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The taste sensory evaluation of medicinal plants and Chinese medicines

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Abstract

The purpose of this study was to investigate the use of the artificial taste sensor in the evaluation of 11 medicinal plants and 10 Chinese medicines with bitter and/or astringent tastes, and to assess the possible application of the sensor in the evaluation of taste and quality control of medicinal products.

Aqueous extracts of the six bitter medicinal plants could be classified into three types, and those of the five astringent medicinal plants into two types, on the basis of sensor output pattern profiles. These differences seem to derive from the different structures of the main components.

In the principal component analysis of the taste sensor output of 10 Chinese medicines, a new measure developed, the 'Euclidean distance', defined as the distance between a control and the targeted substance on the principal component map. This measure offers a possibility for indicating the different tastes of Chinese medicines.

Lastly, we confirmed that berberine adsorption on the surface of the artificial membrane of the taste sensor was of the Langmuir type. The berberine content in extracts of medicinal plants could be evaluated by the taste sensor, and it was shown to be possible to use the taste sensor for the quality control of medicinal plants.

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Keywords: Taste sensor; Medicinal plants; Chinese medicine; Bitterness; Astringency; Berberine

1. Introduction

Medicinal plants and Chinese medicines have been available on the Japanese market for a long time. They have varied tastes (predominantly sweet, bitter, pungent, or astringent), some of which are particularly complex as they have several active constituents. Products which are predominantly bitter or astringent need to be taste-masked in order to improve compliance. To our knowledge, there has been no previous quantitative evaluation of the taste of medicinal plants or Chinese medicines.

The artificial taste sensor has already been used quite extensively to characterize the taste of foods or beverages such as beer, sake, green tea, etc. (Toko, 1998; Tan et al., 2001a,b; Taniguchi and Ikezaki, 2001; Kim et al., 2005). Up to now, there have been comparatively few applications of the taste sensor in the field of pharmaceutical development, although this is an area which is currently under examination (Legin et al., 2004). We have previously demonstrated the usefulness of the taste sensor in

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predicting the bitterness of a number of medicines (Miyanaga et al., 2002), and it has also been shown to be useful in the evaluation of bitterness suppression (Uchida et al., 2003).

In the present study, the application of the taste sensor was examined in the evaluation of the taste (bitterness or astringency) of extracted solutions of commercial medicinal plants and/or Chinese medicines. First, the taste sensor outputs for 11 typical medicinal plants included in Chinese products available on the Japanese market were examined. Principal component analysis was then carried out to distinguish between the bitter and/or astringent medicinal plants. Secondly, the sensor outputs of 10 Chinese medicinal products with bitter and/or astringent tastes were classified into one of two types: either Coptis Rhizome and/or Phellodendron Bark type or tannin type, using principal component analysis of the taste sensor output, with berberine and tannin solutions, respectively, as controls. The 'Euclidean distance', defined as the distance between control and targeted substances, was proposed as a new criterion to denote the taste of Chinese medicines. Thirdly, we looked at various concentrations and corresponding sensor outputs of solutions of berberine, the main component of a number of particularly bitter medicinal plants, such as Coptis Rhizome and Phellodendron Bark.

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Table 1A Medicinal plants used in the study

Crude drugs name	Family	
Gentian	Gentianaceae	
Swertiae Herb	Gentianaceae	
Bitter Orange Peel	Rutaceae	
Picrasma Wood	Simaroubaceae	
Coptis Rhizome	Ranunculaceae	
Phellodendron Bark	Ranunculaceae	
Geranii Herba	Geraniaceae	
Houttuynia Herb	Saururaceae	
Rhubarb	Polygonaceae	
Lupli Strobilus	Moraceae	
Chinese Nutgalls	Anacardiaceae	

Finally, the amounts of berberine in Coptis Rhizome and Phellodendron Bark from various locations were evaluated using both the taste sensor and HPLC, in an effort to evaluate the accuracy of the taste sensor data and its application in the quality control of medicinal plants.

2. Experimental

2.1. Materials

The bitter medicinal plants used in the study were Gentian, Swertiae Herb, Bitter Orange Peel, Picrasma Wood, Coptis Rhizoma, and Phellodendron Bark, while the astringent plants were Geranii Herb, Houttuynia Herb, Rhubarb, Lupli Strobilus and Chinese Nutgalls. The Chinese medicines used were Orengedokuto (three products), Unseiin (four products), and Akadama abdobt medicines (three products). Names and families of the medicinal plants and Chinese medicines used are listed in Tables 1A and 1B.

The medicinal plants were all purchased from Nippon Funmatsu Yakuhin Co. Ltd. (Osaka, Japan). Berberine chloride standard for crude drug testing was purchased from Wako Pure Chemical Industries (Osaka, Japan) and dissolved in 900 mL of hot water. The solution was made up to 1000 mL with cold water and this solution was diluted with 10 mmol/L KCl to obtain solutions of 0.003, 0.012, 0.031, 0.078, 0.201, 1.226, and 2.452 mmol/L. All other reagents were of special reagent grade.

Table 1B			
Chinese medicine	used in	the	study

Trade name	Chinese medicine	Company name	
0-1		А	
O-2	Orengedokuto	В	
O-3		С	
U-1		D	
U-2	Unseiin	В	
U-3		С	
U-4		А	
A-1	Akadama	Е	
A-2	abdomen	F	
A-3	medicines	G	

2.2. Preparation of sample solutions for taste sensor and HPLC analysis

Pulverized samples of each medicinal plant (about 0.2 g each, except for Coptis Rhizome and Phellodendron Bark, for which the sample size was about 0.05 g) were accurately weighed and placed in a beaker to which 90 mL of water was added. In the case of commercial Chinese medicines, 0.02 g packages of Orengedokuto and Unseiin, and 0.1 g package of Akadama abdobt medicine were used. In the case of pulverized Coptis Rhizome and Phellodendron Bark, about 0.05 g of each was used. The samples were stirred for 30 min using an agitator at room temperature, after which 5 mL of 0.2 mol/L KCl was added, and the suspension made up to exactly 100 mL with purified water. Amount of each medicinal plant for extraction was determined to keep quantitative analysis for sensor or HPLC. As an extraction time, 30 min was employed since in advance we tried 20, 30, 40, and 60 min extraction time and confirmed drug amount evaluated by sensor output or HPLC method became almost constant after over 30 min extraction (detail data not shown). In addition, water was employed as an extraction medium during the experiment, and solvent such as an alcohol might remove various components from artificial sensor and thereby cause damage in sensor characteristics. Fifty milliliters of the above extracted solution was used for sensor measurement and, after filtration through a membrane with 0.45-µm pore size, for HPLC.

The conditions for HPLC were essentially the same method as described in the evaluation of berberine in JPXV. The 20 µL of the prepared sample was injected onto a chromatograph (Shimadzu LC-10AT, Kyoto, Japan) equipped with an ultraviolet absorption photometer detector (Shimadzu SPD-10AV, Kyoto, Japan), an integrator (Shimadzu C-R6A, Kyoto, Japan) and a reversed-phase column (CAPCELL PAK C18, 4.6 mm × 250 mm i.d., Shiseido Co. Ltd., Tokyo, Japan). As mobile phase, 3.4 g of potassium dihydrogen phosphate and 1.7 g of sodium lauryl sulfate were dissolved in 1000 mL of a mixture of water and acetonitrile (1:1). The flow rate was adjusted so that the retention time for the berberine peak could be maintained at about 11 min. The wavelength was set at 345 nm. Standard deviations for the berberine peak area after five-time repeated experiments were within 1.5% as relative value and its reproducibility was almost the same level as defined in the JPXV.

2.3. Sensor measurement and data analysis

The taste-sensing system SA402 of Intelligent Sensor Technology Co. Ltd., Atsugi, Japan, was used in the study. The detecting sensor part of the equipment consists of five electrodes composed of lipid polymer membranes, whose components are shown in Table 2. The measurement procedure was the same as that described in a previous paper (Yoshikawa et al., 1994; Miyanaga et al., 2002; Uchida et al., 2003). The relative sensor output represents the difference $(V_s - V_r)$ between the potentials of the sample (V_s) and of the reference solution (V_r) . Fresh 30 mmol/L KCl solution containing 0.3 mmol/L tartaric acid (corresponding to saliva) was used as a reference sample and

Table 2 Lipids component used in this study

Channel	Lipids component	
1	Phosphoric acid di- <i>n</i> -decyl ester	
	Dioctyl phenyl-phosphate	
2	Phosphoric acid di-n-decyl ester	
	2-Nitrophenyl octyl ether	
3	Hexadecanoic acid	
	Dioctyl phenyl-phosphate	
4	Dioctyl phenyl-phosphate	
5	Tetradodecylammoniumbromide	
	Dioctyl phenyl-phosphate	

also to rinse the electrodes after each measurement. The measurement interval was set at 30 s, and electrodes were thoroughly rinsed after each measurement.

S-PLUS 2000J (Mathematical Systems, Inc., Tokyo, Japan) was used as calculation software for multiple regression

analysis. Principal component analysis was performed using five-channel data for the medicinal plants and Chinese medicines extracts.

2.4. Calculation of Euclidean distance

In general, the difference between the control and the targeted sample was calculated based on the Euclidean distance of sample A (control) and sample B according to the following equation:

$$\sqrt{(A1 - B1)^2 + (A2 - B2)^2} \tag{1}$$

where A1 is the first principal ingredient score of control, A2 the second principal ingredient score of control, B1 the first principal ingredient score of the sample, and B2 is the second principal ingredient score of the sample. We tried to use this value as a criterion for bitterness or astringency. In the actual calculation of the 'Euclidean distance' (defined as the distance between control

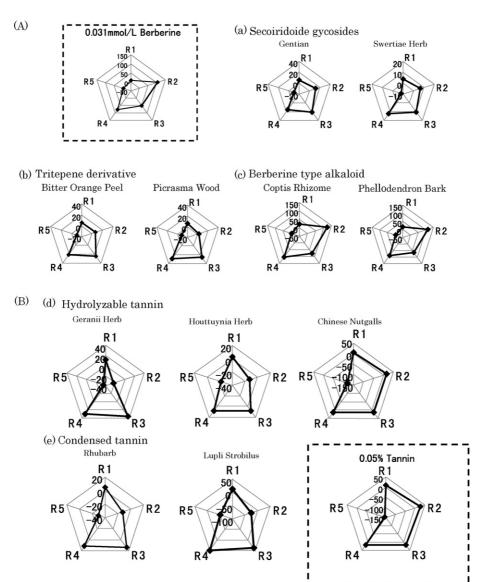


Fig. 1. (A) Sensor output profiles of six bitter and/or astringent medicinal plant extracts. The data of berberine is given as bitterness control. (B) Sensor output patterns of four astringent medicinal plants. The data of tannin is given as astringency control.

and the targeted substance), either 0.031 mmol/L of berberine or 0.05% of tannin was employed as control.

2.5. Relationship between concentration of berberine and sensor output

The sensor output value was plotted along the horizontal axis and the berberine concentration (0.003, 0.012, 0.031, 0.078, 0.201, 1.226, and 2.452 mmol/L) along the vertical axis. The correlation between the two sets of values was evaluated. The correlation between the reciprocal of the berberine concentration (horizontal axis) and the reciprocal of the sensor output value (vertical axis) was also examined.

3. Results and discussion

3.1. Sensor analysis of medicinal plant extracts

Fig. 1A shows the sensor output profiles for the six bitter medicinal plant extracts. These could be divided into three groups. The bitter tastes of Gentian and Swertiae Herb seemed due to their component secoiridoid glucosides (gentiopicnoside and swertiamarin, respectively). In Picrasma Wood and Bitter Orange Peel, the main components conferring a bitter taste are the triterpene derivatives, quassin and D-limonene, respectively, while the plants in the bitterest group, Coptis Rhizome and Phellodendron Bark, contain berberine-type alkaloids. The Coptis Rhizome and Phellodendron Bark extracts showed large output values in channel 2, which corresponds to bitterness.

The sensor output patterns of the five astringent medicinal plants could be divided into two groups, as shown in Fig. 1B. The most astringent showed a comparatively large response on channel 5, which contains tetradodecyl ammonium bromide in the sensor membrane, with positively charged tetra-ammonium ions. Our pilot study shows that relative value on channel 5 well-reflected gustatory sensation of astringency feeling (detail data not shown). The astringency of all five astringent medicinal plants appeared to be due to tannin derivatives: geraniin in Geranium Herb (Okabe et al., 2001), quercitrin in Houttuynia Herb (Fabjan et al., 2003), tannin in Chinese Nutgalls, rhatannin in Rhubarb (Yokozawa et al., 1991), and xanthohumol in Strobilus (Wang et al., 2004). Iiyama et al. (1994) have performed a brief evaluation of the astringency of gallic acid, using tannin as control. Even in the present study, tannin was used as astringent control.

As shown in Fig. 2, principal component analysis was used to estimate the largest and second largest relative contribution factors (PC1 and PC2) from the sensor data. The relative contributions of PC1 and PC2 are 69% and 18%, respectively, with the two axes indicating bitterness and astringency, respectively. The data for different concentrations of quinine and tannin solutions (bitterness and astringency controls, respectively) are also shown in Fig. 2. The six medicinal plants said to show bitterness were located between the low and high concentrations of quinine solution. The data for Coptis Rhizome and Phellodendron Bark were located close to the most concentrated quinine solution. It is suggested that the extracts of Coptis Rhizome and

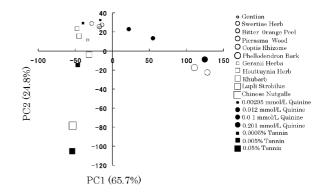


Fig. 2. Principal component analysis using data from 11 medicinal plants. The largest and second largest relative contribution factors, PC1 and PC2, from all the sensor data. The relative contributions of PC1 and PC2 are 69% and 18%, respectively, and *x* and *y* axes represent bitterness and astringency, respectively.

Phellodendron Bark mainly contained berberine, which has a bitterness intensity similar to that of quinine.

The four astringent medicinal plants were close to the lower tannin concentration, indicating that the taste of the extracts is similar to that of low concentrations of tannin solution.

Since the medicinal samples used here were the complex mixture of various compounds such as alkaloids, other nitrogen containing compounds, and flavonoids, we have to examine their response to the present sensor and develop the specific sensors responsive to those components in near future.

3.2. Sensor analysis of Chinese medicine extracts

3.2.1. Sensor output profiles of Chinese medicines

Sensor output profiles for extracts of the 10 Chinese medicines (three Orengedokuto products, O-1, O-2, & O-3; four Unseiin products, U-1, U-2, U-3, & U-4; and two Akadama abdobt products, A-1 & A-2) are shown in Fig. 3. The sensor patterns of the Orengedokuto and Unseiin products, which contain Coptis Rhizoma and Phellodendron Bark, were very similar to that of berberine, as expected, berberine being the main component of Coptis Rhizoma and Phellodendron Bark. The Akadama abdobt products A-1 & A-2 contain Chinese Nutgalls, which are very astringent; sensor output profiles of these two products were similar to that of tannin. The sensor profile of A-3, which contains Geranii Herba in addition to Coptis Rhizoma, and Phellodendron Bark, was slightly different from those of A-1 & A-2, being less bitter and astringent.

3.2.2. Principal component analysis for Chinese medicines

Fig. 4 shows the principal component analysis using data from the above 10 Chinese medicines. The largest and second largest relative contribution factors, PC1 and PC2, had relative contributions of 69% and 18%, respectively, and the axis of PC1 almost coincided with the calibration curve of berberine (0.003 mmol/L, 0.031 mmol/L, 0.201 mmol/L). Orengedokuto (O-1, O-2, and O-3) and Unseiin (U-1, U-2, U-3, U-4) products, which contain berberine, were all directly located on the calibration curve of berberine. Therefore, the bitterness intensity of these seven samples can be calculated from the bitterness intensity of berberine in human gustatory sensation results. The data

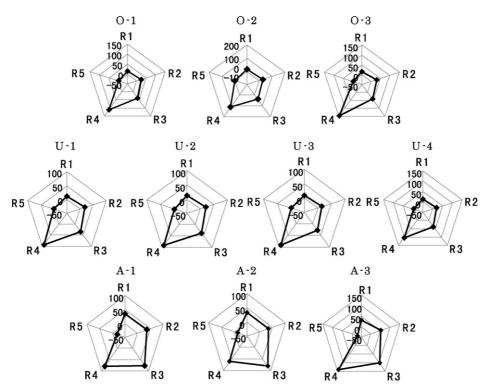


Fig. 3. Sensor output profile for extracts of three kinds of Chinese medicine (10 products).

suggest that the bitterness of the O-3 extract was greater than that of both O-1 and O-2, which might suggest a difference in the berberine content.

The location of the various concentrations of tannin solution increased along the berberine axis as the concentration of tannin increased. The two products (A-1 & A-2) which contained Chinese Nutgalls, were located very close to the standard tannin solutions and were therefore likely to be strongly bitter. A-3, which contained Geranii Herba, was located between berberine and tannin.

3.2.3. Use of 'Euclidean distance' in analysis of Chinese medicine extracts

As mentioned above, the sensor output patterns of the 10 bitter and/or astringent Chinese medicinal products could be classified into two types, Coptis Rhizome and/or Phellodendron Bark type, and tannin type. In the principal component analysis

0.2 0-3 U-1 U-211.3U-4 A-1 PC2(17.9%) A-2 A-3 0.00295 mmol/L Quinine -100 -50 150 -20 0.012 mmol/L Quinine 0.031 mmol/L Quinine 0.00295 mmol/L Berberine 0.012 mmol/L Berberin 0.031 mmol/L Berberine 0.0005% Tannir 0.005% Tannin -80 0.05% Tannir PC1 (69.4%)

Fig. 4. Principal component analysis using data from 10 Chinese medicines to estimate the largest and second largest relative contributions.

of the taste sensor output of these Chinese medicines, we measured the 'Euclidean distance' (the distance between control and the targeted sample in the principal component map), and evaluated the possibility of using this as a measure of the different tastes of Chinese medicines.

In the calculation of the 'Euclidean distance', the bitterness and astringency control points were taken as 0.031 mM berberine and 0.05% tannin acid, respectively. The calculated 'Euclidean distances' between the test samples and controls are summarized in Table 3. Coptis Rhizome and/or Phellodendron Bark extracts show comparatively small 'Euclidean distances' which means their taste resembles that of the control (0.031 mmol/L berberine), that is, quite bitter. In the previous section, it was shown that the bitterness intensity of O-3 was greater than that of O-1 or O-2. This was confirmed by the

Table 3	
Euclidean distance for analysis of 10 Chinese medicines	

	Euclidean distance		
	0.031 mmol/L Berberine	0.05% Tannin	
0-1	105.6	85.0	
O-2	104.1	84.0	
O-3	67.8	105.0	
U-1	127.1	84.6	
U-2	129.2	78.4	
U-3	132.0	87.8	
U-4	115.9	84.0	
A-1	144.8	36.9	
A-2	160.8	40.4	
A-3	92.3	66.9	

'Euclidean distance' of O-3 (67.8), being appreciably less than those of O-1 (105.6) and O-2 (104.1).

In the case of the 'Euclidean distance' for astringency, values of 36.9 and 40.4 were calculated for A-1 and A-2, respectively (distance between samples and control 0.05% tannin), while 66.9 was obtained for A-3, which contains less Chinese Nutgalls than A-1 and A-2, indicating that the astringency of A-3 is expected to be less than that of A-1 or A-2. In the map of principal component analysis, A-3 is located between the 0.031 mmol/L berberine and 0.05% tannin solutions.

In the case of the Unseiin products, the 'Euclidean distance' values for bitterness of U-1, U-2, U-3, and U-4 (127.1, 129.2, 132.0, and 115.9, respectively) were larger than those of O-1, O-2, and O-3 (106.5, 104.1, and 67.8, respectively), indicating that the bitterness intensity of the Unseiin products is expected to be less than that of Orengedokuto products. The 'Euclidean distance' values for astringency were about the same for both Unseiin and Orengedokuto products, which indicate that the astringency of two groups is similar.

3.3. Relationship between concentration of berberine and sensor output value

The relationship between the concentration of berberine and the sensor output value of channel 2 was examined using berberine solutions of 0.003, 0.012, 0.031, 0.078, 0.201, 1.226, and 2.45 mmol/L. The following scheme was used to describe the binding of berberine to the taste sensor membrane with constant surface area.

If the interaction between a group or free receptor P in a sensor membrane and a berberine molecule D is written

$$P + D = PD \tag{1'}$$

The equilibrium constant K is written

$$K = \frac{[\text{PD}]}{[\text{P}][\text{D}]} \tag{2}$$

where K is the association constant, [P] is the free receptor concentration in the sensor membrane, [D] the concentration of berberine, and [PD] is the concentration of the receptor-berberine complex.

If the total sensor membrane is designated [Pt], we can write

[Pt] = [P] + [PD]

or

$$[P] = [Pt] - [PD] \tag{3}$$

Substituting the expression for [P] from Eq. (3) to Eq. (2) gives

$$[PD] = K[D]([Pt] - [PD])$$

$$\tag{4}$$

[PD] + K[D][PD] = K[D][Pt](5)

$$\frac{[\text{PD}]}{[\text{Pt}]} = \frac{K[\text{D}]}{1 + K[\text{D}]} \tag{6}$$

If *r* is the number of moles of berberine bound [PD] per mole of total free receptor concentration on the membrane [Pt], then r = [PD]/[Pt] or

$$r = \frac{K[D]}{1 + K[D]} \tag{7}$$

The ratio r may also be expressed in other dimensions, such as mM of berberine bound per x mM of receptor concentration y. Eq. (7) is one form of the Langmuir adsorption isotherm.

Although it is quite useful for expressing berberine binding data, the use of this formula does not necessarily require that receptor binding be an adsorption phenomenon. Expression (7) can be converted to a linear form, convenient for plotting, by inverting it

$$\frac{1}{r} = \frac{1}{K[D]} + 1$$
 (8)

If v independent binding sites are available, the expression for r, Eq. (7), is simply v times that for a single site or

$$r = v \frac{K[D]}{1 + K[D]} \tag{9}$$

and Eq. (8) becomes

$$\frac{1}{r} = \frac{1}{vK} \frac{1}{[D]} + \frac{1}{v}$$
(10)

An alternative manner of writing Eq. (9) is to rearrange it first to

$$r + rK[D] = vK[D] \tag{11}$$

and subsequently to

$$\frac{r}{[D]} = vK - rK \tag{12}$$

Data presented according to Eq. (12) is known as a Langmuir plot. Although the above model and corresponding equations have previously been used in the field of protein binding, they may also be suitable for use in the case of drug-sensor membrane binding.

As shown in Fig. 5A, the maximum sensor value of the vertical axis corresponds to the maximum number of theoretical bound sites per unit area, if the adsorption is of the Langmuir type. Toko et al. demonstrated a linear relationship between the concentration of electrolytes and corresponding sensor potential in the range of 0.05–300 mV membrane potential, which means there is no saturation of the measurement capacity in this range (Shimakawa et al., 2004). We also confirmed that there was no saturation of the sensor potential when various concentrations of amino acid solutions were used (unpublished data).

As shown in Fig. 5B, good linearity was obtained between the reciprocal of the concentration of berberine, and the reciprocal of the sensor output value [y=0.00011x+0.0054 (r=0.992)].

In relation to the value of v obtained in the present study, we have stated that the maximum vertical axis value in Fig. 5A represents the maximum number of theoretical drug binding sites available. In fact, we actually observed the electric potential

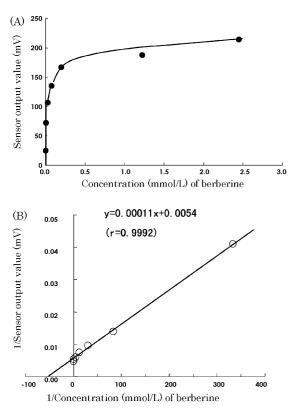


Fig. 5. (A) The relation between sensor output (mV) and various concentrations of berberine (mmol/L). The data indicates Langmuir adsorption. (B) The relation between the reciprocal of the berberine concentration and the reciprocal of the sensor output value.

rather than the theoretical bound sites per unit area on the sensor membrane. In the present study, v = 185.3 mV was obtained from the intercept of the reciprocal graph of Fig. 5B. This might suggest that we have to be able to detect berberine concentrations at much lower levels than 185.3 mV, in other words, in the unsaturated area.

3.4. The possible use of the taste sensor in quality control of medicinal plants

The possibility of quantitative determination of berberine in Coptis Rhizome and Phellodendron Bark from different locations was examined. Fig. 6 shows the sensor response pattern of channels 1-5 for three kinds of Coptis Rhizoma (C-1, China (Hubei); C-2, Japan (Fukui); C-3, China (Sichuan)) and three kinds of Phellodendron Bark (P-1, Japan (Tokushima); P-2, China (Hunan); P-3, China (Sichuan)) using the taste sensor. In this study, we used 0.031 mmol/L berberine as standard. Although there were differences in sensor output values of Coptis Rhizome and Phellodendron Bark from different locations, the sensor response patterns of the sensor were similar in all cases, and the output value of channel 2 showed the highest value in every case. The results suggest that the berberine content of Coptis Rhizome and Phellodendron Bark could be predicted by the sensor output value of channel 2. We then tried to draw a calibration curve using the relation between the sensor output value and the concentration of berberine. The relationship

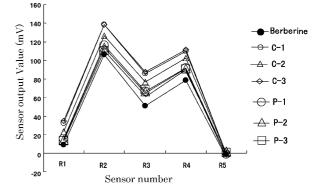


Fig. 6. Sensor response pattern of channels 1–5 for six different samples of Chinese medicine. Coptis Rhizoma (C-1, C-2, C-3); Phellodendron Bark (P-1, P-2, P-3).

between the logarithmic value of the concentration of berberine (0.003, 0.012, 0.031, 0.078, and 0.201 mmol/L) and taste sensor output value was shown to be linear (Fig. 7), represented by the straight line: x = 0.013 (R2) – 2.85 (r = 0.9998), where the y axis is the taste sensor output value (R2 represents the relative value of channel 2) and the x axis is the logarithmic value of the concentration of berberine (mmol/L).

The berberine content of Coptis Rhizome and Phellodendron Bark samples from six different areas was measured using both the taste sensor and an HPLC method. The results are shown in Table 4. Coptis Rhizome was found to contain about twice as much berberine as Phellodendron Bark, but there were not large differences among berberine contents for samples of plants taken from different locations. The berberine contents evaluated by the taste sensor were almost same as those evaluated by HPLC. This suggests that it is possible to predict the berberine content of Coptis Rhizome and Phellodendron Bark using the taste sensor.

As mentioned above, the use of the taste sensor in quality control screening would allow the rapid evaluation of many samples in a single run. The taste sensor seems therefore to be a

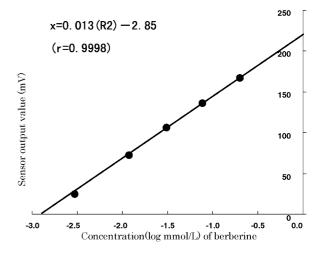


Fig. 7. The relationship between the logarithmic value of the concentration of berberine (0.003, 0.012, 0.031, 0.078, and 0.201 mmol/L) and taste sensor output value (*R*2, relative value of channel 2). The *y*-axis gives the taste sensor output value of channel 2, and the *x*-axis value gives the logarithmic value of the concentration of berberine (mmol/L).

Contents of Berberine-type alkaloid in	n Coptis Rhizoma and Phe	llodendron Bark using HPLC and taste sensor	
Name of medicinal plant	Lot no.	The place of production	Contents

Name of medicinal plant	Lot no.	The place of production	Contents (mmol/L)	
			HPLC	Taste sensor
Coptis Rhizome	C-1	China (HUBEI)	0.090 (0.001)	0.088 (0.002)
-	C-2	Japan (Fukui)	0.072 (0.002)	0.069 (0.002)
	C-3	China (SICHUAN)	0.113 (0.002)	0.109 (0.003)
Phellodendron Bark	P-1	Japan (Tokushima)	0.039 (0.001)	0.042 (0.001)
	P-2	China (HUNAN)	0.041 (0.000)	0.041 (0.001)
	P-3	China (SICHUAN)	0.041 (0.001)	0.040 (0.001)

The contents were represented as the mean value and standard deviation in parenthesis (n = 5).

useful tool, not only for discriminating between many kinds of medicinal plants but also for their quantitative evaluation. There are, however, some problems to be overcome. The taste sensor used in the present study could not recognize differences in the chirality of substances such as *R*- and *S*-phenylalanine. However, Chibvongodze et al., 2001 recently developed a taste sensor with stereoselectivity. In their article, changes in the membrane impedance of optically active membranes due to interactions between amino acids and the membrane were used successfully to discriminate between D- and L-amino acids. Recently, Marx et al. (2004) have developed a highly selective and sensitive sensor, based on molecularly imprinted sol–gel films. Thus, it is possible to improve the sensitivity and specificity of the sensor membrane to allow accurate quality control of different kinds of medicinal plants.

4. Conclusions

T-1-1- 4

Eleven medicinal plants could be classified into two groups (bitter and astringent products) using principal component analysis of taste sensor data from aqueous plant extracts. The six bitter-tasting medicinal plants could be further divided into three groups on the basis of the type of compound to which they owed their bitterness: group 1, secoiridoid glucosides (Gentian, Swertiae Herb); group 2, deformed triterpene derivatives (Bitter Orange Peel, Picrasma Wood); and group 3, berberine-type alkaloids (Coptis Rhizome, Phellodendron Bark). The five astringent medicinal plants could be divided into two groups on the basis of the principal component analysis of taste sensor data.

Ten Chinese medicines could be classified into two groups (bitter Coptis Rhizome and/or Phellodendron Bark type and astringent tannin-type products) using principal component analysis of taste sensor data from aqueous plant extracts. On principal component analysis of the taste sensor output, the seven bitter products were located close to the standard berberine solutions, while the two products which contained Chinese Nutgalls were located close to the standard tannin solutions. Thus, in the present study, the new measure 'Euclidean distance', seems to be able to distinguish between the tastes of different Chinese medicines with respect to bitterness and astringency.

The relation between the concentration of berberine and the sensor output value of channel 2 of the taste sensor (bitterness) was shown to resemble Langmuir-type adsorption, more berberine being adsorbed on the sensor membrane as the concentration of berberine increased.

Prediction of the berberine content of Coptis Rhizome and Phellodendron Bark samples was possible using the output value of channel 2 of the taste sensor as well as by HPLC. There were no significant differences between the berberine content of various aqueous extracts of these medicinal plants when evaluated by either method.

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References

- Chibvongodze, H., Hayashi, K., Toko, K., 2001. Discrimination of D-amino acids from L-amino acids using electric potential changes of a membrane. Sens. Mater. 13, 99–108.
- Fabjan, N., Rode, J., Kosir, I.J., Wang, Z., Zhang, Z., Kreft, I., 2003. Tartary buckwheat (*Fagopyrum tataricum* Gaertn.) as a source of dietary rutin and quercitrin. J. Agric. Food Chem. 72, 6452–6455.
- Iiyama, S., Toko, K., Matsuno, T., Yamafuji, K., 1994. Responses of lipid membranes of taste sensor to astringent and pungent substances. Chem. Senses 19, 87–96.
- Kim, N., Park, K.R., Park, I.S., Cho, Y.J., Bae, Y.M., 2005. Application of a taste evaluation system to the monitoring of Kimchi fermentation. Biosens. Bioelectron. 20, 2283–2291.
- Legin, A., Rudnitskaya, A., Clapham, D., Seleznev, B., Lord, K., Vlasov, Y., 2004. Electronic tongue for pharmaceutical analytics: quantification of tastes and masking effects. Anal. Bioanal. Chem. 380, 36–45.
- Marx, S., Zaltsman, A., Turyan, I., Mandler, D., 2004. Parathion sensor based on molecularly imprinted sol–gel films. Anal. Chem. 76, 120–126.
- Miyanaga, Y., Tanigake, A., Nakamura, T., Kobayashi, Y., Ikezaki, H., Taniguchi, A., Matsuyama, K., Uchida, T., 2002. Prediction of bitterness of single-, binary- and multiple-component amino acid solutions using a taste sensor. Int. J. Pharm. 248, 207–218.
- Okabe, S., Suganuma, M., Imayoshi, Y., Taniguchi, S., Yoshida, T., 2001. New TNF-α releasing inhibitors, geraniin and corilagin, in leaves of Acer nikoense, Megusurino-ki. Biol. Pharm. Bull. 24, 1145–1148.
- Shimakawa, H., Habara, M., Toko, K., 2004. Bitterness-masking effect of phospholipids on lipid/polymer membranes. Sens. Mater. 16, 301–307.
- Tan, T., Schmitt, V., Isz, S., 2001a. Electronic tongue: a new dimension in sensory analysis. Food Technol. 55, 44–50.
- Tan, T., Schmitt, V., Isz, S., Saint Martin, E., 2001b. The electronic tongue; a time-saving tool for off-taste detection, bitterness masking study and gold

reference assessment in the beverage industries. Eur. Food Drink Rev. 3, 65–75.

- Taniguchi, A., Ikezaki, H., 2001. The taste sensor. FFI J. 193, 47-56.
- Toko, K., 1998. Electronic tongue. Biosens. Bioelectron. 13, 701-709.
- Uchida, T., Tanigake, A., Miyanaga, Y., Matsuyama, K., Kunimoto, M., Kobayashi, Y., Ikezaki, H., Taniguchi, A., 2003. Evaluation of the bitterness of antibiotics using a taste sensor. J. Pharm. Pharmacol. 55, 1479–1485.
- Yokozawa, T., Fujioka, K., Oura, H., Nonaka, G., Nishioka, I., 1991. Effects of rhubarb tannins on uremic toxins. Nephron 58, 155–160.
- Yoshikawa, M., Yamaguchi, S., Kunimi, K., Matsuda, H., Okuno, Y., Yamahara, J., Murakami, N., 1994. Stomachic principles in ginger. III. An anti-ulcer principle, 6-gingesulfonic acid, and three monoacyldigalactosylglycerols, gingerglycolipids A, B, and C, from Zingiberis Rhizoma originating in Taiwan. Chem. Pharm. Bull. 42, 1226–1230.
- Wang, Q., Ding, Z.H., Lin, J.K., Zheng, Y.T., 2004. Xanthohumol, a novel anti-HIV-1 agent purified from Hops Humulus lupulus. Antiviral Res. 64, 189–194.