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FORMULATION AND *IN-VITRO* EVALUATION OF MUCOADHESIVE BUCCAL TABLETS OF GLICLAZIDE

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ABSTRACT

The aim of the present study involved the formulation and evaluation of mucoadhesive buccal tablets of Galiclazide, with objective of avoiding first pass metabolism and to improve its bioavailability with reduction in dosing frequency. Mucoadhesive buccal tablets of Gliclazide were prepared by direct compression method. The mucoadhesive polymers used in the formulation were carbopol 940, HPMC K15 LV, sodium alginate, guar gum in different ratios. The compatibility study by FTIR confirmed that mucoadhesive polymers were compatible with the drug. The results of pre-compression and post-compression parameter of all the formulated tablets were shown satisfactory results which complies with official limits. The comparative *in-vitro* study of the optimized formulation H4 showed better sustained release 71.70 % than the other formulation. Among the formulations the combination of HPMC K15 LV and Carbopol-940 has shown optimum bioadhesive strength. Formulation H4 showed maximum percentage of swelling index 193.66 after 8 hrs. The accelerated stability of the optimized formulation was studied and no significant changes were detected in hardness, % of drug content, surface pH, bioadhesive strength and percentage of drug release. The *in-vitro* release kinetics studies revealed that all formulations fit well with Peppas model kinetics and followed Non-Fickian diffusion mechanism.

KEYWORDS

Gliclazide, *In-vitro* drug release, Buccal tablets, Mucoadhesive polymers and Swelling.

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INTRODUCTION

Buccal mucosa is the preferred site for both systemic and local drug action. The mucosa has a rich blood supply and it is relatively permeable. In buccal drug delivery systems mucoadhesion is the key element so various mucoadhesive polymers have been utilized in different dosages form. Bioadhesion can be defined as a phenomenon of interfacial molecular

attractive forces in the midst of the surfaces of biological substrate and the natural or synthetic polymers, which allows the polymer to adhere to biological surface for an extended period of time[1]. If the adhesive attachment is to a mucous coat, then the phenomenon is known as mucoadhesion. Mucosal layer represents potential sites for the attachment of any bioadhesive systems because mucosal layer lines number of the body including the gastro intestinal tract, the urogenital tract, vaginal tract, eye, ear, and nose. Recently the oral transmucosal drug delivery gaining important than other mucoadhesive delivery systems like vaginal delivery, rectal delivery, nasal delivery, ocular delivery[2].

Gliclazide is an oral antihyperglycemic agent used for the treatment of non-Insulin-dependent diabetes mellitus (NIDDM). It belongs to the sulfonylurea class of Insulin secretagogues, which act by stimulating β cells of the pancreas to release Insulin. Sulfonylureas increase both basal Insulin secretion and meal-stimulated Insulin release. Gliclazide having half-life of 10.4 hrs and molecular weight (323.412 g/mol). Prior research work revealed that it has good general tolerability, low incidence of hypoglycemia and low rate of secondary failure. In addition; it has the potential for slowing the progression of diabetic retinopathy. For these reasons, it appears to be a drug of choice in prolonged therapy for the control of NIDDM[3,4]. Hence, this the present study we plan to formulate buccal tablets of Gliclazide to increase its permeability and bioavailability.

MATERIALS AND METHODS

Gliclazide was a gift sample from Bal pharmaceuticals, Bangalore. Carbopol-940 was gift sample from Rolex laboratory reagent. HPMC K15 LV was gift sample from Shreeji chemicals Ltd, Mumbai. Sodium alginate was gift sample from Loba chemicals Ltd, Mumbai. Guar gum was gift sample from Merch specialities Ltd, Mumbai. Mannitol, Talc, Magnesium stearate from S D fine chemical Ltd, Mumbai.

Preparation of Gliclazide mucoadhesive buccal tablets[5,6]

Mucoadhesive tablets of Gliclazide were prepared by direct compression using an 8 mm flat- faced punch of 8 station compression machine. Carbopol 940, HPMC E15 LV, sodium alginate 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, polymers and excipients were weighed accurately according to the batch formula was shown in the Table No.1 and screened through sieve # 60, than mixed thoroughly for 10 mints before compression In all the formulations the amount of Gliclazide and carbopol 940 was kept constant at 80 mg and 20 mg. The polymers like HPMC E15 LV, sodium alginate and xanthan gum were used in different concentrations in combination. Total weight of the tablet was kept constant at 200 mg.

Drug-polymer compatibility studies

The compatibility of the drug and polymer were studied by the FTIR spectrometer using Shimadzu 8400-S, Japan. Two percent (w/w) of the sample with respect to a potassium bromide disc was mixed with dry KBr. The mixture was grind into a fine powder using an agate mortar and then compressed into a KBr disc in a hydraulic press at a pressure of 1000 psi. The characteristic peaks were recorded. FT-IR spectrum of Gliclazide was compared with FT-IR spectra of drug and polymers.

Evaluation parameters of mucoadhesive buccal tablets[7,8]

Weight variation test

Twenty tablets were weighed individually and all together. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference should be within the permissible limits (± 7.5%).

Thickness

Six randomly selected Gliclazide buccal tablets from each formulation were used for thickness determination. Thickness of each tablet was measured in mm using a digital caliper. The average values were calculated.

Friability test

Roche type friabilator was used for testing the friability using the following procedure. Permitted

friability limit is 1.0 %. Previously weighed 10 tablets from each batch were taken in Roche friabilator apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 100 revolutions, the tablets were weighed and the percentage loss was determined. The percentage friability was measured using the following formula-

$$\textbf{Percentage friability} = W_0 - W / W_0 \times 100$$

Where, W_0 = Initial weight of tablet

W = Weight of tablets after revolution.

Hardness test

The hardness of six randomly selected Gliclazide buccal tablets from each batch was measured using Monsanto tester and expressed in kg/cm^2. The mean and standard deviation values were calculated and reported.

% of drug content

Twenty tablets from each formulation were taken, crushed in a mortar and mixed. From the mixture 80 mg of Gliclazide equivalent of mixture was extracted thoroughly with 100 ml of pH 7.4 phosphate buffer. The contents were shaken periodically and kept for 24 hrs for solvation of drug completely. The mixtures were filtered, appropriately diluted, and the amount of drug present in each extract was determined using UV spectrophotometer at 226 nm against blank reference. The procedure was repeated thrice and this average was chosen.

Measurement of surface pH

The microenvironment pH (surface pH) of the buccal tablets 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. A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping it in contact with 5 ml of distilled water (pH 6.5 ± 0.05) for 2 hrs at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablets and allowing it to equilibrate for 1 min.

% of swelling studies

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

$$\textbf{Swelling index} = W_2 - W_1 / W_1 \times 100$$

Where, W_1= initial weight of the tablet

W_2= Weight of the tablet after swelling

Mucoadhesive strength[9,10]

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 sheep buccal mucosa obtained from local slaughterhouse was cut into pieces, washed with distilled water followed by phosphate buffer pH 7.4. 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. 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 minutes 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. The excess weight on the left pan *i.e.,* total weight minus 5 g was taken as adhesive strength. Three films of each formulation is tested for mucoadhesive strength, average and standard derivations was calculated-

Fabricated bio-adhesion= bio-adhesive strength X 9.81/100

Whereas 9.18 is acceleration due to gravity (m/sec^2).

***In-vitro* dissolution studies**

The *in-vitro* release of buccal tablets was determined using a dissolution apparatus USP type-II XXIII by paddle method using 900 ml of phosphate buffer pH 7.4, which was maintained at

37 ˚C and stirred at 100 rpm. Aliquotes of 5 ml of samples were withdrawn at specified time intervals of 1, 2, 4, 6, and 8 hrs and replaced with equal volume of phosphate buffer pH 7.4 at each withdrawal and filtered through whatman filter paper. The samples were then analysed using UV spectrophotometer at 226 nm and the cumulative amount of drug released at various time intervals was calculated.

Accelerated stability study[11]

The purpose of accelerated stability study is to provide evidence on the quality of a drug substance or drug product, which varies with time under the influence of a variety of environmental factors such as temperature, humidity and light. The optimized formulations were subjected to accelerated stability studies as per ICH (The International Conference of Harmonization) guidelines *i.e.,* 40 ˚C ± 2 ˚C and 75% RH ± 5% RH. The accelerated stability studies data was recorded at intervals of 3, 6 months. Tablets were evaluated for the different physicochemical parameters *i.e.,* hardness, content uniformity, surface pH, bioadhesive strength and percentage of drug release.

RESULTS AND DISCUSSION

Compatibility studies

An FT-IR spectroscopy study was carried out to check the compatibility between the drug Gliclazide and the polymers. The FTIR was performed for drug, polymers and physical mixture of drug and polymers. The spectral data of pure drug and various drug-polymers are presented in (Figure No.1-4). The results indicate that there was no chemical incompatibility between drug and excipients used in formulation

Evaluation of pre-compression characteristics of powder blend

The powder blends were also evaluated for various pre-compression parameters. The results are shown in Table No.2. These blends displayed angle of repose values between 25.03±0.45 - 27.26±0.60 indicating good flow property. As it is below 30˚ it indicates good flow properties of blend. Bulk density was found to be between 0.41±0.14 - 0.51±0.22 g/cm^3 and tapped density between 0.56±0.05 - 0.62±0.06 g/cm^3 for all the formulations. From the density data, % compressibility was calculated. The results showed that Hausner's ratio value of 1.14±0.01- 1.19±0.01 and good Carr's index value of 12.67±0.47 - 16.19±0.83 % for all pre compressional mixtures. Hence, powder mixture was found suitable for direct compression method.

Evaluation of Gliclazide mucoadhesive buccal tablets

Tablet thickness, hardness and friability

The thickness of the batch from H1-H4, S1-S4, G1-G4 was found to be in the range of 3.17-3.51 mm and hardness was found to be 4.91-5.66 kg/cm^2 as. Thus tablets were having good mechanical strength. The friability of all the formulated tablets of Gliclazide was found to be between 0.52 - 0.85 % are reported in Table No.3 and all the formulated tablets of Gliclazide confirmed that % friability within the official limits (*i.e.,* not more than 1 %).

Weight variation

Prepared tablets were evaluated for weight variation and percentage deviations from the average weight are reported in Table No.3. It was found to be within (±7.5) the prescribed limits.

Percentage of Drug content

The drug content of all the formulations of Gliclazide tablets were found to be within the range of 99.09±0.67 - 100.31±0.98 % which were within the limits of IP specifications *i.e.,* ±5%. The drug content of all the formulations of Gliclazide tablets are shown in Table No.4.

Surface pH

The surface pH was determined in order to investigate the possibility of any side effects in the oral cavity as acidic or alkaline pH is found to cause irritation to the buccal mucosa, hence an attempt has been made to keep the surface pH close to the neutral pH. Surface pH of all the formulations was found to be in the range of 6.21±0.46 - 6.61±0.35. This pH is near to the neutral and also these results revealed that all the formulation provide an acceptable pH in the range of salivary pH (5.5 to 7.0). Hence, it was concluded that all formulations could not produce any local irritation to the mucosal

surface. The surface pH of all the formulations is shown in Table No.4.

Swelling studies

Swelling index was determined with respect to time. The swelling index of the tablets was increased with increasing concentration of polymer. Swelling study was performed on all the batches of Gliclazide mucoadhesive buccal tablets for 8 hrs. The swelling index of all formulations was in the range of 103±6.24 - 193.66±6.02 %. Maximum swelling was observed with the formulations (H1, H2, H3, H4) containing Carbopol 940 and HPMC K15 LV than the remaining formulations. The results of swelling index studies are shown in the Table No.4 and Figure No.5.

Mucoadhesive strength

The values of the mucoadhesive strength of Gliclazide mucoadhesive buccal tablets are given in Table No.4. The bioadhesion characteristics were affected by the concentration of the bioadhesive polymers. Adhesion occurs shortly after the beginning of swelling but the bond formed between mucosal layer and polymer is not very strong. The mucoadhesive strength was influenced by the nature and proportions of the bioadhesive polymers used in the formulations. In all the formulations, as the polymer concentration increased, the mucoadhesive strength also increased. The order of mucoadhesive strength of bioadhesive polymers used in the formulations can be given as carbopol 940 and HPMC K15 LV < carbopol 940 and sodium alginate < carbopol and guar gum. Very strong mucoadhesion could damage the epithelial lining of the buccal mucosa.

***In-vitro* release studies**

All formulations were formulated by using three different mucoadhesive polymers in varying concentration. The formulations H1-H4 were formulated with the help of HPMC K15 LV in concentration 10 mg, 30 mg, 60 mg, 80 mg respectively. The formulations S1-S4 were formulated with the help of sodium alginate in concentration 10mg, 30 mg, 60 mg, 80 mg respectively. The formulations G1-G4 were formulated with the help of guar gum in concentration 10 mg, 30 mg, 60 mg, 80 mg respectively. The *in-vitro* release of Gliclazide from mucoadhesive buccal tablet was found to vary according to the type and ratio of polymer used. The release of Gliclazide was decreased with increasing concentration of HPMC K15 LV, sodium alginate, guar gum. The percentage of the drug released from the formulations H1, H2, H3, H4 was found to be 82.94±0.54 %, 78.26±0.99 %, 74.21±0.86 %, 71.70±0.53 % respectively. The percentage of the drug released from the formulations S1, S2, S3, S4 was found to be 92.00±0.56 %, 88.12±0.60 %, 83.09±0.47 %, 80.60±0.48 % respectively. The percentage of the drug released from the formulations G1, G2, G3, G4 was found to be 75.43±0.47 %, 72.62±0.58 %, 69.44±0.39 %, 60.89±0.34 % respectively. The formulation H4 is considered as a optimized formulation because of its better sustained release 71.70±0.53 %. The data for *in-vitro* drug release of formulations was shown in the Table No.5-7. The *in-vitro* drug release profiles were shown in Figure No.6-8.

Kinetic model data analysis

In-vitro drug release data of all formulations were fitted to Zero order, First order, Higuchi and Korsmeyer-Peppas equations to ascertain the pattern of drug release. Upon the application of different drug release model kinetics is given in Table No.8. It was found that all formulation follows Peppas model. The 'n' values for all the formulations were found to be more than 0.5. This indicates that the release approximates non-Fickian diffusion mechanism.

Accelerated stability study

Accelerated stability studies were carried out for the Formulation H4 by storing at 40 ˚C±2 ˚C / 75 % RH± 5% RH .The tablets were evaluated for physical appearance, hardness, % drug content, surface pH, bioadhesive strength and percentage of drug release. The stability study revealed that there was negligible changes occurred from the initial value, which confirmed that the optimized tablets were stable during storage. The results are shown in Table No.9.

Table No.1: Formulation design of Gliclazide mucoadhesive buccal tablets

S.No	Ingredients (mg)	H1	H2	H3	H4	S1	S2	S3	S4	G1	G2	G3	G4
1	Gliclazide	80	80	80	80	80	80	80	80	80	80	80	80
2	Carbopol-940	20	20	20	20	20	20	20	20	20	20	20	20
3	HPMC E15 LV	10	30	60	80	-	-	-	-	-	-	-	-
4	Sodium alginate	-	-	-	-	10	30	60	80	-	-	-	-
5	Guar gum	-	-	-	-	-	-	-	-	10	30	60	80
6	Mannitol	80	60	30	10	80	60	30	10	80	60	30	10
7	Talc	5	5	5	5	5	5	5	5	5	5	5	5
8	Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5
9	Total weight	200	200	200	200	200	200	200	200	200	200	200	200

Table No.2: Results of Pre-compression parameters

S.No	Formulation Code	Angle of repose (θ)*	Bulk Density* g/cm^3	Tapped Density* g/cm^3	Hausner's ratio*	Carr's index* %
1	H1	26.47±0.55	0.50±0.14	0.59±0.03	1.19±0.01	15.84±0.72
2	H2	25.18±0.97	0.49±0.19	0.56±0.05	1.17±0.02	15.03±0.76
3	H3	26.01±0.60	0.50±0.18	0.62±0.06	1.18±0.02	16.19±0.83
4	H4	27.26±0.60	0.49±0.21	0.60±0.07	1.18±0.02	15.33±0.63
5	S1	25.04±0.62	0.50±0.22	0.58±0.07	1.14±0.01	13.28±0.87
6	S2	25.38±0.66	0.50±0.23	0.57±0.08	1.17±0.01	14.74±0.41
7	S3	26.04±0.45	0.51±0.22	0.61±0.07	1.18±0.02	15.48±0.97
8	S4	25.03±0.45	0.50±0.22	0.58±0.06	1.17±0.01	13.31±0.62
9	G1	25.37±0.75	0.50±0.23	0.57±0.06	1.14±0.01	12.67±0.47
10	G2	26.33±0.50	0.50±0.19	0.58±0.050	1.16±0.01	13.73±0.99
11	G3	25.12±0.66	0.50±0.18	0.57±0.04	1.16±0.02	14.57±0.65
12	G4	25.20±0.68	0.41±0.14	0.59±0.02	1.19±0.01	15.64±0.89

***All values are expressed as mean ±SD, n=3**

Table No.3: Results of Post-compression parameters

S.No	Formulation Code	Thickness*(mm)	Hardness*(kg/cm^2)	Friability(%)	Weight variation**(%)
1	H1	3.32±0.15	5.16±0.40	0.85	0.073±0.43
2	H2	3.40±0.10	4.91±0.49	0.83	0.068±0.55
3	H3	3.44±0.41	5.41±0.37	0.84	0.047±0.46
4	H4	3.51±0.14	5.16±0.60	0.72	0.022±0.52
5	S1	3.25±0.15	5.33±0.51	0.65	0.068±0.48
6	S2	3.30±0.11	5.58±0.37	0.85	0.020±0.54
7	S3	3.17±0.09	5.50±0.54	0.65	0.020±0.65
8	S4	3.26±0.16	5.16±0.60	0.73	0.096±0.57
9	G1	3.23±0.12	5.25±0.41	0.52	0.068±0.57
10	G2	3.36±0.10	5.66±0.40	0.82	0.019±0.63
11	G3	3.28±0.12	5.50±0.44	0.75	0.020±0.16
12	G4	3.43±0.14	5.25±0.52	0.61	0.071±0.56

***Mean ± SD, n = 6. ****Mean ± SD, n = 20**

Table No.4: Results of % of drug content, surface pH, swelling index, bioadhesive strength

S.No	Formulation Code	(%) Drug content*	Surface pH**	Bioadhesive strength*** (gm)	% Swelling index*** after 8 hrs
1	H1	99.45±0.95	6.35±0.32	15.46±0.35	187.33±5.50
2	H2	100.24±0.60	6.56±0.45	15.83±0.30	189.66±5.03
3	H3	99.43±0.85	6.48±0.33	16.23±0.25	192.33±5.50
4	H4	99.09±0.67	6.45±0.50	16.51±0.36	193.66±6.02
5	S1	99.73±0.95	6.53±0.41	18.86±0.11	135.66±6.02
6	S2	99.62±0.52	6.21±0.46	19.26±0.15	137.85±7.02
7	S3	99.78±0.73	6.25±0.37	19.86±0.25	141.21±8.18
8	S4	99.94±0.78	6.35±0.36	20.36±0.11	145.61±9.84
9	G1	100.11±0.70	6.33±0.40	22.30±0.25	103.00±6.24
10	G2	99.32±0.39	6.61±0.35	22.40±0.10	106.00±5.56
11	G3	99.10±0.58	6.55±0.33	23.21±0.17	109.66±6.02
12	G4	100.31±0.98	6.58±0.21	23.63±0.75	113.33±7.50

***Mean ± SD, n = 20. **Mean ± SD, n = 6. ***Mean ± SD, n = 3**

Table No.5: *In vitro* drug release data of Gliclazide tablets containing HPMC K15 LV

S.No	Time (hrs)	% of Cumulative drug release			
		H1	H2	H3	H4
1	0	0	0	0	0
2	0.5	16.65±0.53	14.88±0.24	13.55±0.34	10.45±0.51
3	1	23.70±0.47	20.68±0.57	18.68±0.41	15.49±0.38
4	2	36.02±0.80	33.76±0.30	31.69±0.48	32.22±0.49
5	4	56.64±0.47	51.75±0.49	47.01±0.71	44.19±0.67
6	6	65.96±0.14	63.70±0.49	58.15±0.91	56.14±0.72
7	8	81.94±0.54	78.26±0.99	74.21±0.86	71.70±0.53

Mean ± SD, n = 3

Table No.6: *In vitro* drug release data of Gliclazide tablets containing Sodium alginate

S.No	Time (hrs)	% of Cumulative drug release			
		S1	S2	S3	S4
1	0	0	0	0	0
2	0.5	21.56±0.56	18.83±0.36	15.89±0.27	16.85±0.28
3	1	34.83±0.28	32.14±0.87	30.55±0.47	27.96±0.10
4	2	57.44±0.40	52.41±0.38	46.20±0.60	41.37±0.27
5	4	65.97±0.12	61.61±0.51	57.34±0.46	49.76±0.38
6	6	84.19±0.32	79.71±0.38	75.90±0.21	69.56±0.65
7	8	92.00±0.56	88.12±0.60	83.09±0.47	80.60±0.48

Mean ± SD, n = 3

Table No.7: *In vitro* drug release data of Gliclazide tablets containing Guar gum

S.No	Time (hrs)	% of Cumulative drug release			
		G1	G2	G3	G4
1	0	0	0	0	0
2	0.5	8.78±0.29	7.77±0.21	6.88±0.31	6.48±0.48
3	1	19.36±0.44	13.62±0.47	11.02±0.27	9.45±0.37
4	2	28.60±0.31	27.79±0.35	22.83±0.20	18.19±0.35
5	4	34.85±0.25	30.62±0.38	27.36±0.40	25.06±0.23
6	6	51.47±0.23	48.46±0.60	47.75±0.35	42.81±0.32
7	8	75.43±0.47	72.62±0.58	69.44±0.39	60.89±0.34

Mean ± SD, n = 3

Table No.8: Best fit modle for all formulation

S.No	Formulation code	Zero order	First order	Higuchi matrix	Peppas plot		Best fit modle
		r^2	r^2	r^2	r^2	'n'	
1	H1	0.950	0.984	0.993	0.997	0.576	PEPPAS
2	H2	0.961	0.990	0.991	0.997	0.606	PEPPAS
3	H3	0.966	0.985	0.987	0.995	0.615	PEPPAS
4	H4	0.965	0.985	0.979	0.987	0.695	PEPPAS
5	S1	0.875	0.983	0.983	0.990	0.511	PEPPAS
6	S2	0.892	0.985	0.982	0.987	0.538	PEPPAS
7	S3	0.907	0.986	0.989	0.993	0.569	PEPPAS
8	S4	0.930	0.980	0.989	0.994	0.537	PEPPAS
9	G1	0.961	0.922	0.935	0.973	0.688	PEPPAS
10	G2	0.963	0.917	0.915	0.977	0.746	PEPPAS
11	G3	0.973	0.930	0.903	0.978	0.796	PEPPAS
12	G4	0.984	0.954	0.908	0.989	0.790	PEPPAS

Table No.9: Accelerated stability studies for the formulation H4

S.No	Specification or study	Parameters	Duration in Months		
			0	3	6
1	40 ˚C±2 ˚C and 75% RH±5%RH	Hardness*	5.16±0.60	5.16±0.60	5.06±0.60
		% of drug content**	99.09±0.67	98.12±0.57	97.92±0.48
		Surface pH***	6.45±0.50	6.42±0.33	6.12±0.46
		Mucoadhesive strength***	16.51±0.36	16.12±0.28	15.24±0.35
		% CDR at 8hrs***	71.70±0.53	71.12±0.61	70.10±0.58

*Mean ± SD, n = 6. **Mean ± SD, n = 20. ***Mean ± SD, n = 3

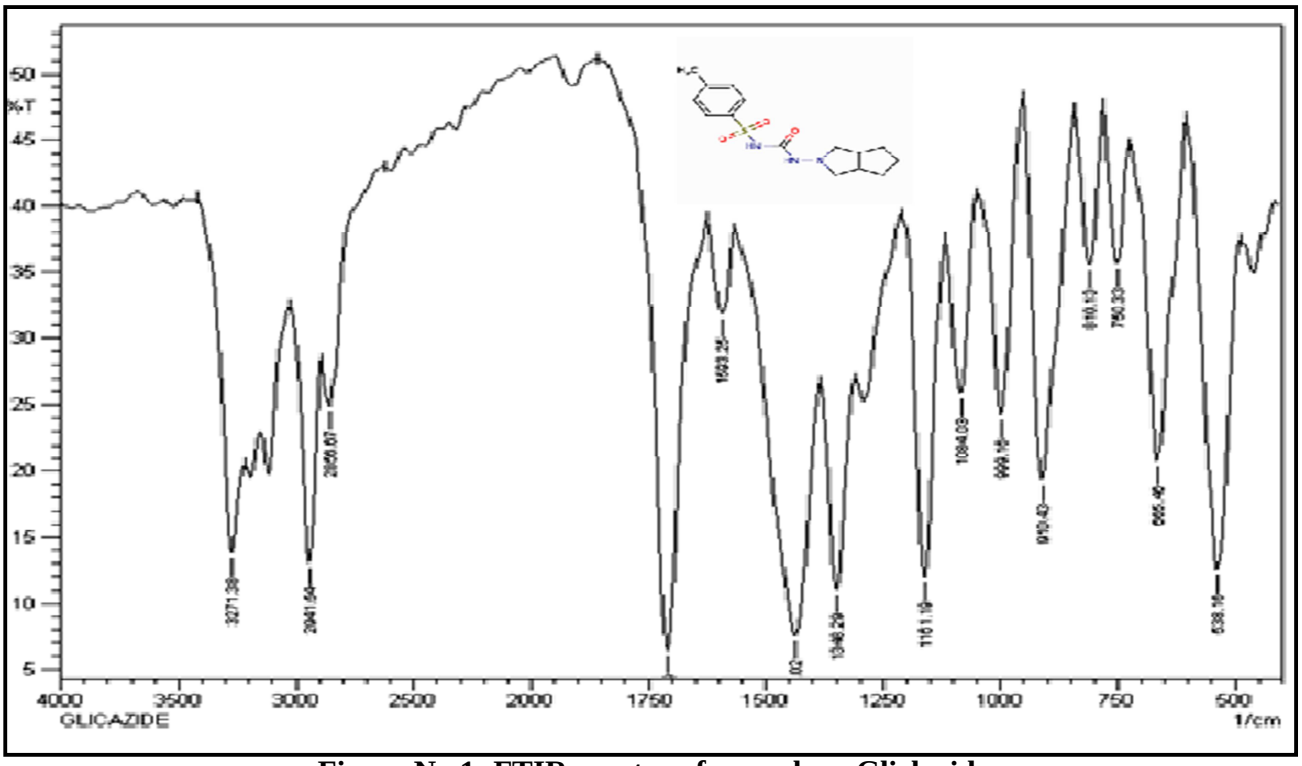


Figure No.1: FTIR spectra of pure drug Gliclazide

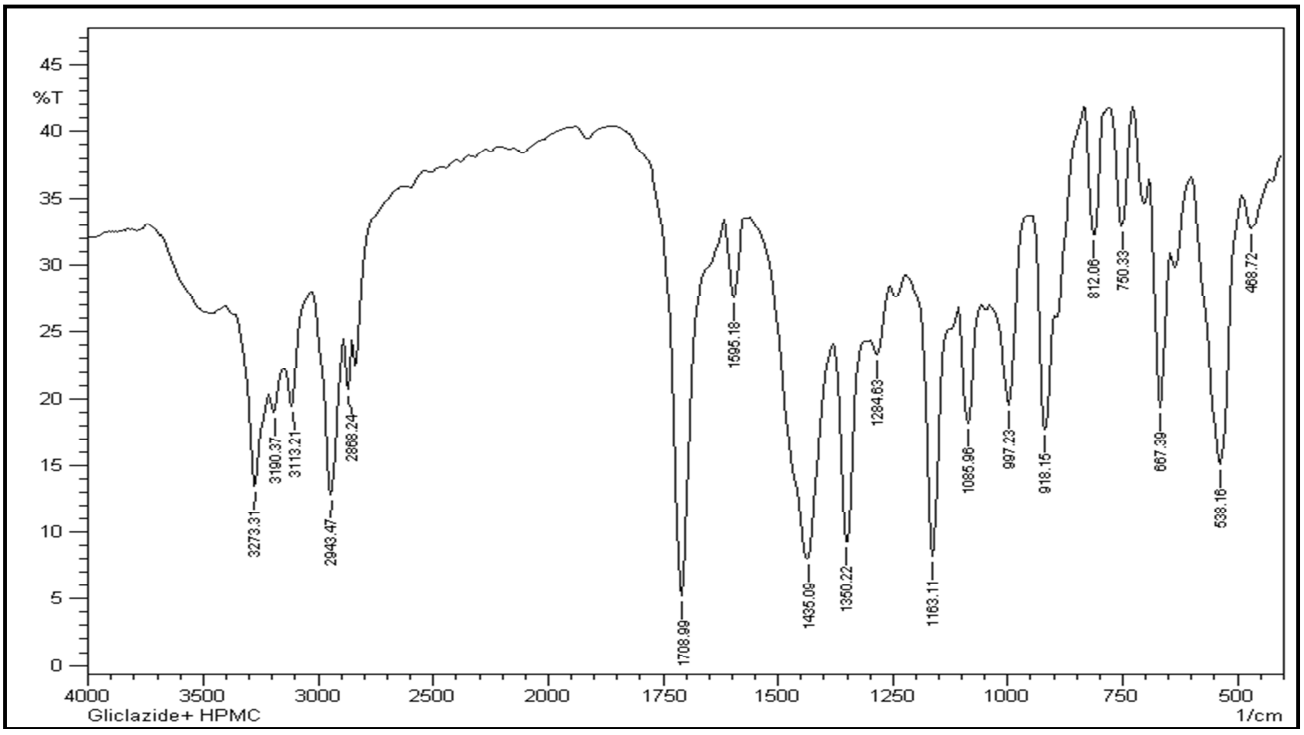


Figure No.2: FTIR spectra of Gliclazide+HPMC K15 LV

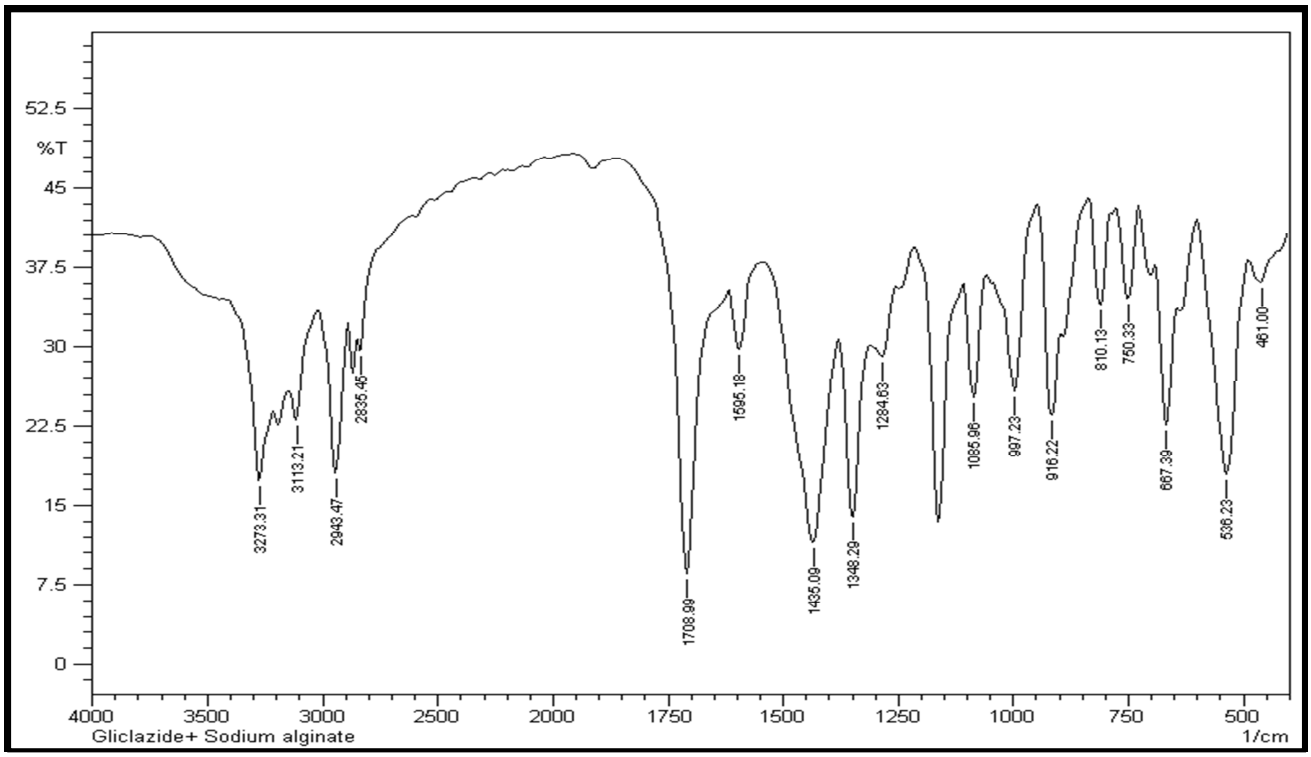


Figure No.3: FTIR spectra of Gliclazide+Sodium alginate

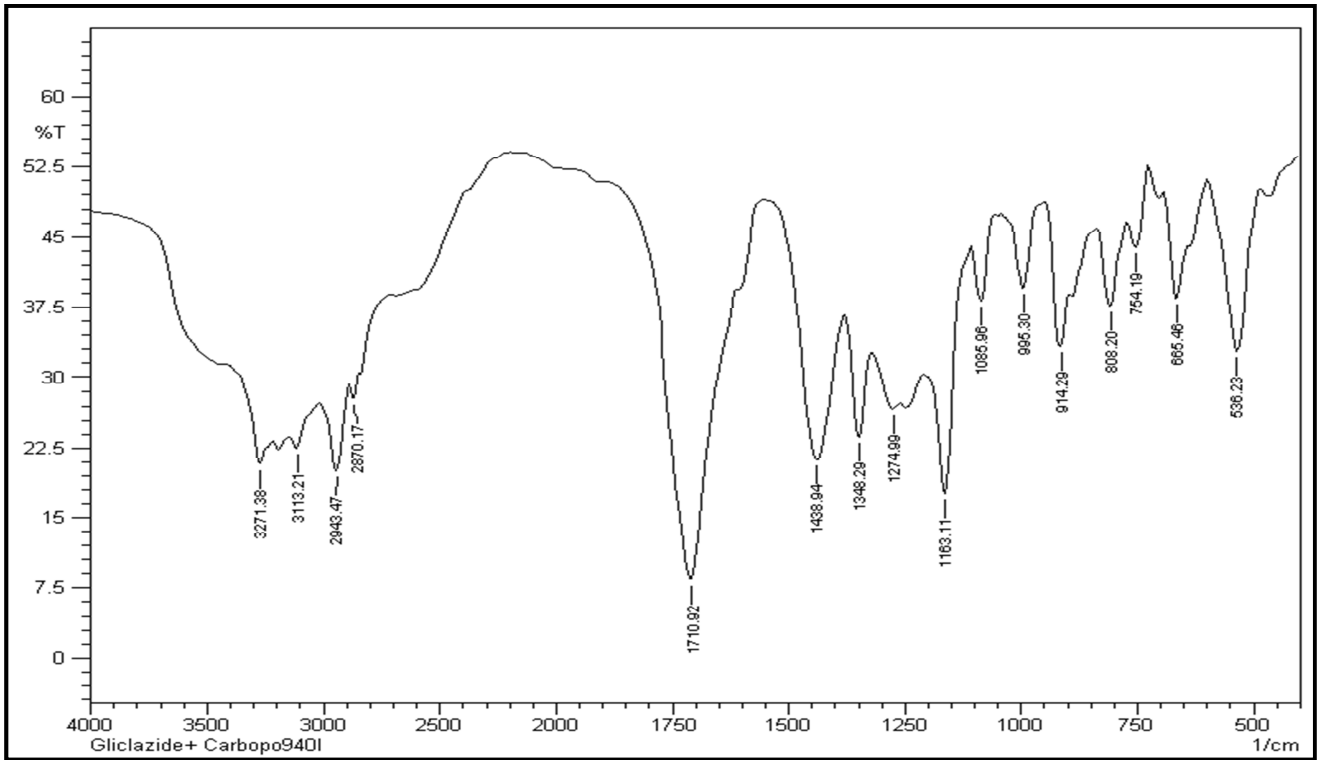
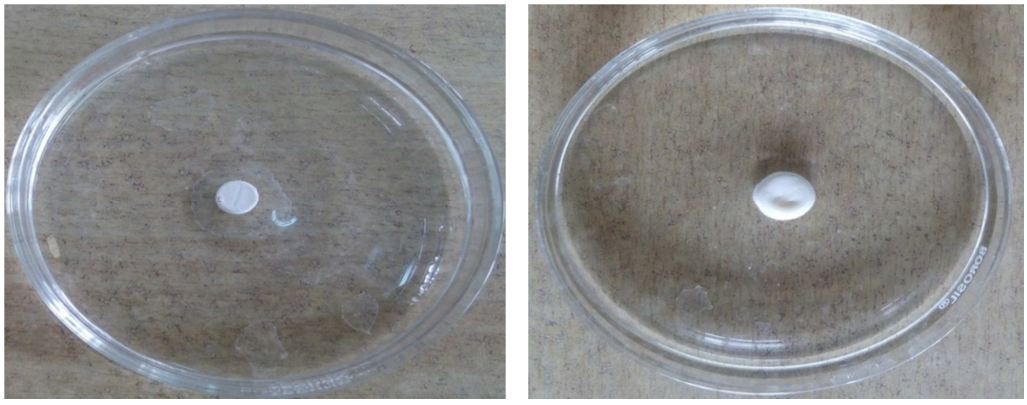


Figure No.4: FTIR spectra of Gliclazide+Carbopol-940



Swelling study at initial time (0hr) **Swelling study after 8hrs**

Figure No.5: Swelling study of selected formulation H4

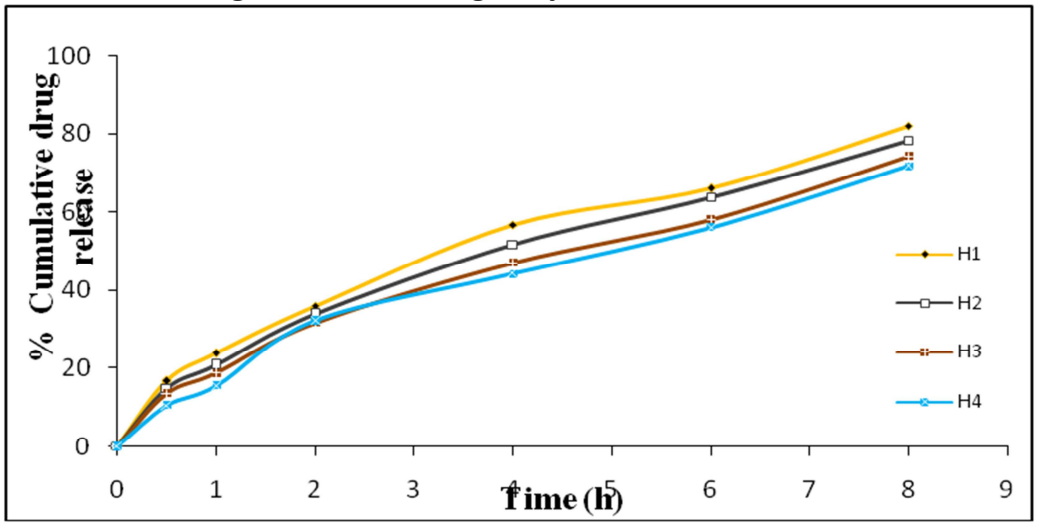


Figure No.6: *In-vitro* drug release profile of formulations H1 – H4

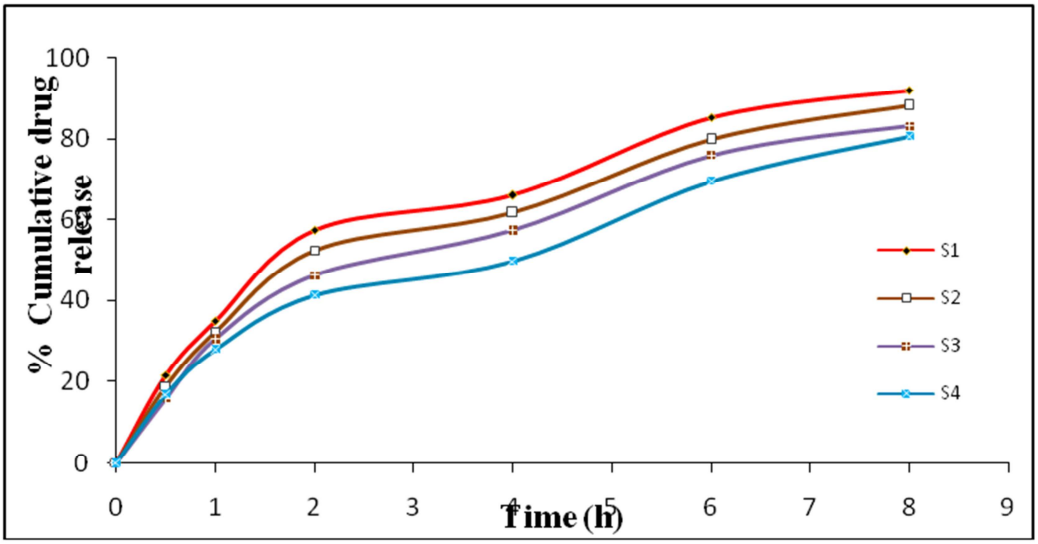


Figure No.7: *In-vitro* drug release profile of formulations S1 – S4

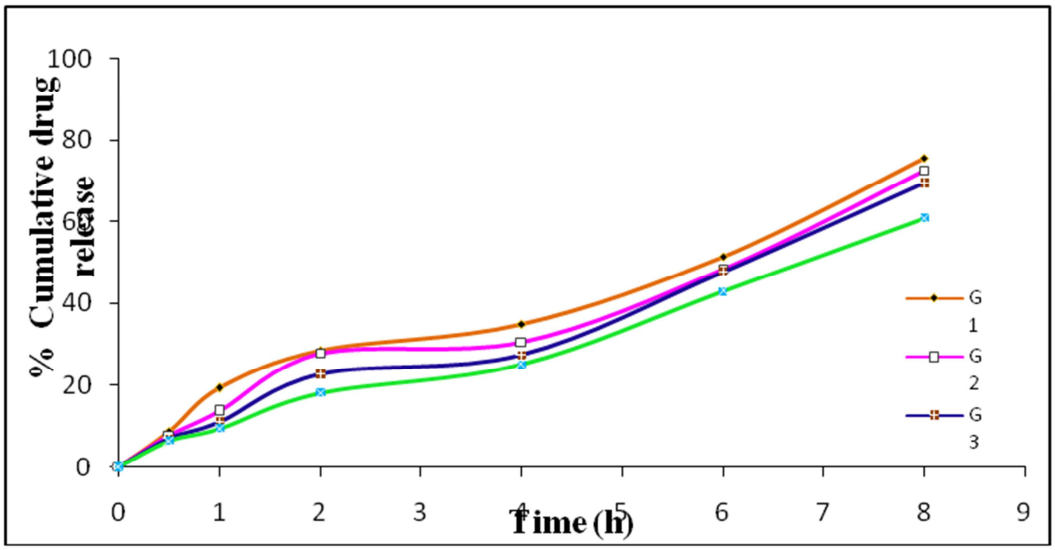


Figure No.8: *In-vitro* drug release profile of formulations G1 – G4

CONCLUSION

Development of mucoadhesive buccal drug delivery of Gliclazide tablets is one of the alternative routes of administration to avoid first pass effect and provide prolongs release. Gliclazide mucoadhesive buccal tablets could be formulated using the drug, Carbopol 940, HPMC K15 LV, Sodium alginate and Guar gum with different ratios. The twelve formulations *i.e.*, H1-H4, S1-S4, G1-G4 were evaluated for physicochemical parameters *i.e.*, hardness, thickness, weight variation, friability, % of drug contents, surface pH, bioadhesive strength, % Swelling index, *In-vitro* drug release studies, *In-vitro* drug release kinetic studies and stability studies. The best formulation H4 was showed the optimum sustained drug release *i.e.*, 71.70±0.53 % at the end of 8 hrs by using drug and polymer in the ratio of 1:1. The *in-vitro* drug release kinetics studies revealed that all the formulations fits to Peppas order kinetics followed by non-Fickian diffusion mechanism. Hence it can be concluded that the formulation H4 will be useful for buccal administration of Gliclazide. So, the mucoadhesive buccal tablets of Gliclazide may be a good choice to bypass the hepatic first pass metabolism with an improvement in the bioavailability of Gliclazide through buccal mucosa.

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CONFLICT OF INTEREST

None declared.

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