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DESIGN AND CHARACTERISATION OF SALBUTAMOL SULPHATE MUCOADHESIVE BUCCAL PATCHES

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ABSTRACT

Among the various transmucosal routes, buccal mucosa has excellent accessibility, an expanse of smooth muscles and relatively immobile mucosa, hence suitable for administration of retentive dosage form. Buccal administration of drugs provides a convenient route of administration for both systemic and local drug actions. The mucoadhesive buccal films of Salbutamol sulphate were prepared by solvent casting technique using various concentrations of mucoadhesive polymers such as HPMC, PVP and Sodium alginate. The formulated patches were evaluated for their physicochemical parameters like thickness, weight variation, surface pH, folding endurance and swelling studies. In vitro release studies were performed with pH 6.8 phosphate buffer solution. Good results were obtained both in physicochemical and in vitro studies. The films were exhibited controlled release more than five hours. The best mucoadhesive performance and matrix controlled release was exhibited by the formulation F6.

INTRODUCTION

Buccal drug delivery has gained significant attention and momentum since it offers remarkable advantages. Over past few decades, buccal route for systemic drug delivery using mucoadhesive polymers to significantly improve the performance of many drugs has been of profound interest[1]. The buccal mucosa is relatively permeable with a rich blood supply, robust in comparison to the other mucosal tissues and the buccal region is drains directly into the jugular vein and bypassing the liver[2-4]. However, the preferred site for retentive oral transmucosal delivery systems and for sustained and controlled release delivery devices is the buccal mucosa, mainly because of the differences in permeability characteristics between the two regions and the buccal mucosa's expanse of smooth and relatively immobile mucosa. Buccal mucosal administration improves the performance of many drugs, as they are having prolonged contact time with the mucosa. Easy access to the membrane sites so that the delivery system can be applied, localized and removed easily.The adhesive properties of such drug delivery platforms can reduce the enzymatic degradation due to the increased intimacy between the delivery vehicle and the absorbing membrane[1].

Salbutamol sulphate is β-adrenoreceptor agonist, used in bronchodilator in asthma, bronchitis and obstructiveairways diseases. As its biological half-life is about 4 hours and is eliminated rapidly, repeated daily administrationsare needed to maintain effective plasma levels. Because of the low t issue permeability for compounds such as peptides, buccal administration is then often ranked as l ess effective when compared to nasal delivery, and better than transdermal delivery. In the case of a sufficiently potent peptide, therapeutic levels can be expected to be reached with a buccal or a sublingual delivery system[5,6].

Not much work has been reported on salbutamol sulphate buccal delivery. The patches of Poly vinyl alcohol (PVA), Hydroxy propyl methyl cellulose (HPMC) and Chitosan in presence of Poly vinyl pyrrolidone (PVP) and Carbopol already reported earlier[7]. The salbutamol patches composed of different compositions of Eudragit RL 100, Ethyl cellulose (EC) and HPMC are reported[8]. The salbutamol sulphate buccal patches using mucoadhesive polymers like chitosan, Polyvinyl pyrrolidone (PVP), and Poly vinyl alcohol (PVA) are reported[9]. Thus, the objective of this work was to design and characterize the buccal patches of salbutamol sulphate employing HPMC, PVP and Sodium alginate as buccal mucoadhesive polymers.

MATERIAL AND METHODS

Salbutamol sulphate obtained as gift sample from Halmark pharmaceuticals Pvt Ltd, Secunderabad; HPMC obtained from Merck specialties Pvt Ltd, Mumbai; PVP and Sodium alginate were obtained from SD fine chem.. Ltd, Mumbai; The other chemicals were used are of analytical grade.

PREPARATION OF MUCOADHESIVE BUCCAL PATCHS[10,11]:

Buccal films of salbutamol sulphate were prepared by solvent casting technique using films forming polymers. Required amount of HPMC according to the polymer. Required amount of water was added to the above polymer solution and the dispersion was stirred. Simultaneously salbutamol sulphate was accurately weighed and dissolved in 10ml of distilled water in another beaker. Then the drug solution was added to polymer solution and 5ml of 10% w/v glycerol as plasticizer was mixed thoroughly with the help of a magnetic stirrer. The glass mould (petridish) having diameter 8.7cm whose surface was lubricated with liquid paraffin was placed over a flat surface and 10 ml of resulting solution with the help of measuring cylinder was transferred into petridish slowly drop by drop and spread it uniformly. Inverted funnel was placed over the petridish to have uniform evaporation. The petridish containing polymeric solution of drug was kept 12 hrs at room temperature for drying. After drying the films were observed and checked for possible imperfections and upon their removal from moulds then they were cut into the required sizes they were covered with wax paper and preserved in dessicator till evaluation tests were performed. The films were examined in order to select the films having the best characteristics. Similarly formulations F_2,F_3,F_4,F_5, and F_6 were prepared.

EVALUATION OF THE PATCHES

Thickness uniformity of the patches[12]

The thickness of each patch was measured using screw gauge at five different positions of the patch and the average was calculated.

Folding endurance[13]

Folding endurance of the patches was determined by repeatedly folding one patch at the same place till it broke or folded upto 300 times manually, which was considered satisfactory to reveal good patch properties. This test was done on five patches.

Uniformity of weight of the patches[14]

Patches sizes of 1x1 cm^2 were cut. The weights of five patches were taken and the weight variation was calculated.

Swelling studies of the patches[15]

A drug-loaded patch of 1x1 cm^2 was weighed on a preweighed cover slip. It was kept in a petridi sh and 50 ml of phosphate buffer, pH 6.8 was added. After every five min, the cover slip was re moved and weighed after each hour till period of 6 hr. The difference in the weights gives the we ight increase due to absorption of water and swelling of patch. The percent swelling, %S was cal culated using the following equation:

$$\%S = \frac{X_t - X_\circ}{X_\circ} \times 100$$

Xt is the weight or area of the swollen patch after time t and Xo is the original patch weight or ar ea at zero time.

Surface pH[16]

Buccal patches were left to swell for 1 h on the surface of the agar plate, prepared by dissolving 2% (w/v) agar in warmed isotonic phosphate buffer of pH 6.8. The surface pH was measured by means of pH paper placed on the surface of the swollen patch.

In vitro release study[9]

This was carried out in a USP dissolution apparatus type 1 (eight-station dissolution apparatus, TDT 08L, Electro lab, India), with a modification in order to take care of the small volume of dissolution medium. The dissolution medium, 50 ml IPB, pH 6.8, maintained at 37± 0.5^0C was kept in a glass beaker placed inside the dissolution flask. The patch was attached to end of the shaft (without basket) with the help of cyanoacrylate adhesive, so that the drug release only for one side and kept for 50 rpm. Samples 2 ml were withdrawn at intervals of 30, 60, 90, 120, 150, 180, 210, 240, 270, and 300 and filtered using Whatman filter paper. The withdrawals were compensated using equal volumes of IPB kept at the same temperature. The concentration of drug released in the medium was assayed spectrophotometrically at 276 nm after suitable dilution with the dissolution medium whenever necessary. The experiment was carried out three times.

RESULTS AND DISCUSSION

Buccal films of salbutamol sulphate were prepared by the method of solvent casting technique employing a glass petri dish with mucoadhesive polymers of HPMC, PVP and Sodium Alginate. Glycerol was used as the plasticizer. The prepared buccal patches were evaluated or characterized based upon their physicochemical properties like thickness, weight variation, and surface pH, folding endurance and swelling percentage studies. The results were shown in Table2.

The thickness (Table 2) of formulated patches was ranges from 0.16 ± 0.04 to 0.38 ± 0.03 mm, while the average weight of patch from each batch ranges from 57 ± 1.63 to 108.3 ± 1.25 mg. The higher values of thickness and weight variation might be due to increasing concentration of water soluble mucoadhesive polymers like HPMC, Sodium alginate. Assessment of the swelling behavior was done by measuring weight of swollen patch. Excessive increase in patch diameter might cause discomfort and/or dislodgment of the swollen patch. The swelling values after 6 h were in the range of 25.3± 2.4 % to 76.6± 0.2 %. Higher swelling values would result in excessively increased surface area which could result in unmanageable faster release of the drug. Also, higher swelling may cause patient discomfort due to occupying of larger space in the oral cavity and chances of dislodgement. Water soluble mucoadhesive polymers increased the surface wettability and consequently water penetration within the matrix, hence increased weight of the patches. The surface pH of patches was ranges from 6.22 ± 0.28 to 6.73 ± 0.33 were found around neutral pH. Films did not show any cracks even after folding for around 250 for all batches. The cumulative percentage of drug dissolved in buffer pH 6.8 for the period of 5 hrs at temperature 37± 0.5^{o}C are analyzed by using UV-Spectrophotometer at 276 nm wavelength. The maximum in vitro release was found to be 81.50 % over a period of 5 h in batch F6, containing 1:4 of Sodium alginate and HPMC. The drug release finding was also supported by the reported swelling studies where the highest swelling index was also exhibited by batch F6, indicating that the increase in water-soluble polymer content result in faster swelling and release from patches. The films also subjected to FTIR studies showed no interaction between the polymers and the drug, salbutamol sulphate and not found any interactions of polymers with the drug.

CONCLUSION

A new buccoadhesive patches for controlled released of Salbutamol sulphate was developed by HPMC & Sodium alginate in appropriate ratio. Sodium alginate has both film forming and good

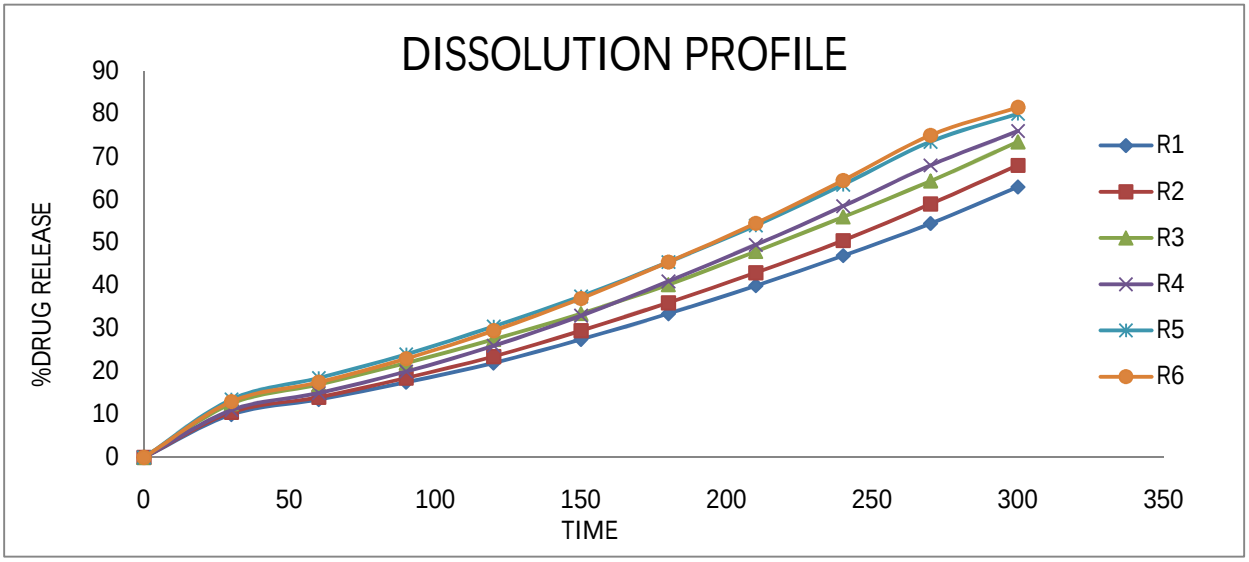
mucoadhesion properties with drug salbutamol sulphate. Optimized formulation F6 shows good Folding endurence, in-vitro drug release and optimum swelling. HPMC with Sodium alginate can meet the ideal requirement for buccal mucoadhesive dosage form. Thus, it can be concluded that the present studies established the usefulness of buccoadhesive dosage form as potential alternative to conventional dosage form for Salbutamol sulphate.

TABLE-1: Formulation of salbutamol sulphate buccal mucoadhesive patches

S.No	Formulations	F_1	F_2	F_3	F_4	F_5	F_6
1	Salbutamol sulphate	50	50	50	50	50	50
2	HPMC(mg)	1000	2000	3000	4000	3000	4000
3	PVP(mg)	-	-	1000	1000	-	-
4	Sodium alginate(mg)	-	-	-	-	1000	1000
5	Glycerol (10%v/v) (ml)	5	5	5	5	5	5
6	Distilled water (ml)	30	30	40	40	40	40

TABLE-2: Physicochemical characteristics of prepared buccal patches of salbutamol sulphate

Formulation	Film thickness (mm)	Weight (mg)	Surface PH	Folding endurance	Swelling index
F1	0.16	57	6.22	258	50.2
F2	0.30	108.3	6.40	264	61.2
F3	0.32	78.3	6.70	245	25.3
F4	0.28	97	6.73	241	34.6
F5	0.28	88	6.66	270	41.6
F6	0.38	95.3	6.70	276	76.6



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