Novel Umami Ingredients: Umami Peptides and Their Taste

Yin Zhang, Chandrasekar Venkitasamy, Zhongli Pan, Wenlong Liu, and Liming Zhao

Abstract: Umami substances are very important for food seasoning and healthy eating. In addition to monosodium glutamate and some nucleotides, recent investigations have revealed that several peptides also exhibit umami taste. In recent years, 52 peptides have been reported to show umami taste, including 24 dipeptides, 16 tripeptides, 5 octapeptides, 2 pentapeptides, 2 hexapeptides, 1 tetrapeptide, 1 heptapeptide, and 1 undecapeptide. Twenty of these peptides have been examined for the present of umami taste. In this review, we have listed these umami peptides based on their category, source, taste, and threshold concentration. The evidence for peptides showing umami taste, the umami taste receptors on the human tongue, and the peptides whose umami taste is controversial are also discussed.

Keywords: hydrolysate, synthesis, peptides, protein, umami

Introduction

Umami taste has been widely accepted as the 5th basic form of taste, along with the other 4 basic tastes of sweet, sour, salty, and bitter. This acceptance has been mainly attributed to the identification of G protein–coupled receptors for glutamate such as mGluR4 (Chaudhari and others 2000) and the heteromeric T1R1+T1R3 receptor (Nelson and others 2002). Umami ingredients are very important for food seasoning and are widely used in food production. They also show many health benefits, including reducing fat deposition, weight gain, and plasma leptin levels in rats (Kondoh and Torii 2008; Nakamura and others 2008). Umami ingredients were found to regulate gastrointestinal functions (Nakamura and others 2008) and to decrease the risk of stroke and coronary heart disease in adults by reducing sodium intake in their diets (Yamaguchi 1998; Aburto and others 2013). These food-seasoning and health-improving functions of umami ingredients have provoked more investigations to find new umami substances and evaluate their taste properties (Kunishima and others 2000; Masic and Yeomans 2014).

Monosodium glutamate (MSG) was the 1st molecule reported to have umami taste (Ault 2004). Then, in 1967, ribonucleotides such as guanosine monophosphate (GMP) and inosine monophosphate (IMP) were found to have synergistic effects with MSG (Yamaguchi 1967; Zhang and others 2013). Later, succinic acid (Med. 1974), theanine, gallic acid, theogallin (Kaneko and others 2006), pyroglutamic acid (Buckholz and Scharpf 1994), N-glycosides (Schlichtherle-Cerny and others 2002), pyroglutamyl peptides (Amado and Schlichtherle-Cerny 2003), N-acetylglycine (Grigorov and others 2003), succinoyl amides of amino acids (Frerot and BENZI 2004), and glycopeptides (Iwasaki and others 2004) were all reported to have umami taste. Alapyridaine, which is a product of the Maillard reaction (Soldo and others 2003a), and morelid, which is found in Morel mushrooms (Rotzoll and others 2005), were also found to enhance umami taste (Ley and others 2006). In addition to these natural and synthesized umami compounds that have been proven to possess or enhance umami taste (Kondoh and Torii 2008; Nakamura and others 2008), recent investigations have demonstrated that a few peptide molecules produced from hydrolysates of fish protein, beef bouillon, or other foods, have umami taste, as do some synthesized peptides (Arai and others 1973; Tamura and others 1989b; Winkel and others 2008). However, umami peptides are widely questioned for their taste characteristics. Several researchers believe that umami peptides have umami taste, but others disagree. There is an ever-increasing demand for natural food products and ingredients (Winkel and others 2008). Umami peptides have also been found to be desirable natural ingredients, with a high demand for their full development and application in food products. This article provides a review of research carried out on umami peptides and their taste characteristics; umami taste receptors; and the disputes regarding the umami taste of umami peptides.

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Peptides Showing Umami Taste

Umami taste is called a meaty, broth-like, or savory taste, as it has been used to describe the taste of savory and meat broth foods (Lioe and others 2010; Coulier and others 2011). One of the earliest reports on umami-taste peptides was on the glutamyl umami oligopeptides (3 dipeptides and 1 tripeptide; Table 1), which were separated and purified from α-chymotrypsin-modified soybean protein hydrolysate (Arai and others 1972). Arai and others (1973) investigated the correlation between the chemical structures and taste characteristics of L-glutamyl oligopeptides and reported that the highly acidic (hydrophilic) L-glutamyl oligopeptides might have a umami taste that contributes to the favorable flavor of food protein hydrolysate. They thought that interactions of the cationic amino and anionic carboxyl groups induced by the 5-member L-glutamyl ring structure were the reason for the brothy taste. Fujimaki and others (1973) used 5 proteases (pepsin, rapidase, papain, pronase, and bioprase) to hydrolyze the protein concentrate of fish and found that the acidic oligopeptide fraction (molecular weight lower than 1000) tasted brothy and had an amicable after-taste. They isolated 4 dipeptides and tripeptides from the enzymatic hydrolysate that had a flavor resembling that of MSG (Table 1; Noguchi and others 1975). Yamasaki and

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Table 1–Peptides reported to have umami taste.

Type and number of peptides	Amino acid sequence of umami peptide	Source	Taste as reported (pH)	Reported threshold concentration of umami	Authors
24 Dipeptides	Asp-Ala	Soy sauce	Umami	–	Oka and Nagata (1974)
	Ala-Asp	Synthesized	Bitter > Umami	13 mM	Ohyama and others (1988)
	Ala-Glu	Synthesized	Umami (neutral)	1.5 mM	Ohyama and others (1988)
	Asp-Asp	Synthesized	Salty/umami (6.0)	4.79 mM	Tamura and others (1989a)
	Asp-Glu	Synthesized	Salty/umami(6.0)	1.25 mM	Tamura and others (1989)
	Asp-Leu	Synthesized	Umami (neutral)	2.5 mM	Ohyama and others (1988)
	Glu-Asp	Proteinase-modified soybean protein	Brothy	–	Arai and others (1972)
		Synthesized	Brothy (6.0)	200 mg%	Arai and others (1973)
		Fish protein hydrolysate	MSG-like	200 mg%	Noguchi and others (1975)
		Synthesized	Salty/umami (6.0)	3.14 mM	Tamura and others (1989)
	Glu-Glu	Proteinase-modified soybean protein	Brothy	–	Arai and others (1972)
		Synthesized	brothy (6.0)	1% solution	Arai and others (1973)
		Fish protein hydrolysate	MSG-like (6.0)	150 mg%	Noguchi and others (1975)
		Synthesized	Salty/umami(6.0)	2.73 mM	Tamura and others (1989)
		Synthesized	Umami	1% (g/mL)	Maehashi and others (1999)
	Glu-Leu	Synthesized	Umami	3 mM	Ohyama and others (1988)
	Glu-Lys	Synthesized	Umami (6.0)	3.12 mM	Tamura and others (1989)
	Glu-Orn	Synthesized	Umami/sour	3.12 mM	Tamura and others (1989)
	Glu-Ser	Proteinase-modified soybean protein	Brothy	–	Arai and others (1972)
		Synthesized	Weak brothy (6.0)	–	Arai and others (1973)
		Fish protein hydrolysate	MSG-like (6.0)	200 mg%	Noguchi and others (1975)
	Glu-Thr	Synthesized	Brothy taste	–	Arai and others (1973)
	Glu-Val	Synthesized	Umami/sweet	1% (g/mL)	Maehashi and others (1999)
	Gly-Asp	Synthesized	Umami	6 mM	Ohyama and others (1988)
	Gly-Glu	Synthesized	Umami > bitter	0.8 mM	Ohyama and others (1988)
	Leu-Glu	Synthesized	Umami > bitter	1.5 mM	Ohyama and others (1988)
	Lys-Gly·HCl	Synthesized	Salty/umami (6.0)	1.22 mM	Tamura and others (1989)
	Orn- Orn·2HCl	Synthesized	Umami	1.5 mM	Tamura and others (1989)
	Orn-Ala·HCl	Synthesized	Salty/Umami	1.25 mM	Tamura and others (1989)
	pGlu-Pro	Deamidated wheat gluten hydrolysate	MSG-like	–	Schlichtherle-Cerny and Amadò (2002)
	Thr-Glu	Fish protein hydrolysate	MSG-like	300 mg%	Noguchi and others (1975)
	Val-Asp	Synthesized	Bitter>umami	25 mM	Ohyama and others (1988)
	Val-Glu	Synthesized	Umami>Bitter	1.5 mM	Ohyama and others (1988)
16 tripeptides	Ala-Asp-Ala	Synthesized	Umami>Bitter	3 mM	Ohyama and others (1988)
	Ala-Glu-Ala	Synthesized	Umami (neutral)	0.8 mM	Ohyama, et al. (1988)
	Asp-Glu-Ser	Fish protein hydrolysate	MSG-like	300 mg%	Noguchi and others (1975)
	Glu-Asp-Glu	Fish protein hydrolysate	MSG-like	300 mg%	Noguchi and others (1975)
	Glu-Gln-Glu	Fish protein hydrolysate	MSG-like	200 mg%	Noguchi and others (1975)
	Glu-Glu-Leu	Synthesized	Umami	–	Frerot and Escher (1998)
	Glu-Gly-Ser	Proteinase-modified soybean protein	brothy	–	Arai and others (1972)
		Fish protein hydrolysate	MSG-like(neutral)	200 mg%	Noguchi and others (1975)
	Gly-Asp-Gly	Synthesized	Umami(neutral)	1.5 mM	Ohyama and others (1988)
	Gly-Glu-Gly	Synthesized	Umami = Bitter	1.5 mM	Ohyama and others (1988)
	Leu-Glu-Glu	Synthesized	Umami	–	Frerot and Escher (1998)
	pGlu-Pro-Gln	Deamidated wheat gluten hydrolysate	MSG-like	–	Schlichtherle-Cerny and Amadò (2002)
	pGlu-Pro-Glu	Deamidated wheat gluten hydrolysate	MSG-like	–	Schlichtherle-Cerny and Amadò (2002)
	pGlu-Pro-Ser	Deamidated wheat gluten hydrolysate	MSG-like	–	Schlichtherle-Cerny and Amadò (2002)
	Ser-Glu-Glu	Fish protein hydrolysate	MSG-like	200 mg%	Noguchi and others (1975)
	Val-Asp-Val	Synthesized	Umami	13 mM	Ohyama and others (1988)
	Val-Glu-Val	Synthesized	Umami (neutral)	1.5 mM	Ohyama and others (1988)

(*Continued*)

Table 1–Continued.

Type and number of peptides	Amino acid sequence of umami peptide	Source	Taste as reported (pH)	Reported threshold concentration of umami	Authors
1 Tetrapeptide	Glu-Ser-Leu-Ala	Synthesized	Sour > astringent > umami > bitter	–	Yamasaki and Maekawa (1980)
2 Pentapeptides	Glu-Glu-Ser-Leu-Ala	Synthesized	Sour > astringent > umami > bitter	–	Yamasaki and Maekawa (1980)
	Glu-Glu-Asp-Gly-Lys	Synthesized	Sour/umami /sweet	1.25 mM	Nakata and others (1995)
2 Hexapeptides	Asp-Glu-Glu-Ser-Leu-Ala	Synthesized	Sour > astringent > umami > sweet > bitter	–	Yamasaki and Maekawa (1980)
	Cys-Cys-Asn-Lys-Ser-Val	Jinhua hams	Umami	–	Dang and others (2014)
1 Heptapeptide	Ala-His-Ser-Val-Arg-Phe-Tyr	Parma hams	Umami	–	Dang and others (2014)
5 Octapeptides	Lys-Gly-Asp-Glu-Glu-Ser-Leu-Ala	The gravy of beef meat	Delicious taste	–	Yamasaki and Maekawa (1978)
		Synthesized	Umami, sour, sweet	–	Yamasaki and Maekawa (1980)
		Synthesized	Umami/sour	1.41 mM	Tamura and others (1989)
	Lys-Gly-Ser-Leu-Ala-Asp-Glu-Glu	Synthesized	Sour/umami/sweet	0.78 mM	Nakata and others (1995)
	Ser-Leu-Ala-Asp-Glu-Glu-Lys-Gly	Synthesized	Umami/sour	1.25 mM	Nakata and others (1995)
	Ser-Leu-Ala-Lys-Gly-Asp-Glu-Glu	Synthesized	Sour/umami	1.50 mM	Nakata and others (1995)
	Ser-Ser-Arg-Asn-Glu-Gln-Ser-Arg	Peanut hydrolysate	Umami	–	Su and others (2012)
1 Undecapeptide	Glu-Gly-Ser-Glu-Ala-Pro-Asp-Gly-Ser-Ser-Arg	Peanut hydrolysate	Umami	–	Su and others (2012)

"–", not reported.

Maekawa (1978) isolated H-Lys-Gly-Asp-Glu-Glu-Ser-Leu-Ala-OH from the gravy of papain-treated beef meat (beef umami peptide, BMP). When BMP was reported, there were many arguments about its taste, and no new findings on umami peptides or peptides contributing to the umami taste of hydrolysate were published for the next several years. Twenty-four years after BMP was 1st reported, Schlichtherle-Cerny and Amadò (2002) found 4 MSG-like pyroglutamyl peptides from flavourzyme-hydrolyzed deamidated wheat gluten. Winkel and others (2008) studied the structure, taste threshold level, and solubility of these proglutamyl peptides and opined that binding of the GMP/IMP or glutamate to an umami receptor might be the reason for the umami taste of these pyroglutamyl peptides. Recently, Rhyu and Kim (2011) found that low molecular weight acidic peptides (F-IV; 1000> MWP500) were the component compounds that contributed to the umami taste of doenjang water extract. Su and others (2012) found 2 novel umami peptides, an octapeptide and an undecapeptide, from peanut hydrolysate. Bagnasco and others (2013) reported that medium-to-small size polypeptides contributed to the umami taste of hydrolysate of rice middlings. Dang and others (2014) isolated 2 umami peptides from water-soluble extractions of 2 kind of hams (Table 1).

Table 1 enumerates a total of 52 peptides that were reported to show umami taste, along with their category, source, taste, and threshold concentration. These 52 peptides include 24 dipeptides, 16 tripeptides, 5 octapeptides, 2 pentapeptides, 2 hexapeptides 1 tetrapeptide, 1 heptapeptide, and 1 undecapeptide. Comparison of the taste of the synthesized and naturally formed dipeptides and tripeptides in Table 1, such as Glu-Ser, Glu-Asp, Glu-Glu, and Glu-Gly-Ser, shows that both dipeptides and tripeptides have similar tastes. From Table 1, the threshold concentration of MSG is 1.5 mM (Ohyama and others 1988; Soldo and others 2003b), which shows that the umami taste of most dipeptides and tripeptides is weaker than that of MSG, but the umami taste of Gly-Glu (0.8 mM) and Ala-Glu-Ala (0.8 mM) is stronger than that of MSG. The tastes of tetrapeptides, pentapeptides, hexapeptides, and heptapeptides were found to be different. The synthesized hexapeptides and heptapeptides showed weaker umami taste than the naturally formed hexapeptides and heptapeptides. The naturally formed octapeptides showed umami taste, but the synthesized octapeptides showed not only umami taste but also sour and sweet tastes.

Comparing the taste of all naturally formed and synthesized peptides in Table 1, it can be found that the peptides from hydrolysates showed umami taste, but their tastes changed after they were synthesized. This tendency became more obvious as the size of the umami peptide increased. For all reported umami peptides, taste confirmation of most of the naturally formed umami peptides was performed using the synthesized peptide. There is a high possibility that this practice of using synthesized peptides to confirm the taste of naturally formed peptides might be the cause of many disputes about the taste of umami peptides.

Disputes about the Taste of Umami Peptides

There are 20 peptides whose tastes are in controversy, including 14 dipeptides, 5 tripeptides, and 1 octapeptide (Table 3). Some peptides were reported to show umami taste when they were separated from hydrolysate but became controversial when the peptide was synthesized to confirm the taste. In 1978, Yamasaki and Maekawa (1978) stated that BMP had umami potency that was higher than glutamate itself. Later, they synthesized BMP and compared it with isolated BMP, finding that the taste of the synthesized BMP was savory, sour, and sweet even though the synthesized and isolated BMPs were identical in many aspects (Yamasaki and Maekawa 1980). Both Tamura and others (1989a) and Spanier and others (1995) synthesized BMP, investigated its taste and found that BMP tasted umami, but Tamura and others (1989a) did not perceive the sweet taste of BMP. However, van

Wassenaar and others (1995) did not agree with the findings of Tamura and others (1989a), and they experimentally claimed that BMP had no savory taste. They synthesized BMP and characterized it. BMP was tasted by a trained flavor panel, and it was found that the synthesized BMP and a few peptide fragments did not have any taste, umami, or otherwise. van Wassenaar and others (1995) opined that impurities in the synthesized BMP might have caused disturbance in the taste evaluation of the BMP synthesized by Tamura and others (1989a) and Spanier and others (1995). They speculated that the impurities might have originated from side reactions, racemization, or truncation of sequences (van Wassenaar and others 1995). van den Oord and van Wassenaar (1997) re-examined 12 dipeptides and 4 tripeptides that Tamura and others (1989a), Arai and others (1973), Ohyama and others (1988), and Noguchi and others (1975) reported as having umami or savory tastes. They analyzed the taste of 16 peptides at pH 4.0 and 6.0, with or without 0.6% sodium chloride, and discovered that not any of the peptides had a distinct umami taste, even at concentrations much higher than the reported thresholds. To test possible synergy between the peptides and ribonucleotides, van den Oord and van Wassenaar (1997) mixed 5.4 mM Glu-Glu at pH 6.0 with 0.6 mM IMP and reported that the taste of the mixture was perceived to be the same as that of IMP alone under the same conditions. However, Maehashi and others (1999) performed similar experiments and found that there was an enhancement of taste between 1% Glu-Glu solution and 0.02% IMP. van den Oord and van Wassenaar (1997) attributed the discrepancy between their results on the taste of peptides and those of other researchers to the following 2 reasons. (1) The discrepancy might be caused by the presence of bitter peptides and derivatives of amino acids. These chemicals might have influenced the taste evaluation. A similar problem has reported when evaluating the salty taste of ornithyl peptides (Tada and others 1984; Tuong and Philippossian 1987). (2) The discrepancy might have originated from the actual tasting procedures and cultural differences of the taste panelists. However, they concluded that the actual tasting procedures and cultural differences had little influence on umami taste analysis by comparing the perception difference of umami taste between panelists of American and Japanese, and between panelists of Dutch and Japanese.

In our opinion, taste disputes might be caused by the following 4 other factors. The 1st reason is that the method of preparation of umami peptides might influence the taste analysis of the peptides. The investigation of Maehashi and others (1999) is taken as an example; they reexamined the taste of 11 umami peptides obtained from hydrolysate. They synthesized the 11 umami peptides and found that few showed an independent umami taste. The second reason might be that the isomeric structural differences of the peptides might also have influenced their flavor properties. For example, MSG exists in 2 forms, namely, D and L. The L form is the naturally occurring form, and only the L form possesses flavor activity. Similarly, there are 3 possible isomeric forms of nucleotides, namely, 2′, 3′, and 5′, and only 5′ nucleotides showed umami enhancing effect (Maga and Yamaguchi 1983). The third reason could be that differences in the spatial structure of the umami peptides from hydrolysate and synthesized ones might have disturbed the taste analysis. Figure 1 shows the spatial structures of the natural BMP and BMP with one D-form amino acid. It demonstrates that if one D-form amino acid is used during the synthesis of BMP, it will result in an obvious difference in its spatial structure. According to an umami receptor investigation (Chaudhari and others 2000; Nelson and others 2002), the spatial structure of an umami substance is a key to the recognition of umami taste. Therefore, the spatial structural changes resulting from the isomeric forms of amino acids during the synthesis of a peptide may influence the umami taste of the peptide. The 4th reason might be that the interactions of umami peptides with other compounds might have disturbed the proper assessment of their taste.

Interactions between Umami Peptides and Other Compounds

The taste interactions of newly found umami peptides and other flavor compounds are characterized as shown in Table 2. Recent investigations have demonstrated that there are 3 types of interactions of umami peptides, the interactions of peptide with peptide, peptide with nucleotide, and peptide with cation.

Tamura and others (1989a) examined the taste of a mixture containing N-terminal dipeptide (Lys-Gly), acidic tripeptide (Asp-Glu-Glu), C-terminal tripeptide (Ser-Leu-Ala), and salty dipeptide (Orn-β-Ala). They found that all the combinations produced an umami taste with the same character and almost the same strength as BMP. According to the sensory analysis results of Tamura and others (1989a), the tastes of Lys-Gly, Ser-Leu-Ala, Asp-Glu-Glu, and Orn-β-Ala are umami, sour, bitter, and bitter/sweet, respectively. The taste of the mixture was similar to the umami taste of BMP, indicating that there were interactions that enhanced, suppressed or masked taste, as well as synergistic interactions that affected taste.

Maehashi and others (1999) found that one synthesized peptide (Glu-Val) and 5 synthesized tripeptides (Ala-Asp-Glu, Ala-Glu-Asp, Asp-Glu-Glu, Ser-Pro-Glu, and Glu-Glu-Asn) showed umami taste when they were mixed with 0.2% IMP. The taste of peptide mixtures (Glu-Glu+Glu-Val+Asp-Glu-Glu+Glu-Glu-Asn and Asp-Glu-Ser+Glu-Glu+Asp-Glu-Glu) combined with 0.02% IMP also showed umami taste. Among these peptides, Glu-Glu, Glu-Val and Asp-Glu-Ser were found to elicit weak umami taste (Noguchi and others 1975), but their tastes were enhanced when they were mixed with IMP. Other di- or tripeptides did not show umami taste on their own, but they showed umami taste when they were mixed with 0.02% IMP. These results indicated that there are complicated interactions between IMP and peptides.

Nakata and others (1995) investigated the interactions of acidic peptides with Na^+ and K^+ and found that as pH levels increased to 6 using NaOH and KOH, the sodium salts of the acidic dipeptides showed both meaty and salty tastes. The potassium salts of each peptide showed a blurred taste that could not be categorized as umami or salty. The sensory analysis of the salts of acidic peptides suggested that the sequence of Glu and Asp in the peptide might be a key factor establishing salty and umami tastes.

Winkel and others (2008) compared the threshold limit values of the taste of MSG, GMP, lactoyl GMP, and acetyl GMP in water, sodium chloride solutions, and model broths. They found that the taste threshold value of MSG in water (5 ppm) > GMP in 0.5% NaCl and 0.05% MSG solution (0.5 ppm) > lactoyl GMP in bouillon (0.03 ppm) > acetyl GMP in bouillon (0.01 ppm). These results implied that the media used to dissolve the umami peptide might also have affected their taste assessment.

The results of taste evaluation of peptides are impacted by other peptides, nucleotides, and cations, and possibly by the dissolved media. These substances might disturb the accurate evaluation of umami peptides. The interactions of umami peptides with sour,

sweet, or bitter substances and the dissolved media should be further investigated. However, only limited investigations have been performed in recent years on these aspects. The possible reasons might include (1) controversy on the taste of umami peptides, preventing more detailed investigations on the interactions of umami peptides with other taste substances; and (2) umami peptides are zwitterionic, which makes the interactions between peptides and other flavor substances too complex to differentiate the taste characteristics. To further prove the existence of umami taste and prevent disturbance caused by other factors during umami taste evaluation, recent studies have focused on umami receptors.

Umami Receptors

Taste plays an important role in assessing the nutritional value of food and prevents the absorption of toxic substances (Chandrashekar and others 2006). Taste receptor cells are gathered into taste buds. Sweet, bitter, sour, salty, and umami ingredients stimulate the taste buds and are recognized by different cells containing specialized receptors. The obtained stimulating signals will be transformed into neural signals. Thus, the taste quality of taste ingredients will be felt (Chandrashekar and others 2006). Because umami taste was established as one of the 5 basic tastes, several discoveries of umami receptors in the taste buds have been reported (Uneyama and others 2009).

The 1st umami receptor, called taste-metabotropic glutamate 4 (mGluR4), was discovered in 2000 (Chaudhari and others 2000). Taste-mGluR4 is an unusual dimeric G protein–coupled receptor (GPCR; Kunishima and others 2000), and a truncated version of the famous glutamate receptor mGluR4. The 2nd umami receptor, T1R1+T1R3, was found in 2002 (Li and others 2002; Nelson and others 2002), and the 3rd, an unusual mGlu receptor, which is relevant to the brain glutamate receptor mGluR1, was found in 2005 (San Gabriel and others 2005). Among these receptors, T1R1+T1R3 is broadly considered as the major receptor for umami stimuli (Behrens and others 2011). The umami receptor T1R1+T1R3 is special in that it belongs to the class C GPCR family of proteins and has 7 transmembrane sections (Temussi 2009). Most of the class C GPCRs are homodimers, but the umami receptor T1R1+T1R3 is a heterodimer (Nelson and others 2002). The typical model of the umami receptor T1R1+T1R3 was reported by Temussi (2012) and Chandrashekar and others (2006). The monomer of T1R1 is considered critical for sensing umami taste (Mouritsen and Khandelia 2012). It makes up of an extracellular Venus flytrap domain (VFTD). The VFTD was found as the ligand-binding site within homologous proteins such as mGluRs (Kunishima and others 2000). In mGluRs, 2 lobes of the VFTD could keep open or close together with the conformations of the protein (Kunishima and others 2000; Tsuchiya and others 2002; Ahmed and others 2007; Muto and others 2007). Taking Glu and 5'-ribonucleotides as examples, Glu stabilizes the closed conformation (Mouritsen and Khandelia 2012), and this makes Glu have umami taste. IMP and GMP bind to the outer garment of the VFTD and markedly strengthen the response of the mGluRs to glutamate (Zhang and others 2008). Therefore, both of them intensify the taste of Glu.

The umami taste of Asp-Glu-Ser was doubted by Maehashi and others (1999), and the umami tastes of Glu-Asp, Glu-Glu, and Glu-Ser were questioned by van den Oord and van Wassenaar (1997). However, Kim and others (2015) presented 5 umami peptides (Glu-Asp, Glu-Glu, Glu-Ser, Asp-Glu-Ser, and Glu-Gly-Ser) with a bitter substance (salicin) in a Ca^{2+}-flux signaling assay. They found that these umami peptides markedly reduced the salicin-induced intracellular calcium influx with time increase. They reported that the results provided evidence to prove that umami peptides restrain bitter taste by bitter taste receptor(s).

A few recent studies have suggested that other receptors might also be participated in umami taste sensation. Damak and others (2003) reported that T1R3-knockout mice retained the taste response to monosodium glutamate. Maruyama and others (2006) found that taste buds lacking T1R3 mice still showed markedly

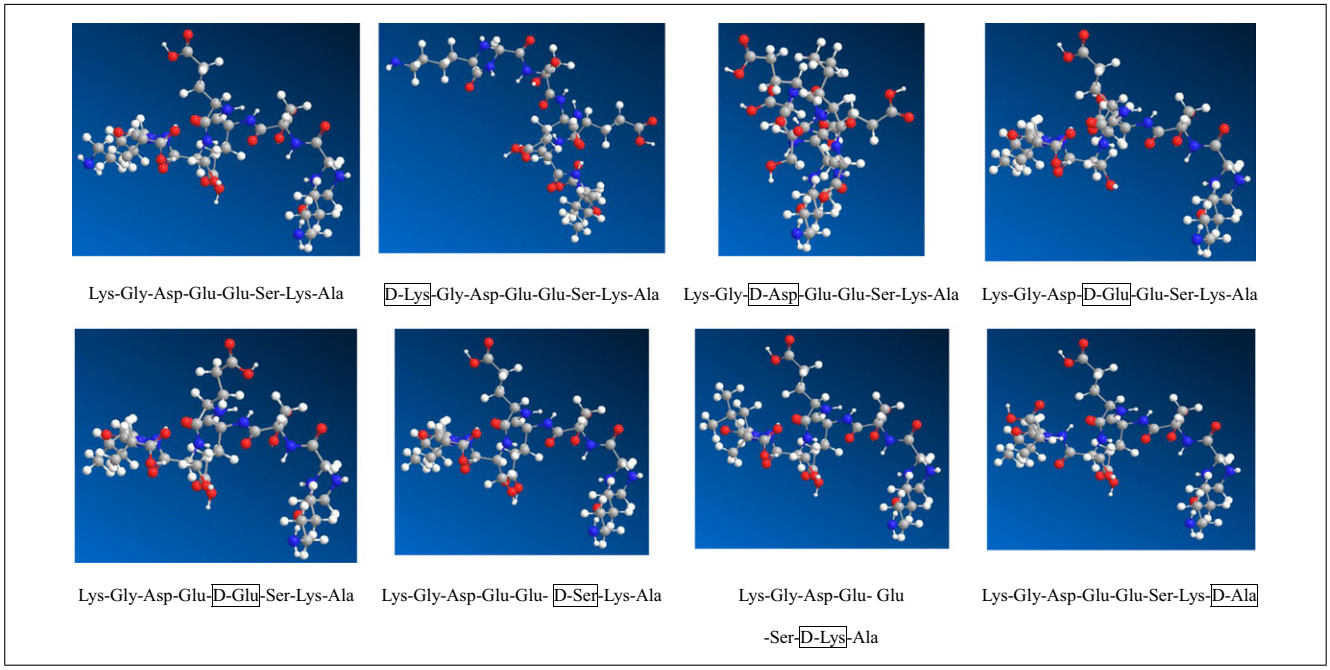

Figure 1–Spatial structures of natural BMP and BMP with one D-form amino acid.

Table 2–Peptides that show umami taste when mixed with other ingredients.

Interaction category	Peptide and interaction ingredients	Flavor	Threshold concentration reported (mM)	Author
Peptide with peptide	Lys-Gly + Asp-Glu-Glu + Ser-Leu-Ala	Umami/sour	1.41	Tamura and others (1989a)
	Orn-β-Ala + Asp-Glu-Glu + Ser-Leu-Ala	Umami/sour	1.41	Tamura and others (1989)
	Lys-Glu + Glu-Glu + Ser-Leu-Ala	Umami/sour	0.94	Tamura and others (1989)
Peptide with nucleotide	0.5% Glu-Glu + 0.02% IMP	umami/salty/sweet	–	Maehashi and others (1999)
	0.5% Glu-Val + 0.02% IMP	Umami/sour	–	Maehashi and others (1999)
	0.5% Ala-Asp-Glu + 0.02% IMP	Umami/bitter	–	Maehashi and others (1999)
	0.5% Ala-Glu-Asp + 0.02% IMP	Umami/sour	–	Maehashi and others (1999)
	0.5% Asp-Glu-Glu + 0.02% IMP	Umami/salty	–	Maehashi and others (1999)
	0.5% Ser-Pro-Glu + 0.02% IMP	Umami/bitter/salty	–	Maehashi and others (1999)
	0.5% Glu-Glu + 0.5% Glu-Val + 0.5% Asp-Glu-Glu + 0.5% Glu-Glu-Asn + 0.02% IMP	Umami/sour/salty	–	Maehashi and others (1999)
	0.5% Asp-Glu-Ser + 0.5% Glu-Glu + 0.5% Asp-Glu-Glu + 0.02% IMP	Sour/umami/bitter	–	Maehashi and others (1999)
Peptide salt	Asp-Asp + Na^+	Salty/umami	3.33	Nakata and others (1995)
	Asp-Asp + K^+	Indistinct umami	3.24	Nakata and others (1995)
	Asp-Glu + Na^+	Umami/salty	3.32	Nakata and others (1995)
	Asp-Glu + K^+	Indistinct umami	3.72	Nakata and others (1995)
	Glu-Asp + Na^+	Salty/umami	1.74	Nakata and others (1995)
	Glu-Asp + K^+	Indistinct umami	1.71	Nakata and others (1995)
	Glu-Glu + Na^+	Umami/salty	2.22	Nakata and others (1995)
	Glu-Glu+K^+	Indistinct umami	3.62	Nakata and others (1995)
	Asp-Asp-Asp + Na^+	Salty/umami	3.23	Nakata and others (1995)
	Asp-Asp-Glu+Na^+	Umami/salty	2.06	Nakata and others (1995)
	Asp-Glu-Asp + Na^+	Umami/salty	2.68	Nakata and others (1995)
	Glu-Asp-Asp + Na^+	Salty/umami	3.23	Nakata and others (1995)
	Asp-Glu-Glu + Na^+	Umami/salty	2.09	Nakata and others (1995)
	Glu-Asp-Glu + Na^+	Salty/umami	3.09	Nakata and others (1995)
	Glu-Glu-Asp + Na^+	Umami/salty	3.47	Nakata and others (1995)
	Glu-Glu-Glu + Na^+	Umami/salty	2.09	Nakata and others (1995)
Peptide with other taste ingredients	Lys-Gly-Asp-Glu-Glu-Ser-Leu-Ala + MSG	Umami increased	–	Wang and others (1996)
	Lys-Gly-Asp-Glu-Glu-Ser-Leu-Ala + NaCl	Umami increased	–	Wang and others (1996)

[a]–", not reported.

glutamate-evoked Ca^{2+} responses. Single-unit recordings on taste sensory neurons indicated that umami taste responses did not need T1R3-containing receptors (Yoshida and others 2009). The receptor type GPR92 is activated by peptide hydrolysates and free amino acids (Choi and others 2007a, 2007b), and it was expressed in enteroendocrine cells of the gastric mucosa and in G cells, which secreted gastrin upon stimulus with protein hydrolysate (Haid and others 2012). These results indicated that umami cells might react to both amino acids and peptides in protein hydrolysates (Haid and others 2013). Similar to the umami receptor T1R1+T1R3, the sweet receptor T1R2+T1R3 is also a heterodimer (Chandrashekar and others 2001; Li and others 2002). T1R3 is a common component of both the T1R1+T1R3 and the T1R2+T1R3. However, the sweet receptor T1R2+T1R3 recognizes not only sweet amino acids (glycine and D-tryptophan) but also a sweet dipeptide (aspartame) and sweet proteins such as monellin, brazzein, and thaumatin (Hatada and others 1985; Li and others 2002; Temussi 2002). The large cavity on the T1R3 promoter and the molecular structure of the sweet protein are the key factors for the recognition of the sweet protein (Temussi 2002, 2011). Molecular mechanics demonstrates that T1R1+T1R3 binds points in a comparatively mini binding hole (Zhang and others 2008). These investigations of umami and sweet receptors suggested the existence of umami peptides and that their spatial structure might greatly influence their flavor. Therefore, it will be worth further investigating the interactions of peptide spatial structures with umami receptors and the taste characteristics of these peptides.

Based on the results of the reported investigations, it is suggested that more research on umami peptides and their tastes should be required, focusing on (1) the preparation of natural peptides using peptide gene expression methods to investigate differences in taste with synthesized peptides; (2) the spatial structure of synthesized and naturally produced umami peptides should be characterized in their taste confirmation, as changes in the spatial structure might influence the interactions of peptides with umami receptors; (3) the clarification of the interactions of umami peptides themselves or with other taste ingredients; and (4) the ability to increase the purity of the synthesized peptides, as the maximum purity of synthesized peptides currently reported was >98%.

Table 3–Controversial umami peptides.

Type and number of peptides	Peptide	Taste as reported (pH)	Reference reported	Taste (pH) perceived in present work	Authors
14 Dipeptides	Ala-Glu	Umami (neutral)	Ohyama and others (1988)	Not umami, no other taste	van den Oord and van Wassenaar (1997)
	Asp-Ala	Umami	Oka and Nagata (1974)	Tasteless	Maehashi and others (1999)
	Asp-Asp	Salty/umami (6.0)	Tamura and others (1989a)	Not umami, no other taste at either level	van den Oord and van Wassenaar (1997)
	Asp-Glu	Salty/umami (6.0)	Tamura and others (1989)	Not umami, no other taste at either level	van den Oord and van Wassenaar (1997)
	Asp-Glu	Salty/umami (6.0)	Nakata and others (1995)	Not umami, no other taste at either level	van den Oord and van Wassenaar (1997)
	Asp-Leu	Umami (neutral)	Ohyama and others (1988)	Not umami, no other taste	van den Oord and van Wassenaar (1997)
	Asp-Leu	Umami (neutral)	Ohyama and others (1988)	Bitter(6.0)	Noguchi and others (1975)
	Glu-Asp	Brothy(6.0)	Arai and others (1973)	Not umami, no other taste at either level	van den Oord and van Wassenaar (1997)
		MSG-like (neutral)	Noguchi and others (1975)		
		Salty/umami(6.0)	Tamura and others (1989)		
		Salty/umami(6.0)	Nakata and others (1995)		
	Glu-Glu	Brothy(6.0)	Arai and others (1973)	Not umami, slightly bitter at any level	van den Oord and van Wassenaar (1997)
		MSG-like (6.0)	Noguchi and others (1975)		
		Salty/umami(6.0)	Tamura and others (1989)		
	Glu-Leu	Umami (neutral)	Ohyama and others (1988)	Not umami, no other taste at either level	van den Oord and van Wassenaar (1997)
		Umami (neutral)	Ohyama and others (1988)	bitter (6.0)	Arai and others (1973)
	Glu-Lys	Umami (6.0)	Tamura and others (1989)	Not umami, no other taste at any level	van den Oord and van Wassenaar (1997)
	Glu-Ser	Weak brothy (6.0)	Arai and others (1973)	Not umami, no other taste	van den Oord and van Wassenaar (1997)
		MSG-like (6.0)	Noguchi and others (1975)		
	Glu-Val	Umami/sweet	Maehashi and others (1999)	flat	Arai and others 1973
	Lys-Gly	Salty/umami (6.0)	Tamura and others (1989)	Not umami, slightly bitter at any level	van den Oord and van Wassenaar (1997)
5 Tripeptides	Ala-Glu-Ala	Umami (neutral)	Ohyama and others (1988)	Not umami, no other taste at any level	van den Oord and van Wassenaar (1997)
	Asp-Glu-Ser	MSG-like	Noguchi and others (1975)	Sour, salty	Maehashi and others (1999)
	Glu-Glu-Glu	MSG-like (6.0)	Noguchi and others (1975)	Not umami, no other taste at either level	van den Oord and van Wassenaar (1997)
	Gly-Asp-Gly	Umami (neutral)	Ohyama and others (1988)	Not umami, no other taste at any level	van den Oord and van Wassenaar (1997)
	Val-Glu-Val	Umami (neutral)	Ohyama and others (1988)	Not umami, no other taste at any level	van den Oord and van Wassenaar (1997)
1 Octapeptide	Lys-Gly-Asp-Glu-Glu-Ser-Leu-Ala	Umami, sour, sweet	Yamasaki and Maekawa (1978); Yamasaki and Maekawa (1980); Tamura and others (1989)	Not umami or other taste	van Wassenaar and others (1995),

Conclusions

There are 52 peptides that have been reported to show umami taste, but 20 of them have been questioned. New umami peptides and peptides contributing to the umami taste of hydrolysate have been continuously reported. Investigation of umami receptors has suggested that umami peptides might show umami taste. Therefore, more investigation should be conducted to prove the taste of umami peptides. In particular, new methods should be adopted to produce the natural peptides and then confirm their taste. This will be beneficial to finding new umami substances and supplying sound materials for the investigation of umami peptide receptors. It will also be useful to investigate the flavor interactions with taste receptor responses and other physiological responses.

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