Evaluation of palatability for 10 commercial famotidine orally disintegrating tablets by combination of disintegration apparatus for orally disintegrating tablet and taste sensor

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ABSTRACT SUMMARY
The palatability of the original and nine generic versions of famotidine orally disintegrating tablets (FODTs) was evaluated by means of human gustatory sensation tests, comparison of disintegration time using disintegration method for ODT and bitterness intensity using taste sensor.

INTRODUCTION
Orally disintegrating tablets (ODTs) are often prescribed for older people and children whose swallowing abilities are poor, as they disintegrate easily in saliva in the mouth without the need for additional water. Recently, ODT formulations have been developed for various medicines, and many generic products are now available on the market. When ODTs disintegrate in the mouth, the concentration of dissolved drug in the mouth is greater than that which is found when conventional tablets are kept in the mouth. Thus, taste masking is an important issue for ODTs.

Famotidine orally disintegrating tablet (FODT) was the first ODT on the Japanese market. After expiry of the patent, there are many generic forms of this product on the market. The palatability of a medicine is an important factor in determining compliance.

Disintegration of ODT is suggested to be a factor of the palatability of ODTs. OD-mate is one of the disintegration devices for ODTs. It has an advantage over other device in that it can be used at low volume characterized from the oral cavity and it is not complicated to use. OD-mate was used for measuring the disintegration time of FODT in this study.

Bitterness, a factor of the palatability, is known to decrease patient compliance. Taste plays an important role in the development of a pharmaceutical formulation, so the use of an taste sensor for pharmaceutical purposes is an important step forward. Bitterness intensity of FODTs was evaluated in human sensation test and taste sensor in this study.

EXPERIMENTAL METHODS

Materials
Ten different 10-mg FODTs were used in the present study: the original product, Gaster®D (Astellas Pharma Inc., Tokyo, Japan) were named product A, and nine generic products. Nine generic products were randomly named products B to J.

The gustatory sensation test
The gustatory sensation test for bitterness intensity were performed with 10 well-trained volunteers, using quinine sulfate at concentrations of 0.0029, 0.012, 0.031, 0.078 and 0.20 mM as a standard for bitterness. Scores of 0, 1, 2, 3 and 4 were allocated to the increasing concentrations of the standard solutions. The in vivo disintegration time of the placebo ODTs was determined by 10 well-trained volunteers. Before testing, the volunteers were asked to rinse their mouths with a cup of water, and then a test placebo ODT was placed on the tongue. The protocol and experimental design for all gustatory sensation tests was approved in advance by the ethical committee of Mukogawa Women’s University.

Disintegration test of FODTs using OD-mate
The in vitro oral disintegration time was measured using OD-mate (Model IMC-14D1, Higuchi Inc., Tokyo, Japan). An ODT is placed on a trapezoidal mesh flat-bottomed test tube corresponding to tongue, and compressed by two weights (30 g of inner weight and 100 g of outer weight) corresponding to upper palate.
The test media was 20 mL of purified water at 37°C. The measurement was started immediately after the test tube contacted the water, and the elapsed time to disintegrate the tablet (until the inner weight reaches to the test tube) was recorded.

**Taste sensor**

SA501C, of Intelligent Sensor Technology Inc. (Atsugi, Japan) was used to determine bitterness intensity of the sample solution. The bitterness intensity of FODT at 10 s, 20 s, 30 s after starting disintegration of FODT using OD-mate evaluated by taste sensor. 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 is defined as Vs. The relative sensor output is represented by the difference (Vs − Vr) between the potentials of the sample and the reference solution and corresponds to the so-called ‘The momentary taste after including 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 the membrane potential caused by adsorption (CPA) and corresponds to the so-called ‘aftertaste’. In this study, the CPA was used as bitterness intensity. The measurement of each sample is repeated four times and the average value of the last three measurements is used in the data analysis.

**RESULTS AND DISCUSSION**

Initially, disintegration time and bitterness intensity of FODTs were evaluated in gustatory sensation test. Secondly, disintegration time of orally disintegrating tablets using OD-mate and bitterness using taste-sensor of FODTs were evaluated. There is high correlation between disintegration times of 10 FODTs by human gustatory test and those using OD-mate (Fig.1). The bitterness intensity of FODT at 10 s, 20 s, 30 s after starting disintegration of FODT using OD-mate evaluated by taste sensor was high correlation to bitterness intensity by gustatory sensation test. It is suggested that disintegration and bitterness intensity of FODTs can be predicted by OD-mate and taste sensor.

![Figure 1. Correlation between disintegration time by OD-mate and that by gustatory sensation test.](image)

**CONCLUSION**

The factors contributed to palatability of FODTs, disintegration and bitterness intensity of FODTs were suggested to predicted using OD-mate and taste sensor. The combination of OD-mate and taste sensor may be useful for predicting the disintegration and bitterness intensity of ODT in the mouth.

**REFERENCES**


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