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DEVELOPMENT AND EVALUATION OF BUCCAL DRUG DELIVERY SYSTEM FOR POORLY WATER SOLUBLE DRUG, GLICLAZIDE

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Abstract

The main objective of the present work was to prepare solid dispersion of poorly water soluble drug GLICLAZIDE to enhance its in–vitro dissolution rate and aqueous solubility. Mucoadhesive drug delivery systems promote the residence time and act as sustained-release dosage forms. The aim of this work was to develop and characterize a buccoadhesive controlled-release tablet of gliclazide. The buccal route was chosen because of its good accessibility, robustness of the epithelium, facile removal of the dosage form, relatively low enzymatic activity, natural clearance mechanisms for elimination of the drug from buccal area, satisfactory patient acceptance, avoiding the hepatic first pass metabolism and increase in bioavailability. Hence it was envisaged to develop buccoadhesive dosage form of gliclazide using various buccoadhesive polymers

1. Introduction

Many drugs cannot be delivered effectively through the conventional oral route. Because after oral administration some of drugs are subjected to hepatic first pass metabolism, which often leads to a lack of significant correlation between membrane permeability, absorption and bioavailability. Difficulties associated with parenteral delivery and poor oral availability provided the impetus for exploring alternative routes for the delivery of such drugs. These include pulmonary, ocular, nasal, rectal, buccal, sublingual, and vaginal and transdermal routes of drug administration. In absence of external stimuli to facilitate absorption, use of these alternative routes has limited success. Various strategies have been implemented to promote the bioavailability of these drugs, including supplemental administration of enzyme inhibitors, use of absorption enhancers, novel formulation strategies and reversible chemical modifications. One of the determinant factors for absorption of drug is its dissolution which is influenced by solubility of drug in gastrointestinal fluid. Consideration of Noyes-Whitney equation provide some

hints as to how the dissolution rate of even very poorly water soluble compounds might be improved to minimize the limitations to oral bioavailability.

dc/dt =AD(Cs-C)/h

Where,

dc/d t = Rate of dissolution.

A = Surface area available for dissolution.

D = Diffusion coefficient of compound.

Cs = Solubility of compound in dissolution medium.

C = Concentration of drug in bulk of solution at time t.

H = Thickness of diffusion boundary layer adjacent to surface of the dissolving compound.

According to Noyes–Whitney equation analysis, the main possibilities for improving the dissolution are:

Increasing the surface area of drug.

Optimizing the wetting characteristics of compound surface.

Improving apparent solubility of drug.

Out of the various options, the most attractive option for increasing the release rate is improvement of solubility through formulation approaches.

2. Materials and methods

2.1. Materials

Sr. No.	**Chemicals and Reagents**	**Manufacturer**
1.	Gliclazide	Zhejiang Jiuzhou Pharma
2.	Chitosan	Noveon, USA
3.	Carbopol 934P	Lubrizol USA .
4.	Sodium alginate	Noveon, USA
5.	SodiumCarboxymethyl cellulose	Alkem Laboratories, Mumbai.

6.	Hydroxypropylmethylcellulose-K4M	Colorcon, Goa
7.	Ethyl cellulose	Colorcon, Goa
8.	Lactose (spray dried)	Neel Raj Agencies
9.	Talc	Aravali Minerals and Chemicals
10	Magnesium stereate	S.Kanth Healthcare Ltd.
11	Potassium dihydrogen orthophosphate	Loba chemie, India
12	Sodium hydroxide	Caliron Chemicals Ltd.

2.2 Preparation of calibration curve of Gliclazide

2.2.1 Preparation of phosphate buffer pH 6.6

Phosphate buffer pH 6.6 was prepared as per IP 1996.

2.2.2 Scanning for absorbance maxima

Scanning was done in phosphate buffer pH 6.6. Gliclazide solution 10µg/ml was prepared in phosphate buffer pH 6.6 and scanning was recorded in the wavelength range from 200-400 nm.

2.2.3 Calibration curve for Gliclazide

Gliclazide 10 mg was dissolved in 100 ml of pH 6.6 phosphate buffer solution. A series of dilutions were made from the above stock solution to get the solution of concentration ranging from 2 -20 µg/ml. The absorbance of solutions was measured spectrophotometrically at 228 nm.

2.3 Preparation of solid dispersions of gliclazide with PEG 6000 and gliclazide with poloxamer by solvent evaporation method

Solid dispersions of Gliclazide in PEG 6000 and poloxamer containing two different weight ratios (1:1, 1:2) and denoted as SD PEG (1:1, 1:2) and SD POL (1:1, 1:2) respectively were prepared by the solvent evaporation method. To a solution of gliclazide (1g) in dichloromethane (20ml), appropriate amount of PEG 6000 or poloxamer was added. The solvent was then evaporated at 45^{o}C and resulting residue was dried in hot air oven for 3 hours and stored for 24 hours in a desiccator subsequently, the dispersion was ground and passed through sieve No.150.

3. Results and discussion

3.1 Preparation of solid dispersions of gliclazide

Solid dispersions of gliclazide with PEG 6000 or poloxamer were prepared by solvent evaporation method. Solid dispersion of gliclazide with PEG 6000 or poloxamer prepared by melting was found to be sticky, waxy and hence difficult for processing of formulation development. The products of solvent evaporation method were found non-sticky and easy for processing in formulation of dosage form development.

3.2 Analysis of drug content in solid dispersions and physical mixtures

The solid dispersion or physical mixtures equivalent to 25 mg of gliclazide were used to determine drug content. The drug content of solid dispersions and physical mixtures is shown in table 10.

Table 10: Drug content in solid dispersions and physical mixtures.

Sr. No.	**Solid dispersion or physical mixture**	**Drug content (%) (Mean ± S.D.)**
1	PM PEG 1:1	96.65 ± 0.65
2	PM PEG 1:2	96.98 ± 1.43
3	PM POL 1:1	97.76 ± 0.87
4	PM POL 1:2	97.32 ± 1.05
5	SD PEG 1:1	96.78 ± 0.94
6	SD PEG 1:2	98.89 ± 0.76
7	SD POL 1:1	96.87 ± 0.54
8	SD POL 1:2	98.78 ± 0.65

3.3 Saturation solubility studies

The saturation solubility's of drug, physical mixtures and solid dispersions in pH 1.2, 6.6 and 7.4 buffer are shown in table 11.

Table-11: Solubility of gliclazide in physical mixtures and solid dispersions in different pH 1.2, 6.6 and 7.4 buffer solutions.

Sr. No.	Sample	Solubility of gliclazide (mg/ml)		
		pH 1.2 buffer	pH 6.8 buffer	pH 7.2 buffer
1	Gliclazide	0.79 ± 0.05	0.57 ± 0.04	0.45 ± 0.04
2	PM PEG 1:1	0.81 ± 0.01	0.52 ± 0.02	0.45 ± 0.04
3	PM PEG 1:2	0.82 ± 0.01	0.59 ± 0.01	0.51 ± 0.02
4	PM POL 1:1	0.82 ± 0.03	0.54 ± 0.04	0.56 ± 0.05
5	PM POL 1:2	0.83 ± 0.06	0.67 ± 0.03	0.54 ± 0.05
6	SD PEG 1:1	1.54 ± 0.02	0.85 ± 0.05	0.83 ± 0.02
7	SD PEG 1:2	1.79 ± 0.03	1.02 ± 0.03	1.01 ± 0.04
8	SD POL 1:1	2.54 ± 0.02	1.49 ± 0.02	1.47 ± 0.04
9	SD POL 1:2	2.94 ± 0.04	2.32 ± 0.05	2.16 ± 0.03

3.4 Dissolution studies

As shown in figure 6.2 gliclazide solid dispersions presented better dissolution performance over the corresponding physical mixtures and the pure drug. This may be due to the improved wettability of drug particles and intrinsically higher rate of dissolution of the soluble polymer component of the solid dispersion. The dissolution profiles of gliclazide, physical mixtures and solid dispersions in pH 6.6 are shown in table 12.

Table-12: *In-vitro* dissolution profile of gliclazide, physical mixtures and solid dispersions of gliclazide in pH 6.6 phosphate buffer

Sr. No	Sample	Cumulative % drug release					
		15 min	30 min	45 min	60 min	90 min	120 min
1	Gliclazide	4.08 ± 0.25	7.56 ± 0.38	10.48 ± 0.50	12.54 ± 0.59	17.74 ± 0.80	21.15 ± 0.95
2	PM PEG 1:1	19.98 ± 0.01	31.21 ± 0.45	37.59 ± 0.21	43.29 ± 0.66	52.04 ± 0.13	58.91 ± 0.15
3	PM PEG 1:2	21.76 ± 0.17	37.59 ± 0.13	43.09 ± 1.81	51.47 ± 0.75	61.71 ± 0.53	69.91 ± 0.45
4	PM POL 1:1	37.13 ± 0.02	43.58 ± 019	49.17 ± 0.4	52.65 ± 0.11	59.16 ± 0.6	64.56 ± 0.5
5	PM POL1:2	52.94 ± 0.09	67.0 ± 0.01	74.33 ± 0.21	79.14 ± 0.89	86.17 ± 0.43	89.89 ± 0.83
6	SD PEG 1:1	23.33 ± 0.12	39.85 ± 0.54	50.02 ± 0.32	56.12 ± 0.37	57.05 ± 0.85	61.32 ± 0.71
7	SD PEG 1:2	27.54 ± 0.19	43.42 ± 0.2	53.61 ± 0.1	59.17 ± 0.37	64.46 ± 0.62	70.66 ± 0.43
8	SD POL 1:1	37.65 ± 0.27	51.44 ± 0.32	61.40 ± 0.03	66.64 ± 0.58	74.69 ± 0.83	78.06 ± 0.17
9	SD POL1:2	50.71 ± 0.15	65.75 ± 0.37	74.56 ± 0.53	78.76 ± 0.26	85.99 ± 0.39	91.58 ± 0.21

3.5 Characterization of solid dispersion of gliclazide

Infra red spectroscopy

The FT-IR spectrum of blend of drug with carriers did not show the presence of any additional peaks for new functional groups indicating no chemical interaction between gliclazide and carriers.

The FT- IR spectrum of drug and blend containing drug and carrier is shown in figure 6.4 to 6.8 respectively.

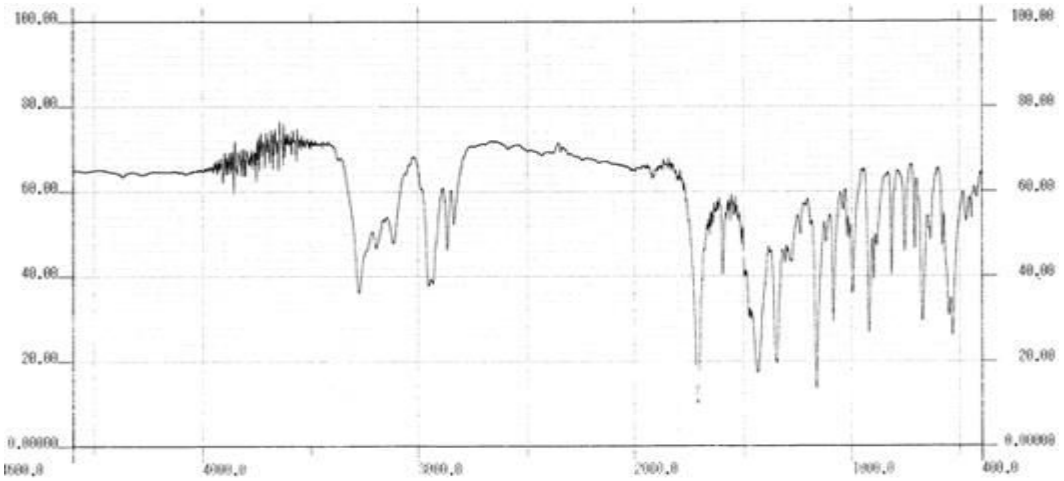


Figure 6.4 FT-IR spectra of gliclazide.

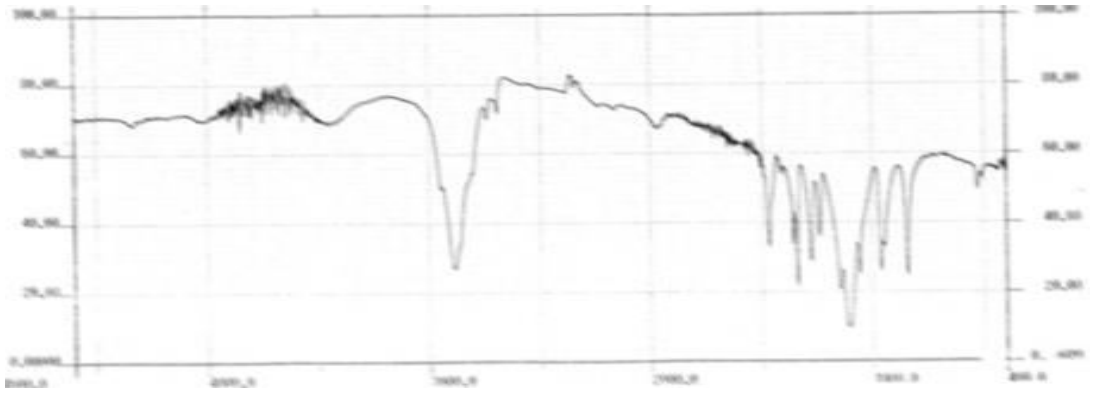


Figure 6.5 FT-IR spectra of PEG 6000.

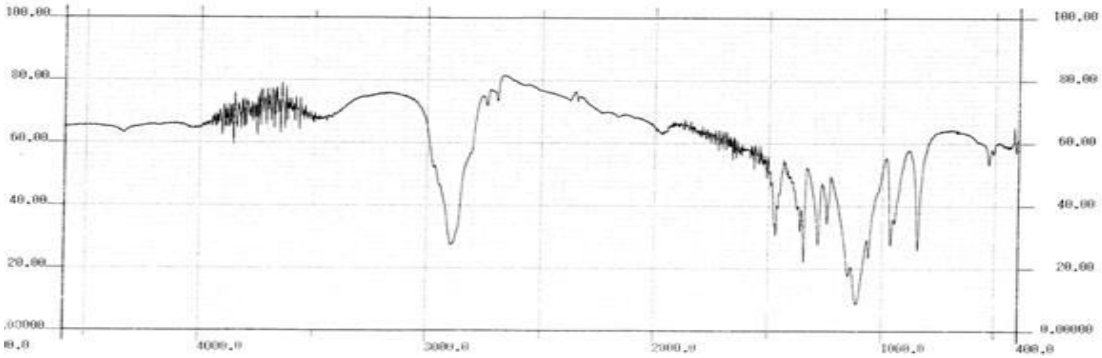


Figure 6.6 FT-IR spectra of Poloxamer.

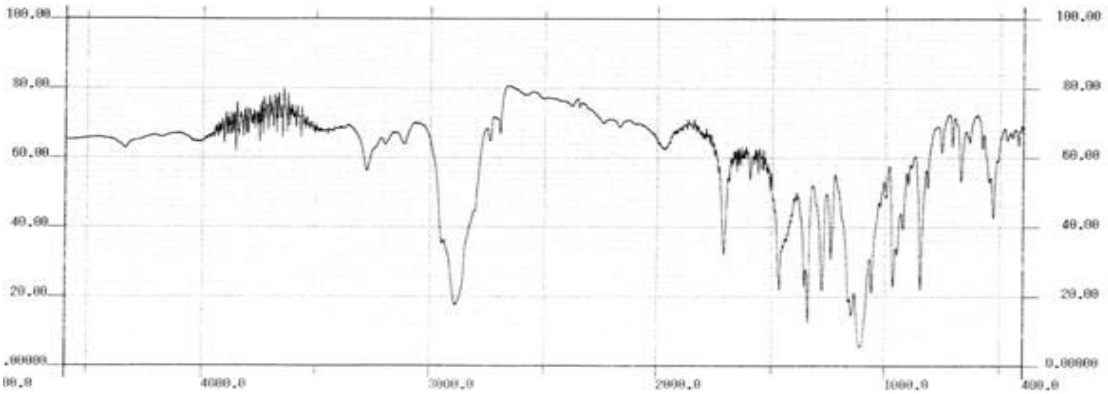


Figure 6.7 FT-IR spectra of solid dispersion of gliclazide and PEG 6000 (1:2 ratio).

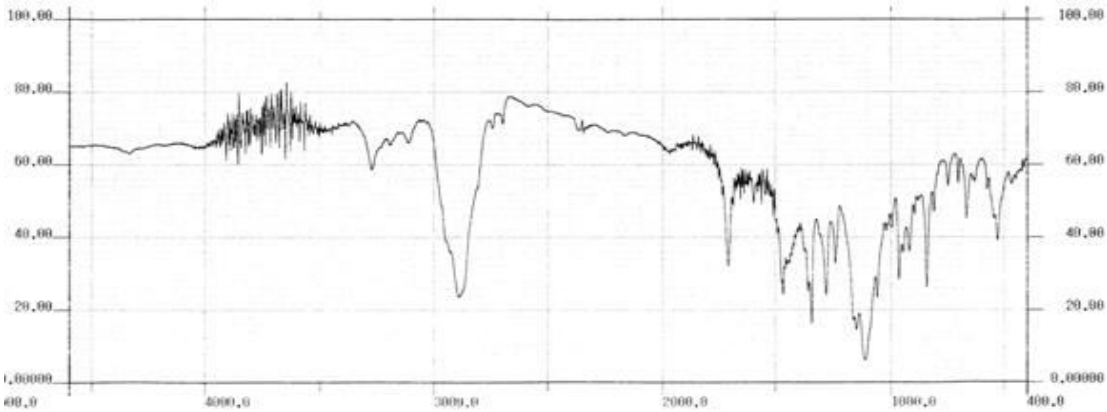


Figure 6.8 FT-IR spectra of solid dispersion of gliclazide and Poloxamer (1:2 ratio).

3.6 Evaluation of buccal tablets

3.6.1 Physical parameters of buccal tablets

Evaluation of various parameters of buccoadhesive tablets was done for hardness, thickness, weight variation, friability, drug content and surface pH. The physical parameters of different formulation batches are shown in table 13.

Table-13: Physical parameters of formulation batches F_1 to F_8.

Formulation Batch	Hardness (Newton)	Thickness (mm)	Weight Variation (mg)	Friability (%)	Drug Content (%)	Surface pH
F_1	39.5	2.42	149.90 ± 0.98	0.64	99.49 ± 0.75	6.83
F_2	36.3	2.39	149.65 ± 1.27	0.55	98.31±1.11	6.63
F_3	38.2	2.61	148.85 ± 1.02	0.74	98.43 ±0.86	6.27
F_4	31.2	2.39	149.99 ± 1.43	0.62	99.20 ±0.35	6.40
F_5	38.3	2.42	150.07 ± 1.12	0.71	98.86 ±0.69	6.82
F_6	33.2	2.36	149.46 ± 1.06	0.69	99.63 ±0.95	6.64
F_7	31.8	2.35	149.17 ± 1.72	0.56	99.23 ±0.55	6.27
F_8	39.2	2.34	150.10 ± 1.61	0.51	98.69 ±0.89	6.34

Table-14: Swelling index of batches F_1 to F_4.

Time (hours)	Swelling index			
	F_1	F_2	F_3	F_4
1	1.27 ± 0.14	1.15 ± 0.11	0.69 ± 0.20	1.29 ± 0.21
2	1.87 ± 0.09	1.87 ± 0.10	1.18 ± 0.11	1.55 ± 0.17
3	2.36 ± 0.08	2.23 ± 0.12	1.45 ± 0.15	1.95 ± 0.11
4	2.63 ± 0.12	2.34 ± 0.16	1.62 ± 0.13	Eroded
5	3.15 ± 0.07	2.79 ± 0.18	Eroded	Eroded
6	3.42 ± 0.11	2.90 ± 0.04	Eroded	Eroded
7	3.87 ± 0.10	3.22 ± 0.09	Eroded	Eroded

8	3.98 ± 0.13	3.30 ± 0.07	Eroded	Eroded

Table 15 Swelling index of batches F_5 to F_8

Time (hours)	Swelling index			
	F_5	F_6	F_7	F_8
1	1.22 ± 0.10	1.35 ± 0.14	1.18 ± 0.16	1.23 ± 0.20
2	1.38 ± 0.06	1.68 ± 0.12	1.71 ± 0.25	1.60 ± 0.36
3	1.81 ± 0.14	2.28 ± 0.15	1.77 ± 0.21	1.73 ± 0.23
4	2.19 ± 0.17	2.42 ± 0.20	2.37 ± 0.15	Eroded
5	2.64 ± 0.11	2.81 ± 0.16	Eroded	Eroded
6	2.76 ± 0.16	3.35 ± 0.27	Eroded	Eroded
7	3.15 ± 0.11	3.50 ± 0.19	Eroded	Eroded
8	3.32 ± 0.06	3.78 ± 0.17	Eroded	Eroded

3.6.2 Swelling studies of buccal tablets

The degree of swelling of bioadhesive polymers is an important factor affecting adhesion. Uptake of water results in relaxation of the originally stretched entangled or twisted polymer chains, resulting in exposure of all polymer bioadhesive sites for bonding to occur. The faster the swelling of the polymer, the faster the initiation of diffusion and formation of adhesive bonds resulting in faster initiation of bioadhesion. Figure 6.9 and 6.10 shows the swelling indices of formulation batches F_1 to F_8.

The results of swelling studies are represented in tables 14 and 15 and figures 6.9 and 6.10 respectively for all formulation batches F_1 to F_8. The formulation batches F_3, F_4, F_7 and F_8 which contains CP-934P and sodium CMC has shown erosion after 4 and 3 hours respectively. Maximum swelling was seen in the formulation batches F_1 which contain chitosan. It was also observed that swelling index decreased in order of chitosan > sodium alginate > carbopol > sodium CMC.

Figure 6.9: Swelling indexes of batches F_1 to F_4

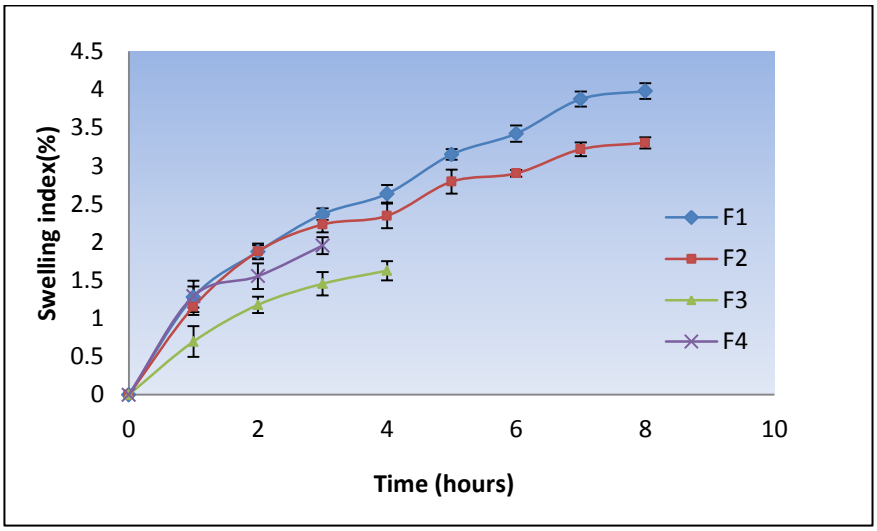
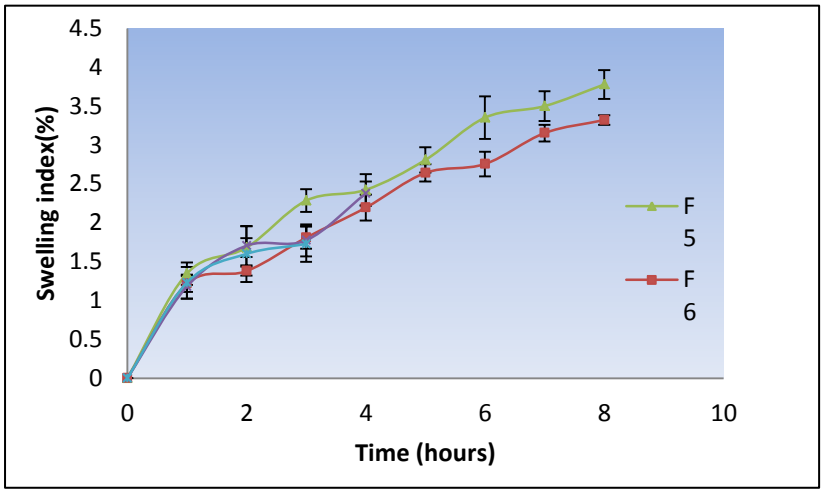


Figure 6.10: Swelling index of batches F_5 to F_8



3.6.3 Bioadhesion studies of buccal tablets

The bioadhesion study of tablets was performed by measuring bioadhesion force using porcine buccal mucosa. The bioadhesion force for the formulation batches F_1 to F_8 is shown in figure 6.11.

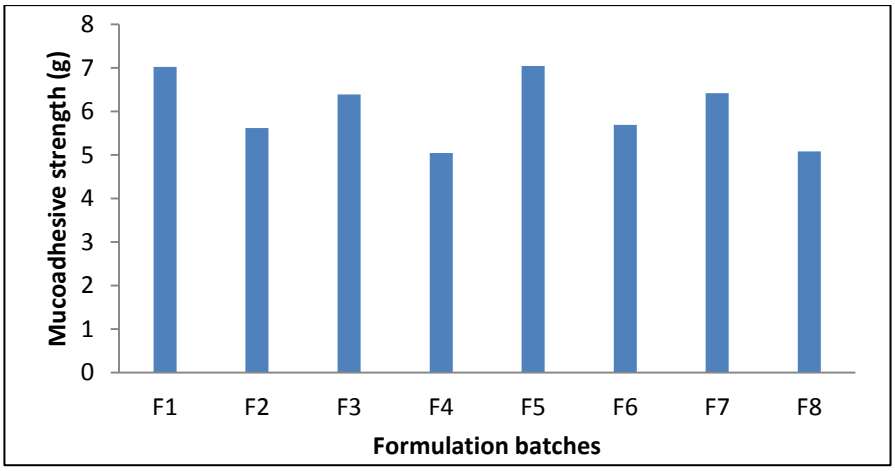


Figure 6.11 Bioadhesion force of formulation batches F_1 to F_8

The maximum bioadhesion force was observed in formulation F_5 (4.486N) containing chitosan and hydroxypropy methylcellulose, formulation batches containing sodium alginate and sodium CMC has shown the lowest bioadhesion force. The bio-adhesive strength of the formulations changes with type of polymer and also those containing the same polymer was found to be a function of the concentration of the polymer. It was also observed that bioadhesion force was decreased in order of chitosan > CP-934P > sodium alginate > sodium CMC.

3.6.4 In-vitro drug release studies

Drug release from hydrophilic matrices is dependent on factors like swelling and dissolution of the polymers, giving rise to mass erosion of the system, concomitantly with dissolution and diffusion of drug. Initially, the matrix thickness increases due to hydration and swelling of polymer then the matrix thickness decreases and finally disappear due to polymer dissolution as well as dissolution of the drug. The release profile of gliclazide from formulation batches F_1 to F_8 is shown in figure respectively.

3.6.5 Evaluation of buccal tablets with backing layer

a. Physical parameters

Evaluation of various parameters of buccoadhesive tablets was done for hardness, thickness, weight variation, friability, drug content and surface pH. The physical parameters of different formulation batches are shown in table 19.

Weight variation results were found to comply as per IP. The hardness of tablets was found to be 40-50N.

The friability of tablets was found to be 0.41-0.61 %.

Thicknesses of tablets were found to be 2.73–2.97 mm.

The surface pH of the tablets was found to be 6.26 -6.83

b. Swelling studies of buccal tablets with backing layers

To study the effect of backing layer on swelling index of buccal tablets containing backing layer the swelling index of formulation batches F_9 to F_{16} is shown in figure 6.14 and 6.15.

As shown in figure, it was observed that the buccoadhesive tablets containing backing layer of different composition has shown no significant affect on swelling index of tablet. The small reduction in swelling index initially was found due to the backing layer of tablets which retards the entry of water into core and increase in hardness of tablets.

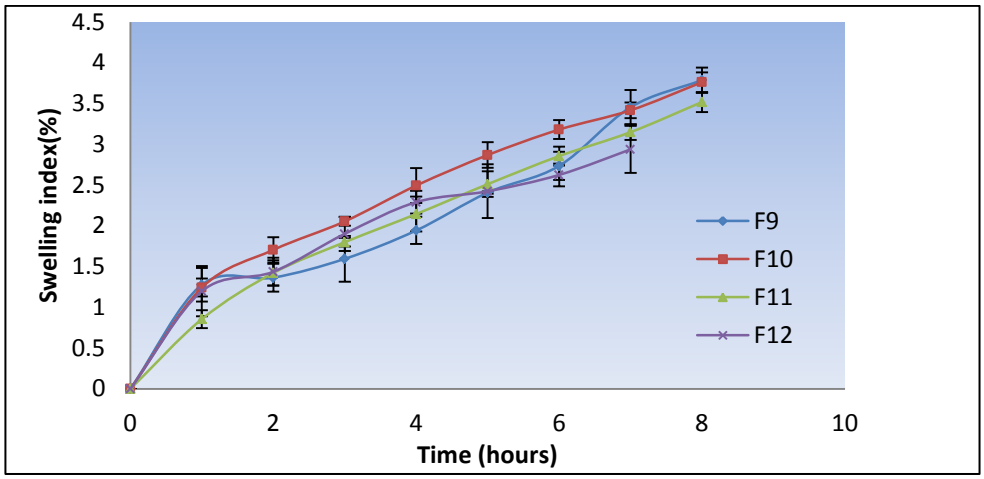


Figure 6.14 Swelling index of batches F_9 to F_{12}

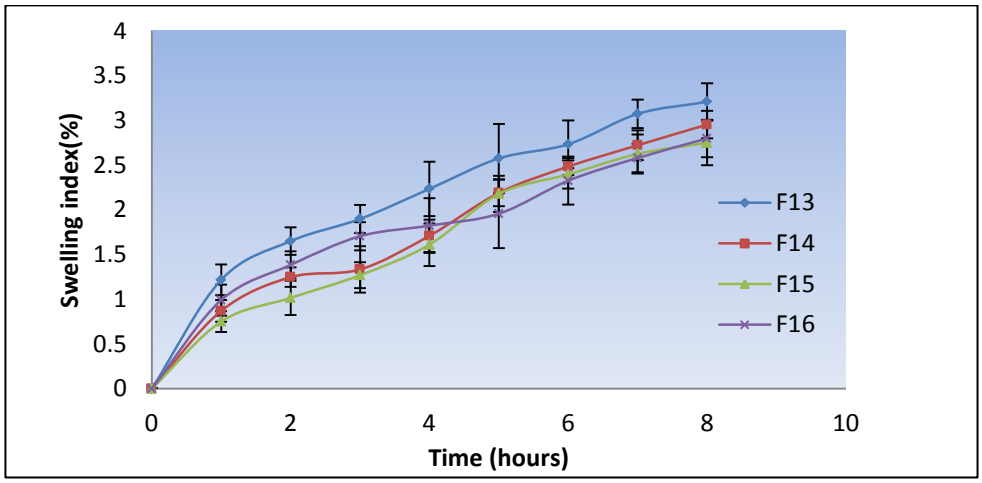


Figure 6.15 Swelling index of batches F_{13} to F_{16}

c. Bioadhesion studies of buccal tablets with backing layer

The effect of backing layer on bioadhesion force of bilayered formulation batches F_9 to F_{16} is shown in table 22 and in figure 6.16.

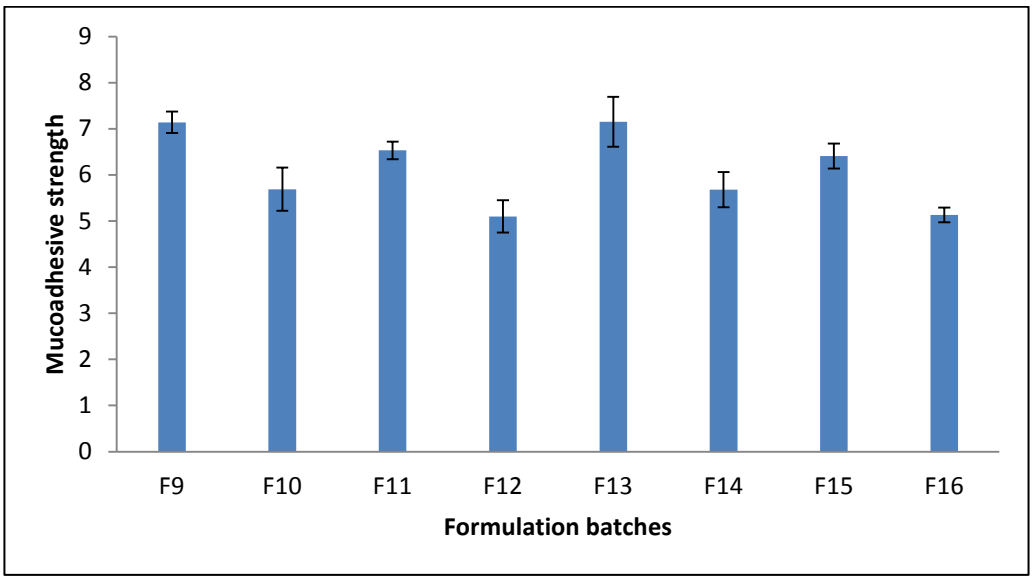


Figure 6.16 Bioadhesion force of formulation batches F_9 to F_{16}

Table 22 Bioadhesion strength of batches F_9 to F_{16}

Formulation batches	Bioadhesion strength (g)	Bioadhesion force (N) ±SD
F_9	7.14 ± 0.23	0.070
F_{10}	5.69 ± 0.47	0.056
F_{11}	6.53 ± 0.19	0.064
F_{12}	5.10 ± 0.35	0.050
F_{13}	7.18 ± 0.54	0.071
F_{14}	5.68 ± 0.38	0.055
F_{15}	6.41 ± 0.27	0.062
F_{16}	5.17 ± 0.16	0.051

Formulation batches F_9 to $F_{16,}$ having backing layer of ethyl cellulose did not show any significant differences in bioadhesion force. The maximum bioadhesive force among the formulations F_9 to F_{16} was observed in the formulation batch $F_{13.}$

It was observed that, formulation batches F_9 to F_{16} having backing layer of ethyl cellulose did not affect bioadhesive force significantly.

3.6.6 Release kinetics studies

The mechanism of drug release from tablet was determine by fitting the *in-vitro* release profile of optimized batches with zero order, first order, Matrix, peppas and Hixon-Crowell models. The obtained correlation coefficient is given in the following table 26.

Table 26 Correlation coefficient values of drug release kinetics of formulation batches.

Formulation	Zero order	First order	Matrix	Korsmeyer-Peppas	Hixson-Crowell
F1	0.9374	0.9316	0.9142	**0.9982**	0.9667
F2	0.9257	0.9377	0.9084	**0.9964**	0.9680
F3	0.9427	0.9867	0.9724	0.9954	**0.9979**
F4	0.9727	0.9855	0.9801	0.9948	**0.9963**
F5	0.9667	0.7684	0.9088	**0.9997**	0.8992
F6	0.9538	0.8104	0.9019	0.9824	**0.9938**
F7	0.9311	0.8909	0.9605	**0.9960**	0.9670

F8	0.9868	0.9143	0.9688	**0.9983**	0.9734
F9	0.9557	0.9370	0.9141	**0.9978**	0.9691
F10	0.9378	0.9272	0.9156	0.9762	**0.9953**
F11	0.9458	0.9078	0.9067	**0.9988**	0.9533
F12	0.9668	0.9411	0.9144	0.9878	**0.9916**
F13	0.9465	0.7886	0.9088	**0.9970**	0.9088
F14	0.9895	0.8117	0.8892	**0.9965**	0.9112
F15	0.9939	0.8728	0.9592	**0.9989**	0.9555
F16	0.9877	0.8875	0.9681	**0.9986**	0.9636

In-vitro drug release studies of buccal tablets with backing layer

Effect of backing layer of ethyl cellulose on drug release from buccal tablets was studied in the formulation batches F_9 to F_{16} is shown in figures 6.17 and 6.18. Figure 6.18 shows the release profile of drug from F_9 to F_{16} formulation batches shown unidirectional drug release over the period of 8 hours.

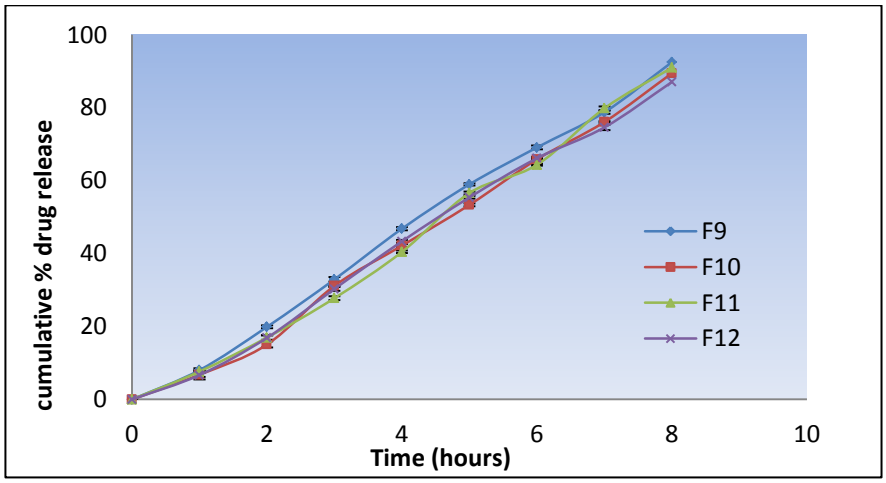


Figure 6.17 Cumulative % drug releases of batches F_9 to F_{12}

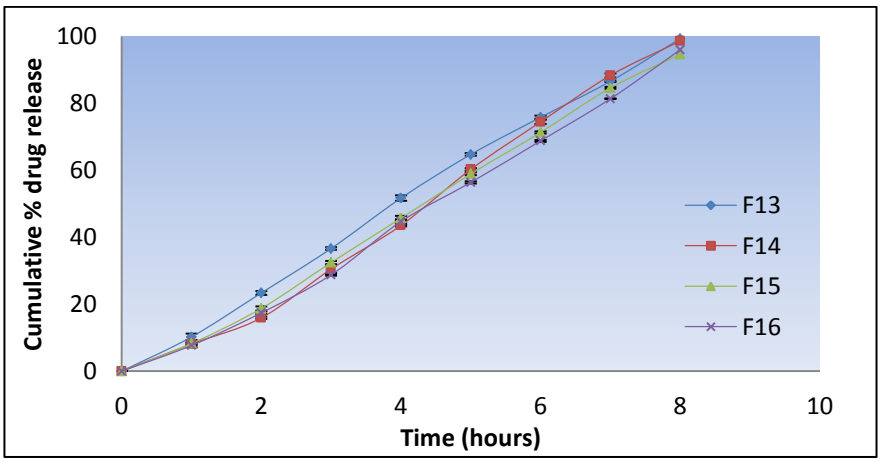


Figure 6.18 Cumulative % drug releases of batches F_{13} to F_{16}

3.6.7 Stability studies

The stability studies of the optimized formulation (F_{13}) of buccoadhesive tablets with backing layer revealed that no significant changes in the physical parameters, bioadhesive force and released profile when stored at temperature and humidity conditions of 40 ± 2°C/ 75 ± 5 %RH and at room temperature.

3.6.8 Bioadhesion Studies

The optimum formulation did not show any significant change in bioadhesion force after 60 days when kept at 40°C. The bioadhesion force results for stability study has shown in table 28 and in figure 6.21

Table 28 Bioadhesion force of formulation batch F_{13} at room temperature and at 40 °C

Parameter	**Room Temperature**		**40 ^{0}C**
	0 Day	30 Day	30 Day
Bioadhesive strength (g)	7.18 ± 0.54	7.17 ± 0.63	7.14 ± 0.47
Bioadhesive force (N)	0.071	0.070	0.070

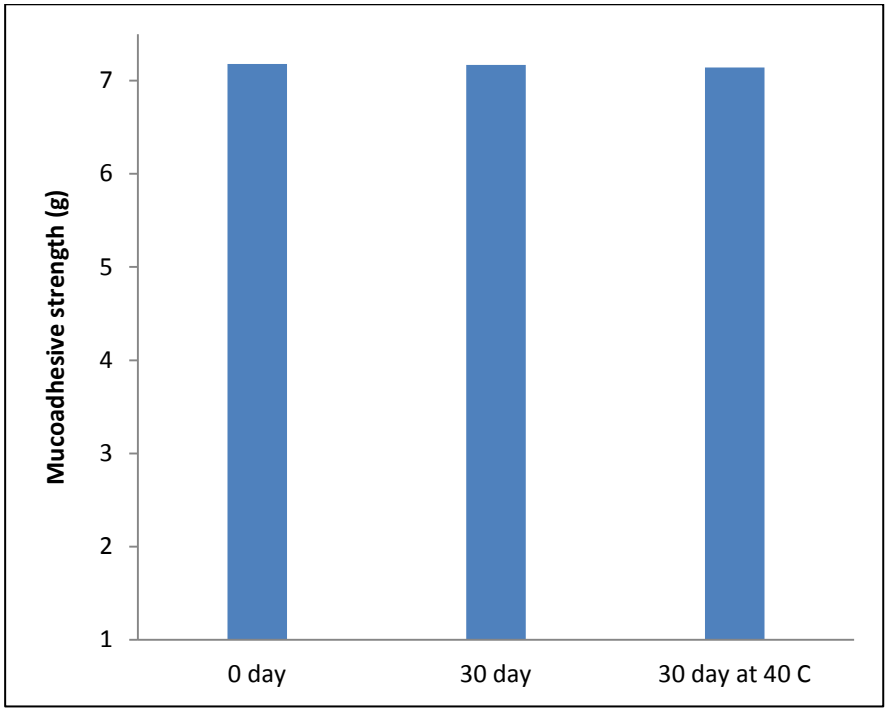


Figure 6.21 Bioadhesive force of formulation batch F_{13} at room temperature and at 40^0 C

3.6.9 *In-vitro* drug release studies

The optimum formulation did not show any significant changes in drug release profile after 30 days when kept at 40°C. The drug release data for stability study is shown in table 29 and in figure 6.22 and 6.23

Table 29 Cumulative % drug released of formulation batch F_{13} at room temperature and at 40°C

Time (hours)	Cumulative % drug released		At 40^0 C
	0 day	30 days	30 days
1	10.238 ± 0.63	10.059 ± 0.47	10.089 ± 0.37
2	23.369 ± 0.98	23.287 ± 0.73	22.779 ± 0.65
3	36.648 ± 0.59	35.576 ± 0.46	36.134 ± 0.49
4	51.705 ± 0.41	50.695 ± 0.93	50.237 ± 0.58
5	63.738 ± 0.82	61.649 ± 0.79	61.658 ± 0.76
6	75.841 ± 0.38	74.725 ± 0.28	73.874 ± 0.64
7	86.591 ± 0.47	84.478 ± 0.41	85.731 ± 0.38
8	99.345 ± 0.25	98.247 ± 0.63	98.786 ± 0.43

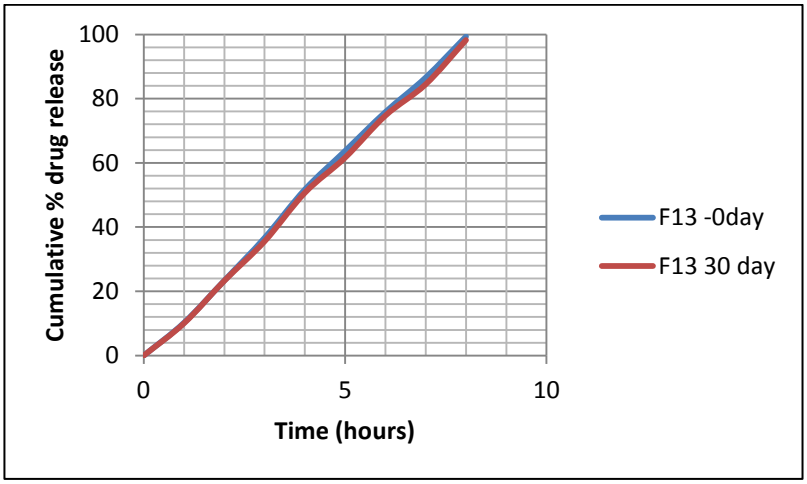


Figure 6.22 Drug release profile of formulation batch F_{13} at room temperature.

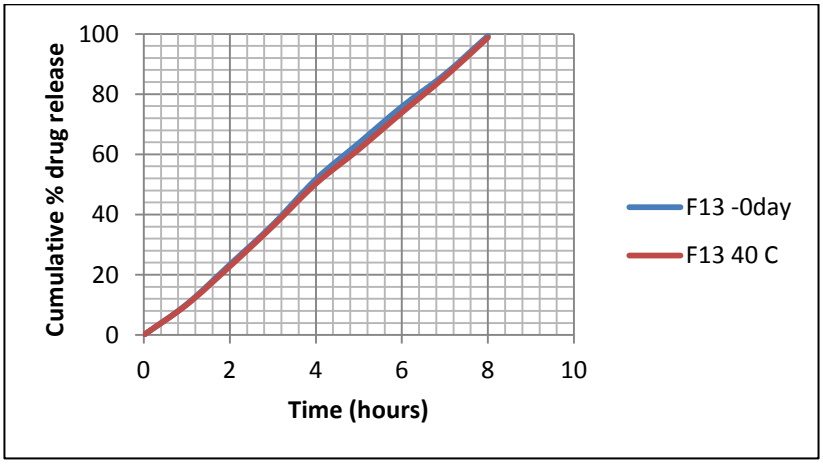


Figure 6.23 Drug release profile of formulation batch F_{13} at 40^oC temperature.

Improving the dissolution characteristics of poorly water soluble drug is important to achieve better bioavailability and reduced side effects. Solid dispersion is one of the best promising approach in this direction.

The buccal route has gained significant attention because of its good accessibility, robustness of the epithelium, facile removal of the dosage form, relatively low enzymatic activity, and natural clearance, mechanisms for elimination of the drug from buccal area, satisfactory patient acceptance and avoiding the hepatic first pass metabolism.

Gliclazide is second generation oral hypoglycaemic used in the treatment of diabetes. It is practically insoluble in water and its absorption is dissolution rate limited. Gliclazide gives negligible release due to its poor aqueous solubility. To enhance the dissolution rate of gliclazide, solid dispersion of gliclazide were prepared using the carriers PEG 6000 and poloxamer. Gliclazide is extensively metabolized in liver to metabolite without significant hypoglycemic activity. So it is rational to develop buccoadhesive dosage form of gliclazide to avoid its first pass effect and to increase its bioavailability.

Solid dispersion of gliclazide were prepared using the carriers PEG 6000 and poloxamer in 1:1 and 1:2 ratio by solvent evaporation method. It was observed that solid dispersion SD POL 1:2 gave the maximum drug release in 2 hours.

Bioadhesive polymers were selected on the basis of their mucoadhesive properties and non-toxicity. The chitosan, carbopol-934P, sodium alginate, sodium CMC and hydroxylpropyl methylcellulose were used in combination.

Buccoadhesive tablets with and without backing layer were prepared by direct compression method. Formulations batches were evaluated for physical parameter, swelling studies, bioadhesion studies and *in-vitro* drug release. Bioadhesion studies were carried out to determine mucoadhesive potential of prepared tablets.

The buccoadhesive tablets without backing layer were evaluated for *in-vitro* drug release study for period of 8 hours using USP type- II apparatus, it was observed that tablets containing chitosan has shown faster rate of drug release from the tablets. The formulation batch prepared using poloxamer solid dispersion containing chitosan has shown maximum drug release rate and bioadhesion.

The prepared batches were back coated with Ethocel and the effect of backing layer on bioadhesive potential, swelling index, and *in-vitro* drug release was studied.

It was concluded that there was no significant effect of backing layer on bioadhesive force of tablets. There was slightly change on swelling index of tablets due to backing layer. The buccoadhesive tablets with backing layer shown unidirectional drug released from the tablets.

The *in-vitro* diffusion study on porcine buccal mucosa shows maximum amount of drug gets diffused through buccal mucosa within 8 hours.

The stability studies were conducted on most promising formulation batch F_{13} under accelerated storage condition of temperature and humidity, no significant reduction in drug content and bioadhesion force were found over a period of one month.

Thus, it can be concluded that the present studies established the usefulness of buccoadhesive dosage form as potential alternative to conventional and form for gliclazide.

4. Conclusion

Improving the dissolution characteristics of poorly water soluble drug is important to achieve better bioavailability and reduced side effects. Solid dispersion is one of the best promising approach in this direction.

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