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FORMULATION AND EVALUATION OF BUCCAL TABLETS OF GLIMEPIRIDE

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Keywords:

Glimepiride, buccal tablets, HPMC K15M, Carbopol 934P, Starch acetate

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ABSTRACT

The aim of the work was to develop a tablet for the buccal delivery of the poorly soluble drug (glimepiride) which is an antidiabetic agent. In that an attempt was made to enhance bioavailability,reduce dose dependent side effects and frequency of administration. Buccal tablets containing the drug were prepared using different concentrations of mucoadhesive polymers (such as carbopol 934p, HPMC K15Mand starch acetate). The buccal tablets were evaluated for various parameters like content uniformity, *in-vitro* drug release, drug content, swelling index, drug-excipient interactions (FTIR and DSC). IR and DSC studies indicated that there was no drug-excipient interaction. The rate of drug release decreased with increase in the polymer concentration. Among the mucoadhesive polymers used buccal tablets prepared with HPMC K15M and Starch acetate showed sustained drug release. Release kinetics study showed that release exponent ‘n’ was between 0.5-1.0 indicating a non fickian diffusion as the release mechanism for all the prepared tablets.

INTRODUCTION

Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike. However, peroral administration of drugs has disadvantage such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain class of drugs.[1]

The oral cavity is an attractive site for the administration of drugs because of ease of administration. Various dosage forms like tablets, capsules and liquid oralsare administered by oral route. Inrecentyears, delivery of therapeutic agents throughbuccal mucosa has gained significant attention. Administration of the drug via themucosal layer is novel method that can render treatment more effective and safe.There are opportunitiesfor mucosal (local effect) and transmuosal (systemic effect) drug administration. The mucosal administration of drugs is to achieve site-specific releaseofdrugsonthe mucosa, whereas, in thelatter, transmucosal administrationinvolvesdrug administration throughmucosalbarriertoreachthesystemiccirculation. Among thevarious transmucosal routes like nasal, rectal, vaginal, ocular,pulmonary and buccal routes, thebuccal mucosa isanattractivealternativeto the oralrouteofdrugadministrationand itis apotential site forthedelivery ofdrugs tothesystemic circulation.[2] Diabetes mellitus isachronic metabolicdisorder characterized by highblood glucose concentration-hyperglycemia-caused by insulin deficiency, often combined with insulin resistance[3]. Glimepiride,an important drug of sulfonylurea class, is currently available for treating hyperglycemia in Non-Insulin Dependent DiabetesMellitus (NIDDM); buthasbeen associated with severe and sometimes fatal hypoglycemia and gastric disturbances like nausea, vomiting, heartburn, anorexia and increased appetite after oral therapy.[4] Since these drugs are usually intended to be taken for a long period, patient compliance is also very important.[5-7] Hence in the present study,we have formulated the buccaltabletsof glimepiride.

MATERIALS AND METHODS

Materials

Glimepirideis a generous gift from Karnataka Antibiotic Private Limited, Banglore, India. Potato starch,HPMC K15M and Carbopol 934P were obtained from Yarrow Chemicals. Talcand magnesium stearate (analytical grade) were purchased from S.D. FineChemicals Ltd. (Mumbai, India). All the other ingredients were of analyticalgrade.

Methods

Preparation of starch acetate:[8]

Potato starch (20 parts), acetic anhydride (80 parts) and sodium hydroxide 50% solution (4.4 parts) were mixed and refluxed for 5 h at 150˚C. The reaction mixture was added to cold water to precipitate the starch acetate formed. The product was collected by vacuum filtration, washed repeatedly with water and dried at 80˚C for 2 h.

Drug polymer compability:

The drug and polymer compability was also checked using Infrared spectroscopy and DSC.

Preparation of Glimepiride buccal tablets:

Accurately weighted quantity of glimepiride, polymer, andlactose were taken in mortar and mixed. Mixture of water: isopropyl alcohol (1:1) was added to dry blend gradually with constant kneading to ensure a homogenous mass.The dough mass was passed through a #12 mesh sieve. Then granules were dried at 60°C for 2hrs and dried granules were lubricated with magnesium Stearate and compressed into tablets using 8 mm punches. Each tablet contains 4 mg of glimepiride.

Table1: Formulation composition of buccal tablets of Glimepiride:

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Glimepiride	4	4	4	4	4	4	4	4	4	4	4	4
Carbopol 934P	20	40	60	80	-	-	-	-	-	-	-	-
HPMC K15M	-	-	-	-	20	40	60	80	-	-	-	-
Starch acetate	-	-	-	-	-	-	-	-	20	40	60	80
Lactose	172	152	132	112	172	152	132	112	172	152	132	112
Magnesium stearate	4	4	4	4	4	4	4	4	4	4	4	4
Total(mg)	200	200	200	200	200	200	200	200	200	200	200	200

PRE COMPRESSION STUDIES:

Angle of Repose (θ):[9]

It was determined by funnel method. A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity.

$$Angle\ of\ Repose\ (\theta) = tan^{-1}\ (h/r)$$

Density:[10,12]

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of accurately weighed powder (bulk) from each formula, previously shaken to break any agglomerates formed was introduced into a 25 ml measuring cylinder.After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 seconds interval. LBD and TBD were calculated using following formula;

$$LBD = \frac{Weight\ of\ powder}{Tapped\ volume\ of\ packing}$$

$$LBD = \frac{Weight\ of\ powder}{Volume\ of\ packing}$$

Carr's Compressibility Index:[10,11]

The compressibility index of the granules was determined by Carr's compressibility index. Grading of the powders for their flow properties according to Carr's Index is given in Table below

Evaluation of tablets:

Weight variation: Twenty tablets were randomly selected from each batch individually weigh, the average weight and standard deviation of 20 tablets calculated.[13]

Thickness: The thickness of the tablet was measured by using venire caliper, twenty tablets from each batch were randomly selected and thickness was measured.[13]

Hardness: Hardness was measured using Monsato hardness tester, for each batch three tablets were tested.[14]

Friability: Twenty tablets were weight and placed in the Roche friabilator and apparatus was rotated at 25 rpm for 4 min. After revolution the tablets were dusted weight.[15]

Uniformity of drug content:

Five tablets were powdered in a mortar. Weighed of the tablet equivalent to 100 mg of glimepiride and transferred to a 100ml volumetric flask containing few ml of methanolic hydrochloride and mixed well, made up the volume up to 100ml with phosphate buffer pH 6.8. Pipette out 10 ml from the stock solution into another 100ml volumetric flask and made up the volume with phosphate buffer pH 6.8. From the above solution withdrew the aliquots 1ml and

volume was made up to 10 ml with phosphate buffer pH 6.8. The absorbance was measured at 228 nm using phosphate buffer pH 6.8 as blank.

Swelling index:[16]

The extent of swelling was measured in terms of percentage weight gain by the tablets. One tablet from each formulation was kept in petri dish containing phosphate buffer pH 6.8. At the end of 1, 2, 4 and 6h tablets were withdrawn, soaked on tissue paper and weighed, and then percentage weight gain by the tablet was calculated using formula.

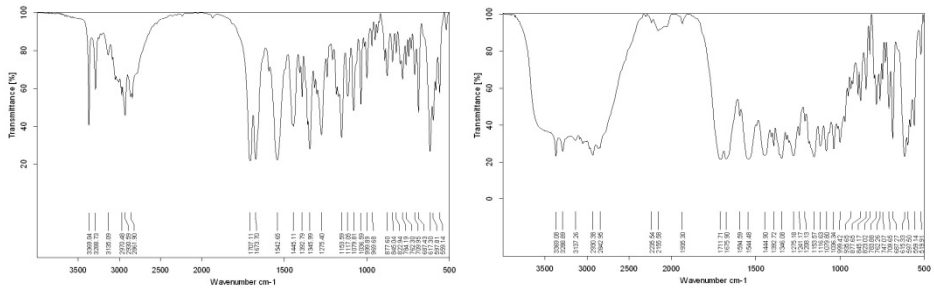
In-vitro dissolution studies:[17,18]

The in-vitro dissolution studies were performed using the USP-II (Paddle) dissolution apparatus at 50 rpm. The dissolution medium consisted of 900ml of phosphate buffer pH 6.8, maintained at 37±0.5^{0}C. An aliquot (5ml) was withdrawn at specific time intervals and drug content was determined by UV-visible spectrometer (UV-1700 Shimadzu corporation, Japan.) at 228nm. The study was performed in triplicate.

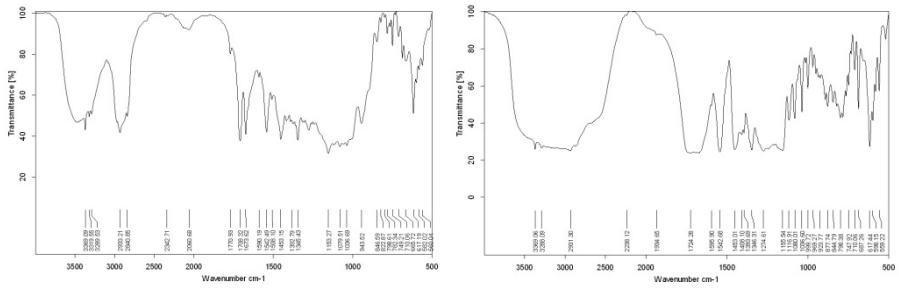
RESULTS

Drug polymer compability:

IR spectrometry:



IR spectra of GPDIR spectra ofGPD + starch acetate

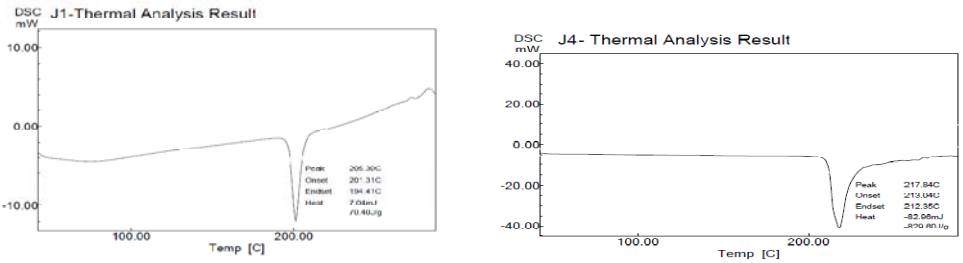


IR spectra of GPD + HPMC K15MIR spectra of GPD + Carbopol 934P

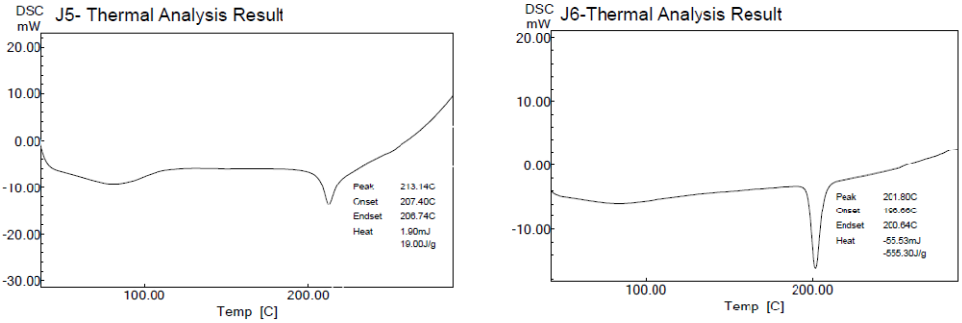
Table-2: Data obtained from compatibility study of drug and polymer by IR:

	NH stretching	CH stretching	C=0 stretching	C-N vibrational	S=O stretching	C=C stretching
Standard Range (cm^{-1})	3400-3500	2960-2850	1705-1725	1000-1400	1050-1400	1450-1600
Glimepiride	3369.04	2970.48	1707.11	1392.79	1079.81	1542.65
Glimepiride + Carbopol 934p	3369.06	2931.30	1724.28	1393.69	1080.01	1542.68
Glimepiride + HPMC K15M	3369.09	2933.21	1708.32	1392.79	1079.51	1542.49
Glimepiride + Starch acetate	3369.08	2930.38	1711.71	1392.72	1079.80	1544.46

Differential scanning calorimetry (DSC):



DSC thermogram of GPDDSC thermogram of GPD + starch acetate



DSC thermogram of GPD + HPMC K15MDSC thermogram of GPD + carbopol 934p

Table-3: Data obtained from compatibility study of drug and polymer by DSC:

Drug/ polymer	Characterization of peak
Glimepiride	205.30˚C
Glimepiride + starch acetate	217.84˚C
Glimepiride + HPMC K15M	213.14˚C
Glimepiride + carbopol 934P	201.80˚C

Table-4: LB Density, TB Density and Carr's Index, hausner's ratio and angle of repose

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Hausner's ratio	Angle of repose
F1	0.33±0.03	0.36±0.2	8.33	1.09	25.5
F2	0.32±0.04	0.38±0.6	15.78	1.18	29.74
F3	0.31±0.06	0.34±0.1	8.82	1.09	28.13
F4	0.37±0.08	0.39±0.3	5.12	1.05	27.42
F5	0.39±0.02	0.42±0.2	7.14	1.07	25.68
F6	0.28±0.05	0.31±0.1	9.67	1.10	26.90
F7	0.41±0.01	0.43±0.5	6.97	1.07	27.59
F8	0.31±0.03	0.34±0.8	8.82	1.09	24.41
F9	0.385±0.06	0.41±0.1	6.09	1.06	28.13
F10	0.26±0.0	0.29±0.5	10.34	1.11	26.65
F11	0.36±80.01	0.385±0.8	6.49	1.06	27.09
F12	0.28±0.03	0.31±0.6	9.67	1.10	25.51

EVALUATION OF BUCCAL TABLETS:

Table-5: Evaluation of buccal tablets:

Formulation Code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)
F1	203±2	7.4±0.2	3.09±0.05	0.19	96.4 ± 1.77
F2	204±3	6.8±0.5	3.12±0.07	0.54	97.71 ± 1.68
F3	202±1	6.9±0.6	3.13±0.03	0.59	97.23 ± 2.84
F4	198±2	7.2±0.3	3.18±0.09	0.39	96.07 ± 1.62
F5	204±4	7.3±0.3	3.08±0.04	0.20	94.34 ± 3.94
F6	201±3	6.4±0.4	3.17±0.06	0.19	95.46 ± 2.56
F7	204±4	6.3±0.8	3.18±0.03	0.34	97.54 ± 1.92
F8	203±2	7.8±0.7	3.20±0.07	0.70	97.67 ± 1.47
F9	201±4	6.3±0.5	3.08±0.02	0.55	95.6 ± 4.97
F10	202±5	8.1±0.6	3.11±0.01	0.59	98.72 ± 1.87
F11	200±3	6.3±0.7	3.04±0.01	0.79	95.44 ± 2.39
F12	198±4	8.4±0.8	3.16±0.01	0.89	97.72 ± 1.85

In-vitro drug release:

Table-6 Percent drug release buccal tablets of glimepiride and carbopol 934p:

Sl. No.	Time	Carbopol 934P buccal tablets			
		F1	F2	F3	F4
1	0	0	0	0	0
2	1	31.23 ±1.2	27.15 ±2.4	20.47 ±1.8	15.1 ±2.3
3	2	42.15 ±2.3	36.5 ±3.5	29.11 ±2.3	21.21 ±2.6
4	3	49.38 ±3.4	42.29 ±1.2	38.58 ±3.1	32.36 ±1.8
5	4	56.54 ±1.8	49.25 ±1.9	43.24 ±2.4	38.62 ±3.1
6	5	64.75 ±3.1	56.36 ±2.3	50.2 ± 1.5	44.37 ±2.7
7	6	73.66 ±2.2	63.45 ±3.2	57.33 ±2.3	52.63 ±1.8
8	7	84.2 ± 0.8	75.29 ±2.6	65.86 ±2.7	62.1 ± 2.5
9	8	93.45 ±1.3	83.15 ±3.4	73.33 ±3.4	66.64 ± 1.7
10	9	--	91.69 ±2.5	77.71 ±1.8	73.29 ±2.4
11	10	--	98.34 ±1.4	82.41 ±2.1	77.79 ±1.9
12	11	--	--	88.79 ±2.6	79.94 ±2.3
13	12	--	--	90.98 ±3.4	88.75 ±3.4
14	13	--	--	96.07 ±2.8	94.58 ±1.5

*** Value are mean ± SD (n=3)**

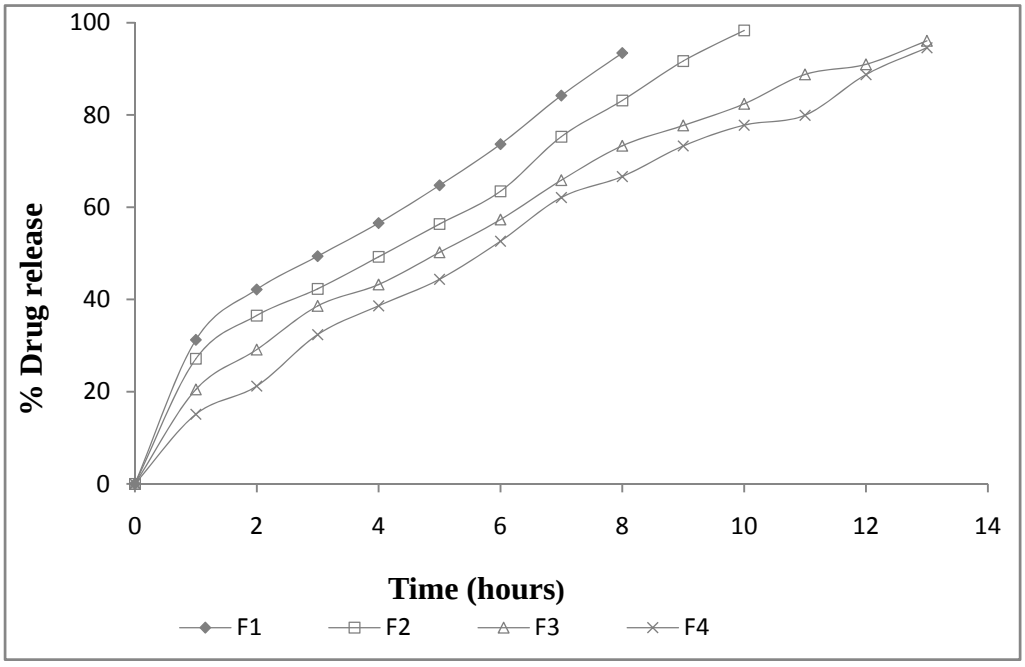


Fig-1 Dissolution profile of glimepiride with carbopol 934P

Table-7 Percent drug release buccal tablets of glimepiride and HPMC K15M

Sl. No.	Time	HPMC K15M buccal tablets			
		F5	F6	F7	F8
1	0	0	0	0	0
2	1	24.35±2.3	18.41±1.9	14.26±2.3	5.26±1.8
3	2	31.26±2.6	23.27±2.4	19.35±2.1	8.42±1.9
4	3	36.41±1.8	30.94±3.2	28.32±3.4	12.68±2.4
5	4	43.33±1.7	39.45±2.8	33.48±2.6	18.75±4.3
6	5	54.84±3.4	47.84±4.1	38.85±3.1	22.15±2.6
7	6	61.5±3.1	54.24±2.7	44.39±4.2	29.22±2.7
8	7	69.75±2.7	62.34±1.8	50.94±1.8	34.5±1.9
9	8	77.48±1.9	71.45±2.1	57.81±2.3	42.67±2.1
10	9	85.66±0.8	79.67±3.8	62.75±1.6	49.34±2.4
11	10	91.12±2.9	86.44±1.3	67.53±1.9	57.25±3.1
12	11	96.71±2.1	92.53±2.6	72.25±2.3	62.31±2.8
13	12	--	--	79.46±2.4	68.89±1.7
14	13	--	--	85..64±1.8	73.65±2.4
15	14	--	--	91.75±3.1	81.32±1.8

*** Value are mean ± SD (n=3)**

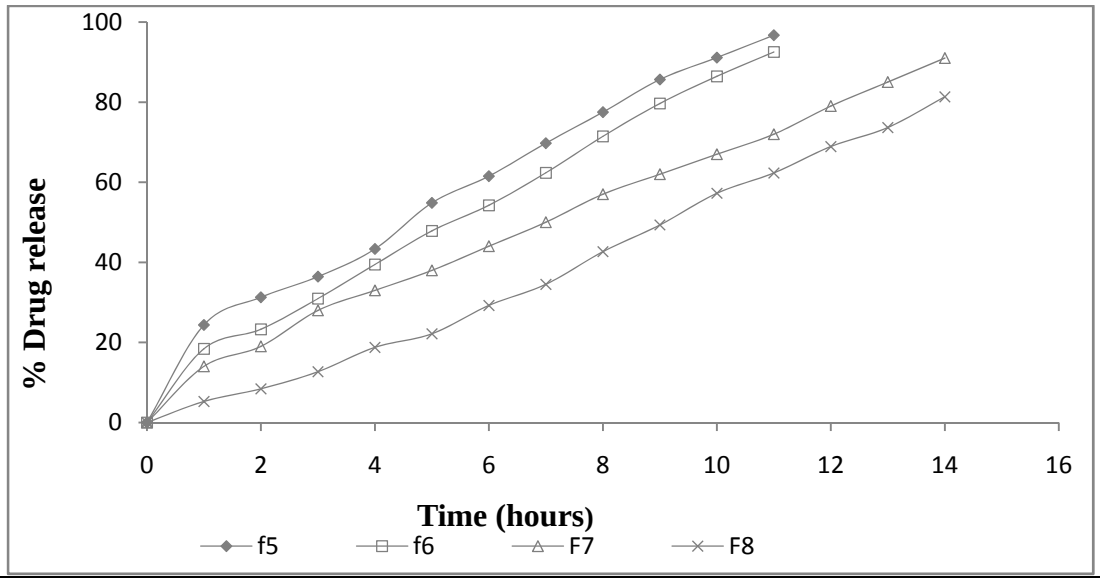


Fig-2Dissolution profile of glimepiride with HPMC K15M

Table-8 Percent drug release buccal tablets of glimepiride and starch acetate:

Sl. No.	Time	Starch acetate buccal tablets			
		F9	F10	F11	F12
1	0	0	0	0	0
2	1	26.17±0.6	11.28±2.5	6.25±2.6	3.76±0.6
3	2	32.82±2.3	21.46±2.4	14.31±3.1	8.13±2.6
4	3	42.63±0.5	37.37±2.3	24.48±2.7	17.45±1.2
5	4	52.45±1.6	41.25±1.6	32.73±1.2	26.68±0.8
6	5	64.37±3.2	49.29±0.9	40.47±0.8	37.19±1.2
7	6	77.94±0.9	58.24±2.5	49.68±0.4	45.26±1.6
8	7	83.18±1.6	67.29±3.1	56.96±1.3	53.35±2.3
9	8	88.65±2.5	83.47±0.7	64.24±2.1	61.44±2.8
10	9	97.34±1.7	92.65±0.9	68.72±0.8	67.57±2.5
11	10	--	98.21±1.6	77.18±0.7	74.88±1.9
12	11	--	--	83.93±1.6	79.25±2.5
13	12	--	--	89.48±2.4	85.42±1.8
14	13	--	--	95.05±2.8	91.37±2.3

*** Value are mean ± SD (n=3)**

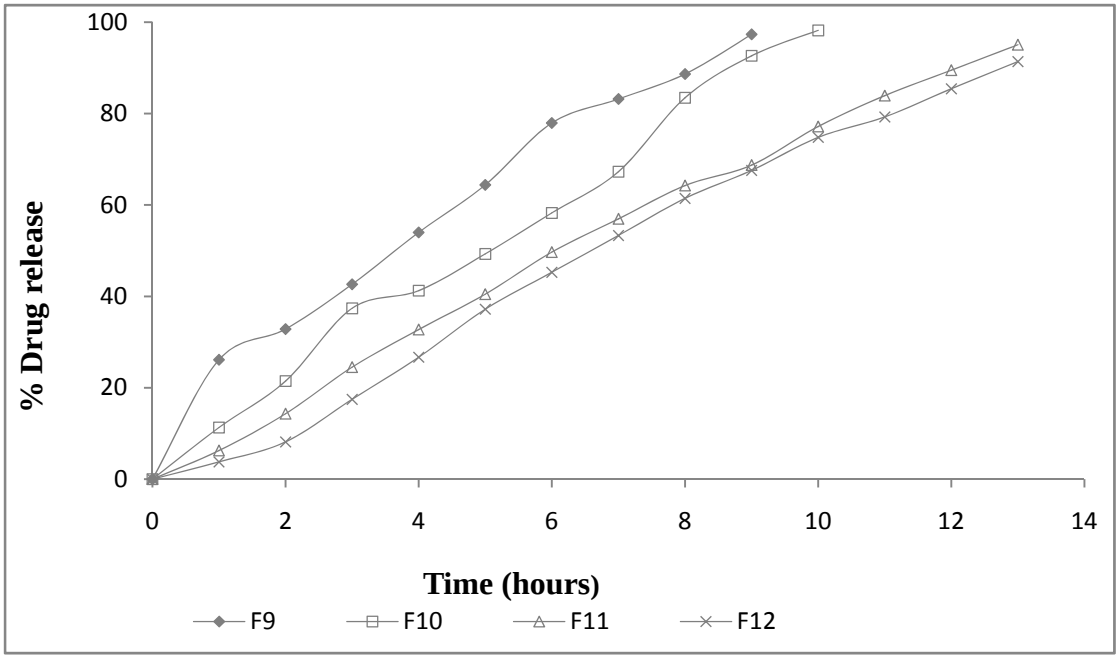


Fig-3 Dissolution profile of glimepiride with starch acetate

Drug release kinetics:

Table-9 Correlation co-efficients(r) of different mathematical models for formulations with carbopol 934P

Code	Zero	First	Higuchi	Peppas	
				r^2	n
F1	0.9483	0.9702	0.9845	0.5509	0.5261
F2	0.9711	0.9389	0.9698	0.6044	0.5791
F3	0.9691	0.9522	0.9851	0.6740	0.6376
F4	0.9834	0.945	0.9696	0.7433	0.7619
F5	0.9795	0.8822	0.9687	0.6436	0.6277
F6	0.9928	0.9123	0.9500	0.7065	0.7408
F7	0.9934	0.9175	0.9579	0.7601	0.7506
F8	0.993	0.9288	0.8844	0.9260	1.1853
F9	0.9736	0.8733	0.9706	0.6237	0.6534
F10	0.9926	0.7941	0.923	0.7832	0.9692
F11	0.9949	0.9004	0.9412	0.876	0.9701
F12	0.9921	0.9364	0.9189	0.9382	0.9991

SWELLING INDEX:

Table-10: %Swelling index of glimepiride buccal tablets in phosphate buffer pH 6.8

Formulation code	1 hr	2 hrs	4 hrs	6 hrs
F1	40.2 ±2.6	70.6 ±1.8	100.4 ±2.3	130.7 ±6.3
F2	50.3 ±1.5	80.1 ±3.4	123.1 ±1.6	159.5 ±5.7
F3	63.5 ±2.9	94.8 ±4.7	142.6 ±3.5	183.2 ±6.1
F4	84.6 ±5.4	114.5 ±3.1	165.7 ±3.9	207.6 ±7.4
F5	30.4 ±8.6	57.3 ±4.6	83.1 ±4.3	112.3 ±5.8
F6	43.9 ±7.2	72.2 ±2.5	98.3 ±5.6	134.1 ±4.9
F7	51.2 ±1.6	84.9 ±1.8	104.5 ±7.2	157.8 ±6.8
F8	64.5 ±2.3	97.2 ±2.2	128.4 ±5.3	164.4 ±7.2
F9	27.3 ±4.2	54.3 ±2.3	80.6 ±4.6	109.2 ±4.9
F10	40.5 ±6.2	69.6 ±3.6	95.2 ±5.6	131.8 ±5.3
F11	48.9 ±5.1	81.8 ±4.2	101.3 ±5.1	154.5 ±6.7
F12	61.6 ±2.6	94.2 ±1.5	125.8 ±4.8	171.4 ±4.5

DISCUSSION

Drug polymer compatibility studies

Fourier transform infrared radiation (FTIR)

Data obtained from compability study of drug and polymer by IR is shown in table-2. This showed that there is no chemical interaction taking place between drug and polymers.

Differential scanning calorimetry (DSC)

The thermograms obtained by subjecting the pure glimepiride and mixture of glimepiride with different polymers showed no possible drug polymer incompatibility. The DSC thermograph of pure glimepiride showed one sharp endothermic peak at 205.3^{o}C. In the DSC thermograms of mixture of glimepiride and the polymers, the pure drug peak was still present but slightly shifted from its original position which could be possibly due to an ionic interaction and this characteristic feature of drug melting suggested that there was no incompatibility. Some modification of drug peak, such as changes in area, shape or peak temperature were found, but they arose from mixing the components. Thus these minor changes in the melting endotherm in the drug could be due to the mixing of the drug and excipients which lower the purity of each component in the mixture. The data is given in table-3.

Pre-compression parameters evaluation for powder flow:

Bulk density may influence compressibility, tablet porosity, dissolution and other properties and depends on the particle size, shape and tendency to adhere together. The bulk density of granules was found to be between 0.27±0.01 to 0.41±0.06 g/cm^3. This indicates good packing capacity of granules and indicative of the flowability of the material. The tapped density was in the range of 0.29±0.09 to 0.43±0.05gm/cm^3, which indicate powder was not bulky. The angle of repose of the powder was in the range of 26.05 to 31.56, which indicate good flow of the powder and Carr's index was found to be in the range of 5 to 15 indicating compressibility of the tablet powder is good as reported in table-4.

POST-COMPRESSION PARAMETERS:

Thickness and Hardness:

All the formulations were evaluated for various parameters like thickness, and hardness of all tablets from batch F1 to F12 are shown in Table 5. As there was no much variation in thickness of tablets in each formulation, it shows that powder blends were consistent in particle size and uniform behavior during compression process. Thickness and diameter of tablets of all batches was measured by vernier caliper and there are no any changes in thickness and diameter of tablets respectively. Thickness was in range of 3.05±0.03 to 3.21±0.02.The hardness of tablet was measured by Monsanto hardness tester. The hardness was in range of 6.8 to 8.7kg/cm^2.

Friability test:

The values of friability are given in Table 5 and are within the limit. The tablets are within the limit and the slight variation in friability because of the variation in compression force applied and its total weight. The friability of tablets is also depends on type of filler and moisture contents in it. The friability was in range of 0.19±0.023 to 0.89±0.046%.

Uniformity of Weight:

The values of average weight are given in above Table 5 and are in within limits.

Drug content:

The values of drug content are given in Table 5. Drug content was in range of 95.52±0.21% to 101.2±1.44% indicating good content uniformity in the prepared formulation.

CONCLUSION

The drug and polymers were subjected to compability study using FT-IR and DSC, which suggested that there was no interaction between drug and polymers. The entire formulations were evaluated for different parameters like weight variation, content uniformity, hardness, thickness,

drug content and percentage friability and showed acceptable results. In vitro drug release studies revealed that release of glimepiride from different formulations varies with characteristics and composition of mucoadhesive polymers. The release of glimepiride from tablets was slow and spread over 14h. The decrease in glimepiride was dependent on the percent polymer in the tablet. The formulations containing HPMC K15M have shown more sustained drug release compared to rest of the formulation. The release kinetics show that the drug follows zero order release in allthe formulations. Analysis of drug release mechanism showed that the drug release followed non-Fickian diffusion.

REFERENCES

1. Amir H. Shojaei, Richard KC, XiaodiGuo, Beth AB, Richard AC. Systemic drug delivery via the buccal mucosal route. Pharm tech june 2001; 70-81.
2. Velmurugan S, Deepika B, Nagaraju k, Vinushitha S. Formulation and invitro evaluation of b uccal tablets of piroxicam. Int J Pharmtech res 2010;2(3): 1958-68.
3. M. S. Nolte & J. H. Karam, Pancreatic hormones and antidiabetic drugs. In: Katzung BG (eds). Basic and clinical pharmacology. 8th ed., Lange Medical Books/ McGraw-Hill Publishing Division, New York; 2001, 711-734.
4. S. N. Davis & D. K. Granner, Insulin oral hypoglycemic agents, and the pharmacotherapy of the endocrine pancreas. In: Hardman JG: Limbird LE (eds), The pharmacological basis of therapeutics. 9th ed., McGraw-Hill Co., New York; 1996, 1487-1517.
5. Y. Takahshi, K. Furuya, M. Iwata, H. Onishi, Y. Machida & S. Shirotake, Trial for transdermal administration of sulfonylureas. YakugakuZassi. 1997; 12:1022-1027.
6. S. Mutalik, & N. Udupa, Transdermal delivery of glibenclamide and glipizide: In vitro permeation studies through mouse skin. Pharmazie. 2002; 12:838-841.

7. Chowdary KPR, Radhaa GV. Synthesis, characterization and evaluation of starch acetate as rate controlling matrix for controlled release of nifedipine. Int J Chem Sci 2011; 9(2): 449-56.
8. Indian Pharmacopoeia 2007, vol 1, pg.241.
9. Martin A, Micro meritics. In: physical pharmacy. 4th ed. Philadelphia: lippincottwilliams&wilkins, 2001: 423-52.
10. Rajiv G. Pre-formulation: A need for dosage form design. Pharmainfo. Net; 2008; 6.
11. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. Philadelphia, pa: lea and febiger, 1987; 317-318.
12. Bhanja S, Ellaiah P, Martha SK, Singh P, Panigrahi, Bibhuti B, Das D. Design and in-vitro evaluation of mucoadhesive buccal tablets of repaglinide. Int J Pharma Sci Tech: 4(1), 2010; 42-53.
13. S. Mutalik, & N. Udupa, Formulation development, in vitro and in vivo evaluation of membrane controlled transdermal systems of glibenclamide. J. Pharm. Pharmaceut. Sci. 2005; 8(1):26-38.
14. VimalKY, AB Gupta, Raj K, JaideepSY, Brajesh K. Mucoadhesive polymers: means of improving the mucoadhesive properties of drug delivery system. J Chem Pharm Res 2010; 2(5):418-32.
15. Prasanth VV,SirishaM, SamTM, RinkuM. Buccal tablet as mucoadhesive drug delivery: an over view. J Pharm Res 2011; 4(3): 706-09.
16. Khairnar GA, SayyadFJ. Development of buccal drug delivery systembased on mucoadhesive polymers. IntJ Pharm Tech Res 2010; 2(1): 719-35.
17. Ammar HO, Salama HA, Ghorab M, Mahmoud AA. Formulation and biological evaluation of glimepiride–cyclodextrin–polymer systems. Int J Pharm 2006; 306: 129-38.