Evaluation the palatability of ebastine orally disintegrating tablets using OD-mate; as new apparatus of detecting disintegration time and electronic tongue system

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ABSTRACT SUMMARY

The aim of this study was to predict the palatability of ebastine orally disintegrating tablets (ODTs). The disintegration time of the ODTs was measured using the OD-mate while their bitterness was measured using electronic tongue (e-tongue). The disintegration times determined by the OD-mate correlated well with those obtained in human sensation tests, while the Euclidean distances calculated from e-tongue analysis correlated with the bitterness scores obtained in human sensation tests. The ability of the OD-mate and the e-tongue to predict palatability will be useful in evaluating ODTs without using human sensation tests.

INTRODUCTION

Orally disintegrating tablets (ODTs) are of particular benefit to older patients and children with poor swallowing ability, as well as patients with busy lives, as they can be taken at any time and in any place with little or no water. However, the main advantage of ODTs, that the solid dosage forms disintegrates in saliva or in small volumes of liquid, creates another problem: that of taste. Taste-masking is almost always necessary for ODTs because most active pharmaceutical ingredients produce an unpleasant taste sensation, such as bitterness, when they dissolve in the oral cavity. Therefore, the ideal ODT formulation disintegrates quickly but without expressing bitterness.

Ebastine is a second-generation H₁-receptor antagonist with an oxypiperidine-based structure. In this study, we evaluated the disintegration time and taste of ebastine ODTs in order to predict their palatability using artificial apparatuses¹. There are several ebastine ODTs on the market in Japan. We randomly chose five of them in our study, one original and four generic products, manufactured using different additives and processes. The disintegration time of the ODTs was measured using two disintegration tests, one being the traditional disintegration test and the other using the newly developed OD-mate. The taste of each ODT was measured in human gustatory tests and using electronic tongue, α-ASTREE II. These results were combined in an overall evaluation of palatability.

EXPERIMENTAL METHODS

Materials: Five different 10-mg ODTs, all containing ebastine as active ingredient, were used in this study: the original product, EBASTEL® OD (Dainippon Sumitomo Pharm Co., Ltd, Osaka, Japan) identified as product A, and the four generic products were randomly assigned letters B to E.

Disintegration time: Disintegration time was measured using two apparatuses: Riken’s disintegration tester (HM-21D) being the conventional method according to the Japanese Pharmacopoeia, XVIth edition (JP16) and the OD-mate (Model IMC-14D1), a new method which has already been used successfully to predict the disintegration time of amlodipine OD tablets².

E-tongue system: The ASTREE II e-Tongue system, developed by Alpha MOS, was used for taste evaluation of the test sample solution. Samples of the ODTs (ten tablets) were put in a stainless-steel mesh basket which was lowered into a 100 ml beaker. The beaker was put into a thermostatically controlled shaking water bath (37°C at 25 rpm) containing 100 ml of distilled water. After 10 and 60 s the suspensions were filtered under reduced pressure. Solutions were then measured by the e-tongue.
Human Sensation test: Before testing, the subjects (n=6) were asked to keep the bitterness standard quinine hydrochloride solutions (0.01, 0.03, 0.10, 0.30 and 1.00 mM as scores of 0, 1, 2, 3 and 4 respectively) in their mouths and memorize the bitterness score of each solution. In individual subject, each ODT was held between the tongue and upper jaw in the mouth and the bitterness score was evaluated after 10 and 60 seconds. In addition, the time it took for each ODT to disintegrate completely in the mouth was determined and the bitterness score at that time was also evaluated. The experimental design was given prior approval by the ethical committee of Mukogawa Women's University (No. 12-47; approved on 18 May 2013).

RESULTS AND DISCUSSION
The disintegration time as determined by the JP16 disintegration test was 25 s for product A, while for the other products it was >30 s (Fig. 1(a)). There was poor correlation between the disintegration time as determined by the disintegration test in JP16 and that determined in human testing (Fig. 1(b)). The disintegration time determined by the OD-mate was 34 s for product A, while for the other products it was 40–80 s (Fig. 1(c)). There was good correlation between the disintegration time determined by the OD-mate and that determined by human testing (Fig 1(d)).

The Euclidean distances from quinine 0.1 mM to each sample at 10 s and 60 s is shown in Figure 2(a). There was good correlation between the Euclidean distances and the bitterness scores determined by human gustatory sensation testing (Fig 2(b)).

The results show that product A has the highest palatability because of its prompt disintegration and low bitterness. In fact, products A, D and E all had prompt disintegration and low bitterness; product B had slow disintegration and moderate bitterness, while product C had prompt disintegration and moderate bitterness.

CONCLUSION
The OD-mate and Euclidean distances derived from data produced by the electronic tongue, were found to be useful for determining the disintegration time and bitterness of ebastine ODTs. The combination of disintegration time and bitterness are the most important factors involved in predicting the palatability of ODTs.

REFERENCES

ACKNOWLEDGMENTS
This work was supported by Grant-in-Aid for Scientific Research (C) from the Japan Society for Promotion of Science 24590226 (to Takahiro Uchida).