

Formulation and Characterization of Glimepiride Buccal Tablet

¹Himanshu Verma , ²Sarika Gupta

(Research Scholar) and (Associate Professor) Agra Public Institute of Technology and Computer Education vermahimanshu23011998@gmail.com

Abstract:

In order to increase Glimepiride bioavailability by bypassing first pass metabolism, buccal tablets were developed. The polymers HPMC K15M, Chitosan, Guar gum, and Carbopol-934 were chosen, and several formulations were created by combining these polymers in varied ratios. Chitosan Polymer is also employed in a 1:2 ratio to increase the formulation's solubility when the Glimepiride medication is poorly soluble in water. Angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio were all used to describe the pre-compression blend of Glimepiride buccal tablets. All results showed that the blend had good flow characteristics and superior compression qualities. The formulations made with Carbopal-934 and Chitosan at concentrations of 3 mg and 10 mg (F7) demonstrated superior 99.48% drug release and were subsequently improved. For the formulations that showed the desired drug release, swelling studies were conducted. Maximum flow and permeability coefficient values were displayed in the chosen formulations. Thus, the buccal tablets of Glimepride with increased bioavailability were effectively created, and they lower high blood sugar levels in persons with type 2 diabetes. **Keywords:** Glimepiride, Buccal Tablet, Type 2-diabetes. Increased bioavailability

DOI: 10.48047/ecb/2023.12.Si12.140

Introduction:

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetics) and sudden episodes of coughing during the common cold, allergic condition and bronchitis [1-2].

Oral administration is the most versatile, convenient and commonly employed route of drug delivery for systemic action. Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation [3-4].

A controlled drug delivery system with prolonged residence time in the stomach is of particular interest for drugs that are locally active in the stomach, have narrow absorption window in gastrointestinal tract, are primarily absorbed from stomach and upper part of GIT, are unstable in the intestinal or colonic environment, disturb normal colonic bacteria and exhibit low solubility at high pH values. Gastro retentive dosage form can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs [5-6].

Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drugs that are less soluble in a high pH environment. Gastro retention helps to provide better availability of new products with suitable therapeutic activity and substantial benefits for patients [7-10].

Diabetes Mellitus:

Diabetes Mellitus is a group of metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. [Diabetes care 2004] Chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of various organs especially the eyes, kidney, nerves, heart, and blood vessels.

Materials and Methods: Materials:

S. No.	Chemicals	Brand
1	Glimepiride	Om Biotec Daryaganj, New Delhi
		110002.
2	HPMCK15M	Agra Public Institute of Technology &
		Computer Education, Artoni, Agra
3	Chitosan	Nanowiztech Pvt, Ltd, Ganaur, Dist.
		Sonipat
4	Carbopol-934	Agra Public Institute of Technology &
		Computer Education, Artoni, Agra
5	Guar gum	Agra Public Institute of Technology &
		Computer Education, Artoni, Agra
6	Mannitol	Agra Public Institute of Technology &
		Computer Education, Artoni, Agra
7	Mg-Streate	Agra Public Institute of Technology &
		Computer Education, Artoni, Agra
8	Talc	Agra Public Institute of Technology &
		Computer Education, Artoni, Agra

Table.1: Materials used in Preparation

Instruments:

S.No.	Equipment	Source
1	UV- visible spectrophotometer	Shimadzu 1800, Japan
2	FTIR spectrophotometer	8400S, Shimadzu, Japan.
3	Tablet dissolution tester USP 2 6-Station electro lab Mumbai, Ind	
4	Friabilator	Roche
5	Hardness tester	Monsanto
6	Electronic balance	Shimadzu BL 220H, Japan
7	Hot air oven	Tempo equipments, India
8	Digital weighing balance	Adventurer USA
9	12 Station D/B Tooling Compression Machine	Fluid Pack Ahmadabad.
10	Stability Chamber	Labtop House Mumbai.

Preformulation Study: Characterization of the Drug: Organoleptic Properties:

The sample of Glimepiride was studied for Organoleptic properties such as colour, odour and

appearance.

Melting Point:

The melting points of Glimepiride were determined by melting point apparatus. Observed value was compared with the reported value.

Solubility:

Solubility of Glimepiride was checked in various solvents Like Methanol and Water.

UV Spectroscopy:

A solution of containing the concentration $10\mu g/$ ml was prepared in 0.1N HCl. UV spectrum was taken using Double beam UV Spectrophotometer (Labindia-3000+). The solution was scanned in the range of 200-400nm.

Preparation Calibration Curve:

10mg of drug was accurately weighed and dissolved in 10ml 0.1N HCl in 10ml volumetric flask, to make (1000µg/ml) standard stock solution (1). Then 1ml stock solution (1) was taken in another 10ml volumetric flask to make (100µg/ml) sub stock solution (2), and then final concentrations were prepared 5-25µg/ml with 0.1N HCl. The abs. of standard solution was determined using UV Spectrophotometer (Lab India 3000+) at 236nm. Linearity of standard curve was assessed from the square of correlation coefficient (r2) which determined by least-square linear regression analysis.

Fourier Transformation Infra – Red Analysis:

Drug- Excipients compatibility studies the infra red absorption spectra of unmixed drug & with unalike ingredient were hold in the scale of four hundred thousand to four hundred cm-1 using KBr dise procedure, 1-2 milligram of material to be analyse was mixed with 300-400 mg, specified quantity of minute powder & dried KBr these sum are mainly enough to give a circle of 10-15 diameter and pellet of right strength by a hydraulic press [11].

Micrometries Study:

Angle of Repose:

Mostly funnel was used in this method, firstly weight of the powder and it taken in a funnel, the height (h) funnel was place in a stand, after the powder is place in the funnel to freely flow, then the angle of repose of the powder is find out. Range of repose can zero degree. The angle of repose of the powder is found out the following formula [12].

Tan
$$\theta = h/r$$

Therefore,

 $\theta = tan \ h / \ r$

Here,

 θ = angle of repose.

h = height of the pile.

r = radius of the pile base.

Bulk Density:

Bulk density was calculated by adding a known mass powder to a cylinder. The density was calculated as mass. Tapped density in this method firstly we have to weigh the known powder and then the known powder transfer in a 10ml mechanically tapping cylinder. The tapping was started until the little further volume changed was observed [13].

Calculated by following equation:

Loosen Bulk Density = Total Mass of Powder /Volume of Powder

Tapped Bulk Density = Powder Wt. / Tapped Volume

Carr's index:

Carr's index help in measuring the power need to breakdown the friction into the particle & the hopper. Carr's index > 25 % is carefully to be a sign of low flow capability, and under 15, of good flow property It can be calculated by following equation [14-16].

Carr's Index (%) = [(Total Bulk Density –Loosen Bulk Density) ×100]/TBD

Where,

TBD = Tapped Bulk Density

Hausner Ratio:

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner's Ratio = Tapped density / Bulk Density

Preparation of Glimepiride Buccal Tablets:

The buccal tablet was formulated using direct compression method all the ingredients were screened through sieve no.100. Carbopol-934, Chitosan, Guar gum, HPMC K15M are the biodegradable polymers used in this preparation of buccal mucoadhesive drug delivery systems. Glimepiride was mixed manually with different ratios of Carbopol 934, Chitosan, Guar gum, HPMC K15M and Mannitol as Diluents for 10min. The blend was mixed with Talc & Mg-stearate for 3-5min. Then the powder blend was compressed into tablets by the direct compression method using 6mm flat faced punches. The tablets were compressed using 10 station Lab Press rotary tablet-punching machine. The weight of the tablets was determined using a digital balance and thickness with digital screw gauge. Composition of the prepared buccal tablet formulations of Glimepiride were given in Table.2.3. Eight batches of the most suitable formulation were prepared by direct compression (Yadav Deepak et al., 2011).

Evaluation of Glimepiride loaded Buccal Tablets:

Weight Variation:

Weight variation was define as to ensure that each of tablet carry proper amount of drug. This method was performed as, weight of 20 individual tablet using analytical balance, after that calculate the average weight of tablet, and after that calculate the individual tablet weight to the average [17].

Hardness of Drug:

Monsanto hardness tester was used to carry out the hardness test on buccal tablet. Individual tablet kept in between plungers and applying pressure until the buccal tablet crackdown into two parts completely and the reading on the scale was noted down in lb/cm2.

Friability:

For the determination of friability test randomly selected buccal tablets were placed in friabilator and rotated at 25rpm for 4 minutes percent deviation in final weight loss is determined.

Thickness:

The vernier caliper (Pico India) device was used to determine the thickness of the mucoadhesive tablet.

Tablet Swelling Index Study:

The tablets were evaluated for rate of hydration when come in contact with phosphate buffer in petridishes. In different time interval for 24 hours, tablets were withdrawn from the petri-dish and weighed after removal of excess moisture from the surface [18-20].

Drug Content Uniformity:

For this at least 30 tablets were randomly selected. Out of 30 tablets, 10 tablets were crushed into fine powder and assayed individually. The powder was dissolved in 500ml of 0.1N HCl, filtered and the specific aliquots were taken and analyzed spectrophotometrically (Shimadzu, SPD-10AVP, Kyoto, Japan) at 228nm [21-23].

Mucoadhesion Strength:

A modified physical balance was used to measure the strength of mucoadhesive-ness. The apparatus consisted of a double beam physical balance in which the right side has a pan, and the left side of the balance has a string that was hanged and at the bottom of the string was a suctioned glass slide. This was the place where the tablets were placed using an adhesive. The porcine buccal mucosa was placed

on top of an inverted 50ml beaker which was placed inside a 500ml beaker that was filled with phosphate buffer with pH 6.8 kept at 37 °C. The buffer amount was just enough so that it reaches the buccal mucosa surface. Exactly five gram of weight was placed on the right pan before putting the porcine buccal tablet in place. The weight was then removed to lower the glass slide with the attached buccal tablet. The tablet was to be in contact with the porcine buccal mucosa membrane and this was not disturbed for 5 minutes. After 5 minutes, weights were added on the right side of the pan to separate the tablet from the membrane. The accumulated weight on the right side was then noted and subtracted with 5g. The value was taken as the measure for the Mucoadhesion strength of the tablet [24].

The Bioadhesive force was calculated using the formula:

$$N = W \times g / 1000$$

Where,

N = Bioadhesive force.

W = Weight required for detachment of the tablet from the porcine buccal mucosa in grams.

g = Acceleration due to gravity at 9.81m/sec2 (Fatima et al., 2015 & Lodhi et al., 2013; Prasad et al., 2010). Fig.1 shows the modified physical balance.



Fig.1: Modified Physical Balance for Mucoadhesive Studies

Surface pH Study:

The tablets to be evaluated were moistened in water and allowed to swell. After sometime the pH meter was to measure the surface pH of the tablet. The significance of this measurement is to avoid mucosal irritation caused by pH change.

In-Vitro Drug Release Study:

In-vitro drug release studies were tested using USP dissolution test apparatus II, the paddle type with dissolution medium of phosphate buffer with a pH of 6.8. It was performed at $37^{\circ}C + 0.5^{\circ}C$ with a speed of 50 rpm. The sample at 5ml was withdrawn at time interval of 15, 30, 45, 60, 90, 120, 150, 180 minutes and was replaced with 5ml of fresh phosphate buffer. The amount of Glimepiride was determined at 228nm using UV spectrophotometer (Vikram et al., 2012; Yadav Deepak et al., 2011). **Kinetic Study:**

The dissolution view of main acceptable preparation was provide to zero order, 1st order & higuchi model to know the mechanism modelling of liberate the model was adopted for determining the proper model [25].

Zero Order:

A zero order response in few reactions, the measure was adequately equivalent of the reactant concentration the rate of zero order reaction dose not very neither greater nor lowering reactants alternativeness means equal to the rate continual, (k) of the reaction.

First Order Reaction:

First order reaction is defined as that proceeds at a rate on rectilinear on single reactant concentration.

Higuchi Model:

A huge number of modified release formulation have few sort matrix system in such instances, the moiety dissolve from the matrix, the dissolution pattern of drug is dictated by H2O perforation, in this higuchi method, a plot of cumulative % moiety released v/o square root of time is linear.

Ft=Kht1/2

Koresmeyer-Peppas Model:

The Koresmeyer Peppas model empirical related the function of time for diffusion-controlled mechanism; it is given as followed:

$$Mt / M\infty = ktn$$

Here,

 $Mt/M\infty$ = Fraction of drug release time.

Kt = Release rate constant.

n= the release exponent.

Stability:

The tablets were stored for 3 months and the samples were tested after a period of 30, 60, and 90 days (Yadav Deepak et al., 2011). The samples were analyzed using the quality control tests such as Hardness, Friability, Drug Content Uniformity, Mucoadhesive strength and Drug release.

Results and Discussion

Preformulation Study:Organoleptic Properties:

 Table.3: Identification Tests of Glimepiride

Parameter	Reported value	Observed value	
Appearance	Crystalline	Crystalline	
Colour	White	White	
Odour	Odourless	Odourless	

Melting Point:

The melting point was determined by melting point apparatus and the melting point was found to be. **Table.4:** Melting Point of Glimepiride

Parameter	Standard	Observed
Melting Point	207°C-214°C	210°C

Solubility:

Solubility of Glimepiride was checked in various solvents.

Table.5: Determination of drug solubility in various solvents

S. No.	Solvent	Descriptive Term
1	Methanol	Slightly Soluble
2	Water	Low soluble

UV Spectroscopy:

The absorbance for various concentrations measured at 228nm is as follows:

Table.6: Standard Graph of Glimepiride in 0.1N HCL

S.	No.	Conc. (µg/ml)	Abs. at 228nm
----	-----	------------------	---------------

1	5	0.096
2	10	0.188
3	15	0.276
4	20	0.368
5	25	0.464
6	30	0.566



Fig.2: Standard Graph of Glimepiride in 0.1N HCL

FTIR Study:

IR Spectra of Pure Drug:

The FTIR spectrums of Pure Drug with different polymers were used in formulation was showed in Figures.



Fig.3: FTIR spectrum of Glimepiride







Fig.7: FTIR spectrum of Glimepiride + Guar gum **Table.7:** Interpretation of FTIR Spectrum

Functional Groups	Peaks Observed (wave no. (cm-1))								
	Glimepiride	Glimepiride + HPMC K115M	Glimepiride + Chitosan	Glimepiride + Carbopol 934	Glimepiride + Guar gum				
O=C= stretching	1848.25CM ⁻¹	1858.20 CM ⁻¹	1867.19 CM ⁻¹	1886.16 CM ⁻¹	1808.12 CM ⁻¹				
N-H stretching	3369.18CM ⁻¹	3318.89CM ⁻¹	3302.78CM ⁻¹	3309.54CM ⁻¹	3352.80 CM ⁻¹				
C-H stretching	2930.71c CM ⁻¹	2986.62CM ⁻¹	2974.60 CM ⁻¹	2990.53CM ⁻¹	2988.50CM ⁻¹				
C=O bending	1137.31 CM ⁻¹	1150.45CM ⁻¹	1147.20CM ⁻¹	1132.05CM ⁻¹	1130.01CM ⁻¹				
N=O stretching	1350.78CM ⁻¹	1550.65CM ⁻¹	1505.36CM ⁻¹	1507.28CM ⁻¹	15t02.20CM ⁻¹				
S=O stretch	1153.94CM ⁻¹	1120.56CM ⁻¹	1118.54 CM ⁻¹	1115.42 CM ⁻¹	1178.51CM ⁻¹				

Micrometry Study:

 Table.8: Evaluation of Powders for Glimepiride

Formulation Code	Angle of Repose (θ)	Bulk density (gm/ml)	Carr's index (%)	Tapped density (gm/ml)	Hausner's ratio
F1	25°.52′	0.496	22.15	0.618	1.252
F2	22°.82′	0.464	24.67	0.608	1.190
F3	23°.32′	0.448	21.40	0.619	1.273
F4	24°.06′	0.476	25.58	0.584	1.288
F5	27°.36′	0.450	26.30	0.576	1.292
F6	28°.30′	0.464	20.50	0.648	1.245
F7	27°.90′	0.436	24.15	0.590	1.214
F8	28°.92′	0.424	23.54	0.580	1.264

Discussion:

The physical mixtures for Glimepiride Powder are evaluated with respect to Angle of repose was found b/w 22°.82' to 28°.92' and Carr's index values are found 20.50 to 26.30% the powder of all batches excellent to poor flow ability and compressibility. Hausner ratio is found to be 1.190 to 1.292. Bulk density ratio 0.424 to 0.496 and Tapped density ratio 0.576 to 0.648 for all the batches indicating that possible and poor flow properties.



Fig.8: Powder Evaluated with respect to Bulk & Tapped Density



Fig.9: Powder Evaluated with respect to Angle of repose, Carr's index & Hausner's Ratio **Preparation:**

S. No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
1	Glimepiride	2mg	2mg	2mg	2mg	2mg	2mg	2mg	2mg
2	HPMC K15M	5	10	15	20	5	10	15	20
3	Chitosan	5	10	5	10	5	10	5	10
4	Carbopol 934	10	20	30	10	20	30	10	20
5	Guar gum	10	15	20	10	15	20	10	-
6	Mannitol	QS	QS	QS	QS	QS	QS	QS	QS
7	Mg-Stearate	2.5	2.5	2.5	3.5	3.5	3.5	2.5	3.5
8	Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Table.9: Preparation of Mucoadhesive Glimepiride Buccal Tablets

Evaluation Parameters:

 Table.10: Evaluation of Compressed Glimepiride Loaded Mucoadhesive Buccal Tablets

Formulation Code	Weight variation Average wt in (mg)	Hardness (Kg/cm2)	Thickness in (mm)	Friability (%)
F1	182.32	3.50±0.34	2.56±0.20	0.33±0.12

F2	180.46	3.12±0.68	2.26±0.14	0.40±0.16
F3	201.38	2.86±0.62	2.82±0.08	0.60±0.16
F4	195.27	3.06±0.78	2.72±0.06	0.50±0.20
F5	201.28	4.25±0.26	2.40±0.04	0.67±0.10
F6	199.50	3.15±0.10	2.72±0.12	0.70±0.18
F7	198.36	3.82±0.32	2.78±0.03	0.62±0.11
F8	197.78	3.64±0.20	2.10±0.03	0.58±0.13
Formulation	Drug Content	Tablet Swelling	Surface pH	Mucoadhesion
Code	TIm:forme:try	T., J., C4., J.,	04 1	C4 41
Code	Uniformity	Index Study	Study	Strength
F1	98.50±1.10	25.82	7.01	>12
F1 F2	98.50±1.10 97.80±1.50	25.82 36.68	7.01 6.90	>12 >11
F1 F2 F3	98.50±1.10 97.80±1.50 96.26±1.76	25.82 36.68 46.92	Study 7.01 6.90 6.70	Strengtn >12 >11 >15
F1 F2 F3 F4	98.50±1.10 97.80±1.50 96.26±1.76 96.78±1.45	11dex Study 25.82 36.68 46.92 62.96	Study 7.01 6.90 6.70 7.16	Strengtn >12 >11 >15 >14
F1 F2 F3 F4 F5	98.50±1.10 97.80±1.50 96.26±1.76 96.78±1.45 97.96±1.25	11dex Study 25.82 36.68 46.92 62.96 76.42	Study 7.01 6.90 6.70 7.16 7.30	Strengtn >12 >11 >15 >14 >16
F1 F2 F3 F4 F5 F6	98.50±1.10 97.80±1.50 96.26±1.76 96.78±1.45 97.96±1.25 98.98±1.12	11dex Study 25.82 36.68 46.92 62.96 76.42 90.90	Study 7.01 6.90 6.70 7.16 7.30 7.04	Strengtn >12 >11 >15 >14 >16 >14
F1 F2 F3 F4 F5 F6 F7	98.50±1.10 97.80±1.50 96.26±1.76 96.78±1.45 97.96±1.25 98.98±1.12 99.98±1.10	111dex Study 25.82 36.68 46.92 62.96 76.42 90.90 95.42	Study 7.01 6.90 6.70 7.16 7.30 7.04 7.00	Strengtn >12 >11 >15 >14 >16 >14 >12

Values are intimate as design \pm SD (n = 3)



Fig.10: A Diagrammatically Representation of Hardness, Thickness & Friability



Fig.11: A Diagrammatically Representation of Wt. Variation, Tablet Swelling Index Study



Fig.12: A Diagrammatically Representation of Surface pH Study & Mucoadhesion Strength





Table.11: Release studies F1-F	8
--	---

Time/Hrs	% Release Drug							
Formulat	F1	F2	F3	F4	F5	F6	F7	F8
ion								
0	0	0	0	0	0	0	0	0
		42.40±0.2	46.60±0.2		47.40±0.6		46.42±1.2	
1	45.75±2.6	4	0	44.04 ± 0.96	2	48.42 ± 1.30	0	42.82±1.32
		48.66±0.9	54.42±0.4		56.85±0.7		58.78±1.1	
2	56.90±2.4	2	6	52.34±1.33	8	57.78±1.25	5	54.78±1.28
		58.04±0.7	59.54±0.7		60.58±1.3		66.47±1.2	
3	62.70±2.1	2	0	63.13±1.28	4	63.47±1.20	6	60.47±1.21

		(0.0(0.0	(5.00.00				76.00 1.1	
		68.26±0.3	65.30±0.8		6/.44±1./		/6.89±1.1	
4	70.15±0.4	4	4	69.49±1.22	5	75.89±1.18	6	72.89±1.17
		75.78±1.2	76.72±0.5		77.98±1.2		84.45±0.9	
5	80.32±0.6	3	7	72.21±0.98	5	87.45±0.78	2	82.45±0.90
		80.25±1.0	79.42±0.2		80.43±1.4		89.45±0.7	
6	84.58±0.9	8	8	78.16±0.88	2	92.25±1.77	2	88.22±0.73
		85.94±1.1	86.20±0.7		88.78±1.4		96.64±1.2	
7	90.29±0.5	0	2	88.29±0.68	6	95.67±1.57	3	94.36±1.22
		92.83±1.3	95.70±0.3		96.38±1.9		99.48±1.8	
8	94.54±0.7	4	8	94.90±0.48	3	97.96±0.82	5	97.16±1.80

Point are communicate as mean \pm standard deviation (n = 3)



Fig.14: A Diagrammatically Representation of % Release Drug

Release Kinetics of In-vitro Drug Release:

Different kinetic models, including zero order, first order, Higuchi, and Korsmeyer-Peppas, were used to analyze in-vitro drug release data in order to derive the drug's release kinetics. Table.12 Summaries the findings in further detail.

Formulation	Zero Order	1 st Order	Higuchi	Peppas	Best Model
Code	r^2	r^2	r^2	r^2	
F1	0.835	0.838	0.858	0.468	Higuchi
F2	0.870	0.874	0.880	0.588	Higuchi
F3	0.843	0.848	0.855	0.463	Higuchi
F4	0.847	0.874	0.863	0.473	1 st Order
F5	0.835	0.872	0.851	0.460	1 st Order
F6	0.836	0.838	0.863	0.472	Higuchi
F7	0.842	0.843	0.867	0.476	Higuchi
F8	0.874	0.876	0.887	0.494	Higuchi

Table.12: Release Kinetics of In-vitro Drug Release



Fig.17: Higuchi Model F1-F7



Fig.18: Peppas Model F1-F7

Stability Studies:

Formulation F7 was deemed to be the best of the seven formulations based on the findings. Thus, stability experiments were conducted on Formulation F7. Percentage yield, Drug content and in vitro drug release were measured for each month up to three months for Formulation F7. Results are reported in Table.13.

S. No.	Parameters	Initial	1 Month	2Month	3Month		
2	Hardness	3.82±0.32	3.70±0.32	3.40±0.22	3.10±0.18		
3	Friability	0.62±0.11	0.60±0.10	0.52±0.08	0.46±0.04		
4	In-Vitro Drug Release	99.48±1.85	99.40±1.80	99.00±1.52	98.70±1.34		
5	Drug Content Uniformity	99.98±1.10	99.86±1.10	99.10±1.09	98.90±1.08		
6	Mucoadhesive strength	>12	>12	>11.5	>11		

Table.13: Stability Study for Best Formulation F7

Discussion:

The duration of stability studies of the Formulation 7, there is no major variation, the minor variation found in Hardness, Friability and In vitro drug release, Drug Content Uniformity & Mucoadhesive strength that is adjustable, All data evaluated according to ICH guidelines at $40\pm2^{\circ}C/75\pm5\%$ RH for 90 days.

Conclusion:

Glimepiride was formulated as buccal tablets to improve its bioavailability by avoiding first pass metabolism. HPMC K15M, Chitosan, Guar gum and Carbopol-934 were selected as polymers and various formulations were prepared by using these polymers in different ratios. Glimepiride drug low soluble in water then Chitosan Polymer also used 1:2 ratio to enhance solubility of formulation. The Pre-compression blend of Glimepiride Buccal tablets were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio and all the results indicated that the blend was having good flow nature and better compression properties. The formulations prepared with Carbopal-934 and Chitosan in the concentration of 3mg and 10mg (F7) was showing better result 99.48% drug release and is thus optimized. The swelling studies were performed for the formulations which were shown desired drug release. The selected formulations were showing maximum flux value and permeability coefficient value. Thus the buccal tablets of Glimepride were prepared successfully with improved bioavailability and *reduce high blood sugar levels in people with type 2 diabetes*.

References

1. Seager, H., Drug delivery products and Zydis fast dissolving dosage form, 1998, 50, 375-382.

- Gunter Muller, the Mode of Action of the Antidiabetic Drug Glimepiride-Beyond Insulin Secretion Current Medicinal Chemistry - Immunology, Endocrine & Metabolic Agents volume 5, 2005, Pg no 499-518. 499 - 518.
- 3. Hotamisligil GS. Molecular mechanisms of insulin resistance and the role of the adipocyte. Int J Obes Relat Metab Disord. 2000;24:S23.
- 4. Wu X, Motoshima H, Mahadev K, Stalker TJ, Scalia R, Goldstein BJ. Involvement of AMPactivated protein kinase in glucose uptake stimulated by the globular domain of adiponectin in primary rat adipocytes. Diabetes. 2003;52:1355.
- 5. Bähr A, von Holtey M, Müller G, Eckel J. Direct stimulation of myocardial glucose transport and glucose transporter-1 (GLUT1) and GLUT4 protein expression by the sulfonylurea glimepiride. Endocrinol. 1995;136:2547.
- 6. Hausenloy DJ, Wynne AM, Mocanu MM, Yellon DM. Glimepiride treatment facilitates ischemic preconditioning in the diabetic heart. J Cardiovasc Pharmacol Ther. 2013;18:263-9.
- 7. Müller, G.; Geisen, K. Characterization of the molecular mode of action of the sulfonylurea, glimepiride, at adipocytes. Horm Metab Res. 1996;28:469.
- Takada Y, Takata Y, Iwanishi M, Imamura T, Sawa T, Morioka H, Ishihara H Ishiki M Usui I, Temaru R, Urakaze M, Satoh Y, Inami T, Tsuda S, Kobayashi M. Effect of glimepiride (HOE 490) on insulin receptors of skeletal muscles from genetically diabetic KK-Ay mouse. Eur J Pharmacol. 1996;308:205.
- Kramer W, Müller G, Girbig F, Gutjahr U, Kowalewski S, Hartz D, Summ HD. Differential interaction of glimepiride with the β-cell sulfonylurea receptor II. Photoaffinity labeling of a 65 kDa protein by [3 H] glimepiride. Biochim Biophys Acta. 1994;1191: 278-90.
- 10. Müller G. The mode of action of the antidiabetic drug glimepiride beyond insulin secretion. Curr Med Chem Immun Endoc Metab Agents. 2005;5:499-518.
- 11. Hadi, Mohd Abdul, V. Lokeswara Babu, and Narottam Pal. "Formulation and evaluation of sustained release matrix tablets of glimepiride based on combination of hydrophilic and hydrophobic polymers." *J Appl Pharm Sci, no.* 2 (2012): 101-107.
- 12. Sajal Kumar Jha, Thilothama LR, Parameshwar K, Radhika Reddy M and Sandeep K. "Design Development and In-Vitro Characterization of Stavudine Matrix Porous Tablets." *Asian Journal of Pharmaceutics9*, no. 4 (2018): 26-33.
- 13. Guerra-Ponce, Wendy Leticia, Sandra Leticia Gracia-Vásquez, Patricia González-Barranco, Ivonne Antonieta Camacho-Mora, Yolanda Araceli Gracia-Vásquez, Elizabeth Orozco-Beltrán, and Linda Anne Felton. "In vitro evaluation of sustained released matrix tablets containing ibuprofen: a model poorly water-soluble drug." *Brazilian Journal of Pharmaceutical Sciences52*, no. 4 (2016): 751-759.
- 14. Kumar, C.H., M. Reddy, Nalini Krishna, and Namany Archana."Formulation and Evaluation of Sustained Release Matrix Tablets of Quetiapine Fumarate." *International journal of pharmaceutical and pharmacological research4*, no.4 (2015): 244-248.
- 15. Chandra sekhar y, vani prasanna, mohan, t Sagarika. "Formulation and in vitro evaluation of sustained release floating matrix tablets of enalapril maleate." *An International Journal of Advances in Pharmaceutical Sciences* 2, no. 1 (2010): 308-312.
- 16. Awan, Ammar Ashraf, Nazar M. Ranjha, and Umar Farooq. "Design and optimization of extended release tablets of vildagliptin by matrix diffusion system using directly compressible co-processed excipients." *World Journal of Pharmacy and Pharmaceutical Science5*, no. 3 (2016).199-215.
- 17. Mohammed, Moiz, Prathima Srinivas Maringanti, and Sadanandam Mamidi. "Formulation and evaluation of bioadhisive tablet levocetrizine dihydrochloride using natural and synthetic polymers." *International Journal of Drug Delivery* 3, no. 4 (2011): 597.
- 18. Navade, Kirankumar, B. Someswara Rao, and Suresh V. Kulkarni. "Formulation and Evaluation of Sustained Release Matrix Tablets of Flurbiprofen by Using Natural and Synthetic Polymers." *Journal of Pharmaceutical Sciences and Research7*, no. 6 (2015): 274.
- 19. Gupta SK, Singhvi IJ, Shirsat M, Karwani G, Agarwal A, Aditi A. Buccal adhesive drug delivery system: a review. Asi J Biochem Pharm Res 2011 april;2(1):105-14.
- 20. Chen YS, Squier CA. The structure and function of oral mucosa. Pergamon Press, Oxford 1984:7-30.

- 21. Ross & Wilson. Anatomy & physiology in health and illness. 9th ed. Edinburgh Publishers;2001:289-93.
- 22. Jain NK. Controlled and novel drug delivery. 1st ed. New Delhi: CBS Publishers & Distributors; 1997:52-81.
- 23. Kumar V, Aggarwal G, Zakir F, Choudhary A. Buccal bioadhesive drug delivery- a novel technique. Int J Pharm Bio Sci 2011;1(3):89-102.
- 24. Gandhi PA, Patel MR, Patel KR, Patel NM. A review article on mucoadhesive buccal drug delivery system. Int J Pharm Res Dev 2011 july;3(5):159-73.
- 25. Nazila SM, Montakarn C, Thomas PJ. The use of mucoadhesive polymers in buccal drug delivery. Adv Drug Deli Rev 2005 july;57:1666-91.