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Evaluation of a Mucoadhesive Buccal Patch for Delivery of Atenolol : *In vitro* Screening of Bioadhesion

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Mucoadhesive buccal patches of Atenolol for local delivery of the drug to the oral cavity were formulated by Solvent casting technique. Different mucoadhesive polymers, namely Polyvinyl alcohol (PVA), Sodium carboxymethyl cellulose (NaCMC) and Chitosan of different grade were incorporated into the patches to modify their mucoadhesive properties as well as the rate of drug release, using glycerol as plasticizer. Different concentrations of polymer were used for the preparation of patches. The patches were evaluated on the basis of their physical characteristics like surface pH, folding endurance, mucoadhesive performance, and release rate. The in-vitro drug release was carried out in *Franz diffusion cell*, with commercially available dialysis membrane. Formulation P-10 (10 % polyvinyl alcohol, 5 % glycerol and 2 % Atenolol) showed sustained release upto 18 hours and also obeyed Higuchi kinetic release pattern.

Keywords: Mucoadhesive Buccal Patch, Atenolol, Bioadhesion.

The main aim of the study was to develop and evaluate mucoadhesive patches of Atenolol for the treatment of cardiac diseases. Development of new drug delivery system has been one of the major thrust area of pharmaceuticals these days. Buccal cavity has a wide variety of functions and it acts as an excellent site for the absorption of drugs. In the present investigation focus was given to design Atenolol buccal patches with different polymers. The study also indicated that the permeability of all-epithelial was similar, with most selective for positively charged molecules. Atenolol is a β-blocker widely used in the treatment of hypertension. Since the buccal route by-pass the hepatic first pass effect, the dose of Atenolol could be reduced. The physio-chemical properties, its suitable half life (6-7 hours) and low molecular weight (266.3) make it a good candidate for administration by the buccal route.

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The effectiveness of mucoadhesive formulation was greatly determined by the nature of polymer composition used.

MATERIALS AND METHODS

Atenolol was a gift sample by Dabur India Limited, Ghaziabad (INDIA), Polyvinyl alcohol (PVA) and Sodium carboxymethyl cellulose (NaCMC) were procured from Central Drug House, New Delhi (INDIA). Chitosan was a gift sample by Central Institute of Fisheries Cochine (INDIA). Other chemicals used were of A.R. grade.

Preparation of mucoadhesive patches

All the patches were prepared by solvent casting technique. The polymer studied, PVA, NaCMC and Chitosan were applied in concentration of 10% (P-10), 3% (S-3) and 2% (C-2) w/v respectively. In all cases 5% v/v glycerol was added as plasticizer. For polyvinyl alcohol patches 10% w/v PVA was dissolved in hot water (80-100°C) under constant stirring.

For sodium carboxymethyl cellulose patches 3% NaCMC dissolved in distilled water and stirrer by means of magnetic stirrer.

For Chitosan patches 2% w/v Chitosan was dissolved in 1.5% v/v acetic acid solution with stirring for 48 hours, then added 5% v/v glycerol and 2% w/v Atenolol (10mg for each patch) in all cases with continuous stirring. The resultant viscous solution was filtered and left to stand until all the air bubbles disappeared. The solution was poured in a clean, dry, glass petridish and allowed to dry in an oven at 40°C till a flexible film was formed. The Chitosan patches were dry at room temperature. The patches of 10 mm diameter were cut and packed in aluminium foil.

Evaluation of patches content uniformity

From the prepared patches, one patch was dissolved in 10 ml of buffer solution (pH 6.8), shaken vigorously for 5 min and then diluted to 10 ml with buffer. The solution was filtered through whatman filter paper (No.42) and drug content was then determined after proper dilution and absorbance was measured spectrophotometrically at 225 nm against a blank.

Patch Thickness

The thickness of 10 patches was measured using of screw gauge. The data were analyzed for sample mean and standard deviation.

Mass Uniformity

The mass of each of 10 individual patches was determined by placing it on an electronic balance. The mass data from the patches were analyzed for sample mean and standard deviation.

Surface pH

The patches were left to swell for one hour on the surface of agar plate, prepared by dissolving 1% w/v agar in buffer solution (pH 6.8) under stirring. The surface pH was measured by means of a pH paper placed on the surface of swollen patches.

Radial Swelling

The radial swelling of patches was determined by weighing three patches (W_1) and placed separately in beakers containing phosphate buffer (pH 6.8). The beakers were stored at room temperature, after 8 hours the patches were removed and excess water on their surface was carefully absorbed using filter paper, and weighed (W_2). The % radial swelling was calculated as:

$$RS\ (\%) = (W_2 - W_1 / W_1) \times 100$$

Folding Endurance

Folding endurance of the patches was determined manually by repeatedly folding the patch at the same place till it broken or folded upto 300 times, patches without breaking gave the value of folding endurance.

Mucoadhesive Force

The tensile strength required detaching the mucoadhesive patch from the mucosal surface was applied as a measure of the bioadhesive performance. The apparatus was locally assembled, which consist of three parts, a tissue mount fixed on the glass dish, a patch holder with a nylon thread and a light pan. The tissue holder with pig intestine portion was allowed to hang on an iron stand. The patch was fixed on tissue by applying a force by thumb and the pan was attached to patch holder. The water was added in the pan till the patch was detached. The total weight of water in the pan require for the complete detachment of patch was recorded and

Table 1. Physico-chemical characteristics of Patches

Composition	Batch code		
	P-10	S-3	C-2
Patch thickness (μm)	390±3.8	440±4.1	310±1.2
Patch mass (μg)	374.1±2.9	408.7±2.5	337.5±2.2
Surface pH	≈7	≈7	≈7
Drug content (%)	99.2 ±0.15	98.2±0.10	98.7 ±0.11
Redial swelling (%)	20.15±0.50	37.99±0.28	9.1±0.9
Folding endurance	>300	>300	>300
Bioadhesive force	402 ±7.1	120.1 ±1.8	78.91±3.2
In vitro release (18hours)	92.71±1.1	88.12±1.4	85.32±1.9

mucoadhesive force was calculated per unit area of the patch as

$$F = (W \times g / A) \times 100.$$

where F is the mucoadhesive force (Kg $m^{-1}s^{-2}$), W is weight of water (gm), g is acceleration due to gravity (cm s^{-2}) and A is the area patch (cm^2).

***In vitro* Release Study**

Commercially available dialysis membrane (obtained from Himidia chemicals Mumbai, INDIA) was employed for the study. The membrane used was transparent and a regenerated cellulose type, which was permeable to low molecular weight substances. The in-vitro release study was done in Franz diffusion cell. The diffusion cell consists of two parts: upper donor compartment and a bottom receptor compartment. The receptor compartment was enclosed by water jacket to control the temperature. An O-ring seal couple with a membrane and patch to separate the top and bottom compartment, for allowed 10 mm of diffusion area. In the receptor compartment the phosphate buffer (pH 6.8) was filled, cell was placed on magnetic stirrer and maintained at 37°±0.5°C, the buffer solution was stirrer at a speed of 20 rpm and the sample were collected from the chamber after every hour upto 18 hours and analyzed spectrophotometrically at 225nm.

RESULTS AND DISCUSSION

Physical characteristics of the patches shown in Table 1. The thickness of patches was varied from 310±1.2 to 440±4.1µm. The patches prepared with different polymers were transparent, dry and flexible. The mass ranges from 337±2.2 to 408±2.5 µg/cm^2. Surface pH of all formulations was nearer to neutral i.e. 7.0; hence no mucosal irritation was expected.

Drug content in the formulations was uniform with a maximum variation of 0.51%, this indicates that drug was dispersed uniformly throughout the film. All the patches showed a folding endurance more than 300, when folded manually. The radial swelling of the patches were found to be maximum in case of NaCMC followed by PVA and Chitosan. The values after 8 hours were 40.92±1.5, 20.15±0.50, and 11.37±0.5 % respectively. The lowest swelling recorded for Chitosan (11.37±0.5) may be attributing to its poor solubility in water. The mucoadhesive strength of formulation was found to be depends upon the type of polymer used. Among the formulations PVA, exhibited maximum strength followed by NaCMC and Chitosan patches.

The *in vitro* drug release profiles of Atenolol from patches were shown in Fig. 1.

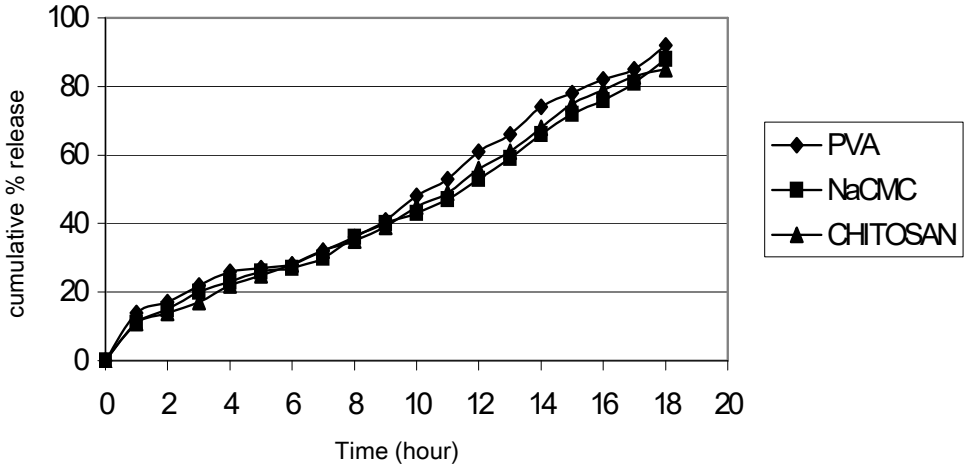

Fig. 1. *In vitro* release profiles of different patches

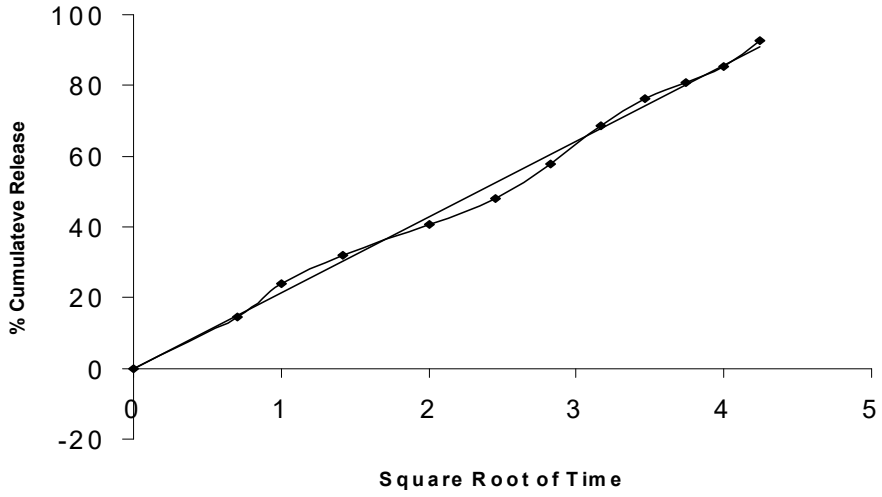

Fig. 2. Higuchi release kinetics for optimized PVA patch

The PVA patches provided maximum drug release (92.71±1.1), fallowed by Chitosan (85.72±3.2) and NaCMC (85.41±2.2) % in 18 hrs. The PVA patches followed Higuchi release pattern like depicted in Fig. 2. When a graph between square root of time and cumulative % release was plotted a straight line obtained.

CONCLUSION

It may be concluded that mucoadhesive patches were promising drug delivery system for Atenolol. The PVA patch shows a good release for a long time (18 hours) Physicochemical evaluation was performed for all patches and the patches were found to be suitable for further studies. The drug was uniformly distributed throughout the system and patches were uniform in thickness.

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