Original Research Article

Design, evaluation and *in vitro - in vivo* correlation of glibenclamide buccoadhesive films

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Abstract

Background: Glibenclamide (G) is a popular anti-diabetic drug, belonging to the class of sulfonylurea. The drug is widely used for treating type II diabetes but it undergoes first-pass effect. A novel aspiration in treatment of diabetes, to provide greater therapeutic effect, bypass first pass effect and to improve patient compliance upon administering buccal drug delivery of Glibenclamide (G) have not been tested literally. Hence, the present study was designed to develop the buccal mucoadhesive films of glibenclamide by solvent casting technique; that is by using different polymers such as Hydroxy Propyl Methyl Cellulose 15 cps (HPMC), carbopol (CP), and poly vinyl pyrrolidone. Propylene glycol, which served the purpose of plasticizer as well as penetration enhancer and the backing membrane used was aluminium foil. **Materials and Methods:** The films were subjected to physicochemical parameters, *in-vitro* drug release and *ex vivo* bucco adhesive strength. **Results:** The satisfactory results were obtained in all prepared formulation and based on the results G14 [HPMC (150 mg) + CP(20 mg) + PVP (30 mg)] was the best one compared to others. The drug release of all formulation follows zero order kinetics by diffusion mechanism of non-fickian diffusion type. *Ex vivo*, *buccal* permeation studies by using sheep buccal mucosa and finally stability studies by using human saliva were carried out for the optimized formulation G14.Good correlation was observed between *in-vitro* and *in vivo* correlation, thus revealing the ability of the formulation to reproduce the in-vitro release pattern through the *in vivo*. **Conclusion:** Glibenclamide muck-adhesive buccal films could be promising one as they, increase bioavailability by bypassing the first pass effect, minimize the dose, reduces the side effects, and improve patient compliance and also glibenclamide might be a right and suitable candidate for oral controlled drug delivery via buccoadhesive films.

Key words: Buccoadhesive films, carbopol, *in-vitro in vivo* correlation, diabetes, glibenclamide, hydroxyl propyl methylcellulose, poly vinyl pyrolidone

INTRODUCTION

Buccal drug delivery is an alternative method of systemic drug delivery that offers several advantages over both inject able and enterable methods. The parenteral route may give excellent bioavailability but suffers from poor patient compliance and various risks such as anaphylaxis and extravasations infection per oral administration of pharmaceutical compositions have some drawbacks. For instance, it is difficult to keep the medicament at the desired location so that it can be absorbed, distributed, and metabolized easily. These limitations have driven the development of alternative routes of administration. Absorptive mucosa has been attracting extensive research, as they offer many benefits, such as noninvasive administration, rapid onset of action, good bioavailability, elimination of hepatic first pass metabolism, reduced dose, and low dose-related side effects.[1]

Many of the initial goals for buccal drug delivery have been selectively achieved with currently marketed products, such as providing a convenient, painless method of drug delivery, improving patient compliance, reducing adverse delivery, reducing adverse effects, and maintaining more consistent and prolonged blood levels than those achieved with oral or parenteral dosing. Patients and clinicians alike quickly accepted the technology, and films were viewed as a desirable platform for a variety of therapeutic uses, including motion sickness, hypertension, and angina, hormone therapy, smoking cessation, and pain control.[2]

Glibenclamide (G) is a popular anti-diabetic drug, belonging to the class of sulfonylurea. The drug is widely used for treating type II diabetes. It undergoes first-pass effect and the most frequently reported side effects are gastric disturbances like

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nausea, vomiting, anorexia, and increased appetite after oral therapy. Since these drugs are usually intended to take for a long period, patient compliance is very important. [3,4]

The aim of this work was designed to develop 12 hours therapeutic system of glibenclamide via buccal route to avoid hepatic first pass metabolism, to overcome gastrointestinal incompatibility,[5] reduce the frequency of administration, overcome the side effects and to obtain greater therapeutic efficacy to improve patient compliance.

MATERIALS AND METHODS

Materials

Glibenclamide obtained from Sri Raghavendra Chemicals and Suppliers, Bangalore. Hydroxy propyl methylcellulose (15 cps), Poly vinyl pyrrolidine, Carbopol (934P) obtained from Drugs India, Hyderabad. Ethanol, O. R Distilleries, Renigunta. Propylene glycol, Karnataka fine chem. Industries, Bangalore. All other chemicals used for this study were of analytical grade.

Pre formulation studies

Determination of partition coefficient

The partition co-efficient of the drug was determined using *n* – Octanol: Water system. The *n*-octanol- water partition coefficient serves as a parameter of lipophilicity. *n*-Octanol and water were pre saturated with each other for at least 24 h before the experiment. An accurately weighed quantity of drug was dissolved in 10 ml of the n-octanol phase and shaken at 37°C for 24 h against 10 ml aqueous phase in a sealed container. The separated n-octanol phase was assayed by UV spectroscopy to determine its residual concentration and hence the amount partitioned into the aqueous phase.[6,7] The partition coefficient was expressed as the concentration of drug in the n-octanol phase (% w/v) divided by the concentration in the aqueous phase.

Drug–excipient interaction study

The pure drug, glibenclamide and a mixture of it with the polymers, Hydroxyl propyl methyl cellulose, Poly Vinyl Pyrrolidone and, Carbopol were mixed separately with IR grade KBr in the ratio of 100:1 and corresponding pellets were prepared by applying 5.5 metri ton of pressure in a hydraulic press.[8] The pellets were scanned over a wave number range of 4000–400 cm^{-1} in Thermo Nicolet USA, FTIR instrument.

Fabrication of glibenclamide buccal films

The buccal mucoadhesive films were prepared by the method of solvent casting technique[9] employing 'O' shape ring placed on a glass surface as substrate by using different polymers like Hydroxy Propyl Methyl Cellulose 15 cps (HPMC), Carbopol (CP) and Poly Vinyl Pyrrolidone (PVP).

The calculated quantities of polymers were dispersed in ethanol (70% v/v). The carbopol polymeric solution was neutralized using triethanolamine. An accurately weighed 10 mg glibenclamide was incorporated in polymeric solutions after levigation with 30% w/w propylene glycol, which served the purpose of plasticizer as well as penetration enhancer.[10] The solution was casted on a glass surface employing 'O' shape ring and allowed to dry at room temperature over night. The dried films were separated and the backing membrane used was aluminium foil.[11]

The compositions of formulation of glibenclamide buccal films were given in [Table 1].

Physico-chemical evaluation

Thickness and weight of films

The thickness of the each film was measured by using a digital Vernier caliper at six different positions of the film, the average thickness was calculated, the weights of three films were taken, and the weight variation was calculated.[12]

Drug content uniformity

A film was cut into three pieces of equal diameter were taken in separate 100 ml of pH. 6.8 phosphate buffer was added and continuously stirred for 24 h.[12] The solutions were filtered, suitably diluted and analyzed at 229 nm in a UV Spectro photometer.

Folding endurance

Folding endurance of the film was determined by repeatedly folding one film at the same place till it broke or folded up to 300 times manually, which was considered satisfactory to reveal good film properties.[13]

Surface pH

Buccal films were left to swell for 2 h on the surface of 2% (w/v) an agar plate. The surface pH[12] was measured by means of a pH meter placed on the surface of the swollen buccal film.

Percentage moisture absorption

The percent moisture absorption test was carried out to check the physical stability of the buccal films at high humid conditions.

Table 1: Composition of films prepared using glibenclamide

Formulation code	Polymers in mg			Solvents in ml	
	HPMC	CP	PVP	Ethanol (70%)	PG
G1	200	0	-	9.5	0.5
G2	190	10	-	9.5	0.5
G3	180	20	-	9.5	0.5
G4	170	30	-	9.5	0.5
G5	160	40	-	9.5	0.5
G6	150	50	-	9.5	0.5
G7	190	-	10	9.5	0.5
G8	180	-	20	9.5	0.5
G9	170	-	30	9.5	0.5
G10	160	-	40	9.5	0.5
G11	150	-	50	9.5	0.5
G12	150	40	10	9.5	0.5
G13	150	30	20	9.5	0.5
G14	150	20	30	9.5	0.5
G15	150	10	40	9.5	0.5

Drug loaded in each film: Glibenclamide: 10 mg, Plasticizers: Propylene Glycol; Backing membrane: Aluminium foil

In the present study, the moisture absorption capacity of the films was determined as follows. Three 1 cm diameter films were cut out and weighed accurately then the films were placed in desiccators containing saturated solution of aluminum chloride, keeping the humidity inside the desiccators at 79.5%. After 3 days, the films were removed, weighed and percentage moisture absorption was calculated. Average percentage moisture absorption of three films was found.[12]

$$\text{Percentage Moisture Absorption} = \frac{\text{Final weight - Initial weight}}{\text{Initial weight}} \text{X100}$$

Percentage moisture loss

This test was also carried to check the integrity of films at dry condition. Three 1-cm diameter films was cut out, weighed accurately, and kept in desiccators containing fused anhydrous calcium chloride. After 72 hours, the films were removed and weighed. Average percentage moisture loss of three films was found out.[12]

$$\text{Percentage Moisture Loss} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \text{X100}$$

Swelling percentage

Drug-loaded films were placed in a thoroughly cleaned petridish and a graph paper was placed beneath the petridish, to measure the increase in area due to swelling of the film. [14] Fifty ml of pH. 6.8 phosphate buffer was poured into the petridish. An increase in the weight of the patch was noted in 15 min intervals for 60 min and the weight was calculated. The swelling percentage was calculated using the following formula:

$$\%\, S = \frac{X_t - X_0}{X_0} \text{X100}$$

Where, % S -swelling percentage, X_t -the weight of swollen film after time t, X_0 -weight of film at zero time zero.

Water vapour transmission rate

For this study, vials of equal diameter were used as transmission cells. These cells were washed thoroughly and dried in an oven. About 1 g of calcium chloride was taken in the cell and the polymeric films measuring one cm^2 area were fixed over the brim with the help of an adhesive. The cells were weighed accurately and initial weight was recorded, and then kept in a closed desiccators containing saturated solution of potassium chloride. The humidity inside the desiccators was found in between 80–90% RH. The cells were taken out and weighed after 18, 36, 54, and 72 hrs.[15] In addition, the rate at which water vapour transmitted was calculated by using the following formula.

$$\textit{Water Vapour Transmission Rate} = \text{WL/S}$$

Where, W is water vapour transmitted in mg, L is thickness of the film in mm, S is exposed surface area in cm^2.

Stability study in human saliva

The stability study of patches was performed in natural human saliva. Samples of human saliva were collected from 10 humans (ages 18-40 years) and filtered. The films were placed in separate petridishes containing 5 mL of human saliva and put in a temperature-controlled oven at 37°C±0.2°C for 6 hours. At regular time intervals, films were examined for changes in color, shape, collapse and physical stability.[16]

Measurement of buccoadhesive strength

A modified balance method was used for determining the *ex-vivo* buccoadhesive strength.[17,18] Fresh sheep buccal mucosa was obtained from a local slaughterhouse and used within 2 h of slaughter. The mucosal membrane was separated by removing the underlying fat and loose tissues. The membrane was washed with distilled water and then with isotonic phosphate buffer (IPB) pH. 6.8 as moistening fluid. Sheep buccal mucosa was fixed on the plane surface of glass slide attached (with adhesive tape) to bottom of smaller beaker, kept inverted in 500 ml beaker attached to the bigger beaker. Isotonic phosphate buffer pH. 6.8 was added to the beaker up to the upper surface inverted beaker with buccal mucosa. The buccal film was stuck to the lower side of the upper clamp with cyanoacrylate adhesive. The exposed patch surface was moistened with IPB and left for 30 s for initial hydration and swelling. Then the platform was slowly raised until the patch surface came in contact with mucosa. Two sides of the balance were made equal before study by keeping a weight on the right hand pan. A weight of 5 g was removed from the right hand pan, which lowered the pan along with the patch over the mucosa. The balance was kept in this position for 5 minutes contact time. Then weights were slowly added to the right hand pan until the patch detached from the mucosal surface. This detachment force gave the buccoadhesive strength of the buccal patch in grams. The following parameters were calculated from the bioadhesive strength.

Force of adhesion (N) = (Bioadhesive strength (g) ×9.8)/1000

In vitro drug release studies

The *in vitro* release studies were performed in phosphate buffer solution (pH 6.8, 100 ml) at 37°C using a modified dissolution apparatus. The modified dissolution apparatus consisted of a 250 ml beaker as a receptor compartment and an open-end tube as a donor tube. The magnetic stirrer assembly with an attached hot plate was adopted for the study. The dissolution medium consisted of 100 ml of phosphate buffer (pH 7.5) maintained at 37±1°C by means of a thermo-regulated hot plate. Film was placed into the donor chamber of the assembly separated from the medium by a semi-permeable membrane. The donor tube was then dipped into the receptor compartment containing dissolution medium, which was maintained at 37±1°C and stirred at a constant speed of 100 rpm using a magnetic bead.[19] One-milliliter samples were withdrawn at predetermined time intervals for all the batches. For each sample withdrawn, an equivalent volume of phosphate buffer was replaced to the dissolution medium to maintain constant volume and sink condition. A ten-fold dilution of each of the withdrawn sample was made and the diluted solutions were thereafter analyzed spectrophotometrically at 229 nm.

Ex vivo permeation studies

An *ex vivo* diffusion study of glibenclamide was carried out using a fresh sheep buccal mucosa[20,21] using modified diffusion cell at 37±1°C. Fresh sheep buccal mucosa was mounted between the donor and receptor compartments. Sheep buccal mucosa was tied to one end of an open ended cylinder, which acts as a donor compartment. The film should be placed in such a way that it should be stuck on the mucous membrane. The receptor compartment was filled with isotonic phosphate buffer pH. 6.8. The assembly was maintained at 37 °C and stirred magnetically. Samples were withdrawn at predetermined time intervals and analyzed using UV spectrophotometer at 229 nm.

In vivo drug release study

Selection of animals and method

Rabbits [*Orytolagus cuniculuss*] 10 – 12 weeks old weighing 2.5 to 3 kg was selected.

A healthy rabbit.[22] weighing 2.5 to 3 kg was taken, which was already checked for absence of any diseases. The dose of glibenclamide was adjusted based on the rabbit weight.[23] The film was placed in the buccal membrane with the help of a clip. Dextrose solution was transfused continuously throughout the period of study. Periodically 1 ml of blood sample was taken by syringe, which already contained 1 ml of heparin solution to prevent blood clotting. These blood samples were subjected for centrifuging at 2,500 rpm for about 30 minutes. 1 ml of supernatant was taken, and after suitable dilution, analyzed at 229 nm using UV spectrophotometer.

In vitro-in vivo correlation

In vitro and *in vivo* correlation was carried out to compare the release of drug. It is governed by the factors related to both *in vitro* and *in vivo* characteristics of the drug. The cumulative percentage of drug release both in *in vitro* and *in vivo* was plotted.[24]

RESULTS AND DISCUSSION

The glibenclamide buccoadhesive films were prepared by the method of solvent casting technique employing 'O' shape ring placed on a glass surface as substrate by using different polymers such as Hydroxy Propyl Methyl Cellulose - 15 cps (HPMC), Carbopol-P 934 (CP) and Poly vinyl pyrrolidone (PVP). Ethanol (70%) is used as the solvents. Propylene glycol serves as the plasticizer as well as penetration enhancer. Triethanolamine was used to neutralize the carbopol polymeric solution.

Pre formulation studies

Partition coefficient

Partition coefficient of Glibenclamide in n-octanol/water system.[6,7] was found to be 3.16, favorable for the buccal drug delivery system.

Drug–excipient interaction study

The physicochemical compatibility of the drugs and the polymer was established through FTIR studies.[8] In the physical mixture of Glibenclamide with HPMC, CP and PVP; the major peaks of glibenclamide were 1714, 1638 (C = O Stretching), 1415 (CH_2 Bending), 1342, 1300 (SO_2 Asymmetric Stretching), 1244, 1158 (C – N Stretching) wave numbers. However, additional peaks were absorbed in physical mixtures, which could be due to presence of polymers and indicated that there was no chemical interaction between glibenclamide and other excipients, which are shown in Figure 1.

Physico-chemical evaluation

Thickness and weight of films

The film thicknesses were observed[12] by using digital Vernier caliper and found to be in the range of 0.20±0.01 mm to 0.62±0.01 mm. The weight of the films was found to be in the range of 200.12±1.06 mg to 153.18±0.9 mg.

Drug content uniformity

The observed results of content uniformity[12] indicated that the drug was uniformly dispersed and with minimum intra batch variability. Recovery was possible to the tune of 8.1±0.26 to 9.9 ±0.2.

Folding endurance

The folding endurance was found to be greater than 300 times in case of all the formulations.[13] This makes the system acceptable

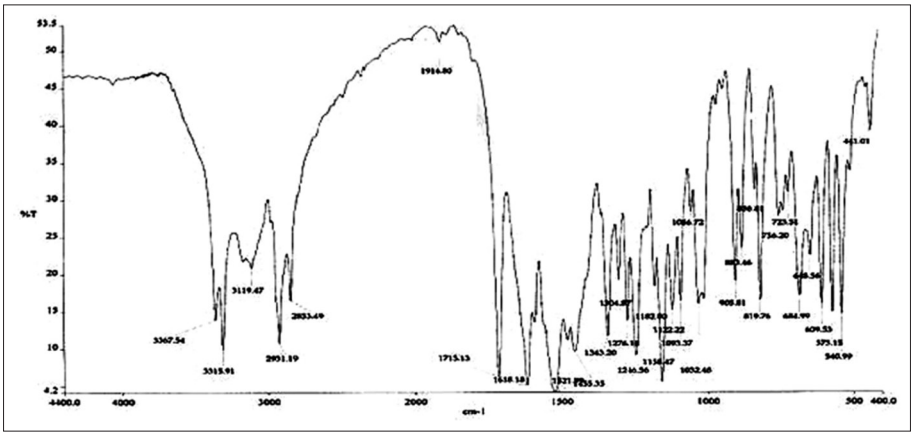

Figure 1a: IR spectra of Glibenclamide

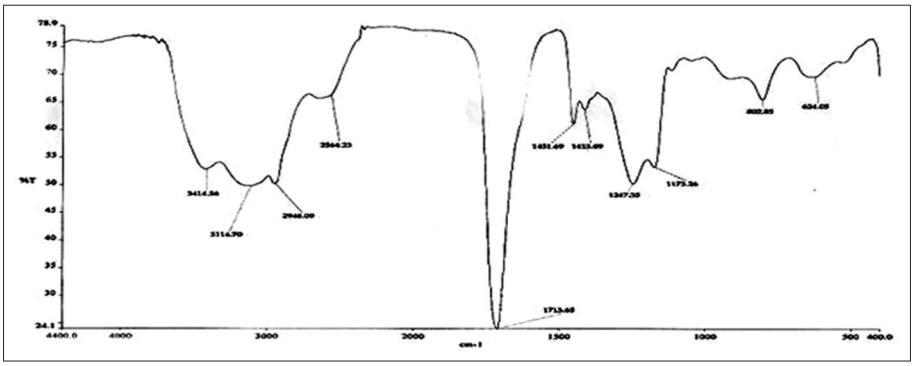

Figure 1b: IR spectra of Carbopol 934

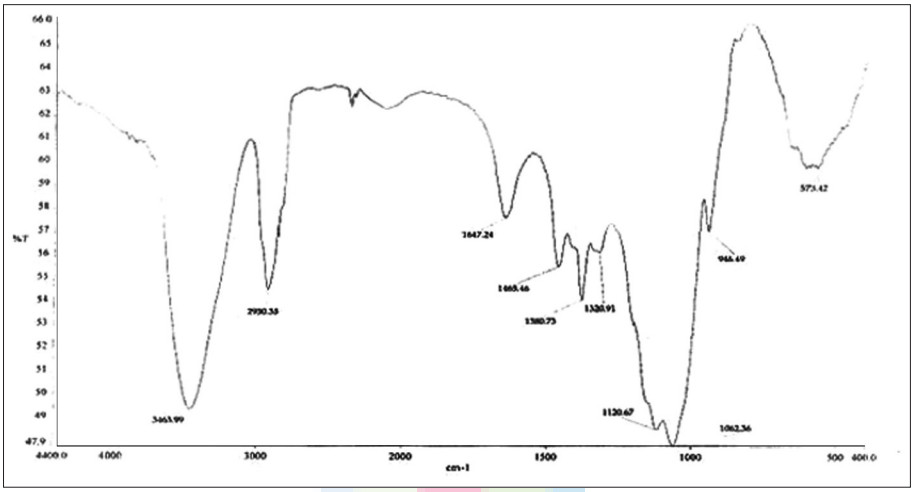

Figure 1c: IR spectra of HPMC

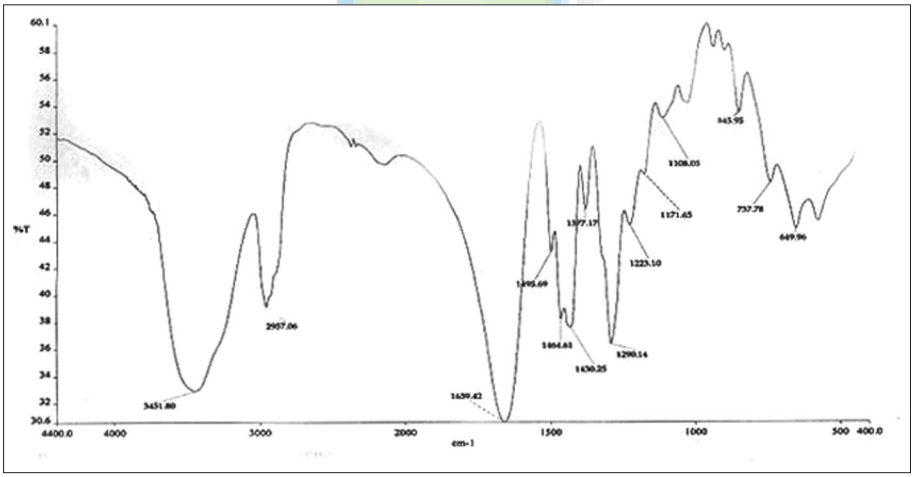

Figure 1d: IR spectra of PVP

for movement of mouth, indicating good strength and elasticity. Folding endurance test results indicated that the films would maintain the integrity with buccal mucosa when applied.

Surface pH

Considering the fact that acidic or alkaline pH may cause irritation to the buccal mucosa and influence the rate of hydration of the polymers, the surface pH of the films was determined.[12] The results are found that there is no significant difference of surface pH in all the formulations and the pH range lies within the range of salivary pH, i.e., 6.5 to 6.8, hence do not cause irritation and achieve patient compliance.

Percentage moisture absorption and percentage moisture loss

Checking the physical stability of the film at high humid conditions and integrity of the film at dry conditions,[12] the films were evaluated for PMA and PML. The percentage moisture uptake in

the formulation G6 (150 mg, HPMC, 50 mg CP) has shown the highest value of moisture absorption 14.29±0.06. This may be due to the presence of higher concentrations of CP along with HPMC.

The formulation G11 (150 mg, HPMC; 50 mg PVP) shows higher value of moisture loss 11.29±0.06, which is due to presence of higher concentration of PVP and formulation G6 (150 mg, HPMC; 50 mg CP) shows low value of 3.89±0.02.

Swelling percentage

The swelling behavior of the polymer was reported to be crucial for its bioadhesive character. The adhesion occurs shortly after swelling but the bond formed is not very strong. The adhesion increases with the degree of hydration until the point of distanglement at the polymer tissue surface, which leads to abrupt drop in adhesive strength due to over hydration.[14] The formulation G6 (150 mg, HPMC, 50 mg CP) shows higher value of swelling percentage, 138.02±0.85, which is due to presence of higher concentration of carbopol.

Water vapour transmission rate

Water vapor transmission studies indicated that all the films were permeable to water vapour.[15] The formulation G11 (150 mg, HPMC, 50 mg PVP) has shown maximum water vapor transmission of 12.44±0.48 among all the films. This may be due to the presence of high amount of PVP.

The formulation G6 (150 mg, HPMC; 50 mg CP) has shown lower water vapor transmission of 5.39±0.32 among all the films. This may be due to the presence of high amount of carbopol.

Stability in human saliva

The stability study of the optimized films (G 14) was done in natural human saliva. The films did not exhibit any significant changes in their color, shape and satisfactory physical stability.

Measurement of buccoadhesive strength

The buccoadhesive properties of the fabricated films were shown in Figure 2. CP being an anionic polymer gives the highest bioadhesive force. The bioadhesive strength exhibited by glibenclamide buccal films was satisfactory for maintaining them in oral cavity.[17,18] The combination of HPMC and CP shows good adhesion. Upon addition of PVP, the bioadhesive strength increases, which may be due to hydrogen bond formation and Vanderwaals forces. The highest buccoadhesive strength was found to be in formulation G 14.

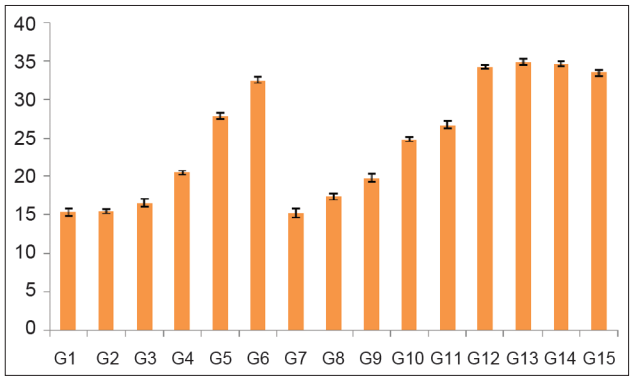

Figure 2: Buccoadhesive strength of all formulations

In vitro drug release studies

Distinguishable difference was observed in the release of Glibenclamide in all formulations shown in [Table 2].

Formulations G1, G2, G3 containing HPMC alone and combination of CP and HPMC gave a reasonable Glibenclamide release up to 10 h.

Formulations G4, G5 and G6 containing combination of CP and HPMC gave a reasonable Glibenclamide release up to 11 h.

In vitro drug release and higuchi's plot of formulations G1, G2, G3, G4, G5, and G6 has shown that the drug release followed by zero order kinetics, which was evinced from the regression value (R). The diffusion exponent (n) obtained by Peppa's plot, which confirms that the diffusion mechanism involved in the drug release, was Non-fickian release in case of formulations G1 and G2 and Super case II transport type in of case of formulations G3, G4, G5, and G6.

Formulations G7, G8, G9, G10, and G11 containing combination of HPMC and PVP gave a reasonable Glibenclamide release up to 11 h.

In vitro drug release and higuchi's plot of formulations G7, G8, G9, G10, G11, and G12 has shown that the drug release followed by zero order kinetics, which was evinced from the regression value (R). Peppa's plot, which confirmed that the diffusion mechanism involved in the drug release, was Non-fickian release in case of formulations G7 and Super case II transport type in the case of formulations G8, G9, G10, and G11.

Table 2: Drug release parameters of various formulations

Drug release studies	Percentage drug release at the end of 12th hour
In-vitro drug release study	
G-1	95.2±1.3
G-2	96±1.1
G-3	95.6±1.2
G-4	98.1±1.2
G-5	96.2±1.2
G-6	94.4±1.3
G-7	96.6±1.2
G-8	95.2±1.4
G-9	94±1.3
G-10	93.2±1.3
G-11	91±1.2
G-12	94.4±1.3
G-13	96.2±1.3
G-14	98.2±1.4
G-15	97±1.3
Exvivo buccal permeation study for G-14	84±1.8
In vivo drug release study for G-14	90.4±1.4

All values expressed as Mean±SD, (n=3)

Formulations G12, G13, G14, and G15 containing combination of HPMC, CP, and PVP gave a reasonable glibenclamide release up to 12 h.

In vitro drug release and higuchi's plot formulations G12, G13, G14, and G15 has shown release has shown that the drug release followed by zero order kinetics, which was evinced from the regression value (R). Peppa's plot was drawn, which confirmed that the diffusion mechanism involved in the drug release was Non-fickian release in case of formulations G14, shown in [Figure 3] and Super case II transport type in of case of formulations G12, G13, and G15.

At pH. 6.8, carbopol is present in ionized state and as a result,[19] the polymeric network is loosened comparatively, attributing for the higher drug release. The addition of PVP decreases the glibenclamide release may be due to enhancement in swelling of the polymer, which in turn increases the barrier effect and decreases the drug release, there by controlling the drug release approximately 12 h.

The incorporation of carbopol and PVP into HPMC films, the drug release was found to maximum at the end of 12 h.

Ex vivo permeation studies

The oral mucosa represents a barrier to drug permeation and it is intermediate between skin epidermis and the gut in its permeability characteristics. The effectiveness of the buccal barrier[20,21] and whether buccal absorption could provide means for glibenclamide administration can be determined by *ex vivo* permeation studies. Permeation studies were carried out on formulation G 14. The cumulative amount of drug permeated was 68.8% maximum in 12 h. The values are tabulated in [Table 2] and shown in [Figure 4].

In vivo studies

In vivo drug release studies[22] were conducted for the glibenclamide buccal film G-14 in rabbits showed zero order release pattern and values tabulated in [Table 2]. The *in vivo* studies of buccal films of glibenclamide in rabbits did not show any inflammation or any other sensitization reactions at the administration site.

In vitro in vivo correlation

In vitro and *in vivo* correlation was carried out for the therapeutic efficacy of a pharmaceutical formulation and is governed by the factors related to both *in vitro* and *in vivo* characteristics of the drug. A graph was plotted by taking cumulative *% in vitro* release on X-axis and cumulative*% in vivo* drug release on Y-axis for the same period of time and the release rate follows zero order (R^2 = 0.9957) and shown in [Figure 5].

CONCLUSION

The glibenclamide buccal films were prepared by solvent casting technique using ethanol (70% v/v) as a solvent, employing 'O' shape ring placed on a glass surface as substrate and by using different polymers like Hydroxy Propyl Methyl Cellulose - 15 cps

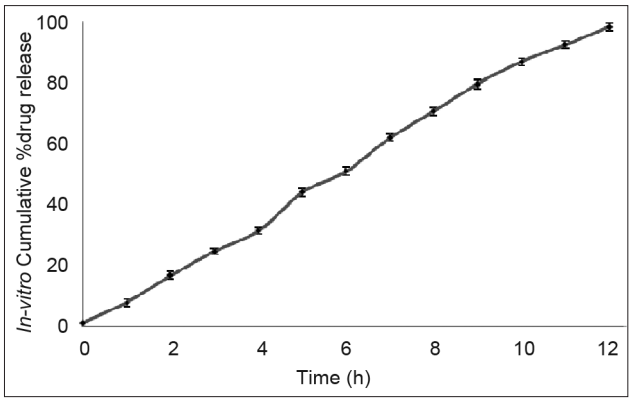

Figure 3: *In vitro* drug release for best formulation G-14

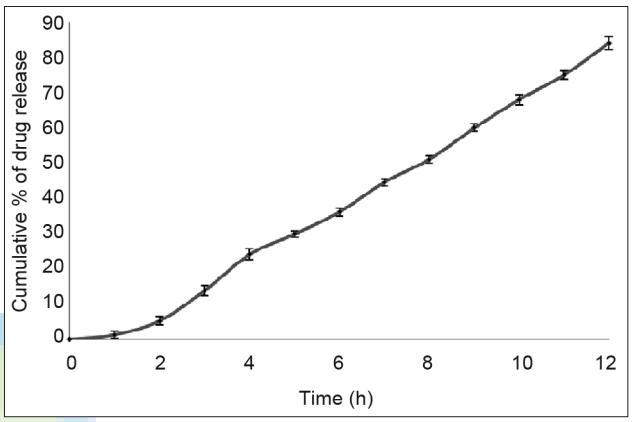

Figure 4: *Ex vivo* drug release for best formulation G-14

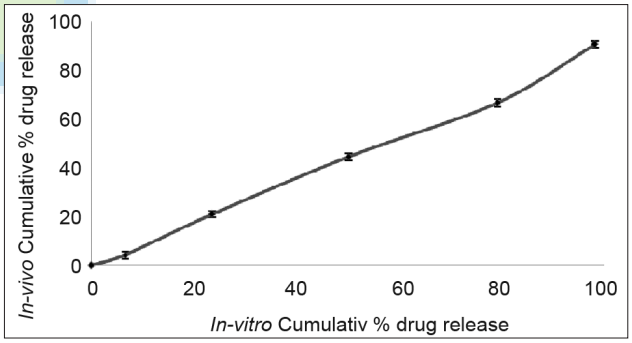

Figure 5: *In vitro-in vivo* correlation of formulation G-14

(HPMC), Carbopol (CP), and Poly vinyl pyrrolidone (PVP). The polymeric solutions are levigated with 30% w/w propylene glycol, which served the purpose of plasticizer as well as penetration enhancer. The prepared glibenclamide buccal films were characterized based upon their physico-chemical characteristics like surface pH, PMA, PML, swelling percentage, thickness, weight, folding endurance and drug content. The *ex vivo* buccoadhesive strength, *in vitro* release studies, *ex vivo* permeation studies and *in vivo* studies were performed.

The satisfactory results were obtained in all prepared formulation and based on the results G 14 [HPMC (150 mg) + CP (20 mg) + PVP (30 mg)] was the best one when compared to other. Good correlation was observed between *in vitro* and *ex vivo*

profile, revealed the ability of the formulation to reproduce the *in vitro* release pattern through the biological membrane. Hence, glibenclamide mucoadhesive buccal films could be promising one as they increase bioavailability, minimize the dose, reduces the side effects, and improve patient compliance; glibenclamide might be a right and suitable candidate for oral controlled drug delivery via mucoadhesive buccal films.

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