Food Additive Toxicology

edited by

Joseph A. Maga

Anthony T. Tu

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6
Flavoring Agents

Robert Leslie Swaine, Jr.
The Procter & Gamble Company
Cincinnati, Ohio

I. INTRODUCTION

The objective of this chapter is to provide the toxicologist with insight and perspective as to the origin, manufacture, use, and safety considerations of flavoring agents. It is not a toxicology reference manual, rather it is written for the toxicologist who wants to obtain an introduction to flavoring agents. The chemical nature and derivation of flavoring substances will be stressed, and while several examples of known toxins will be discussed, the safety and toxicological data for all flavoring agents is beyond the scope of this chapter. For comprehensive individual toxicological studies, the reader is referred to resources such as *The National Toxicology Program Technical Report Series* and *The Registry of Toxic Effects of Chemical Substances*, available through the U.S. Department of Health and Human Services.

It is appropriate, if not ironic, to include flavoring agents (flavorings) in this endeavor since many flavoring agents are pharmacologically active and, of course, according to the dose, may be toxic to some organisms, even humans. For example, vanilla extract is toxic to humans, but the LD_{50} is estimated to be 4.0 pounds (Hodge and Downs, 1961). Actually, much of modern flavor chemistry has its roots in the early pharmaceutical industry. A search of official compendia, some as late as NF XII, reveals the codification of many of today's flavorings and flavoring agents not only for their organoleptic value but also for their pharmaceutical actions (Table 1). Some flavorings still exist in current compendia. Their use, however, is almost exclusively as a flavoring, more specifically as a masking agent for unpalatable medicinal principles. Exceptions include clove bud oil, used as a local anesthetic for toothaches, and enteric-coated peppermint oil, used for irritable bowel syndrome (Evans and Rhodes, 1979).

The reasons for using flavorings and flavoring agents may appear obvious, but a closer examination of such agents reveals perhaps as many subtleties and nuances

Table 1 Early Flavoring Agents Codified as Pharmaceuticals

Agent	Action
Anethole	Calmative
Anise oil	Calmative
Caraway oil	Calmative
Cardamom oil	Calmative, aromatic, stomachic
Cinnamon oil	Calmative
Clove oil	Aromatic
Coriander oil	Stomachic
Ethyl vanillin	Preservative
Eucalyptol	Antiseptic, inhalant
Eucalyptus oil	Bacteriostat, expectorant
Fennel oil	Calmative
Lavendar oil	Calmative, aromatic
Methyl salicylate	Counterirritant
Nutmeg oil	Calmative, G.I. stimulant
Peppermint oil	Calmative, antiseptic, local anesthetic
Phenyl ethyl alcohol	Antibacterial
Pine needle oil	Inhalent
Rosemary oil	Rubifacient
Spearmint oil	Calmative
Tolu balsam	Expectorant

as a good flavoring itself. Flavor is that property of a food or beverage that causes the simultaneous reaction of taste on the tongue and odor in the olfactory center of the nose. Flavoring agents are those substances that, when added to a food or beverage, impart flavor, i.e., evoke those simultaneous responses. The classical flavorist, then, uses flavorings with one of three main objectives (Swaine, 1972):

1. To impart the characteristic flavor of the flavoring: e.g., vanillin to give the flavor of vanilla to ice cream
2. To augment, complement, or modify a flavor: e.g., vanillin to modify the flavor of chocolate or cocoa
3. To mask the original flavor: e.g., anise to cover bitter medicinals

Recently the use of flavorings has been expanded to include interesting new roles.

1. Antioxidant
   Various spices and herbs and their extracts have been shown to exhibit antioxidant properties in a variety of food systems (Simon, 1990). These include:

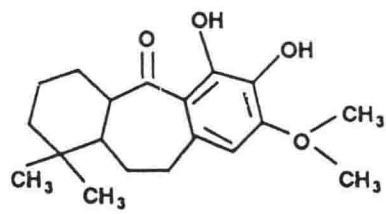
Allspice	Clove
Mace	Cinnamon
Ginger	Oregano
Black pepper	White pepper
Bay	Coriander
Sage	Rosemary

   The compounds responsible for the antioxidant activity in extract of rosemary

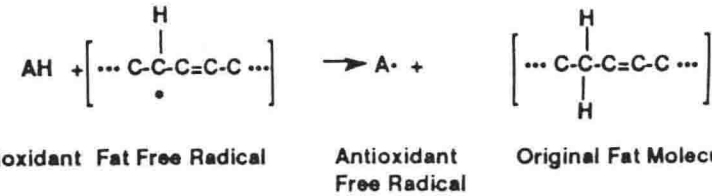
are phenolic in nature. One such compound, rosmaridiphenol and the mechanisms of antioxidants are shown in Figure 1.

2. Antimicrobial (Bactericidal)
Both clove bud oil and cinnamon oil have long been used in oral care and skin care preparations. Today they are common components in dentrifices and oral rinses. Garlic oil, because of its selective bactericidal action, is part of the current revival of folk-type medicines. Garlic oil acts selectively in food systems such as salami to prevent the growth of unwanted bacteria while permitting desirable microbes to flourish and produce the desired flavor and color.

Kubo et al. (1991) have demonstrated antimicrobial activity in the 10 most abundant chemicals in cardamom. These constituents—1,8-cineole, α-terpinyl acetate, linalool, linalyl acetate, geraniol, limonene, α-terpinene, safrole, methyl eugenol, and eugenol—are all common flavoring agents or constituents of flavoring (essential) oils.



These phenolic compounds interrupt free radical formation by donating a hydrogen ion to a free radical to reform the original molecule.



They also may donate hydrogen ions to peroxides, forming hydroperoxides and preventing free radical formation in other molecules.

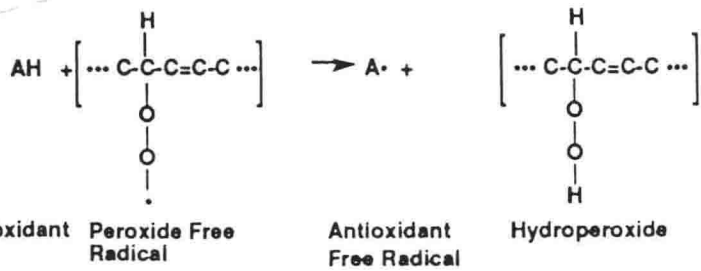


Fig. 1 Natural phenolic antioxidant.

Pellecuer et al. (1983) have established the antibacterial spectrum for certain gram-positive and gram-negative bacterial flora using thyme oil, rosemary oil, and lavender oil. Antimicrobial activity may allow the food scientist to reduce or eliminate added preservatives. This may have significant economic and consumer implications.

3. Color
   Paprika and turmeric, both as ground spices and as extracts, are used to add color to culinary items.
4. Enzymatic Activity
   Certain herbs and spices contain proteolytic and lipolytic enzymes. These are involved in flavor generation in many traditional dishes and ripened foods, such as certain Scandinavian fish preparations.
5. Physiological Effects
   Several herbs and spices are used for their side effects as well as for their characteristic flavor. Digestive beverages and breath fresheners, especially common in Europe, make use of cardamom, caraway, sweet marjoram, and thyme. Mustard also has been reported to stimulate the digestive process. Procter & Gamble (Tsai et al., 1990) has demonstrated that extracts of green tea ameliorate the state of anxiety and agitation induced by caffeine.
6. Health Benefits
   Schiffman (1986) at Duke University theorizes that obesity may be caused by the requirement of certain individuals for greater organoleptic signals, such as taste and odor in their food, i.e., obese people may have an exaggerated flavor setpoint. The implications are that low-calorie foods with high intensity flavor profiles may be beneficial as part of antiobesity therapy.

   Providing a more palatable, appealing and varied diet is important in insuring the consumption of sufficient nutrients. Lyman (1989) has shown in preliminary experiments that eating in general makes one happier. The effect, however, was dependent on the subject's initial mood. Generally his results suggest that flavor associations enhance the existing mood. If subjects are in a positive mood and the association is positive, then they feel better; if they are in a negative mood and the association is unpleasant, they will feel worse!
7. Aromacology
   While olfaction, both from a biochemical and cognitive point of view, is still not completely understood, researchers in the new field of aromacology are studying the effect of aromas on the function of the mind and the body (van Toller, 1991). Common biological measurements such as skin potential level, eye movement, pupil dilation, pulse wave, and blood pressure are unreliable indicators of the effects of aromas and flavorings. Recently, however, the use of electroencephalographic measurement, particularly CNV (contingent negative variation), of brain electrical activity is providing enlightening insights. Data on individual flavoring agents will eventually allow the creative flavorist to compound flavorings that, when added to a beverage or chewing gum, for example, will stimulate or relax the consumer.
8. Therapeutic Agent
   Several flavoring oils or oil components are now being studied for their anticancer activity. Organosulfur compounds from garlic oil may stimulate the activity of anticancer enzymes in the liver. d-Limonene, the major component

in citrus oils, has been implicated in breast cancer prevention in animals. Other flavoring agents with antioxidant properties may also find application in anticancer therapy. Antioxidants have been shown to exhibit anticancer effects, most probably by complexing with free radicals prior to any deleterious effects on the body cells nucleic acids (Cheetham and Lecchini, 1988).

The impact of flavorings on the food and beverage industry is dynamic and involves more applications than one could have envisioned even a few decades ago.

II. HISTORY AND INDUSTRY PERSPECTIVE

The discovery and evolution of flavoring agents and subsequently the flavor industry was most probably serendipitous. While the exact origins are still unknown, archeologists and flavor chemists alike can speculate as to the historical role of flavoring agents.

Archeologists do, however, believe that the knowledge and use of seasonings can be traced as far back as 50,000 years. Primitive experiences with flavoring agents could have been when humans cooking meat over different types of wood observed the variation in flavor (Swaine, 1972). Early humans may also have used leaves to protect food from dirt only to discover that upon heating (cooking) a most enjoyable flavor resulted from certain leaves. They probably also learned, probably too late, that certain flora were to be avoided. This most likely led people to gather other leaves, roots, and berries, perhaps blending them in unique proportions or mixing them with wild honey, thus preparing some of the first flavorings. These crude flavoring agents added variety to the rather monotonous diet. They may even have discovered that certain concoctions or processes made palatable food that may have otherwise been unfit for human consumption, a custom that was to be practiced for centuries to come.

Spices played an important part in several religions. Spices are referred to in the scriptures of the Assyrians (ca. 3000 B.C.). There are numerous references in the Bible to spices and the spice trade. When the Queen of Sheba visited King Solomon (I Kings 10) (ca. 1000 B.C.) she brought offerings of spice (Hodson, 1981).

In the Orient spices were used to introduce variety into a diet consisting mainly of rice. Cassia, for example, was known as early as 2700 B.C.

In the main, spices that have come to be significant items of commerce were indigenous to the East, India, Ceylon, Sumatra, Java, Bali, and the Molucca Islands. The spice trade that developed between the Mediterranean region (the ancient Greek and Roman civilizations) and the East was most likely the beginning of the flavor industry as we know it today. Among the more popular spices (flavoring agents) of the ancient Greeks and Romans were pepper, cassia, cinnamon, ginger, anise, caraway, fennel, coriander, and mint.

The Greek and Roman cultures spread throughout Europe and with them the appreciation for and knowledge of spices. Mustard, for example, was introduced into England in 50 B.C. by Roman soldiers. These new spices were not only flavorings but also valuable barter. The trade between Europe and the Orient ceased with the decline of the great civilizations of the ancient world. During this period the Islamic empire was rapidly expanding. Its newly found control over the spice trade ensured and strengthened its commercial position and religious posture. The

Muslims held captive the spice market for several hundred years. It was in the tenth century A.D. that the European spice trade enjoyed a revival. Spices were quite dear to the Europeans. One must be mindful that the diet at this point in history was at best monotonous and more often than not putrid or at least partially spoiled. Spices provided a welcome change and even a sense of adventure and romance since the spices came from faraway lands whose origins were shrouded in mystery. Further, the spices made spoiled food palatable.

During the late thirteenth century the monopoly on spice trade ended. Following his expeditions through the New East, Central and South Asia, and the exotic Pacific islands, Marco Polo recounted his exploits including his rediscovery of spices: ginger in China, cinnamon in Ceylon, pepper in Borneo, and nutmeg in the Pacific islands. The next several centuries saw exploration by sea and new trade routes develop in the East, Central America, and the Caribbean. New spices such as paprika, cayenne, and allspice were introduced into the kitchens of Europe.

The Middle Ages saw the early use of chemistry to develop flavoring agents. The alchemist in his search for "the elixir of life" used distillation to prepare or to concentrate essences from herbs. History actually credits Avicenna, an Arab physician in the tenth century, as being the first to isolate volatile oils from plant material using distillation. These extracts or volatile oils became increasingly more important to the alchemist, the druggist, the doctor, and finally to the creative flavorist. By the beginning of the sixteenth century only 13 volatile oils were widely used (Short, 1973): benzoin, rosemary, calamus, sage, cedarwood, spike (Lavender), costus, turpentine, mastic, juniperwood, rose, frankincense, and cinnamon. During the next century 66 volatile oils were used, and by the mid-1700s the number of oils had reached 100.

The crystallization of vanillin from an extract of vanilla beans in 1858 and the subsequent synthesis of vanillin in 1876 by Tiemann and Haarmann signaled the beginning of modern flavor chemistry. The organic chemist now began to assemble for the creative flavorist a much larger palette, containing both natural isolates and synthetic flavor chemicals. The advent of affordable sophisticated analytical instruments led to the identification of literally thousands of volatile aroma and flavor chemicals for foods and beverages. At last count some 6200 compounds had been identified in 320 foods (Maarse and Visscher, 1990). Figure 2 demonstrates the proliferation of flavor chemicals and patents during the past 2½ decades. The compounds identified still vastly outnumber the chemicals listed in the United States as generally recognized as safe (GRAS) for flavorings when used under conditions of intended use in accordance with Good Manufacturing Practices as defined by the Food, Drug and Cosmetic Act, section 182.1. The permutations of natural products and synthetic compounds seem, however, limited only by the imagination of the creative flavorist.

The flavor industry today records sales in excess of $3 billion per year. Since many flavor houses are still privately held, exact turnover is impossible to establish. Best estimates place third-party sales of compounded flavorings at $1.7 billion for 1986, $2.3 billion for 1987, and most recently $3.2 billion for 1990, $4.5 billion if one includes the sale of essential oils as well as of compounded flavorings (Broekhof, 1987; Matheis, 1989a; Unger, 1989; Abderhalden, 1991). Figure 3 demonstrates the use of flavoring according to industry. The 10 largest flavor houses account for approximately one third of this business. Aroma chemicals required

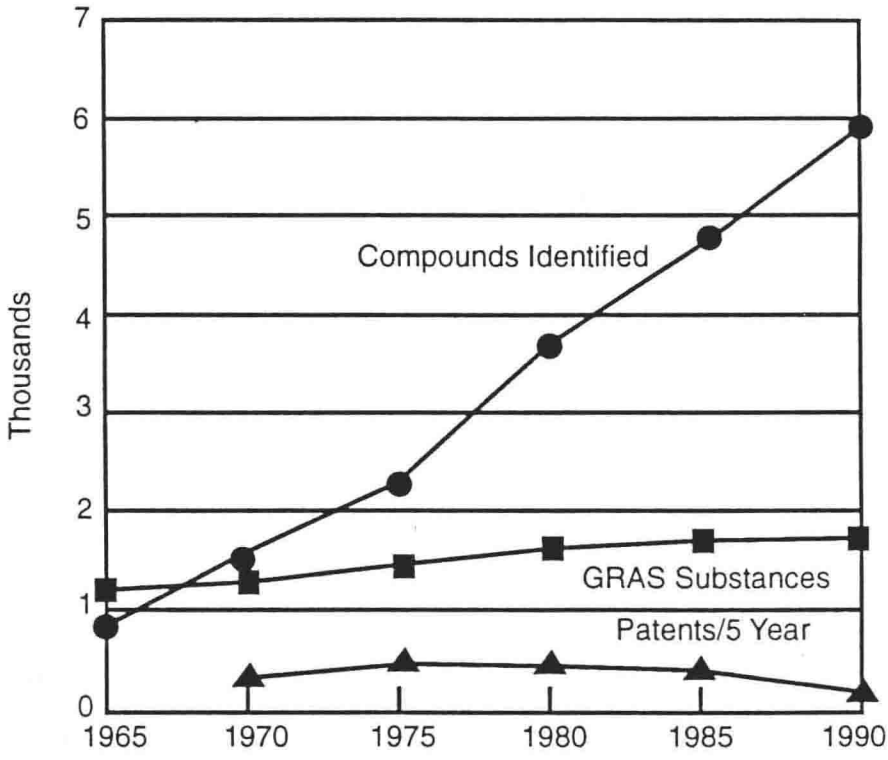


Fig. 2 Proliferation of flavor chemicals and patents. (From Maarse and Visscher, 1990.)

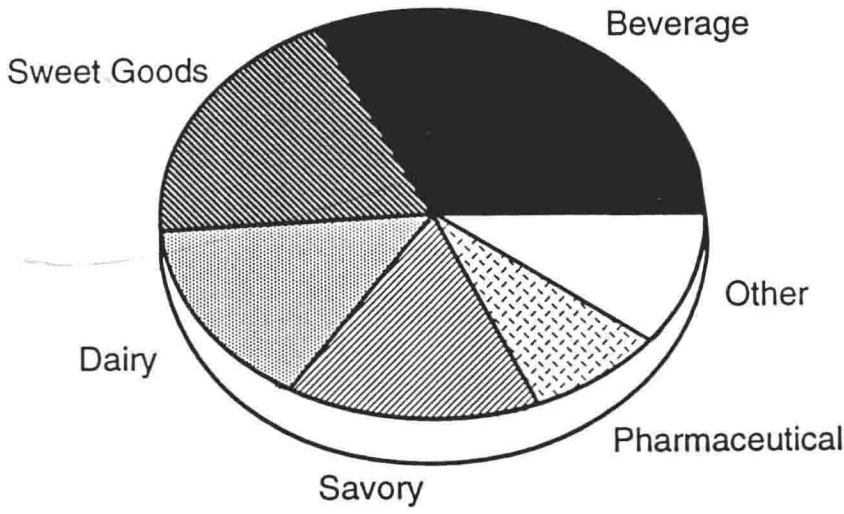


Fig. 3 Industry use of flavorings.

to support this volume may total another $750 million per annum. A healthy growth of 5–6% per year is anticipated through the turn of the century.

III. LEXICON

The flavor industry has developed a terminology reflective of the idiosyncrasies of the flavor chemist. Since certain terms are expressions of subjective observations and measurements, it may be difficult to define them. For example, is the essential oil of lemon citrusy, fruity, or is it refreshing? This may become clearer as individual terms are defined. Often research chemists and creative flavorists must discuss specific project requirements and review or develop new vocabulary at the inception of a project. The following are arbitrary definitions based on common industry practice and specific work in the Flavor Technology Laboratory of Procter & Gamble.

Absolute A highly concentrated form of plant material whose flavor is extremely similar to the starting material. An absolute is prepared by removing the alcohol-soluble portion of a concrete.

Accord A group of flavor notes that blend together to form one unique and harmonious composition.

Agrumen Flavor notes characteristic of citrus: orange, lemon, lime, tangerine, grapefruit, bergamot, and bitter orange.

Aldehydic Note from aliphatic fatty aldehydes containing 8–12 carbons. They possess fatty, waxy, and floral notes.

Aldehyde (So-Called) A potent flavor chemical, for example, γ-decalactone (aldehyde C14), or γ-nonalactone (aldehyde C 18). Many early synthetic flavoring agents were true aldehydes. They possessed great strength and diffusiveness. Flavorists came, therefore, to also call several new, potent flavor chemicals aldehydes.

Animalic Odor and flavor character of civet and castoreum. It is sometimes known as fecal.

Anosmia Loss of the sense of smell.

Aromatic Chemical A volatile chemical that has an odor and flavor property. This is a flavorist's term and should not be confused with a pure chemist's definition. It does not have to contain the typical benzene ring structure.

Balsamic A sweet, warm note typified by cinnamic alcohol or resinous plant exudates.

Blender A compound that has the ability to smooth or round a flavor, tying together the various notes to produce a harmonious effect. A blender such as vanilla may even introduce a flavor of its own.

Bottom Note The evaporative residue; the aroma present when the top and middle notes are gone. These tend to be higher molecular weight chemicals or resinous compounds.

Bulking A method used to ensure uniformity of flavoring agents. This principle is extremely important with natural raw materials that vary from season to season. Usually materials from various lots are mixed.

Burnt A charred or scorched note, or a smoky character.

Camphoraceous Fresh, clean medicinal flavor notes characterized by a resemblance to camphor.

Caramel Flavor of browned or burned sugar. Furaneol® is an example.

Compound 1. A true chemical compound. 2. A flavoring or part of a flavoring composed of two or more individual flavorings.

Concrete A waxy solid or semisolid extract produced by extraction, usually with a hydrocarbon solvent. It contains the essential oil, waxes, pigments, and fixed oil. The term concrete usually applies to flower material.

Deepener As with β-ionone in raspberry, a compound that enhances or reinforces the main theme.

Diffusive Flavor or odor that most rapidly permeates the air. Ylang Ylang is quite diffusive.

Earthy The odor of moist soil or a damp basement.

Essence A concentrated flavoring agent containing alcohol.

Essential Oil A volatile oil, usually possessing the characteristic odor and flavor of the plant from which it was isolated. These oils were once thought to be essential to the plant's life processes or communication.

Ethereal A spiritous, sharp, penetrating aroma.

Extract A water-soluble solution obtained by passing alcohol or a hydroalcoholic mixture through a substance. These should not be confused with official extracts, where the solvent is removed and the active constituent or flavoring subsequently standardized.

Fatigue Loss of the sensation of smell with respect to a specific odorant or flavoring. This is usually caused by continued exposure in sufficient concentration to an odorant.

Fixative A compound that reduces the overall volatility of a flavoring and results in a reduction in the loss of more volatile compounds.

Floral Odor reminiscent of flowers.

Fold Denotes the strength of a flavoring agent, particularly an essential oil or an extract.

Green A class of flavor notes characterized by intense fresh leafy odor. Six-carbon alcohols and aldehydes are green.

Isolate A chemical or fraction composed of several chemicals obtained from a natural source. Citronellal may be chemically isolated from citronella oil.

Main Note This is also known as the heart or the middle note. It is characteristic for a particular flavor system.

Masking Agent A compound that covers unwanted odors and flavors, e.g., as lemon oil covers fishiness.

Modifier A compound that changes (slightly) the overall character of a flavoring, e.g., citral in an orange composition.

Note A singular characteristic of a flavoring agent. Any flavoring, however, may be a blend of several notes and accords.

Oleoresin A resinous plant extractive prepared by extraction with a nonaqueous, usually hydrocarbon solvent. An oleoresin contains both the volatile fraction and the nonvolatile fraction, which may include pigments, waxes, fixed oils, gums, and resins. The nonvolatile portion contains, in the case of ginger and pepper, the pungent principles.

Safety Reasonable certainty that a substance is not harmful under the conditions of use. This is a most difficult thing to determine on an absolute scale.

Tinctures Cold alcoholic or hydroalcoholic solutions prepared from vegetable materials, essential oils, or chemical substances.

Topnote The volatile note first observed upon exposure to a flavoring. It may be smelled or tasted and is usually suggestive of the flavor identity.

Woody Flavor note provided by certain natural woods and their isolates. These have excellent fixative properties.

Many terms, especially those used to describe flavor sensations, are subjective. Commonly available chemicals and natural products that exemplify key flavor notes are shown in Table 2.

IV. FLAVOR PROCESSES

A. General Considerations

This section will discuss methods to commercially isolate or generate flavoring agents from natural raw materials. Natural raw materials in this context are botanical or animal products containing flavorful compounds or the precursors to flavoring agents. It is not the intention here to define natural products of flavorings for any legal or regulatory purpose. Flavor-labeling regulations still vary among

Table 2 Flavor Notes

Flavor note	Examples
Aldehydic	Decanal, undecanal, dodecanal
Alliacious	Allyl disulfide, onion oil, garlic oil
Almond	Benzaldehyde
Animalic	Civet, indole
Anise	Anethole
Balsamic	Balsam Peru, benzyl cinnamate
Bite	Capsicum, oleoresin black pepper
Brown	Maltol
Buttery	Diacetyl
Camphoraceous	Isobornyl acetate, marjoram
Citrus	Orange oil, lemon oil
Peachy	Aldehyde C14 (so called)
Phenolic	Guaiacol, clove bud oil
Roast	2,3-Dimethyl pyrazine
Skunky	Dimethyl sulfide
Smoky	Guaiacol
Soapy	Decanal
Spicy	Eugenol, cinnamic aldehyde
Sweet	Vanillin
Vegetable	Galbanum, maté
Violet	β-Ionone, methyl octyne carbonate
Waxy	2,4-Decadienal
Woody	Sandalwood, Vetiver, γ-methyl ionone