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MUCOADHESIVE DOSAGE FORM OF GLIBENCLAMIDE: DESIGN AND CHARACTERISATION

Sarfaraz Md, Venubabu.P, Doddayya Hiremath, Prakash. S.G*

Department of Pharmaceutics,
N.E.T Pharmacy College, Mantralayam Road,
Raichur-584103, Karnataka, India.
***Corresponding Author Email:** Sarfindia@gmail.com

ABSTRACT

The purpose of the present investigation was to design mucoadhesive dosage form of glibenclamide and characterize them for their physicochemical, ex vivo and in vitro parameters. Glibenclamide is an oral hypoglycemic agent of the sulphonylurea group and is frequently prescribed for the treatment of late-onset (non-insulin dependent) diabetes mellitus. Preformulation and micromeritic studies were carried out for the mucoadhesive tablets. The controlled-release glibenclamide tablets were produced by direct compression method using bioadhesive polymers like Carbopol 934P (CP934), polyvinylpyrollidone (PVP-K30) and Xanthan gum. The tablets were evaluated for surface pH, in-vitro bioadhesion strength, swelling index, in-vitro release and stability studies. The formulation F2 containing Carbopol 934P, PVP-K30 and mannitol was found to be promising. Formulation F 2 showed maximum drug release (89.19%) in 8 hrs along with satisfactory bioadhesion strength (3.74 gms).The optimized formulation F2 showed a surface pH of 6.31 and swelling index 67%. The stability of the optimized formulation was studied and no significant changes were detected in drug content and in vitro release studies. The formulations followed zero order and non-fickian release kinetics. FT-IR and DSC studies revealed the absence of any chemical interaction between drug and polymers used. Glibenclamide mucoadhesive tablets for buccal delivery could be prepared with required bioadhesive strength and in vitro release properties.

KEYWORDS: *Glibenclamide, buccal tablets, in-vitro release, bioadhesion strength, ex-vivo studies.*

INTRODUCTION

Oral route is perhaps the most preferred for the patients. However, oral administration of drugs has disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs. Within the oral mucosal cavity, the buccal region offers an attractive route of administration for systemic drug delivery. Buccal routes of drug delivery offer distinct advantages over oral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of pre-systemic elimination within the GI tract, these factors make the oral mucosal cavity a very attractive and feasible site for systemic drug delivery. Moreover, rapid onset of action can be achieved relative to the oral route and the formulation can be removed if therapy is required to be discontinued. It is also possible to administer drugs to patients who are unconscious and less co-operative. Considering the low patient compliance of rectal, vaginal, sublingual and nasal drug delivery for controlled release, the buccal mucosa has rich blood supply and it is relatively permeable. To prevent accidental swallowing of drugs adhesive mucosal dosage forms were suggested for oral delivery, which included adhesive tablets, adhesive gels, adhesive patches and many other dosage forms with various combinations of polymers, absorption enhancers[1]. Mucoadhesion is a state

in which two materials, one of which is mucus or a mucous membrane, is held together for an extended period of time [2]. Various mucoadhesive polymers are generally hydrophillic macromolecules that contain numerous bond forming groups, and will hydrate and swell when placed in contact with aqueous solution. These material needs to be in the hydrated form to become adhesive [3]. Among various routes of delivering the mucoadhesive dosage forms buccal route is most preferred. Diabetes mellitus is a chronic disorder with interrelated metabolic and vascular components. A relative or absolute deficiency of insulin secretion and activity is associated with hyperglycemia and altered lipid and protein metabolism. Type II diabetes mellitus is a chronic disease characterized by hyperglycemia and numerous other metabolic abnormalities. Its chronic complication include retinopathy, neuropathy, accelerated atherosclerosis which result in blindness, end-stage renal disease, amputation and premature cardiovascular mortality [4]. The medications that are used to treat diabetes can be categorized into two broad areas; oral antidiabetic agents and insulin. The oral agents, which may be further subcategorized into sulfonylureas and biguanides, are effective only in type II (non-insulin dependent) diabetes [5].

Glibenclamide has actions and uses similar to those of the other sulfonylureas. Glibenclamide is used for the treatment of patients with Non-Insulin Dependent Diabetes Mellitus (NIDDM) [6]. Glibenclamide inhibits ATP sensitive potassium channels in pancreatic beta cells. This inhibition causes cell membrane depolarization, which causes voltage-dependent calcium channels to open, which causes an increase in intracellular calcium in the beta cell, which stimulates insulin release. Glibenclamide is a weak acid (p*K*a = 6.3) practically insoluble in water and acidic solutions but highly permeable (class 2) according to the Biopharmaceutical classification System (BCS)[7]. The oral absorption is uniform, rapid and complete with nearly 100% bioavailability. The usual initial dose is 2.5 to 5 mg. The dose may be increased by maximal increments of 2.5 to 5 mg at weekly intervals and should be based on blood glucose level [8].

MATERIALS AND METHODS

Materials

Glibenclamide was obtained as gift sample from Arvind Remedies Ltd, Kakkalur, Tamil nadu. Poly vinyl pyrolidone (PVP-K30) was gifted by S.D Fine Chemicals Mumbai. Xanthan gum was from Krystal colloid Ltd. Mumbai., and Carbopol 934P was gifted by Hi media Laboratories Pvt. Ltd. All other materials were of analytical or pharmacopoeial grade and used as received.

Mucoadhesive tablet preparation

Mucoadhesive tablets of Glibenclamide were prepared by direct compression of the drug with mucoadhesive polymers using an 8 mm flat-faced punch of 10 station Rimek compression machine (**Table 1**). Carbopol 934P, PVP-K30 and xanthan gum were used as mucoadhesive polymers and mannitol was used as diluent. Magnesium stearate and talc were added to the above blend as flow promoters. All component ingredients including drug, polymer and excipients were weighed accurately according to the batch formula (**Table 1**) and screened through sieve # 60, than mixed thoroughly for 10 min before compression. In all the formulations the amount of glibenclamide was kept constant at 10 mg. The polymers like carbopol 934P, PVP-K30 and xanthan gum were used in different concentrations in combination. Total weight of the tablet was kept constant at 200 mg. The mass of the tablets were determined using a digital balance, hardness with monsanto hardness tester and thickness with a vernier calliper.

Table 1: Composition of glibenclamide mucoadhesive buccal tablets

Ingredients (mg)	Formulation code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Glibenclamide	10	10	10	10	10	10	10	10	10
Carbopol-934P	46	30.66	36.8	55.2	46	30.66	36.8	55.2	92
PVP-K30	46	61.33	55.2	36.8	-	-	-	-	-
Xantan gum	-	-	-	-	46	61.33	55.2	36.8	-
Mannitol	94	94	94	94	94	94	94	94	94
Magnesium stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Total weight	200	200	200	200	200	200	200	200	200
Polymer Ratio	1:1	1:2	2:3	3:2	1:1	1:2	2:3	3:2	

Evaluation of mucoadhesive buccal tablets

The prepared mucoadhesive buccal tablets were evaluated for thickness, diameter, hardness, friability, weight variation, drug content, surface pH, *ex vivo* bioadhesive strength, swelling index, *in vitro* drug release, short-term stability and drug-excipients interaction. Hardness and friability of the tablets were determined by using Monsanto hardness tester and Roche friabilator respectively. For weight variation twenty tablets were selected at random and weighed individually. The individual weights were compared with the average weight for determination of weight variation.

Estimation of drug content

For drug content an accurately weighed quantity of powder equivalent to 10 mg of glibenclamide was taken into 100 ml volumetric flask, dissolved in phosphate buffer of pH 7.4 and the solution was filtered through whatman filter paper no.41. The filtrate was collected and suitably diluted with phosphate buffer of pH 7.4. The drug content was determined at 300 nm by UV-spectrophotometer [9, 10].

Measurement of surface pH

A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping them in contact with 5 ml of distilled water for 2 hrs and pH was noted by bringing the electrode in contact with the surface of the formulation and allowing it to equilibrate for 1 min as showing in (**Figure 1**).

Figure 1: Measurement of surface pH

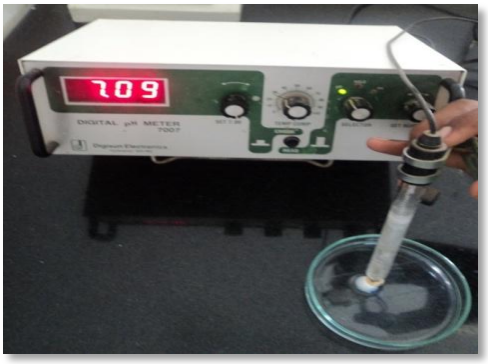


Figure 2: Measurement of *ex vivo* bioadhesive strength

Ex vivo bioadhesive strength

In this study, an instrument was designed to evaluate the tensile force. This instrument consists of a modified physical balance.This method was used for determination of the *ex vivo* bio adhesion strength. The balance was

modified by replacement of one pan with the metal shaft 5 gm heavier in weight than pan. Fresh ox buccal mucosa obtained from local slaughterhouse was cut into pieces, washed with distilled water followed by phosphate buffer pH 7.4 containing 8.4% methanol and 0.24% tween 80. A piece of buccal mucosa was fixed in a petri dish with instant adhesive, which was filled with phosphate buffer pH 7.4 so that it just touched the mucosal surface. The tablet was stuck to the lower side of a shaft with instant adhesive. The two sides of the balance were made equal before the study, by keeping 5 gm weight on the right hand pan as showing in (**Figure 2**). A weight of 5 gm was removed from the right hand pan, which lowered the shaft along with the tablet over the mucosa. The balance was kept in this position for 3 min contact time. The weight was added slowly to the right hand pan until the tablet detached from the mucosal surface. This detachment force gave the bioadhesion strength of the buccoadhesive tablet in gm (total weight on right hand pan minus 5 gm).

Swelling studies

The extent of swelling was measured in terms of % of weight gained by the tablet. One tablet from each formulation was weighed and kept in petri dish containing 15 ml of phosphate buffer of pH 7.4. At the end of specified time intervals tablets were withdrawn from petri dish and excess buffer blotted with tissue paper and weighed as shown in **Figure 3**. The % of weight gained by the tablet was calculated by using following formula:

$$\text{Swelling index} = \frac{W_b - W_a}{W_a} \times 100$$

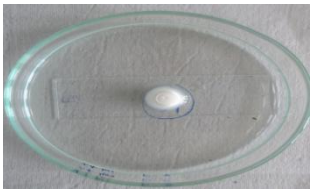
Where,

W_a- initial weight of the tablet,

W_b- weight of the tablet after swelling [11, 12].

Figure 3: Swelling study of selected formulation F2 before and after swelling study

Before Swelling study



After Swelling Study

***In vitro* drug release study**

The dissolution of the buccal tablet was performed using USP type II XXIII dissolution apparatus (paddle method) using 900 ml of phosphate buffer pH 7.4 containing 8.4% methanol and 0.24% tween 80 as the dissolution medium [13], which was maintained at 37°C and stirred at 50 rpm. Aliquots of 5 ml of samples were withdrawn with a bulb pipette at different time intervals of 1, 2, 3, 4, 5, 6, 7 and 8 hrs and replaced with equal volume of phosphate buffer pH 7.4 at each withdrawal, filtered it through what man filter paper No. l. The samples were then analysed using UV spectrophotometer at 300 nm and the cumulative amount of drug released at various time intervals was calculated. The experiment was run in triplicate.

Stability study

The best formulation was subjected for one month stability study by exposing the tablets in their final packing mode to the temperature 40±2°C and relative humidity 75±5 % in programmable environmental test chamber. At the end of one month the tablets were analyzed for any change in appearance, physical attributes, drug content, % swelling index and in vitro drug release.

Fourier Transform Infrared Spectroscopy (FTIR) studies

The pure drug, physical mixtures and optimized formulations were subjected for FTIR analysis. The samples were prepared on KBr-press (Startech Lab, India). The samples were scanned over a range of 4000-400 cm^{-1} using Fourier

transformer infrared spectrophotometer. Spectra were analysed for drug polymer interactions.

Differential scanning calorimetry (DSC) studies

The pure drug and optimized formulation were subjected to differential scanning calorimeter equipped with an intra cooler (NETZSCH, Japan.). Indium/zinc standards were used to calibrate the DSC temperature and enthalpy scale. The sample were sealed in aluminum pans and heated at a constant rate 20°C/min over a temperature range of 20-250°C. An inert atmosphere was maintained by purging nitrogen gas at a flow rate of 50 ml/min.

RESULTS AND DISCUSSION

In the present investigation an attempt was made to design Mucoadhesive buccal tablets containing glibenclamide. The method employed for preparation of mucoadhesive buccal tablets in this study was direct compression for which the drug or the mixture of drug and polymer should possess good flow properties. Plain glibenclamide exhibited angle of repose (45.10 ± 0.48°) indicating extremely poor flow property. It was further supported by high Carr's index value (25.37 ± 0.26%) and Hausner's ratio (1.34 ± 0.82). Hence it was necessary to use directly compressible vehicles like spray dried mannitol to improve the flow property of glibenclamide.

A total of nine formulations of mucoadhesive buccal tablets of glibenclamide were prepared and evaluated for physical and mechanical parameters. The blends were also evaluated for various pre compression parameters. These blends displayed angle of repose values were between 24.95 – 26.30° indicating good flow property. As it is below 30° it indicates good flow properties of blend. Bulk density was found to be between 0.49 - 0.54 gm/cm^3 and tapped density between 0.57 - 0.63 gm/cm^3 for all the formulations. From the density data, % compressibility was calculated. It was further supported by Hausner's ratio of 1.14 - 1.18 and good Carr's index value of 12.28 - 15.87% for all pre compressional mixtures (**Table 2**). Hence powder mixture was found suitable for direct compression method. According to work plan, the tablets were evaluated for their thickness, hardness, friability, weight variation, drug content uniformity, surface pH, *ex vivo* bioadhesive strength, swelling index, *in vitro* drug release. The mucoadhesive tablets were uniform with respect to thickness (4.8 to 5.1 mm) diameter (6.8 to 7.1 mm) and hardness (5.5 to 6.3 kg/cm^2) except F9 where the hardness is 7.2 kg/cm^2 because of presence of Carbopol 934P alone. The friability (0.42 to 0.72 %) and weight variation (1.7 to 2.2 %) of different batch of tablets were found within prescribed limits (**Table 3**).

Table 2: Micromeritic properties of glibenclamide mucoadhesive buccal tablets

Code	Angle of repose (θ)*	Bulk density* g/cm^3	Tapped density* g/cm^3	Hausner's ratio*	Carr's index* %
Glibenclamide	45.10 ± 0.48	0.50 ± 0.26	0.67 ± 0.44	1.34 ± 0.82	25.37 ± 0.26
F1	24.95 ± 0.21	0.49 ± 0.11	0.57 ± 0.02	1.16 ± 0.02	14.28 ± 0.36
F2	25.19 ± 0.36	0.50 ± 0.15	0.59 ± 0.05	1.18 ± 0.04	14.03 ± 0.57
F3	25.32 ± 0.26	0.53 ± 0.19	0.63 ± 0.06	1.18 ± 0.05	15.87 ± 0.52
F4	26.30 ± 0.38	0.51 ± 0.02	0.60 ± 0.12	1.17 ± 0.08	15.00 ± 0.53
F5	25.18 ± 0.22	0.50 ± 0.14	0.57 ± 0.16	1.14 ± 0.04	12.28 ± 0.45
F6	25.56 ± 0.70	0.54 ± 0.01	0.63 ± 0.18	1.16 ± 0.02	14.28 ± 0.33
F7	24.98 ± 0.56	0.50 ± 0.22	0.57 ± 0.08	1.14 ± 0.08	12.28 ± 0.18
F8	25.44 ± 0.65	0.51 ± 0.05	0.60 ± 0.18	1.17 ± 0.06	15.00 ± 0.22
F9	25.04 ± 0.38	0.49 ± 0.42	0.57 ± 0.21	1.16 ± 0.04	14.03 ± 0.78

a) * All values are expressed as mean ± SD. n=3.

Table 3: Physico-chemical evaluation of glibenclamide mucoadhesive buccal tablets

Code	Thickness (mm) *	Diameter (mm) *	Hardness (kg/cm^2) *	Friability (%)*	Weight variation (%)*
F1	4.8 ± 0.04	6.9 ± 0.08	5.9 ± 0.24	0.62 ± 0.03	1.7 ± 0.29
F2	4.9 ± 0.01	6.8 ± 0.05	5.5 ± 0.33	0.72 ± 0.01	2.2 ± 0.14
F3	4.9 ± 0.01	7.0 ± 0.04	5.6 ± 0.55	0.68 ± 0.02	1.8 ± 0.19
F4	4.8 ± 0.04	7.1 ± 0.07	5.8 ± 0.64	0.65 ± 0.01	2.0 ± 0.37
F5	4.9 ± 0.06	7.0 ± 0.05	6.1 ± 0.30	0.60 ± 0.03	2.1 ± 0.48
F6	5.1 ± 0.02	6.9 ± 0.06	5.5 ± 0.28	0.68 ± 0.06	2.0 ± 0.65
F7	5.0 ± 0.01	6.9 ± 0.06	5.8 ± 0.35	0.62 ± 0.01	1.9 ± 0.16
F8	5.1 ± 0.03	7.1 ± 0.02	6.3 ± 0.40	0.54 ± 0.04	1.7 ± 0.75
F9	4.9 ± 0.01	7.0 ± 0.03	7.2 ± 0.48	0.42 ± 0.03	1.9 ± 0.15

a)*All values are expressed as mean ± SD. n=3.

Estimation of drug content

Drug content (97.50 to 99.52 %) was found uniform within the batches of different tablets as shown in **Table 4**.

Surface pH

Tablets of all formulations except F9 showed surface pH values in range of 5.65 to 6.45, indicating no risk of mucosal damage or irritation. Tablets of formulation F9 showed lower surface pH value of 4.61 which is due to presence of higher amount of polyacrylic acid in Carbopol 934P. This observation indicates that Carbopol 934P alone is not suitable in designing mucoadhesive tablets and a combination of polymers produces tablets with surface pH that are safe for mucosal membrane. The results are reported in **Table 4**.

Bioadhesive strength

The mean bioadhesive strength values were found in range of 3.20 to 7.18 gm for the buccal tablets F1 to F9. This study showed that addition of secondary polymer to the Carbopol 934P was found to decrease the bioadhesive property of buccal tablets as observed from formulation F9 (Carbopol 934P alone) and other formulations F1 to F8. It was also observed that as the concentration of Carbopol 934P is increased, the mucoadhesive strength also increased. When all different polymeric ratios are considered formulations containing Carbopol 934P and PVP-K30 (F1, F2, F3 and F4) show more adhesion than formulations containing Carbopol 934P and xanthan gum, i.e. (F5 to F8). The results are reported in **Table 4**.

Table 4: Physico-chemical evaluation of glibenclamide mucoadhesive buccal tablets

Formulation Code	(%) Drug Content*	Surface pH*	Bioadhesive Strength (gm)	% swelling index* after 8 hrs
F1	98.82 ± 0.04	6.22 ± 0.042	4.57	117 ± 0.48
F2	99.22 ± 0.09	6.31 ± 0.053	3.74	67 ± 1.61
F3	99.51 ± 0.20	6.18 ± 0.043	3.78	100 ± 0.67
F4	98.41 ± 0.18	5.65 ± 0.016	4.93	153 ± 1.62
F5	99.34 ± 0.40	6.38 ± 0.063	4.12	330 ± 0.66
F6	98.69 ± 0.06	6.45 ± 0.055	3.20	300 ± 1.21
F7	99.52 ± 0.33	6.40 ± 0.012	3.21	310 ± 1.55
F8	97.50 ± 0.16	5.83 ± 0.072	4.26	350 ± 0.41
F9	99.24 ± 0.37	4.61 ± 0.052	7.18	223 ± 0.38

a)* All values are expressed as mean ± SD. n=3.

Swelling study

Swelling ratio describes the amount of water that is contained within the hydrogel at equilibrium and is a function of network structure, hydrophilicity and ionization of functional group. Swelling study was performed on all the batches of glibenclamide mucoadhesive buccal tablets for 8 hrs. The

swelling index of all formulations was in the range of 67 – 350%. Maximum swelling was seen with the formulations (F5, F6, F7 and F8) containing Carbopol 934P and xanthan gum than the remaining formulations. Tablets containing Carbopol 934P and secondary polymers (like PVP-K30, Xanthan gum) showed increased swelling index by increasing amount of Carbopol 934P in the formulations. Swelling index and bioadhesion studies indicate that there is a linear relationship between them. The results of swelling index studies are tabulated in **Table 4**.

***In vitro* release study**

In vitro release profile of all formulations F1-F9 was ranging from 71.55-89.19% (**Figure 4 - 5**). The formulation F2 containing Carbopol 934P and PVP-K30 in the ratio of 1:2 showed highest 89.19% drug release in 8 hrs. The dissolution profiles of tablet were influenced by type of polymer. Dissolution profiles of formulations containing different CP: PVP-K30 polymer ratios i.e., F1, F2, F3 and F4 showed that as the concentration of Carbopol 934P increased in the formulation the release rate decreased. This property may be due to hydrophilic and swellable nature of Carbopol 934P as supported by swelling studies (**Table 4**). From the same data it was observed that as the concentration of secondary polymer PVP-K30 was increased in the formulations the release rate of glibenclamide also increased. In case of formulations containing xanthan gum (F5, F6, F7 & F8) as secondary polymer the release rate decreased with increase in polymer concentration. This increase in the polymer concentration increases the viscosity of the gel and gel layer with longer diffusion path. This causes a decrease in the effective diffusion co-efficient of drug and therefore reduction in drug release rate. Among all these formulations F2 gave 89.19% drug releases in 8 hrs and was selected as best formulation.

Figure 4: *In-vitro* release profile of glibenclamide mucoadhesive buccal tablets in pH 7.4 buffer.

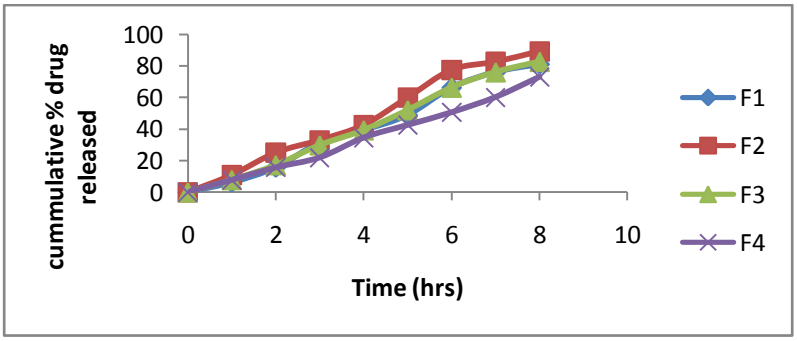
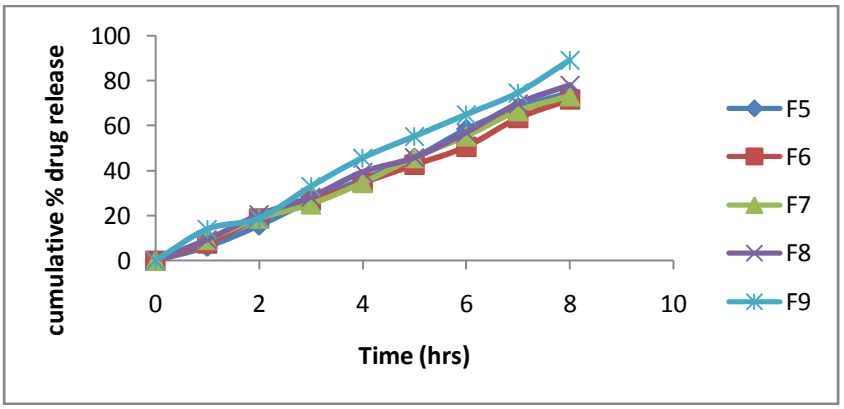


Figure 5: *In-vitro* release profile of glibenclamide mucoadhesive buccal tablets in pH 7.4 buffer.



Mechanism of drug release

It was evident from **Table 5**, that the optimized formulations F2, F3, F5 and F8 followed zero-order process as correlation coefficient (r^2) values were 0.988, 0.995, 0.996 and 0.997 respectively.

This indicated that the dissolution rate of the drug was independent of the amount of drug available for dissolution. Further, when the drug release data was put into Higuchi equation, good correlation coefficient (r^2) value 0.891-0.907 were obtained, indicating that the drug release was diffusion controlled. The n values of different glibenclamide mucoadhesive buccal tablets were found in the range of 1.536 – 1.647 with lower correlation coefficient values ranging from 0.779-0.860, indicating non-Fickian super case II type transport mechanism.

Table 5: Kinetic analysis of release data based on best curve-fitting method for optimized glibenclamide mucoadhesive buccal tablets

Formulation code	Zero order		First order		Higuchi		Korsmeyer-peppas	
	n	r^2	n	r^2	N	r^2	n	r^2
F2	11.72	0.988	-0.120	0.935	34.20	0.905	1.591	0.779
F3	10.93	0.995	-0.095	0.946	31.55	0.891	1.647	0.838
F5	9.823	0.996	-0.075	0.961	28.32	0.891	1.646	0.860
F8	9.730	0.997	-0.078	0.944	28.28	0.907	1.536	0.791

FTIR studies

FTIR spectral studies revealed that the positions of the characteristic absorption bands for different functional groups and bonds of the pure drug are not changed considerably. This study indicates that there is no interaction of the drug with polymers and other excipients used (**Figure 6, 7 & 8**).

Figure 6: FTIR spectra of glibenclamide pure drug

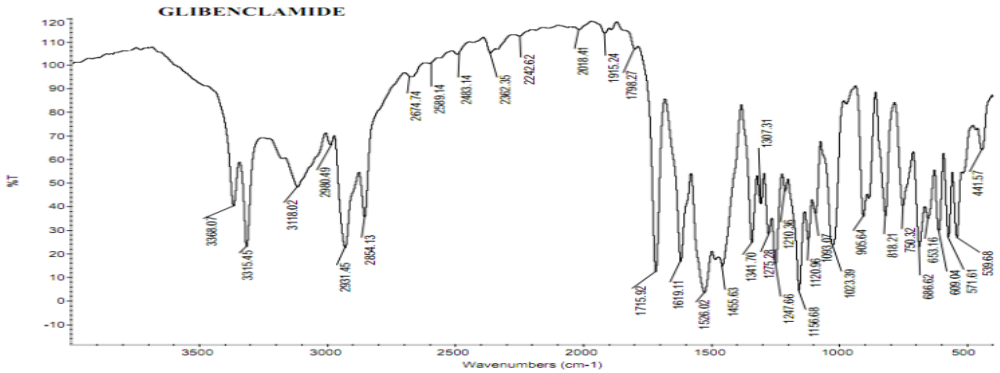


Figure 7: FTIR spectra of Glibenclamide + Carbopol 934P + PVP-K30.

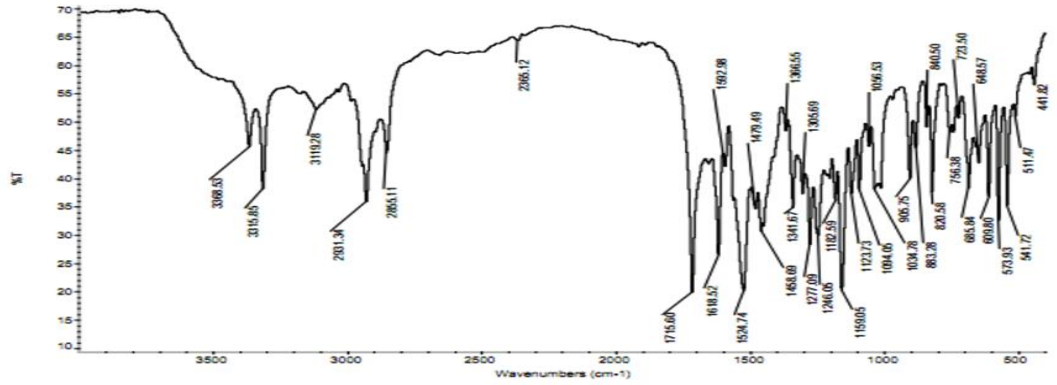
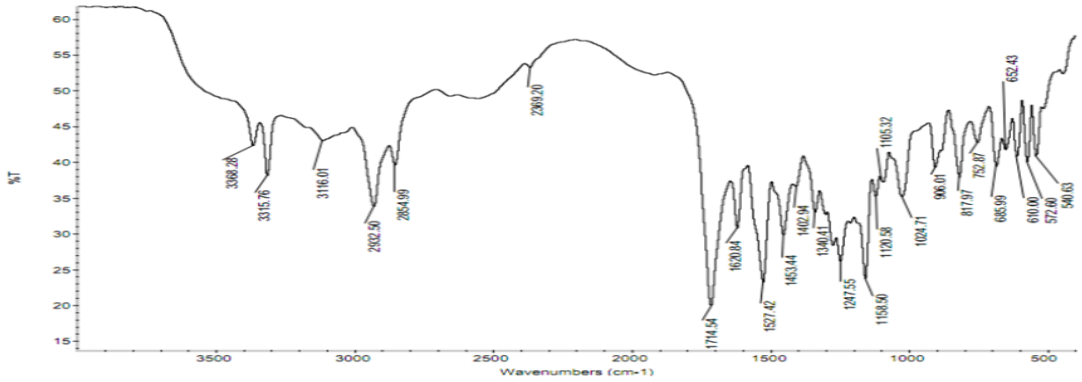


Figure 8: IR spectra of Glibenclamide + Carbopol 934P + Xanthan gum



DSC studies

As there was no appreciable change in the thermal properties of the drug and formulations as indicated by the thermographs, it was concluded that there is no interaction of the drug with the polymer and other excipients (**Figure 9 & 10**).

Figure 9: DSC thermogram of glibenclamide pure drug

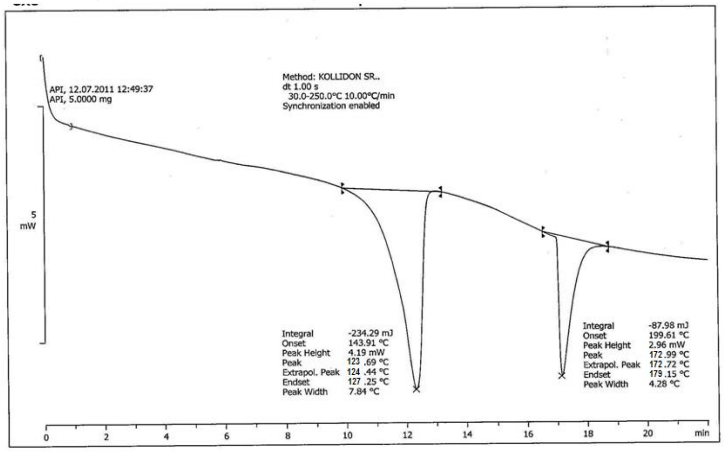
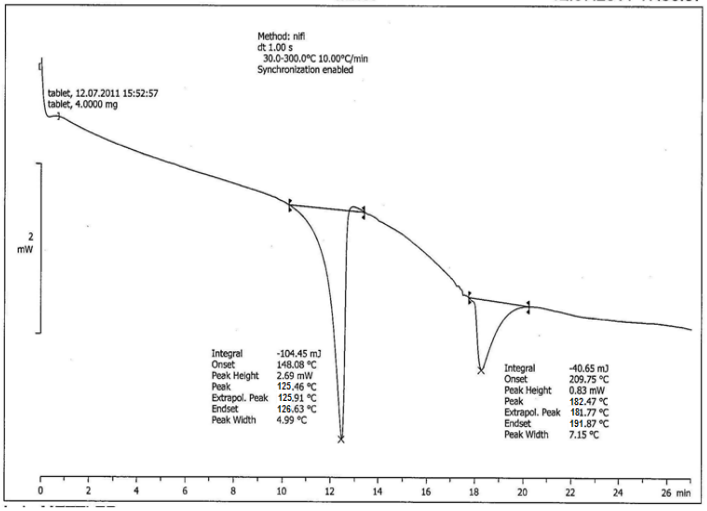


Figure 10: DSC thermogram of formulation F2 (CP934 + PVP-K30)



Stability Study

The stability studies revealed that there is not much considerable change in appearance, physical attributes, drug content, % swelling index and in vitro drug release. The glibenclamide mucoadhesive tablets were found to be stable with respect to stability studies.

CONCLUSION

Preformulation studies on glibenclamide fairly corroborate with the reported literature limits; pre compression studies indicated good micromeritic properties of the powder blend. The adopted method yielded uniform and reproducible mucoadhesive buccal tablets with all the polymers used. Hardness, friability, weight variation, drug content, surface pH, bioadhesive strength, swelling index and *in vitro* release were uniform and reproducible. Tablets of all formulations except F9 showed surface pH values in the range of 5.65 to 6.45 indicating no risk of mucosal damage or irritation, the mean bioadhesive strength values were found to be in range of 3.20 to 7.18 gm for the buccal tablets F1 to F9, indicating sufficient adhesiveness to stick to the mucosa, swelling index was found to be higher with xanthan gum than PVP-K30, increase in Carbopol 934P concentration increased the swelling index, mucoadhesive buccal tablets F2 gave 89.19% controlled drug release over a period of 8 hrs as compared to all other formulations. The mechanism of drug release was found to be non-Fickian diffusion controlled, zero order kinetics. FT-IR and DSC studies revealed the absence of any chemical interaction between drug and polymers used.

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***Corresponding Author:**
Sarfaraz Md*
Department of Pharmaceutics, N.E.T Pharmacy College, Mantralayam Road, Raichur-584103, Karnataka, India
E-Mail address: Sarfindia@gmail.com
Ph. No.: 09448711094