



Investigating the Pharmaco-Mechanical Characteristics of Buccal Patches and Their Interaction with Loaded Antihypertensive Drug Permeation

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ABSTRACT

Atenolol buccal patches have the mucoadhesive layers built into their design, which extends across the whole patch. The medication and control release polymer (HPMC K15M or HPMC K4M) were the main components chosen for the matrix layer, whereas gum karaya was the prominent element in the mucoadhesive layer. Various assessments, including thickness uniformity, average weight, folding endurance, mucoadhesion strength, and swelling behavior, were performed on the developed patches. Permeation tests confirmed that the patches' physicochemical qualities were adequate. A dialysis membrane was used to perform an 8-hour in vitro permeation research in a phosphate buffer with a pH of 6.8. Each batch's permeation profile was almost linear, and the total medication penetrated from formulation ranged from 32% to 49%. The flow ranged from 1.43 to 1.85 mg cm⁻² hr⁻¹, and the permeability coefficient was determined to be between 0.041 and 0.053 cm/hr.

KEY WORDS: Buccal patch, mucoadhesion, Swelling, Permeation.

INTRODUCTION

There are a number of significant advantages to the buccal medication delivery technique over the more traditional methods of dosing. Drugs that are unstable at stomach pH, have a short biological half-life, a low molecular weight, a poor water solubility, and a strong first pass effect may be conveniently delivered using this method. [1]

There are currently a number of buccal formulations available, including films, patches, gels, ointments, strips, and disks. But the patches are more accommodating, and they make the patient feel better. Their removal from the application site and administration are both made easy. Therefore, compared to alternative dose forms, patient compliance is higher. However, the buccal area is also quite vascular. Therefore, it is quite easy to go there. The drug has a high rate of bioavailability because it may enter the systemic circulation via the jugular vein with relative ease. [2] In Many macromolecular drugs, including peptides, proteins, and nucleic acids, with improved pharmacological efficacy, site specificity, and decreased unwanted and toxic effects, have been generated as a consequence of rapid optimization in molecular biology and gene technology. the third

Because of their large presystemic metabolism and instability in acidic environments, these medicines have poor and unpredictable oral absorption, which is the fundamental problem with their oral administration as possible therapeutic agents. These medications are thus most effectively administered via buccal route, as the oral mucosal membrane is vascular, very permeable, and easily accessible; this permits the painless and continuous absorption of medicines into the system. [4]

Mucoadhesive polymers with a release retardant and a strong swelling characteristic are Gum Karaya and HPMC. The inert, viscoelastic, hydrophilic polymer known as hydroxy propyl methyl cellulose is a semi-synthetic substance. It may connect with mucin in the mucosal layer by strong hydrogen bonding.

There are benefits to using natural polymers instead than synthetic or semi-synthetic ones. This is due to the fact that they are readily accessible, inexpensive, and harmless. Gums derived from plants are a kind of natural polymer. Carbohydrates, with

trace amounts of proteins and minerals, make up the bulk of natural gums. These gums may be used as thickeners in food and cosmetic preparations due to their high safety margin and accessible availability. The sticky exudate of the *Sterculia urens* tree is known as gum karaya. It is a member of the Sterculiaceae family. Deacetylation by alkali treatment renders Gum karaya water soluble, and the existence of an acetyl group determines the gum's swelling behavior. When submerged in water, gum karaya may expand by about 100% and by 60% in alcohol. Gum karaya is indigestible and cannot be absorbed by the body. The culinary and cosmetic industries also make use of gum karaya, in addition to the pharmaceutical sector. Gum karaya can withstand a 10% hydrochloric acid solution at ambient temperature for a minimum of eight hours because of its high uronic acid concentration.

On this page The buccal patches will now include atenolol. The solubility of atenolol, a medication belonging to BCS class III, is dependent on pH. A permeability range of 50-84% is considered moderate. One of the most common uses for the beta blocker medicine atenolol is the treatment of hypertension and chest discomfort caused by the heart. Migraine prophylaxis and the therapy of certain arrhythmias are two more applications. It may be administered intravenously or orally. Additionally, it is compatible with other drugs that lower blood pressure. Feeling exhausted, fainting, depressed, and short of breath are common adverse effects. Bronchospasm is another major adverse effect. [5]

MATERIALS

The Dehradun, India-based Windlas Biotech LTD generously donated Atenolol. Colorcon Pvt Ltd. of India offers a variety of grades of Hydroxypropyl methyl cellulose, including HPMC K4M and HPMC K15M. Ingredients supplied by Indian Drug House: ethyl cellulose and glycerine. Purchase Gum Karaya in Hyderabad from Nutriroma.

Drug-Polymer Interaction Research Infrared Spectroscopy and Fourier Transform Analysis

Using a Fourier transform infrared spectrophotometer (Perkin Elmer, spectrum GX FTIR), we investigated the drug-excipient compatibility. The atenolol infrared spectra were captured by means of a Fourier transform infrared spectrophotometer that used the diffuse reflectance principle. Prior to sampling, the material was mixed with potassium bromide (KBr), ground in glass mortar, and then placed in the sample holder. The frequency range that was examined in the spectrum was 4000-400 Hz. cm⁻¹. We measured the infrared absorption spectra of both the pure drug and a physical mixing of the drug and polymer. [6]

Buccal Patch Preparation Background Membrane Preparation

We used PVA (Poly-vinyl Alcohol) to make the backing membrane. Four milligrams of PVA were measured. This was followed by heating the double distilled water to 80 °C. A suitable viscous solution was created by adding the weighed PVA while stirring continuously. The next step was to transfer the mixture to the mold.

The Method of Solvent Casting

To begin, the polymers were agitated while dissolving in a solvent. After that, the medicine was added while stirring constantly until a thick solution was formed. The plasticizer was then added while the mixture was still being stirred. Humectants were subsequently added. The solvent was then evaporated by pouring it into a mold. Patches with unidirectional drug release are the result of backing membrane preparation in the mold. A coating of gum karaya was applied on the other side of the backing membrane to facilitate the muco adherence of the patch after its preparation. [7]

Application of Gum Karaya's Mucoadhesive Layer

2. Grams Twenty milliliters of double distilled water containing gum Karaya was heated to a temperature of eighty-five degrees Celsius and swirled constantly using a magnetic stirrer. A coating of the sticky solution was poured around the patch once it had been properly mixed.

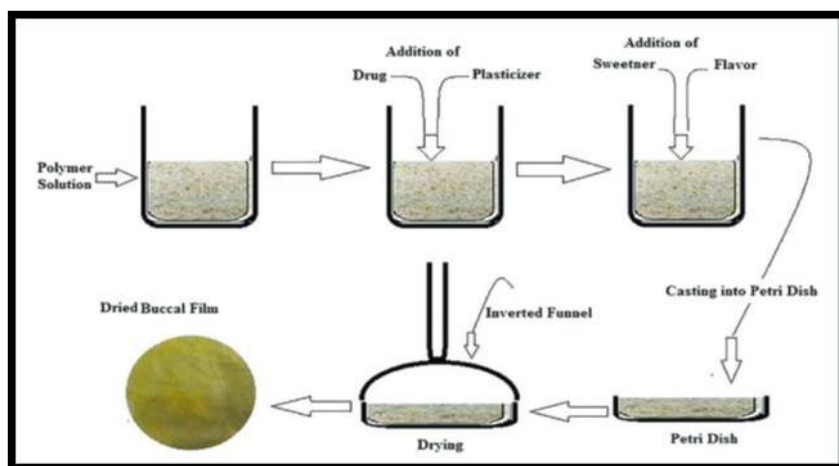


Fig. 1: Preparation of Buccal Patches.

Table 1: Components of the formulations.

Formula	HPMC K4M:Ethyl Cellulose	HPMC K15M:Ethyl Cellulose	HPMC (K4M+K15M):Ethyl Cellulose
B1	1:1		
B2	3:1		
B3		1:1	
B4		3:1	
B5			0.5:0.5:1
B6			1.5:1.5:1

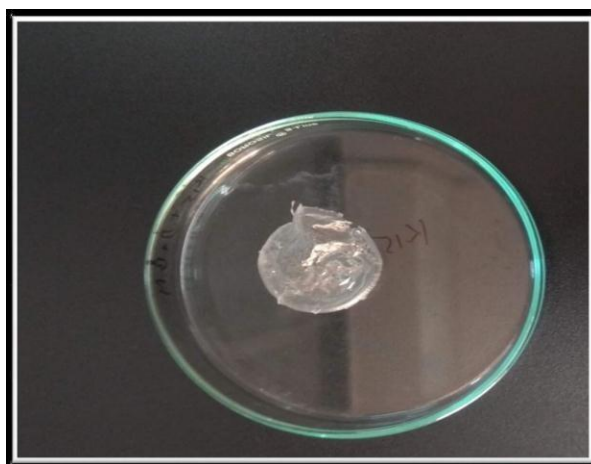


Fig. 2: Buccal Patch.

Drug Content Study

After dissolving a 5.72 cm² patch in 100 ml of methanol and vigorously shaking it for 24 hours at room temperature, the drug contents in the buccal patches were measured. Using Whatman® filter paper, these solutions were diluted. A UV-VIS spectrophotometer was used to measure optical density at 274 nm against a blank after the appropriate dilution. The concentration of the medication was calculated by constructing a calibration curve that included concentration ranges of 1 to 5 µg/ml. Linearity, accuracy, and precision were all checked to ensure the approach was legitimate. The calibration curve's regression equation was $Y = 0.103X$.

Consistency in patch thickness:

Using a screw gauge, we measured the thickness of each patch five times throughout the patch and then averaged the results. [8] Folding resistance To test the patches' folding durability, we folded them in the same spot until they broke or until we reached a suitable number of hand folds—300—to indicate that the patches had excellent qualities. The value of the folding endurance was determined by the number of times the patch could be folded in the same spot without breaking. The patches underwent this testing. [9] Strength of Mucoadhesion

An adjusted mucoadhesive test assembly was used to gauge the patch's mucoadhesive strength. The bottom of a pan on the balance was patched using glue. A little amount of phosphate buffer (pH 6.8) was used to saturate the patch, and then the side of the patch that was facing the ongoing gum karaya was allowed to adhere to a glass slide. An exact calculation of the force required to move the patch away from the glass slide was carried out. The patch's mucoadhesive strength in vitro is represented by that weight.

The bond strength, expressed as a number in Newtons per square meter, is equal to the force of adhesion divided by the surface area, divided by 1000.

Small-Scale Picture

A digital microscope was used for the microscopic imaging. Along with a high-speed digital signal processor (DSP), a 640×480 optimal DSP resolution, 5x digital zoom, calibration ruler, digital measurement software, and compatibility with USB 3.0, 2.0, and 1.1, this device also has an HD color CMOS sensor.

Disparity in Mass

We used an analytical balance (Shimadzu, Japan) to measure the weight of each patch separately before averaging them. Moisture Content and Absorption Determination The anhydrous calcium chloride-containing desiccators were used to store the precisely weighted buccal patches. After three days, the patches were removed and their weight was recorded. By plugging the percentage of moisture loss into the above formula, we were able to ascertain the moisture content:

The percentage of moisture is equal to 1 divided by the difference between the initial and final weights, multiplied by 100. Before being inserted in the desiccators with Sodium Hydroxide, the buccal patches were precisely weighed. We removed and weighed the films after three days. The formula was used to determine the percentage of moisture absorption. The formula for moisture absorption as a percentage is expressed as $[(\text{Final weight} - \text{Initial weight}) / \text{Initial weight}] \times 100$.

Surface pH The pH of the prepared patches was tested by dipping them into a 6.8 phosphate buffer for one minute. To see whether any of the films irritate the buccal mucosa, we measured their surface pH. For one minute, the pH probe was left in touch with the surface of the film to enable it to acclimate. [10]

Experimental permeability

Using a modified Franz diffusion model, we calculated the rate and amount of atenolol mucosal penetration via cell. In a nutshell, the solvent was PBS (pH 6.8) added to the receptor compartment (78 mL) and mixed at 50 rpm while the temperature was maintained at 37.0 ± 0.5 °C. Diffusion cell donor and receptor compartments on dialysis membrane were sandwiched by the patch. The receptor medium was removed in 5 mL portions at regular intervals and promptly replaced with PBS (pH 6.8) in equal amounts. To find out how much Atenolol was released into the receptor media, the absorbance at 274 nm was measured in comparison to a blank.

RESULTS AND DISCUSSION

At a pH of 6.8, 1 gram of Atenolol was dissolved in 25 milliliters of phosphate buffer. The mixture was continually stirred in a B.O.D. shaker for three days, with 24-, 48-, and 72-hour pauses in between. At various intervals, 1 ml of the sample was removed and its absorbance at 274 nm was measured. When tested at pH 6.8, atenolol dissolved at a concentration of 15.37 mg/ml.

Prior to developing a novel formulation, it is crucial to determine the drug-excipient interaction. Researchers have turned to Fourier Transform Infrared Spectroscopy spectra as one of the many tools at their disposal to learn more about the molecular level interactions between excipients and drugs [6]. Shown in Figure 3 are the infrared spectra of the drug, the polymer, and the drug-polymer combination. Transmission spectroscopy has shown changes across wave numbers (3400-3550 cm^{-1}) and (1630 - 1500 cm^{-1}). The functional groupings for those locations are mostly caused by stretches. Since no significant change in peak positions has been seen, the FTIR spectra imply the possibility of physical interactions as a result of the formation of weak bonds.

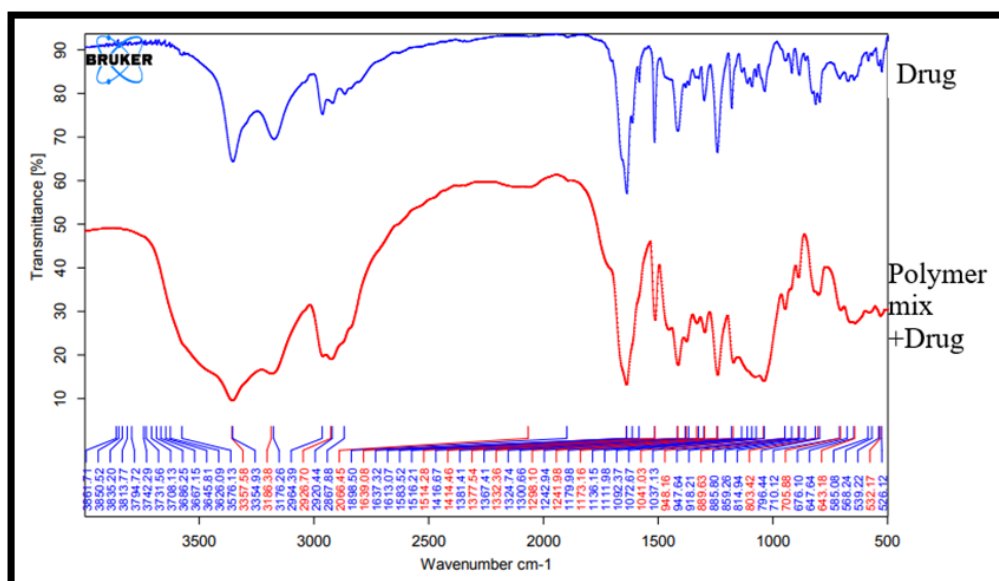


Fig. 3: Overlaid FTIR Spectra of Polymer mix with Drug and Drug individually.

Table 2: Physico mechanical parameters.

PARAMETERS	B1	B2	B3	B4	B5	B6
Drug Content	99.51	99.51	96.85	96.85	97.75	97.75
Thickness Uniformity (mm)	0.12 ± 0.00707	0.13 ± 0.00608	0.11 ± 0.11402	0.12 ± 0.10502	0.9 ± 0.11402	0.10 ± 0.1245
Folding Endurance	>300	>300	>300	>300	>300	>300
Mucoadhesion Strength (gm)	15.2 ± 1	17.2 ± 1	19.30 ± 1	21.23 ± 1	16.50 ± 1	18.1 ± 1
Weight Variation (%)	125.10	126.15	127.17	128.18	127.16	125.25
Moisture Uptake (% w/w)	7.2	6.9	3.45	3.13	5.7	4.9
Moisture Content (% w/w)	5.26	5.50	4.90	4.98	5.10	5.12
Surface pH	6.80	6.85	6.85	6.85	6.80	6.80

Measurement of Mucoadhesion Strength

There was a shift in mucoadhesion strength among formulations as a result of these testing, which were performed on all of the formulations. that proportion of hydrophobic polymer to ethyl cellulose. Formulation B1 had the lowest mucoadhesion strength of 15.2 g while formulation B4 had the highest, measuring 21.23 g. In Table 2.

When a bioadhesive polymer binds to mucus, this phenomenon is known as mucoadhesion or bioadhesion. Wetting, interpenetration, adsorption, and the creation of secondary chemical bonds between the polymer and mucus membrane are the four main steps in mucoadhesion. Polymer swelling degree, contact duration with membrane, and molecular weight are a few of the variables that influence mucoadhesion strength. As hydration level rises, adhesion will also rise. An increase in HPMC in conjunction with gum karaya was associated with an increase in the degree of edema.

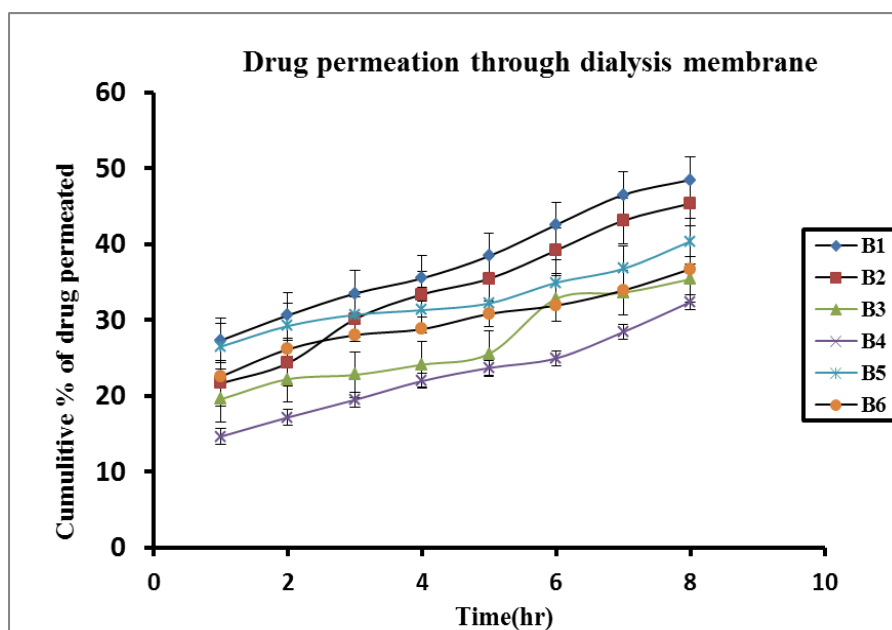
Because acidic or alkaline pH may irritate the buccal mucosa, measuring the buccal patches' surface pH allowed researchers to speculate on the potential irritation consequences. Results showed that the surface pH of all formulations ranged from 6.80 to 6.85, which is close to neutral. It was assumed that the buccal mucosa would not be irritated by the formulation's neutral pH.

Fragments of dialysis membrane were attached to the Franz diffusion cell in order to study the drug permeation kinetics. The medication release site was kept lower by affixing a buccal patch over the dialysis membrane. The receiver compartment was filled with phosphate buffer with a pH of 6.8. After 5, 15, 30, 45, and 60 minutes, samples were obtained. After that, every hour up to 8 hours, new buffer was changed. Flow cytometry was used to analyze the formulations. Formulation B1 had the highest cumulative drug permeation rate at 49%, whereas formulation B4 had the lowest at 32%.

While the medication was being studied, zero-order kinetics may be used to characterize the penetration (Fig:3). We found the permeability coefficient (P) by dividing the slope of the line (J) by the surface area of the dialysis membrane (S), where Cd is the drug concentration in the receiver chamber, and P is the permeability coefficient itself. Each batch's permeation profile was almost straight. There was a flow of 1.43–1.83 mg cm⁻² hr⁻¹, and a permeability coefficient of 0.041–0.052 cm/h.

Table 3: Drug Permeation.

TIME(h)	CUMULATIVE PERCENTAGE OF DRUG PERMEATION					
	B1	B2	B3	B4	B5	B6
1	27.29	21.64	19.54	14.62	26.48	22.52
2	30.60	26.42	22.19	17.14	29.19	30.51
3	33.47	30.09	22.75	19.46	30.66	32.10
4	35.48	33.35	23.95	21.94	31.29	34.52
5	38.41	35.42	25.54	23.67	32.18	35.19
6	42.53	39.16	32.78	24.94	34.89	36.63
7	46.48	43.08	33.59	28.41	36.74	41.69
8	49.84	46.30	35.36	32.37	40.35	44.64

**Fig. 3: Drug Permeation from Formulation B1, B2, B3, B4, B5, B6.****Table 4: Flux, Permeation coefficients of the formulations.**

Formulation	Slope	Flux ($\text{mg cm}^{-2} \text{h}^{-1}$)	Permeation Coefficient (cm /h)
B1	3.067	1.79	0.042
B2	3.442	1.61	0.041
B3	2.3723	1.43	0.045
B4	2.663	1.85	0.051
B5	1.7669	1.65	0.052
B6	1.8075	1.53	0.049

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