herbivore- or wound-induced vocabularies have been modified by silencing genes involved in either the biosynthesis of particular volatiles or the oxylipin signal cascade represent potential mute emitter plants (Fig. 1).

Mutants whose perception of specific VOCs is impaired ("deaf" plants) represent another tool for analyzing the consequences of VOC signaling as illustrated by the ethylene-insensitive tobacco plants, *etr1-1*. The produce industry long ago developed a sophisticated ethylene trapping and releasing technology, but the first clear demonstration of the functional significance of ethylene signaling in competitive interactions required plants that were "deaf" to this VOC (*20*). Receptors for most of the herbivore-induced VOCs remain to be discovered, but transcriptional responses to VOC exposure can be used in mutant screens to identify new VOC receptors. Identification of these genetic elements and the creation of VOC-reporter plants [with β-glucuronidase (GUS) or green fluorescent protein] will allow researchers to readily determine the quantity of signals that are perceived by receivers at different distances from an emitter. Combining deaf and mute plants with wild-type plants in natural settings will clarify the relevance of VOC signaling for a plant's performance and/or fitness in the real world. Because differences in performance among plants that are unable to produce or perceive certain volatiles are likely to be subtle, the analysis will likely require long-term studies in natural settings. The more deaf plants that are available to complement the growing list of available mute plants, the more tools researchers will have to fully evaluate the significance of volatile signaling among plants in natural settings. These experiments will determine whether being a native speaker enhances a plant's fitness in its community.

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REVIEW

Plant Volatile Compounds: Sensory Cues for Health and Nutritional Value?

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Plants produce many volatile metabolites. A small subset of these compounds is sensed by animals and humans, and the volatile profiles are defining elements of the distinct flavors of individual foods. Flavor volatiles are derived from an array of nutrients, including amino acids, fatty acids, and carotenoids. In tomato, almost all of the important flavor-related volatiles are derived from essential nutrients. The predominance of volatiles derived from essential nutrients and health-promoting compounds suggests that these volatiles provide important information about the nutritional makeup of foods. Evidence supporting a relation between volatile perception and nutrient or health value will be reviewed.

Plants are capable of synthesizing tens to hundreds of thousands of primary and secondary metabolites with diverse biological properties and functions. Plant volatile organic compounds (defined hereafter as volatiles) generated from both primary and secondary metabolites are generally low molecular weight lipophilic compounds (*1*, *2*). More than 7000 flavor volatiles have been identified and cataloged from foods and beverages (*3*, *4*). Many volatiles are produced in plant tissues at specific developmental stages—for example, during flowering, ripening, or maturation. Although a single fruit or vegetable synthesizes several hundred volatiles, only a small subset generates the "flavor fingerprint" that helps animals and humans recognize appropriate foods and avoid poor or dangerous food choices.

Although perception of flavor is often described as a combination of taste and smell (*5*), appearance, texture, temperature, mouth feel, and past experience also play major roles in flavor perception, indicating that multiple distinct sensory inputs are processed to generate the overall sensation (Fig. 1). Integration of this sensory information in the brain ultimately results in a flavor preference or aversion with a strong influence on subsequent perception and behavior. Studies of flavor preferences and aversions suggest that flavor perception may be linked to the nutritional or health value associated with the perceived foods (*6*–*11*). For example, fatty acids that stimulate taste responses are essential long-chain cis-polyunsaturated fatty acids rather than nonessential saturated fatty acids (*11*). Flavor preferences begin to develop before birth and develop rapidly in the newborn

(*12–16*). Several feeding experiences are generally required to develop flavor preferences (*17*, *18*), although flavor aversions are learned much more rapidly (*18*, *19*).

The human genome encodes a few dozen functional taste receptors and several hundred olfactory receptors (*20*, *21*). These sensory receptors have evolved to allow recognition of specific foods and their compositions. Taste receptors monitor five distinct modalities of salty, sweet, sour, bitter, and umami (*22–24*). Bitter compounds are sensed by a large family of receptors and are used as a warning of undesirable constituents (*25*). Whereas the taste sensory system provides information on major nutrients such as carbohydrates, proteins, and lipids, the olfactory sensory system and the food volatiles with which they interact provide the basis for the diversity of flavors found in the human diet. To more fully understand the links between flavor preferences, volatiles, and nutrition, we consider the volatile chemicals that contribute to tomato flavor. Tomato is a model for fruit development, and more is known about the chemicals contributing to tomato flavor than for any other fruit or vegetable. Virtually all of the major tomato volatiles can be linked to compounds providing health benefits to humans. In most instances, the link is to essential human nutrients. Frequently these volatiles or their precursors have antimicrobial or other health-promoting activities. Thus, flavor volatiles can be perceived as positive nutritional signals.

The impact of a chemical on flavor perception is determined by both its concentration and the odor threshold (our ability to sense it). When expressed as the log ratio of concentration over odor threshold, the value for compounds present at levels exceeding the threshold is positive. Only a small number of the more than 400 volatiles detected in tomato have a positive impact on the flavor profile. Table 1 lists these volatiles in their approximate order of importance. Odor thresholds of these volatiles vary by as much as six orders of magnitude, and some of the most important volatiles are present in very small quantities.

Volatile emissions have evolved to facilitate seed production and dispersal. In that context, the foundations for the flavors associated with most fruits and vegetables existed before crop domestication. Generally, domestication has had a negative effect on tomato flavor and volatile production. Breeding programs have historically focused on yield, color, shape, and disease resistance. Flavor is a complex, multigenic trait providing unique challenges to breeders and has not been a high priority. Selection for yield, fruit size, and shelf-life characteristics in particular has had unintended negative consequences on fruit flavor. Table 1 lists the concentrations of volatiles emitted by fruits for two different tomatoes: *Lycopersicon esculentum* var. *cerasiforme*, a wild accession, and Flora-Dade, a commercial cultivar released in 1976. Whereas the former is indicative of volatiles produced by the undomesticated species, the latter is typical of most commercial cultivars grown for fresh market consumption. Overall, the sugars, organic acids, and volatiles associated with tomato flavor are somewhat reduced in cultivated varieties (although the yield may be enhanced). A major exception is 6-methyl-5-hepten-2-one, a volatile derived by oxidative cleavage of lycopene. This reflects breeders' emphasis on selection of cultivars with enhanced red color (dependent on lycopene). Another fruit that has been intensively domesticated with similar consequences is strawberry. Cultivated strawberries have different volatile profiles and are considered to be less flavorful than the wild species. A large part of this difference can be attributed to loss of a single enzyme during domestication (*26*).

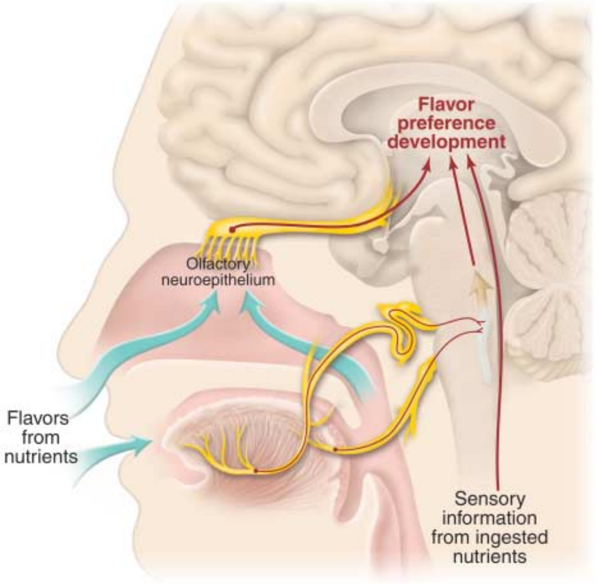

Fig. 1. Taste and olfactory sensory stimulation are integrated with a variety of sensory inputs including visual, tactile, and nutrient-sensing from the gastrointestinal tract to generate the overall flavor perception of specific foods. Experience modulates flavor preferences and aversions.

The metabolic pathways for synthesis of many important plant flavor volatiles are not fully elaborated. However, on the basis of structural considerations, predicted precursor-product correlations, isotope feeding studies, and, in some instances, gene cloning, the precursors of most of the major tomato flavor volatiles are known (Table 1) (*27*). The most abundant volatiles in tomato fruits are derived from catabolism of essential fatty acids (*28*). These volatiles are associated with flavors described as "tomato," "green," or "grassy." They are derived from linoleic acid (hexanal) and linolenic acid (*cis*-3-hexenal, *cis*-3-hexenol, *trans*-2-hexenal) via lipoxygenase activity (*29*) and are, therefore, indicators of the presence of free fatty acids classified as essential to the human diet. The six-carbon aldehydes and alcohols derived from omega-3-linolenic acid are also important constituents of the flavors of a diverse group of plant products including apple, sweet cherry, olive, bay leaf, and tea. Breakdown of linoleic acid generates the decadienoate esters important for pear flavor (*30*), as well as butanoate esters and hexanol that are important for banana flavor (*31*, *32*). Essential fatty acids are also degraded to lactones in peaches, apricots, and coconuts, and many of the fruit aliphatic esters, alcohols, acids, and carbonyls are derived from essential fatty acids.

A second class of volatiles that contribute positively to tomato flavor is derived from the essential amino acids leucine, isoleucine, and phenylalanine (*27*). Thus, these volatiles are indicative of free amino acid content. These volatiles (2- and 3-methylbutanal, 3-methylbutanol, phenylacetaldehyde, 2-phenylethanol, methyl salicylate) are important flavor constituents of many fruits, including strawberries and apples as well as processed foods such as breads, cheeses, wines, and beer. 2- and 3-methylbutanal are also potato flavor volatiles. Methyl salicylate is commonly known as oil of wintergreen and is the methylated derivative of salicylic acid (aspirin), a known anti-inflammatory and analgesic compound. Although some nonessential amino acids are metabolized to volatiles, most notably cysteine being the precursor of allicin, none is considered a major contributor to tomato flavor. Allicin is an important flavor component of garlic and has reported antibacterial and antifungal activities (*33*, *34*).

A third class of tomato volatiles, the apocarotenoids, is derived from oxidative cleavage

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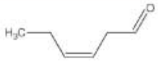
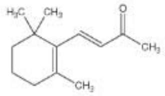
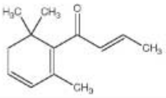
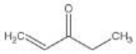
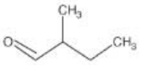
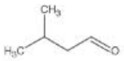
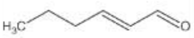
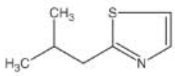
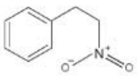
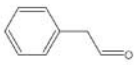
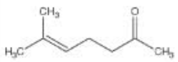
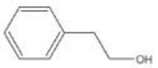
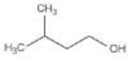
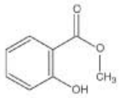
Table 1. Volatile compounds, structures, and their precursors in two varieties of tomato. Shown are volatile chemicals positively contributing to tomato flavor. The rank order of volatiles is based on the work of Buttery and Ling (*27*). The concentrations of volatile emissions were determined for two varieties of tomato. *L. esculentum* var. *cerasiforme* LA1673 is a wild accession isolated by C. Rick in Peru. Flora-Dade is a commercial cultivated tomato released by the University of Florida in 1976. Odor thresholds in parts per billion (ppb) are taken from Leffingwell and Associates (*62*). FW, fresh weight; ND, not determined.

Volatile	Structure	Precursor	Concentration (nl/g FW/hour *cerasiforme*)	Concentration (nl/g FW/hour Flora-Dade)	Odor threshold (ppb)
cis-3-Hexenal		Fatty acid	16.28	5.25	0.25
β-Ionone		Carotenoid	0.03	0.02	0.007
Hexanal		Fatty acid	27.21	17.15	5
β-Damascenone		Carotenoid	ND	ND	0.002
1-Penten-3-one		Fatty acid	0.21	0.03	1
2-Methylbutanal		Isoleucine	0.75	0.25	1
3-Methylbutanal		Leucine	0.67	0.18	0.2
trans-2-Hexenal		Fatty acid	0.7	0.26	17
Isobutylthiazole		Unknown	0.32	0.8	3.5
1-Nitro-2-phenylethane		Phenylalanine	0.018	0.013	2
trans-2-Heptenal		Fatty acid	0.16	0.13	13
Phenylacetaldehyde		Phenylalanine	0.06	0.09	4
6-Methyl-5-hepten-2-one		Carotenoid	0.99	1.84	2000
cis-3-Hexenol		Fatty acid	19.83	13.29	70
2-Phenylethanol		Phenylalanine	0.21	0.32	750
3-Methylbutanol		Leucine	3.83	1.23	120
Methyl salicylate		Phenylalanine	0.08	0.04	40

of carotenoids. Carotenoids are light-harvesting pigments and essential antioxidants in plants. They also provide important visual cues associated with fruit ripeness. Carotenoids have been reported to serve as antioxidants in the human diet and are implicated in many aspects of human health (*35*, *36*), although these benefits remain controversial (*37*, *38*). Nonetheless, the pro–vitamin A carotenoids, principally β-carotene, are essential precursors of retinol, retinal, and retinoic acid. Humans have a much lower odor threshold for β-ionone (the oxidative cleavage product of β-carotene) than for linear carotenoids such as 6-methyl-5-hepten-2-one (derived from lycopene), although both are readily detectable in tomato fruits. Apocarotenoids are important for flavor in diverse food products. For example, β-damascenone, in addition to tomato, is found in berries, apples, and grapes (as well as wine). Safranal, found in saffron, grapefruit, and green tea, is derived from the carotenoid zeaxanthin. Likewise, dihydroactinidiolide and 4-oxoisophorone are flavor components of carotenoid origin found in teas, tobacco, lemon balm, and saffron.

Although a few tomato flavor volatiles are produced in detectable quantities throughout fruit development, most are principally associated with ripening (Fig. 2). Synthesis of the apocarotenoids β-ionone, geranyl acetone, and 6-methyl-5-hepten-2-one increases 10- to 20-fold as fruits reach a fully ripened stage (*27*, *39*). The specific association of these volatiles with ripe fruits and their relative absence from vegetative tissues suggests a role in signaling ripeness and attracting seed-dispersing organisms, including humans. Thus, tomato flavor can be viewed as a set of cues that together reflect the ripeness and nutritional quality/nutrient availability of the fruit. Sweet taste receptors respond to the sugars, principally glucose and fructose that accumulate only upon ripening. Sour taste receptors respond to citrate, malate, and ascorbate. Umami taste receptors respond to the buildup of glutamate and aspartate released from proteins. These signals are integrated with olfactory-system stimulation by volatiles derived from fatty acids, amino acids, and carotenoids. Fruit ripening thus involves a conversion of higher molecular weight precursors to smaller chemical components that provide maximal nourishment to the seed and attraction to seed-dispersing species. Volatiles released during fruit ripening are sensed as principal flavor constituents that signal the ripeness of the fruit and therefore the highest nutrient bioavailability.

Unlike ripening fruits, vegetables produce most of the volatiles sensed as flavors only after their cells are disrupted (*28*). This disruption mixes substrates with the enzymes responsible for generating flavor volatiles. For example, garlic, onions, and mustards, as well as certain other vegetables, produce the volatiles allyl isothiocyanate and allicin after cellular disruption. These volatile flavor compounds exhibit antimicrobial activity when present in a variety of foods. Thioglucosidase activity in various *Brassicaceae* releases volatiles from glucosinolates, which have anticancer activities but can be toxic at high doses. Both the development of flavors and the availability of nutrients are promoted by cell lysis in vegetables.

The volatiles synthesized in popular spices found throughout the world again suggest that flavor perception is linked with specific health properties. Curcumin, a major flavor volatile of the spice turmeric, is reported to have both anti-inflammatory and anti-tumor activities (*40*–*42*). Likewise, curcumene, gingerol, and gingerone from the spice ginger have reported antioxidant and anti-tumor activities. Many spices with distinct preferred flavors in a variety of cultures are reported to have antimicrobial activities, including allicin from garlic, thymol, borneol, isoborneol, eugenol, allyl isothiocyanate, and cavracol from rosemary, sage, clove, mustard, chili pepper, and thyme (*43*–*45*). These observations have led to the proposal that spice use in different parts of the world helps preserve food and provide a safer food supply (*43*). A preference for the flavors found in these spices is believed to have developed due to the health benefit of less contaminated food.

Although bitter taste is generally considered a negative sensation and a warning of toxin content, some bitter flavors are preferred in specific food products. For example, the lupulins from hops, quinine from cinchona, and methyl cinnamate, cineol, and camphor from the spice galangal are preferred bitter flavors in some foods or beverages. Specific health benefits have been reported to be associated with these bitter flavors: Quinine is a well-known antimalarial compound, hops are used as a preservative in beer, and camphor and methyl cinnamate are reported to have antimicrobial activity. Likewise, the bitter gluconsinolates such as sinigrin from brussels sprouts are reported to have anticarcinogenic and immune-boosting activities.

The question of whether a sensory feedback system involving plant-produced volatiles is quantitative or qualitative remains unanswered. Although there is frequently a direct correlation between precursor content and volatile emissions, as with carotenoids (*39*, *46*, *47*), there is not always a direct correlation between essential nutrients and their volatile metabolites. However, this does not exclude a quantitative response because such a response need not be linear. Indeed most biological systems are linear over a limited range. Although excessively high concentrations of many volatiles can be perceived as off-odors, the cues provided by individual volatiles must be considered in the context of the food and the learned experiences associated with that food. Thus, humans respond to a tomato as a whole food with certain nutritional benefits.

Although the physiological mechanisms responsible for monitoring the nutritional or health value of a specific food remain unresolved, behavioral research supports a connection between sensory perception, flavor preferences, and health benefits. For example, rodent feeding studies demonstrate that preferences for bitter or otherwise undesirable flavors can be learned when those flavors are associated with desirable nutrients (*48*). Herbivores learn to consume toxin-containing plants with additional foods that neutralize the toxic effects (*49*–*52*). Even nematodes, with only a few hundred neurons, avoid foods with detrimental health consequences via learned olfactory-mediated responses (*53*). In addition, invertebrate predators forage selectively to acquire specific dietary nutrients (*54*), and grasshoppers feed selectively to maintain dietary protein and lipid content (*55*). Caterpillars regulate their protein and carbohydrate intake (*56*). Tiger moth caterpillars display enhanced taste responses to alkaloid-containing plants when

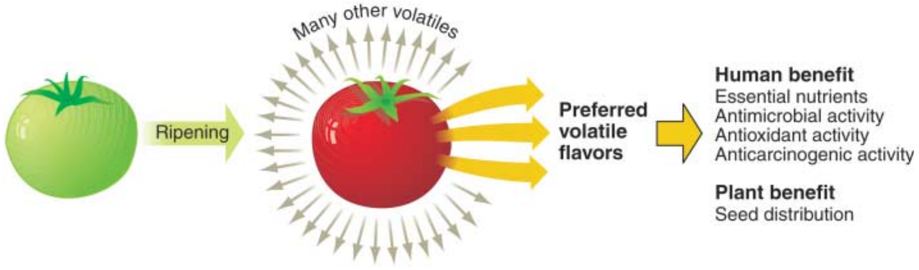


Fig. 2. Tomato fruits produce a volatile emission profile that is both attractive to humans and an indicator of ripeness. Of the more than 400 volatiles emitted by tomato fruits, only a small number, almost all of which are derived from essential human nutrients, are detected and integrated into a preferred volatile aroma. This pattern of volatile emissions is mutually beneficial. Thus, volatile emissions are both positive indicators for the presence in the fruit of compounds with positive health benefits and attractants that promote seed dispersal.

parasitized, resulting in feeding behavior that eliminates the parasites (*57*). Sensory systems expressed throughout the gastrointestinal tract may provide feedback on the quality and quantity of ingested nutrients (*58–61*).

In conclusion, a correlation exists between health and the volatiles that contribute to the positive perception of foods. It is likely that volatile emissions have evolved in part to provide positive information to seed-dispersing organisms. For tomato, almost every important volatile is derived from an essential nutrient. Not all desirable volatiles are expected to be derived from essential nutrients, nor will all volatiles derived from essential nutrients be viewed as desirable across all populations. For example, many flavor volatiles are derived from terpenoids that are not directly related to essential nutrients. But many of these terpenoids are also known to have strong antimicrobial activity. Also, nutrients such as essential fatty acids can be metabolized to produce off-flavors in certain circumstances such as the off-flavors generated by lipoxygenase activity in soybean processing. Despite the exceptions, essential nutrient-derived volatile flavors are positive indicators of their precursors. The molecular mechanisms underlying nutrient monitoring remain undiscovered, but implications for food production and consumption are suggested. Much of the developed world faces a nutritional crisis, where obesity and diet-related health issues are becoming an increasing burden to society. Processed foods prevalent in developed countries today often combine natural or synthetic flavors with low nutrient content. Dissociation of flavors from their natural nutritional context may create undesirable health consequences such as the overconsumption of highly processed starch or saturated fats. Flavor preferences together with health benefits should be considered in future food production and in crop-enhancement strategies.

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