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FORMULATION EVALUATION AND DEVELOPMENT OF MUCOADHESIVE BUCCAL TABLET OF VILDAGLIPTIN

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Abstract:

Mucoadhesive drug delivery systems interact with the mucus layer covering the mucosal epithelial surface, and mucin molecules increase the duration of the dosage form at the positioning of absorption. Mucosal coating characterizes potential sites for the add-on of any bio adhesive systems for the reason that mucosal layer lines number of the body with the gastric tract, the urogenital tract, vaginal tract, the eye, ear, and nose. The mucoadhesive layer tablets containing of dual various forms of drug particles and that they display on set of actions on their specific sites. This analysis defines the structure of mucosal layer, mechanism of action of mucoadhesion, and planning of tablets and evaluation parameters of tablets

KEYWORDS- Buccal Tablet, Vildagliptin, Mucoadhesive

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1. INTRODUCTION:

Current innovation in pharmaceuticals determine the merits of mucoadhesive drug delivery system is especially relevant than oral control release. By the buccal drug delivery system the medication are directly pass via into circulation, easy administration without pain, brief enzymatic activity, less hepatic metabolism and excessive bioavailability. This literary criticism is an overview of buccal dosage form, mechanism of Mucoadhesion, in-vitro and in-vivo Mucoadhesion testing technique. The oral route is most ancient still as preferred by the patient being convenient to require. However, per oral administration of medicine has shortcomings like hepatic first-pass metabolism and enzymatic degradation within the duct On the contrary of per oral route, mucosal layer (nasal, rectal, vaginal, ocular and oral cavity) are often considered as potential sites for drug administration and having distinct advantages for systemic drug delivery. These advantages include possible liver bypass effect, avoidance of presystemic elimination within the duct with improved absorption and hence better bioavailability

2. DRUG PROFILE

2.1 Vildagliptin

Vildagliptin is an oral antihyperglycemic agent used for the treatment of non-insulin dependent diabetes (NIDDM).

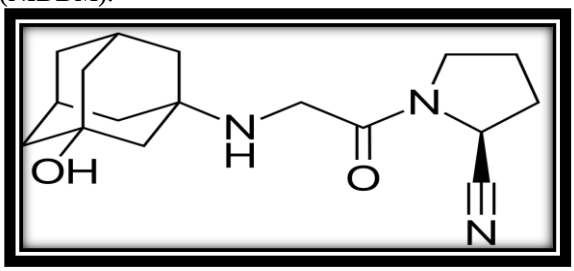

Fig. No.1 Vildagliptin

3. MATERIAL AND METHODOLOGY:

Before visiting direct compression all the ingredients were screened through sieve no. 100 except lubricant (mg. stearate). All the ingredients were thoroughly blended within the glass mortar with pestle for15 mins. After sufficient mixing, lubricant was added and again mixed for extra 2-3 mins. Before compression, hardness was adjusted an compressed into 200 mg each tablet using tablet compression machine equipped with 250 mm flat faced, bevel edge punches on 12th station rotary tablet machine and same hardness was used for the specified number of the tablets.

3.1 Methodology

3.1.1 Pre-formulation Studies

Pre-formulation could also be described as a phase of the dosage form development process that consists of characterization of the physical, chemical and mechanical properties of recent drug substances, so as to develop stable, safe & effective dosage forms. Here Pre-formulation studies were conducted for the both the drug and excipients. a. Identification and characterization of the drug b. Description: The drug samples obtained were examined for his or her state, appearance, color, odour etc.

3.1.2 Solubility Studies:

The solubility of Vildagliptin in phosphate solution pH 6.8 make up my mind by phase equilibrium method. Vials were closed with rubber caps and constantly agitated at temperature for twenty-four hr using rotary shaker. After 24 hr, the answer was filtered through 0.2µm Whatman's paper. the number of drugs solubilized was then estimated by measuring the absorbance at 229 nm employing a UV spectrophotometer.

3.1.3 Melting Point:

Melting point of the drug determined by tube method. during this method, touch of the drug was fill within the capillary and one end of the capillary was packed. The capillary tubes were placed within the digital freezing point apparatus and temperature was increased then and text the temp. When drug was start to melt. Repeat this procedure a minimum of three time and take average of them.

3.1.4 Determination of Wave Length (λmax):

Drug 10 mg was accurately weight and transfer in to 10 ml volumetric flask dissolved and volume conjure with the methanol. Take 0.1 ml solution from the stock and transfer in to 10 ml volumetric flask and volume structure with the assistance of ethanol then scanned for determination of wavelength by double beam UV spectrophotometer

3.1.5 Drug- polymer Compatibility Studies:

Infrared spectra of pure drug and combination of drug and excipients remained noted by KBr technique using the Fourier transform infrared spectrophotometer. Within the present study, the salt disc method was employed. The powdered sample

was intimately mixed with dry powdered salt. This mixture was then compressed into transparent pellet under air mass press at a pressure of 1000 psi. The characteristic peaks wer recorded.

3.1.6 Preparation of mucoadhesive buccal tablets of vildagliptin:

Mucoadhesive tablets of Vildagliptin were prepared by direct compression method using single hand punching tablet machine All component ingredients including drug, polymers and excipients were weighed accurately Various batches of vildagliptin buccal tablets were prepared by changing the ratio of Carbopol 934, HPMC E15LV, xanthum gum sodium alginate and xanthan gum were used as mucoadhesive polymers and mannitol was used as diluent. Magnesium stearate and talc were added to the above blend as flow promoters the prepared blend of every formulation was compressed by using tablet punching machine.

3.2 Evaluation parameters of mucoadhesive buccal tablets:

1. Pre-compression Parameters

a. Bulk Density: Bulk Density: it's defined because the total mass of powder to the majority volume of powder. it's expressed in gm/ml or gm/10- 3 L. Sample of known weight was introduced into measuring cylinder. The cylinder was dropped on hard wood surface thrice from height of 1 inch at 2 second interval. From this bulk density was calculated consistent with the formula mentioned below
BD=M/BV
Where, BD=Bulk density, M=Weight of sample in grams, BV=Final volume of blend.

b. Tapped Density (TD): it's defined as ratio of total mass of powder to the tapped volume of powder. it had been measured by tapping the powder by persistently (approximately 750-1000) and tapped volume was noted. it's expressed in "gm/10-3 L from this tapped density calculated in line with the formula mentioned below.
(TD)=M/TV
Where TD =Tapped density, M=Weight of powder in grams, TV=Tapped volume of powder.

c. Angle of Repose: it's defined as maximum angle possible between surface of pile of powder and therefore the horizontal plane. it's an indicative of flow properties of powder. An Improper flow property is because of frictional force between particles. The powdered mixture was allowed to flow through funnel to square at definite height (h). The angle of repose remained then determined by calculating height radius of heap of powdered formed, which is signified as follows:

$\text{Tan}^{\theta} = h/r,$

Where, h=height in cms, r=radius in cms.

d. carr's index or compressibility index: The powder is taken in a very measuring cylinder and bulk volume was noted. Then it had been tapped to notice tapped volume. From then Carr`s index was calculated as follows CI=TD-BD/TDX100 Where, TD=Tapped density of powder, BD=Bulk density of powder, it's expressed in "percentage"

Table 1. Relationship between %compressibility and flow ability

% Compressibility	Flowability
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
23 – 35	Poor
33 – 38	Very Poor
> 40	Extremely Poor

e. Hausner's Ratio: it's defined because the ratio of tapped density to the majority density. it's calculated by the formula as follow46-49
Hausner's ratio= TD/BD
Where, TD= Tapped density, BD=Bulk density.

Table.2 Hausner's Ratio limits

Flow character	Hausner's Ratio
Excellent	1.00-1.11
Good	1.12-1.18
Fair	1.19-1.25
Passable	1.26-1.34
Poor	1.34-1.45
Very poor	1.46-1.59
Very, very poor	>1.60

2. Post Compression Parameters

a. Hardness Test: The stiffness of tablets was determined by Pfizer hardness tester. It's expressed in kg/cm2 three tablets were randomly picked from each formulation and therefore the mean and variance values was calculated.

b. Thickness and diameter: Thickness and diameter of the prepared tablets were evaluated with the assistance of Vernier callipers and screw gauge. it's expressed in mm.

c. Friability Test: The friability of the tablets was resolute using Roche friabilator. 20 tablets were initially weighed and transferred into the friabilator. The friabilator was operated at 25 rpm for 4 min. After 4 min the tablets were weighed again. it's expressed in percentage (%). The friability was then calculated using the formula,

Friability (%) =Initial weight – final weight × 100
Initial weight

d. Weight variation: the load variation test was performed as per procedure of IP. the load of every of 20 individual tablets, selected randomly from each formulation was firm by using balance. The burden data from the tablets were analyzed for sample mean and percent deviation

Table No.3. Limits for weight variation

Sr.No	Average weight of tablet (X mg) as follow USP Guidelines	Percentage deviation allowed	Average weight of tablet(X mg) as per JP/BP
1	130 mg or less	10%	80 mg or less
2	130-324 mg	7.5	More than 80 mg but less than 240 mg
3	More than 324 mg	5	240 mg or more

e. Determination of Drug Content: Determination of Drug Content: The prepared formulations were analysed for drug content. Five mucoadhesive tablets were taken and therefore the contents are powdered. About 200 mg of the formulation was taken in to a 100 ml volumetric flask. Further, the degree was made up to the mark with phosphate buffer 6.8. The drug content was resolute by measuring the absorbance at 229 nm using UV spectrophotometer

f. Swelling Index: Swelling Index: Eight buccal tablets were weighed (W1) and placed separately in Petri dishes with 5ml of phosphate buffer of pH 6.8. At the measure of 1,2,3,4,5,6,7 and eight hrs, tablets were aloof from the Petri dish and excess water was removed carefully using paper. The swollen tablets were then reweighed (W2) and also the percentage hydration were calculated using the subsequent formula53

Swelling Index = [W2—W1] X100 W1

g. Surface pH: The microenvironment pH (surface pH) of the buccal tablets was firm so as to research the chance of any side effects in- vivo. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it had been decided to stay the surface pH as near neutral as possible. A joint glass electrode was used for depth of surface pH. The tablet was allowed to swell by keeping it involved with 4 ml of water (pH 6.5 ± 0.05) for two hrs. at temperature. The pH was measured by bringing the electrode in-tuned with

the surface of the tablets and allowing it to equilibrate for 1 min.

h. In-vitro Drug Release Study: In-vitro Drug Release Study: The USP type II dissolution apparatus was accustomed study the discharge of drug from buccal tablets. the discharge was performed at 37 ± 0.5°C, at a rotating speed of fifty rpm. The slide was put within the bottom of the dissolution vessel, in order that the tablet remained on the top side of the slide. Dissolution was applied and samples of 5 ml, at on every occasion intervals were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through whatman paper and were analysed spectrophotometric ally at 229 nm against phosphate buffer pH 6.8 as blank.

i. Release kinetics: Data of in-vitro release was fitted into different equations to elucidate the discharge kinetics of Vildagliptin release from buccal tablets. The kinetic equations used were zero order and first order equations. A plot of the fraction of drug released against the clock are going to be linear if the discharge obeys zero order release kinetics. A plot of the logarithm of the fraction of drug remained against the clock are going to be linear if the discharge obeys first order release kinetics.

j. Models of drug release mechanism: the discharge data of buccal tablets was fitted into different mechanism models like Higuchi model and Korsmeyer – Peppas model to interpret the drug release mechanism from tablets

k. Higuchi (Diffusion) equation: It defines a linear dependence of the active fraction released per unit of surface (Q) on the root of your time. A plot of the fraction of drug released against root of your time is linear if the discharge obeys Higuchi equation. This equation describes drug release as a diffusion process supported the Fick's law, root time dependent.

l. Korsmeyer – Peppas kinetics: A plot of the fraction of logarithm of % drug released against logarithm of time will be linear if the release obeys Korsmeyer–Peppas equation. Log Q = log k + n log t Where, k is the release rate constant.

m. Ex-vivo mucoadhesive time: The Ex-vivo mucoadhesion time was examined after application of the buccal tablet on freshly cut sheep buccal mucosa. The fresh sheep buccal mucosa was tied on the glass slide, and a mucoadhesive core side of each tabletwas wetted with 1 drop of phosphate buffer pH 6.8 .The glass slide was then put in the beaker, which was filled with 200 mL of the phosphate buffer pH 6.8 and kept at 37 ± 1ºC. After 2 min, a slow stirring rate was applied to simulate the buccal cavity environment, and tablet adhesion was monitored for 8 h. The time for the tablet to detach from the sheep buccal mucosa was recorded as the mucoadhesion time In Preformulation studies.

Color : White crystalline powder;

Odor : Odorless;

Taste : Tasteless;

State : Fine to granular powder.

n. Melting point

Melting point of the Vildagliptin was determined by Capillary Fusion method. One side closed capillary filled with drug and put into the Melting Point Apparatus and finally the temperature was noted as at which solid drug changed to into liquid. Itwas found to be 180ºC.

o. Solubility studies:

Solubility of Vildagliptin was determined in different solvent systems andbuffers.

Table 4: Solubility of Vildagliptin in different solvents

Sr. No	Solvents	Solubility
1	Distilled water	-
2	Methylene chloride	+
3	Acetone	+
Sr. No	**MEDIUM**	**CONCENTATION**
1	Phosphate 6.8 buffer	14.8
2	Phosphate 7.4 buffer	13.7
3	water	12.4

3.3 Preparation procedure for calibration curve of vildagliptin:

100 mg of Vildagliptin was dissolved in PH 6.8 phosphate buffer and volume was made up to 4100 ml (=

1000µg/ml) using the same, which is called as stock-I solution,further dilution were carried out in PH 6.8 phosphate buffer. From this Stock-I solution take 1 ml and diluted with 10ml of PH 6.8 phosphate buffer (= 100µg/ml), which is known as stock-II solution. Then from stock–II solution take 1ml and diluted with 10ml of PH 6.8 phosphate buffer (10µg/ml). From that above stock-III solution carry out serial dilutions were made to obtain solutions of the drug in the concentration ranging from 2, 4, 6, 8, 10 and 12µg/ml. The absorbance of thesolutions was Determined at 330nm using UV-visible spectrophotometer. A graph of concentration vs. absorbance was plotted.

3.4 Preparation of PH 6.8 phosphate buffer:

Dissolve 13.872 g of potassium dihydrogen **phosphate** and 35.084 g of disodium hydrogen **phosphate** in sufficient water to produce 1000 ml of distilled water is called as 1M solution Store in a cold place.

Table 5: Calibration curve of Vildagliptin

Sr.No	Concentrations (µg/ml)	Absorbance at 330nm
1	0	0
2	2	0.197
3	4	0.356
4	6	0.484
5	8	0.622
6	10	0.790

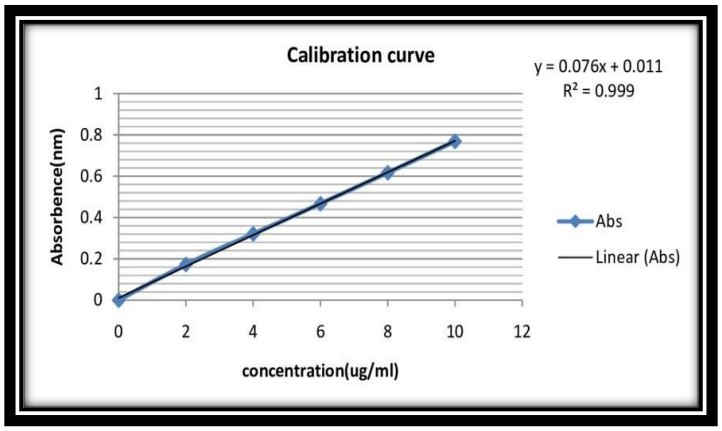

Fig. No 2: Calibration curve of vildagliptin

3.5 FT-IR Compatibility Studies:

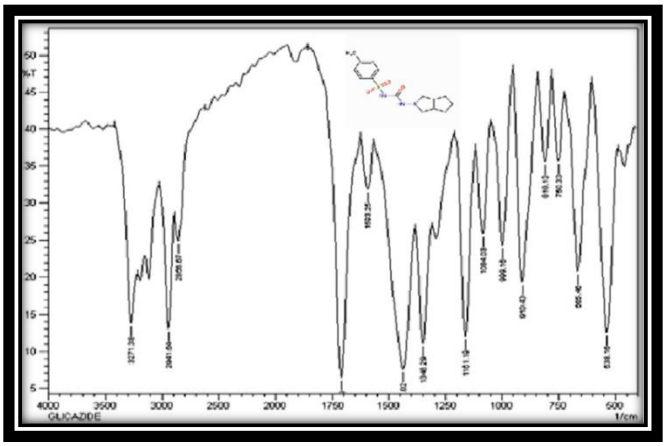

Fig. No 3: FTIR spectra of pure drug Vildagliptin

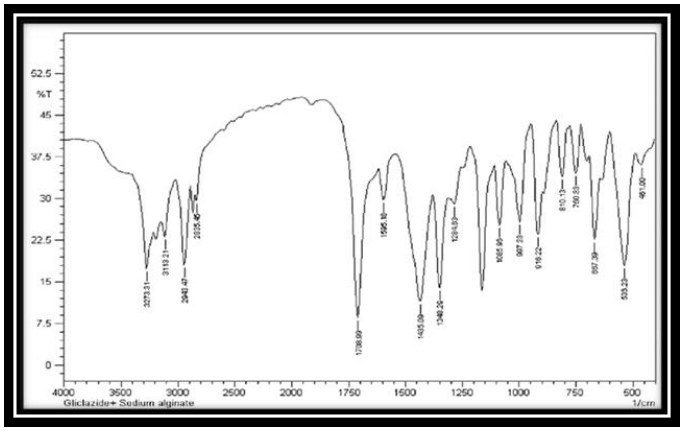

Fig. No 4: FTIR spectra of Vildagliptin+Sodium alginate

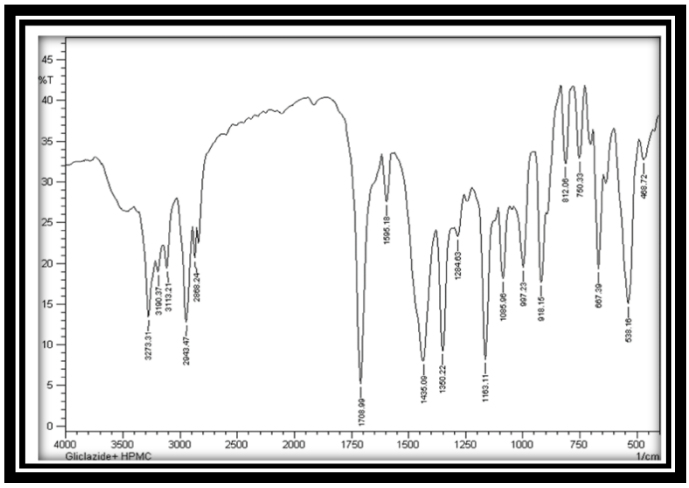

Fig. No 5: FTIR spectra of Vildagliptin+HPMC K15

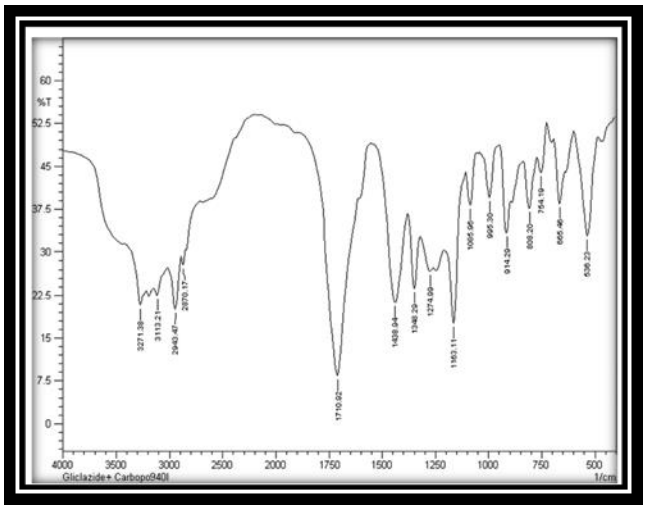

Fig. No 6: FTIR spectra of Vildagliptin+Carbopol-940

3.5.1 Interpretation of FTIR

Table 6: Interpretation of FTIR peaks present in Vildagliptin.

Sr.No.	Wave number in formulation (cm^{-1})	Characteristic Wave number range cm^{-1}	Bond nature and bondattributed
1	3447.78	3000-3700	N-H Stretching
2	1639.47	1600-1700	NH2 deformations
3	2870.17	2700-3300	C-H3asymetrical Stretching
4	1710.23	1600-1900	C-O Stretching
5	1466	1200-1500	O-H Bending
8	1596.55	1500-1800	C=C stretching
9	1348.07	1300-1490	c-c stretching
10	1164.24	1100-1200	C-N stretching

3.6 Precompression Parameter of Powder Blend:

Table 7: Precompression parameter of powder blend.

Sr.No	Formulation Code	Angle of repose (θ)*	Bulk Density* g/cm^3	Tapped Density* g/cm^3	Hausner's ratio*	Carr's index* %
1	H1	26.47±0.55	0.50±0.14	0.59±0.08	1.19±0.05	15.94±0.62
2	H2	25.28±0.97	0.48±0.19	0.56±0.04	1.17±0.03	15.63±0.86
3	H3	26.31±0.60	0.50±0.19	0.62±0.02	1.18±0.01	16.29±0.83
4	H4	27.26±0.70	0.49±0.18	0.60±0.01	1.18±0.02	15.43±0.63
5	S1	25.03±0.62	0.50±0.22	0.58±0.07	1.14±0.01	13.28±0.87
6	S2	25.98±0.66	0.50±0.23	0.57±0.08	1.17±0.01	14.74±0.41
7	S3	26.54±0.45	0.51±0.22	0.62±0.07	1.18±0.02	15.47±0.97
8	S4	25.03±0.55	0.50±0.24	0.58±0.06	1.17±0.01	13.31±0.62
9	G1	25.39±0.75	0.50±0.23	0.57±0.06	1.14±0.01	12.67±0.47
10	G2	26.43±0.50	0.50±0.21	0.58±0.05	1.16±0.01	13.73±0.89
11	G3	25.32±0.66	0.50±0.18	0.57±0.04	1.16±0.02	14.57±0.75
12	G4	25.44±0.68	0.41±0.14	0.59±0.02	1.19±0.01	15.64±0.89

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

3.6.1 Post Compression Parameters

Table 8: Results of Post-compression parameters

Sr.No	Formulation Code	Thickness*(m m)	Hardness* (kg/cm2)	Friability (%)	Weight variation** (%)
1	H1	3.32±0.15	5.16±0.40	0.85	0.073±0.43
2	H2	3.40±0.10	4.91±0.49	0.83	0.068±0.55
3	H3	3.44±0.41	5.41±0.37	0.84	0.047±0.46
4	H4	3.51±0.14	5.16±0.60	0.72	0.022±0.52
5	S1	3.25±0.15	5.33±0.51	0.65	0.068±0.48
6	S2	3.30±0.11	5.58±0.37	0.85	0.020±0.54
7	S3	3.17±0.09	5.50±0.54	0.65	0.020±0.65
8	S4	3.26±0.16	5.16±0.60	0.73	0.096±0.57
9	G1	3.23±0.12	5.25±0.41	0.52	0.068±0.57
10	G2	3.36±0.10	5.66±0.40	0.82	0.019±0.63
11	G3	3.28±0.12	5.50±0.44	0.75	0.020±0.16
12	G4	3.43±0.14	5.25±0.52	0.61	0.071±0.56

Table.9: Results of % of drug content, surface pH, swelling index, bio adhesive strength

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

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

Fig. No.7 Swelling study at initial time (0hr) Swelling study after 8hrs

Table10: In vitro drug release data of Vildagliptin tablets containing HPMCK15 LV

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

Mean ± SD, n = 3

Table 11: In vitro drug release data of Vildagliptin tablets containing Sodiumalginate

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

Table 12: In vitro drug release data of Vildagliptin tablets containing xanthum gm

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

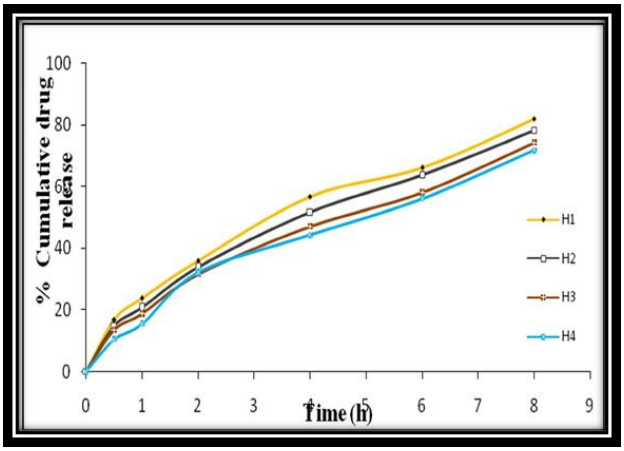

Fig. No. 8: *In-vitro* drug release profile of formulations H1 – H4

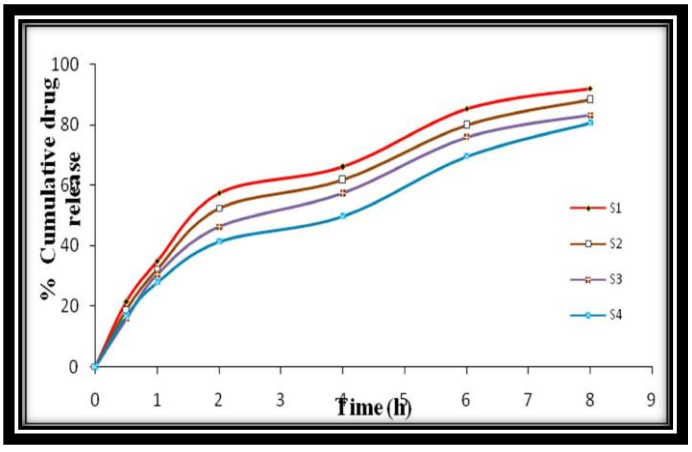

Fig.No.9: In-vitro drug release profile of formulations S1 – S4

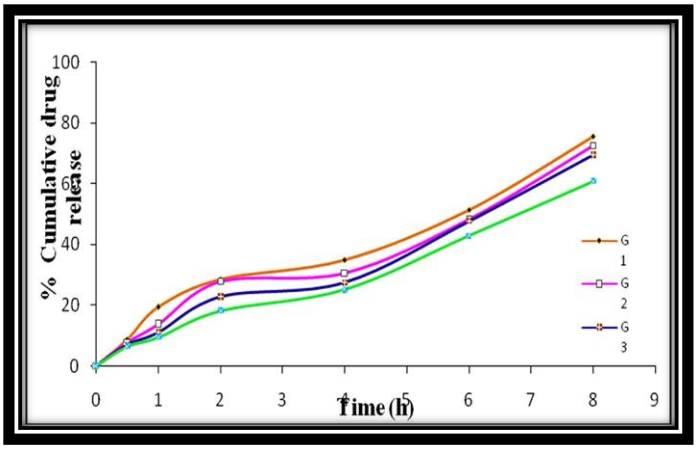

Fig. No.10: *In-vitro* drug release profile of formulations G1 – G4

Table.13: Best fit model for all formulation

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

3.7 Ex vivo permeation studies through porcine buccal mucosa:

The aim of this study was to investigate the permeability of buccal mucosa toVildagliptin.

Table.14: Ex vivo permeation studies through porcine buccal mucosa

Time(hrs.)	H4
0	0
0.5	11.86±0.12
1	19.01±0.22
2	26.16±0.28
3	29.54+0.33
4	36.99±0.38
5	58.81±0.44
6	73.55±0.78
7	75.17±0.42
8	76.64±0.52
Flux (µg.hrs^{-1}cm^{-2})	389.42
Permeability coefficient (cm/h)	0.111

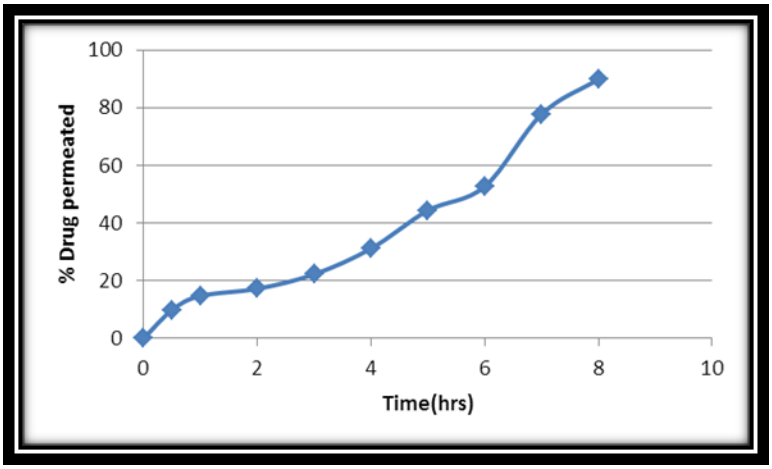

Fig.No.11: Ex-vivo permeation of Vildagliptin drug solution through the porcinebuccal mucosa

4. SUMMARY:

In the present project of Vildagliptin mucoadhesive buccal tablets were prepared and evaluated. As vildagliptin undergoes extensive first pass metabolism its bioavailability when given through Conventional route is 30% and (80x4) doses. So, in order to improve its bioavailability, to decrease the dosing frequency and to bypass the first pass metabolism the study has been planned to prepare vildagliptin buccal tablets

The gift sample of vildagliptin was analyzed by various organoleptic and spectrophotometric methods. The sample of Vildagliptin possesses similar color, odor, and taste and texture s given in officials. The melting point of procured sample was analyzed by capillary fusion method and found 180°C. The qualitative solubility of vildagliptin was determined by various solvent systems. The maximum solubility was found in ethanol, pH 6.8 buffer The solubility of Vildagliptin was shown in Table-11

The calibration curve of Vildagliptin was prepared in pH 6.8 phosphate buffer. The plot of different concentrations of Vildagliptin versus absorbance was found linear inthe concentration range 2-12 µg/ml at 229 nm. The absorbance at different concentrations was shown in Table-12. The data of standard curve was linearly regressed.

The FT-IR spectrum of drug sample was concordant with reference spectra as given in IP 1996. The IR spectra of Vildagliptin sample was shown in Figure-3

and Table-13respectively.

4.1 Compatibility studies

An FT-IR spectroscopy study was carried out to check the compatibility between the drug Vildagliptin and the polymers. The FTIR was performed for drug, polymers and physical mixture of drug and polymers. The spectral data of pure drug and various drug-polymers are presented in (Figure No.3-6). The results indicate that there was no chemical incompatibility between drug and excipients used in formulation

4.2 Evaluation of pre-compression characteristics of powder blend

The powder blends were also evaluated for various pre-compression parameters. The results are shown in Table No.14. These blends displayed angle of repose values between 25.03±0.45 - 27.26±0.60 indicating good flow property. As it is below 30˚ it indicates good flow properties of blend. Bulk density was found to be between 0.41±0.14 - 0.51±0.22 g/cm^3 and tapped density between 0.56±0.05 - 0.62±0.06 g/cm^3 for all the formulations. From the density data, % compressibility was calculated. The results showed that Hausner's ratio value of 1.14±0.01- 1.19±0.01 and good Carr's index value of 12.67±0.47 - 16.19±0.83 % for all pre compressional mixtures.

4.3 Evaluation of Vildagliptin mucoadhesive buccal tablets. Tablet thickness, hardness and friability

Thus tablets werehaving good mechanical strength. The friability of all the formulated tablets of Vildagliptinwas found to be between 0.52 - 0.85 % are reported in Table No.15 and all the formulated tablets of Vildagliptin confirmed that % friability within the official limits (*i.e.*, not morethan 1 %).

4.3.1 Weight variation

Prepared tablets were evaluated for weight variation and percentage deviations from the average weight are reported in Table No.15. It was found to be within (±7.5) the prescribed limits.

4.3.2 Percentage of Drug content

The drug content of all the formulations of Vildagliptin tablets were found to be withinthe range of 99.09±0.67 - 100.31±0.98 % which were within the limits of IP specifications *i.e.*, ±5%. The drug content of all the formulations of Vildagliptin tablets are shown in Table No.16.

4.3.3 Surface pH

The surface pH was determined in order to investigate the possibility of any side effects in the oral cavity as acidic or alkaline pH is found to cause irritation to Surface pH of all the formulations was found to be in the range of 6.21±0.46 - 6.61±0.35. This pH is near to the neutral and also these results revealed that all the formulation provide an acceptable pH in the range of salivary pH (5.5 to 7.0). The surface pH of all the formulations is shown in Table No.16

4.3.4 Swelling studies

Swelling index was determined with respect to time. The swelling index of the tablets was increased with increasing concentration of polymer. Swelling study was performed on all the batches of Vildagliptin mucoadhesive buccal tablets for 8 hrs. The swelling index of all formulations was in the range of 103±6.24 - 193.66±6.02 %. Maximum swelling was observed with the formulations (H1, H2, H3, H4) containingCarbopol 940 and HPMC K15 LV than the remaining formulations. The results of swelling index studies are shown in the Table No.16 and Figure No.7.

4.3.5 Muco adhesive strength:

The values of the mucoadhesive strength of Vildagliptin mucoadhesive buccal tablets are given in Table. Adhesion occurs shortly after the beginning of swelling but the bond formed between mucosal layer and polymer is not very strong. The mucoadhesive strength was influenced by the nature and proportions of the bioadhesive polymers used in the formulations. In all the formulations, as the polymer concentration increased, the mucoadhesive strength also increased. The order of mucoadhesive strength of bioadhesive polymers used in the formulations can be given as carbopol 940 and HPMC K15 LV < carbopol 940 and sodium alginate< carbopol and xanthum gum. Very strong mucoadhesion could damage the epithelial lining of the buccal mucosa.

4.3.6 In-vitro release studies

All formulations were formulated by using three different mucoadhesive polymers in varying concentration. The formulations H1-H4 were formulated with the help of HPMC K15 LV in concentration 10 mg, 30 mg, 60 mg, 80 mg respectively. The formulations S1-S4 were formulated with the help of sodium alginate in concentration 10mg, 30 mg, 60 mg, 80 mg respectively. The formulations G1-G4 were formulated with the help of xanthum gum in

concentration 10 mg, 30 mg, 60 mg, 80 mg respectively. The *in-vitro* release of Vildagliptin from mucoadhesive buccal tablet was found to vary according to the type and ratio of polymer used. The release of Vildagliptin was decreased with increasing concentration of HPMC K15 LV, sodium alginate, guargum.Thepercentage of the drug released from the formulations S1, S2, S3, S4 was found to be 92.00±0.56%, 88.12±0.60%, 83.09±0.47%, 80.60±0.48 % respectively. The percentage of the drug released from the formulations G1, G2, G3, G4 was found to be 75.43±0.47%, 72.62±0.58 %, 69.44±0.39 %, 60.89±0.34 % respectively. The formulation H4 is considered as a optimized formulation because of its better sustainedrelease 71.70±0.53 %. The data for in-vitro drug release of formulations was shown in the Table No.17-19 The in- vitro drug release profiles were shown in Figure No.8-10

4.3.7 Kinetic model data analysis

In-vitro drug release data of all formulations were fitted to Zero order, first order, Higuchi and Korsmeyer-Peppas equations to ascertain the pattern of drug release. Upon the application of different drug release model kinetics is given in Table No.20.It was found that all formulation follows Peppas model. The 'n' values for all the formulations were found to be more than 0.5.

4.3.8 Ex-vivo permeation of drug solution/ EX-vivo mucoadhesion studies:

From the results mentioned in the table-21 it was evident that selected formulation was showing good Flux and permeability coefficient values. The selected formulations H4 formulation was showing maximum flux value and permeability coefficient value i.e., 389.42 (µg.hrs-1cm-2) and 0.111 (cm/h).

5. CONCLUSION:

Development of mucoadhesive buccal drug delivery of Vildagliptin tablets is one of the alternative routes of administration and provide prolongs release. Vildagliptin mucoadhesive buccal tablets could be formulated using the drug, were evaluated for physicochemical parameters *i.e.*, hardness, thickness, weight variation, friability, % ofdrug contents, surface pH, bio adhesive strength, % Swelling index, *In-vitro* drug release studies and In-*vitro* drug release kinetic studies. The best formulation H4 was showed the optimum sustained drug release *i.e.*, 71.70±0.53 % at the end of 8 hrs. by using drug and polymer in the ratio of 1:1. The in-vitro drug release kinetics studies revealed that all the formulations fit to Peppas order kinetics followed by non-Fickian diffusion mechanism. Hence it can be concluded that the formulation H4 will be useful for buccal administration of Vildagliptin.

So, the mucoadhesive buccal tablets of Vildagliptin may be a good choice to bypass thehepatic first pass metabolism with an improvement in the bioavailability of Vildagliptinthrough buccal mucosa

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