J. Pharm. Pharmacol. 1994, 46: 647–650
Received November 16, 1993
Accepted February 1, 1994

Investigating the Surface Properties and Bioadhesion of Buccal Patches

JIAN-HWA GUO

3M Pharmaceuticals, 3M Center, 270-4S-02, St Paul, MN 55144-1000, USA

Abstract—By using a two-roll milling method, a new bioadhesive polymer patch formulation for drug controlled delivery and consisting of Carbopol 934P (CP), polyisobutylene (PIB), and polyisoprene (PIP) was prepared. The effects of different ratios of CP : PIB : PIP on the surface properties, adhesion, and swelling of buccal patches were investigated. It was found that the surface properties of buccal patches were not only dependent on the CP content but also dependent on the PIB:PIP ratio. The strongest peeling strength was found on the buccal patches with a CP : PIB : PIP ratio of 50 : 43·75 : 6·25. The maximum bioadhesion of patches was found following 2- to 8-h contact with the test medium, and this observation could be explained by the interpenetration of macromolecular chains at the polymer-polymer interface (based on the diffusion theory of polymer adhesion).

Absorption of therapeutic agents from the oral mucosa overcomes premature drug degradation within the gastrointestinal tract, and active drug loss due to first-pass hepatic metabolism that may be associated with other routes of administration (Harris & Robinson 1992). 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 (Nagai & Konishi 1987; Gurny & Junginger 1989). 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 (Harris & Robinson 1992). 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. It has been suggested that drugs with biological half-lives between 2 and 8 h are good candidates for sustained-release formulations (Longer et al 1985). The plasma half-life (3 h), duration of action (4–5 h), and other aspects of its pharmacokinetic profile (liver metabolism) make buprenorphine a suitable candidate for administration via a buccal patch that provides controlled drug delivery and by-passes first-pass hepatic metabolism.

The first step in the development of such a patch is the selection and characterization of an appropriate 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 (Anders & Merkle 1989), and a variety of in-vitro methods has previously been employed to measure these parameters (Gurny et al 1984; Smart et al 1984; Park & Robinson 1985). The effects of manufacturing processes on the physical properties of the individual component polymers and the drug dissolution profile of buprenorphine buccal patches have been assessed and evaluated by the present author (1993), who found that the milling process did not alter the viscosity or the thermodynamic and rheologic properties of individual component polymers; data obtained from dissolution studies suggested that the major mechanism of buprenorphine release is patch swelling. Therefore, I suggested that buccal patches consisting of a homogeneous mixture of polyisobutylene, polyisoprene, and Carbopol 934P (CP) formed by a two-roll milling process, appear to possess physical properties that are well suited for the transmucosal controlled delivery of buprenorphine.

A surface energy analysis of mucoadhesion has been made by Lehr et al (1992, 1993), and the contact angle and spreading coefficient was used to predict the mucoadhesive performance of polymers. They found that the measured adhesive performance between polycarbophil and pig small intestinal mucosa was highest in non-buffered saline medium, intermediate in gastric fluid, and minimal in intestinal fluid. In agreement with this trend, they also found that the mismatch in surface polarities between substrate and adhesive, calculated from the contact angle data, increased in the same order. In addition, they described the mucoadhesion as a process driven by the interfacial thermodynamics in a three-phase (solid-liquid-solid) system. They concluded that the formation of a mucoadhesive bond was primarily governed by the aforementioned surface energy effects and spreading processes, and the surface energy concept provided useful information for the search for better mucoadhesive materials and the identification of favoured target sites in the human body for mucoadhesive drug delivery systems.

This paper describes the in-vitro characterization of a newly developed bioadhesive patch for drug controlled delivery via the buccal mucosa. The effects of different ratios of CP : polyisobutylene (PIB) : polyisoprene (PIP) on the surface properties, adhesion, and swelling of buccal patches were investigated.

Materials and Methods

Carbopol 934P (CP) (polyacrylic acid, BF Goodrich, Cleveland, OH), polyisobutylene (PIB) (LMMH grade; Exxon Chemical Co., Houston, TX), and polyisoprene (PIP) (GoodYear Chemical Co., Akron, OH) were homogeneously mixed by a two-roll mill. The polymer mixture

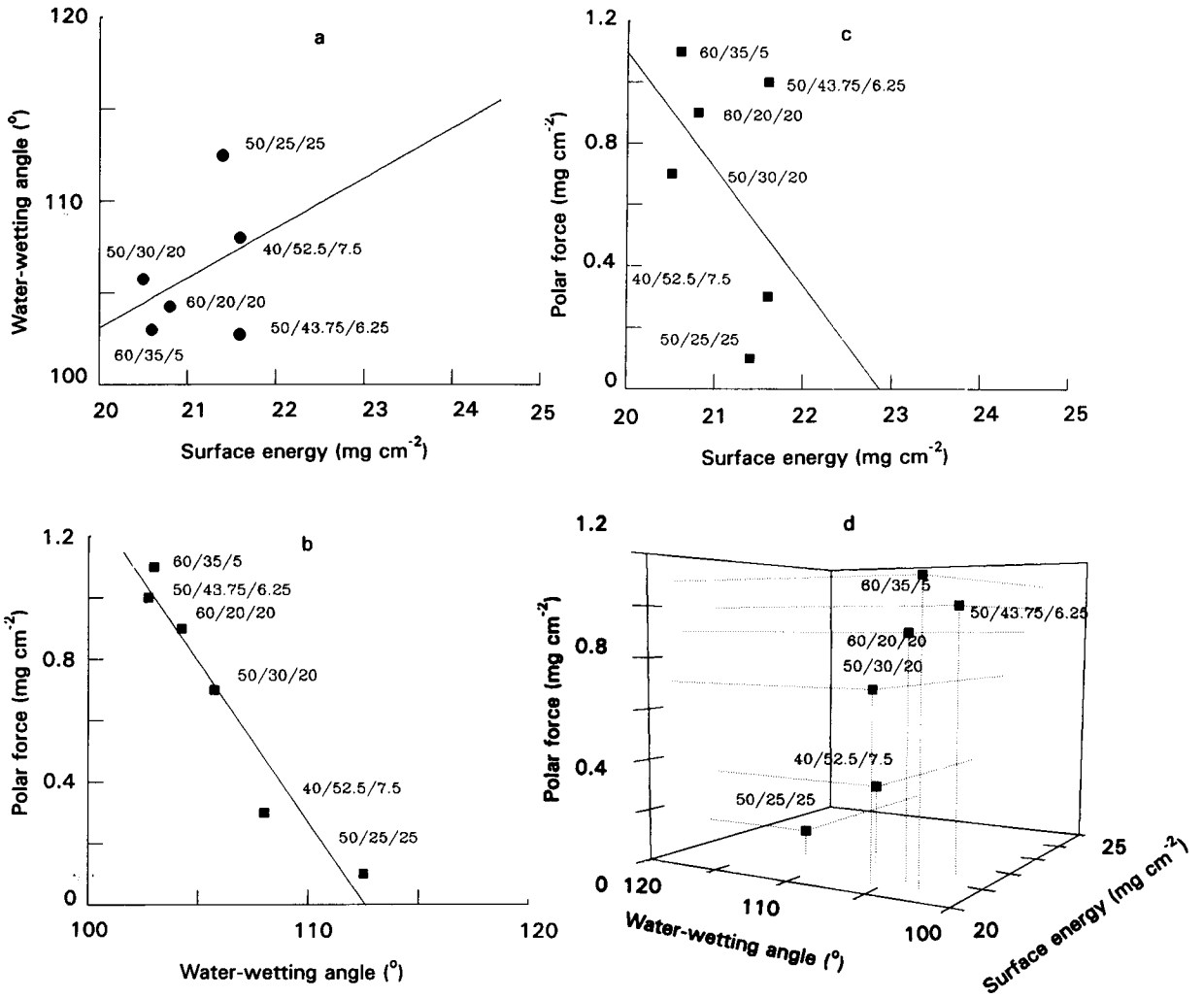

FIG. 1. The surface properties of Carbopol 934P : polyisobutylene : polyisoprene patches. a. The relation between water-wetting angle and surface energy of patches. b. The relation between polar force and water-wetting angle of patches. c. The relation between polar force and surface energy of patches. d. The three-dimensional plot of surface properties of patches.

was compressed to its desired thickness and patches of appropriate sizes were cut or punched out for in-vitro testing. The homogeneity of patches and the effects of manufacturing processes on the physical properties of the individual component polymers have been assessed and evaluated elsewhere (Guo 1993, 1994).

The bioadhesion and adhesion duration between polymer patches and hydrated polyvinyl pyrrolidone/cellulose acetate hydrogel was assessed using Instron Model 4201 (Instron Co., Canton, MA). Adhesion between the patches and the test surface was expressed as the average peeling strength (kg mm^{-1}) or load (kg). A detailed description is given elsewhere (Guo 1994).

By measuring the weight change of each patch with respect to the time, swelling tests were performed in phosphate buffer (pH 7), and swelling ratios and initial swelling rate were calculated. The morphology change of polymer patches during the swelling was studied using scanning electron microscopy.

The surface properties of polymer patches were deter-

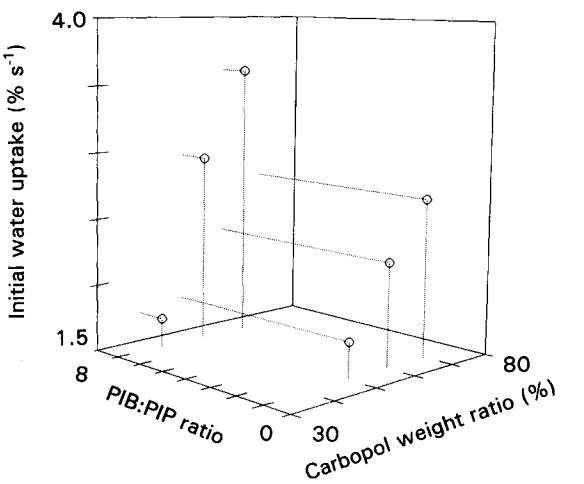

FIG. 2. The effects of Carbopol 934P content and polyisobutylene : polyisoprene ratio on the initial water uptake rate of patches.

Table 1. The effects of Carbopol 934P/polyisobutylene/polyisoprene ratio on the initial water uptake rate of patches.

Composition (CP : PIB : PIP ratio)	Average peeling strength ($kg\,mm^{-1}$)
60 : 20 : 20	0·0077 ± 0·0024
60 : 35 : 5	0·0102 ± 0·0009
50 : 43·75 : 6·25	0·0150 ± 0·0027
40 : 52·5 : 7·5	0·0131 ± 0·0021
30 : 61·25 : 8·75	0·0092 ± 0·0004

mined at ambient temperature by the pendent drop method (Ambwani & Fort 1979; Lehr et al 1992, 1993) using a contact angle goniometer (Model NRL-100, Ramé-Hart, Mountain Lake, NJ), equipped with an environmental chamber.

Results

The surface properties of polymer patches are presented in Fig. 1. The consistent results demonstrated that the water-wetting angle and surface energy decreased with the CP content in the polymer patches at the same PIB : PIP ratio, and decreased with PIB : PIP ratios when the CP ratio in the polymer patches was fixed; the surface properties of buccal patches are not only dependant on the CP content but also dependant on the PIB : PIP ratio.

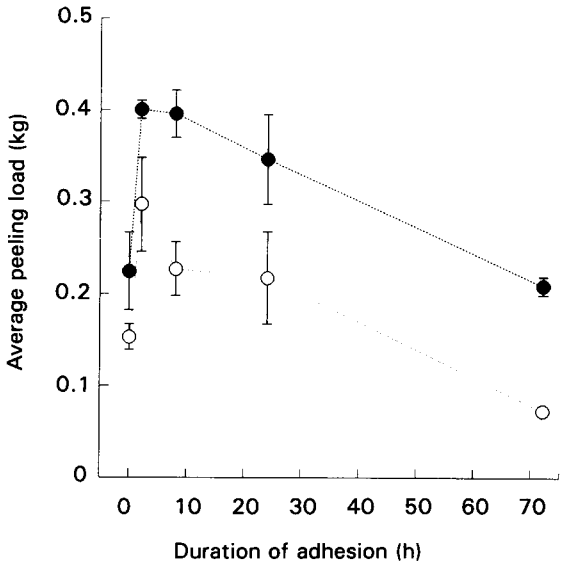

FIG. 3. Change in adhesion with time. ● 50 : 43·75 : 6·25 CP : PIB : PIP, ○ 60 : 35 : 5 CP : PIB : PIP.

The effects of CP content and PIB:PIP ratio on the swelling of buccal patches are shown in Fig. 2. The initial water uptake rates of buccal patches were found to be effected by both the CP content and PIB:PIP ratio, and

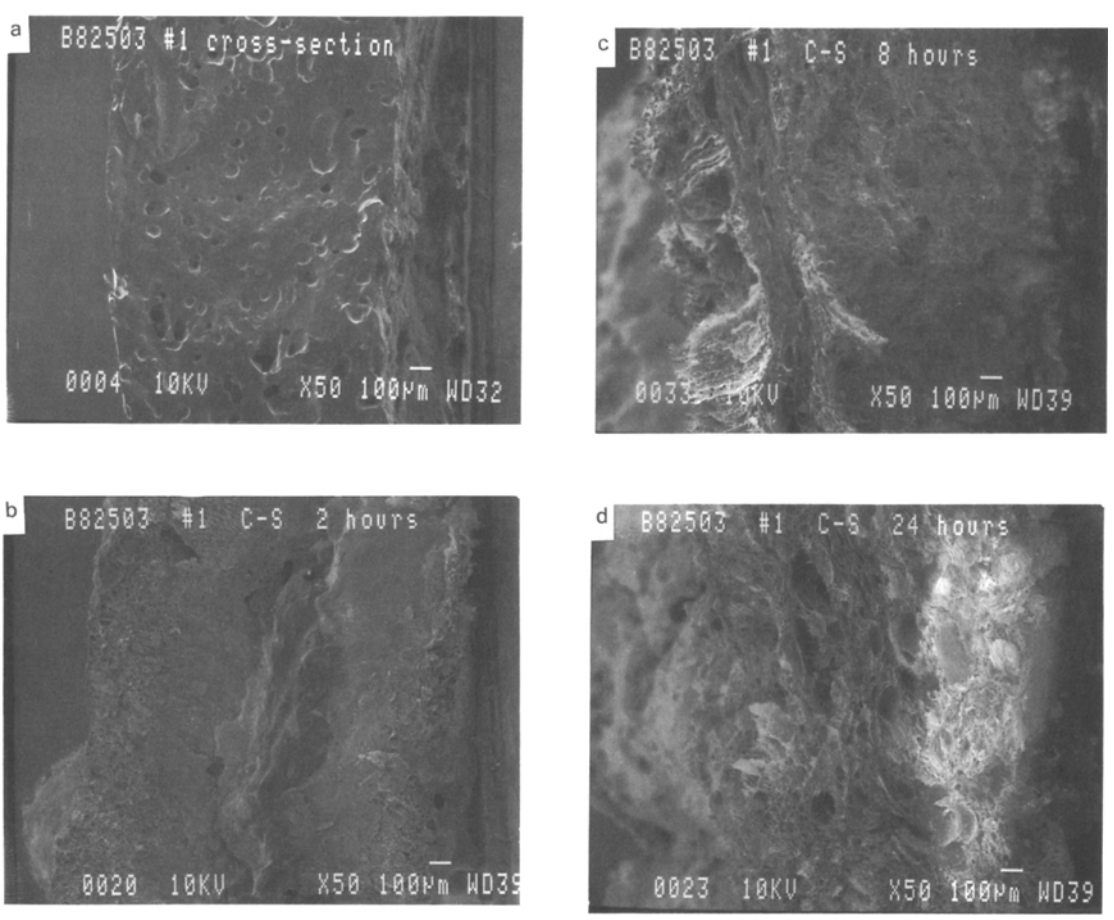

FIG. 4. Scanning electron micrographs of polymer patches (cross-section); a, initial; b, 2-h; c, 8-h; d, 24-h.

the polymer patches which contained higher CP content or PIB : PIP ratio had higher water uptake capacity.

The average peeling strengths of buccal patches which contained different CP : PIB : PIP ratios are shown in Table 1. The strongest peeling strength was found for the buccal patches which contained a CP : PIB : PIP ratio of 50 : 43·75 : 6·25.

The adhesion duration results for both 60 : 35 : 5 and 50 : 43·75 : 6·25 (PIB : PIP ratio is 7 : 1 for both formulations) patches are shown in Fig. 3. A similar phenomenon was seen for these two different kinds of patches. The initial maximum bioadhesion of patches was found following 2–8-h contact with the test medium, and the bioadhesion values decreased with contact time.

The scanning electron micrographs of the polymer patches (cross-section) during the swelling are shown in Fig. 4. A more loose structure of the buccal patch was found when the patch was soaked in the buffer solution for a longer time.

Discussion

The results of surface property studies (Figs 1, 2) show that the polymer patches which contained high CP content and PIB : PIP ratio had low surface energy and water-wetting angle. Initially, it might be supposed that the polymer patches which had low surface energy and water-wetting angle should have higher bioadhesive potential. However, the peeling test results (Table 1) showed that the maximum peeling strength was seen at 50% CP and 7 : 1 PIB : PIP ratio formulation, but not at 60% CP and the same PIB : PIP ratio. The experimental results of Lehr et al (1992) indicated that interfacial energies played an important role in mucoadhesion. Nevertheless, it was found from this study that the bioadhesion of buccal patches could not be predicted by judging from their surface properties only. Since the wetting angle and surface energy results would only represent the initial ability to adhere to the substrate, the relation between bioadhesion and morphological structure of buccal patches should be considered as an important factor. An optimal amount of PIB and PIP is needed for supporting the swelling of CP to achieve the maximum adhesion between patches and substrate.

The increasing bioadhesion of patches was found following 2–8-h contact with the test medium (Fig. 3), and a plausible explanation for this observation (based on the diffusion theory of polymer adhesion) is that the increase is due to the interpenetration of macromolecular chains at the polymer-polymer interface (Peppas & Buri 1985). Using the attenuated total reflection infrared spectroscopy (ATR-FTIR) Jababari et al (1993) have investigated the chain interpenetration at a poly(acrylic acid) and mucin interface. Their results indicated that an important mechanism of mucoadhesion is chain interdiffusion as the mucin swells the cross-linked poly(acrylic acid) matrix. After the buccal patches reached the maximum adhesion, the decrease in adhesion could be explained by the relaxation of CP and the loose structure of the patches. The scanning electron micrographs of buccal patches (Fig. 4) showed that the structure of buccal patches was continuously swelling and becoming more loose after soaking in the buffer solution.

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