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Formulation and Physicochemical Characterization of Buccal Mucoadhesive Films Containing Alfuzocin Hydrochloride

Abikesh P. K. Mahapatra[1*], Sonia P. Nagvenkar[2] and Rajashree Gude[2]

[1]VerGo Pharma Research Laboratories Pvt. Ltd., Verna, 403107, Goa, India.
[2]Goa College of Pharmacy, Panaji, 403107, Goa, India.

Authors' contributions

This work was carried out in collaboration among all authors. Authors APKM and SPN designed the study, wrote the protocol and managed the literature searches. Author RG performed the statistical analysis. All the authors read and approved the final manuscript.

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ABSTRACT

The buccal region of oral cavity is a interesting target for the drug of choice administration. To increase prevent first pass metabolism and bioavailability, Alfuzocin Hydrochloride is embedded in buccal film for a sustained release over a period of 8 hours. The purpose of this study was to develop formulations and systematically evaluate in vitro performances of buccoadhesive films of Alfuzocin hydrochloride using the polymers HPMC K100M, Sodium Alginate and Chitosan. The films were provided with a backing layer of Eudragit RS100 so as to get an unidirectional release pattern. The films were evaluated for their physical characteristics like weight, thickness, content uniformity, folding endurance, bioadhesive strength, surface pH, in vitro drug release, ex vivo buccal permeation and XRD studies. The films, which were prepared by the solvent casting method, were smooth and elegant in appearance; uniform in thickness, weight, and drug content; and showed good folding endurance. The mechanical properties reveal that the formulations were found to be strong but not brittle. The *in vitro* release data were fit to different equations and kinetic models viz. zero order, first order, higuchi's plot and peppas plot. The best mucoadhesive performance and matrix controlled release was exhibited by the formulation A7 (2% HPMC K100 M and 2%

**Corresponding author: E-mail: abikeshmahapatra@gmail.com;*

Chitosan). The correlation coefficient value (r) indicates, the kinetic of drug release was zero order. Stability study of optimized films was done and it was found that both drug and buccal films were stable. It can be concluded that the present buccal formulation can be an ideal system to improve the bioavailability of the drug by avoiding hepatic first-pass metabolism.

Keywords: Alfuzocin hydrochloride; buccoadhesive films; sustained release; HPMC K100M; sodium alginate; chitosan.

1. INTRODUCTION

Many advances have been made in recent years in the area of biopharmaceutical technology. The systemic delivery of drugs through novel methods of administration is one area in which significant changes and improvements have been made [1]. The buccal route, as an alternative to other traditional methods of systemic drug administration, is a subject of growing interest because of its numerous advantages. This route of drug administration has recently been extensively reviewed by Shojaei [2]. Various bioadhesive mucosal dosage forms have been developed, which included adhesive tablets, gels, ointments, patches, and more recently films [3]. The use of polymeric films for buccal delivery has not yet been widely investigated, although they have been extensively employed in pharmaceutical tablet coating formulations to protect tablet cores from environmental extremes, improve appearance, mask undesirable taste, and control the drug release. Buccal film may be preferred over adhesive tablet in terms of flexibility and comfort. In addition, they can circumvent the relatively short residence time of oral gels on the mucosa, which is easily washed away and removed by saliva [4]. Moreover, the buccal film is able to protect the wound surface, thus reduce pain and also could treat oral diseases more effectively. An ideal buccal film should be flexible, elastic, soft yet adequately strong to withstand breakage due to stress from mouth activities. Moreover, it must also possess good bioadhesive strength so that it can be retained in the mouth for a desired duration. Swelling of film, if exists should not be too extensive to prevent discomfort. As such, the mechanical, bioadhesive, and swelling properties of buccal film are critical and essential to be evaluated [5].

Alfuzocin Hydrochloride, a quinazoline derivative, is a selective and competitive alpha-1 adrenoreceptor antagonist. It distributes preferentially in the prostate, compared with plasma, and decreases the sympathetically controlled tone of prostatic smooth muscle. As a result, lower urinary tract symptoms suggestive of benign prostatic hyperplasia (BPH) are improved [6].

Alfuzocin Hydrochloride is freely soluble in water and thus readily absorbed after administration. The oral absorption is significantly aided by the presence of food. The dose of immediate release Alfuzocin tablet is 2.5 mg thrice daily. Recently 10 mg once daily extended release formulation is available in the market which is more convenient for older patients. The absolute bioavailability of Alfuzocin is about 49% under fed conditions, while the corresponding value under fasting conditions is approximately 25% [6]. This shows that food has a significant impact on the oral absorption of Alfuzocin. This originates the need for an alternative route of administration, which can bypass the hepatic first-pass metabolism. Buccal route is an alternative choice of route of administration for such drugs. Various physicochemical parameters like molecular weight, log P value and aqueous solubility of Alfuzocin Hydrochloride are 425.92, 1.51 at a pH of 7.4 and > 10% respectively [6]. These favorable parameters make it an ideal drug candidate for buccal drug delivery. Buccal films offer added advantages such as maintenance of constant and prolonged drug level, reduced frequency of dosing, minimization of inter- and intrapatient variability, self administration, and easy termination of medication, leading to patient compliance.

The present work deals with the formulation and characterization of mucoadhesive buccal films of glipizide using mucoadhesive polymers like Hydroxy propyl methyl cellulose (HPMC K100M), Sodium Alginate and Chitosan.

2. MATERIALS AND METHODS

Alfuzocin Hydrochloride obtained as gift sample from Unichem Laboratories Ltd. Pilerne – Goa India; Hydroxy Propyl Methyl Cellulose (HPMC K100 M) was a gift from Colorcon, Goa; Sodium Alginate was obtained from Snap Alginate, Mumbai; Chitosan was provided by Central

Institute of Fisheries Technology, Cochin as gift sample; Polyvinyl Pyrrolidone K-30 was obtained from Centaur Pharmaceuticals, Mapusa, Goa, India. The other chemicals are of analytical grade. The compatibility study of drug and polymers were carried out with FT-IR spectroscopic study, there was no chemical interaction found (Fig. 6). The films were prepared by solvent casting method.

2.1 Preparation of Buccal Mucoadhesive Films

The buccal mucoadhesive films of Alfuzocin Hydrochloride were prepared by solvent casting method. The polymers, HPMC K100 M, Sodium Alginate and Chitosan were applied in different concentrations as shown in Table 1 for the fabrication of buccal films [7,8,9].

HPMC at concentration of 3% w/v and 4% w/v and Sodium Alginate at 1% w/v and 2% w/v were used for the preparation of Buccal Films. 1% (V/V) glycerine was added as plasticizer. The calculated amount of the polymer was dispersed in a 75% water volume under continuous stirring using a mechanical stirrer. The plasticizer was gradually added and the final volume was adjusted with distilled water. The amount of drug required to dissolve in petridish, so that a film of size 20 mm diameter containing 10 mg of Alfuzocin Hydrochloride could be obtained, was calculated by the ratio of surface area of petri dish and buccal film (20 mm) and it was then added to the final volume. The prepared gels were left overnight at room temperature till clear, bubble-free gels were obtained. The gels were cast into a glass petridish and allowed to dry in an oven maintained at 40°C till a flexible film was formed.

The polymeric solution of chitosan was prepared by soaking 1% w/v and 2% w/v using 1.5% (V/V) acetic acid in distilled water under occasional stirring for 48 h. The resultant viscous solution was filtered through gauze. The filtrate was left to stand until all air bubbles disappeared. To improve elastic and film forming properties of the patches, PVP (1%, m/V) and glycerine (plasticizer) were added. Hydrophilic additives along with the drug were first dissolved in a small volume of distilled water, then added to the polymer solution prepared as described above. The prepared gels were left overnight at room temperature till clear, bubble-free gels were obtained. The gels were cast into a glass petridish and allowed to dry in an oven maintained at 40°C till a flexible film was formed [9].

The dried films (plain patches) were carefully removed from the petridish, checked for any imperfections or air bubbles and cut into films of 20 mm in diameter. The impermeable, protective layer of Eudragit RS 100 was applied by spreading the solution Eudragit RS 100 in iso propyl alcohol to one side of films to achieve unidirectional release pattern.

The samples were packed in aluminum foil and stored in a glass container maintained at room temperature and 58% relative humidity; this condition maintained the integrity and elasticity of the patches [10].

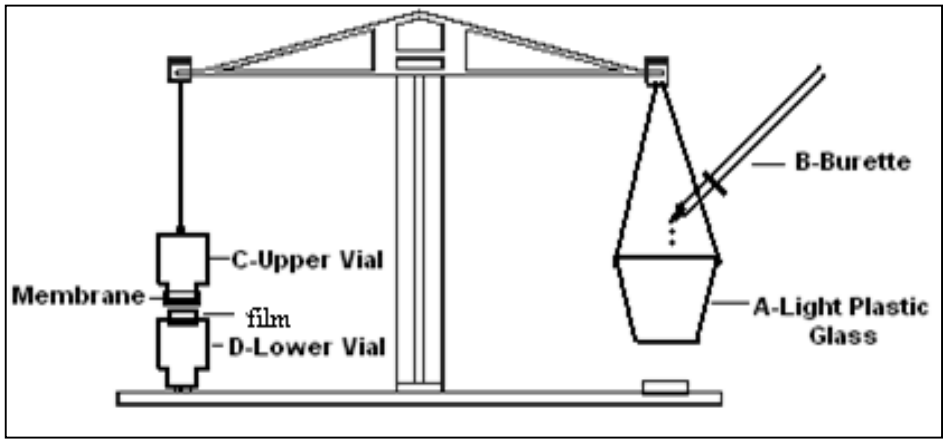


Fig. 1. Schematic diagram of bioadhesive strength tester

Table 1. Composition of buccal mucoadhesive films of alfuzocin hydrochloride

Formulation code	A1	A2	A3	A4	A5	A6	A7	A8
Alfuzocin HCl (mg)	10	10	10	10	10	10	10	10
HPMC K100M	3%	4%	--	--	--	--	2%	2%
Sodium Alginate	--	--	1%	2%	--	--	--	2%
Chitosan	--	--	--	--	1%	2%	2%	--
PVP K-30	1%	1%	1%	1%	1%	1%	1%	1%
Sodium Saccharine	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Glycerine	1%	1%	1%	1%	1%	1%	1%	1%

2.2 Characterization of Buccal Muco-adhesive Films

There is a strong and definite need to quantify and thereby assure certain physical, chemical and biological parameters of buccal dosage forms. The devised Buccal Film formulations were therefore characterized based on the following parameters:

Thickness and Weight Uniformity: The thickness of three randomly selected buccal patches from every batch was determined using a standard screw gauge at six different places and the mean value was calculated [11]. Similarly, for evaluation of film weight three films of every formulation were taken and weighed individually on a digital balance. The average weights were calculated [12].

Surface pH study: The surface pH of the prepared films was determined after soaking each film (1 cm^2) in distilled water (1 ml) for 15 min. After the time of soaking the pH of the wet surface was measured by placing the electrode in contact with the surface of the film. The experiments were performed in triplicate, and average values were reported. The surface pH of the buccal patches was determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible [13,14,15].

Swelling study: Swelling study of prepared buccal patch was calculated by function of weight and area increase due to swelling, which was measured for each formulation as follows.

Weight increase due to swelling: A patch of 20 mm diameter from every batch was weighed on a preweighed cover slip. It was kept in a petridish and 10 ml of phosphate buffer, pH 6.8 was added. After one hour, the cover slip was removed and weighed. The difference in the weights gives the weight increase due to absorption of water and swelling of patch.

Area increase due to swelling: Similarly patch of 20 mm diameter from each batch was placed on cover slip and this cover slip was placed in a petridish. 10 ml of phosphate buffer, pH 6.8, was poured into the petridish. A calibrated measuring scale was used to measure the increase in the area of each patch. An increase in the area in diameter of the patch was noted at one hour intervals for 8 hours and the area was calculated. The swelling index of weight and area was calculated from the following equation:

$$SI = (Xt – Xo / Xo)$$

Where, Xt - weight or area of the swollen patch after time t and Xo - is the original patch weight or area at zero time [12,16].

Content uniformity: Drug content uniformity was determined by dissolving the buccal patch (20 mm in diameter) from each batch by homogenization in 100 ml of phosphate buffer (pH 6.8) for 6 h under occasional shaking. The 5 ml solution was taken and diluted with phosphate buffer pH 6.8 up to 25 ml, and the resulting solution was filtered through a 0.45 mm Whatman filter paper if necessary. The drug content was then determined after proper dilution at 245 nm using a UV-spectrophotometer [17].

Folding endurance: Folding endurance of the film was determined by repeatedly folding one patch at the same place till it broke or folded manually, which was considered satisfactory to reveal good film properties. The number of times of film could be folded at the same place without breaking gave the value of the folding endurance. This test was done for three films [16,9,15].

***In vitro* release study:** The drug release studies were performed with USP dissolution test apparatus (Paddle method). The USP dissolution apparatus was thermo stated at the temperature

of 37±1°C and stirred at rate of 50 rpm. Each film was fixed on a glass slide with the help of cyanoacrylate adhesive so that the drug could be released only from upper face. Then the slide was immersed in the vessel containing 900 ml of pH 6.8 phosphate buffer solution. The aliquots of 10 ml were withdrawn at the time interval of every hour and replaced with equal volume of dissolution medium. The sink condition was maintained throughout the study. The samples were analyzed at 245 nm in a UV-spectrophotometer and cumulative amount of drug release at various time intervals was calculated [18].

***Ex- vivo* buccal permeation study:** The in vitro study of Alfuzocin hydrochloride permeation through the porcine buccal mucosa was performed using a Franz diffusion cell at 37 ± 0.2°C. Porcine buccal mucosa was obtained from a local slaughterhouse (used within 2 hrs of slaughter). Freshly obtained porcine buccal mucosa was mounted between the donor and receptor compartments so that the smooth surface of the mucosa faced the donor compartment. The film was placed on the mucosa and the compartments clamped together. The donor compartment was filled with 1 ml of isotonic phosphate buffer pH 6.8. The receptor compartment (25 ml capacity) was filled with phosphate buffer pH 7.4 and the hydrodynamics in the receptor compartment was maintained by stirring with a magnetic bead at 100 rpm. One ml sample was withdrawn at predetermined time intervals and analyzed for drug content at 245 nm [19,20].

Measurement of Bioadhesive Strength: Bioadhesive strength of the buccal mucoadhesive films was measured on a modified physical balance. A lower vial (D) as shown in Fig. 1 was inverted and fixed in place at the left hand side of the physical balance. The film was attached to the lower vial (D). A fresh piece of porcine buccal mucosa was used as the model membrane for the study. It was fixed to the rubber closure end of the upper vial (C) with the mucosal surface facing outwards. A string was attached to the other end of the upper vial. This string was attached to the left hand side of the physical balance. The weight of the upper vial acted as preload. A plastic container weighing 1.083 gms was placed on the right hand side of the balance. The surface of the film was moistened with simulated saliva fluid pH 6.8 and the upper vial with the mucous membrane was placed on to the tablet, the weight of the upper vial acting as preload. The balance was kept in this position for a period of 5 minutes, and then slowly water was poured into the plastic container on the right hand side of the balance till the tablet just detached from the membrane. The weight of the plastic container was then noted. The total weight minus the weight of the plastic container corresponds to the bioadhesive strength of the film in grams. Before carrying out the study, the two sides of the balance were equilibrated. The mucosa was washed thoroughly before use. The test was carried out on two films from each formulation. Fresh mucosa was used for testing of each film [21,22,23].

Tensile strength measurement: The instrument was designed in our laboratory as per literature. This was used for the measurement of tensile strength. The strip (5 X 1 cms) was clamped at the static end and was attached to the movable rod on a railing with the help of a clip. The weights were gradually added to the pan to increase the pull force till the film was cut. The elongation was determined simultaneously by noting the distance traveled by the pointer before break of the film on the graph paper. The weight required to break the film was noted as the break force [24].

The tensile strength was calculated as follows:

Tensile strength ($kg.mm^{-2}$)

$$= \frac{\text{Force at break (kg)}}{\text{Initial cross sectional area sample (mm2)}}$$

Elongation at break ($\%.mm^{-2}$)

$$= \frac{\text{Initial length (mm)}}{\text{Original length(mm)}} \text{ X } \frac{100}{\text{Cross sectional area(mm2)}}$$

X-Ray diffraction studies: The optimized formulation containing physical mixture of Alfuzocin HCl, HPMC K100 M, Chitosan and PVP K-30 were prepared by simple blending. Powder XRD patterns were measured using a *Ultima IV* X-Ray Diffractometer.

Stability Studies: Stability studies on the optimized formulation batches were carried out to determine the effect of presence of formulation additives on the stability of the drug and also to determine the physical stability of the formulation under accelerated storage conditions.

The films were sealed in aluminum packaging and subjected to, elevated temperature and humidity conditions of 40±2ºC/ 75± 5%RH for 30 days [25].

3. RESULTS AND DISCUSSION

The objective of the present study was to design and optimize Buccal Mucoadhesive Films of Alfuzocin Hydrochloride. The mucoadhesive Buccal Films of Alfuzocin Hydrochloride were prepared using mucoadhesive polymers HPMC K100 M, Sodium Alginate and Chitosan. Glycerine was used as the plasticizer. The films were characterized for their physical characteristics, bioadhesive performance, release characteristics, surface pH, thickness, folding endurance, drug content uniformity and percent swelling. The IR spectra indicate that there was no positive evidence for the interaction between Alfuzocin Hydrochloride and the utilized Bioadhesive polymers. These results clearly indicate the usefulness of utilized Bioadhesive polymers for formulation of buccoadhesive films of Alfuzocin Hydrochloride.

Films of all formulations were circular in shape, with flat surfaces and the patches were translucent, visually smooth surfaced having smooth texture. The size of the films was 20 mm in diameter. There was an absence of odour or any physical flaws. The film thicknesses were observed to be in the range of 0.547 ± 0.028 mm to 1.1 ± 0.032 mm and weight was found to be in the range of 21 ±1.86 mg to 106 ± 0.74 mg. The films did not show any cracks even after folding for more than 200 times for all batches. Considering the fact that acidic or alkaline pH may cause irritation to the buccal mucosa and influence the degree of hydration of polymers, the surface pH of the buccal films was determined to optimize both drug permeation and mucoadhesion. Attempts were made to keep the surface pH as close to buccal/salivary pH as possible. The surface pH of all the films was within the range of salivary pH. No significant difference was found in surface pH of different films. Drug content in formulations was uniform with a range of 9.27 ± 0.006 mg (A6) to 9.69 ± 0.016 mg (A5). On this basis, it was found that the drug was dispersed uniformly throughout the film.

The swelling percentage of the formulated buccal films was observed in pH 6.8 phosphate buffer. The swelling in area and weight was pronounced in formulation A1 and A2 which contain HPMC K100 M alone in concentration of 3% and 4% respectively. The observed swelling index of weight was in order of A2>A1>A7>A8>A4>A3>A6>A5. The observed swelling index of area was found to be in the order of A2>A1=A4=A8>A7>A6>A5.

The Bioadhesive strength of the films was found to be the function of nature and concentration of the polymer. There are several advantages in having Bioadhesive drug delivery systems. As a result of such adhesion, the formulation stays longer at the delivery site and improves the bioavailability of the drug. The bioadhesion force is therefore an important physicochemical parameter for buccoadhesive dosage forms. The Bioadhesive strength of the prepared Alfuzocin Buccal films is shown in Table 3. The average Bioadhesive strength varied between 25.084 to 27.858 gms. The film containing Chitosan and HPMC in combination required maximum force in grams to break the bond between the mucoadhesive film and the buccal mucosa. This was followed by the films containing Sodium Alginate and HPMC in combination and Chitosan films. HPMC showed the minimum force required to detach the films from the mucus membrane. It was suggested that, at alkaline or slightly neutral pH, chitosan has numerous amine and hydroxyl groups as well as a number of amino groups that may increase the interaction with the negative mucin which causes strengthening of the mucoadhesive interface.

Mechanical Properties of ideal buccal film, apart from good bioadhesive strength, should be flexible, elastic and strong enough to withstand breakage due to stress caused during its residence in the mouth. The tensile strength (TS) and elongation at break (E/B) shows the strength and elasticity of the film. A soft and weak polymer is characterized by a low TS and E/B; a hard and brittle polymer is defined by a moderate TS, and low E/B; a soft and tough polymer is characterized by a moderate TS and a high E/B; whereas a hard and tough polymer is characterized by high TS and E/B (Aulton et al., 1981). It is suggested that an ideal buccal film should have a relatively high TS and E/B (Peh and Wong, 1999).

The results of TS and E/B are presented in Table 3. TS increased with the increase in polymeric content but E/B values decreased with the increase in polymer content. Maximum TS was exhibited by A7 film (4.96 ± 0.09 kg.mm–2) and minimum was exhibited by A5 (3.79 ± 0.03 kg.mm–2). Maximum E/B was seen with A1 (8.04 ± 0.81% mm–2) and the least was observed with A6 (6.01 ± 0.08% mm–2).

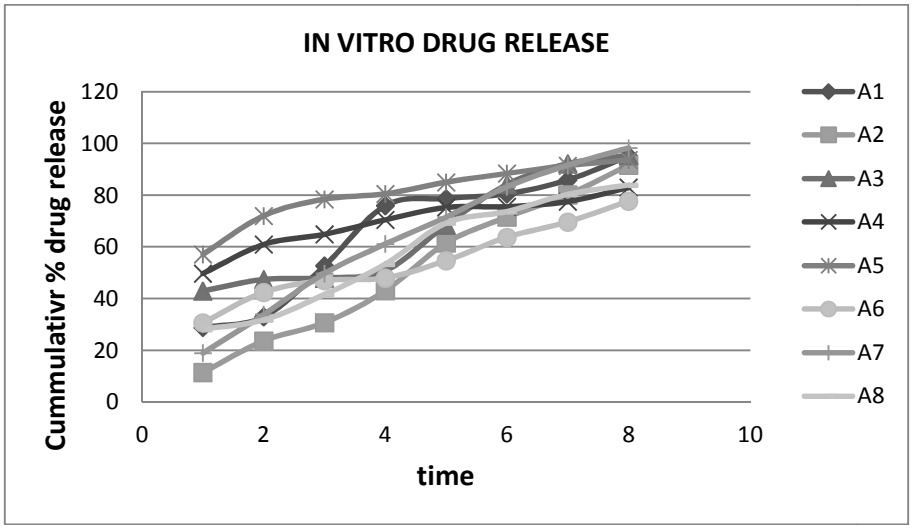


Fig. 2. Comparative dissolution profile of batches A1 to A7

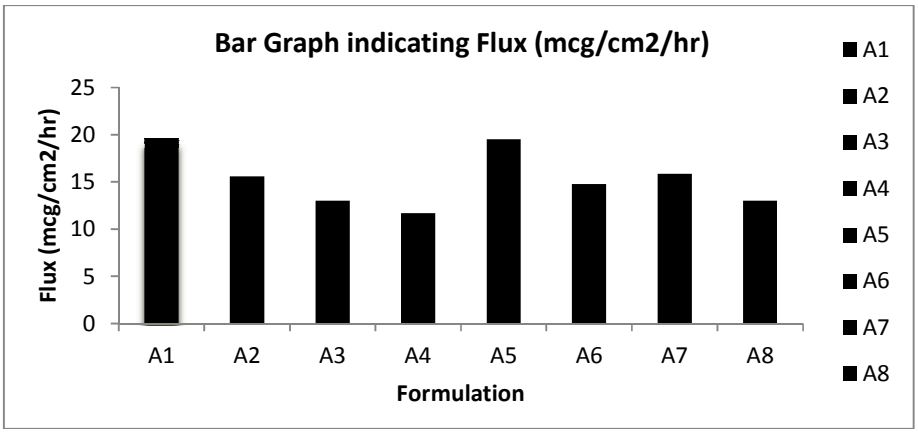


Fig. 3. Bioadhesice flux of films A1 to A7

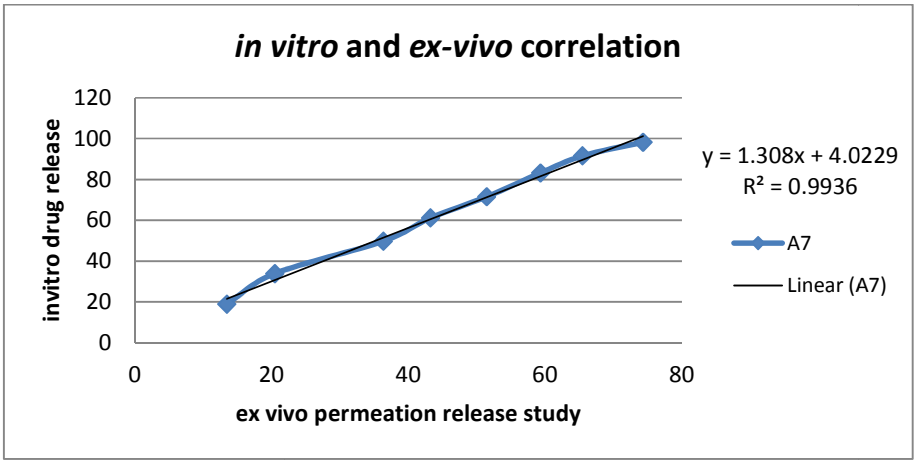


Fig. 4. Correlation coefficient for batch A7

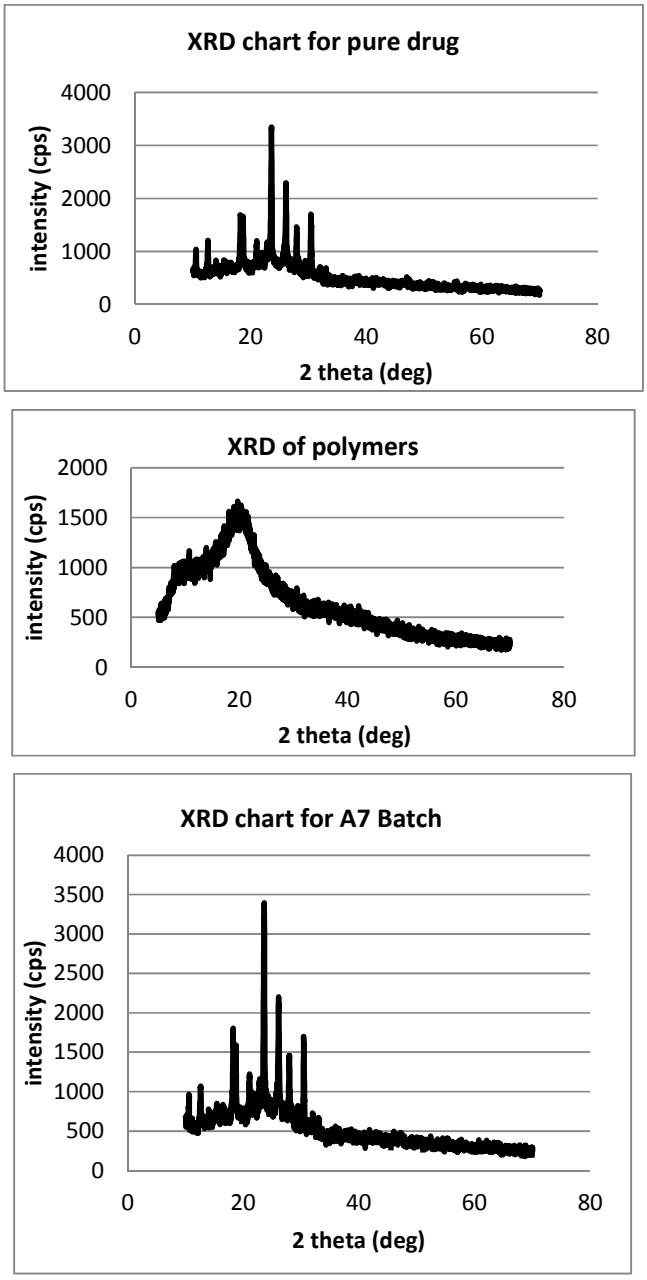


Fig. 5. XRD Charts A. XRD of pure drug; B. XRD of polymers; C. XRD of A7 batch

In vitro release data of alfuzocin from all the films are given in Fig. 2. A perusal to Fig. 2 indicated that the drug release was higher in HPMC (films A1 & A2) and HPMC-chitosan combinations (film A7). *In vitro* dissolution data of Alfuzocin Hydrochloride from the formulated Buccal Mucoadhesive films are given in Table 4.

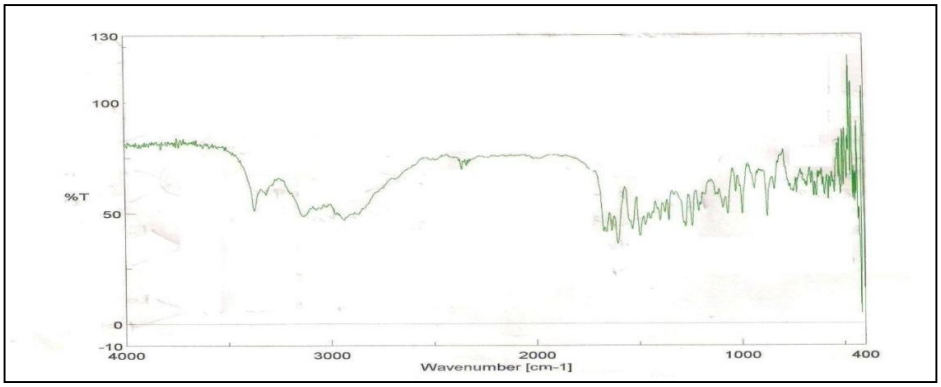
An increase in the polymer content was associated with a corresponding decrease in the drug-release rate. Data of the in vitro release were fit into different equations and kinetic models to explain the release kinetics of alfuzocin from these buccal films. The kinetic models used were a zero-order equation, first-order equation, Higuchi release and Peppas models. The R^2 values for Zero order plots were higher when compared to First order plots which indicates that all formulations best fitted in Zero order kinetics. Similarly the data when treated according to Higuchi's diffusion equation indicated that all formulations exhibit diffusion

mechanism in drug release. The data was subjected to Peppas model where R^2 value revealed that Peppas model best fitted in all dissolution profiles having the highest correlation coefficient nearly approaching 1.0. The values of 'n' as derived from Peppas model are between 0.417 and 0.801. Hence we conclude that mucoadhesive films follow a non- Fickian release. Thus the drug release from mucoadhesive Buccal Films is *Diffusion Controlled* and followed *Zero order kinetics*. On basis of above studies film formulation A7 comprising the combination of HPMC K100M and chitosan was found to be the best formulation for retarding the drug release with 98.72% release after the end of 8 hrs.

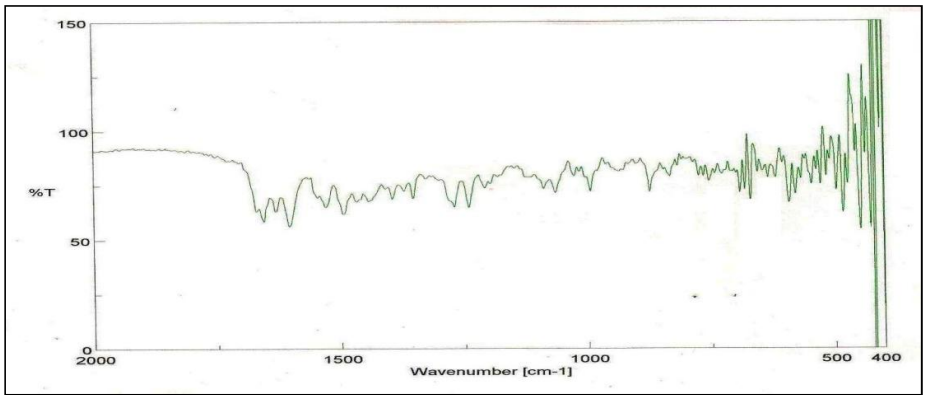
For *ex vivo* diffusion studies, the value of flux (J), show a declining trend with an increase in polymer content. The cumulative amount of drug permeated across the sheep stomach membrane varied between 8.05 and 6.32 mgs per square centimeter of membrane. The values show a declining trend with the increase in polymer content. However the values of Flux (J) show a non linearity with the polymer content.

Table 2. Characteristics of buccal mucoadhesive films of alfuzocin hydrochloride

Batch code	Weight (mg)	Thickness (mm)	Folding endurance	Surface pH	Content uniformity
A1	72±0.043	1.02±0.078	287	6.26	9.57±0.008
A2	84±1.21	1.11±0.032	308	6.46	9.52±0.045
A3	21±1.86	0.65±0.006	212	6.36	9.38±0.034
A4	29±1.23	0.58±0.075	226	5.86	9.61±0.064
A5	51±0.32	0.78±0.044	325	6.1	9.69±0.016
A6	61±0.65	0.85±0.032	367	6.05	9.27±0.006
A7	68±0.97	0.832±0.021	345	6.61	9.57±0.056
A8	106±0.74	0.547±0.028	356	6.19	9.43±0.009



IR Spectra of pure drug



IR Spectra of A7 Batch

Fig. 6. IR Spectra A. pure drug; B. A7 Batch

Table 3. Evaluation of mechanical strength

Formulation code	Bioadhesive strength (g)	Tensile strength (kg/mm^2)	Elongation at break (mm^{-2})
A1	26.792	3.86 ± 0.09	8.04 ± 0.81
A2	25.760	4.86 ± 0.08	6.75 ± 0.07
A3	25.993	4.08 ± 0.10	7.8 ± 0.04
A4	26.745	4.36 ± 0.04	6.57 ± 0.23
A5	25.054	3.79 ± 0.03	6.89 ± 0.07
A6	26.998	4.10 ± 0.19	6.01 ± 0.08
A7	27.858	4.96 ± 0.19	7.41 ± 0.81
A8	27.792	4.13 ± 0.07	6.98 ± 0.03

Table 4. Release kinetic profile for the buccal mucoadhesive films of alfuzocin hydrochloride

Formulation	Zero order plot		First order plot		Higuchi's plot		Peppas plot		
	R^2	K_O	R^2	K	R^2	K	R^2	n	K
A1	0.905	9.694	0.905	22.32	0.939	38.49	0.934	0.628	26.607
A2	0.992	11.73	0.911	0.313	0.971	45.27	0.950	0.830	15.13
A3	0.923	8.539	0.954	0.280	0.858	32.10	0.796	0.417	36.307
A4	0.921	4.199	0.938	0.147	0.970	16.8	0.986	0.433	50.46
A5	0.976	6.992	0.862	0.370	0.978	31.16	0.976	0.461	34.27
A6	0.974	6.215	0.965	0.138	0.951	23.94	0.995	0.621	21.03
A7	0.984	11.36	0.869	0.4836	0.998	44.59	0.996	0.801	19.54
A8	0.969	8.877	0.975	0.2305	0.962	34.48	0.946	0.593	24.37

Batch A7 was optimized based on moderate swelling, a convenient mucoadhesive strength as well as adequate *in-vitro* drug release. The optimized batch (A7) showed 74.30% drug permeation in 480 minutes. The straight line and the high correlation coefficient value (r^2 =0.993) proved the good correlation between *in-vitro* drug release and *ex-vivo* drug permeation studies (Fig. 4).

X-ray diffraction studies were carried out to reveal the crystalline modifications during the preparation of films. Results of the x-ray diffractograms for the A7 formulation of 1:1 ratio chitosan – HPMC K100 M and the drug alfuzocin Hydrochloride were studied (Fig. 5 A. B. C). The physical mixture of the film formulation showed crystallinity supposedly due to the presence of the crystalline form. It presumably suggests that the drug molecule is present in a crystalline state in the film.

The stability studies were carried out on optimized formulation at 40ºC/ 75% RH for a month. After 30 days samples were analyzed for *in vitro* drug release, active drug content and bioadhesion study. The results indicated no significant variations.

4. CONCLUSION

It can be concluded that buccal mucoadhesive films are a promising drug delivery system for Alfuzocin Hydrochloride. These buccal films maintained a satisfactory residence time in the buccal cavity and ensure zero order release of the drug over relatively longer period which made them good candidate for drug delivery system through buccal mucosal route. From the present investigation, one can conclude that the optimized buccoadhesive films of Alfuzocin Hydrochloride with the combination of HPMC and chitosan can meet the ideal requirements for buccal devices, which can be a good way to bypass the extensive hepatic first pass metabolism.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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