candies, where the main taste experienced by the consumer is promoted as a minty or fresh taste, are prevalent. Oral coolants such as N-ethyl-p-menthane-3-carboxamide are used widely in this area. The initial strong minty flavor and cooling sensation experienced often give way quite quickly and need to be enhanced or prolonged in some manner. In addition to being used solely for the purpose of attaining a minty flavor, cooling agents such as menthyl 3-hydroxy butyrate also can extend the longevity of the fresh taste in the mouth as a cooling sensation takes longer to build. This can lead to greater longevity of the flavor of the product and an enhanced experience for the consumer.

Predicted growth in chewing/bubble gum applications (T-4) cements the importance of new product and flavor development as consumers continue to look for new experiences and marketers look to lengthen the life of products and brands.

Beverage

The growth of products entering the beverage market presents new and significant opportunities for the application of cooling agents. Looking at the different types of products in this area and, in particular, the nonalcoholic segment, one can see that there has been a significant development in products that promote extra benefits to the consumer. These products are limited not only to juices and health-related products, but also to sports beverages and "water plus" (T-5 and T-6), where the product not only attempts to refresh the consumer, but also replenishes or replaces vital nutrients that have been lost. The development of flavors of these applications recently has included "ice" or "cool" brand extensions. Flavor development in these categories has been concentrated on products that impart the impression of being thirst-quenching or refreshing. To date, however, few products that actually contain a physiological coolant have reached the market. This could be an ideal area for such materials. What better way to tell the brain that the body feels refreshed than to give the palate a feeling of refreshment?

Other Areas

Other areas in which cooling agents such as menthyl 3-hydroxy butyrate, N-ethyl-p-menthane-3-carboxamide, 2-isopropyl-N,2,3-trimethylbutyramide and menthyl lactate could be used are endless. For the perfumer, applications in which a cooling sensation or feeling of freshness is required can be enhanced using the previously mentioned materials. These areas may not be limited to fine fragrance, but also to any areas in which application of the fragrance can arouse or affect the other senses. For the flavorist, one must ask, "How can the consumer's product experience be enhanced by stimulating other senses?" In some cases, this may be accomplished via the addition of a slow-acting coolant to remove any unwanted aftertaste, leaving the consumer with a more pleasant sensation. In reality, the applications are limited only by the bounds of one's imagination.

World market for chewing gum, bubble gum and chewing gum base: 2001–2011 **T-4**

Year	World market ($ millions)
2001	8,262
2002	8,358
2003	8,459
2004	8,565
2005	8,717
2006	9,113
2007	9,569
2008	10,050
2009	10,556
2010	11,089
2011	11,649

Source: Philip Parker, INSEAD (2005)

Sports beverage market (USA): 2000–2002 (gallons in millions) **T-5**

Year	Gallons	% Change
2000	719.50	5.8
2001	776.70	7.9
2002	867.10	11.6

Source: Global Industry Analysts (2005)

Growth of European market for sports and energy drinks (2000–2010) **T-6**

Product segment	% CAGR (2000-2010)
Energy Drinks	9.2
Sports Drinks	7.1
Total	7.6

Source: Global Industry Analysts (2005)