# Quantitative Taste Evaluation of Total Enteral Nutrients

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Received April 15, 2004; accepted September 1, 2004

**The purpose of this study was to evaluate quantitatively the taste of the various total enteral nutrients marketed in Japan using human gustatory sensation tests and an artificial taste sensor. In the human gustatory sensation test, four basic taste intensities (sweetness, saltiness, sourness, and bitterness), as well as 15 kinds of palatability scales, were evaluated according to the semantic differential (SD) method. Among 15 palatability items, the item; difficult to drink/easy to drink, was adopted as an overall palatability since it shows the highest factor loading by factor analysis. The overall palatability was found to be highly positively correlated with sweetness and sourness, but negatively correlated with bitterness and saltiness. Addition of a flavour to the amino acid-based enteral nutrient Aminoleban®EN significantly improved its palatability. This effect is presumably due to sour components of the flavour, such as citric acid, which reduce the bitterness intensity of branched-chain amino acids in the product. The sweetness and sourness intensities predicted by the taste sensor showed a high correlation with the results obtained in the human gustatory sensation tests. The taste sensor was able to predict the overall palatability of the total enteral nutrients with high accuracy. The products could be classified into three groups (peptide-based, amino-acid-based, and protein-based) by principal component analysis using sensor output of 8 channels. The products could be also classified into four groups; peptide-based, amino-acid-based, and protein-based and flavor addition group by principal component analysis using sensor output of channels 1, 3, 4 and 7, which are specific to basic tastes. The taste sensor could therefore be useful in predicting the taste or palatability of total enteral nutrients, and could contribute to attempts to improve compliance for such products and for enteral nutrients.**

**Key words** enteral nutrients; taste sensor; semantic differential method; sweetness; sourness; bitterness

For patients who need to receive their total nutrition *via* an intravenous or enteral route, the latter route has several advantages. It is easy to manage, carries only a small risk of infection, is economical, and can be regarded as a more physiologically appropriate method as it does not bypass the gastrointestinal tract.[1)]

The total available on the Japanese marketing can be classified into three groups according to differences in nitrogen source. Protein-based nutrients (PrBNs), in which the main protein components are casein and soybean protein; peptide-based nutrients (PeBNs), in which the main protein components are dipeptide and tripeptide solutions; and amino-acid-based nutrients (AaBNs), which contain crystal amino acids.[2)] This latter group includes elemental diets which are used to treat hepatic insufficiency by improving Fischer's rate[3,4)] and contain high concentrations of bitter-tasting branched-chained amino acids (BCAAs). PrBNs contain dextrin and white sugar as carbohydrate sources and 20—30% (w/w) of various kinds of lipid. PeBNs and AaBNs also contain dextrin as a carbohydrate source and 15—25% of fat. The PrBNs are commonly said to taste worse than AaBNs or PeBNs.[2)]

These total enteral nutrients must often be taken for long periods, and their unpleasant taste or smell may decrease compliance or intake. Therefore, many attempts have been made to improve their palatability, such as by dilution, addition of flavours, or by mixing with food or drinks.[5,6)] Recently, bitterness-suppressed elemental diets, containing increased particle sizes of BCAAs, have become commercially available.[7)]

The goal of the present study was to conduct a systematic, quantitative, evaluation of the total enteral nutrients on the Japanese market using human gustatory sensation tests and an artificial taste sensor. In the gustatory sensation tests, we used the semantic differential method to examine various palatability scores and to determine the critical factor(s) for overall palatability. Furthermore, the application of the taste sensor in the evaluation of the palatability of total enteral nutrients was determined.

## Experimental

**Materials** The total enteral nutrients and their associated flavours used in the study were as follows:

PrBNs: Clinimeal®, with or without a coffee flavour (Eisai Co., Ltd. Tokyo, Japan); Ensure® liquid with a coffee flavour (Dainippon Pharmaceutical Co., Ltd. Osaka, Japan); Harmonic-M® (Ajinomoto Pharma Co., Ltd. Tokyo, Japan); Racol® with a milk flavour (Otsuka Pharmaceutical Co., Ltd. Tokyo, Japan). PeBNs: Enterued®, with or without a coffee flavour (Terumo Co., Ltd. Tokyo, Japan); Twinline® (Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan). AaBNs: Elental®, with or without a coffee flavour (Ajinomoto Pharma Co., Ltd. Tokyo, Japan); Hepan ED®, with or without a coffee flavour (Ajinomoto Pharma Co., Ltd. Tokyo, Japan); Aminoleban®EN, with or without pineapple, apple, coffee, fruit-mix, and powdered-green-tea flavours (Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan). Hepan ED® and Aminoleban®EN are used for patients with severe hepatic diseases. Samples of each total enteral nutrient were prepared as described in the package insert of the product, to a concentration of 1 kcal/ml.

**Gustatory Sensation Tests** Samples of Clinimeal®, Enterued®, Elental®, Hepan ED®, and Aminoleban®EN with or without flavours (pineapple, apple, coffee, fruit-mix, and powdered-green-tea) were used for the gustatory sensation tests which were carried out using nine well-trained volunteers. The sample size was 2 ml, and all samples were kept in the mouth for 10 s. After tasting, subjects gargled well before tasting the next sample. Four basic taste intensities and various palatability scores were eval-

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uated using the semantic differential (SD) method.

In the evaluation of four basic tastes, the gustatory sensation test was performed according to the method of Katsuragi,[8] using sucrose at concentrations of 29.2, 87.7, 187.1, 409.4 and 994.2 mM as a standard for sweetness, sodium chloride at concentrations of 20.5, 51.3, 130.0, 273.8 and 616.0 mM as a standard for saltiness, tartaric acid at concentrations of 0.17, 0.60, 1.73, 4.66 and 11.99 mM as a standard for sourness, and quinine sulfate at concentrations of 0.003, 0.012, 0.031, 0.078 and 0.201 mM as a standard for bitterness. Scores of 0, 1, 2, 3, and 4 were allocated to the increasing concentrations of all the standard solutions.

The palatability scores were evaluated by the SD method as follows[9]: the subjects were asked to score the samples on the basis of the following 15 items, which were expressed as symmetrical terms representing both extremities of the item, as follows: (1) Difficult to drink/Easy to drink, (2) Bad flavour quality/Good flavour quality, (3) Cannot drink every day/Can drink every day, (4) Tastes bad/Tastes good, (5) Not agreeable/Agreeable, (6) Not like a meal/Like a meal, (7) Bad sensation in mouth/Good sensation in mouth, (8) Weak flavour/Strong flavour, (9) Does not seem nutritional/Seems nutritional, (10) Taste not too persistent/Taste too persistent, (11) Weak aftertaste/Strong aftertaste, (12) Not easy to get tired of/Easy to get tired of, (13) Not medicine-like/Medicine-like, (14) No distinct taste/Distinct taste, (15) Not acrid/Acrid. The items were scored on the following rating scale: 0, extremely; 1, slightly; 2, neither; 3, slightly; 4, extremely.

In the gustatory sensation test to evaluate the bitterness reduction of BCAA solutions by addition of citric acid concentrations of the BCAAs in the control solution (which were essentially the same as in Aminoleban®EN) were as follows: 77.65 mM L-Leu, 73.28 mM L-Ile, 68.37 mM L-Val, and 1.80 mM L-Trp. Citric acid was added to this control solution at concentrations equivalent to the citric acid content of each flavour (apple 3.64 mM, pineapple 4.42 mM, fruit-mix 3.44 mM, green-tea 0.73 mM) and at 5.21 mM and 7.81 mM. The change of pH caused by the addition of citric acid was recorded.

**Sensor Measurement and Data Analysis** The artificial taste sensor system and the lipid components of the sensor used in the present study are essentially same as those described in previous papers.[10—15] The taste sensor system SA402B (Intelligent Sensor Technology Co., Ltd., Atsugi, Japan) was used to measure the electric potential of the drug suspensions. In this sensor, the electrode set is attached to a mechanically controlled robot arm. The detecting sensor part of the equipment consists of eight electrodes composed of lipid/polymer membranes. Each lipid was mixed in a test tube containing poly(vinylchloride) and dioctylphenylphosphonate as a plasticizer, dissolved in tetrahydrofuran, and dried on a glass plate at 30 °C to form a transparent thin film, almost 200 $\mu$m thick. The electrodes consist of an Ag wire whose surface is plated with Ag/AgCl, with an internal cavity filled with 3 M KCl solution. The difference between the electric potential of the working electrode and the reference electrode was measured by means of a high-input impedance amplifier connected to a computer.

All total enteral nutrients and flavours were prepared as instructed in the relevant package insert. Fresh 30 mM KCl solution containing 0.3 mM tartaric acid (corresponding to saliva) was used as the reference sample (Vr) and also to rinse the electrodes after every measurement. The method used to measure the sensitivity and the selectivity of adsorption of the samples is summarized in Chart 1. The electrode is first dipped into the reference solution (Vr) and then into the sample solution or suspension (Vs). The relative sensor output is represented as the difference (Vs−Vr) between the potentials of the sample and the reference solution. When the electrode is dipped into the reference solution again, the new potential of the reference solution is defined as Vr′. The difference (Vr′−Vr) between the potentials of the reference solution before and after sample measurement is defined as CPA (change of membrane potential caused by adsorption) and corresponds to aftertaste. Each measuring time was set at 30 s, and the electrodes were rinsed after each measurement.

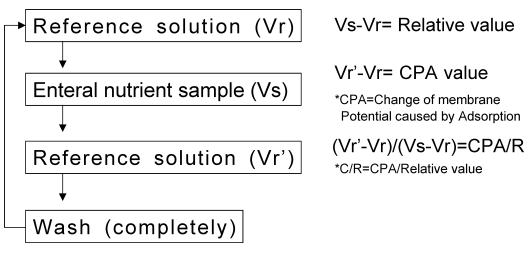


Chart 1. Measuring Procedure in This Study

S-PLUS 2000J (Mathematical Systems, Inc., Tokyo, Japan) was used for factor analysis, regression analysis, and principal component analysis.

The comparison of palatability items was analyzed using the Wilcoxon's rank sum test.

## Results and Discussion

**The Palatabilities of Total Enteral Nutrients Evaluated by the SD Method** Figure 1 shows the palatability scores of the total enteral nutrients as evaluated using the SD method. High scores were obtained for most products on the items 'Distinct taste', 'Taste too persistent' and 'Strong aftertaste'. The palatability scores of the PrBN (Clinimeal®) ranged from 1 to 3, and were therefore all in the average range. The AaBNs (Elental® and Hepan ED®) scored highly on the items 'Difficult to drink', 'Not agreeable', and 'Easy to get tired of', while Aminoleban®EN had a reasonable palatability, similar to that of Clinimeal®. The PeBN (Enterued®) had a high score for 'Acrid', and 'Strong aftertaste'.

About the data obtained by the SD method, a factor analysis (a factor axis was rotated with a varimax method) was performed. As a result, three factors with eigenvalues greater than 1.0 could be extracted. The factor contribution for factor I, II, III are 45.9, 9.7, and 7.5%, respectively. The factors loading of each scale are shown in Table 1. Among 15 palatability items, the item; difficult to drink/easy to drink, was adopted as an overall palatability since it shows the highest factor loading (0.891) by factor analysis.

The actual overall palatability scores for products were shown Fig. 2. In figure, a low Y-axis value means poor palatability. The PeBN Clinimeal® and the AaBN Aminoleban®EN showed moderate overall palatabilities compared to the other AaBNs (Elental® and Hepan ED®) and the PrBN Enterued®, which showed poor palatabilities. When fruit, pineapple, apple, and coffee flavours were added to the Aminoleban®EN the overall palatability was significantly improved. In particular, the scores for 'Agreeable' and 'Good flavour quality' increased, while scores for 'Acrid' decreased (Fig. 1). Thus, the four flavours were effective in improving the palatability of the Aminoleban®EN, a finding which supports the conclusion reached in an earlier report (data not shown in that article).[7]

**Correlation of Various Palatability Item Scores and the Basic Taste Intensities** Among 15 scales in Table 1, we picked up five scales with high factor loading (>0.7), and correlation between four basic taste intensities and intensities of above five scales were examined. The result was summarized in Table 2. It was suggested that the palatability is positively correlated with sweetness and sourness, and negatively correlated with bitterness and saltiness. Amino acids or peptides with bitterness involved in nutrients might be one reason for its bad palatability.

In gustatory sensation test, the addition of flavor into Aminoleban®EN was so useful for improving palatability as shown in Figs. 1 and 2. Especially the addition of fruit flavor was useful for bitterness suppression. The fruit flavor contains organic acids such as citric acid and this component might have capability of bitterness suppression. Therefore, we examined the effect of citric acid on bitterness of the BCAA solution which was the same component solution as Aminoleban®EN product (L-Leu: 77.65 mM, L-Ile: 73.28 mM,

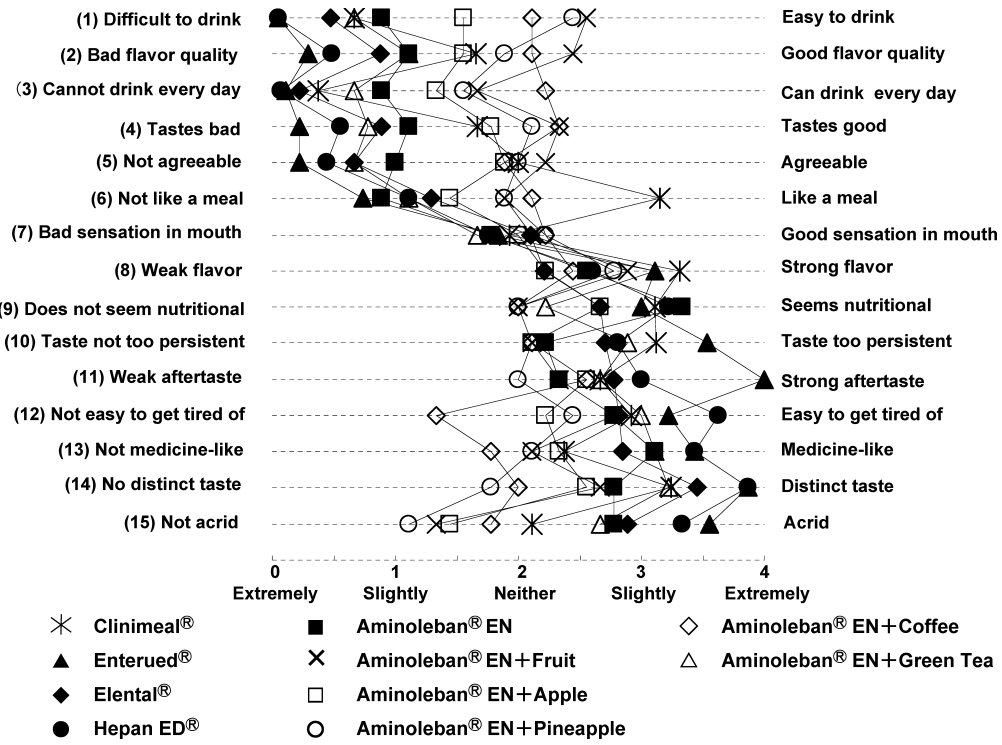


Fig. 1. Various Palatabilty Scores by SD Method for Various Enteral Nutrients in Japanese Market
The data represents the mean of 9 values.

Table 1. The Factor Analysis Result Using a SD Method for Enteral Nutrient Products ($n=9$)

| Scales | | Factor loading | | |
|---|---|---|---|---|
| | | I | II | III |
| Compliance | ( 1 ) Difficult to drink/easy to drink (Overall palatability score) | 0.891 | 0.149 | −0.194 |
| | ( 2 ) Bad flavour quality/good flavour quality | 0.757 | 0.4 | −0.264 |
| | ( 3 ) Cannot drink every day/can drink every day | 0.761 | 0.392 | −0.26 |
| | ( 4 ) Tastes bad/tastes good | 0.713 | 0.505 | −0.259 |
| | ( 5 ) Not agreeable/agreeable | 0.708 | 0.567 | −0.028 |
| | ( 6 ) Not like a meal/like a meal | 0.503 | −0.017 | −0.314 |
| | (12) Not easy to get tired of/easy to get tired of | −0.442 | −0.139 | 0.328 |
| | (13) Not medicine-like/medicine-like | −0.439 | −0.325 | −0.054 |
| | (14) No distinct taste/distinct taste | −0.532 | −0.431 | 0.457 |
| Feeling of taste | ( 7 ) Bad sensation in mouth/good sensation in mouth | 0.055 | 0.392 | −0.04 |
| | ( 9 ) Does not seem nutritional/seems nutritional | −0.192 | −0.317 | 0.114 |
| | (15) Not acrid/acrid | −0.271 | −0.633 | 0.318 |
| Strength of taste | ( 8 ) Weak flavour/strong flavour | −0.056 | 0.003 | 0.569 |
| | (10) Taste not too persistent/taste too persistent | −0.355 | −0.295 | 0.592 |
| | (11) Weak aftertaste/strong aftertaste | −0.146 | −0.224 | 0.643 |

L-Val: 68.37 mM).

The result was shown in Fig. 3. The addition of 8 mM citric acid to a BCAA solution reduced the bitterness intensity of the solution completely.

Tamura[16] reported that the bittereness inhibitory effect of acidic amino acids on bitterness of BCAAs, even though the mechanism was not clearly mentioned in that article. Also in our pilot experiments, the acidic substances such as organic acid being useful for bitterness suppression in many substances with bitterness.

It can therefore be concluded that the improvements in overall palatability of the enteral nutrients brought about by the addition of various flavors are mainly due to the citric acid involved in flavors.

**Prediction of Sweetness or Sourness Intensities of Enteral Nutrients Using the Taste Sensor** Since the sweetness or sourness of the product shows a high correlation with overall palatability, the possibility of predicting these two basic tastes would be extremely useful in any attempt to improve the taste of enteral nutrients. Figure 4 shows the result of a simple linear regression analysis for several of these products using sensor output value and gustatory sensation data for sweetness intensity (A), sourness intensity (B), and bitterness intensity (C). The taste intensity

Table 2. Correlation of the Scale Relevant to a Compliance, and 4 Basic Tastes ($n$=9)

| Palatability items | Sweetness | Sourness | Bitterness | Saltiness |
|---|---|---|---|---|
| (1) Difficult to drink/easy to drink | 0.80 | 0.68 | −0.84 | −0.78 |
| (2) Bad flavour quality/good flavour quality | 0.83 | 0.53 | −0.89 | −0.83 |
| (3) Cannot drink every day/can drink every day | 0.62 | 0.45 | −0.66 | −0.85 |
| (4) Tastes bad/tastes good | 0.77 | 0.55 | −0.87 | −0.82 |
| (5) Not agreeable/agreeable | 0.79 | 0.59 | −0.97 | −0.81 |

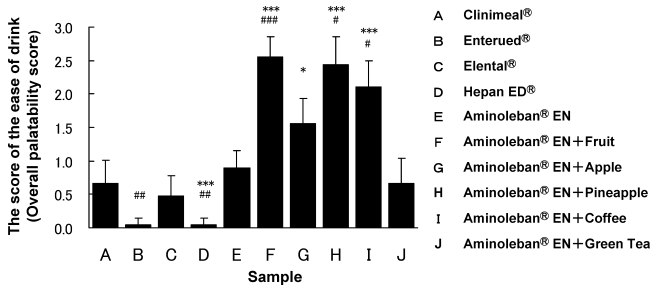


Fig. 2. The Overall Palatability Score (SD Method) of Various Enteral Nutrients

The data represents the mean of 9 values plus standard errors. Significantly different from the Clinimeal®, $*p<0.050$, $***p<0.005$. Significantly different from the Aminoleban®EN, $^{\#}p<0.050$, $^{\#\#}p<0.010$, $^{\#\#\#}p<0.005$.

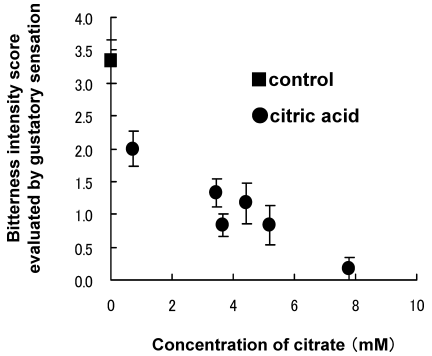


Fig. 3. The Additional Effect of Citric Acid on Obtained Bitterness Intensity

As an standard solution, the BCAA solution (L-Leu 77.65 mM, L-Ile 73.28 mM, L-Val 68.37 mM, L-Trp 1.80 mM) equivalent to an Aminoleban®EN was prepared and citric acid was added, as for bitterness was accepted, so that concentration became high. The data represents the mean of 9 values plus standard errors.

predicted by the sensor output values correlated well with the intensities obtained from the gustatory sensation tests. The regression equation $Y=0.746X+0.260$ ($r=0.864$, $p<0.005$) was obtained for sweetness, $Y=0.776X+0.234$ ($r=0.881$, $p<0.001$) for sourness, and $Y=0.718X+0.328$ ($r=0.847$, $p<0.005$) for bitterness. These results suggest that the taste sensor can predict the palatability of total enteral nutrients with sufficient accuracy. As shown in Fig. 4A, the product containing fruit-based flavours (Aminoleban®EN) showed comparatively high sweetness. As Aminoleban®EN without added flavour had far lower sweetness intensity, the three flavours must contain substances with comparatively strong sweetness.

Aminoleban®EN with fruit, apple, or pineapple flavours also had high sourness intensity, as shown in Fig. 4B. This reflects the fact that these three flavours contain sour substances (organic acids such as citric acids). As already men-

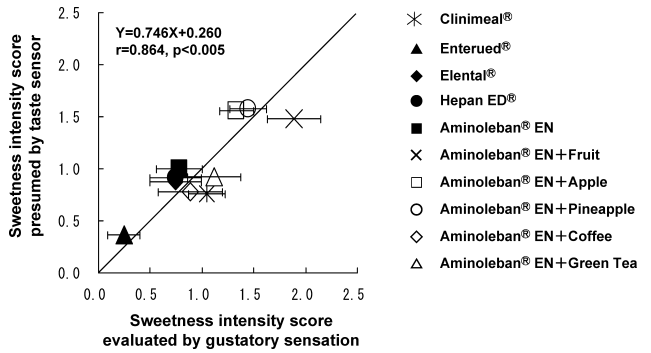


Fig. 4A. Correlationship between the Predicted Sweet Intensity by a Taste Sensor, and Observed Sweet Intensity by a Gustatory Sensation Test for Various Enteral Nutrients

The data represents the mean of 9 values plus standard errors.

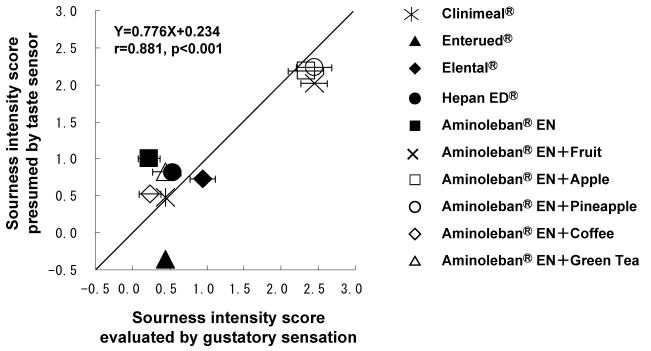


Fig. 4B. Correlationship between the Predicted Sourness Intensity by a Taste Sensor, and Observed Sourness Intensity by a Gustatory Sensation Test for Various Enteral Nutrients

The data represents the mean of 9 values plus standard errors.

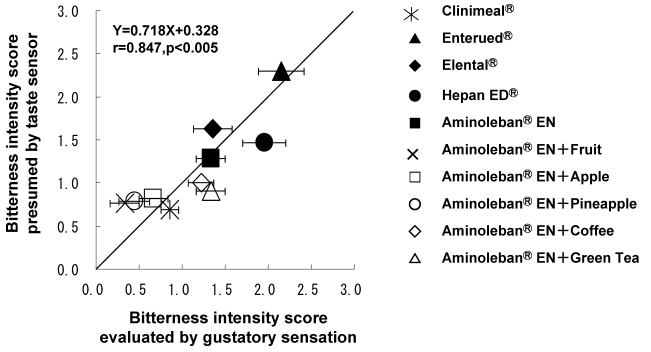


Fig. 4C. Correlationship between the Predicted Bitterness Intensity by a Taste Sensor, and Observed Bitterness Intensity by a Gustatory Sensation Test for Various Enteral Nutrients

The data represents the mean of 9 values plus standard errors.

tioned in Fig. 4, the acidity seems so effective in suppression of bitterness of BCAAs in nutrient.

Thus, both sweet and sour substances must be components of the flavours marketed with Aminoleban®EN, and the addition of these three flavours is effective in reducing the bitterness of the product as shown in Fig. 4C. The taste sensor was able to predict the sweetness or sourness of the products, sweetness or sourness being the critical factors in determining their overall palatability.

The palatability of coffee- or powdered-green-tea flavor was improved (as shown in Fig. 2) even though the intensity of "sweetness" and the "sourness" did not increased as shown in Fig. 4. We did not know the precise reason for it but the improvement in palatability is considered in relation to the preference or inclination of subjects. For example, the some people like beers or beverages with bitterness. Therefore the palatability of nutrient containing flavors depends on not only basic tastes but also on preference or inclination of subjects.

In this study, taste sensor was successfully in prediction of basic tastes of nutrients but not successfully in evaluation of the palatalibity of coffee flavor.

**Principal Component Analysis of the Total Enteral Nutrients by a Taste Sensor** As shown in Fig. 5A, the various enteral nutrients could be divided into three groups on the basis of principal component analysis using sensor output of 8 channels: peptide-based nutrients (PeBN), protein-based nutrients (PrBN), and amino-acid-based nutrients (AaBN). The addition of their associated flavours did not have a significant effect on the positions of Clinimeal® or Aminoleban®EN in this grouping. With Enterued®, although the addition of the coffee flavour moved the place of the product considerably, it remained within its group area.

Whereas as shown in Fig. 5B, the products could be also classified into four groups; PeBN, AaBN, and PrBN and flavor addition group by principal component analysis using sensor output data of channels 1, 3, 4 and 7, which are specific to basic tastes.

Thus, data from the taste sensor could also be used to discriminate between the four groups of products, without the necessity of performing laborious gustatory sensation tests with their inherent inter- and intra-subject variations. The sensor data seemed to be sufficiently accurate and reproducible to allow us to predict the palatability of total enteral nutrients, and the effects of adding various type of flavor to these products.

In conclusion, the following results were obtained from the present study.

(1) Four basic taste intensities (sweetness, saltiness, sourness, and bitterness), as well as 15 kinds of palatability scales, were evaluated according to the semantic differential (SD) method for enteral nutrient. The palatability item; difficult to drink/easy to drink, was adopted as an overall palatability since it shows the highest factor loading by factor analysis. The overall palatability was found to be highly positively correlated with sweetness and sourness, but negatively correlated with bitterness and saltiness.

(2) The addition of three flavours (fruit, apple, pineapple) to reduce bitterness exerts its effect by increasing both sourness and sweetness, and thereby improving overall palatability. The organic acids in the flavours are likely to be

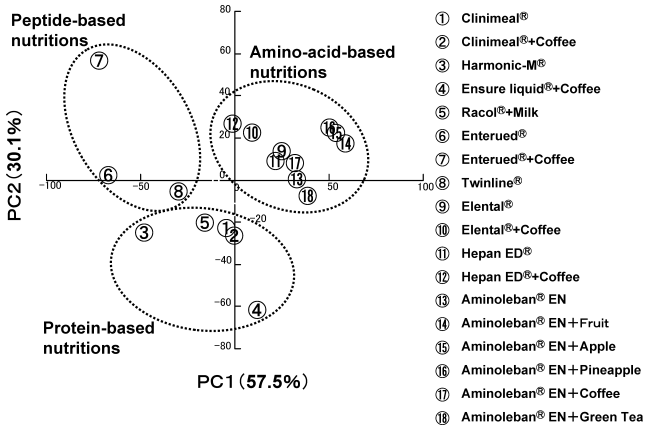


Fig. 5A. The Principal-Component-Analysis Result of the Various Enteral Nutrients Using the Output Value of a Taste Sensor (Using all Sensor Output Data)

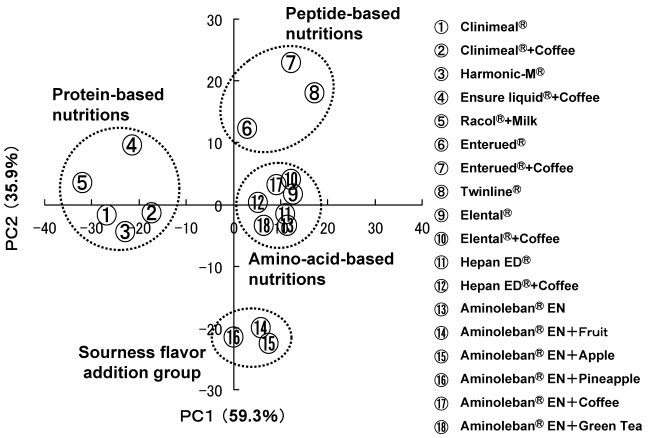


Fig. 5B. The Principal-Component-Analysis Result of the Various Enteral Nutrients Using the Output Value of a Taste Sensor (Using Sensor Output Data of Channels 1, 3, 4 and 7)

primarily responsible for this effect, at least in AaBNs, by reducing the bitterness intensity of BCAAs in the total enteral nutrients.

(3) A high correlation was found between the taste intensity values obtained in human gustatory sensation tests and the intensity scores for sweetness and sourness predicted by the taste sensor. It is postulated that the taste sensor could predict the overall palatability of a total enteral nutrients with good accuracy and repeatability.

(4) The products could be classified into three groups (peptide-based, amino-acid-based, and protein-based) by principal component analysis using all sensor output data. The products could be also classified into four groups; peptide-based, amino-acid-based, and protein-based and flavor addition group by principal component analysis using sensor output data of channels 1, 3, 4 and 7, which are specific to basic tastes.

Thus, prediction of taste or palatability of total enteral nutrients, alone or combination with flavours or other foods, might be possible using the taste sensor. This would facilitate attempts to improve the patient acceptability of total enteral nutrients.

**Acknowledgements** We thank Miss Yoshiko Kanemoto, Sonhi Kin, Ai Saiuchi, Emi Takeda, Emi Tokuyama, Miyuki Nakamura, Nozomi Miyatake,

and Kanako Watanabe for their assistance in sensor measurement. This work was supported by a grant-in-aid from the Ministry of Education, Science, Sports, Culture and Technology of Japan (No.15590146).

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