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RESEARCH PAPER

Physicochemical Characterization and Evaluation of Buccal Adhesive Tablets Containing Omeprazole

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ABSTRACT

The objective of this study was to develop an effective omeprazole buccal adhesive tablet with excellent bioadhesive force and good drug stability in human saliva. The omeprazole buccal adhesive tablets were prepared with various bioadhesive polymers, alkali materials, and croscarmellose sodium. Their physicochemical properties, such as bioadhesive force and drug stability in human saliva, were investigated. The release and bioavailability of omeprazole delivered by the buccal adhesive tablets were studied. As bioadhesive additives for the omeprazole tablet, a mixture of sodium alginate and hydroxypropylmethylcellulose (HPMC) was selected. The omeprazole tablets prepared with bioadhesive polymers alone had bioadhesive forces suitable for a buccal adhesive tablet, but the stability of omeprazole in human saliva was not satisfactory. Among alkali materials, only magnesium oxide could be an alkali stabilizer for omeprazole buccal adhesive tablets due to its strong waterproofing effect. Croscarmellose sodium enhanced the release of omeprazole from the tablets; however, it decreased the bioadhesive forces and stability of omeprazole tablets in human saliva. The tablet composed of omeprazole/sodium alginate/HPMC/magnesium oxide/croscarmellose sodium (20/24/6/50/10 mg) could be attached on the human cheek without disintegration, and it enhanced the stability of omeprazole in human saliva for at least 4 h and gave fast release of omeprazole.

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The plasma concentration of omeprazole in hamsters increased to a maximum of 370 ng/ml at 45 min after buccal administration and continuously maintained a high level of 146–366 ng/ml until 6 h. The buccal bioavailability of omeprazole in hamsters was 13.7% ± 3.2%. These results demonstrate that the omeprazole buccal adhesive tablet would be useful for delivery of an omeprazole that degrades very rapidly in acidic aqueous medium and undergoes hepatic first-pass metabolism after oral administration.

Key Words: *Bioadhesive force; Buccal adhesive tablet; Dissolution; Omeprazole; Pharmacokinetics; Stability in human saliva.*

INTRODUCTION

The substituted benzimidazole omeprazole, 5-methyl-2-{[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfonyl}-1H-benzimidazole, exhibits potent and long-lasting inhibition of gastric acid secretion by selectively interacting with the gastric proton pump (K^+/H^+-ATPase) in the parietal cell secretory membrane (1–3). The bioavailability of omeprazole following oral administration is usually very low since it degrades very rapidly in the stomach and undergoes hepatic first-pass metabolism. Thus, various oral dosage forms of omeprazole, such as enteric-coated granules (4,5) and enteric-coated tablets (6,7), have been developed to improve its bioavailability. Moreover, attempts have also been made to develop an omeprazole rectal suppository as an alternative dosage form; however, the result was unsatisfactory (8).

In this study, an attempt was made to develop an omeprazole buccal adhesive tablet to avoid gastric degradation and first-pass metabolism in the liver. Absorption of drug from the oral cavity and attachment of the tablet to the buccal mucosa without disintegration are the two prime considerations in designing a conventional buccal adhesive tablet. However, an additional consideration in the case of omeprazole is the stability of omeprazole in human saliva since it is very unstable in acidic and neutral media.

To develop an omeprazole buccal adhesive tablet that could be attached to the human cheek without disintegration and could keep the drug without decomposition in human saliva, omeprazole buccal adhesive tablets were prepared with various bioadhesive polymers, alkali materials, and croscarmellose sodium. Their physicochemical properties, such as the bioadhesive force and drug stability in human saliva, were investigated. Furthermore, the release and bioavailability of omeprazole delivered by the buccal adhesive tablets were studied.

EXPERIMENTAL

Materials

Omeprazole, sodium alginate (300–400 cPs), and hydroxypropylmethylcellulose (HPMC 2208, 4000 cPs) were supplied by Chongkundang Pharmaceutical Company (Seoul, Korea), Wako Chemical Company (Tokyo, Japan), and Shin-Etsu Company (Tokyo, Japan), respectively. Carbopol (934P) and polycarbophil were purchased from B. F. Goodrich (Brockville, OH). Potassium phosphate monobasic, sodium phosphate monobasic, and sodium phosphate dibasic were purchased from Junsei Chemical Company (Tokyo, Japan). Magnesium oxide and croscarmellose sodium were USP grade.

Preparation of Omeprazole Buccal Adhesive Tablets

Omeprazole buccal adhesive tablets, 7 mm in diameter and with a hardness of 6–8 KP, were prepared by compressing 20 mg omeprazole and 80–95 mg other ingredients, such as bioadhesive polymers, alkali materials, and croscarmellose sodium, using an Erweka tablet machine (Heusenstamm, Germany).

Measurement of Bioadhesive Force of Buccal Adhesive Tablets In Vitro

The bioadhesive force, detachment stress of the buccal adhesive tablet in vitro, was determined using the measuring device in Fig. 1 according to a method described previously (9,10). In brief, a section of tissue was cut from the fundus of a hamster cheek pouch and secured with the mucosal side out onto each glass vial (C in Fig. 1) using a rubber band and an aluminum cap. The vial with a section of tissue (E) was connected to the balance (A), and the other vial was placed on a height-adjustable pan (F). An omeprazole tablet (D) was added to the tissue

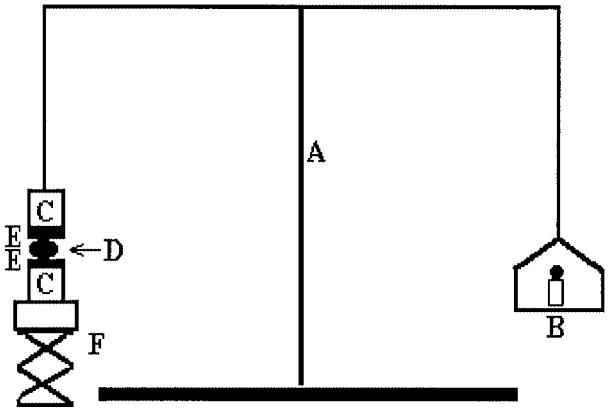

Figure 1. Bioadhesive force-measuring device: (A) modified balance; (B) weights; (C) glass vial; (D) buccal adhesive tablet; (E) hamster cheek pouch; (F) height-adjustable pan.

of the other vial on the pan (F). Then, the height of the vial was adjusted so that the tablet could be placed between the mucosal tissues of both vials. The weights (B) were increased until the two vials were detached. Bioadhesive force, the detachment stress (dyne/cm^2), was determined from the minimal weight that detached the two vials (9,11,13).

Measurement of Bioadhesive Force of Buccal Adhesive Tablets In Vitro

Treatment Group

Three healthy male volunteers, weighing 58–63 kg and 24–27 years old, participated in the study and gave written consent before the test. The test was approved by the Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University. The subjects were all subjected to full clinical examination and were found to be free of renal, hepatic, cardiac, and neurologic diseases, as well as bowel habit disturbances.

Bioadhesive Force In Vivo

Each omeprazole tablet, which had bioadhesive force measured previously in vitro, was attached to a volunteer's cheek. When it was not well attached on the cheek, the surface of the tablet was wetted slightly with a bit of carbonate buffer (pH 9.3). The subject was allowed no access to water and food during the experiments. The threshold of bioadhesive force of the buccal adhesive tablet in vivo was then determined by the observing the attachment of the omeprazole tablet on the volunteer's cheek for 4 h. If it was detached from the cheek within 4 h, the experiment was finished. The threshold of bioadhesive force was arbitrarily determined as the minimum force for keeping the tablet attached to the human cheek for at least 4 h.

Stability of Omeprazole Tablet in Human Saliva

The human saliva was prepared by filtering natural human saliva. Each omeprazole tablet was immersed in 5 ml of human saliva for 4 h and taken out of human saliva at predetermined time intervals. The stability of the omeprazole tablet was then evaluated by its appearance, such as color and shape, and omeprazole concentration.

Release of Omeprazole from Buccal Adhesive Tablets

Each omeprazole tablet was attached to a glass plate with 0.05 ml of carbonate buffer (pH 9.3). The glass plate was then placed in a dissolution tester (DST-600, Fine Chemical, Seoul, Korea). The experiments were performed at 37°C $\pm$ 0.5°C using the paddle method at 50 rpm with 500 ml of carbonate buffer (pH 9.3) as a dissolution medium. Every 30 min, 1 ml of the medium was sampled and filtered. This resulting solution (10 μl) was directly injected onto a Lichrosorb RP-18 column (Waters, 0.5 μm, 25 cm $\times$ 0.46 cm i.d.). The chromatograph consisted of a high-performance liquid chromatograph (HPLC) (Waters TM 717) and a variable ultraviolet (UV) spectrophotometric detector (model SPD-6A). The mobile phase consisted of acetonitrile and pH 7.6 phosphate buffer (35%/65% v/v). The eluent was monitored with a UV/Visible detector set at the wavelength of 310 nm with a flow rate of 1.5 ml/min (14,15).

Pharmacokinetic Study

Preparation of Test Samples

An omeprazole tablet for buccal administration, 2.5 mm in diameter and with a hardness of 6–8 KP, was prepared by compressing 2 mg omeprazole, 2.4 mg sodium alginate, 0.6 mg HPMC, 5 mg magnesium oxide, and 1 mg croscarmellose sodium using the Erweka tablet machine. Omeprazole solution for intravenous administration was prepared by dissolving 20 mg of omeprazole in 2 ml of ethanol/pH 9.3 carbonate buffer (5%/95%).

Administration and Blood Collecting

Male Golden hamsters weighing 100 ± 10 g were anesthetized in an ether-saturated chamber after fasting for 24 h prior to the experiments. An omeprazole buccal adhesive tablet (20 mg of omeprazole per kilogram weight of the hamster) was attached to each hamster cheek pouch. An omeprazole solution (2 ml/kg, equivalent to 20 mg/kg of weight of the hamster) was intravenously administered. Then, 0.5 ml of blood was collected from the inferior vena cava after laparotomy. During the experiment, the attachment of the tablet to the cheek pouch of the hamster was confirmed. Each sample was immediately centrifuged at 3000 rpm for 10 min.

Blood Sample Analysis

Plasma (0.2 ml) was mixed with 150 μl of carbonate buffer (pH 9.3) and 50 μl of 1-chloro-2,4-dinitrobenzene as an internal standard in a 15-ml screw-cap polypropylene tube. Subsequently, omeprazole was extracted with 6 ml of hexane and methylene chloride (50:50, volume ratio). Under N_2 (g), 5 ml of the organic layer was evaporated. The residue was reconstituted in 300 μl of the mobile phase. Then, the resulting solution was analyzed by HPLC (Waters, model TM 717) equipped with a Lichrosorb RP-18 column (Waters, 0.5 μm, 25 cm ± 0.46 cm i.d.) and a UV detector (model SPD-6A). The mobile phase consisted of methanol and triethanolamine (99:1, volume ratio) adjusted to pH 7.7 with 85% (w/v) phosphoric acid. The eluent was monitored at 302 nm with a flow rate of 1.5 ml/min (7,8,16).

RESULTS AND DISCUSSION

Effect of Bioadhesive Polymers on the Physicochemical Properties

In this study, bioadhesive force is the force by which a tablet binds to the buccal mucous membrane. Since buccal mucous membrane consists of oligosaccharide chains with sialic acid, polymers with hydrophilic groups such as carboxyl and hydroxyl groups can bind strongly to these chains, resulting in strong bioadhesive force. The stronger the bioadhesive force, the longer a tablet may stay attached to buccal mucosa (9,11,13). Therefore, in the development of omeprazole buccal adhesive tablets, the bioadhesive force is an important factor.

The threshold of the bioadhesive force of the buccal tablet was evaluated by the minimum force to keep the tablet attached to the human cheek for 4 h, resulting in 4.50 dyne/cm^2. The buccal tablets with bioadhesive forces above the threshold of 4.50 dyne/cm^2 could be attached on the human cheek for at least 4 h. However, the buccal tablets with bioadhesive forces below the threshold of 4.50 dyne/cm^2 were detached from the human cheek within 4 h.

The buccal adhesive tablets were prepared by compressing 20 mg of omeprazole and 80 mg of bioadhesive polymers. HPMC, Carbopol, polycarbophil, and sodium alginate were selected as the bioadhesive polymers. All of these bioadhesive polymers are water soluble or swellable. HPMC, a cellulose derivative, is neutral and swells in water. Carbopol, a polyacrylic acid derivative polymerized with a cross-linking agent (allyl sucrose), is anionic and water swellable. Polycarbophil, a polyacrylic acid derivative polymerized with diethylene glycol, is also anionic and swells in water. Sodium alginate is the sodium salt of alginic acid and is slightly alkali and water soluble. Carbopol, polycarbophil, and sodium alginate are known to be excellent bioadhesive polymers (9–11,13).

The tablets composed of omeprazole (20 mg) and the bioadhesive polymers (80 mg) HPMC, polycarbophil, Carbopol, and sodium alginate had bioadhesive forces of 1.51 ± 0.15, 9.26 ± 0.65, 9.81 ± 0.84, and 17.15 ± 1.68 dyne/cm^2, respectively. Sodium alginate, with a greater portion of hydroxyl groups (OH) than the other polymers tested, could bind more strongly with the oligosaccharide chains than polycarbophil and Carbopol, which contain primarily carboxyl groups (COOH). HPMC, with neutral cellulose groups, bound less than the other three polymers (9,13). Among these bioadhesive polymers tested, sodium alginate had the greatest bioadhesive force. However, the bioadhesive force of a buccal tablet should be controlled since excess bioadhesive force can damage mucous membranes (10,13). HPMC could be used to control the strong bioadhesive force of sodium alginate due to its weak bioadhesive force. Thus, a mixture of sodium alginate and HPMC was selected as the bioadhesive additive for the omeprazole buccal adhesive tablet.

The omeprazole (20 mg) tablets prepared with sodium alginate (80 mg) or HPMC (80 mg) alone did not disintegrate for at least 4 h. However, they turned black and exhibited 70% and 52%, respectively, of the initial omeprazole concentrations at 4 h in human saliva. The stability of omeprazole tablets in human saliva was evaluated by their appearance, such as color and shape, and omeprazole concentrations. The weakly acidic or neutral human saliva that penetrated into the omeprazole tablets decomposed the drug in them since the drug is very unstable in acidic or neutral medium (5,16). Furthermore, it gradually changed the color from white to violet or black due to the decomposition of omeprazole

(1,2,16). In the worst case, it caused the disintegration of tablets, followed by complete decomposition of the omeprazole in the tablets. As a fact by which the omeprazole tablets with sodium alginate or HPMC alone turned black and did not exhibit 100% of the initial omeprazole concentrations at 4 h in human saliva, it was proved that the omeprazole tablets with only the bioadhesive polymers could not stabilize the drug in human saliva (4–7).

Effect of Alkali Materials on the Physicochemical Properties

The omeprazole tablets were prepared by compressing 20 mg of omeprazole, 50 mg of sodium alginate, and 30 mg of alkali materials such as magnesium oxide, potassium phosphate monobasic, sodium phosphate monobasic, and sodium phosphate dibasic in an attempt to stabilize the drug. In the formulation of oral enteric-coated omeprazole granules and tablets, these alkali materials have been used as stabilizers for omeprazole. They prevented the decomposition of omeprazole in acidic gastric fluid that penetrated into the enteric coating walls, providing an alkaline environment for omeprazole (2,4–6). In the formulation of omeprazole buccal adhesive tablets, these alkali materials are used as stabilizers of omeprazole since the omeprazole is decomposed in weakly acidic or neutral human saliva, as well as in acidic gastric fluid (2,4–6,16). The tablets with potassium phosphate monobasic, sodium phosphate monobasic, and sodium phosphate dibasic disintegrated at 1 h. However, the tablet with magnesium oxide did not disintegrate in human saliva until 4 h. These results suggested that magnesium oxide could be a good stabilizer for an omeprazole buccal adhesive tablet. A hydrophobic and insoluble alkali material, magnesium oxide, might protect the tablet matrix from penetration by human saliva due to its strong waterproofing effect (17–19).

To determine the optimal amount of magnesium oxide to stabilize the drug in human saliva, the tablets were prepared by compressing 20 mg of omeprazole and 80 mg of various mixtures of sodium alginate and magnesium oxide (Table 1, A–D). Physicochemical properties such as bioadhesive force and stability in human saliva were evaluated.

Tablets with less than 50 mg of magnesium oxide (A, B, C) had bioadhesive forces of 17.15 ± 0.95, 10.24 ± 1.21, 8.74 ± 0.89 dyne/cm^2, respectively. The tablet with 70 mg magnesium oxide (D) had a bioadhesive force of 2.53 ± 0.19 dyne/cm^2. As the ratio of sodium alginate to magnesium oxide decreased, the bioadhesive forces of the omeprazole tablets decreased (9,12,13).

Tablets with less than 50 mg of magnesium oxide (A–C) did not disintegrate until 4 h. However, the tablet with 70 mg of magnesium oxide (D) disintegrated within 1 h, indicating that the tablets with excess amounts of magnesium oxide rapidly disintegrated in human saliva due to less bioadhesive polymer (10 mg/tablet). The tablets with less than 30 mg of magnesium oxide (A and B) turned black and exhibited 70%–85% of the initial omeprazole concentrations in human saliva at 4 h. However, the tablet with 50 mg of magnesium oxide (C) remained white and exhibited nearly 100% of the initial omeprazole concentration in human saliva at 4 h. On the other hand, the tablet with 70 mg of magnesium oxide (D) and the tablet without magnesium oxide (A) exhibited about 95% and 80%, respectively, of the initial omeprazole concentrations in human saliva at 30 min (Table 1). The omeprazole in the tablet with 70 mg of magnesium oxide (D) was more rapidly decomposed compared to the tablet without magnesium oxide (A) since the tablet D disintegrated within 1 h but tablet A did not. These results suggested that the maintenance of the tablet shape was more important to the stability of the drug than the protection from human saliva penetrating into the tablet matrix (20–22).

Table 1

Composite of Omeprazole Buccal Adhesive Tablets

Ingredients	A	B	C	D	E	F	G	H	I	J	K
Omeprazole	20	20	20	20	20	20	20	20	20	20	20
Sodium alginate	80	50	30	10	24	15	6	0	24	24	24
HPMC	—	—	—	—	6	15	24	30	6	6	6
Magnesium oxide	—	30	50	70	50	50	50	50	50	50	50
Croscarmellose sodium	—	—	—	—	—	—	—	—	5	10	15
Total (mg/tablet)	100	100	100	100	100	100	100	100	100	100	100
Omeprazole concentration (%) in human saliva at 4 h	70.2 ± 3.4	85.4 ± 3.7	99.2 ± 3.1	40.3 ± 6.8	99.1 ± 1.2	98.2 ± 2.8	93.2 ± 3.2	87.5 ± 4.1	99.1 ± 2.5	99.2 ± 3.2	93.6 ± 2.2

Each value represents the mean ± SE (n = 3).

Tablet Formulas Suitable for Omeprazole Buccal Adhesive Tablet

The omeprazole tablets were prepared by compressing 20 mg of omeprazole, 50 mg of magnesium oxide, and 30 mg of various mixtures of sodium alginate and/or HPMC (Table 1, C, E–H). Their physicochemical properties, such as bioadhesive force, stability in human saliva, and release, were evaluated.

Tablets C, E, F, G, and H, with omeprazole/sodium alginate/HPMC/magnesium oxide concentrations of 20/30/0/50 mg/tablet, 20/24/6/50 mg/tablet, 20/15/15/50 mg/tablet, 20/6/24/50 mg/tablet, and 20/0/30/50 mg/tablet, had bioadhesive forces of 8.74 ± 0.89, 6.35 ± 0.62, 4.24 ± 0.89, 3.12 ± 0.17, and 0.55 ± 0.27 dyne/cm^2, respectively. The bioadhesive forces of omeprazole tablets were also affected by the concentrations of bioadhesive polymers. The higher the ratio of sodium alginate to HPMC was, the stronger the bioadhesive forces of the omeprazole tablets were. Among these tablets, tablets C and E had bioadhesive forces above the threshold of 4.5 dyne/cm^2, suggesting that they could be attached on the human cheek for at least 4 h.

All tablets did not disintegrate until 4 h. Tablets G and H turned violet and exhibited 85%–93% of the initial omeprazole concentrations in human saliva at 4 h. However, tablets C, E, and F remained white and exhibited nearly 100% of the initial concentrations in human saliva at 4 h (Table 1). These results indicate that the stability of omeprazole in tablets was enhanced in human saliva as the ratio of sodium alginate to HPMC increased. They indicate that sodium alginate also stabilized the drug due to its alkali property.

Figure 2A illustrates the effect of composition ratio of sodium alginate to HPMC on the release of omeprazole from buccal adhesive tablets. As the ratio of sodium alginate to HPMC decreased, the release of omeprazole from the tablets increased slightly. The release of omeprazole from tablets was affected by the nature of bioadhesive polymers, particularly their functional groups. The neutral cellulose groups of HPMC have a weak binding force with the drug compared with the hydroxyl groups of sodium alginate (9,10,12).

On the other hand, the long-term attachment of the omeprazole buccal tablet on the cheek pouch might affect the stability of omeprazole, even if it could stabilize the

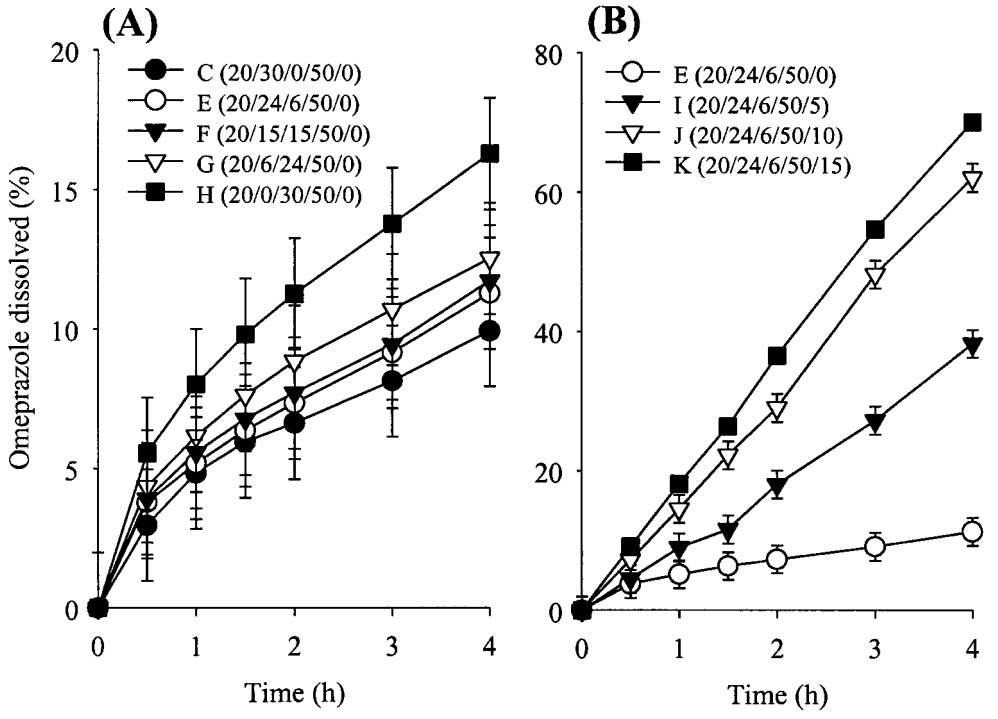

Figure 2. Release of omeprazole from the omeprazole buccal adhesive tablets, omeprazole/sodium alginate/HPMC/magnesium oxide/croscarmellose sodium (mg). Each value represents the mean ± SE (n = 6).

drug in human saliva for at least 4 h. Thus, omeprazole should be released from the omeprazole buccal tablet within the designated time period so that the drug could be completely absorbed from the oral cavity before it was decomposed in human saliva. Figure 2A shows that about 10%–16% of omeprazole was released within 4 h from all tablets (C, E–H). These results indicate that the drug was released very slowly from these tablets composed of sodium alginate, HPMC, and magnesium oxide.

Effect of Croscarmellose Sodium on the Physicochemical Properties

To enhance the release of omeprazole from the buccal adhesive tablets, omeprazole tablets were formulated by the addition of varying amounts of croscarmellose sodium to the optimized tablet, with omeprazole/sodium alginate/HPMC/magnesium oxide levels at 20/24/6/50 mg, respectively. Croscarmellose sodium has been used to disintegrate the tablet, resulting in enhancement of the release of drug (18).

Figure 2B illustrates that the released percentages of omeprazole from tablets with 5, 10, and 15 mg of croscarmellose sodium at 4 h (Table 1, I, J, and K) were 38%, 62%, and 70%, respectively. These results suggest that the tablets with 10–15 mg croscarmellose sodium had fast release rates of omeprazole, with 60% released at 4 h. It might be considered that croscarmellose sodium formed porous channels in the tablet matrix due to its fast swelling in water, resulting in fast release of omeprazole (18).

Tablets with less than 10 mg of croscarmellose sodium (E, I, J) had bioadhesive forces of 10.24 ± 2.21, 6.75 ± 0.83, and 5.37 ± 0.45 dyne/cm^2, respectively, above the threshold. However, the tablet with 15 mg of croscarmellose sodium (K) had a bioadhesive force of 3.99 ± 0.20 dyne/cm^2. As concentrations of croscarmellose sodium increased, the bioadhesive forces of the tablets were remarkably reduced. It was very probable that the croscarmellose sodium reduced the strong binding of sodium alginate to the oligosaccharide chains of the mucous membranes (9,11,13).

The tablets with less than 10 mg of croscarmellose sodium (E, I, J) remained white and exhibited nearly 100% of the initial concentrations in human saliva at 4 h. However, the tablets with 15 mg of croscarmellose sodium turned violet and exhibited less than 95% of the initial concentrations in human saliva at 4 h (Table 1). Such a reduced stability of omeprazole in tablets with 15 mg of croscarmellose sodium might be due to the easy penetration of human saliva to the tablet matrix through the porous channels formed in the tablet matrix (17–19).

Based on the current experimental data, only the omeprazole tablet composed of omeprazole/sodium alginate/HPMC/magnesium oxide/croscarmellose sodium at 20/24/6/50/10 mg, respectively, had bioadhesive force suitable for a buccal adhesive tablet, acceptable stability of omeprazole in human saliva, and a fast release rate of drug.

Pharmacokinetic Study

The pharmacokinetic parameters of omeprazole were determined after the dose of buccal adhesive tablet composed of omeprazole/sodium alginate/HPMC/magnesium oxide/croscarmellose sodium at 20/24/6/50/10 mg, respectively, and then compared with those after intravenous administration of omeprazole in hamsters (23–26). During the experiment, the buccal tablets were continuously attached on the hamster cheek pouch.

Figure 3 shows the change of mean plasma concentration of omeprazole after intravenous and buccal administration of omeprazole in the hamster. The plasma concen-

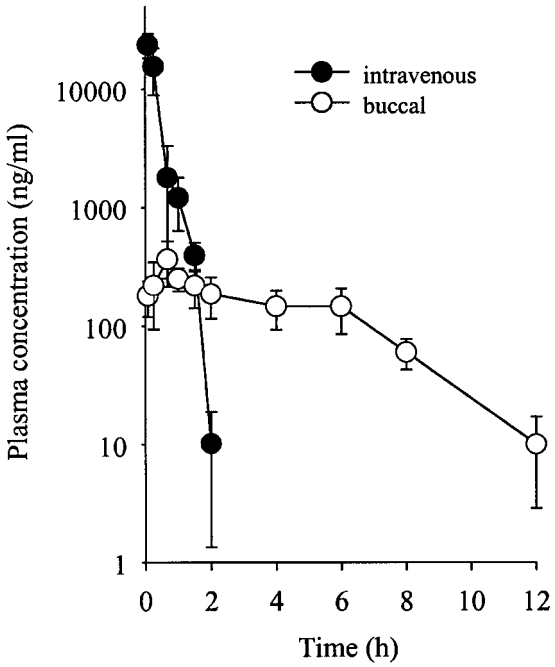

Figure 3. Plasma concentration-time profiles of omeprazole after intravenous and buccal administration in hamsters. Omeprazole buccal adhesive tablet was composed of omeprazole/sodium alginate/HPMC/magnesium oxide/croscarmellose sodium (20/24/6/50/10 mg). Each value represents the mean ± SE (n = 5).

Table 2

Pharmacokinetic Paramters of Omeprazole After Intravenous and Buccal Administration

Parameters	Intravenous	Buccal
AUC (h · μg/ml)	101.01 ± 30.13	13.78 ± 3.23
T_{max}(h)	—	0.67 ± 0.21
C_{max}(μg/ml)	—	0.37 ± 0.13
$t_{1/2}$(h)	0.19 ± 0.05	2.15 ± 0.23

Each value represents the mean ± SE (n = 5).

tration of omeprazole after intravenous administration rapidly decreased to a level ≤10 ng/ml by 2 h after administration. However, the plasma concentration of omeprazole in hamsters increased to reach a maximum of 370 ng/ml at 45 min after buccal administration, continuously maintained a high level of 146–366 ng/ml until 6 h, and then slowly decreased to a level of ≤10 ng/ml by 12 h after administration.

The pharmacokinetic parameters are shown in Table 2. The area-under-the-curve (AUC) values after intravenous and buccal administration were 101.01 ± 30.13 and 13.78 ± 3.23 h·μg/ml, respectively, suggesting that the buccal bioavailability of omeprazole in hamsters was 13.7% ± 3.2%. The half-life $t_{1/2}$ of omeprazole after intravenous and buccal administration was 0.19 ± 0.05 and 2.15 ± 0.23 h, respectively. Thus, our results suggest that the omeprazole buccal adhesive tablet would be useful to deliver omeprazole. Further studies to develop the omeprazole buccal adhesive tablet with an enhancer will be performed to improve the buccal bioavailability of omeprazole.

CONCLUSION

Taken together, it is concluded that the omeprazole buccal adhesive tablet composed of omeprazole/sodium alginate/HPMC/magnesium oxide/croscarmellose sodium at 20/24/6/50/10 mg, respectively, that could be attached on the human cheek without disintegration and could stabilize a drug in human saliva for at least 4 h gave fast release of omeprazole and absolute bioavailability of 13.7% ± 3.2% in hamsters. These results suggest that the omeprazole buccal adhesive tablet would be useful to deliver omeprazole, which degrades very rapidly in acidic aqueous medium and undergoes hepatic first-pass metabolism following oral administration.

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