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COMMUNICATION

Theoretical Approaches and Practical Investigations in Carbopol Buccal Patches for Drug Delivery

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ABSTRACT

This paper describes the theoretical approaches in the peeling test method which can be used to evaluate the bioadhesive patches for buccal drug delivery purposes. The effects of patch thickness and the peeling rate on the bioadhesion of buccal patches were investigated from a theoretical point of view. The influence of a crosslinking agent on the swelling and bioadhesive properties of the patches was also evaluated.

INTRODUCTION

Buccal mucosal bioadhesive patches are a new type of external preparation that can render an effective and safe treatment (local or systemic). Absorption of therapeutic agents from the oral mucosa eliminates the problem of premature drug degradation within the gastrointestinal tract, as well as active drug loss due to first-pass hepatic metabolisms that may be associated with other routes of administration (1). The buccal mucosa was investigated as a potential site for drug delivery several decades ago and interest in this area for transmucosal drug administration is still growing. This portion of the oral mucosa is an ideal surface for the placement of retentive delivery systems such as patches since it contains a large expanse of smooth, immobile tissue. In addition, the buccal site is less permeable than the sublingual site, a difference that makes the former a more suitable choice than the latter if sustained drug delivery is desired. The in-vitro characterization of a newly developed bioadhesive patch for controlled drug delivery via the buccal mucosa was investigated by Guo et al. and Degrande et al. (2–7). They developed patches composed of Carbopol 934P, polyisobutylene, and polyisoprene with the required physical properties for buccal controlled drug delivery.

The first step in the development of such a patch is the selection and characterization of an appropriate

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bioadhesive. Since dissolution of a bioadhesive occurs naturally during oral administration, it is important to establish the duration of adhesive force provided by the chosen polymer (8). A variety of in-vitro methods have previously been employed to measure these parameters (8–10). Scientifically, there are two simplifying advantages of the peel test compared to the other methods. It is the only method in which failure proceeds at a controlled rate; furthermore, the peel force is a direct measure of the work of the detachment (11).

This paper describes that by using the Instron 180° peeling test method, the bioadhesion of a newly developed bioadhesve patch for the controlled delivery of drugs via the buccal mucosa was determined. The effects of patch thickness and the peeling rate on the bioadhesion of buccal patches were investigated from a theoretical point of view. This work also evaluated the influence of a crosslinking agent on the swelling and bioadhesive properties of Carbopol 934P buccal patches.

MATERIALS AND METHODS

The crosslinked Carbopol 934P (BF Goodrich, Cleveland, OH) was prepared by using a condensation reaction in the acetone/water/glycerin mixture (Carbopol/glycerin ratio is 1/0.1). The crosslinked Carbopol 934P was collected by spray-drying the mixture solution. The development of buccal drug patches included the establishment of suitable ratios of uncrosslinked Carbopol 934P or crosslinked 934P, polyisobutylene (LMMH grade; Exxon Chemical Co., Houston, TX), and polyisoprene (GoodYear Chemical Co., Akron, OH). These components were homogeneously mixed by using the two-roll milling method. The polymer mixture was compressed to its desired thickness and patches of appropriate sizes were cut or punched out for in vitro testing. The bioadhesion between hydrated polyvinyl pyrrolidone/cellulose acetate hydrogel and buccal patch was assessed using Instron (Model 4201, Instron Co., Canton, MA). Adhesion between the patch and the test surface was expressed as the average peeling strength (kg/mm). Swelling tests of buccal patches were performed in phosphate buffer (pH 7) solution.

RESULTS AND DISCUSSION

In-vitro testing revealed that the average peeling strength of patches increased with increasing patch thickness and reached a maximum bioadhesion at a thickness of approximately 50 mil (3). Increases in thickness beyond this point did not alter bioadhesive strength. The double-logarithmic plot between the average peeling strength and peeling velocity is presented in Fig. 1, and a sigmoid relation between these two parameters was found. When peeling energy is plotted logarithmically against peeling velocity, the patch responded to a regime of low energy peeling (low velocity) and went through a transition to the normal high energy peeling (high velocity).

For a viscous, uncrosslinked elastomeric adhesive, the peeling energy could be expressed as

$$\Theta = \Phi + (\kappa \cdot h)/2$$

where Θ is peeling energy, Φ is the surface energy, κ is the energy dissipated per unit volume of adhesive, and h is the adhesive layer thickness. The bioadhesive strength of buccal patches was found to increase with increasing thickness up to a maximum value, and this is in agreement with data provided in a review by Gene and Hamed (12). The phenomenon can be explained by an alteration of the dissipation energy of patch polymers of increasing thickness (i.e., increasing yield strength) under conditions of viscoelastic and plastic deformation. The peeling energy is a linearly increasing function of thickness when highly hystereic rubber samples are torn apart (large κ value). However, energy dissipated during peeling then becomes independent of the overall thickness of the adhesive because the dissipation process no longer involves the entire layer of adhesive ($\kappa \sim 0$).

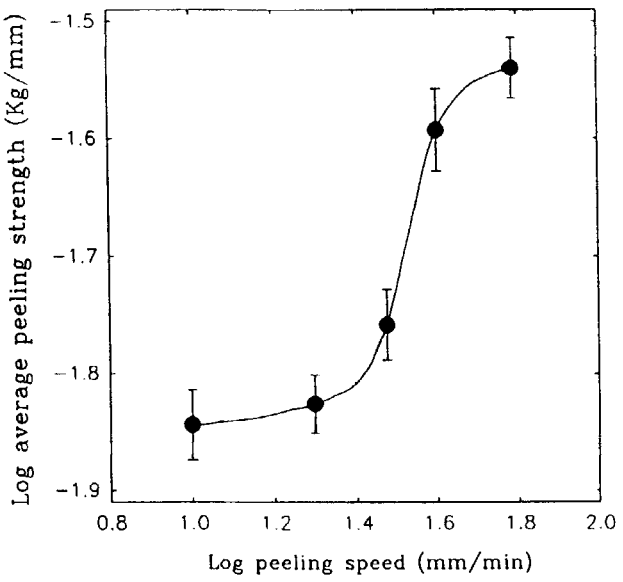

Figure 1. The double-logarithmic plot of peeling strength vs. peeling velocity.

The time-temperature superposition relationship between peeling energy, Θ, and peeling velocity, γ, can be expressed by the following equation:

$$\Theta = \Theta_0 \cdot \Phi(\gamma, T, \xi_0)$$

where Θ_0 is the interfacial bond energy, and Φ is a loss function depending on velocity γ, temperature T, and strain ξ_0. A related observation is that time–temperature superposition of the plot of log Θ against log γ will only be obtained if the energy losses encompassed by the loss function Φ are thermorheologically simple (13). At very low peeling velocities $\Phi \approx 1$ and it is possible in principal to observe a region where Θ becomes independent of rate and temperature and assumes the value Θ_0. At low peeling rates failure is cohesive, with peeling energy Θ increasing with the peeling rate.

Carbopol 934P is a synthetic polymer composed of polyacrylic acid and is only loosely crosslinked. The swelling properties of Carbopol 934P in the buccal patches are dependent on pH and ionic strength of the swelling solution and on the ratios of polyisobutylene and polyisoprene in the patches. As expected the swelling ratio and diameter of buccal patches decreased as the Carbopol 934P was crosslinked with the glycerin. The swelling ratio of uncrosslinked Carbopol 934P patches is almost four times higher than that of crosslinked Carbopol 934P patches after 24-hr hydration in the pH 7 phosphate buffer solution (Fig. 2). The diameter of buccal patches changed from original 1.0 cm to 2.0 cm for uncrosslinked Carbopol 934P patches and to 1.5 cm for crosslinked Carbopol 934P patches after 24 hr of hydration in the pH 7 phosphate buffer solution (Fig. 3).

The decreases of swelling ratio and diameter of buccal patches have reached the goal of crosslinking the

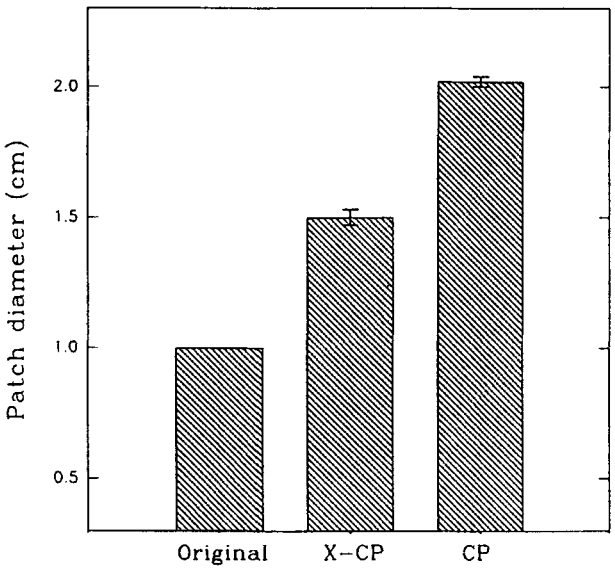

Figure 3. The patch diameter for unsoaked uncrossliked Carbopol 934P patch and crosslinked Carbopol 934P patch (original), soaked uncrossliked Carbopol 934P patch (CP), and soaked crosslinked Carbopol 934P patch (X-CP).

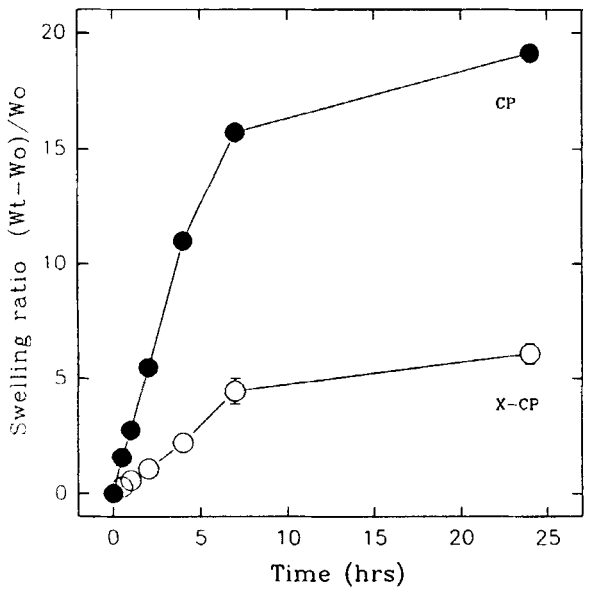

Figure 2. The swelling ratio of uncrossliked Carbopol 934P patch (CP) and crosslinked Carbopol 934P patch (X-CP). Wo: original patch weight, Wt: the patch weight at time t.

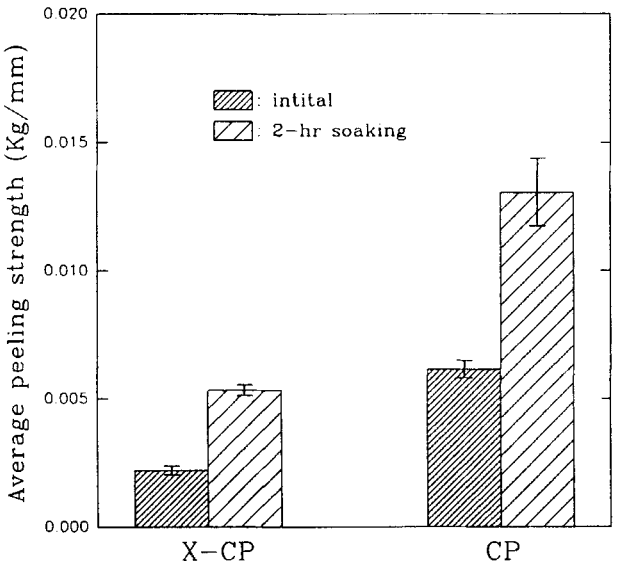

Figure 4. Th peeling strength of uncrossliked Carbopol 934P patch (CP) and crosslinked Carbopol 934P patch (X-CP) at initial and 2-hr soaking time.

Carbopol 934P in this study. However, the bioadhesion of patches also decreased as the Carbopol 934P was crosslinked with the glycerine. Both the initial and 2-hr soaking peeling strengths of uncrosslinked Carbopol 934P patches are nearly one-third of those of crosslinked Carbopol 934P patches (Fig. 4). Therefore, the main consideration when preparing the crosslinked Carbopol 934P patches should be how to balance the swelling profile we need and the bioadhesion we can get from the crosslinked Carbopol 934P patches.

The correlation between the drug (buprenorphine) and water uptake of buccal patches was investigated by Guo (3), and it was found that the swelling of the buccal patch is the major mechanism of drug release. Since the crosslinking agent would change the swelling profile of buccal patches, the drug release from the crosslinked Carbopol 934P patches would need to be investigated in the future.

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