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Development and evaluation of buccoadhesive patches of Glipizide using polymer blend of Ethylcellulose and Polyvinylpyrrolidone K-30

K.M. Lokamatha Swamy* and B. Keerthana

Department of Pharmaceutics, V.L. College of Pharmacy, Raichur, Karnataka, India

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ABSTRACT

In the present study, an attempts were made to formulate buccal patches of glipizide using bioadhesive polymers to avoid the hepatic first pass metabolism, to achieve controlled release and to improve better clinical efficacy. Buccal patches of glipizide were designed using ethylcellulose (EC) alone and blends of EC:Polyvinylpyrrolidone (PVP K-30) at different ratios using glycerol as plasticizer adopting solvent evaporation method. All patches were evaluated for physical appearance, surface texture, weight uniformity, thickness uniformity, folding endurance, surface pH, swelling index, moisture content and absorption, bioadhesive strength, drug content uniformity. Various bioadhesive parameters like bioadhesive strength, force of adhesion, and bond strength exhibited by various patches of glipizide was satisfactory. All buccal patches of glipizide showed sustained and prolonged release the drug over a period of 8 h. When the patches were prepared with the blends of EC:PVP the flux and permeation rates were increased compared to patches prepared with EC alone. The increasing order of drug release from the EC:PVP patches was found in the order, A4 > A3 > A2 > A1 (i.e., 1:1 > 1:0.75 > 1:0.5 > 1:0.25). Further, increase in concentration of EC has a negative effect on drug release i.e., drug release decreased with increase in concentrations of EC. The release of glipizide from all patches followed Higuchi kinetic model and the mechanism of drug release was concluded as non–Fickian diffusion controlled.

Key words: Glipizide, buccal drug delivery system, buccal patches, ethylcellulose, polyvinylpyrrolidone K-30.

INTRODUCTION

Buccal delivery of drugs provides an attractive alternative to other conventional methods of systemic drug administration, since buccal mucosa is relatively permeable with rich blood supply and acts as an excellent site for the absorption of drugs [1]. The administration of drugs via buccal route facilitates a direct entry of drug molecules into the systemic circulation, avoiding the first-pass metabolism and drug degradation in the harsh gastrointestinal environment, which are often associated with oral administration [2,3]. Buccal patches also show good buccoadhesive strength so that it can be retained in the mouth for a desired duration. Buccal patches are preferred over adhesive tablets in respect of its flexibility and patients comforts. In addition, a patch can circumvent the problem of the relatively short residence time of oral gels on mucosa, since the gels are easily washed away by saliva [4]. Bioadhesive polymers are used to control the buccal drug delivery due to their ability to localize the dosage form in specific regions to enhance drug bioavailability. Buccal route of drug delivery provides direct access to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability. Various mucoadhesive formulations such as buccal patches, buccal tablets and adhesive gels are suggested for buccal delivery. Among them, buccal patches may be preferred over adhesive tablets in terms of flexibility and comfort. Hence, the present study was planned to formulate buccal patches of glipizide in order to overcome its drawbacks associated with oral administration.

Glipizide (GLP) is one of the most effective antidiabetic agent in the management of Type II diabetes. The model drug requires controlled release due to its short biological half-life (3.4 ± 0.7 h) which necessitates its administration

in two or three doses of 2.5 to 10 mg per day [5]. Furthermore, 90% of the drug is metabolized in the liver forming several inactive metabolites [6]. Hence, the aim of this study was to develop and evaluate buccal mucoadhesive patches of glipizide to achieve controlled release and to improve better clinical efficacy. It is also be possible to avoid the hepatic first pass metabolism by administering the drug through buccal mucosa.

MATERIALS AND METHODS

1.1 Materials: Glipizide was obtained from Micro Labs Limited. It was passed through 100 mesh before use. The S.D. Fine Chemicals supplied EC, PVP K-30 and glycerol. All other chemicals used were of laboratory reagent grade.

1.2 Methods

1.2.1 Compatibility studies: Infrared spectra were obtained using a Shimadzu FT-IR-1700 spectrophotometer. The spectra were recorded for pure GLP, EC, PVP K-30, and physical mixture of drug and polymers. The samples were prepared by the potassium bromide (KBr) disc method. The KBr disks were prepared by compressing the powder and scanning range was kept from 4000 to 400 cm^{-1}.

1.2.2 Formulation of buccoadhesive patches of glipizide: Each batch of buccoadhesive patch (4 cm^2) containing 10 mg of GLP was prepared by the method of casting on mercury surface as shown in table 1. Calculated amount of EC was dissolved in 10 ml of solvent blend of methanol: dichloromethane (1:1v/v). Then, glipizide was dissolved in above polymeric solution with continuous stirring. Known amount of PVP K-30 is dissolved in 2 ml of water and added to above organic solvent mixture. After complete dispersion of drug and polymers, glycerol was added plasticizer and stirred to form a homogeneous solution. The resultant solution was left overnight at room temperature to ensure a clear, bubble-free solution. The solution was casted onto mercury substrate, then kept in hot air oven at 40ºC for 24 h. Dried films were carefully removed, checked for any imperfections or air bubbles and cut into patches of 4 cm^2 in diameter. Dried films were packed in aluminum foil and stored in desiccators at room temperature for further studies.

Table 1: Formulae of buccoadhesive patches of glipizide

Sl. No	Batch code	Drug	Polymer ratio (mg)	
			EC	PVP K-30
1	Control	GLP	1	
2	A1	GLP	1	0.25
3	A2	GLP	1	0.5
4	A3	GLP	1	0.75
5	A4	GLP	1	1
6	A5	GLP	1.25	1
7	A6	GLP	1.75	1

1.2.3 Evaluation of buccoadhesive patches of glipizide

a) Physical appearance: The films were observed visually for their physical appearance such as color and transparency.

b) Surface texture: The surface textures of the films were evaluated by pressing the film with finger.

c) Weight uniformity: Three films of each formulation were taken and weighed individually by using single pan balance and average weight films were calculated and standard deviation was computed.

d) Thickness uniformity: Four Films of each formulation were taken and the thickness of the film was measured using screw gauge at different places. The average film thickness was calculated and standard deviations were computed.

e) Folding Endurance: Three films of each formulation of size (2×2 cm) were cut by using sharp blade. Folding Endurance was determined by repeatedly folding a small strip of film at the same place till it broke. The number of times, the film could be folded at the same place without breaking gave the value of folding endurance. The mean value of three readings and standard deviation were computed**.**

f) Surface pH of films: Three films of each formulation were allowed to swell for 2 h on the surface of an agar plate (2% W/V in warmed phosphate buffer of pH 6.6). The surface pH was measured by means of a pH paper placed on the surface of the swollen patch. A mean of three readings was recorded.

g) Swelling studies [7]: After determination of the original film weight and diameter, the samples were allowed to swell on the surface of agar plate (2% W/V in warmed phosphate buffer of pH 6.6) kept in an incubator maintained at 37 ± 0.2°C. Increase in the weight of the films (*n* = 3) was determined at preset time intervals up to 2h. The percent swelling, (%S), was calculated using the following equation

$$\text{Swelling index} = \frac{W2 - W1}{W2} \times 100$$

Where, W1 = Dry weight of the film
W2 = Wet weight of the film

h) Determination of moisture content and moisture absorption [8]**:** The buccal patches were weighed accurately and kept in desiccators containing anhydrous calcium chloride. After 3 days, the patches were taken out and weighed. The moisture content (%) was determined by calculating moisture loss (%) using the formula.

$$\text{Moisture content (\%)} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Buccal patches were weighed accurately and placed in a desiccator containing 100 ml of saturated solution of aluminum chloride, which maintains 76% and 86% humidity (RH). After 3 days, films were taken out and weighed. The moisture absorption was calculated using the formula.

$$\text{Moisture absorption (\%)} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

i) *In vitro* bio-adhesion test [9]**:** The bioadhesive strength of patches was measured using a modified physical balance as shown in figure 1. The sheep buccal mucosa was used as the model membrane and phosphate buffer pH 6.6 was used as the moistening fluid. The sheep buccal mucosa was stuck on to the inner surface of the petridish using suitable glue such that mucosal surface faces upwards. Then, phosphate buffer pH 6.6 was added in to petridish so that the buffer is contacted with the mucosal membrane. The petridish containing mucosal membrane was kept below the right hand set up of the balance. The test patches were stuck on to a lower flat side of hanging glass assembly (glass vial). Two sides of the balance were made equal before the study i.e., by keeping a required weight on the left side. Then weight from the left pan was removed. This lowered the glass assembly along with patch so that patch comes in contact with the surface of the buccal mucosa and kept undisturbed for 3 min. Then, the weights on the left hand side were slowly added till the patch just separated from the membrane surface. Then added weight required to separate the patch from the surface was noted. This weight was then subtracted from the weight required making the balance equal on both sides before starting the experiment is the bioadhesive strength. Then, force of adhesion and bond strength is calculated as follows,

$$\text{Force of adhesion (N)} = \text{bioadhesive strength} \times \frac{9.81}{1000}$$

$$\text{Bond strength} \left(\frac{\text{N}}{\text{m}^2}\right) = \frac{\text{force of adhesion (N)}}{\text{surface area (m}^2\text{)}}$$

Figure 1: Modified bioadhesive tester

j) Drug content [7]**:** Drug content uniformity was determined by taking patch area of 2 cm^2 from each formulation and it was placed in 100 ml of volumetric flask contained 50 ml of methanol and 50 ml of phosphate buffer of pH 6.6. It was shaken in sonicator and kept aside for 6 h. The solution is filtered and then 1 ml of above stock solution is taken in 10 ml volumetric flask and made up to the mark with phosphate buffer of pH 6.6. The drug content was determined by UV Spectrophotometer. Average of three determinations was calculated.

k) *In vitro* permeation studies [7]**:** The *in vitro* permeation study of mucoadhesive buccal patches of glipizide through excised sheep buccal mucosa was performed using the modified keshary-chein diffusion cell. A 2.0 cm diameter patch of each formulation (equivalent to 10 mg) under study was placed in intimate contact with the sheep buccal mucosa. Teflon bead was placed in the receptor compartment filled with pH 6.6 phosphate buffer. The cell contents were stirred with a magnetic stirrer and temperature of 37 ± 1ºC was maintained with the water jacket throughout the experiment. The amount of drug permeated into the receptor solution was determined by removing 1 ml of sample at hourly intervals up to 8 h. The withdrawn volume was replaced with an equal volume of fresh buffer solution. The drug permeated through the buccal mucosa was determined by analyzing the samples at 223 nm using UV spectrophotometer. The studies were carried out in triplicate.

RESULTS AND DISCUSSION

3.1 Drug and polymer interaction studies: Measurement of possible incompatibilities between drug and excipient is an important part of preformulation studies. Hence, FTIR was studied to assess any interaction between the drug and the polymers.

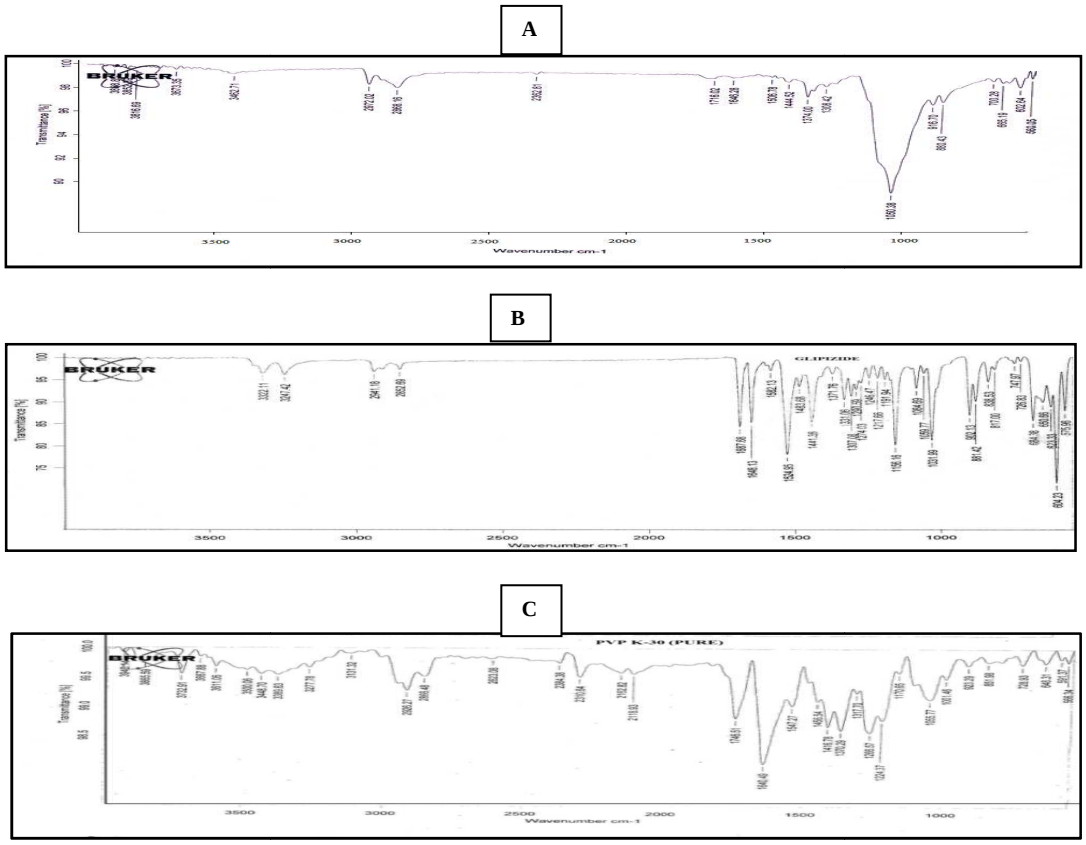

Figure 2: FTIR spectra of (A) GLP (B) EC (C) PVP

The IR spectra of GLP (A), EC (B) and PVP K-30 (C) are shown in figure 2. The IR spectra of physical mixtures of drug:EC and drug:PVP K-30 are shown in figure 3. The IR spectrum of glipizide exhibited its characteristic peaks at 3322.11 cm^{-1} for N-H stretching of NH_2, 3247.42 cm^{-1} for CONH, 2941.18 cm^{-1} for aromatic C-H stretching, 2852.69 cm^{-1} for C-H aliphatic stretching, 1687.68 cm^{-1} and 1648.13 cm^{-1} for C=O stretching, 1582.13 cm^{-1} for C=N and 1524.95 cm^{-1} for C=C stretching. The IR spectrum of physical mixture of drug:EC and drug:PVP K-30 were compared with the IR spectra of pure drug. No significant changes in the functional groups between the two spectra were observed and ensured the compatibility of polymers with the drug.

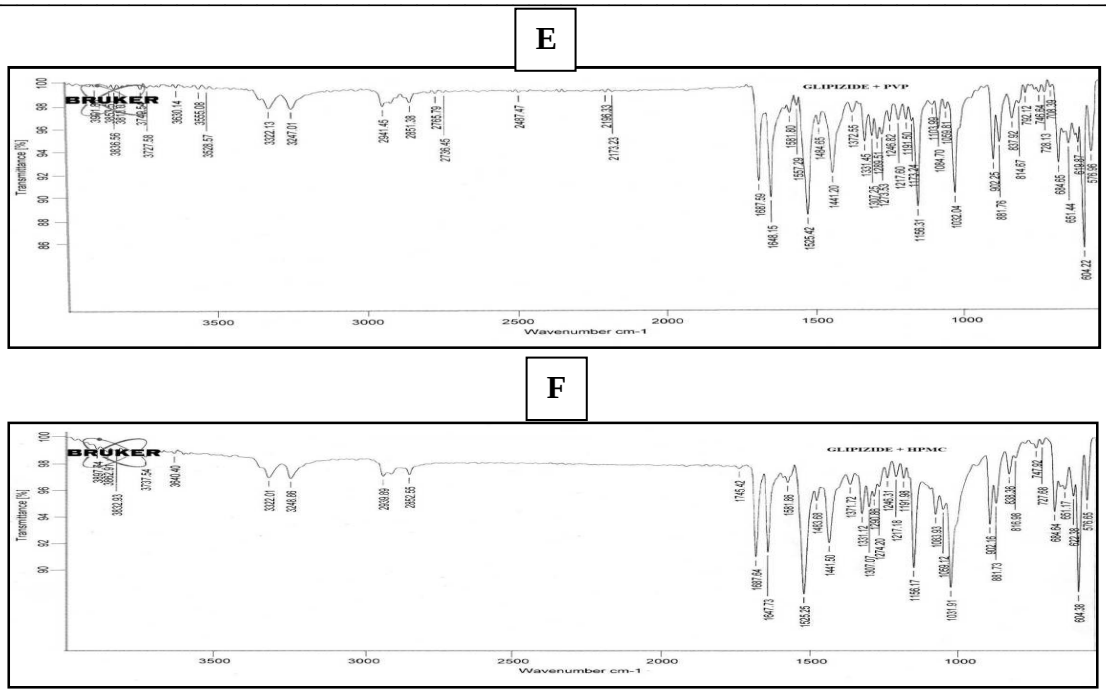

Figure 3: FTIR spectra of physical mixture of (E) GLP:EC (F) GLP:PVP

3.2 Physicochemical characteristics of buccal patches: All prepared buccal patches of glipizide.They were found smooth surface, flexible and slightly opaque. The physical parameters such as thickness, weight variation, folding endurance and surface pH are tabulated in table 2.

Table 2: Thickness, weight variation, folding endurance and surface pH of GLP patches prepared from EC alone (control), EC:PVP K-30 (A1-A6)

Sl. No	Batch code	Thickness ± SD	Weight ± SD	Folding endurance	Surface pH
1	Control	0.105 ± 0.005	0.045 ± 0.001	188 ± 2.154	6.56 ± 0.115
2	A1	0.116 ± 0.004	0.050 ± 0.008	120 ± 3.115	6.58 ± 0.096
3	A2	0.121 ± 0.012	0.055 ± 0.002	116 ± 4.157	6.64 ± 0.154
4	A3	0.125 ± 0.005	0.063 ± 0.005	113 ± 1.146	6.67 ± 0.114
5	A4	0.129 ± 0.003	0.070 ± 0.001	108 ± 2.142	6.68 ± 0.084
6	A5	0.134 ± 0.001	0.079 ± 0.001	114 ± 2.102	6.66 ± 0.094
7	A6	0.141 ± 0.009	0.088 ± 0.003	118 ± 1.194	6.65 ± 0.141

The patches exhibited variable thickness and weight because of differences in their composition. The thickness and weight of the patches were found to increase with increasing concentrations of PVP K-30 compared to patch prepared with EC alone (i.e., control). Folding endurance of all patches were measured manually and found to be good with EC:PVP K-30 compared to EC alone patches. Nevertheless, all patches exhibited good physical and mechanical properties. The surface pH of all buccal patches was varied between 6.56 ± 0.115 to 6.68 ± 0.084. No significant difference was found in surface pH of different formulations and was close to the oral pH and so no mucosal irritation was expected.

Table 3: % Moisture content, % moisture uptake, % swelling index and % drug content of GLP patches prepared from EC alone (control), EC:PVP K-30 (A1-A6)

Sl. No	Batch code	% Moisture content	% Moisture uptake	% Swelling index at 2 h	% Drug content
1	Control	3.85 ± 0.02	5.10 ± 0.03	No swelling	95.27 ± 0.295
2	A1	4.07 ± 0.01	4.56 ± 0.02	81.58 ± 0.18	94.12 ± 0.134
3	A2	4.14 ± 0.01	4.49 ± 0.01	83.49 ± 0.09	93.24 ± 0.815
4	A3	4.26 ± 0.01	4.40 ± 0.03	85.24 ± 0.28	94.68 ± 0.110
5	A4	4.32 ± 0.02	4.32 ± 0.02	86.38 ± 0.19	96.03 ± 0.571
6	A5	4.05 ± 0.01	4.01 ± 0.01	84.29 ± 0.34	93.46 ± 0.542
7	A6	4.00 ± 0.01	3.94 ± 0.01	83.96 ± 0.07	95.28 ± 0.314

Further, % moisture content, % moisture uptake, % swelling index and % drug content of buccoadhesive patches of glipizide are tabulated in table 3. All patches were subjected at high humid conditions and also at dry conditions to check the physical stability and integrity of the patches respectively. The patch prepared only with EC (control) was containing less moisture content and less moisture uptake compared to all other EC:PVP K-30 batches (figure 4).

The results revealed that moisture content and moisture uptake was found to increase with increasing concentrations of PVP K-30 which can be attributed to the hydrophilic nature of the polymers (i.e., A1 to A4). The comparative percentage swelling of various formulations was in order of A4 > A3 > A2 > A1 (figure 5).

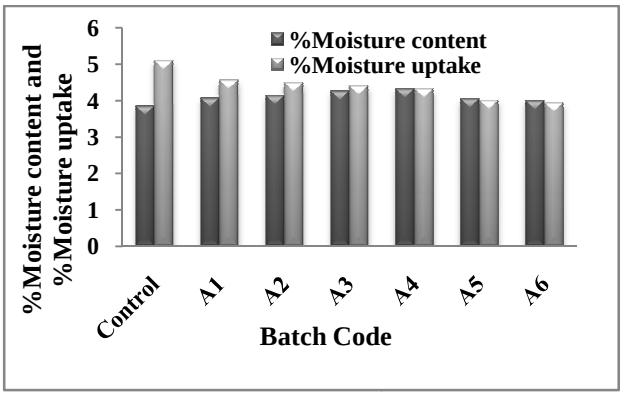

Figure 4: Comparative percentage of moisture content and moisture uptake of GLP from EC alone (control) and EC:PVP K-30 (A1-A6)

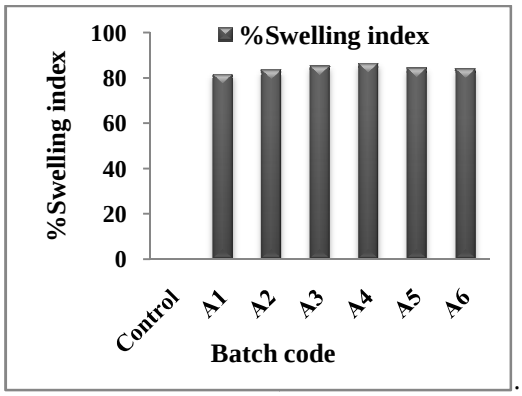

Figure 5: Comparative percentage swelling index of GLP from EC alone (control) and EC:PVP K-30 (A1-A6)

Additionally, it was found that moisture content and moisture uptake were decreased with decrease in concentrations of PVP K-30 (i.e., A5 and A6). Similar types of results were observed with swelling studies. However, no swelling was found in case of patch prepared with EC alone. Amongst all formulations, high % swelling was observed in EC:PVP K-30 patches (A4) due to high concentration hydrophilic polymer and consequently extent of hydration and swelling was more with these patches. The drug content estimated in buccal patch prepared only with EC was 95.27 ± 0.295, whereas in case of various EC:PVP K-30, it was varied from 93 to 96% (table 3). The low SD values ensured uniform of drug distribution in each batch of patches.

3.3 *In vitro* bio-adhesion strength: Bioadhesive strength of buccal patches may be defined as the adhesion between buccal patches and buccal mucosa. In this study, fresh sheep buccal mucosa was used as biological membrane. Bioadhesive strength studies of patches prepared have shown variable results. Table 4 clearly shows that bioadhesive strength of patches varied widely due to differences in the composition of polymers in the formulations. The strength of bioadhesion might have affected by various factors like biological membrane used in the study, molecular mass, flexibility, hydrogen bonding capacity, cross-linking density, charge, concentration, and swelling rate of polymers present in the formulation [10].

Table 4: *In vitro* bioadhesion strength of GLP patches prepared from EC alone (control), EC:PVP K-30 (A1-A6)

Batch code	Bioadhesive strength (G) ± SD	Force of adhesion (N) ± SD	Bond strength (Nm^{-2}) ± SD
Control	1.45 ± 0.020	0.0142 ± 0.001	3.55 ± 0.56
A1	1.87 ± 0.011	0.0183 ± 0.004	4.57 ± 0.21
A2	1.92 ± 0.015	0.0188 ± 0.003	4.70 ± 1.25
A3	2.16 ± 0.020	0.0211 ± 0.001	5.27 ± 0.12
A4	2.25 ± 0.016	0.0220 ± 0.005	5.50 ± 1.45
A5	1.90 ± 0.014	0.0186 ± 0.003	4.65 ± 0.54
A6	1.82 ± 0.023	0.0178 ± 0.003	4.45 ± 0.37

The comparative bioadhesive strength of various formulations was in the order of A4 > A3 > A2 > A1 **(**figure 4). Among all formulations A4 and B4 showed maximum bioadhesive strength (2.24 and 2.18 G), force of adhesion (0.0220 and 0.0170 N), and bond strength (5.50 and 5.23 N m^{-2}). When the concentration of the polymer is too low, the number of penetrating polymer chains per unit volume of the mucus is small, and the interaction between polymer and mucus is unstable [11]. In general, the more concentrated polymer would result in a longer penetrating chain length and better adhesion. However, bioadhesive strength was found decreased with decrease in concentrations of PVP K-30 in some patches (i.e., A5 and A6). In these formulations, concentration of EC (hydrophobic) is more than the concentrations of PVP K-30 and hence decreased the strength of bioadhesion due to decrease in hydration as well as swelling of the polymers. Since, hydration is one of the important polymer-related characteristic required for a mucoadhesive polymer. Further, polymer swelling permits a mechanical entanglement by exposing the bioadhesive sites for hydrogen bonding and/or electrostatic interaction between the polymer and the mucous network [12].

3.4 *In vitro* permeation studies of glipizide through sheep buccal mucosa: The *in vitro* drug release studies through excised sheep buccal mucosa were performed up to 8 h for all the prepared buccal patches of glipizide in phosphate buffer pH 6.6 using modified Keshary-Chein diffusion cell. The cumulative amount of drug permeated per unit area was plotted against time, and the slope of the linear portion of the plot was estimated as steady-state flux (Jss). The permeability coefficient (Kp) was calculated by using the equation Kp = Jss/Cv, where Cv is the total concentration of drug present in the patches. Variable release profiles of glipizide from the different patches were observed from the *in vitro* permeation studies. All buccal patches of glipizide showed prolonged release of drug over a period of 8 h. The comparative drug release profiles of GLP from EC alone (control) and EC:PVP K-30 (A1-A6) patches are tabulated in table 5 and flux and permeability coefficient data are summarized in table 6. The flux and permeability coefficient was very low with patch prepared with EC alone and release was prolonged but incomplete even after 8h. This could be attributed to the hydrophobic nature of the polymer which helps to retain the drug in the matrix system by reducing the penetration of solvent molecules into patches.

Table 5: Comparative *in vitro* permeation rate profiles of GLP from EC alone (control) and EC:PVP K-30 (A1-A6) patches

Time (h)	Cumulative % drug released						
	Control	A1	A2	A3	A4	A5	A6
1	20.456	24.126	26.742	33.062	36.460	30.276	28.135
2	28.171	35.142	37.199	44.903	48.301	42.061	40.387
3	32.939	42.359	46.257	54.078	59.446	52.676	49.135
4	39.695	48.246	53.409	64.406	68.518	58.730	55.527
5	43.923	53.350	60.482	71.044	77.579	65.428	63.353
6	48.220	59.353	66.283	77.180	83.771	72.713	68.426
7	51.635	63.690	70.037	83.445	91.382	78.658	73.339
8	55.304	68.567	75.437	88.345	94.731	82.860	78.052

However, when the patches were prepared with the blends of EC:PVP K-30, the flux and permeation rates were increased compared to patches prepared with EC alone. In case of EC:PVP K-30 patches, the drug release rate was progressively increased with the increase in the PVP K-30 concentration in the formulations. The highest percent of drug release was observed with EC:PVP K-30 1:1 ratio (94.73%) and lowest with EC:PVP K-30 1:0.25 ratio (68.56%) at the end of 8 h.

Table 6: The flux and permeability coefficient data of buccal patches of GLP prepared from EC alone (control), EC:PVP K-30 (A1-A6)

Sl. No	Batch code	Flux (mg/cm^2/h)	Permeability coefficient (cm/h)
1	Control	2.903	3.8142×10^2
2	A1	3.590	4.290×10^2
3	A2	4.000	4.912×10^2
4	A3	4.650	5.226×10^2
5	A4	5.019	4.675×10^2
6	A5	4.370	4.315×10^2
7	A6	4.111	3.577×10^2

The comparative drug release profiles of GLP from EC alone (control) and EC:PVP K-30 (A1-A6) patches are shown if figure 6. The increasing order of drug release from the EC:PVP K-30 patches was found in the following order, A4 > A3 > A2 > A1 (i.e., 1:1 > 1:0.75 > 1:0.5 > 1:0.25). Furthermore, it has been found that increase in concentration of EC polymer has a negative effect on drug release i.e., drug release decreased with increase in concentrations of EC. This has been found in buccal patches prepared with blends of EC:PVP K-30 patches (1.25:1 and 1.75:1) and EC:HPMC (1.25:1 and 1.75:1) patches (i.e., A5 and A6; and B5 to B6). It may probably because of the hydrophobic nature of EC which restricts drug diffusion from the patches. From the over all *in vitro* permeation profiles it was observed that, when patches were prepared with blends of hydrophobic and hydrophilic polymers, flux and permeability of drug through the patches was increased. And glipizide release from patches was highly influenced by the concentration of hydrophobic and hydrophilic polymers used in the formulation. The permeability of drug through polymeric patch is dependent on the characteristics of the polymer [13].

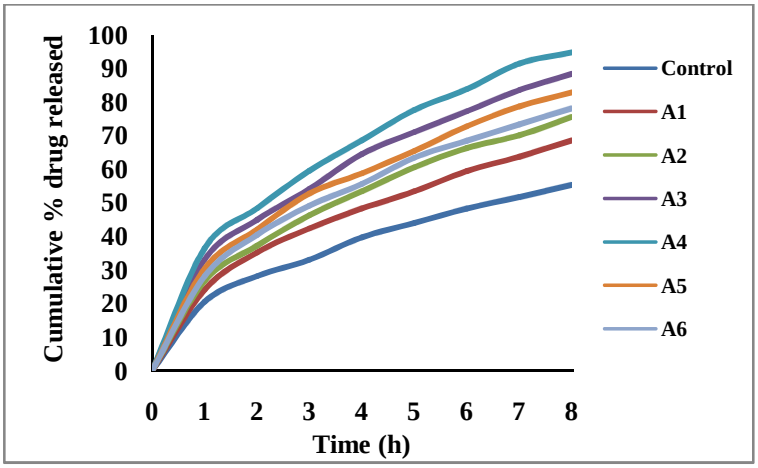

Figure 6: Comparative *in vitro* permeation rate profiles of GLP from EC alone (control) and EC:PVP K-30 (A1-A6) patches through sheep buccal mucosa

3.5 Mechanism of drug release: In order to find out the mechanism of drug release, *in vitro* release data of all patches were treated with various kinetic models such as Higuchi, first order and zero order equations. The comparative kinetic values obtained from the data are given in table 7.

Table 7: Mathematical modeling and comparative kinetic values of GLP patches prepared from EC alone (control) and EC:PVP K-30 (A1-A6)

Batch code	Zero order equation		1st order equation		Higuchi's equation		Hix.Crow equation	
	Ko(%mg/h)	r	$K_1X10^2(min^{-1})$	r	K_h(%mg)	r	$K_{HC}X10^2(mg^{IR}.min^{-1})$	r
Control	8.0745	0.8803	-0.1102	0.9577	19.6139	0.9995	-0.0330	0.9369
A1	9.9593	0.8820	-0.1520	0.9767	24.1891	0.9998	-0.0436	0.9546
A2	11.0167	0.8880	-0.1814	0.9872	26.7377	0.9998	-0.0505	0.9667
A3	12.9995	0.8750	-0.2594	0.9945	31.6002	0.9996	-0.0667	0.9813
A4	14.0859	0.8715	-0.3344	0.9857	34.2542	0.9992	-0.0794	0.9903
A5	12.1776	0.8777	-0.2219	0.9923	29.5927	0.9996	-0.0593	0.9737
A6	11.4879	0.8744	-0.1959	0.9872	27.9300	0.9996	-0.0538	0.9645

The release of the drug from the patches followed predominantly Higuchi model compared to other kinetics. The drug release was proportional to square root of time which indicates that the drug release from buccal patches was diffusion controlled. To know precisely whether Fickian or non-Fickian diffusion, the data obtained were also put in Korsemeyer-Peppas model in order to find out the value of 'n', which is the indicative of mechanism of drug release. In the present study, the value of 'n' determined from the EC:PVP K-30 patches ranged from 0.4739 to 0.5032 ($0.5 < n < 1$) with correlation coefficient values of 0.9988 to 0.9996. This indicated that the drug release mechanism from all buccal patches followed non-Fickian diffusion controlled [14].

CONCLUSION

The buccal route of administration is capable of avoiding the hepatic first pass effect, thus achieving higher systemic bioavailability of drugs. In the present study, attempts were made to develop and evaluate buccal patches of glipizide utilizing polymers like EC and PVP K-30 to achieve controlled release in order to minimize adverse effects associated with oral administration. From the overall studies it could be concluded that buccoadhesive patches of glipizide prepared with blends of EC:PVP K-30 in different ratios holds potential for buccal delivery of model drug to systemic circulation which gives a slow and controlled release up to 8 h. These developed patches also provide an added advantage of circumventing the hepatic first pass metabolism of glipizide and thus improving their oral bioavailability.

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REFERENCES

[1] V.M. Patel, B.G. Prajapati, M.M. Patel. *Acta. Pharm.*, **2007**, 57, 61-72.
[2] L. Vashmi Vishnu, K. Chandrasekhar, G. Ramesh, Y.Madhusudan Rao. *Curr. Drug. Deliv.*, **2007**, 4, 2739.

[3] A. Khairnar , P. Jain, D. Baviskar, D. Jain . *Int. J. Pharm. Sci.*, **2009**, 1(1), 91-95.
[4] T. Johnston, S. Miller, M. Chittchang, *Adv. Drug. Deliv. Rev.*, **2005**, 57, 1666-1691.
[5] C.R. Kahn, Shechter Y. Oral hypoglycemic agents and the pharmacology of the endocrine pancreas. In: Theodore WR, Alan SN, Taylor P, Gilman AG (ED). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ED. New York, NY: McGraw-Hill; **1991**; 1484.
[6] R.H. Foster, G.L. Plosker. *Pharmacoeconomics.*, **2000**, 18, 289-306.
[7] C. Amit, N. Upendra, R. Bhavya. *J. Adv. Pharm. Edu. & Res.*, **2012**, 2(4), 239-246.
[8] R.B. Samyuktha. *Int. J. Inv. Pharm. Sci*., **2013**, 1(1), 15-21.
[9] B.K Satishbabu, B.P. Srinivasan. *Indian. J. Pharm. Sci.*, **2008**, 70(2), 175-179.
[10] N. Salamat-Miller, M. Chittchang, T.P. Johnston. *Adv. Drug. Deliver. Rev.*, **2005**, 57, 1666-1691.
[11] N.A. Peppas, P.A. Buri, *J. Control. Release.*, **1985**, 2:257-275.
[12] J.M. Gu, J.R. Robinson, S.H.S. Leung. *Crit. Rev. Ther. Drug. Carr. Syst.*, **1998**, 5, 21-67.
[13] H. Arwidson, B. Johanson . *Int. J. Pharm.*, **1991**, 76, 91-97.
[14] R.W. Korsmeyer, R. Gurny, E. Doelker, P. Buri, N.A. Peppas. *Int. J. Pharm*., **1983**, 15-25.