Special report

Developments in Taste Perception

The latest findings and their application to the flavor, food and beverage industries

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Considerable progress in taste perception research has been made during the past decennium. Taste receptors (TRs) for tastants with sweet, bitter, umami and fatty qualities have been identified. The primary processes of taste perception for these modalities are now better understood. Within the bitter taste quality, for instance, tens of different receptors exist.

The mechanism for the response of more polar tastants with salty, sour and alkaline qualities has been proposed. The coming years will see the development of a practical use of TRs in vitro on membranes or chips to determine the quality and intensity of tastants in flavors, foods or beverages.

Taste Perception

For the maintenance of life and species, every living organism — including humans — needs nutrition, e.g., food and drink. To find, select and appreciate nutrients requires both physical (touch, sight and hearing) and chemical (smell and taste) means. The chemical communication for the sense of taste in vertebrates starts in the mouth with the intake of water- or saliva-soluble tastants. Papillae with taste buds containing nerve cells with TRs are situated on the tongue, palate and larynx. Those TRs can distinguish among sweet, bitter, umami, fatty, salty, sour and alkaline tastants. Whereas sweet taste perception may provide information about palatable food, the bitter modality may warn and protect against the ingestion of poisonous materials. (Many naturally occurring poisonous substances taste bitter to humans.) Because all animals show an aversion to bitter-tasting compounds, it may be concluded that bitter perception is a defense mechanism against the intake of harmful substances, which, in turn, may explain why mammals possess a large number of bitter TRs.

Although thousands of publications on taste perception have appeared, it was not until 2000 that the first identity of a TR was confirmed.[1-3] Genes that encode bitter, sweet, umami and fatty TRs also have been identified.

Herein we will discuss the primary mechanism of taste reception of these modalities. The mechanism of salty, sour and alkaline tastants, which may be different, will be shown.

Previous Research

In 1994, van der Wel presented an excellent review of the relation between chemistry and taste during a course on "sensorial investigations."[1] During this lecture for Dutch industrial experts, van der Wel summarized the state of the art (ca 1994) of the biological functioning of TRs, as well as the relationships between chemical structures and taste qualities. Hereafter, some citations from his lecture will be made.

In 2003, Atkins devoted a chapter of his "Atkins Molecules" to taste, smell and pain.[2] In this chapter, he revealed the structures of compounds with the qualities sweet, bitter, sour, umami, hot, spicy and cool.

For more than 25 years, van Gemert collected odor and taste threshold values from the literature.[3] He analyzed several thousand publications with up to 20,000 threshold values. Some important tastants from these studies will be shown for qualities and threshold values.

Sugita has reviewed umami taste.[4]

Since 2000, considerable developments have been made in the identification and working mechanism of TRs for the qualities sweet, bitter, umami and fatty.[5-14] Throughout the past year or so, several publications have appeared addressing behavioral studies of taste perception.[17-23]

The Primary Mechanism of Taste Perception

It is well known that the sense of taste is located mainly on the tongue, but the palate and larynx also play important roles.[1,2] There are numerous (up to 10,000) papillae on the surface of the tongue, which, according to their form, can be subdivided into:

- fungiform, with a diameter of about 0.2 mm, and occurring at the front two-thirds of the tongue
- foliateform, consisting of a number of small canals located at the sides and the end of the tongue
- circumvallate, laying in a V-form at the end of the tongue
- filiform, occurring over the whole tongue and containing no taste buds (see F-1)

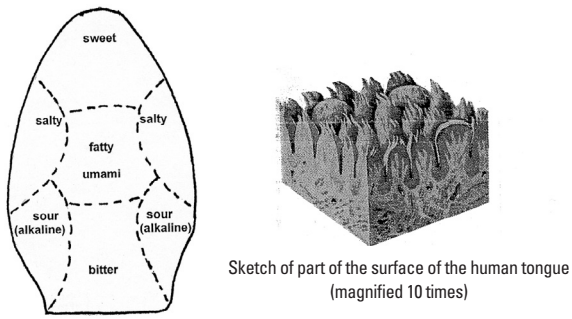
Each papilla contains a number (ca 100) of pear-form organellas, or taste buds (about 0.05 mm in diameter), which are connected to the oral cavity by a small opening. The real taste cells are located in the taste buds. The cells have a long form and are arranged like the segments of an orange. At the top, the cells possess a number of small finger-formed microvilli that are situated in the opening of the taste bud — the so-called tasteporus — which connects the bud with the oral cavity. This is where the primary contact with the stimulus (tasting compound) occurs. Thin nerve fibers can be found in a deeper part of the taste bud. These make synaptic contact with taste cells, which unify under the taste bud in a dense network.

Three types of nerve bundles have been recognized:

- *chorda tympani*, part of the *nervus facialis*, on the front two-thirds of the tongue
- *nervus glossopharyngeus* on the rear third of the tongue
- *nervus vagus*, located on the throat and larynx

According to van der Wel, a chemical signal is converted into an electrical signal during taste perception. The tasting chemosensory process is a reversible physicochemical interaction between two molecular species: a population of stimulating molecules and a population of receptor sites on the sensory epithelium. The sensation occurs when a chemical compound (tastant or stimulus) penetrates the tasteporous, thus interacting with the microvilli and resulting in a response. Minor electrical potential occurs between the inside and outside of the cell via stimulation. The electrical charge of the cell changes by depolarization. A widely accepted theory assumes that the stimulus is absorbed at the surface of the receptor and that the magnitude of the response is proportional to the number of absorbed molecules. The interaction of the tasting molecule and the receptor site may cause a disturbance in the geometry of the receptor molecule, resulting in a weak absorption energy of 2-3 kcal/mole.

Putative regions of the tongue that respond to different taste modalities **F-1**

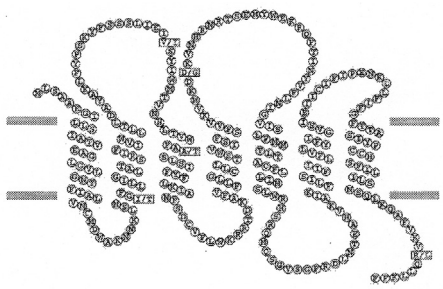


Sketch of part of the surface of the human tongue (magnified 10 times)

In order to taste a chemical compound (a tastant of a flavoring substance), it has to be water- or saliva-soluble. Saliva-soluble molecules reach the microvilli at the end of a taste cell and may come to a reversible interaction with the cell wall or with a TR in this wall. This interaction may be due to hydrogen bonds, weak van der Waals forces or Coulomb attractions.

The TRs are G protein-coupled receptors (GPCRs). A G protein of 250-350 amino acids repeats seven times in a spiral form through the cell wall (so-called seven-*trans*-membrane-domain protein), with the NH2-endgroup outside the cell and the -COOH-endgroup within the cell (see F-2).

Predicted seven transmembrane domain topology of a taste receptor protein (mT2R5) in mice (each dot is an amino acid: about 300 in total)[9] **F-2**



Matsunami et al. have mentioned that the candidate receptors for bitter taste in humans and mice are encoded by the TRB genes on chromosomes 5 and 12,

and share sequence motifs with one another, uniting them as members of the same receptor family.[5,7] Although they possess the seven-transmembrane domain structure characteristics for GPCRs, they are unrelated in sequence to both mGluR4, which detects glutamate (umami), and the candidate sweet TRs TR1 and TR2. In addition, mGluR4, TR1 and TR2 have long extracellular amino-terminal domains that are proposed to bind ligands, whereas TRBs have very short N-termini, suggesting that they use a different ligand binding.

After interaction of a tastant molecule with the receptor or cell wall, the ion permeability of the cell membrane changes, and a receptor potential occurs. Intracellular messengers play a role during this change in permeability. Cyclic adenosine-3',5'-monophosphate (cAMP) seems to be one of the messengers, which connects the reception of the stimulus to the response. This compound is responsible for a cAMP-dependent enzyme (protein kinase), which inactivates the potassium ion channel. In this way, it influences the transport through the membrance. In T-1, a scheme is shown that reveals the possible events during interaction and transduction of a sweet tastant.

Scheme of chronological order of events during putative interaction of a sweet tastant with receptor cell and the transduction of the signal **T-1**

Saliva-soluble tastant molecules reach receptor cell at microvilli of cell in taste bud
Reversible interaction between tastant molecule and G protein-coupled receptor
Chemical stimulation of the TR (seven-*trans*-membrane-domain protein)
Activation of protein guanidine triphosphate (GTP-binding protein)
Stimulation of adenyl cyclase
Enhancement of intracellulary cyclic adenosine-3',5'-monophosphate (cAMP)
Closing of apical potassium ion-channel
Depolarization of the taste cell (neuron)
Opening of the voltage-dependable calcium ion-channel
Allowance of calcium ions influx to synapsis
Causing neurotransmitter release at synapsis

The Umami, Bitter and Sweet Taste Modalities

The umami, bitter and sweet taste modalities are treated under one heading because the TRs (T1Rs, T2Rs and mGluR4) of these qualities have been studied in detail.[5-13]

Umami: Umami (Japanese) taste also is described as savory with a pleasant and piquant quality. Umami was discovered as a taste quality in 1908 by Kikunae Ikeda, of the Tokyo Imperial University.[4] In 1986, Sugita, from the Society for Research on Umami Taste, reviewed the recent developments in umami research.[4]

Umami is defined as the taste of a group of sodium salts of amino acids and 5'-nucleotides, such as glutamates, inosinates and guanylates. The most important representative for this taste quality is monosodium glutamate (MSG). In Chinese, MSG is referred to as *wei ching*, or taste refiner. Sugita presented a series of data on this taste modality in characterizing umami as an independent fundamental taste, along with the four basic tastes: sweet, salty, sour and bitter. Nine important umami-tasting substances related to nucleotides with their relative potency of taste quality are presented in T-2.

Substances with umami taste[4] **T-2**

Substance (disodium salt)	Relative umami potency
5'-adenylate	0.18
5'-xanthylate.3H_2O	0.61
5'-inosinate.7.5H_2O	1.00
5'-guanylate	2.30
N2-methyl-5'-guanylate.5.5H_2O	2.30
2-methyl-4-mercaptopurine ribose-5'-phosphate	8.00
N'-methyl-2-methylthio-5'inosinate	8.40
2-ethoxyethylthio-5'-inosinate	13.00
2-furfuryl-5'-inosinate.H_2O	17.00

The identity of the umami receptor remained illusive until 2000 with the work of Chaudhari and co-workers.[7] The researchers described a modified TR, mGluR4 in which the end of the molecule is missing. The strong binding of glutamate to mGluR4 requires this terminal region, and so the absence of the molecular end explains why the truncated form of mGluR4 is less sensitive to glutamate. The authors confirmed that the truncated molecule, which they called "taste-mGluR4," has all the properties that one would predict of an umami receptor. Most importantly, they showed that it responded to glutamate at the same concentrations at which glutamate can be tasted and that chemicals that mimic the taste of glutamate also activate the receptor.

In a 2000 press release from *Nature Neuroscience* regarding the identification of the umami TR, the following announcement was made: "Now the hunt is on to find the receptors for sweet and bitter, which are still not known."[8]

That same year, Adler et al. already had discovered a novel family of mammalian TRs.[9] The researchers

identified a novel family of 40-80 human and rodent G protein-coupled receptors expressed in subsets of TR cells of the tongue and palate epithelia.

According to Adler et al., the sweet, bitter and umami taste transduction is believed to be mediated by G protein-coupled receptor (GPCR) (seven transmembrane domain protein) signaling pathways. These cell surface receptors interact with tastants and initiate signaling cascades that culminate in neurotransmitter release. The researchers also mentioned that, following this interaction, afferent nerve fibers from cranial nerve ganglia relay signals via the thalamus to cortical centers, where information is processed and integrated. Thereafter, a series of publications followed about the identification of TRs for bitter, sweet and (again) umami modalities.[10-13]

In 2003, Zhang et al. studied the coding of sweet, bitter and umami tastes and found different receptor cells sharing similar signaling pathways.[11] The authors' findings can be summarized as follows: Two unrelated families of receptors (T1Rs and T2Rs) mediate responses to sweet, amino acids and bitter compounds. The researchers demonstrated that knockouts of TRPM5, a taste TRP ion channel, or PLCbeta2, a phospholipase C selectively expressed in taste tissue, abolish sweet, amino acid and bitter taste reception, but do not impact sour or salty tastes. Therefore, despite relying on different receptors, sweet, amino acid and bitter transduction converge on common signaling molecules.

Using PLCbeta2 taste-blind animals, a fundamental question in taste perception was examined: How are taste modalities encoded at the cellular level? Mice engineered to rescue PLCbeta2 function exclusively in bitter-receptor expressing cells respond normally to bitter tastants, but do not taste sweet or amino acid stimuli. Thus, bitter is encoded independently of sweet and amino acids, and TRs are not broadly tuned across these modalities.

In the same year, Zhao et al. reported on the receptors for mammalian sweet and umami taste.[12] They stated that sweet and umami (the taste of MSG) are the main attractive taste modalities in humans. T1Rs are candidate mammalian TRs that combine to assemble two heteromeric G protein-coupled receptor complexes: T1R1+3, an umami sensor, and T1R2+3, a sweet receptor.

They reported the behavioral and physiological characterization of T1R1, T1R2 and T1R3 knockout mice. They demonstrated that sweet and umami taste are strictly dependent of T1#-receptors, and showed that selective elimination of T1R-subunits differentially abolishes detection and perception of these two taste modalities. To examine the basis of sweet tastant recognition and coding, they engineered animals expressing either the human T1R2-receptor (hT1R2) or a modified opioid receptor (RASSL) in sweet cells. Expression of hT1R2 in mice generates animals with humanized sweet taste preferences, while expression of RASSL drives strong attraction to a synthetic opiate, demonstrating that sweet cells trigger behavioral outputs, but their tastant selectivity is determined by the nature of the receptors.

In T-3, the sodium glutamate taste threshold value for the umami quality is shown.

Geometric means of taste threshold values of different tastants in water **T-3**

Taste modality	Compound	No. of publications	Geometric mean of threshold values in mg/kg water
umami	sodium glutamate	28	120
sweet	sucrose	120	3,000
	glucose	21	3,880
	fructose	12	1,120
	maltose	6	4,450
	saccharine	17	5
bitter	quinine	16	1.6
	quinine.hydrochloride	43	2.0
	6-propyl-2-thiouracil	30	11
salty	sodium chloride	195	150
	ammonium chloride	16	100
sour	hydrochloric acid	48	20
	acetic acid	23	50
	citric acid	63	57
alkaline	sodium hydroxide	12	50
	potassium hydroxide	9	70

Bitter Taste

It is generally accepted that bitter taste detection functions as an important sensory input to warn against the ingestion of toxic and noxious substances.[13] Scientists at the University of California and the (US) National Institutes of Health carried out pioneering investigations about the receptors and coding logic for bitter taste.[5-13]

In 2000, Chandrashekar et al. published a study about a large family of receptors (T2Rs) functioning as bitter TRs. They summarized their findings as follows:

> Bitter taste perception provides animals with critical protection against ingestion of poisonous compounds. The characterization of a large family of putative mammalian TRs (T2Rs) is

reported. A heterologous expression system is used to show that specific T2Rs function as bitter TRs. A mouse T2R (mT2R-5) responded to the bitter tastant cycloheximide, and a human and mouse receptor (hT2R-4 and mT2R-8) responded to denatonium and 6n-propyl-2-thiouracil. Mice strains deficient in their ability to detect cycloheximide have amino acid substitutions in the mT2R-5 gene; these changes render the receptor significantly less responsive to cycloheximide. mT2R-5 was expressed in insect cells and demonstrated specific tastant-dependent activation of gustducin, a G protein implicated in bitter signaling. Because a single TR cell expresses a large repertoire of T2Rs, these findings provide a plausible explanation for the uniform bitter taste that is evoked by many structurally unrelated toxic compounds.

Also in 2000, Matsunami et al. reported the identification of a family of candidate TRs (the TRBs) that are members of the G protein-coupled receptor superfamily and are expressed specifically by TR cells.[5] A cluster of genes encoding human TRBs is located adjacent to a Prp gene locus, which in mice is linked tightly to the SOA genetic locus involved in detecting the bitter compound sucrose octaacetate. Another TRB gene is found on a human contig assigned to chromosome 5p15, the location of a genetic locus (PROP) that controls the detection of the bitter compounds 6-n-propyl-2-thiouracil (PROP) in humans.

Recently, Mueller et al. wrote that the sense of taste provides animals with valuable information about the nature and quality of food.[13] Tastant receptors (T2Rs) are a family of approximately 30 high-divergent G protein-coupled receptors (GPCRs) that are expressed selectively in the tongue and palate epithelium, and are implicated in bitter tasting. Using a combination of genetic, behavioral and physiological studies, the researchers demonstrated that T2R receptors are necessary and sufficient for the detection and perception of bitter compounds, showing that differences in T2Rs between species (human and mouse) can determine selectivity of bitter taste responses. In addition, Mueller et al. showed that mice engineered to express a bitter TR in "sweet cells" became strongly attracted to its cognate bitter tastants, whereas expression of the same receptor (or even a novel GPCR) in T2R-expressing cells resulted in mice that were averse to the respective compounds.

Taken together, these results illustrate the fundamental principle of bitter taste coding at the periphery: Dedicated cells act as broadly tuned bitter sensors that are wired to mediate behavioral aversion. T-3 displays the taste threshold values of some bitter tastants.

Sweet Taste

Hundreds of publications have appeared regarding compounds with sweet taste.[3] The preference

for sweet has been known since ancient times. This preference may be an evolutionary adaptation. For the maintenance of the species, e.g., to find calorie-rich food in nature, mammals need sweet-tasting compounds, such as sugars. The main representative of these sugars is sucrose, a so-called disaccharide consisting of two monosaccharides: glucose and fructose. The advantage of sucrose is that it is pure and sweet, and has no aftertaste. The consumption of too much sucrose, however, has severe disadvantages, such as obesity and dental caries. It must be noted, however, that sucrose's importance goes far beyond its role as a delicious sweetener. The material affects other properties of the end product (foodstuff or drink), such as viscosity, consistence, structure, freezing point, conservation (preservative) and odor.

The tasting unit (feature) responsible for sweetness is called a glucophore. The molecular structure of a glucophore interacts with the structure of a protein in a TR in a taste bud near the front of the tongue. The interaction of the glucophore molecule and the protein-TR takes place primarily via hydrogen bonds, but is also possible via van der Waals or Coulomb attractions. After this interaction, transduction occurs, and a signal is sent to the brain (see T-1).

A good sweetener should meet the following requirements:

- water-soluble
- stable in solution
- stable at low and high pH
- stable at cooking (boiling and frying) temperature
- no off taste or aftertaste

Atkins mentioned that there are many odd features of taste, and sweetness in particular.[2] For instance, a substance of unknown structure in a fruit known as agbayun (*Synsepalum dulcificum*) modifies the sweet receptor mechanism so that it will respond to hydrogen ions, which are normally the cause of sourness. Eating the fruit causes sour substances to taste sweet for about an hour.

Look under the umami section for the Zhao et al. studies regarding receptors for mammalian sweet taste.[11] T-3 contains taste threshold values of some sweeteners.

Fatty Taste

Mankind always has had a need and preference for fatty food. Consumption of fats is a necessity for the maintenance of the species. Every human being is familiar with the mouthfeel of fatty food. Klosse mentioned that the filming mouthfeeling of a fat or fatty product is important for the appreciation of a meal.[17] One may wonder whether there exists a specific TR for fats or fatty food.

In 2005, Laugerette et al. demonstrated that a protein called CD36 performed as a fatty TR on the tongues of rats and mice.[14] Said the authors: "Rats and mice exhibit a spontaneous attraction for lipids."

Such a behavior raises the possibility that an orosensory system is responsible for the detection of dietary lipids. The fatty acid transporter CD36 appears to be a plausible candidate for this function because it has a high affinity for long-chain fatty acids (LCFAs) and is found in lingual papillae in rats.

To explore this hypothesis further, experiments were conducted in rats and in wild-type and CD36-null mice. In mice, RT-PCR experiments with primers specific for candidate lipid-binding proteins revealed that only CD36 expression was restricted to lingual papillae, although absent from the palatal papillae. Immunostining studies showed a distribution of CD36 along the apical side of circumvallate taste cell buds. CD36 gene inactivation fully abolished the preference for LCFA-enriched solutions and solid diet observed in wild-type mice. Furthermore, in rats and wild-type mice with esophageal ligation, the deposition of unsaturated LSFAs onto the tongue led to a rapid and sustained rise in flux and protein content of pancreatobiliary secretions. These findings demonstrate that CD36 is involved in

oral LCFA detection and raise the possibility that an alteration in the lingual fat perception may be linked to feeding dysregulation.

Salty, Sour and Alkaline Tastes

The salty, sour and alkaline tastes are treated under one heading because the taste modalities are caused by strong polar ions (electrically charged atoms or atom groups), and their primary mechanism of perception probably differs from those for the aforementioned qualities. Adler et al. suggest that sour and salty tastants modulate TR cell function by direct effects on specialized membrane channels.

Salty Taste

It is common knowledge that sodium chloride is the most important representative of compounds with a salty taste. This salt makes food more tasteful. Up to 100 million metric tons sodium chloride are isolated every year from natural sources. Less than 10 percent of this amount is used for human consumption. The remaining 90-plus percent finds use in the chemical industry for the production of sodium hydroxide, sodium carbonate and hydrochloric acid.

Sodium chloride has found use throughout human history. In Roman times, the material was scarce and in so much demand that wages were paid with regimented weights of the material — a payment known as *salarium*, from which the name salt is derived.

Humans require about 1 g of sodium chloride daily for biological purposes. However, the average intake per person in, for example, the Netherlands, is more than 9 g. In the United Kingdom, this level reaches 11 g.[18] This overconsumption is due mainly to relatively high concentrations of sodium chloride in foods — for instance, in bread and prepared meat products. Excessive sodium chloride intake may lead to severe health problems, including high blood pressure. Studies have been conducted for the replacement of sodium chloride in food (see **Application of Recent Findings**).

In chemistry, the general name of a salt is reserved for compounds that are formed from an alkaline metallic hydroxide (metal kation) and an acid (anion). The salty-tasting sodium chloride can be formed from the alkaline-tasting sodium hydroxide and the sour-tasting hydrochloric acid. Although sodium chloride has a pure salty taste, not all salts have this quality. Many inorganic salts, such as magnesium salts, possess a bitter taste.

According to van der Wel, it is thought that, as a response to the stimulation of sodium chloride, sodium ions directly enter receptor cells through passive ungated channels in the apical membrane.[1] Amiloride, for instance, suppresses the taste of sodium and lithium salts, but not that of potassium salts. The polarization of taste cells in response to potassium chloride seems to be the result (at least in part) of an influx of potassium ions through the apical membrane. Changing of the phase-border-layer potentions can

contribute to the response for salts, as well as for other stimuli.

Adler et al. mentioned that electrophysiological studies suggest that salty and sour tastants modulate TR cell function by direct effect on specialized membrane channels.[9] Thus, it has been suggested that salty, sour and alkaline compounds can act directly on taste cells without the intervention of specific TRs.

Because many salts have bitter and even sweet strong off tastes and/or aftertastes, one may question whether the primary process of taste perception may have a combinatorial receptor code for the tastants.

T-3 displays the taste threshold values of several salts.

Sour Taste

According to van der Wel, the original function of the sour taste was not food enjoyment, but, rather, safety. Sour taste's purpose initially was to demonstrate the presence of undesired circumstances in the direct proximity of the animal. Almost all natural (plant) products are more or less acidic and, as a consequence, have a sour taste. Unripe fruits, however, are more acidic (lower pH) than ripe fruits, although their sourness is a good indication for the palatability of the nutrients.

Sourness is due to the presence of free hydrogen ions (H+), which are released by acids. The intensity of the sourness seems to be totally dependent on the concentration of these hydrogen ions. There exist acids in which the cation may stimulate one response (e.g., sour), while the anion stimulates another (e.g., sweet). Salicylic acid, for instance, is said to have a sweet taste.[2]

With some acids it is possible to make a (practically) neutral (pH = 7) solution by adding a large amount of a buffer salt. However, this solution would still taste sour. In solutions with a pH higher than 3.2, the concentration of the free protons (H+ ions) probably doesn't contribute to the sour taste as much as the concentration of the undissociated acid.

In general, it can be stated that the sourness of a solution not only depends on the concentration of the protons, but also on the undissociated acid. T-3 displays the taste threshold values of some acids for sour quality.

Alkaline Taste

As described previously, no one doubts that there exist specific TRs for sour or acidic taste modality. One may question whether there are TRs for the counterpart of the acidic quality — namely, an alkaline modality. It seems very probable that if certain taste cells can interact with protons (acidic), then there also exist those that are sensitive to hydroxyl ions (alkaline). During our studies on taste threshold values, we encountered some publications in which the term "alkaline taste" was used for sodium hydroxide and potassium hydroxide.[3] It should be noted that the modalities "sweet" and "bitter" also were assigned to the same products.

In December 2005, an unwanted experiment was conducted accidentally on elementary schools in Rotterdam, the Netherlands. Three hundred to 400 children consumed chocolate milk that was contaminated with <1 percent sodium hydroxide (a cleaning agent). Experts declared that the contaminated drinks caused a dirty chemical taste with a light burnt feeling in the throat. A minor number of children experienced some stomach complaints. Reports stated that the taste of sodium hydroxide was comparable to that of a concentrated solution of sodium carbonate.

In investigating the taste of sodium salts of higher fatty acids in nutrients, Paulet et al. found a soapy modality.[16]

T-3 features taste threshold values for sodium hydroxide and potassium hydroxide for an alkaline quality.

Pain Perception and Mouthfeel

The perception of pain and mouthfeel plays an important role in the appreciation of food and drink. Pain perception in the mouth may, for instance, occur by stimulation of the nerve endings of the trigeminus.

Atkins discussed the effects of pain stimulation in detail. He wrote:

> Hot, spicy and cool tastes are chemical stimulations of pain. There are two types of pain nerves. Class A nerves are slender fibers that carry signals rapidly (at about 20 meters per second); class C nerves are thicker and carry signals more slowly (at about 1 meter per second). Their signals are referred to as fast pain and slow pain, respectively. Fast pain is the response to injury and often is sharply localized. Slow pain often is a dull, aching sensation that is usually less sharply localized. Both types of nerve fibers enter the signal cord, together with nerves responsible for sensation of temperature; there, they stimulate neurons that lead to the brain, and their signals undergo some local processing. An important feature of pain nerves is the interaction of the two types in a gelatinous part of the spinal cord called the *substantia gelatinosa.* Signals arriving along the A fibers excite cells of the *substantia gelatinosa*, but those arriving along the C fibers inhibit them. The net effect can be to inhibit cells that are responsible for transmitting A and C signals to their processing center in the brain (the thalamus). Hence, there is a complex interplay between the signals arriving initially as fast and slow pain (a point that will be illustrated in what follows). Moreover, in response to pain signals, the brain can separate its own analgesics — the endorphins and encephalins. Both are polypeptides, with the endorphins having long chains and the encephalins having short chains, that affect the transmission of nerve signals, and both are mimicked by opiates. The pain receptors that initiate all this complex signaling are highly branched nerve endings themselves; they are not specific innervated pain receptors.
>
> There are, however, receptors that respond to thermal stimulation. They are essentially of two types — one of which responds to hot and the other to cold; the latter are more numerous by a factor of about 10. Their signals, like pain signals, are carried by class A and class C nerve fibers, ultimately to the thalamus, so that intense thermal stimulation can be interpreted as pain. Many of the spices used in curries and other foods stimulate pain-detecting nerve endings in the mouth (and elsewhere), but the relation between molecular structure and response is not known. "Noxious heat" (above 52 C) stimulates one receptor, moderate heat (42 C) and capsaicin stimulate another receptor, and coolness (below 22 C) and menthol stimulate a third receptor. The missing receptor for the range 22-42 C was identified only in 2002, and is found in the skin, on the tongue, and in brain and nerve tissue. It is speculated that such widespread occurrence of the receptor is related to its role in response to injury and inflammation.

Klosse, a famous restaurant keeper in the Netherlands, received his PhD degree at the University of Maastricht on the subject of an objective approach to the sense of taste and its subdivision in taste-styles.[17] He argued that the so-called primary tastes — sweet, sour, salty and bitter — play only a supporting role during cooking. Klosse stated that the real basic tastes are mouthfeel and taste richness. Mouthfeel is featured by two main aspects — namely, tight, or astringent, and filming. Mouthfeel can be subdivided into the terms warm, cold, hard, soft, vivid, fatty, dry, crisp, sharp, pungent, hot, sour, sweet and salty. Salty, sour, cold, crisp and dry are clear examples of the tight/astringent mouthfeel. At the same time, the aspects sweet, vivid and fatty are characterized by a filming mouthfeel. A filming mouthfeel imparts a relaxing effect in the mouth by leaving a thin layer.

Pungency of natural products in Scoville units[17] **T-4**

Natural products	Pungency, in Scoville units (x 1,000)
paprika	0.1
new Mexican peppers	0.5-1.0
Espanola peppers	1.0-1.5
ancho and pasilla peppers	1.0-2.0
cascabel peppers	1.0-2.5
jalapeño peppers	2.5-5.0
serrano peppers	5.0-15.0
cayenne and tabasco	30.0-50.0
chiltepín	50.0-100.0
Thai	100.0-350.0
habanero	200.0-300.0
homocapsaicin	800.0-900.0
nordihydrocapsaicin	900.0-1,000.0
capsaicin	16,000.0

Astringent and filming ingredients can be mixed together, as for instance in a salad dressing containing both vegetable oil and vinegar. Taste richness concerns the quantity of taste and intensity. Flavoring materials enhance taste richness. Herbs and spices, for instance, have a great influence on the taste richness of a prepared food. Moreover, taste richness is determined by cooking techniques, such as boiling, baking, frying and grilling. Klosse discussed seven taste styles and gave for each style nine recipes with accompanying wines. He devoted one chapter to recipes for pungent meals and afforded a list of naturals with their pungency in Scoville units (see T-4).

Behavioral Studies of Taste Perception

Recently, scientists at the American Academy of Pediatrics discovered that children with gene TAS2R38 strongly dislike bitter tastants and have a great preference for sweet.[19] An investigation with 143 children and mothers revealed that 60 percent of the mothers possessed this gene. Fifty percent of the mothers with the gene detected a bitter tastant in the lowest concentration. Children with the gene had a preference for stronger sucrose solutions, as well as sweeter cereals and drinks. Black children with the gene more frequently (76 percent) added sugar to their cereals before consumption than white children (43 percent) did. How disapproval (rejection) of bitter is connected with a preference for sweet is not clear.

Bitter and sweet preference: In November 2005, Djin Gie Liem obtained his PhD for a study about children's preference for the sour modality.[20] During a study at the Monell Chemical Senses Center in Philadelphia, he found that among 61 American children, one-third had a preference for extreme sour puddings, whereas all their mothers strongly disliked them. In studies with Dutch children, he also proved that children not only have a preference for sweet, but also for sour. He could not explain the differences by physiological features, but it seems that preference for sour may be related to the personality of the children.

Crossroads of the academic and the culinary: During a 2005 symposium, Dutch cooks and scientists from the University of Wageningen investigated orange taste in ice cream.[21] They demonstrated the preparation of orange ice cream in which the flavorings isolated from orange peel brought about a real taste explosion. The presenters declared that, with the study of the chemical and physical processes that occur in the kitchen, the University of Wageningen will contribute to a renovation of gastronomy and quality of life.

Corporate adaptation to regional taste variations: At the end of 2005, Moleman wrote an article entitled "Wal-Mart Accommodates to Chinese Taste." At the time, Wal-Mart (Bentonville, AR, United States), the biggest chain of supermarkets in the world, opened its 52nd location in Yuri, Yunnan, China. The firm has more than 4,000 supermarkets worldwide, with 1.6 million employees and 140 million clients. The company imports 70 percent of its raw materials (a value of more than $20 billion) from China, a figure which had increased 20 percent since 2004. The hypercenter in Shanghai was a very big department for fresh vegetables, meat and fish. The quality of the food at the firm's Chinese sites is oriented completely toward the Chinese sensibility. One encounters tender duck head, pig tongue and cow intestine in excess, as well as an impressive collection of tofu varieties. Moreover, for each middle-class Chinese table, the company offers the taste refiner *wei ching* (umami).

Fat-restricted diets: A recent publication of the Women's Health Initiative Dietary Modification stated that a reduction of daily fat intake is no guarantee for weight loss.[23] An investigation was carried out with almost 50,000 post-menopausal women, of whom 20,000 were placed on a diet with a 20 percent reduction in daily fat intake. After one year, the low-fat diet women showed an average weight loss of 2 kg. However, after five years, these women generally returned to their original weight. Among the complete group of 50,000, 20 percent of the women who ate less fat and more fiber lost the most weight after seven and a half years. The general conclusion was that average body weight throughout the years was dependent on the total daily intake of caloric energy and of the variation in food.

Because the overconsumption of saturated fats, sugar (sucrose) and salt (sodium chloride) is the main cause of human disease, it is clear that many future studies will examine ways to decrease and/or replace the consumption of these products.

Application of Recent Findings

One may rightly question how these cited findings can be applied to the flavor, food and beverage industries. To begin with, if it is possible to isolate genes that, for instance, encode the sweet, bitter, umami and fatty TRs, several possibilities become apparent. First, the genes (about 50) can be separated and multiplied. With each separated gene, the individual TR protein (T1Rs, T2Rs, mGluR4 and CD36) can be prepared and fixed on a suitable support, such as a synthetic membrane or chip. A light-emitting protein may be

added to the TRs in such a way that the complex fluoresces after light exposure if/when there is an interaction of the TR and tastant molecules. This "synthetic" biological system affords a method for measuring tasting properties in vitro.

Within such a system, the following investigations are possible:

- Making a library of all the different TRs (e.g., for sweet, bitter, umami and fatty) that interact with a known tastant (flavoring) at a certain concentration (patterns for thousands of different tasting molecules)
- Determining the active TRs within one taste quality for food or beverages (for instance, the activated TRs for the bitterness of coffee; quality control of raw materials)
- Finding activated sites in TRs for salty, sour and alkaline qualities (sodium chloride replacers)
- Testing the tasting quality of a new tastant molecule by comparing its activated TRs with those in the library (human subjective evaluation no longer is necessary)
- Confirming taste intensity by testing at various concentrations
- Finding the patterns of activated TRs in flavoring mixtures, food and beverages (to improve tasting qualities)

Moreover, studies will reveal activated sites in TRs for salty, sour and alkaline qualities (to produce sodium chloride replacers).

The future is now: Already, some US biotechnological companies, such as Linguagen and Senomyx, are carrying out experiments according to these routes. Food and beverage giants, such as Campbell's and The Coca-Cola Company, in addition to flavor and fragrance houses, such as Givaudan and Floridienne, have invested in these endeavors. In Belgium, Chemcom is also active in this area. At the same time, Unilever has interests in fat replacers, whereas Akzo-Nobel and Quest have been working together on new tastants for the (at least partial) replacement of human sodium chloride consumption.

References

1. H. van der Wel, *Relation Chemistry and Taste.* TNO Course Sensorial Investigation, Zeist, the Netherlands (1994).
2. P. Atkins, *Taste, smell and pain.* In: *Atkins Molecules.* Second Edn., pp 121-141, Cambridge University Press, Cambridge, UK (2003).
3. L.J. van Gemert, *Compilation of flavour threshold values in water and other media.* BACIS, 21/1272 GB Huizen, the Netherlands (2003).
4. Y.-H. Sugita, *Recent Developments in Umami Research.* In: *Developments in Food Flavours.* Edits., G.G. Birch and M.G. Lindley, pp 63-79, Elsevier Applied Science London and New York (1986).

5. H. Matsunami et al., *A family of candidate taste receptors in human and mouse.* Nature, **404**, 601 (2000).

6. M.A. Hoon et al., *Putative mammalian taste receptors: a class of taste-specific GPCRs with distinct topographic selectivity.* Cell, **96**, 541 (1999).

7. N. Chaudhari et al., *A metabiotropic glutamate receptor variant functions as a taste receptor.* Nature Neurosci., **3**, 113 (2000).

8. B. Lindemann, *Umami Taste Receptor Identified.* Press Release, Nature Neurosci., February (2000).

9. E. Adler et al., *A Novel Family of Mammalian Taste Receptors.* Cell, **100**, 693 (2000).

10. Y. Zhang et al., *Coding of Sweet, Bitter and Umami Tastes: Different Receptor Cells Sharing Similar Signaling Pathways.* Cell, **112**, 293 (2003).

11. G.Q. Zhao et al., *The Receptors for Mammalian Sweet and Umami Taste.* Cell, **115**, 255 (2003).

12. J. Chandrashekar et al., *T2Rs Function as Bitter Taste Receptors.* Cell, **100**, 703 (2000).

13. K.L. Mueller et al., *The receptors and coding logic for bitter taste.* Nature, **434**, 225 (2005).

14. F. Laugerette et al., *CD36 involvement in orosensory detection of dietary lipids, spontaneous fat preference and digestive secretations.* J. Clin. Invest., **115**, 3177 (2005).

15. NRC-Handelsblad, *Schoolmelk met NaOH*. December 15 (2005).

16. G. Paulet et al., *Le gout de savon dans les produits alimentaires: effet de la lipase du poivre blanc.* Rev. Franc. Corps. Gras., **21**, 611 (1974).

17. P. Klosse, *PhD Thesis Univ. Maastricht*. In: *Spelen Met Smaak.* Pp 13-18, Tirion Uitgevers BV, Baarn, the Netherlands (2005).

18. B. Scholtens, *Bitterzout.* de Volkskrant, May 21 (2005).

19. The American Academy of Pediatrics, *Children's Aversion Towards Bitter Taste with TAS2R38 Taste Gene.* Pediatrics, February (2005).

20. Djin Gie Liem, PhD, Thesis Univ. Wageningen, *Children's preference for sour taste.* Wageningen, the Netherlands, November (2005).

21. *Cooks and Scientists Searching for the Ultimate Taste of Orange.* Univ. Wageningen (*www.wur.nl*), Symposium with Cook & Chemist, December (2005).

22. H. Moleman, *Wal-Mart Accommodates to Chinese Taste.* De Volkskrant, December 31 (2005).

23. *Women's Health Initiative Dietary Modification*. J. Amer. Med. Assn., January (2006).

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