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Research Paper

Evaluation of palatability of 10 commercial amlodipine orally disintegrating tablets by gustatory sensation testing, OD-mate as a new disintegration apparatus and the artificial taste sensor

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Keywords
amlodipine; bitterness; disintegration method for orally disintegrating tablet; gustatory sensation test; taste sensor

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Abstract

Objectives The purpose of this study was to evaluate and compare the palatability of 10 formulations (the original manufacturer's formulation and nine generics) of amlodipine orally disintegrating tablets (ODTs) by means of human gustatory sensation testing, disintegration/dissolution testing and the evaluation of bitterness intensity using a taste sensor.

Methods Initially, the palatability, dissolution and bitterness intensity of the ODTs were evaluated in gustatory sensation tests. Second, the disintegration times of the ODTs were measured using the OD-mate, a newly developed apparatus for measuring the disintegration of ODTs, and lastly, the bitterness intensities were evaluated using an artificial taste sensor.

Key findings Using factor analysis, the factors most affecting the palatability of amlodipine ODTs were found to be disintegration and taste. There was high correlation between the disintegration times of the 10 amlodipine ODTs estimated in human gustatory testing and those found using the OD-mate. The bitterness intensities of amlodipine ODTs 10, 20 and 30 s after starting the conventional brief dissolution test and the values determined by the taste sensor were highly correlated with the bitterness intensities determined in gustatory sensation testing.

Conclusions The OD-mate and the taste sensor may be useful for predicting the disintegration and bitterness intensity of amlodipine ODTs in the mouth.

Introduction

Amlodipine is a member of the 1,4-dihydropyridine class of antihypertensive drugs used in the treatment of hypertension and angina. It acts as a calcium antagonist and inhibits the transmembrane influx of calcium ions into vascular smooth muscles and cardiac muscles, which in turn affects their contractile process and results in reduced blood pressure.[1] Amlodipine is the most commonly used antihypertensive in the world.

Amlodipine orally disintegrating tablets (ODTs) were the most popular ODTs on the Japanese market, and currently, after expiry of the patent, 23 generic forms of this product have been introduced. ODTs are often prescribed for older people and children whose swallowing abilities are poor, as they disintegrate easily in the mouth without the need for additional water.[2] The convenience of ODTs is appreciated by both patients and medical staff, and the number of ODT products will undoubtedly increase in the future.[3–5]

When ODTs disintegrate in the mouth, the concentration of dissolved drug is greater than that found when conventional tablets are held in the mouth. Thus, taste-masking is an important issue for ODTs. Although some characterization of generic ODT products has been reported previously,[6–8] articles in which the palatability of the original and generic products are compared are few,[9,10] and the

palatabilities of the original and generic formulations of amlodipine ODT have not previously been compared.

The palatability of a medicine is an important factor in determining compliance. The equivalent concentration testing method and semantic differential (SD) method are representative methods that have been used in the evaluation of palatability scores determined in gustatory sensation testing. Moreover, factor analysis (a factor axis rotated using a varimax method) of data obtained by the SD method has been performed to extract the factors contributing to the palatabilty of medicine.[11,12]

The disintegration time of an ODT is suggested to be a factor determining its palatability. Of the three main pharmacopoeias, that is the Japanese Pharmacopeia (JP), United States Pharmacopeia (USP), and European Pharmacopeia (EP), the EP has categorized orodispersible tablets as tablets, which disintegrate in less than 3 min as determined by a conventional test.[13] More recently, in the USP, ODTs are defined as solid oral preparations that disintegrate rapidly in the oral cavity, with an *in vitro* disintegration time of approximately 30 s or less, as determined by the USP disintegration test.[14] The JP has not yet defined a disintegration test for ODT. The OD-mate is one of several disintegration devices for ODTs on the market.[5,15–17] In the evaluation of the *in vitro* oral disintegration time was also measured using the OD-mate, an ODT is placed on a trapezoidal mesh in a flat-bottomed test tube corresponding to the tongue and compressed by two weights corresponding to the upper palate of OD-mate. The measurement was started immediately the test tube contacted the test media, and the time taken for the tablet to completely disintegrate was recorded. OD-mate permits the adjustment of volume of the test media. The disintegration of ODTs is expected to relate the quantity of salivation. The quantity of salivation is affected by disease state, age of patient and so on. It has an advantage over other devices in the adjustment of volume of the test media and can simulate the environment of the oral cavity more practically. The OD-mate was used for measuring the disintegration time of ODTs in this study.

Bitterness, a major factor affecting palatability, is also known to decrease patient compliance. Evaluations of the bitterness of medicines in human sensation tests[18] using cell culture[19] or using the taste sensor[20] have been reported previously. We evaluated the bitterness of berberine, an herbal medicine that is extremely bitter, using the equivalent concentration testing method and gustatory sensation tests in a previous paper.[12]

Taste plays an important role in the development of a pharmaceutical formulation. Many active pharmaceutical ingredients exhibit an unpleasant taste, so taste-masking has become increasingly important. The use of an 'electronic tongue' or taste sensor for pharmaceutical purposes is an important step forward, as it reduces dependence on human gustatory sensation testing. The taste sensor is an analytical sensor array system that is able to detect specific substances by means of different artificial membranes using electrochemical techniques. We have evaluated the bitterness of various pharmaceutical products using taste sensors.[20–25] The bitterness intensities of amlodipine ODTs were evaluated both in human gustatory testing and using the taste sensor in this study.

The aims of this study were therefore to compare the original and nine generic versions of amlodipine ODT with respect to palatability in human gustatory sensation tests, disintegration time using the OD-mate and bitterness intensity using an artificial taste sensor. The novelty of this study is to show the possibilities of predicting the disintegration and the bitterness intensity, both of factors in palatability, of amlodipine ODTs using the disintegration device and the artificial taste sensor.

Materials and Methods

Materials

Ten different 5-mg ODTs containing amlodipine as active ingredient were used in this study: the original product, Amlodine® OD (Dainippon Sumitomo Pharma Co., Ltd, Osaka, Japan) identified as product A, and the following nine generic products: amlodipine OD (Takata Seiyaku Co., Ltd, Tokyo, Japan), amlodipine OD tablets 5 mg 'KRM' (Kyorin Rimedio Co., Ltd, Tokyo, Japan), amlodipine OD (Nichi-Iko Pharmaceutical Co., Ltd, Toyama, Japan), amlodipine OD tablets 5 mg 'Towa' (Towa Pharmaceutical Co., Ltd, Osaka, Japan), amlodipine (Tava Pharma Japan, Inc., Aichi, Japan), amlodipine (Sawai Pharmaceutical Co., Ltd, Osaka, Japan), amlodipine OD tablets 5 mg 'Meiji' (Meiji Seika Pharma Co., Ltd, Tokyo, Japan), amlodipine tablets (Nipro Pharma Corporation, Osaka, Japan), amlodipine (Kyowa Pharmaceutical Industry Co., Ltd, Osaka, Japan). The nine generic products were randomly assigned letters B to J.

Quinine hydrochloride was purchased from Sigma Chemical Co. (St. Louis, MO, USA). All other reagents were special reagent grade.

Gustatory sensation tests

Gustatory sensation testing

The protocol and experimental design for all gustatory sensation tests was approved in advance by the ethical committee of Mukogawa Women's University. Six healthy female subjects, 26 ± 9 years old, participated in the sensation tests in which various tastes and textures were evaluated. No subject reported having a cold or other respiratory tract infection in the week before testing. The subjects were asked

to refrain from eating, drinking or chewing gum for at least 1 h before testing. All subjects were non-smokers and signed an informed consent before the experiments. The experimental protocol was approved in advance by the ethical committee of Mukogawa Women's University. The experimental protocol of this study (No. 09–33) was approved on 15 December 2009 by the ethical committee of Mukogawa Women's University.

The gustatory sensation test to measure bitterness intensity was performed with six well-trained volunteers according to a previously described method,[11,12,20–25] using quinine hydrochloride at concentrations of 0.01, 0.03, 0.10, 0.30 and 1.0 mM as a standard for bitterness. Scores of 0, 1, 2, 3 and 4 were allocated to the increasing concentrations of the standard solution. Before testing, the volunteers were asked to keep the abovementioned standard quinine solutions in their mouths and were told the concentration and bitterness score of each solution. They were then asked to give each of the amlodipine ODT samples bitterness scores. Each sample was kept in the mouth and the bitterness evaluated after 10, 20 and 30 s. The disintegration time of the ODT in the mouth was determined. The palatability of each ODT (in the mouth and after splitting out) was also evaluated. After tasting each sample, subjects gargled well and waited for at least 20 min before tasting the next sample.

Evaluation using the SD method

The palatability scores were evaluated by the SD method as follows:[9] the subjects were asked to score the samples on the basis of 24 items in five groups, expressed in symmetrical terms representing both extremities of the item, as follows:

Before putting in mouth: (1) small tablet/large tablet, (2) easy to take tablet out of packaging/difficult to take tablet out of packaging, (3) good smell/bad smell, (4) good colour/bad colour.

Just after putting in mouth: (5) smooth before disintegration/rough before disintegration, (6) smooth after disintegration /rough after disintegration, (7) easy to make disappear/difficult to make disappear.

Thirty seconds after holding in mouth: (8) strong bitterness/weak bitterness, (9) strong sweetness/weak sweetness, (10) good taste/bad taste, (11) strong astringency/weak astringency, (12) powder-like/not powder-like, (13) pulp-like/not pulp-like, (14) bubble-like/not bubble-like, (15) cool sensation/not cool sensation, (16) sticky/watery.

After a gargling: (17) feel aftertaste/not feel aftertaste, (18) good aftertaste/bad aftertaste, (19) bitter aftertaste/not bitter aftertaste, (20) sweet aftertaste/not sweet aftertaste, (21) cool sensation/not cool sensation, (22) smooth/rough.

General impression: (23) hope to take this tablet again/not hope to take tablet again, (24) favourable/not favourable. The items were scored on the following rating scale: 1, extremely; 2, slightly; 3, neither; 4, slightly; 5, extremely.

The in vivo *disintegration time*

The *in vivo* disintegration time of the 10 ODTs was determined by six well-trained volunteers. Before testing, the volunteers were asked to rinse their mouths with a cup of water, and then an ODT was placed on the tongue. They were allowed to move the tablet freely on the tongue, although they were not allowed to chew it. The time taken for all the noticeable granules or fragments to disintegrate was measured with a chronometer. The swallowing of saliva was prohibited during the test, and saliva was rinsed out after each test.

Disintegration testing

Conventional method

Disintegration time was measured with a conventional disintegration tester (HM-21D, Riken's disintegration tester, Miyakomo Riken Ind., Co., Ltd, Osaka, Japan) according to the Japanese Pharmacopoeia, XVIth edition (JP16). The test media was 900 ml purified water at 37°C. The test was conducted with six tablets, and the average measurement was taken as the disintegration time.

Using the OD-mate

The *in vitro* oral disintegration time was also measured using the OD-mate (Model IMC-14D1, Higuchi Inc., Tokyo, Japan). The OD-mate is a unique disintegration testing device intended to simulate the disintegration time of an ODT in the human oral cavity.[17] An ODT is placed on a trapezoidal mesh in a flat-bottomed test tube corresponding to the tongue and compressed by two weights (30 g inner weight and 100 g outer weight) corresponding to the upper palate. The test media was 20 ml of purified water at 37°C. The measurement was started immediately, the test tube contacted the water, and the time taken for the tablet to completely disintegrate (the time taken for the inner weight to reach the test tube) was recorded. The experiment was conducted six times, and the average was taken as the *in vitro* oral disintegration time of the ODT.

The brief conventional dissolution test

The brief conventional dissolution test is reported to have a closer relation to the dissolution of a tablet in the mouth than the dissolution test described in JP16.[26] The brief conventional dissolution test was performed as follows: Ten tablets were placed in a stainless-steel basket (diameter 20 mm, depth 30 mm) that was then placed in 100 ml of purified water in a beaker in the water-bath and shaken at

25 rpm through a distance of about 30 mm. The temperature of the purified water in the beaker was maintained at 37°C. After the tablet had been shaken for 10, 20 and 30 s, the stainless-steel basket containing the tablet was removed from the beaker. The solution in the beaker was filtered and the concentration of drug in the filtrate determined by HPLC. The HPLC system consisted of an LC-10ADvp pump (Shimadzu, Kyoto, Japan), a Shimadzu SPD-10Avp uv-vis detector, a Shimadzu SIL-10ADvp auto injector and a Shimadzu SCL-10Avp system controller. The system was equipped with a Capcellpak C18 UG120 column (5 μm, 4.6 × 150 mm; Shiseido, Japan). The mobile phase consisted of MeOH: 30 mM phosphate buffer (pH 6.0) (13 : 7, v/v) and was delivered at a flow rate of 1.0 ml/min at 25°C. Detection was monitored at a UV wavelength of 237 nm. Under these conditions, the coefficient of the intraday and interday variations was below 5%. The bitterness intensity of the medium was also determined by the taste sensor.

The taste sensor

The taste sensor, SA501C (Intelligent Sensor Technology, Inc., Atsugi, Japan) was used to determine the bitterness intensity of the sample solutions. Sensor AN0, which was developed specifically to detect basic bitter substances, was used to determine the bitterness intensity. In the first step, a reference solution (corresponding to saliva) is measured, and the electric potential obtained (mV) is defined as Vr. Then, a sample solution is measured, and the electric potential obtained is defined as Vs. The relative sensor output, represented by the difference (Vs–Vr) between the potentials of the sample and the reference solution, corresponds to the 'taste immediately after putting in the mouth'. The electrodes are subsequently rinsed with a fresh reference solution for 6 s. When the electrode is dipped into the reference solution again, the new potential of the reference solution is defined as Vr0. The difference (Vr0–Vr) between the potentials of the reference solution before and after sample measurement is the 'change in membrane potential caused by adsorption' (CPA) and corresponds to the so-called 'aftertaste'. In this study, the relative sensor output was taken as the bitterness intensity. The measurement of each sample was repeated four times, and the average value of the last three measurements was used in the data analysis.

Statistical analysis

S-PLUS (Mathematical Systems, Inc., Tokyo, Japan) was used for factor analysis. Correlation between the actual and predicted measurements of disintegration time and the bitterness of amlodipine ODT were examined using Spearman's test. Bonferroni test was used for multiple comparisons in amlodipine concentrations of 10 amlodipine products determined using the brief conventional dissolution test. The 5% level of probability was considered significant.

Results

The palatability of amlodipine ODTs as determined in human gustatory sensation tests

The palatability of amlodipine ODTs as determined using the SD method

Figure 1 shows the average score in each item which involved in palatability for 10 commercial amlodipine ODTs as determined using the SD method. The score level of each item showed various values by pharmaceutical products. In items (6) smooth after disintegration/rough after disintegration, just after holding in mouth, and (10) good taste/bad taste, 30 s after holding in mouth, the scores of amlodipine ODT product A (original product) were lower than that of the generic products. In items (8) strong bitterness/weak bitterness at 30 s after holding in mouth and (19) bitter aftertaste/no bitter aftertaste, after gargling, the scores of all the generics were lower than that of product A.

Factor analysis of palatability of amlodipine ODTs

Factor analysis (rotated using the varimax method and performed according to the method of Mukai *et al*.[17]) was performed on the data obtained using the SD method. As a result, two factors with values greater than 1.0 were identified. The contributions of these factors (factors I and II) were 47.14% and 17.15%, respectively (Figure 2). Among the 24 palatability items, items (10) good taste/bad taste 30 s after holding in mouth and (18) good aftertaste/bad aftertaste after gargling showed high factor loadings for factor I. 'Taste of product' was adopted as the composite factor for these items. Two items, item (5) smooth before disintegration/rough before disintegration, just after placing in mouth, and (6) smooth after disintegration/rough after disintegration, just after placing in mouth, showed high factor loadings for factor II. 'Intraoral sense' was adopted as the composite factor for these items.

The factor scores show the relation between each group and each factor. A scatterplot of factor scores for factors I and II are shown in Figure 3. High scores for factor I indicate less 'taste of product', and low scores indicate strong 'taste of product'. High scores for factor II indicate strong 'intraoral sense', and low scores indicate weak 'intraoral sense'. Product A (original product) had low scores for both factors. Consequently, the palatability of product A was found to be greater than that of the generic products.

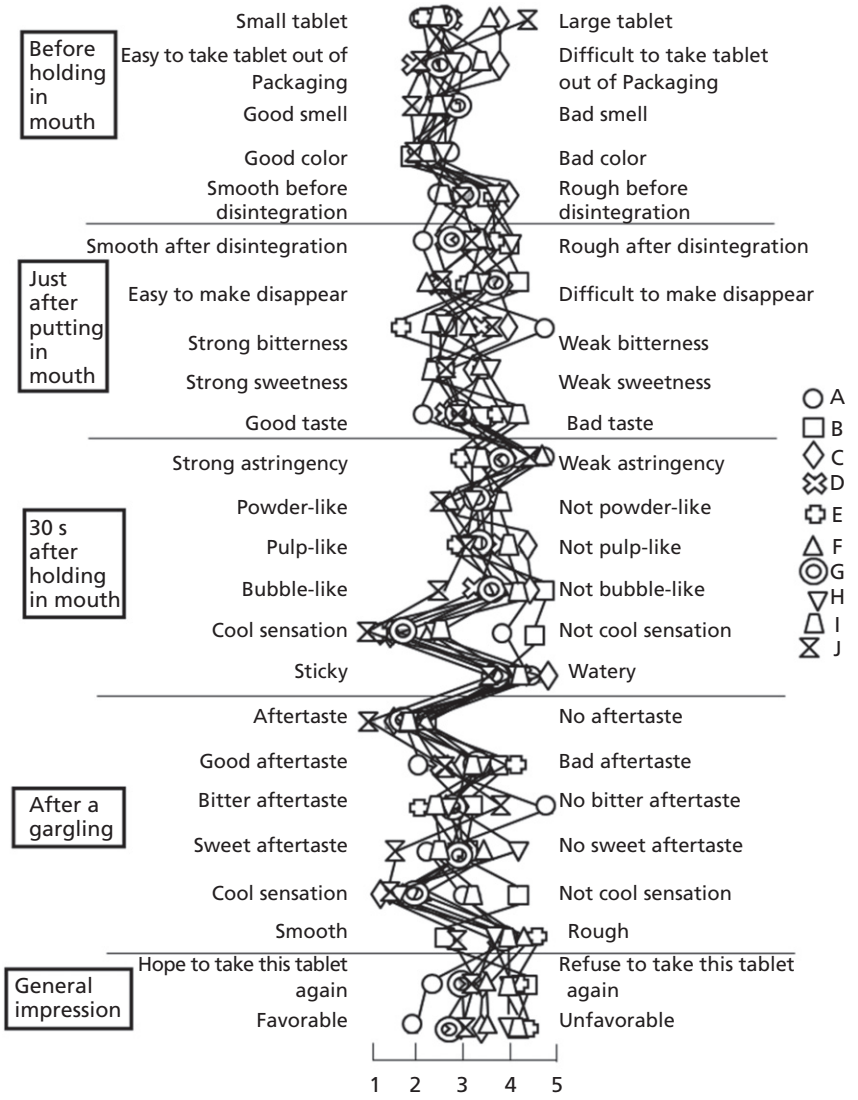

Figure 1 Evaluation of the palatability of 10 commercial amlodipine orally disintegrating tablets using the semantic differential method ($n = 6$). The items were scored using a rating scale of symmetrical terms representing both extremities of the item: 1, extremely; 2, slightly; 3, neither; 4, slightly not; 5, extremely not (see text).

The disintegration time of amlodipine ODTs

The relationship between disintegration time obtained using the pharmacopoeia method and the *in vivo* oral disintegration time is shown in Figure 4. This suggests that the pharmacopoeia disintegration test may not be an appropriate method for estimating the oral disintegration time in the mouth (Figure 4a). On the other hand, a good correlation was observed between *in vitro* oral disintegration time obtained using the OD-mate and the *in vivo* oral disintegration time (rs = 0.9451, $P < 0.01$, Spearman test) (Figure 4b). It was concluded that the disintegration time obtained using the OD-mate was an accurate reflection of the *in vivo* oral disintegration time of amlodipine ODTs.

Dissolution of amlodipine ODTs according to the brief conventional dissolution test

The dissolution of the 10 amlodipine ODTs was determined using the brief conventional dissolution test. The dissolution media were maintained at 37°C to mimic the tablets being kept in the mouth. The dissolved amlodipine concentration was found to increase in a time-dependent manner (Figure 5).

Bitterness intensities of amlodipine ODTs determined using the taste sensor

Figure 6a shows the correlation between the score for taste 'just after putting in mouth' as determined using the SD

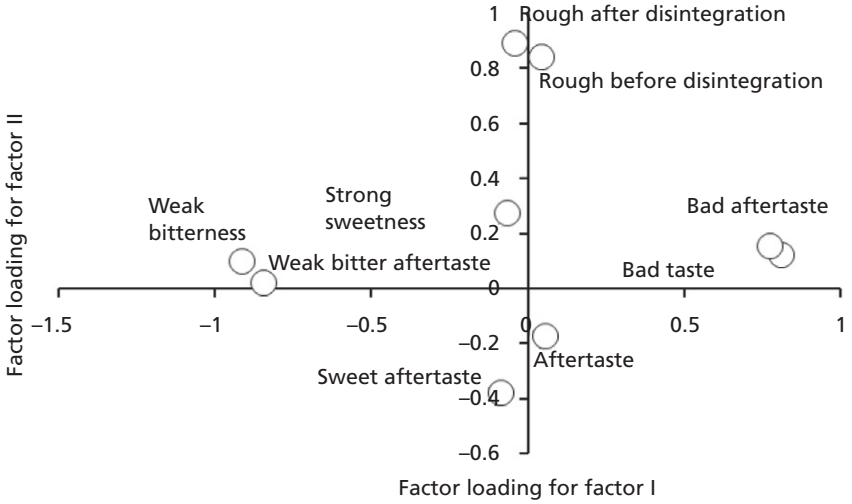

Figure 2 Factor loading for factors I and II obtained using the semantic differential method to assess the palatability of 10 commercial amlodipine orally disintegrating tablets ($n = 6$). The contribution of factor I was 47.14% and of factor II 17.15%.

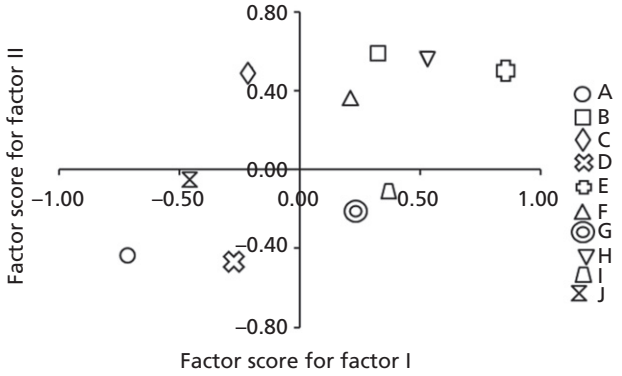

Figure 3 A scatterplot of factor scores for factors I and II obtained using the semantic differential method to assess the palatability of 10 commercial amlodipine orally disintegrating tablets ($n = 6$).

method and the bitterness intensity determined by the gustatory sensation test (rs = 0.8023, $P < 0.01$, Spearman test). Figure 6b shows the correlation between the score for aftertaste obtained using the SD method and the bitterness intensity determined by the gustatory sensation test (rs = 0.9106, $P < 0.01$, Spearman test). The relation between 'taste of product' extracted by factor analysis is suggested to be related to the bitterness intensity of the products. Thus, the bitterness intensity was extracted as the most important factor in determining palatability. The both score of taste just putting in mouth and aftertaste after a gagling of product A (original product) is the best in 10 amlodipine products.

The relationship between the CPA value observed using the AN0 sensor and the bitterness intensity measured in gustatory sensation tests is shown in Figure 7. The CPA value and bitterness intensities obtained were used in the regression analysis. The derived regression equation was: $y = 0.0694 \times CPA_{AN0} - 0.285$ ($r^2 = 0.54$), where y is the predicted bitterness intensity score, and CPA_{AN0} is the CPA value observed in AN0. A relationship was found between the CPA value observed in AN0 measured by taste sensor at 10, 20 and 30 s, and the bitterness intensity measured in gustatory sensation tests (rs = 0.8040, $P < 0.01$, Spearman test; Figure 7). The CPA values from AN0 can therefore be used to predict the bitterness of amlodipine ODTs.

Discussion

The SD method, developed by Osgood *et al.*[27] to characterize the 'emotional meaning' of words, has been extended to a large variety of concepts. It has also been proved to be a useful method for identifying the most important factors in evaluating the palatability of medical products. For example, the palatabilities of products for nutrition[11] and kampo medicines[12] have been evaluated in previous studies.

The SD method was therefore used to find the main factors contributing to the palatability of amlodipine ODTs. It is suggested that one of the two factors found, 'intraoral sense', represents the disintegration of amlodipine ODT in mouth. The disintegration time measured by the OD-mate is intended to simulate this, and indeed, there was a good correlation between the disintegration time determined by the OD-mate and the disintegration time determined in gustatory sensory tests (rs = 0.9451, $P < 0.01$, Spearman test). This suggests that the disintegration time determined by the OD-mate can predict the disintegration time in the human oral cavity. No correlation was observed between

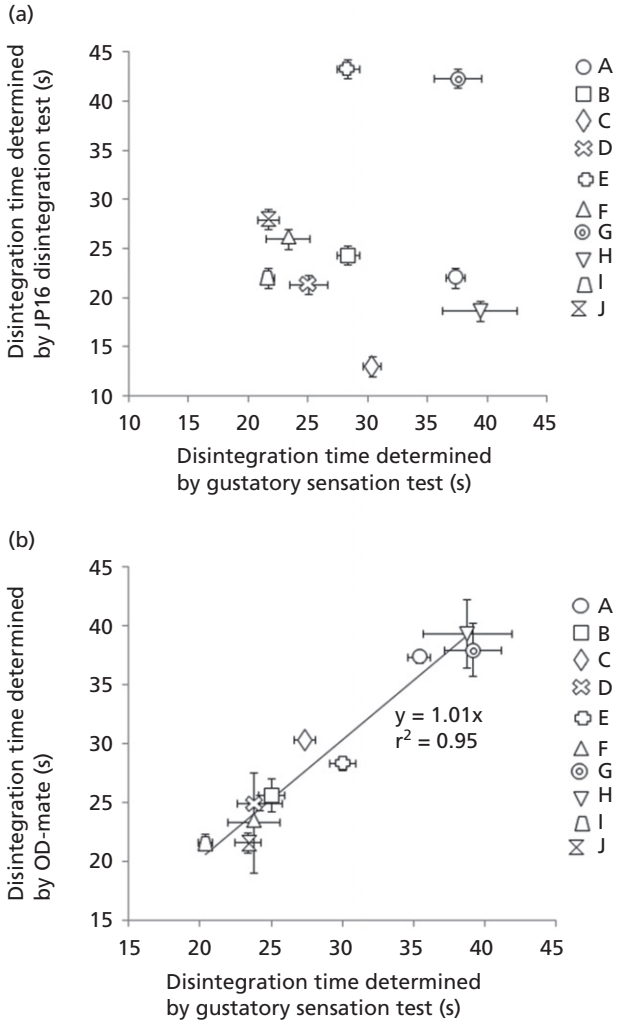

Figure 4 (a) Correlation between disintegration time obtained using the disintegration test in JP16 and that obtained in gustatory sensation testing. Data are presented as mean values ± standard error of the mean ($n = 6$). The equation was obtained by single regression. (b) Correlation between the disintegration time obtained using the OD-mate and that obtained in gustatory sensation testing. Data are presented as mean values ± standard error of the mean ($n = 6$). The equation was obtained by single regression (rs = 0.9451, $P < 0.01$, Spearman's test).

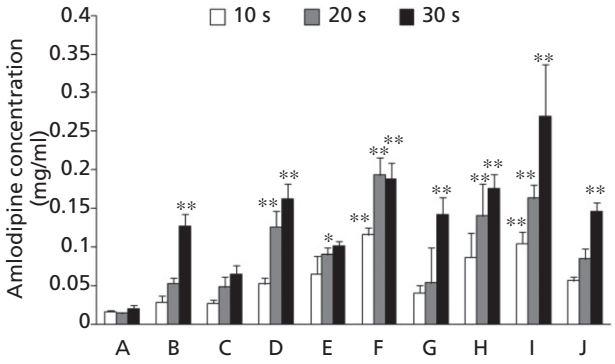

Figure 5 Amlodipine concentrations obtained in the brief dissolution test for amlodipine ODTs. Data are presented as mean values ± standard error of the mean ($n = 6$). * and **: Significant difference from A corresponding to each time (10, 20 or 30 s) at $P < 0.05$ and $P < 0.01$, respectively.

disintegration time obtained in the disintegration test described in JP16 and the *in vivo* oral disintegration time. OD-mate was suggested to be more appropriate for estimating of the oral disintegration time in humans than the disintegration test described in JP16.

The other factor obtained using the SD method, 'taste of product', had equilateral correlations with the bitterness intensities of each product as determined by gustatory sensation tests (Figure 6a and 6b), which in turn were correlated with the amlodipine concentrations obtained using the brief dissolution test. Data from the brief dissolution test showed that dissolution increased in a time-dependent manner (Figure 5). There was no significant correlation between the amlodipine concentrations determined using the brief dissolution test and the disintegration time determined in gustatory sensory tests. It was suggested that the disintegration of amlodipine ODTs had no influence on the bitterness intensity of amlodipine. The bitterness intensity of amlodipine ODTs also increased with dissolution in a time-dependent manner. In the previous paper, the ambroxol concentration dissolved from tablet had a higher correlation with the bitterness intensity in the oral cavity than those obtained using the JP16 dissolution test.[17] Even though the similar time-dependent increasing tendency was seen in the amlodipine concentrations determined using the brief dissolution test and the bitterness intensities of the amlodipine ODTs, there was no significant correlation between the amlodipine concentrations determined using the brief dissolution test and the bitterness intensities of the amlodipine ODTs in this study. As the reason of this result, influence of taste-masking agents contained in amlodipine ODTs was expected. ODTs differ from conventional tablets in that they are designed to be dissolved on the tongue rather than swallowed whole. Various taste-masking agents are contained for bitterness masking of active pharmaceutical ingredients in ODTs. Taste-masking agents like sweeteners contained in amlodipine ODTs were expected to decrease bitterness intensity of amlodipine ODTs without changing amlodipine concentration. Depending on the volume and the types of taste-masking agents, the degree in decrease of bitterness intensities were expected to be different. The difference of taste-masking agents contained in amlodipine ODTs was suggested to decrease correlation between the amlodipine concentrations determined using the brief dissolution test and the bitterness intensities of the amlodipine ODTs.

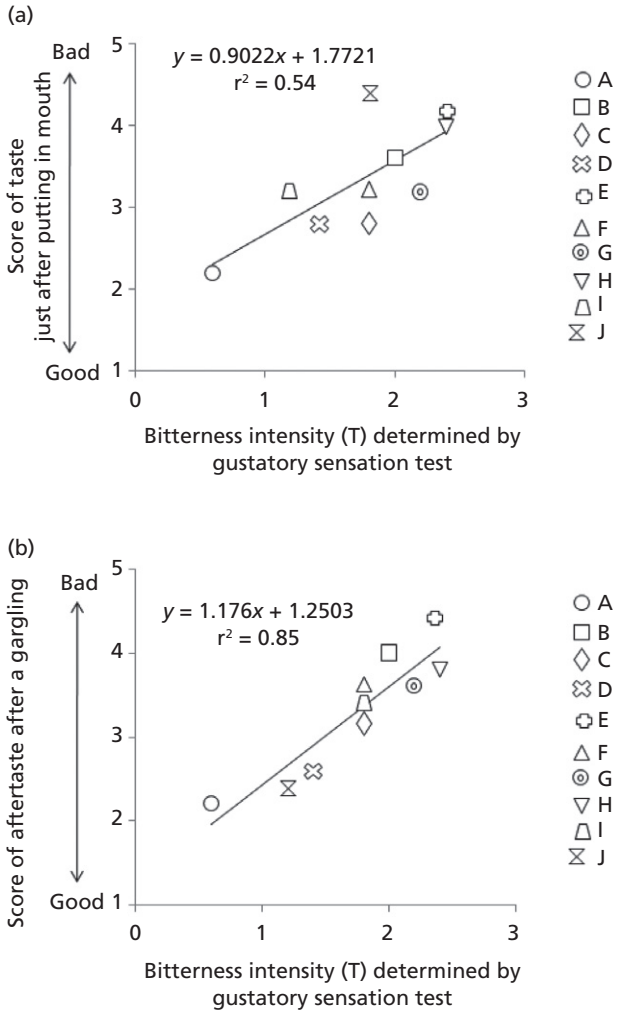

Figure 6 (a) Correlation between the score for 'taste just after putting in the mouth' obtained using the semantic differential method and the bitterness intensity determined by gustatory sensation testing. Data are presented as mean values ± standard error of the mean ($n = 6$). The equation was obtained by single regression (rs = 0.8023, $P < 0.01$, Spearman test). (b) Correlation between score for 'aftertaste after gargling' obtained using the semantic differential method and the bitterness intensity determined by gustatory sensation testing. Data are presented as mean values ± standard error of the mean ($n = 6$). The equation was obtained by single regression (rs = 0.9106, $P < 0.01$, Spearman test).

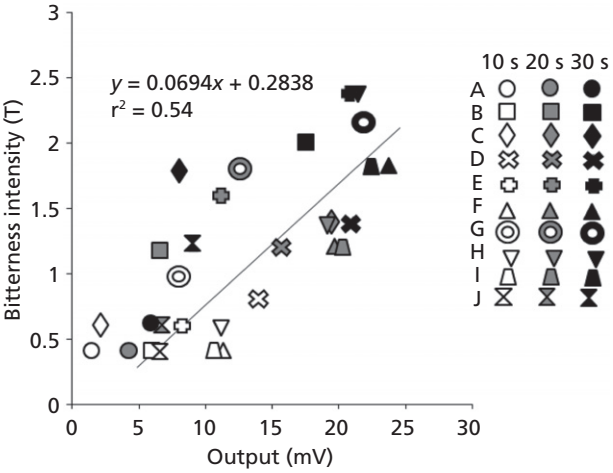

Figure 7 Correlation between the CPA value obtained in AN0 and the bitterness intensity determined by gustatory sensation testing. Data are presented as mean values ± standard error of the mean ($n = 6$). The equation was obtained by single regression (rs = 0.8040, $P < 0.01$, Spearman test).

It has previously been reported that the CPA values obtained using the taste sensor are correlated with the bitterness intensities of some elemental diets.[28] In this study, the CPA value observed in AN0 was highly correlated with the bitterness intensities determined in gustatory sensory testing (rs = 0.8040, $P < 0.01$, Spearman test, Figure 7).

It is suggested that the bitterness intensities of ODTs depend not only on the concentration of the active ingredient but also on their affinity with the sensor probe that best reflects the bitter taste receptor. It was therefore suggested that the taste sensor may be useful in prediction of the bitterness intensity of amlodipine ODTs in the human mouth.

In conclusion, the OD-mate and the taste sensor are together capable of predicting the main factors contributing to the palatability of amlodipine ODTs.

Conclusion

The main factors contributing to the palatability of 10 formulations of amlodipine ODT were extracted by factor analysis of data obtained from human gustatory sensation testing using the SD method. These factors are 'intraoral sense' and 'taste of product'. 'Intraoral sense' is suggested to reflect the disintegration of amlodipine ODT in the mouth. The disintegration time was measured by the OD-mate, a unique disintegration tester intended to simulate the disintegration time of ODTs in the human mouth. The disintegration time measured by the OD-mate was highly correlated with the disintegration time determined in gustatory sensory testing and is therefore suggested to predict the disintegration time in the human mouth. 'Taste of product' is suggested to reflect the bitterness intensity of amlodipine ODTs. The bitterness intensity of amlodipine ODTs predicted by the taste sensor using the CPA value obtained from the AN0 sensor was highly correlated with the bitterness intensity measured by gustatory sensory testing. The bitterness intensity can therefore be predicted using the taste sensor. In conclusion, the main factors determining the palatability of amlodipine ODTs, disintegration and bitterness intensity, can be predicted using the OD-mate and the taste sensor.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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