Amino Acids (2012) 43:2349–2358
DOI 10.1007/s00726-012-1315-x

ORIGINAL ARTICLE

Gustatory sensation of L- and D-amino acids in humans

Misako Kawai · Yuki Sekine-Hayakawa · Atsushi Okiyama · Yuzo Ninomiya

Received: 17 December 2011 / Accepted: 24 April 2012 / Published online: 16 May 2012

Abstract Amino acids are known to elicit complex taste, but most human psychophysical studies on the taste of amino acids have focused on a single basic taste, such as umami (savory) taste, sweetness, or bitterness. In this study, we addressed the potential relationship between the structure and the taste properties of amino acids by measuring the human gustatory intensity and quality in response to aqueous solutions of proteogenic amino acids in comparison to D-enantiomers. Trained subjects tasted aqueous solution of each amino acid and evaluated the intensities of total taste and each basic taste using a category-ratio scale. Each basic taste of amino acids showed the dependency on its hydrophobicity, size, charge, functional groups on the side chain, and chirality of the alpha carbon. In addition, the overall taste of amino acid was found to be the combination of basic tastes according to the partial structure. For example, hydrophilic non-charged middle-sized amino acids elicited sweetness, and L-enantiomeric hydrophilic middle-sized structure was necessary for umami taste. For example, L-serine had mainly sweet and minor umami taste, and D-serine was sweet. We further applied Stevens' psychophysical function to relate the total-taste intensity and the concentration, and found that the slope values depended on the major quality of taste (e.g., bitter large, sour small).

Keywords Amino acid · Taste · Human psychophysics

M. Kawai · Y. Ninomiya
Section of Oral Neuroscience, Graduate School of Dental Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

M. Kawai (✉) · Y. Sekine-Hayakawa
Institute for Innovation, Ajinomoto Co., Inc., 1-1 Suzuki-cho, Kawasaki-Ku, Kawasaki 210-8582, Japan
e-mail: misako_kawai@ajinomoto.com

A. Okiyama
Quality Assurance & External Scientific Affairs, Ajinomoto Co., Inc., 1-15-1 Kyobashi, Chuo-Ku, Tokyo 104-8315, Japan

Introduction

Taste stimuli are important for mastication, swallow, and digestion of foods through secretion of digestive fluids such as saliva, pancreatic juice (Ohara et al. 1988) etc. Recently, many of taste receptors have been detected in various tissues other than taste receptor cells in taste buds on tongue, and their contribution to nutrient sensing is becoming clear. For example, sweet receptor, T1r2/T1r3, in L cells of gut was found to regulate secretion of an incretin, GLP-1 (Jang et al. 2007). Amino acids elicit taste, however, very little has been known about the taste properties of amino acids because of their complexity.

Among the proteogenic amino acids, L-glutamate (Glu) has the best-known taste properties. Glu is one of prototypical substances responsible for umami (savory) taste, which has been proposed as a fifth basic taste, along with sweetness, saltiness, sourness, and bitterness (Ikeda 1909; Yamaguchi 1987; Ninomiya and Funakoshi 1989). A heterodimeric G-protein coupled receptor, T1r1/T1r3, has been proposed as a candidate receptor for Glu and its elicitation of umami taste (Li et al. 2002; Nelson et al. 2002). However, few human psychophysical studies have been conducted on the taste of amino acids other than Glu.

Solms showed that many L-amino acids elicit sweet or bitter tastes, while most D-amino acids have primarily a sweet taste (Solms et al. 1965). Schiffman and her colleagues (Schiffman and Dackis 1975; Schiffman et al. 1981) also examined the taste quality of L- and D-amino acids by asking

subjects to rate amino acid powders for 45 attributes, including hedonic components such as good/bad, using a semantic differential scale. Taste intensity was evaluated using amino acid solutions and subjects were asked to evaluate the overall taste intensity by magnitude estimation without standard stimulus, i.e. modulus. Therefore, taste intensity could not be compared between amino acids. Ninomiya et al. (1966) measured the taste properties of L-amino acid solutions. They used the iso-intense NaCl concentration as a measure of the overall taste intensity and a subjective ratio of each basic taste to the overall taste intensity for taste quality. Yoshida and Saito (1969) used a multidimensional scaling method to analyze the relationship between taste qualities of L-amino acids. These studies provide information about the intensity of overall taste, but do not explain the intensity of each basic taste and its importance in defining the complex taste of an individual amino acid.

Since 2000, in addition to the above umami receptor T1r1/T1r3, the gustatory receptors for the other four basic tastes have been identified by genetic analysis and molecular biology techniques (Chandrashekar et al. 2000; Nelson et al. 2001; Li et al. 2002; Huang et al. 2006; Chandrashekar et al. 2010). Mechanisms of receptor binding also have been explored by studies on the response of mutated receptors to taste molecules and by study of the docking of a taste molecule onto the predicted receptor structure especially about umami and sweet tastes (Zhao et al. 2003; Zhang et al. 2008). However, little is yet known about the taste of amino acids other than Glu.

In the present study, we addressed the potential relationship between the structure and the taste properties of proteogenic amino acids by measuring of human gustatory responses elicited by aqueous solutions. Taste of their D-enantiomers was also measured for comparison. A more in-depth evaluation of taste complexity was obtained by rating of the intensities of total taste (TT) and each basic taste, that is, sweetness (Sw), saltiness (Sa), sourness (So), bitterness (Bi) and umami taste (Um), using a category-ratio scale, labeled magnitude scale (LMS) (Green et al. 1993).

Materials and methods

Subjects

All psychophysical tests followed the regulations for sensory evaluation of the Ajinomoto Co., Inc. Eight subjects (4 men and 4 women, non-smokers, 20–40 years old) who were working for food research and development at Ajinomoto Co., Inc. and familiar to the sensory evaluation of foods participated as subjects after providing informed consent. The subjects had no chronic disease and required no medical treatment. They were given a suprathreshold solution for each basic taste in order to instruct them with regard to each basic taste; these solutions consisted of 150 mmol/l sucrose (Sw), 100 mmol/l NaCl (Sa), 0.67 mmol/l L-tartaric acid (So), 3.1 mmol/l caffeine (Bi), and 100 mmol/l monosodium L-glutamate (MSG) (Um). All subjects were able to discriminate the five basic taste qualities from the following dilute aqueous solutions: 11.7 mmol/l sucrose, 22.4 mmol/l NaCl, 0.33 mmol/l L-tartaric acid, 1.04 mmol/l caffeine, and 2.7 mmol/l MSG, and water.

Prior to evaluation, the subjects were trained to rate the intensity of each quality of taste with the LMS following a previously published procedure (Green et al. 1993, 1996) using suprathreshold solutions representing each basic taste or a mixture of tastes. They were instructed to choose the nearest descriptor to the perceived intensity, then to adjust the position on the LMS. They were strictly instructed to imagine that the descriptor "strongest imaginable" at the top of the LMS meant the strongest oral sensation that would be equivalent to severe pain. Before the sessions for amino acids, subjects had experienced the evaluation of each taste quality of single or mixture solutions (e.g., various concentrations of NaCl solutions, NaCl plus sucrose mixed solutions) using LMS repeatedly. As all of the subjects rated the 150 mmol/l NaCl solution near "moderate" on the LMS, 150 mmol/l NaCl solution was provided to the subjects as the reference for "moderate" in TT intensity at the start of every session. Subjects were asked to quit session when they perceived that the first sample was different from usual. They were asked to refrain from eating or drinking 1 h prior to the evaluation procedure.

Stimuli

Aqueous solutions were prepared using ultrapure water purified using a Milli-Q water purification system (Nihon Millipore K.K, Japan) and guaranteed reagent grade L-form protein amino acids and their D-form enantiomers (Table 1). L- and D-tyrosine were omitted because they were barely soluble in water and their saturated solutions had no taste. Amino acids in free form (i.e., not in salt form) were purchased from Nacalai Tesque, Inc. (Japan). The purity of each amino acid was higher than 98.0 %, except for L-lysine (97.0 %). Three geometrically progressive concentrations, low (L), medium (M), and high (H), for each amino acid were determined by two or three trained subjects before the sessions. The range of concentration was set so that TT intensity was stronger than "weak" and weaker than "strong" on the LMS to avoid the range subthreshold or over sensationally saturated concentration.

Psychophysical methods

Solutions and ultrapure water for a mouth rinse were kept at room temperature, 20–25 °C, when they were presented

Table 1 Test solutions

Type[a]	Amino acid	Physicochemical properties				L-form				D-form			
		Size	Hydrophobicity	pI	Functional group	pr[b]	L[c]	M[c]	H[c]	pr[b]	L[c]	M[c]	H[c]
I	Gly	Small	Low	Neutral		4.0	63	250	1,000				
	Ala				Aliphatic	3.0	67	200	600	3.0	67	200	600
	Ser				Hydroxyl	4.0	63	250	1,000	2.0	250	500	1,000
	Thr				Hydroxyl	2.5	100	250	625	2.5	112	280	700
II	Cys	Small–medium	Medium	Neutral	Sulfhydryl	2.0	100	200	400	–	–	–	–
	Met				Sulfide	4.0	12.5	50	200	2.0	50	100	200
	Val				Aliphatic (branched)	2.0	25	50	100	2.0	50	100	200
III	Leu	Large	High	Neutral	Aliphatic (branched)	2.5	16	40	100	2.0	30	60	120
	Ile				Aliphatic (branched)	2.5	16	40	100	–	–	90	–
	Phe				Aromatic	3.0	8.3	25	75	2.5	8.0	20	50
	Tyr				Aromatic, hydroxyl	–	–	–	–	–	–	–	–
	Trp				Heterocyclic (indol)	2.5	4.0	10	25	4.0	1.0	4.0	16
IV	Asp	Small–medium	Low	Acidic	Carboxyl	2.0	1.5	3.0	6.0	3.0	0.67	2.0	6.0
	Glu				Carboxyl	4.0	0.63	2.5	10	3.0	0.67	2.0	6.0
V	Asn[d]	Medium	Low	Neutral	Amide	3.0	16.7	50	150	3.0	16.7	50	150
	Gln				Amide	2.0	62.5	125	250	2.0	50	100	200
VI	His	Medium–large	Medium–high	Basic	Heterocyclic (imidazole)	2.0	25	50	100	3.0	10	30	90
	Lys				Amine	2.0	50	100	200	–	–	–	–
	Arg				Guanidino	2.0	5.0	10	20	2.5	8.0	20	50
VII	Pro	Medium	Medium	Neutral	Imino acid	4.0	63	250	1,000	2.0	95	190	380

L low, *M* medium, *H* high concentration (mmol/l)

[a] Classified by psychophysical properties

[b] Progressive ratio for concentration of the test solutions

[c] Concentration of the test solutions

[d] Both L-and D-forms of Asn monohydrate were used

to the subjects. Approximately 40 ml of each solution was served in a plastic cup. After three mouth rinses with water, subjects sipped approximately 10 ml of each amino acid solution, tasted the solution, and then spat it out. To reduce the effects of odor on taste ratings, subjects wore nose clips during the tasting. Subjects were asked to rate the intensity of each taste quality, TT, Sw, Sa, So, Bi and Um, using an LMS 100 mm in length. Oral sensation which could not be ascribed to basic tastes was also evaluated as other taste (Ot). The relative position of each descriptor, "barely detectable (BD)", "weak (W)", "moderate (Mod)", "strong (S)", "very strong (VS)" and "strongest imaginably (SI)", was the same as that of the original LMS. Subjects were allowed to taste repeatedly after the mouth rinse until all taste qualities were rated. Solutions of 2 or 3 amino acids (6–9 solutions) were presented in one session. The order of presentation of L-or D-amino acids was randomized. The subjects participated the sessions up to once a day and up to three times a week.

Data analysis

Labeled magnitude scale ratings were transformed into logarithmic values after zero ("no sensation") was replaced with a very small number, "0.01". Average and standard error of were calculated using logarithmic values for the intensity of TT, Sw, Sa, So, Bi, Um, and Ot. Stevens' law was applied to relate concentration and TT intensity. The goodness of fit of the linier regression was evaluated by one-way ANOVA. The concentration at Mod-TT intensity was calculated according to the psychophysical functions for the comparison of absolute intensity. The correlation of the slope values or the concentrations at

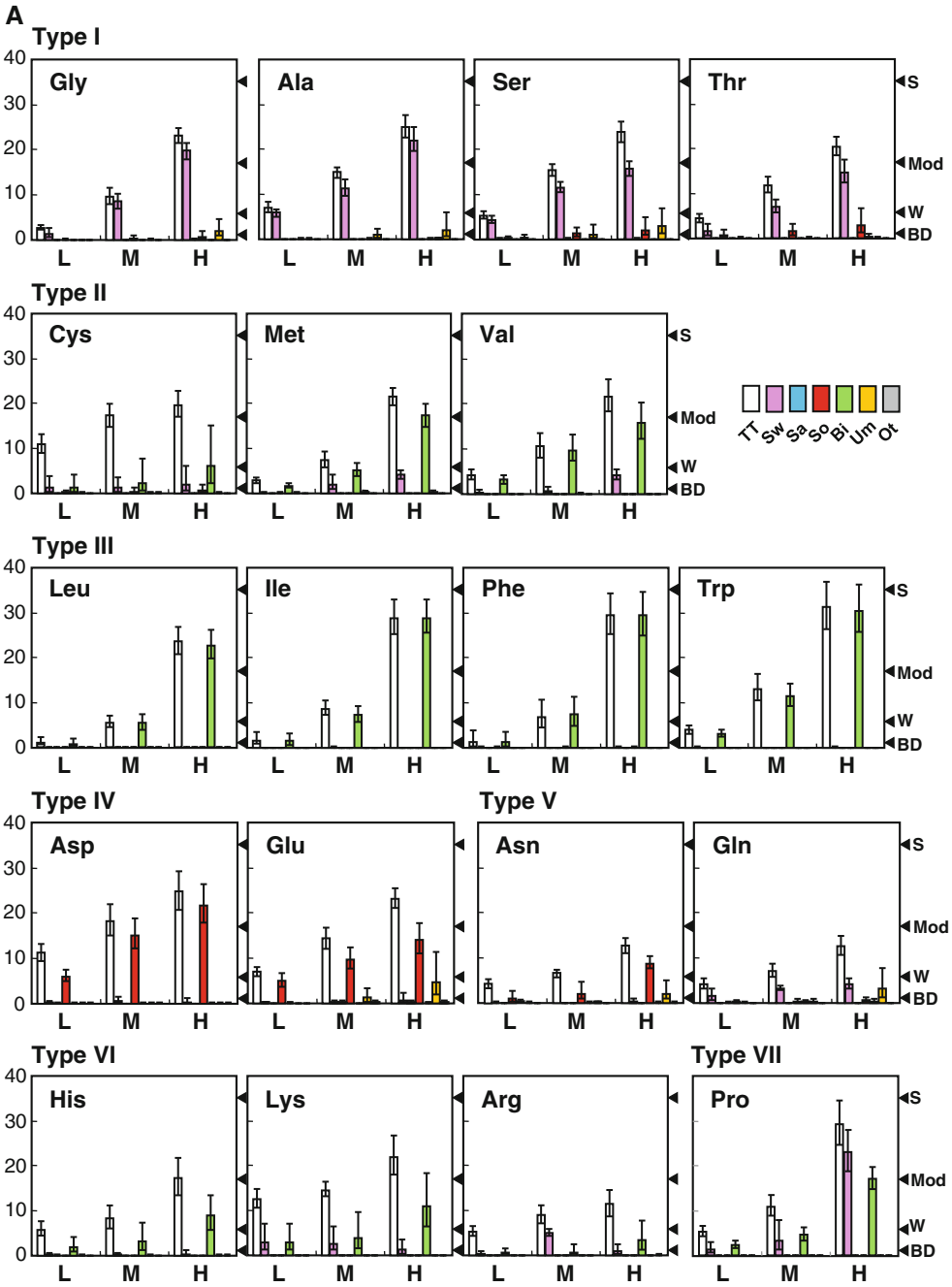


Fig. 1 Taste of each amino acid solution. Taste of L-amino acids (**a**), and D-amino acids (**b**). Each *bar* represents geometric mean ± geometric standard error for each quality of taste, TT (*white*), Sw (*pink*), Sa (*light blue*), So (*red*), Bi (*yellow green*), Um (*orange*) and Ot (*gray*). *Horizontal axis* represents three concentration levels L, M and H (see Table 1). The labels on the *right hand y* axes represent the descriptors on the LMS. Graph for Gly is presented in both **a** and **b**

Mod-TT intensity between L- and D-forms was evaluated by Spearman's correlation coefficient (r).

Results and discussion

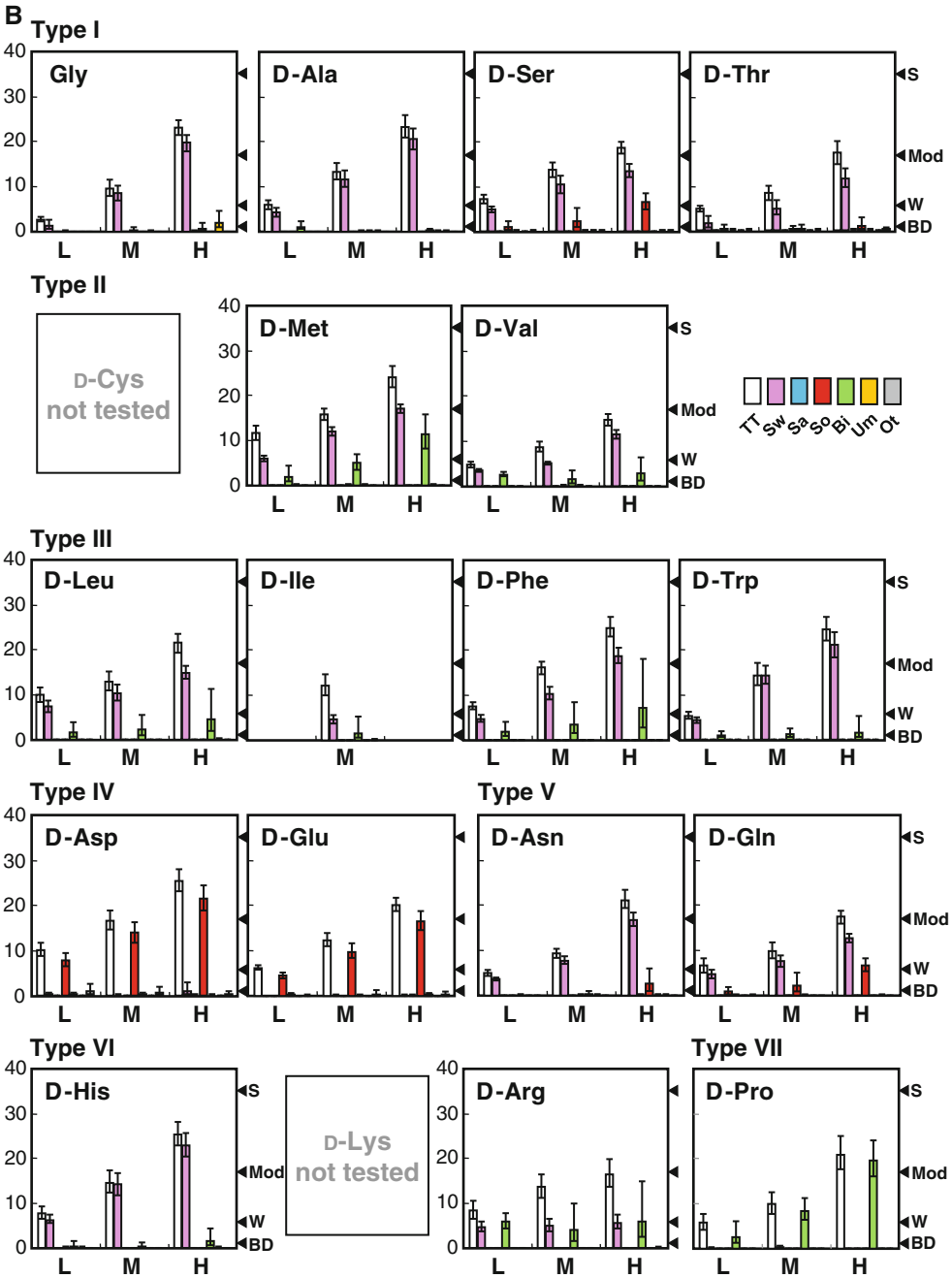
In this study, we asked subjects to taste each amino acid solution and to rate the intensities of TT and each basic taste, Sw, Sa, So, Bi and Um, and Ot using a category-ratio scale, LMS. This method allowed measurement and comparison of the qualitative and quantitative properties of taste for each amino acid.

The results are summarized by the type of amino acids, classified by physicochemical properties, that is, hydrophobicity, size, isoelectric point (pI) and the functional group of the side chain (Table 1).

Taste quality

Mean intensities of TT, Sw, Sa, So, Bi, Um and Ot of each amino acid solution are shown in Fig. 1a for L-amino acids, and Fig. 1b for D-amino acids. The taste quality of each solution was summarized in Table 2.

Fig. 1 continued



For L-amino acids, the most predominant taste qualities could be categorized based on their physicochemical properties; type I (Gly, Ala, Ser, Thr): Sw, type II (Cys, Met, Val): Bi, type III (Leu, Ile, Phe, Trp): Bi, type IV (Asp, Glu): So, type V (Asn, Gln): So or Sw, type VI (His, Lys, Arg): Bi, type VII (Pro): Sw. On the other hand, most of D-amino acids had predominantly Sw except for types IV and VII amino acids. L-Amino acids of types I, IV and V elicited Um at high concentration. On the contrary, none of D-amino acids elicited Um.

Many of the L- and D-amino acids were evaluated as having more than just a single basic taste. In addition, changes in taste quality, the ratio of intensity of each basic taste, were noted in response to the concentration.

Sweetness and bitterness

Sweetness and Bi of neutral amino acids of types I, II and III were linked to hydrophobicity, size and chirality, similar to previous reports (Shallenberger et al. 1969; Birch and Kemp 1989). In L-amino acid cases, Sw and Bi strongly depended on hydrophobicity (>Val: Bi, Cys>: Sw) and size (>Cys: Bi, Met>: Sw). Thus, hydrophilic small type I amino acids elicited Sw without Bi, and

Table 2 Summary of taste quality

Type	Amino acid	L-form			D-form		
		L	M	H	L	M	H
I	Gly	Sw	Sw	SwUm			
	Ala	Sw	Sw	SwUm	Sw	Sw	Sw
	Ser	Sw	Sw	SwUmSo	Sw	SwSo	SwSo
	Thr	Sw	Swso	Swso	Sw	Sw	Sw
II	Cys	Bi	Bi	BiSw	–	–	–
	Met	Bi	Bisw	Bisw	SwBi	SwBi	SwBi
	Val	Bi	Bi	Bisw	SwBi	SwBi	SwBi
III	Leu	Bi	Bi	Bi	SwBi	SwBi	SwBi
	Ile	Bi	Bi	Bi	–	SwBi	–
	Phe	Bi	Bi	Bi	SwBi	SwBi	SwBi
	Trp	Bi	Bi	Bi	Sw	Sw	SwBi
IV	Asp	So	So	So	So	So	So
	Glu	So	So	SoUm	So	So	So
V	Asn	So	So	SoUm	Sw	Sw	SwSo
	Gln	Sw	Sw	SwUm	Sw	Swso	SwSo
VI	His	Bi	Bi	Bi	Sw	Sw	SwBi
	Lys	SwBi	BiSw	Bi	–	–	–
	Arg	Bi	Sw	Bi	BiSw	SwBi	BiSw
VII	Pro	BiSw	BiSw	SwBi	Bi	Bi	Bi

Taste qualities are written according to intensity. Tastes in large letters represent the strongest taste, and the taste that was stronger both than half of the strongest taste and BD. Tastes in small letters represent the taste that was weaker than half of the strongest taste, and stronger both than 1/10 of the strongest taste and BD

hydrophobic large type III amino acids elicited Bi without Sw. Type II amino acids whose properties are between types I and III had Sw and Bi mixed taste. Meanwhile, Sw of D-amino acids had reverse tendency, hydrophobic and large amino acid showed strong Sw, and D-Trp was the sweetest as reported by Deutsch and Hansch (1966). His, a type VI amino acid with a imidazol group, also elicited Bi as the L-form, while the D-form elicited Sw comparable to D-Phe. The particularly strong Sw of D-Trp, D-Phe and D-His might be due to pi–pi interaction between the side chain of these amino acids and the aromatic residues on the Sw receptor proteins. The Bi side taste of D-amino acids of types II and III, and D-His was supposed to be derived from the hydrophobic large side chain like Bi of L-amino acids.

In the case of imino acid Pro, D-Pro was expected to be Sw because its hydrophobicity and size were intermediate between types I and III. However, Pro was predominantly Sw in L-form, and Bi in D-form. This relationship between L- and D-forms was reverse of other amino acids.

In the cases of Lys and L-/D-Arg of basic type VI amino acids, dominant taste was evaluated as Bi and/or Sw, although these amino acids showed complicated taste.

Sourness and umami taste

Amino acids with lower pI than Ser and lower hydrophobicity than Thr, except for Gln and D-Thr had So. Acidic amino acids of type IV (Asp, Glu) elicited primarily a So response.

Though Asp elicited BD Um within the range of the experimental concentration, neutralized salt of Glu and Asp e.g., monosodium L-glutamate and monosodium L-aspartate, are well known to have Um without So (Yamaguchi et al. 1971). In addition to type IV L-amino acids, types I and V amino acids of higher pI than Ala and of smaller than Gln were found to elicit Um at high concentrations. We have shown previously by a human psychophysical experiment that synergistic Um enhancement (Kuninaka 1960; Yamaguchi 1967) occurs when L-amino acids of types not only IV but also types I and V are mixed with 5′-inosine monophosphate (Kawai et al. 2002). This phenomenon is similar to responses seen in in vitro experiments with murine T1R1/T1R3-expressing cells, in which the cellular response to many L-amino acids, such as Gly and Ser, can be enhanced by 5′-guanosine monophosphate (Nelson et al. 2002). The weak Um response of L-amino

acids alone is therefore possibly enhanced by adding nucleotides, suggesting that the T1R1/T1R3 heterodimeric receptor for acidic L-amino acids might be involved in the reception of these L-amino acids. However, unlike a previous report on human T1R1/T1R3 by Li et al. (2002), we found that a wider variety of amino acids could elicit the umami taste in our experiment.

On the other hand, no D-amino acid elicited Um, even if a response was elicited for their L-forms. The phenomenon whereby many L-amino acids, apart from the well known type IV Asp and Glu, elicited umami taste might be consistent with the concept that umami is a signal for protein nutrition.

Taste intensity

The relationships between log-transformed concentration and TT intensity are shown in Fig. 2a for L-amino acids, and Fig. 2b for D-amino acids, with the regression lines of Stevens' psychophysical function. The main effect of the regression was highly significant, except for Cys, Lys, Arg and D-Arg ($p < 0.05$). Slope value and estimated concentration at Mod-TT intensity are summarized in Table 3.

Slope values for psychophysical functions

The order of mean ranks of slope value of psychophysical functions for L-amino acids was types III, I, II, VII, V, VI, IV. For D-amino acids, it was types VII, I, V, II, III, IV, VI. No correlation was noted for slope values between L- and D-amino acids [$r = 0.314$ ($p = 0.240$)] (Fig. 3). In particular, the difference in slope between L- and D-amino acids was substantial when their dominant quality of taste was different, as observed especially in types III and VII; e.g., one enantiomer was Sw, while the other was Bi. In summary, a relationship was noted between the predominant taste and the slope value common to L- and D-amino acids, with "Bi > Sw > So". The phenomenon that amino acids have the same slope values for Stevens' psychophysical functions can be interpreted as the amino acids having apparent multiple concentrations. That is, when amino acids A and B have similar taste quality, the following relationship holds:

$$f_{\mathrm{A}}(x_{\mathrm{A}}) = f_{\mathrm{A}}(l \times x_{\mathrm{B}})$$

where f_{A} is the psychophysical function for amino acid A, x_{A} is the concentration of amino acid A, and l is a constant.

However, the observed tendency of the slope differed from that reported in previous studies by Schiffman and Clark (1980), Schiffman et al. (1982). For example, they reported that the slope values for most of the D-amino acids were larger than those for L-amino acids, and no conclusive relationship could be determined between slope values and either structure or taste quality. Contrary to our results, they reported a substantial difference between the slopes of Leu (0.475) and Ile (0.675), even though Leu and Ile are very similar in structure.

Among the Sw–Bi amino acids, type VI basic amino acids, Lys, Arg, and D-Arg, had Bi and/or Sw intensities that were weakly dependent on concentration as shown in Fig. 1. However, Bi intensity of neutralized salts of these basic amino acids showed a strong concentration-dependency (data not shown), suggesting that these bulky side chains might be linked to Bi taste. Alkaline pH of solution of these basic amino acids could perturb Sw and Bi taste sensation.

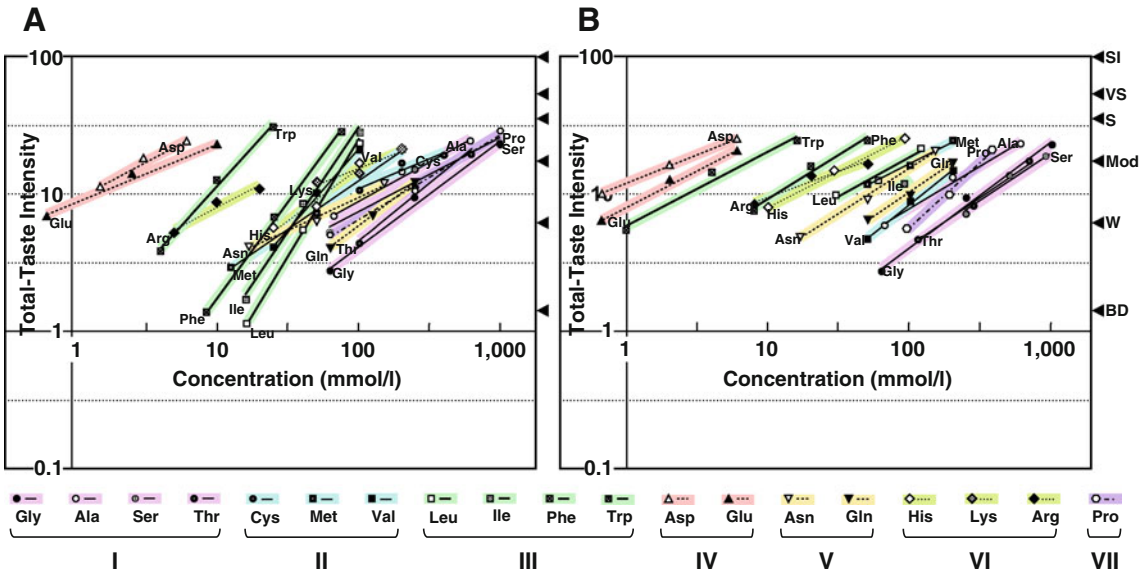


Fig. 2 Total-taste intensity. TT intensity with regression lines for psychophysical function of L-amino acids (**a**), and D-amino acids (**b**)

Table 3 Summary of taste intensity

Type	Amino acid	L-form			D-form			Ratio (L/D)	
		Slope[a]	p[b]	Mod-TT[c]	Slope[a]	p[b]	Mod-TT[c]	Slope	Mod
I	Gly	0.78	1.64E−09	6.4E+02					
	Ala	0.57	6.21E−08	2.9E+02	0.62	3.91E−07	3.4E+02	0.92	0.85
	Ser	0.54	7.34E−09	4.5E+02	0.69	3.45E−06	8.2E+02	0.78	0.54
	Thr	0.84	4.81E− 07	4.6E+02	0.71	4.06E−06	7.3E+02	1.19	0.63
II	Cys	0.42	1.73E−02	2.6E+02	–	–	–	–	–
	Met	0.72	2.07E−07	1.5E+02	0.52	4.39E−05	1.1E+02	1.37	1.41
	Val	1.18	7.20E−05	8.1E+01	0.83	2.32E−06	2.4E+02	1.42	0.34
III	Leu	1.51	5.84E−05	8.2E+01	0.56	1.10E−03	8.8E+01	2.68	0.93
	Ile	1.38	1.88E−04	6.8E+01	–	–	–	–	–
	Phe	1.14	3.26E−03	5.0E+01	0.66	4.17E−09	2.6E+01	1.74	1.91
	Trp	1.14	3.05E−07	1.4E+01	0.54	3.11E−07	7.3E+00	2.09	1.93
IV	Asp	0.57	3.08E−03	3.0E+00	0.42	2.72E−05	2.3E+00	1.35	1.29
	Glu	0.43	2.08E−06	4.6E+00	0.54	2.50E−08	4.2E+00	0.81	1.10
V	Asn	0.49	1.50E−04	3.1E+02	0.66	5.09E−09	1.2E+02	0.75	2.67
	Gln	0.79	9.44E−04	3.7E+02	0.69	9.61E−04	2.0E+02	1.14	1.82
VI	His	0.77	9.39E−03	1.1E+02	0.53	4.16E−05	4.2E+01	1.46	2.59
	Lys	0.40	2.55E−02	1.2E+02	–	–	–	–	–
	Arg	0.53	2.80E−02	4.0E+01	0.37	2.66E−02	4.9E+01	1.44	0.82
VII	Pro	0.62	3.87E−06	4.6E+02	0.95	1.11E−03	3.2E+02	0.66	1.43

[a] Slope value of the Stevens' psychophysical function

[b] Significance of fitting

[c] Concentration at Mod-TT intensity estimated by the psychophysical function (mmol/l)

Relative taste intensity

The concentration at Mod-TT intensity, calculated according to psychophysical function, showed a strong correlation between L- and D-amino acids [$r = 0.882$ ($p = 0.001$), for 15 amino acids] (Fig. 4). This relationship was coincident with the correlation in threshold of L- and D-forms observed by Schiffman et al. (1981). In addition, a high correlation was noted between the concentrations at Mod-TT intensity and the threshold concentrations reported by Schiffman et al. (1981), $r = 0.676$ ($p = 0.004$) for

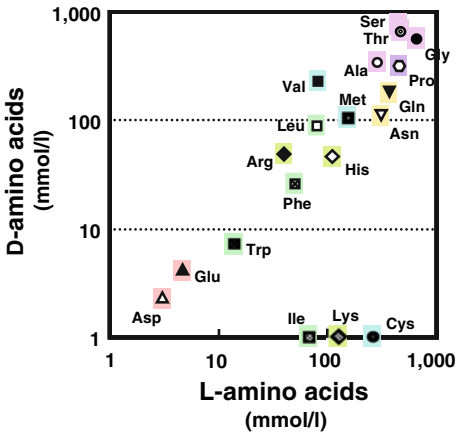


Fig. 3 Correlation of slope values between L- and D-amino acids. *Symbols* on the *horizontal axis* indicate that data are not available for D-amino acids

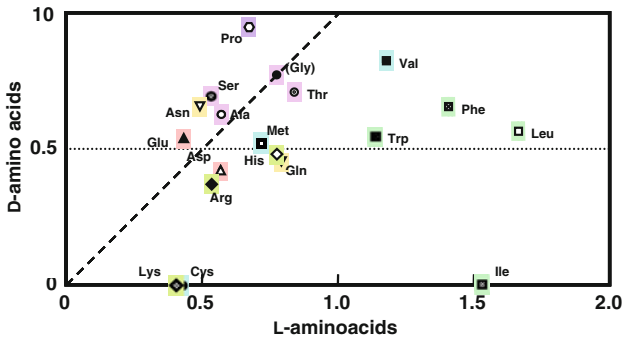


Fig. 4 Correlation of log-transformed concentrations at moderate total-taste intensity between L- and D-amino acids. *Symbols* on the *horizontal axis* indicate that data are not available for D-amino acids

19 L-amino acids (except Tyr), $r = 0.910$ ($p = 0.001$) for 15 D-amino acids (except for Cys, Ile, Lys, Arg and Tyr). However, the mechanism that gives rise to the correlation in taste intensity between L- and D-amino acids that completely differ from each other in taste quality is not clear because it is likely that their receptors may differ from each other. Fine structure analysis of receptors will be necessary to determine the underlying mechanism.

Possible mechanism for the mixed taste of amino acids

The taste of amino acids was apparently perceived as a mixed sensation of basic tastes. The present results suggest that the taste quality and intensity are linked to the combination of the taste properties based on the partial structure of the amino acid. That is, amino acids may interact with more than one taste receptor, as occurs for the odorant receptor system, in which one odorant molecule is received by multiple odor receptors according to its structure (Malnic et al. 1999; Araneda et al. 2000). Hence, the change in taste quality by concentration could have been observed through the taste which was hidden at low concentration and perceived at high concentration.

However, several exceptions to this hypothesis were observed in the cases where Bi was a minor taste of type III D-amino acids, and for So of L- and D-enantiomers of Glu and Ser. In the former case, although Bi of D-Trp was expected to be the stronger than that of D-Phe due to the hydrophobicity and size of the side chain, Bi of D-Trp was in fact weaker than that of D-Phe. In the case of Glu and Ser, each enantiomer was expected to elicit the same So intensity as they have the same pH at a given concentration. However, the So of the L-form was weaker than that of the D-form. One possible mechanism might be a suppression of Bi by Sw (Kroeze and Bartoshuk 1985) or a suppression of So by Um (Yamaguchi and Kimizuka 1979) which are known to occur due to inter-molecular interactions. Such intra-molecular taste–taste interaction might be also involved in complex taste of amino acids.

Conclusion

We measured the qualitative and quantitative properties of taste of amino acids using a category-ratio scale, LMS. The complex taste of amino acids could be described by a combination of the intensities of five basic tastes according to taste properties that depended on the partial structure of each individual amino acid.

Conflict of interest Misako Kawai, Yuki Sekine-Hayakawa, Atsushi Okiyama are employees of Ajinomoto Co., Inc.

References

Araneda RC, Kini AD, Firestein S (2000) The molecular receptive range of an odorant receptor. Nat Neurosci 3:1248–1255

Birch GG, Kemp SE (1989) Apparent specific volumes and tastes of amino acids. Chem Senses 14:249–258

Chandrashekar J, Mueller KL, Hoon MA, Adler E, Feng L, Guo W, Zuker CS, Ryba NJ (2000) T2Rs function as bitter taste receptors. Cell 100:703–711

Chandrashekar J, Kuhn C, Oka Y, Yarmolinsky DA, Hummler E, Ryba NJ, Zuker CS (2010) The cells and peripheral representation of sodium taste in mice. Nature 464:297–301

Deutsch EW, Hansch C (1966) Dependence of relative sweetness on hydrophobic bonding. Nature 211:75

Green BG, Schaffer GS, Glimore MM (1993) Derivation and evaluation of a semantic scale of oral sensation magnitude with apparent ratio properties. Chem Senses 18:683–702

Green BG, Dalton P, Cowart B, Shaffer G, Rankin K, Higgins J (1996) Evaluating the 'Labeled Magnitude Scale' for measuring sensations of taste and smell. Chem Senses 21:323–334

Huang AL, Chen X, Hoon MA, Chandrashekar J, Guo W, Tränkner D, Ryba NJ, Zuker CS (2006) The cells and logic for mammalian sour taste detection. Nature 442:934–938

Ikeda K (1909) New seasonings. J Tokyo Chem Soc 30:820–836 [in Japanese]

Jang H-J, Kokrashvili Z, Theodorakis MJ, Carlson OD, Kim B-J, Zhou J, Kim HH, Xu X, Chan SL, Juhaszova M, Bernier M, Mosinger M, Margolskee RF, Egan JM (2007) Gut-expressed gustducin and taste receptors regulate secretion of glucagon-like peptide-1. Proc Natl Acad Sci USA 104:15069–15074

Kawai M, Okiyama A, Ueda Y (2002) Taste enhancements between various amino acids and IMP. Chem Senses 27:739–745

Kroeze JH, Bartoshuk LM (1985) Bitterness suppression as revealed by split-tongue taste stimulation in humans. Physiol Behav 35:779–783

Kuninaka A (1960) Studies on taste of ribonucleic acid derivatives. J Agric Chem Soc Jpn 34:487–492 (in Japanese)

Li X, Staszewski L, Xu H, Durick K, Zoller M, Adler E (2002) Human receptors for sweet and umami taste. Proc Natl Acad Sci USA 99:4692–4696

Malnic B, Hirono J, Sato T, Buck LB (1999) Combinatorial receptor codes for odors. Cell 96:713–723

Nelson G, Hoon MA, Chandrashekar J, Zhang Y, Ryba NJ, Zuker CS (2001) Mammalian sweet taste receptors. Cell 106:381–390

Nelson G, Chandrashekar J, Hoon MA, Feng L, Zhao G, Ryba NJ, Zuker CS (2002) An amino-acid taste receptor. Nature 416:199–202

Ninomiya Y, Funakoshi M (1989) Peripheral neural basis for behavioural discrimination between glutamate and the four basic taste substances in mice. Comp Biochem Physiol A Comp Physiol 92:371–376

Ninomiya T, Ikeda S, Yamaguchi S, Yoshikawa T (1966) Studies on the taste of various amino acids. Rep. 7th Sensory evaluation symposium, JUSE, pp 109–123 (in Japanese)

Ohara I, Otsuka S, Yugari Y (1988) Cephalic phase response of pancreatic exocrine secretion in conscious dogs. Am J Physiol 254:G424–G428

Schiffman SS, Clark TB 3rd (1980) Magnitude estimates of amino acids for young and elderly subjects. Neurobiol Aging 1:81–91

Schiffman SS, Dackis C (1975) Taste of nutrients: amino acids, vitamins, and fatty acids. Percept Psychophys 17:140–146

Schiffman SS, Sennewald K, Gagnon J (1981) Comparison of taste qualities and thresholds of D- and L-amino acids. Physiol Behav 27:51–59

Schiffman SS, Clark TB 3rd, Gagnon J (1982) Influence of chirality of amino acids on the growth of perceived taste intensity with concentration. Physiol Behav 28:457–465

Shallenberger RS, Acree TE, Lee CY (1969) Sweet taste of D and L-sugars and amino-acids and the steric nature of their chemoreceptor site. Nature 221:555–556

Solms J, Vuataz L, Egli RH (1965) The taste of L- and D-amino acids. Experientia 21:692–694

Yamaguchi S (1967) The synergistic taste effect of monosodium glutamate and disodium 5′-inosinate. J Food Sci 32:473–478

Yamaguchi S (1987) Fundamental properties of umami in human taste sensation. In: Kawamura Y, Kare MR (eds) Umami: a basic taste. Marcel Dekker Inc, NY, pp 41–73

Yamaguchi S, Kimizuka A (1979) Psychometric studies on the taste of monosodium glutamate. In: Filer LJ Jr., Garattini S, Kare MR, Reynolds AW, Wurtman RJ (ed) Glutamic acid: advances in Biochemistry and Physiology. Raven Press, NY, pp 35–54

Yamaguchi S, Yoshikawa T, Ikeda S, Ninomiya T (1971) Measurement of the relative taste intensity of some L-α-amino acids and 5′-nucleotides. J Food Sci 36:846–849

Yoshida M, Saito S (1969) Multidimensional scaling of taste of amino acids. Jpn Psychol Res 11:149–166

Zhang F, Klebansky B, Fine RM, Xu H, Pronin A, Liu H, Tachdjian C, Li X (2008) Molecular mechanism for the umami taste synergism. Proc Natl Acad Sci USA 105:20930–20934

Zhao GQ, Zhang Y, Hoon MA, Chandrashekar J, Erlenbach I, Ryba NJ, Zuker CS (2003) The receptors for mammalian sweet and umami taste. Cell 115:255–266