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The Effects of Backing Materials and Multilayered Systems on the Characteristics of Bioadhesive Buccal Patches

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Abstract

The effects of backing materials (ethylcellulose, polyvinylpyrrolidone and cellulose acetate mixture, and poly(ethylene-co-vinyl acetate) on the characteristics (hydration and adhesion) of newly developed bioadhesive patches for controlled drug delivery via the buccal mucosa were investigated.

It was found that the swelling profiles of buccal patches were changed dramatically by the species and amount of the backing materials, and those changes could alter the drug release profile. The drug release profiles of single-layered and multilayered buccal patches were significantly different.

It was demonstrated that the multiple-layer device could be used to modify the drug release for obtaining the ideal clinical pharmacokinetic release profile.

The oral cavity has a number of features that make it a desirable site for drug delivery, including a rich blood supply that drains directly into the jugular vein, bypassing the liver and thereby sparing the drug from first-pass metabolism (Harris & Robinson 1992). Successful buccal polymer-patch delivery requires a bioadhesive to retain the drug in the oral cavity and maximize the intimacy of contact with the mucosa, a vehicle that releases the drugs at an appropriate rate under the conditions prevailing in the mouth and strategies to overcome the low permeability of the oral mucosa.

The in-vitro and in-vivo characteristics of a newly developed bioadhesive patch for controlled drug delivery via the buccal mucosa were investigated by Scherrer et al 1992; Benes et al 1992, 1994; Guo 1994a,b; Karsenty et al 1994. The effects of different ratios of Carbopol 934P, polyisobutylene, and polyisoprene on the surface properties, adhesion, and swelling of buccal patches were also investigated, leading to the development of patches composed of Carbopol 934P, polyisobutylene, and polyisoprene having physical properties suitable for buccal controlled-drug delivery.

An impermeable backing layer is also used for patches to prevent drug loss and convenience of application. Therefore, this paper describes the effects of backing layers on the swelling and adhesion of buccal patches. The drug-release profiles of multilayered buccal patches were also studied.

Materials and Methods

Preparation of polymer patches. A desired ratio of bioadhesive polymer Carbopol (934P grade, BF Goodrich, Cleveland, OH), polyisobutylene (LMMH grade, EXXON Chemical Co., Houston, TX), and polyisoprene (GoodYear Chemical Co., Akron, OH) were mixed homogeneously with drug and additives in a two-roll mill. The elastomer polymer mixture was compressed to a predetermined thickness, and appropriate sizes were cut or punched out. The multi-layer systems were prepared by recompressing two superimposed patches. The patches were spray-coated by air-spray units which contained individual different backing materials for in-vitro testing. The backing layers included: ethylcellulose (ethoxy content 48·5%, viscosity 45 cps, Sigma, MO), polyvinylpyrrolidone (Average molecular weight 40 000, Fisher Chemical, NJ) and cellulose acetate (MW_w = 177 000, FMC Corporation, Newark, NJ) mixture, and poly(ethylene-co-vinyl acetate) (Elvax 40W, E.I. Dupont, Bedford, IL).

The in-vitro bioadhesion between hydrated polyvinyl pyrrolidone/cellulose acetate hydrogel and bioadhesive buccal patches was assessed using an Instron (Model 4201, Instron Co., Canton, MA). The in-vitro drug release through the hydrated polyvinyl pyrrolidone/cellulose acetate hydrogel film was investigated using diffusion cells and phosphate buffer (pH 7) at 37°C. Aliquots were taken at various times up to 24 h and assayed for buprenorphine free base and HCl salt by high-pressure liquid chromatography (HPLC) equipped with a variable-wavelength ultraviolet/visible detector. The gradient system used in this study consisted of mobile phase, CH_3CN/16.6 mM $CH_3(CH_2)_5SO_3Na$ CH_3COOH, 70/29/1, (v/v/v) at flow rate 1·5 mL min^{-1}.

Results and Discussion

Ethylcellulose, a hydrophobic polymer, has very low water permeability, and moderate flexibility; therefore, it is a good candidate for a backing material. The effects of ethylcellulose on the hydration of polymer patches are shown in Fig. 1. W_0 is the initial weight of the patch. W_t represents the weight of patch in the testing time, and the water uptake of the patch is defined as $(W_t-W_0)/W_0$. The water uptake of polymer patches was delayed by the application of ethylcellulose to around 24 h. The polymer patches which had a higher amount of ethylcellulose had a lower hydration rate. A similar effect was found in the adhesion test (Fig. 2). The time for polymer patches to reach the maximum adhesive

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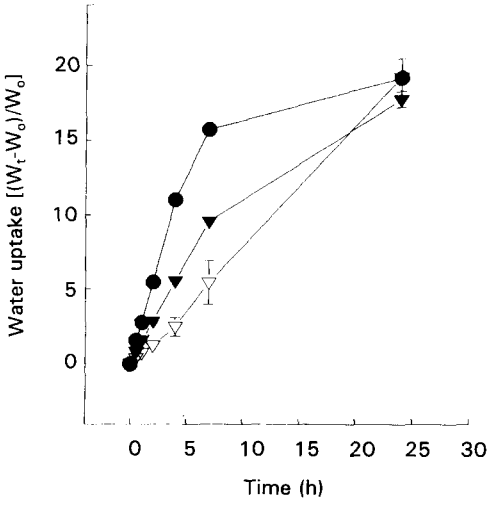

FIG. 1. The effect of ethycellulose (● 0; ▼ 1·26; ▽ 6·47 mg) on the hydration of buccal patches.

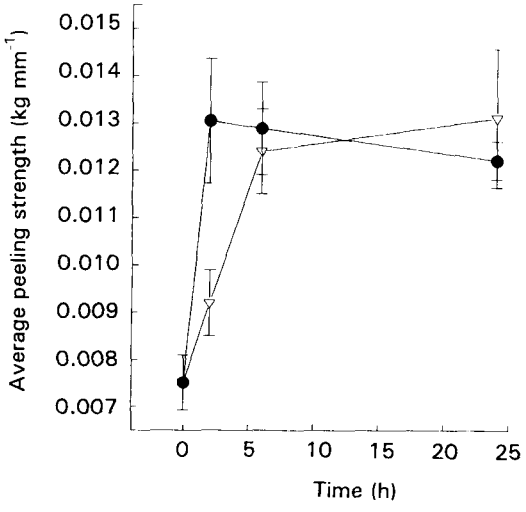

FIG. 2. The effects of ethycellulose (● 0; ▽ 4 mg) on the adhesion duration of buccal patches.

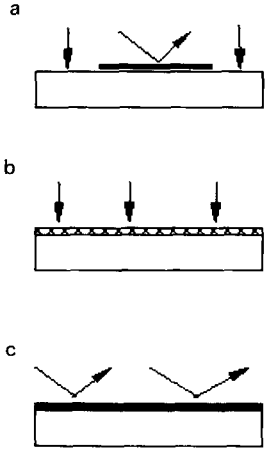

FIG. 3. Schematic illustration of buccal patches with different backing materials. a. Ethylcellulose. Ethylcellulose did not swell with the patch, and water could diffuse into the polymer patch from the surface area which was not covered by ethylcellulose. b. Polyvinylpyrrolidone and cellulose acetate mixture. Water would penetrate the mixture and diffuse into the patch. c. Poly(ethylene-co-vinyl acetate) (Elvax). Water could not penetrate the Elvax film.

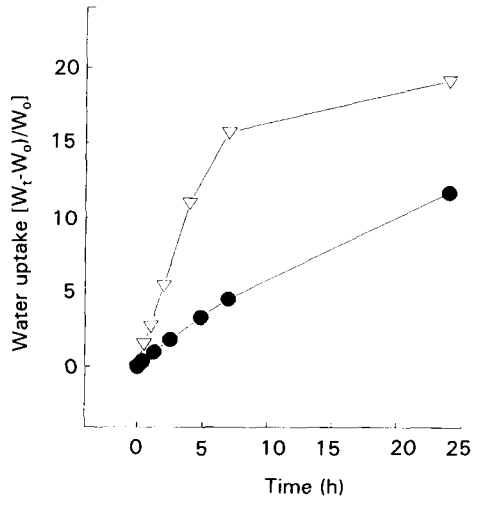

FIG. 4. The effects of poly(ethylene-co-vinyl acetate) (Elvax) (▽ 0; ● 0·5 mg) on the hydration of buccal patches.

strength was prolonged when the patches were backed with ethylcellulose. Since ethylcellulose did not cover the polymer patch when it swelled (Fig. 3), the alternative backing material, polyvinylpyrrolidone and cellulose acetate (PVP/CA) mixture, was studied. The PVP/CA gel did swell with the polymer patch when the polymer patch was hydrated; however this gel has a very high water permeability and could allow the drug to pass through (Fig. 3).

Poly(ethylene-co-vinyl acetate) (Elvax) is another material which has been studied for backing-layer application. Elvax is a very hdyrophobic and elastic polymer, and the effect of Elvax on the patch swelling is presented in Fig. 4. Since most of the swelling force of buccal patch was used to stretch the Elvax film, the swelling ratio of buccal patch significantly decreased when the patch was coated with Elvax (Fig. 3).

The multiple-layer buccal patch device which had no backing layer, was designed to modify the drug-release profile from the patch. The release profiles of buprenorphine

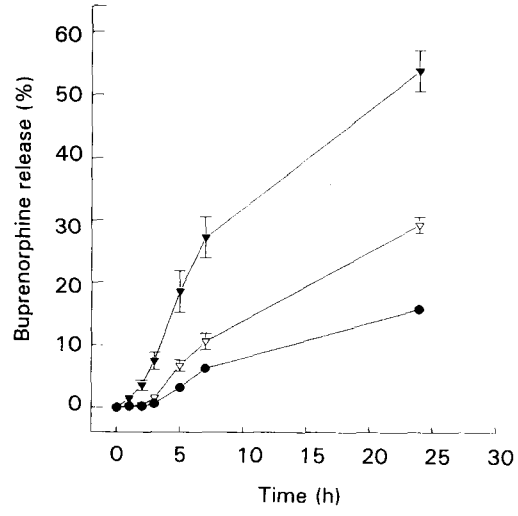

FIG. 5. The drug release profiles of single-layered (▼ 10% loading) and multilayered (▽ 10%/placebo; ● 5%/placebo) buccal patches.

from three different kinds of patches, 10% drug loading single patch, 10% drug/placebo two-layer patch and 5% drug/placebo two-layer patch, are presented in Fig. 5. Significant differences of drug release profiles for these three different kinds of patches were found, and it is apparent that the multiple-layer device could be used to modify the drug release for obtaining optimal clinical pharmacokinetic release profiles.

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