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DESIGN, DEVELOPMENT AND CHARACTERIZATION OF MUCOADHESIVE BILAYER TABLETS OF ACARBOSE

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ABSTRACT

Among the various routes of drug delivery, the oral route is perhaps the most preferred by patients and clinicians alike. However, pre oral administration of drugs has disadvantages, such as hepatic first-pass metabolism and enzymatic degradation within the gastrointestinal tract (GIT). So, there has been a growing interest in the use of delivery of therapeutic agent through various transmucosal routes to provide a therapeutic amount of drug to the proper site in body to promptly achieve and then maintain the desired concentration. In the present investigation buccal bilayer tablets of Acarbose were prepared by direct compression method by using polymers HPMC K_4M and HPMC $K_{15}M$.The prepared tablets were evaluated for physical parameters like appearance, hardness, thickness, weight variation, friability, swelling index and surface pH; biological parameter-Mucoadhesive strength; and other parameters such as drug content uniformity, *in vitro* release, short-term stability and drug excipient interactions (FTIR). Among ten formulations, the formulation $BTA15_1$ containing HPMC $K_{15}M$ was found to be promising, which showed $t_{25\%}$, $t_{50\%}$ and $t_{70\%}$ values of 1.12, 4.24 and 5.48 h respectively and *in vitro* drug release of 93.28% in 8 h along with satisfactory bioadhesion strength (6.40 g). Stability studies on the promising formulation indicated that there are no significant changes in drug content and *in vitro* dissolution characteristics ($p<0.05$). Infrared-spectroscopic studies indicated that there are no drug-excipient interactions. The prepared buccal bilayer tablets of Acarbose could stay in the buccal for a longer period of time, which indicate a potential use of buccal tablets of Acarbose for treating of type 2 diabetes.

INTRODUCTION

Oral drug delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, convenient and most economic method of drug delivery having the highest patient compliance and preferred over conventional capsules and tablets. Their demand is progressively increasing and their product pipelines are fastly intensifying. [1] Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either local or systemic action. All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage form (solid dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology.[3,4] Among the various routes of drug delivery, the oral route is perhaps the most preferred by patients and clinicians alike.

However, peroral administration of drugs has disadvantages, such as hepatic first-pass metabolism and enzymatic degradation within the gastrointestinal tract (GIT). So, there has been a growing interest in the use of delivery of therapeutic agent through various transmucosal routes to provide a therapeutic amount of drug to the proper site in body to promptly achieve and then maintain the desired concentration. Consequently, other absorptive mucosa is considered as potential sites for drug administration. Transmucosal routes of drug delivery (i.e. the mucosal linings of the oral, nasal, rectal, vaginal and ocular cavities) offer distinct advantages over peroral administration for systemic effect.[5]

MUCOADHESIVE DRUG DELIVERY SYSTEMS: [6]

Bioadhesion can be described as adhesion of artificial substances to biological substrates such as adhesion of polymers to skin or other soft tissue. These may be defined as drug delivery systems, which utilize the property of bioadhesion of certain water soluble polymers which become adhesive on hydration and hence can be used for targeting of drug to particular regions of body for extended periods of time. The Mucoadhesive drug delivery system includes following: Buccal drug delivery system, Rectal delivery system, Oral delivery system Nasal delivery system, Vaginal delivery system Ocular delivery system

Overview of oral cavity: [7-12] Oral cavity is that area of mouth delineated by the lips, cheeks, hard palate, soft palate and floor of mouth. The oral cavity consists of two regions. Outer oral vestibule, which is bounded by cheeks, lips, teeth and gingival, Oral cavity proper, which extends from teeth and gums back to the faces with the roof comprising the hard and soft palate. The tongue projects from the floor of the cavity. The Objective of the present research work is to formulate and evaluate Mucoadhesive bilayer tablets containing Acarbose as a drug using different polymers with different ration to avoid hepatic first pas metabolism and to increase bioavailability of drug.

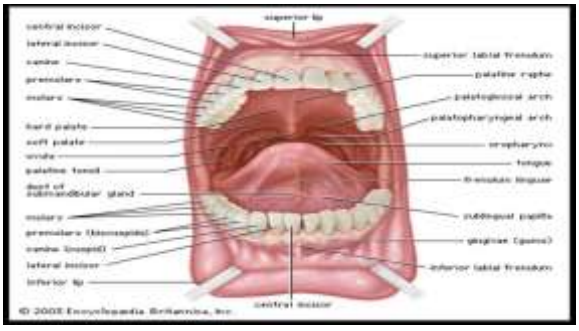

Figure-1: Structure of the oral cavity

Acarbose (INN, trade name Precose) is a drug used with a proper diet and exercises program to control high blood sugar in people with type 2 diabetes. Acarbose is indicated for the treatment of diabetic dyslipidemia and hypertriglyceridemia with type 2 diabetes mellitus not controlled by statin therapy. It has also shown favorable Anti-diabetic medication property by reducing the fasting plasma glucose and HBA1c in diabetes patients. The conventional dosage forms available are associated with bioavailability problem due to extensive first pass metabolism & where in nonsteroidal anti-inflammatory agent area also characterized by biological half life, due to which frequency of dosing is increased, which results in patient incompliance. In order to overcome these draw backs drugs can be developed inform of Mucoadhesive drug delivery system. Buccal delivery of drugs provide an attractive alternative to the oral route of drug administration ,particularly in overcoming deficiencies such as high first pass metabolism and drug degradation in the harsh environment.

MATERIAL AND METHODS

Materials: Acarbose was a gift sample from Cipla, limited Goa. HPMC K_4 M, HPMC K_{15} M, are received sample from Lupin pharmaceuticals Ltd. Aurangabad. Carbopol 934p, Poly Vinyl Pyrrolidine-K30 are purchased from Sd Fine chemicals Ltd. Mumbai. All other ingredients used were analytical grade.

Formulation of Buccal Bilayer Tablets of Acarbose: Direct Compression Method: [13,14,15] Buccal Bilayer Tablets of Acarbose were prepared by direct compression method, using HPMC K_4M and HPMC $K_{15}M$ polymers in different ratios. According to the formulae given in Table 1and 2

EVALUATION OF TABLETS [104,105]

Tablets were subjected to evaluation of properties including drug content uniformity, weight variation, thickness, and tablet hardness, friability, and disintegration time and *in-vitro* drug release studies.

Weight Variation: The weight of the tablet being made was routinely determined to ensure that a tablet contains the proper amount of drug. The IP weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The tablets met the IP specification that not more than 2 tablets are outside the percentage limits and no tablet differs by more than 2 times the percentage limit.

Tablet Thickness: Thickness of the tablet is important for uniformity of tablet size. Thickness was measured using Vernier Calipers. It was determined by checking the thickness of three tablets of each formulation.

Tablet Hardness: The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of each batch of tablet was checked by using digital hardness tester. The hardness was measured in terms of kg/cm^2. Three tablets were chosen randomly and tested for hardness. The average hardness of three determinations was recorded.

Friability: Friability generally refers to loss in weight of tablets in the containers due to removal of fines from the tablet surface. Friability generally reflects poor cohesion of tablet ingredients.

Content Uniformity Test : [18] Ten tablets were weighed and grounded in a mortar with pestle to get fine powder. Powder equivalent to the mass of one tablet was dissolved in water and filtered through a 0.45-µm filter paper. The filtrate was diluted with water (pH6.8).The drug content was analyzed spectrophotometrically at 242 nm using an UV spectrophotometer using a reference to a standard calibration curve of the hydralazine.The results were shown in Table-12.

Swelling Index:[19,20] The swelling rate of the buccal tablet is evaluated by using pH 6.8 phosphate buffer. The initial weight of the tablet is determined (w1). The tablets is placed in pH 6.8 phosphate buffer (6 ml) in a petridish placed in an incubator at 37 ± 1°C and tablet is removed at different time intervals (0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0 and 9.0 h), blotted with filter paper and reweighed (w2). The swelling index is calculated by the formula:

$$\text{Swelling index} = \frac{(w2 - w1)/W1 \ X100}{W1} X100$$

Bioadhesive force:[21-23] The apparatus used for testing bioadhesion was assembled in the laboratory. Bioadhesive strength of the buccal tablets was measured on the "Modified Physical Balance Method" employing the method described by Gupta *et al* using bovine cheek pouch as model mucosal membrane. The method uses sheep buccal membrane as the model mucosal membrane. A double beam physical balance was taken. The left pan was removed. To left arm of a balance, a thick thread of suitable length was hanged. To the bottom side of thread a glass stopper with uniform surface was tied. A clean glass mortar was placed below hanging glass stopper. In this, mortar was placed on a clean 500 ml glass beaker, within which another glass beaker of 50 ml capacity in inverted position was placed and weighed with 50 gm to prevent floating. The pan control system involves placing thermometer in 500 ml beaker and intermittently adding hot water in outer

$$\text{Bioadhesive force} = \frac{mucoadhesivestrenght}{100}(9.81)$$

Dissolution Study: [24-26] *In-vitro* dissolution of a Acarbose buccal bilayer tablets were studied in USP TDT-08L dissolution apparatus. Employing a paddle stirrer. 400 ml of

phosphate buffer pH 6.8 was used as dissolution medium. The stirrer was adjusted to rotate at 50 rpm. The temperature of dissolution media was previously warmed to 37±0.5°C and was maintained throughout the experiment. One tablet was used in each test, 5 ml of sample of dissolution medium were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 246 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Percentage amount of acarbose released was calculated and plotted against time. The results are given in Table-05 to 07 and Figure-03-05. The results of *in-vitro* release data obtained for all formulations were fitted in two or four popular models of data treatments as follows:

1. Zero-order kinetic model (cumulative percent drug released versus time).
2. First-order kinetic model (log cumulative percent drug remaining versus time).
3. Higuchi‟s model (Cumulative percent drug released versus square root of time.
4. Korsmeyer-Peppas equation (Log cumulative percent drug released versus log time)

Table-1: Formulations of Acarbose Buccal Bilayer Tablets Prepared by Direct Compression Method (One Tablet)

Ingredients mg/tablet	Formulation code									
	$BTA4_1$	$BTA4_2$	$BTA4_3$	$BTA4_4$	$BTA4_5$	$BTA15_1$	$BTA15_2$	$BTA15_3$	$BTA15_4$	$BTA15_5$
Acarbose	5	5	5	5	5	5	5	5	5	5
HPMC K_4M	2	4	6	8	10	-	-	-	-	-
HPMC $K_{15}M$	-	-	-	-	-	2	4	6	8	10
Carbopol 934p	10	10	10	10	10	10	10	10	10	10
Mannitol	10	10	10	10	10	10	10	10	10	10
Mg sterate	2	2	2	2	2	2	2	2	2	2
PVP-K30	3	3	3	3	3	3	3	3	3	3
MCC	68	66	64	62	60	68	66	64	62	60
Ethyl Cellulose	50	50	50	50	50	50	50	50	50	50
Total	150	150	150	150	150	150	150	150	150	150

Table-2: Formulations of Acarbose Buccal Bilayer Tablets Prepared by Direct Compression Method (Fifty Tablets)

Ingredients mg/tablet	Formulation code									
	$BTA4_1$	$BTA4_2$	$BTA4_3$	$BTA4_4$	$BTA4_5$	$BTA15_1$	$BTA15_2$	$BTA15_3$	$BTA15_4$	$BTA15_5$
Acarbose	250	250	250	250	250	250	250	250	250	250
HPMC K_4M	100	200	300	400	500	-	-	-	-	-
HPMC $K_{15}M$	-	-	-	-	-	100	200	300	400	500
Carbopol 934p	500	500	500	500	500	500	500	500	500	500
Mannitol	500	500	500	500	500	500	500	500	500	500
Mg sterate	100	100	100	100	100	100	100	100	100	100
PVP-K30	150	150	150	150	150	150	150	150	150	150
MCC	3400	3300	3200	3100	3000	3400	3300	3200	3100	3000
Ethyl Cellulose	2500	2500	2500	2500	2500	2500	2500	2500	2500	2500
Total	7500	7500	7500	7500	7500	7500	7500	7500	7500	7500

RESULTS AND DISCUSSION

In the present study an attempt has been made to design and evaluate buccal bilayer tablets of Acarbose by direct compression method. Buccal tablets were prepared by direct compression method using polymers HPMC K4M and HPMC K15M, and mannitol as a channeling agent. The buccal tablets were evaluated for physical parameters like appearance, hardness, thickness, weight variation, friability, swelling index and surface pH; biological parameter- mucoadhesive strength; and other parameters such as drug content uniformity, *in vitro* drug release, stability studies, drug excipient interaction (IR study). The stability data was also subjected to statistical analysis. The results of all these evaluations are given in table-3 to 8. The appearance of buccal tablets was smooth and uniform on physical examination. The hardness of prepared buccal tablets of Acarbose was found to be in the range of 3.77 to 4.37 kg/cm^2. Results are given in table-4. The thickness and weight variation were found to be uniform as indicated by the low values of standard deviation. The thickness and weight of the prepared buccal tablets were found to be in the range of 2.10 to 2.23 mm and 141.8 to 160.5 mg respectively. Friability values less than 1% indicate good mechanical strength to withstand the rigors of handling and transportations. Results are given in table-4. The drug content of buccal tablets was quite uniform as shown in table-4. The average drug content of buccal tablets was found to be within the range of 90.67 to 105.67 % and low values of standard deviation indicate uniform distribution of the drug within the prepared buccal tablets. 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. Surface pH of all formulations was found to be in the range of 6.99 to 6.70 as shown in table-04. So it is assumed that these formulations do not cause any irritation in the oral cavity. The swelling profile of different batches of the tablets is shown in table-04. These profiles indicate the uptake of water into the tablet matrix, producing an increase in weight. The swelling state of the polymer in the formulation was reported to be crucial for its bioadhesive behavior. Adhesion occurs shortly after the beginning of swelling but the bond formed between mucosal layer and polymer is not very strong. The adhesion will increase with the degree of hydration until a point where over-hydration leads to an abrupt drop in adhesive strength due to disentanglement at the polymer/tissue interface. In formulations, maximum swelling was found with the formulation $BTH4_5$ containing HPMC K_4M (10% w/w of matrix layer). The mucoadhesion of all the buccal tablets of varying ratio of polymers were tested and weight required to pull off the formulation from the mucous tissue is recorded as mucoadhesion strength in grams and results are given in table-4. The mucoadhesivity of buccal tablets was found to be maximum in case of formulation $BTA15_5$ i.e. 10.54 g. This may be due to fact that positive charges on the surface of HPMC K15M could give rise to strong electrostatic interaction with mucous or negatively charged mucus membrane.

In vitro release studies were carried out in USP XIII tablet dissolution test apparatus employing paddle stirrer at 50 rpm and 200 ml of pH 6.8 phosphate buffer as dissolution medium. The *in vitro* dissolution data of all the designed formulations are shown in table-5 & 6 and dissolution profiles depicted in figures-02 & 03. From dissolution data it is evident that designed formulations have displayed more than 52.37% drug release in 8 hr. *In vitro* drug release data of all the buccal tablet formulations of Acarbose was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetics, Higuchi's and Peppas equations to ascertain mechanism of drug release. The results of linear regression analysis including regression coefficients are summarized in table-8. From the above data it is evident that all the formulations displayed zero order release kinetics (r^2 values from 0.908 to 0.999).

Table-3: Pre-compression Parameters of Acarbose Formulations

SI. No.	Formulation code	Angle of Repose (θ)	Bulk Density (gm/cc)	Tapped Density (gm/cc)	Carr's Index (%)	Hausner's Ratio
1.	$BTA4_1$	30.25	0.56	0.67	16.67	1.20
2.	$BTA4_2$	29.26	0.53	0.59	10.53	1.12
3.	$BTA4_3$	28.16	0.50	0.59	15.00	1.18
4.	$BTA4_4$	30.35	0.56	0.67	16.67	1.20
5.	$BTA4_5$	27.68	0.59	0.71	17.65	1.21
6.	$BTA15_1$	28.45	0.67	0.71	6.67	0.94
7.	$BTA15_2$	32.46	0.53	0.59	10.53	1.12
8.	$BTA15_3$	29.31	0.48	0.56	14.29	1.17
9.	$BTA15_4$	28.33	0.59	0.67	11.76	1.13
10.	$BTA15_5$	27.19	0.71	0.77	7.14	1.08

Table-4: Post-compression Parameters of Formulations (BTA4 and BTA15) Prepared by Direct Compression Method

Parameters	Formulation code									
	$BTA4_1$	**$BTA4_2$**	**$BTA4_3$**	**$BTA4_4$**	**$BTA4_5$**	**BTA15 1**	**BTA15 2**	**BTA15 3**	**BTA15 4**	**$BTA15_5$**
Hardness*±SD (kg/cm²)	4.33± 0.15	3.77± 0.15	4.20± 0.10	4.23± 0.06	3.93± 0.15	4.37± 0.21	4.53± 0.31	4.07± 0.15	4.27± 0.21	4.23± 0.15
Thickness*±SD (mm)	2.10± 0.10	2.12± 0.00	2.14± 0.06	2.21±0 .06	2.20±0 .10	2.13± 0.06	2.23±0. 15	2.10± 0.10	2.13± 0.06	2.11± 0.06
Friability (%)	0.68	0.71	0.58	0.91	0.75	0.69	0.57	0.80	0.77	0.83
Percent Drug Content*± SD	95.00± 1.6	95.33± 0.68	95.34± 1.15	95.35± 2.25	95.67± 1.03	95.68± 1.44	96.00± 2.65	97.67± 1.15	98.67± 1.07	105.67± 1.48
Surface pH*± SD	6.33± 0.25	6.99± 1.05	6.10 ±0.67	6.21 ±0.41	6.46 ±0.33	6.43 ±1.12	6.27 ±0.34	6.70 ±0.43	6.19 ±1.20	6.43 ±0.36
Swelling Index (%) (after 8 hr)*± SD	69.33± 1.53	68.00± 2.59	75.33± 1.00	81.33± 0.58	89.67± 0.58	73.00± 1.73	59.33± 2.08	65.68± 2.00	72.00± 2.00	82.33± 2.08
Mucoadhesive Strength (g)*± SD (%)	7.21± 1.74	8.87± 0.93	10.66 ±1.09	9.48± 0.93	8.60± 0.17	6.40± 2.82	7.05± 1.36	6.58± 2.02	8.08± 1.50	10.54± 2.07
Weight Variation -%	(148.8-152.mg) Within the IP limits of ± 7.5%									

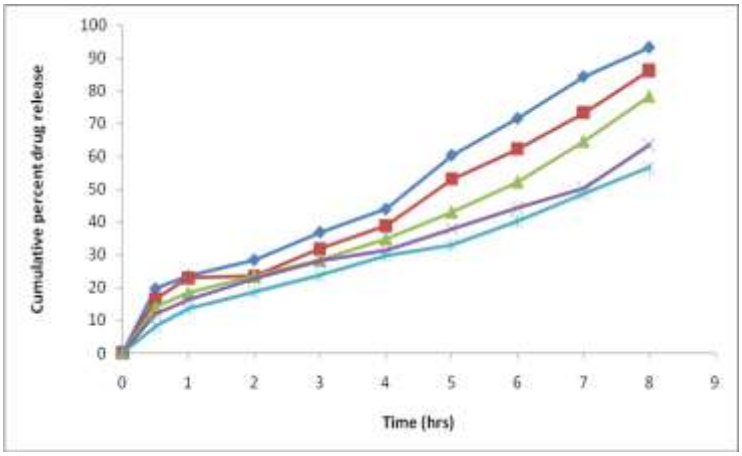

Figure-02: Cumulative percent drug released Vs time plots (zero order) of formulations $BTA4_1$, $BTA4_2$, $BTA4_3$, $BTA4_4$ and $BTA4_5$in pH 6.8 Phosphate Buffer

Table-5: *In vitro* drug release data of formulations $BTA4_1$, $BA4_2$, $BTA4_3$, $BTA4_4$ and $BTA4_5$

Time hrs	Cumulative percent drug release				
	$BTA4_1$	$BTA4_2$	$BTA4_3$	$BTA4_4$	$BTA4_5$
0.5	20.36±1.25	16.93±4.11	14.3±0.57	12.09±1.43	9.38±1.84
1	24.39±2.03	22.08±3.46	19.45±3.45	16.32±2.28	13.64±1.35
2	30.46±0.68	26.92±2.14	22.78±4.31	21.39±0.67	18.64±1.24
3	36.89±2.45	32.57±2.95	27.62±2.17	26.84±1.67	23.48±0.64
4	41.08±1.44	38.68±0.87	34.96±2.34	31.36±2.64	28.04±3.05
5	49.37±2.34	46.27±1.24	41.35±1.64	37.67±3.11	33.69±4.01
6	57.62±1.57	51.23±2.48	46.75±5.34	43.85±2.15	39.58±3.64
7	63.28±1.94	58.39±3.16	54.39±2.44	49.93±3.04	46.31±2.47
8	75.31±1.47	67.17±3.61	63.54±4.36	58.42±1.24	52.37±2.35

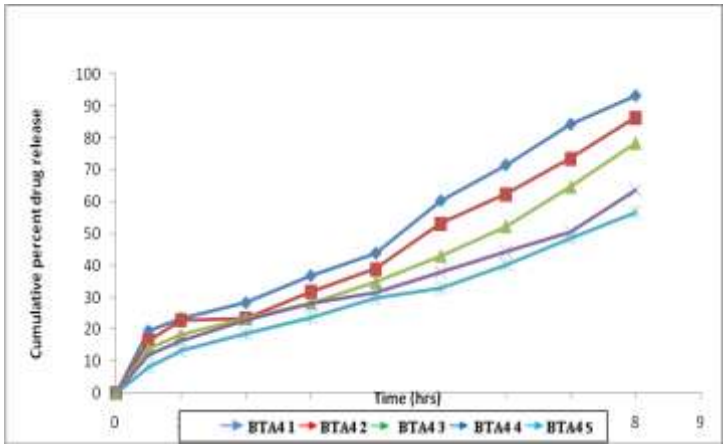

Figure-03: Cumulative percent drug released Vs time plots of formulations $BTA15_1$, BTA152, $BTA15_3$, $BTA15_4$ and $BTA15_5$in pH 6.8 Phosphate Buffer

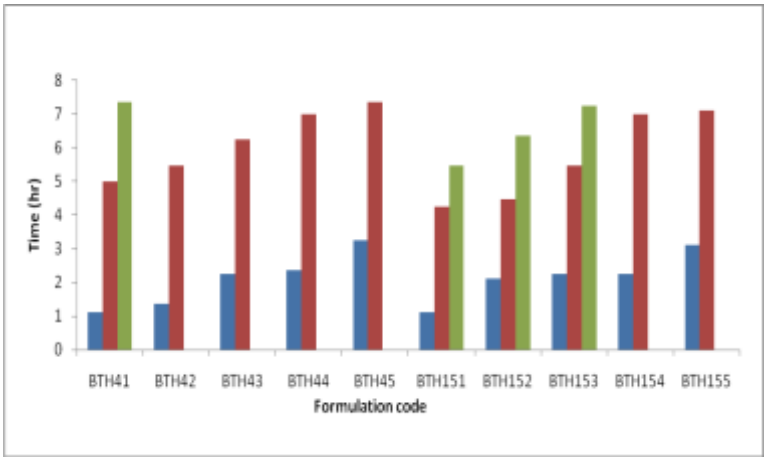

Figure- 04: Comparison of dissolution parameters ($t_{25\%}$, $t_{50\%}$and $t_{70\%}$) of buccal bilayer tablets of Acarbose

Table-6: *In vitro* drug release data of formulations $BTA15_1$, BTA152, $BTA15_3$, $BTA15_4$ and $BTA15_5$in pH 6.8 Phosphate Buffer

Time hrs	Cumulative percent drug release				
	$BTA15_1$	$BTA15_2$	$BTA15_3$	$BTA15_4$	$BTA15_5$
0.5	19.63±1.37	16.46±0.66	13.94±3.55	11.86±3.11	8.23±2.11
1	23.44±1.28	22.89±1.74	18.47±2.77	16.35±2.64	13.45±3.07
2	28.44±1.48	23.45±2.44	23.44±1.67	22.86±1.35	18.63±2.34
3	36.89±4.11	31.87±3.45	28.34±0.67	28.16±1.84	23.72±1.64
4	43.96±2.16	38.92±4.14	34.92±2.34	31.44±0.96	29.81±2.44
5	60.38±0.37	53.17±3.18	43.12±2.77	37.98±0.47	32.98±1.09
6	71.6±1.64	62.35±2.47	52.34±2.14	44.39±1.64	40.38±0.68
7	84.36±1.67	73.49±6.14	64.74±1.34	50.41±1.34	48.67±1.42
8	93.28±1.34	86.39±3.04	78.46±0.64	63.58±2.14	56.73±0.38

Table-7: Dissolution parameters for the formulations

SI. No.	Formulation code	$t_{25\%}$ (hr)	$t_{50\%}$ (hr)	$t_{70\%}$ (hr)	Cumulative % drug released in 8hr
1.	$BTA4_1$	1.12	5.00	7.36	75.31
2.	$BTA4_2$	1.36	5.48	--	67.17
3.	$BTA4_3$	2.24	6.24	--	63.54
4.	$BTA4_4$	2.36	7.00	--	58.42
5.	$BTA4_5$	3.24	7.36	--	52.37
6.	$BTA15_1$	1.12	4.24	5.48	93.28
7.	$BTA15_2$	2.12	4.48	6.36	86.39
8.	$BTA15_3$	2.24	5.48	7.24	78.46
9.	$BTA15_4$	2.24	7.00	--	63.58
10.	$BTA15_5$	3.12	7.12	--	56.73

Table-8: Kinetic data ('r' values) of the formulations

SI. No.	Formulation code	Zero order	First order	Higuchi's Equation	Peppas Equation
1.	$BTA4_1$	0.996	0.967	0.925	0.991
2.	$BTA4_2$	0.983	0.959	0.906	0.938
3.	$BTA4_3$	0.950	0.909	0.919	0.994
4.	$BTA4_4$	0.956	0.985	0.991	0.907
5.	$BTA4_5$	0.979	0.942	0.978	0.927
6.	$BTA15_1$	0.967	0.988	0.893	0.946
7.	$BTA15_2$	0.993	0.978	0.967	0.943
8.	$BTA15_3$	0.908	0.893	0.973	0.958
9.	$BTA15_4$	0.999	0.908	0.970	0.971
10.	$BTA15_5$	0.971	0.978	0.993	0.938

Table-9: Stability data of $BTA15_1$ formulation at 40º±2ºC/ 75 ±5% RH

Sl. No.	Time in days	Physical changes	Percent drug content ±SD*
1.	1^{st} day (initial)	--	88.33±0.08
2.	30^{th} day (1 month)	No changes	88.12±0.05
3.	60^{th} day (2 month)	No changes	87.98±0.05
4.	90^{th} day (3 month)	No changes	87.76±0.07

Table-10: Statistical analysis for drug content data of $BTA15_1$ formulation

Sl. No.	Trials	1st day (A)	90th day (B)	A – B
1.	1	88.26	87.76	0.5
2.	2	88.32	87.82	0.72
3.	3	88.41	87.69	0.57
4.	Mean percent drug content	88.33	87.76	0.60
5.	± SD	± 0.08	± 0.07	± 0.11

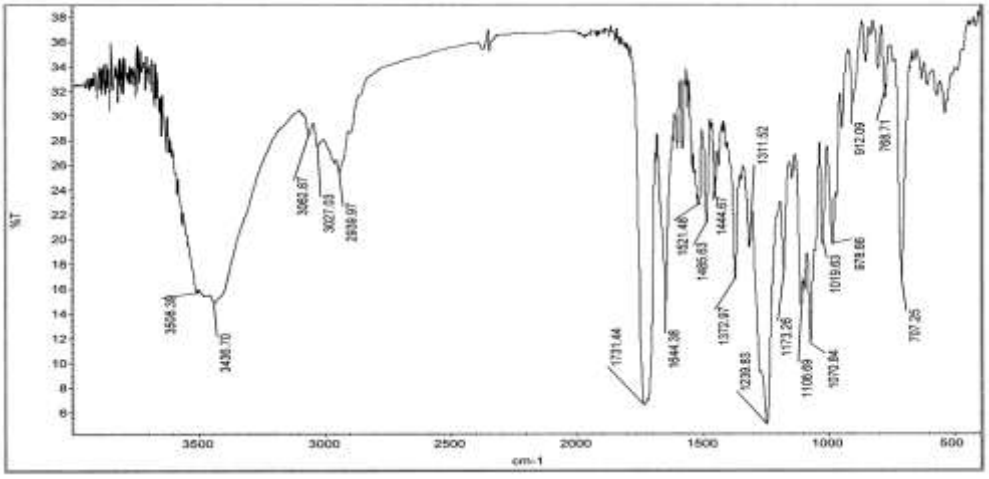

Figure- 05: IR Spectra of drug (Acarbose)

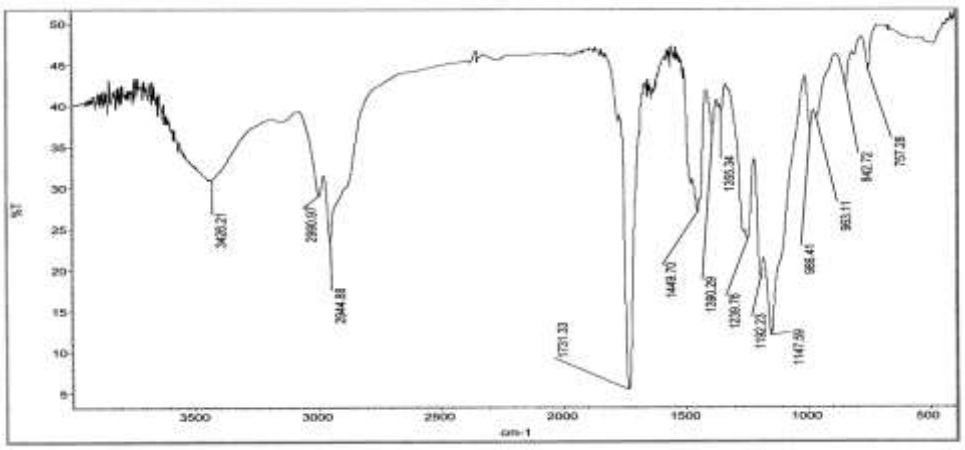

Figure-06: IR of $BTA15_1$ formulation

Higuchi and Peppas data reveals that the drug is released by non-Fickian diffusion mechanism (r^2 values from 0.893 to 0.994). The *in vitro* release parameter values ($t_{25\%}$, $t_{50\%}$, $t_{70\%}$) displayed by the various formulations range from 1.12 to 3.24 hr ($t_{25\%}$), 4.24 to 7.12 hr ($t_{50\%}$), 5.48 to 7.36 hr ($t_{70\%}$) respectively. The formulation $BTA15_1$ containing HPMC K15M (2.0% w/w of matrix layer), carbopol 934p (10% w/w of matrix layer) and mannitol (channeling agent, 10% w/w of matrix layer) was found to be promising, which showed $t_{25\%}$, $t_{50\%}$, $t_{70\%}$ values of 1.12, 4.24, 5.48 hr respectively and *in vitro* drug release of 93.28% in 8 hr along with satisfactory bioadhesive strength (6.40±2.82g). Drug-excipient interactions were ruled out by IR spectroscopy studies on the sample $BTA15_1$ stored for three months at 40±2° C / 75±5% RH. The peaks of 2880.00 cm^{-1} and 1112.00

cm^{-1} are due to C-H group and alkyl aryl ether linkage respectively. The presence of above peaks indicates undisturbed structure of drug in the above formulation. Hence, there are no drug-excipient interactions. IR spectra of Acarbose (pure drug), $BTA15_1$ along with other Excipients are shown in figure- 5 & 6. From the stability studies data it can be seen that the drug content of above formulation BTA151 was not significantly effected at 40±2o C / 75±5% RH after storage for three months. Statistical analysis of the drug content data ('t' test) gives t value of 0.60 which is much less compared to the table value of 3.82 ($p<0.05$).

Stability studies: [27]

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, light and enables recommended storage conditions, re-test periods and shelf lives to be established. ICH specifies the length of study and storage conditions

CONCLUSION: From the present study, the following conclusions can be drawn**:** Buccal bilayer tablets were prepared by direct compression method using various polymers (HPMC K4M, HPMC K15M), mannitol as a channeling agent. All the prepared tablet formulations were found to be good without capping and chipping. As the amount of polymer in the tablets increases, the drug release rate decreases, whereas swelling index and Mucoadhesive strength increases. All the tablet formulations showed good hardness range from 3.77 to 4.37 kg/cm^2. *In vitro* residence test for mucoadhesion indicated good Mucoadhesive property of the prepared tablets. The promising formulation **$BTA15_1$** have showed good Swelling index, which indicates that prepared tablets showed better swelling ability in presence of little amount of water. All the designed formulations of Acarbose buccal tablets have displayed zero order release kinetics and drug release follows non-fickian diffusion mechanism. Stability studies of the promising formulation $BTA15_1$ indicated that there are no significant changes in drug content and dissolution parameter values after 3 months at 40±2°C / 75±5% RH. IR spectroscopic studies indicate that there are no drug-excipient interactions. Among ten formulations, the formulation BTA151 containing HPMC K15M (2.00% w/w of matrix layer), Carbopol 934p (10% w/w of matrix layer) and mannitol (channeling agent, 10% w/w of matrix layer) was found to be promising, which showed t25%, t50%, t70% values of 1.12, 4.24, 5.48 hr respectively and in vitro drug release of 93.28% in 8 hr along with satisfactory Bioadhesive strength (6.40±2.82g). IR spectroscopy studies indicated that there are no drug-excipients interactions

REFERENCES:

1. Kumari, Visht , Fast dissolving drug delivery system: Review article. J Pharm Res 2010;3(6):1444-9.
2. Sayeed , Mouth dissolving tablets: An overview. Int J Res Pharm Biomed Sci 2011;2(3):959-70.
3. Brahmankar, Jaiswal SB.Biopharmaceutics and Pharmacokinetics A Treatise, First Edition, Vallabh Prakashan;1995:337.
4. Chien YW. Concepts and System Design for Rate-controlled Drug Delivery, Chapter 1, Novel Drug Delivery System, 2nd Edition, Marcel Dekker, Inc, New York, 1992; l-42.
5. Shojaei AH, Chang RK, Guo X, Burnside BA. Systemic drug delivery via the buccalmucosal route. Pharm Tech 2001; 70-81.
6. Patel KV, Patel ND, Dodiya HD, Shelat PK.BuccalBioadhesive Drug Delivery System: An Overview. International Journal of Pharmaceutical & Biological Archives 2011; 2(2): 600-609.
7. Ravikumar, Patil SR, Patil MB, Paschapur MS, Mahalaxmi R. Formulation and evaluation of controlled-release diltiazem

hydrochloride buccoadhesive tablets. Scholar Res Libr. 2010;2:48–60.
8. Shojaei AH. Buccal mucosa as a route for systemic drug delivery. J Pharm PharmSci 1998;1(1):15-30.
9. Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Adv Drug Deliv Rev 2005;57(11):1666-91.
10. ToraTora J. In: ToraTora GJ, Gorahowski SR, editors. Principles of anatomy & physiology. 7th ed. Harpet Collins college Publisher; 1992. p. 770-4.
11. Ross & Wilson. In: Waugh A, Goraw A, editors. Anatomy & physiology in health and illness. 9th ed. published by Churchill Livingstone Edinburgh; 2001. p. 289-93.
12. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Adv Drug Deliv Rev 1994;13:43-74.
13. Squier CA, Johnson NW, Hopps RM. The organization of oral mucosa, human oral mucosa, development, structure and function. Oxford: Blackwell Scientific Publications; 1976. p. 7-15.
14. Chen SY, Squier CA. In: Meyer J, Squier CA, Gerson SJ, editors. The ultrastructure of the oral epithelium. The structure and function of oral mucosa. Oxford: Pergamon Press; 1984. p. 7-30.
15. Meyer J, Gerson SJ. A comparison of human palatal and buccal mucosa. Periodontics. 1964; 2:284-91.
16. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets of salbutamol sulphate: A novel drug delivery system. Indian Drugs 2004;41:592-8
17. Roche RC, Sheskey PJ, Weller PJ. Handbook of Pharmaceutical Excipients. 4th ed. Pharmaceutical Press: London; 2003.
18. Cooper J, Gun C. Powder Flow and Compaction. IncCarter SJ, Eds. Tutorial Pharmacy. 6th ed. New Delhi: CBS Publication; 1986. p. 211-33.
19. Martin A, Micromeretics. In: Martin A, ed. PhysicalPharmacy. Baltimores, MD: Lippincott Williams and Wilkins; 2001. p. 423-54.
20. Government of India Ministry of Health & Family Welfare. Indian Pharmacopoeia. Delhi: Controller of Publications; 2007. p. 1689-90.
21. Liberman H, Lachman L. The Theory and Practice of Industrial Pharmacy. 3rd ed. Bombay: Verghese Publication House; 1991. p. 171-93.
22. Jeevanandham S, Dhachinamoorthi D, Formulation and evaluation of naproxen sodium orodispersible tablets- A sublimation technique. Asian J Pharm 2010; 4(1):48-51.
23. Desai KGH, Kumar TMP. Preparation and evaluation of a novel buccal adhesive systems. AAPS Pharm SciTech 2004; 5(3): 1-9. (Article 35)
24. Madgulkar A, Bhalekar M, Wable N, Patel K, Kolhe V. Egg shell membrane as substrate for bioadhesion measures. Indian Drugs 2008; 45(3): 219-21.
25. Deshmukh VN, Jadhav JK, Sakarkar DM. Formulation and *in vitro* evaluation of theophylline anhydrous bioadhesive tablets. Asian J 2009; 3(1): 54-8.
26. Shindhaye SS, Thakkar PV, Dand NM, Kadak VJ. Buccal drug delivery of pravastatin sodium. AAPS Pharm SciTech 2010; 11(1): 416-23.
27. Swamy PV, Pawndeep Singh, Hiremath SN, Shirsand SB, Neelima, Raju SA. Preparation and evaluation of chitosan buccal films of diltiazem hydrochloride. Indian Drugs 2007; 44(2): 137-9.
28. Choi HG, Kim CK. Development of omeprazole buccal adhesive tablets with stability enhancement in human saliva. J Control Release 2000; 68: 397-404.
29. Patel VM, Bhupendra GP, Patel HV, Patel KM. Mucoadhesive bilayer tablets of propranolol hydrochloride. AAPS Pharm SciTech 2007; 8(3): E1-E6. (Article 77).
30. CostaP,LoboJS.Modelingandcomparisonof dissolutionprofiles.EurJ PharmSci 2001;13(2):123–33.