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FORMULATION AND INVITRO EVALUATION OF BUCCAL DRUG DELIVERY SYSTEM OF VENLAFAXINE HYDROCHLORIC ACID TABLETS

M. Purushothaman*, B. Narasimha Rao, V. Viswanath, S. Y. Shasikanth

P. Ramireddy Memorial College of Pharmacy, Prakruthi Nagar,Utukur Road,Kadapa.

Abstract:

In the present study Bilayer buccal tablets were formulated by using ethyl cellulose as backing membrane. From the foregoing investigation it might be close that rate of drug release from the buccal tablets can be govern by the polymer and concentration of the polymer used in the preparation of tablets. Synchronized drug release in first order approach attain in the current study indicates that the hydrophilic matrix tablets of Venlafaxine HCl was prepared using Carbopol 934 and HPMC K100 can successfully be employed as a buccoadhesive controlled released during delivery system. The pre compression mix for all formulations contains various estimation parameters and the outcome found to be within limits. The post compression parameters for all the formulations also originate to be within limits. Slow, controlled and complete release of Venlafaxine HCl over a episode of 9 hours be obtains from matrix tablets formulated HPMC K 100 (F5 Formualtion) with 93.62 % drug release.

Keywords: *Bilayer buccal tablet, Venlafaxine HCl , HPMC, Carbopal.*

Corresponding Author:

Dr. M. Purushothaman,

Principal & Professor,

P.Ramireddy Memorial College of Pharmacy,

Prakruthi Nagar,Utukur Road,

Kadapa.

QR code

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INTRODUCTION:

The unique environment of the oral cavity offers its potential as a site for drug delivery. Because of the rich blood supply and direct access to systemic circulation, the oral mucosa path is suitable for drugs, which are prone to acid hydrolysis in the stomach or which are extentensively metabolized in the liver (first pass effect).

Administration of a drug passing through the buccal mucosa (the lining of the cheek) to the systemic circulation is discrete as buccal delivery. Despite, the buccal mucosa is comprehensively less permeable than the sublingual mucosa generally not able toward provide rapid drug absorption or good bioavailability; it is reasonably more permeable than the skin and also offers other advantage over alternative delivery routes [1-3]. The fact that the buccal mucosa is less permeable than sublingual floor makes it more desirable site for sustained drug delivery. Apart from avoiding enzymatic degradation and first pass metabolism, the non acidic circumstances and lipophilic nature of the buccal tissue supply potential and promises for thriving deliverance of peptide and proteins [4-6].

The various strategies Employed for Buccal Delivery

Bio adhesive Buccal Tablets
Bio adhesive buccal Gels
Bio adhesive Buccal Patches

Bioadhesive Buccal Tablets

Bioadhesive tablets are immobilized drug delivery systems. They can be formulating monolithic, partially coated or multi-layered matrices. Monolithic tablets are easy to fabricate by conservative techniques and provide for the option of loading large amount of drug. In case of bi-layered tablets, drug can be incorporated in the adhesive layer, which comes in contact with the mucosal surface. This drug containing mucoadhesive layer is then confined from the oral cavity environment by a upper inert layer (backing layer), which faces into the oral cavity [7-12].

Bioadhesive Buccal Patches

Adhesive patches can be planned either for unidirectional release into the oral mucosa or for bi-directional release into the oral cavity as well as into the oral mucosa. The adhesive part of the system can be used as drug carrier or as an adhesive for the upholding of a drug loaded non-adhesive layer. In this respect, a peripheral adhesive ring could be casted. The use of an impermeable backing layer will maximize the drug concentration gradient and prolong adhesion because the system is protected from saliva [13-18].

Bioadhesive buccal Gels

Viscous adhesive gels have been designed for local therapy using polyacrylic acid and polymethacrylate as gel forming polymers. Gels are reported to delay residence time on the oral mucosa to a significant level. This not only improves absorption but also allows for sustained release of the active principle [19-21].

MATERIALS AND METHODS:

Venlafaxine HCL obtained from Sura labs, HPMC K15M obtained from Merck Specialities Pvt Ltd, Mumbai, India, HPMC K100M obtained from Merck Specialities Pvt Ltd, Mumbai, India, Microcrystalline cellulose obtained from Merck Specialities Pvt Ltd, Mumbai, India, Magnesium stearate obtained from Merck Specialities Pvt Ltd, Mumbai, India Talc obtained from Merck Specialities Pvt Ltd, Mumbai, India, Ethyl cellulose obtained from Merck Specialities Pvt Ltd, Mumbai, India, Carbopol obtained from Merck Specialities Pvt Ltd, Mumbai, India,

Method of Preparation of Mucoadhesive Tablets:

Buccoadhesive Bilayered Tablets:

Preparation: Direct compression technique has been use to prepare buccal tablets of Venlafaxine HCl using HPMC K15, HPMC K100, and CARBOPOL 934 as polymers.

Procedure: All the ingredient including drug, polymer and excipients were weighed precisely according to the batch procedure (Table-6.1).

- All the ingredients excepting lubricants were mixed in the order of rising weights and blended for 10 min in an exaggerated polyethylene pouch.
- After uniform mixing of ingredients, lubricant was added another time consistent for 2 min. The arranged mix (230 mg) of each formulation was pre-compressed, on multi stationed tablet punching machine at a pressure of 0.5 ton for 30 s to form solitary coated flat-faced tablet of 9 mm diameter.
- Then, 50 mg of ethyl cellulose powder was added and final compression was done at a pressure of 3.5 tons for 30 s to get bilayer tablet.

Table 1: Compositions of the Designed Bilayer Tablets

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
VENLAFAXINE HCL	20	20	20	20	20	20	20	20	20
HPMC K15	20	30	40	----	----	----	----	----	----
HPMC K100	----	----	----	20	30	40	----	----	----
CARBOPOL 934	----	----	----	----	----	----	20	30	40
TALC	3	3	3	3	3	3	3	3	
MAGNESIUM STEARATE	3	3	3	3	3	3	3	3	3
MCC pH 102	QS	QS	QS	QS	QS	QS	QS	QS	QS
ETHYL CELLULOSE	50	50	50	50	50	50	50	50	50
TOTAL	280	280	280	280	280	280	280	280	280

Preformulation Parameters

The quality of tablet, once formulate by rule, is generally dictated by the quality of physicochemical properties of blend. There are many formulations and procedure variables involved in combination and all these can affect the characteristics of blend produced.

Angle of Repose: The frictional force in a loose powder can be calculated by the angle of repose. It is defined as, the maximum slant possible involving the surface of the heap of the powder and the horizontal plane. If more powder is added to the pile, it slides down the side of the pile until the reciprocated friction of the particles producing a surface angle, is in balance with the gravitational force. The fixed funnel technique was in use to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph document that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touch the angle of funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$$\tan \theta = h / r$$

$\tan \theta$ = Angle of repose

h = Height of the cone ,

r = Radius of the cone base

Table 2: Angle of Repose Values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk Density: Bulk density is not an intrinsic property of a material; it can change depending on how the material is handled. For example, a powder poured into a cylinder will have a exacting bulk density; if the cylinder is disturbed, the powder particle will move and usually settle nearer, resulting in a higher bulk density. For this reason, the bulk density of powders is usually reported both as "freely settled" (or "poured" density) and "tapped" density (where the tapped density refers to the bulk density of the powder after a precise compaction process,

usually involving vibration of the container.). The powder was with awareness leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:

$$\text{Bulk Density} = M / V_o$$

Where, M = weight of sample

V_o = apparent volume of powder

Tapped Density: The tapped density increased bulk density attained after mechanically tapping containing a powder sample. It is obtained by mechanically tapping a graduated measuring cylinder containing a powder.

The tapped density was calculated, in gm per L, using the formula:

$$\text{Tap} = M / V$$

Where, Tap= Tapped Density

M = Weight of sample

V= Tapped volume of powder

Measures of Powder Compressibility: The Carr index is indication of the flowability of a powder. In free-flowing fine particles the bulk density and tapped density would be close therefore; the Carr index would be small. On the other hand, in a poor-flowing powder where there is greater interparticle inter procedures the difference between the bulk and tapped density observed would be greater, therefore, the Carr index would be larger.

These differences are reflected in the Compressibility Index which is calculated using the following formulas:

$$\text{Carr's Index} = [(\text{tap} - b) / \text{tap}] \times 100$$

Where, b = Bulk Density

Tap = Tapped Density

Table 3: Carr's index Value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Post compression Parameters:

Characterization of Buccal Tablets of Venlafaxine HCl:

Evaluation of Muco Adhesive Buccal Tablets of Venlafaxine HCl:

Hardness Test: Tablets require a certain amount of force or hardness and resistance to friability, to with stand automatic shocks of managing in manufacture, packaging and shipping. The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm^2.

Thickness:

The thickness of three randomly elected tablets from each formulation was firm in mm using a Screw gauge.

Friability test: It is the phenomenon whereby tablet surface are damaged and/or show evidence of lamination when subjected to mechanical shock or abrasion The friability of tablet was determined by using Roche Friabilator as per IP formula of friability. It is articulated in percentage (%). Twenty tablets were primarily weighed ($W_{initial}$) and transfer into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The percentage friability was then calculated by,

$$F = \frac{W_{inital} - W_{final}}{W_{initial}} X100$$

% Friability of tablets less than 1% is considered acceptable.

Uniformity of Weight: The weight variation test was performing as per formula of IP. The weight (mg) of each of 20 individual tablets, selected erratically from each formulation was determined by each tablet off and introduction it in an electronic balance.

Uniformity of Drug Content: Five tablets were powdered in a glass mortar and the powder equivalent to 50 mg of drug was placed in a 100 ml conical flask. The drug was extract with 40 ml distilled water with vigorous shaking on a automatic gyratory shaker (100 rpm) for 1 hour. Then heated on water bath with occasional quaking for 30 minutes and filtered into 50 ml volumetric flask through and filtrate was made up to the mark by passing more distilled water through filter, dilution were made and absorbance was measured at 220 nm against blank (distilled water).

Swelling Index: The swelling index of the buccal tablet was evaluate in phosphate buffer pH 6.8 The initial weight of the tablet was determined and was placed in 6 ml phosphate buffer pH 6.8 in a petridish and then was incubate at 37^o C. The tablet was removed next to different time intervals (0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0 and 8.0 hrs) blotted with filter paper and reweighed (W_2). The swelling index is calculated by the formula:

$$\text{Swelling index} = 100 (W_2 - W_1) / W_1.$$

Where, W_1 = Initial weight of the tablet.

W_2 = Final weight of tablet.

***In-vitro* Drug Release Study:** The study was carried out in USP XXIII tablet dissolution test apparatus-II Labindia, Mumbai, India, paddle stirrer at 50 rpm and 900 ml of phosphate buffer pH 6.8 as dissolution medium maintain at 37 0.5^0C. At different time interval 5 ml of sample was withdrawn and replaced with fresh medium. The samples were filtered through 0.25 µm filter paper and analyze for Venlafaxine HCl after dilution at 216 nm using Labindia, Mumbai, India UV-Visible spectrophotometer.

Release Kinetics: As a model-dependent approach, the dissolution data was fixed to five popular release models such as zero-order, first-order, diffusion and exponential equations. The order of drug release from matrix systems was described by using zero order kinetics or first orders kinetics. The mechanism of drug release from matrix systems was studied by using Higuchi equation, erosion equation and Peppas-Korsemeyer equation.

Zero Order Release Kinetics: It defines a linear correlation between the fractions of drug released versus time.

$$Q = k_o t$$

Where, Q is the fraction of drug released at time t and k_o is the zero order release rate constant.

A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

First Order Release Kinetics: Wagner assuming that the exposed exterior area of a tablet decrease exponentially with time throughout dissolution process that drug release from most of the leisurely release tablets could be adequately by apparent first-order kinetics. The equation that describes first order kinetics is

$$\text{In } (1\text{-}Q) = - K_1 t$$

Where, Q is the fraction of drug released at time t and k_1 is the first order release rate constant.

Thus, a plot of the logarithm of the fraction of drug remained against time will be linear if the release obeys first order release kinetics.

Higuchi's Equation: It defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time.

$Q=K_2 t^{½}$

Where, K2 is the release rate constant.

A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependant.

Estimation of Venlafaxine HCl:

Determination of λmax of Venlafaxine HCl in phosphate buffer pH 6.8 solutions: Weighed amount 100mg of Venlafaxine HCl is dissolved in phosphate buffer pH 6.8 make up the final volume to 100ml obtain a 1000 µg/ml solution. The 10ml of stock solution was further diluted with phosphate buffer 6.8 in 100ml to get 100 µg/ml .The effect of dilution on absorption maxima was studied by diluting the above solution to 10 µg/ml and scanned from 200-400 nm. From the spectra of drug max of Venlafaxine HCl 216 nm was selected for the analysis. The calibration curve was prepared in the concentration range of 2,4,6,8,10,12 µg/ml at 216 nm. By using the calibration curve, the concentration of the sample solution can be determined.

Standard Calibration Curve of Venlafaxine HCl in Phosphate Buffer pH 6.8 Solution:

Standard Stock Solution: A stock solution containing 1mg/ml of pure drug was prepared by dissolving 100 mg of Venlafaxine HCl in sufficient phosphate buffer pH 6.8 to produce 100 ml solution in a volumetric flask.

Stock solution: From the standard stock solution, 5 ml of the stock solution was further diluted to 50 ml with phosphate buffer pH 6.8 into a 50 ml volumetric flask and diluted up to the mark with phosphate buffer pH 6.8. Aliquots of 0.2, 0.4, 0.6, 0.8, 1 and 1.2 ml of stock solution were pipette out into 10ml volumetric flasks. The volume was made up to the mark with phosphate buffer pH 6.8. These dilutions give 2, 4, 6, 8, 10 and 12 mcg/ml concentration respectively. The absorbance was measured in the UV-Visible spectrophotometer at 216 nm using distilled water as blank and graph of concentration versus absorbance was plotted. The absorbance data for standard calibration curves are given.

Drug – Excipient Compatibility Studies

Fourier Transform Infrared (FTIR) Spectroscopy: The physical properties of the mixture were compared with those of plain drug. sample was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mount in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm^{-1}. The resultant spectrum was compare for any spectrum changes.

RESULTS AND DISCUSSION

The main aim of this work was to develop buccoadhesive bilayered tablets to release the drug at buccal mucosal site in unidirectional pattern for extended period of time without wash out of drug by saliva. Carbopol 934, HPMC K15, HPMC K 100

were selected as buccoadhesive polymers on the basis of their matrix forming properties and mucoadhesiveness, while ethyl cellulose, being hydrophobic, used as a backing material. Ethyl cellulose has recently been reported to be an excellent backing material, given its low water permeability and moderate flexibility.

Table 4: Standard Calibration Graph of Venlafaxine HCl:

Concentration (mcg/ml)	Absorbance* (mean±SD)
2	0.08
4	0.158
6	0.237
8	0.318
10	0.397
12	0.485

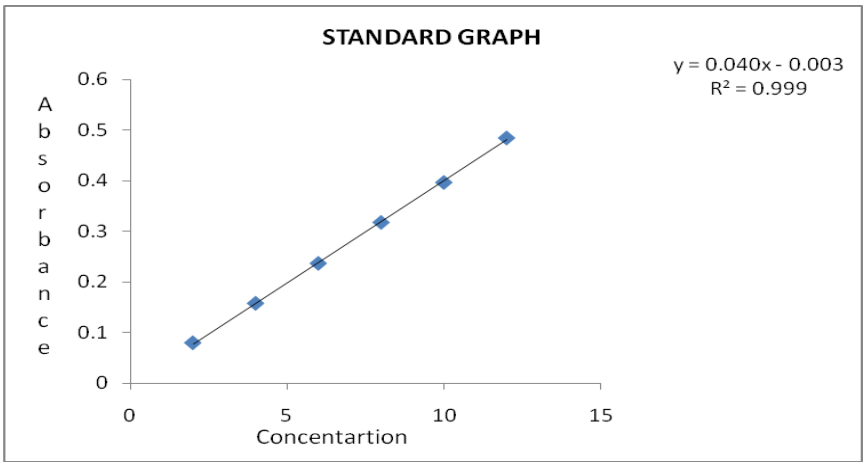

Fig 1: Calibration curve of Venlafaxine HCl

Drug-Excipient Compatibility Studies:

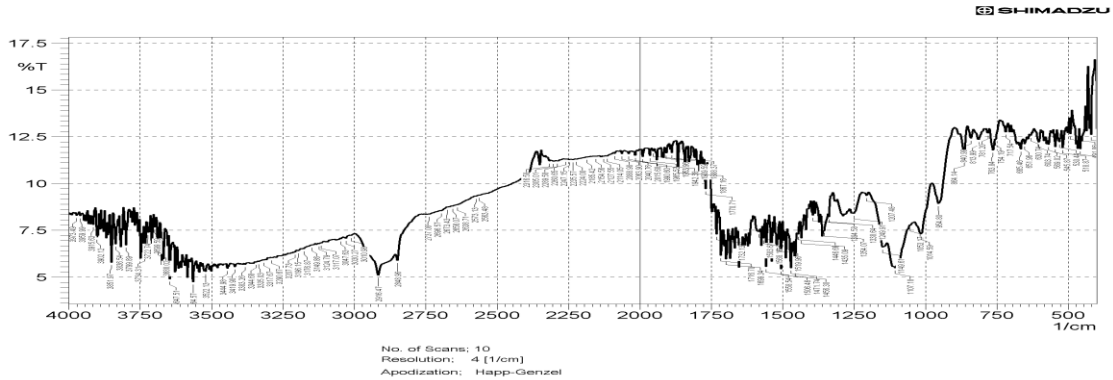

Fig 2: FTIR spectrum of Pure Drug

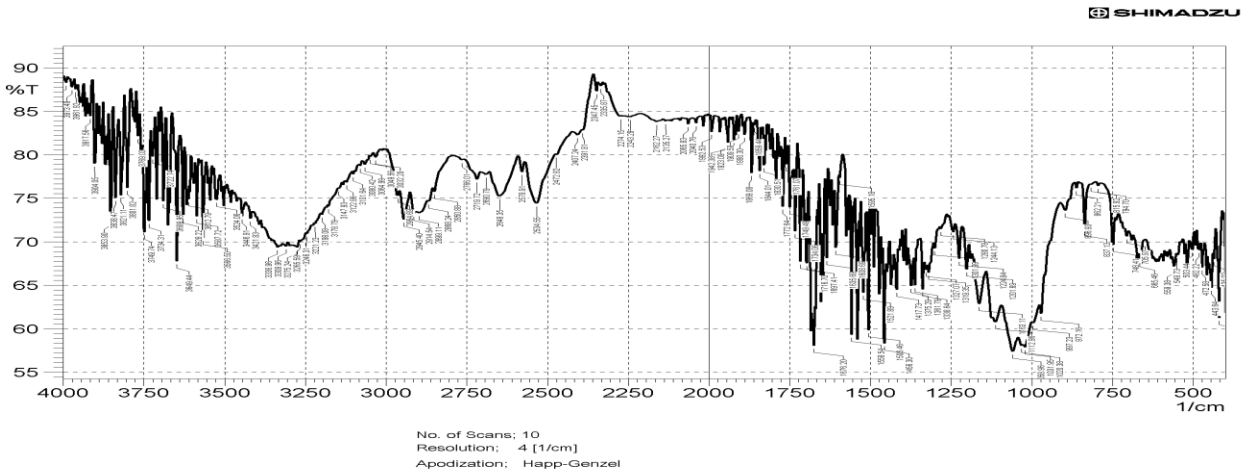

Fig 3 : FTIR Spectrum of Optimised Formulation:

Precompression Evaluation Parameters of Tablets

Table 5: Micromeritics Properties of Powder Blend:

Formulation Code	Bulk density (gm/cm^2)	Tapped density (gm/cm^2)	Compressibility Index (%)	Hausner's ratio	Angle of repose (Θ)
F1	0.49±0.07	0.57±0.01	16.21±0.06	0.86±0.06	28.34
F2	0.56±0.06	0.62±0.05	16.87±0.05	0.98±0.05	27.91
F3	0.52±0.03	0.68±0.07	17.11±0.01	0.64±0.03	26.70
F4	0.54±0.04	0.64±0.08	17.67±0.08	1.12±0.04	26.78
F5	0.53±0.06	0.67±0.03	16.92±0.04	1.2±0.08	29.34
F6	0.56±0.05	0.66±0.06	17.65±0.09	1.06±0.09	28.23
F7	0.58±0.06	0.69±0.04	16.43±0.05	0.76±0.03	29.34
F8	0.48±0.05	0.57±0.02	17.97±0.02	1.15±0.09	29.81
F9	0.54±0.08	0.62±0.03	17.54±0.09	1.17±0.02	27.91

Formulations blend of all the formulations were passed the pre compression parameters like angle of repose, bulk density, tapped density and Hausner's ratio.

Table 6: Evaluation Data of Venlafaxine HCl Buccoadhesive Tablets

Formulation code	Hardness (kg/cm)	Thickness (mm)	Weight variation (mg)	Friability (%)	Drug content (%)
F1	4.8±0.02	2.80±0.00	279.6±0.99	0.79±0.01	100.09±0.56
F2	4.3±0.05	2.83±0.06	278.8±0.99	0.67±0.01	102.73±0.46
F3	4.3±0.05	2.87±0.06	279.8±0.38	0.57±0.01	98.75±0.88
F4	5.7±0.06	2.86±0.06	280.7±0.99	0.55±0.00	99.70±0.34
F5	5.4±0.03	2.87±0.06	279.8±0.38	0.51±0.01	97.95±0.38
F6	5.0±0.02	2.90±0.00	280.1±0.99	0.87±0.03	98.75±0.88
F7	5.6±0.07	2.97±0.06	279.6±0.17	0.46±0.01	103.36±0.83
F8	5.3±0.05	3.01±0.01	281.0±0.40	0.72±0.01	101.09±4.00
F9	5.1±0.02	2.95±0.00	280.0±0.20	0.56±0.02	99.75±0.38

The assayed drug content in various formulations varied between 98.64% and 100.26% (mean 99.68%). The average weight of the tablet was found to be between 281.4 mg and 283.2 mg (mean 280.2 mg), % friability range between 0.46 and 0.76(mean 0.43 %) and thickness of the tablets for all the formulations was found to be between 2.80 mm and 3.00 mm with average of 2.90 mm.

Buccoadhesive tablets containing Carbopol show hardness in the series of 5.00 to 5.60 kg/cm ^{2} and it increased when used in amalgamation with HPMC k100. The hardness of the tablets containing HPMC K15 was much lesser range from 4.30 to 4.8 kg/cm^2 and increased with increasing amounts of HPMC or Carbopol. Drug is liberate by diffusion through the gel layer and/or wearing a way of this layer.

***Invitro* Drug Release Studies:**

Table 7: *In vitro* release data of Venlafaxine HCl mucoadhesive tablets (F1, F2 & F3)

Time (h)	F-1	F-2	F-3
0.5	33.91±0.25	25.46±0.54	17.89±0.91
1	55.97±1.56	35.56±1.19	22.28±0.27
2	88.24±0.74	48.51±0.49	29.96±0.47
3	101.52±0.58	60.03±1.21	46.20±0.21
4		71.23±1.77	50.15±0.65
5		86.59±0.62	59.59±0.25
6		94.82±1.17	68.59±1.54
7		102.95±1.54	76.28±0.53
8		---------	88.24±0.11

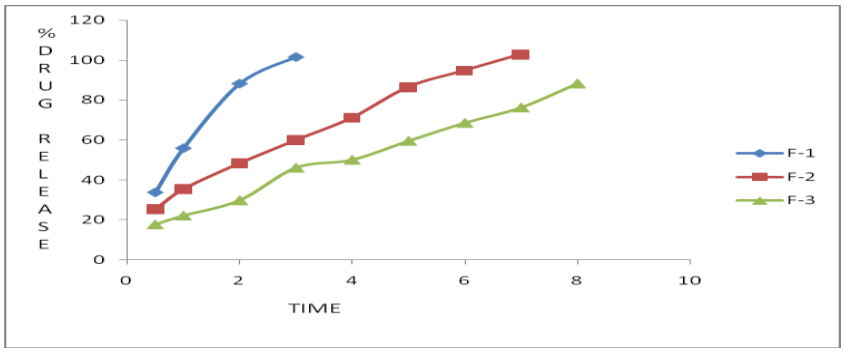

Fig 4: *In vitro* dissolution graph of formulations F1-F3

Table 8: In Vitro Release Data of Venlafaxine HCl Mucoadhesive Tablets Containing HPMC K100 (F4, F5 & F6)

Time (h)	F-4	F-5	F-6
0.5	24.69±0.35	19.86±0.99	17.11±0.08
1	39.73±1.35	27.32±0.25	23.14±1.18
2	48.95±2.36	36.98±1.77	33.20±1.13
3	60.47±2.02	48.40±1.31	43.60±1.10
4	70.35±2.65	57.40±1.95	51.06±0.21
5	82.42±1.95	65.19±0.79	56.02±0.47
6	97.79±0.34	70.46±1.34	60.64±1.65
7	------	78.25±0.38	74.24±1.09
8	------	87.25±0.79	77.75±0.38
9	------	93.62±1.95	83.41±1.31

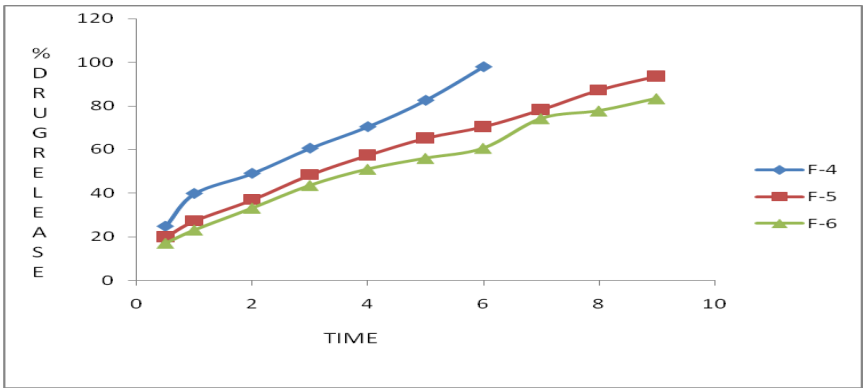

Fig 5: In vitro dissolution graph of formulations F4-F

Table 9: In vitro Release Data of Venlafaxine HCl Containing Carbopol 934 (F7, F8 & F9)

Time (h)	F-7	F-8	F-9
0.5	50.04±0.26	35.56±0.32	21.84±0.44
1	65.63±0.29	40.17±0.18	29.19±0.38
2	68.92±0.72	54.00±0.16	44.02±0.24
3	82.20±2.38	65.96±2.22	58.51±1.59
4	98.89±3.45	74.74±0.33	68.37±0.55
5	------	82.75±0.18	78.36±0.48
6	------	99.43±1.98	87.03±0.82
7	------	------	99.32±1.98

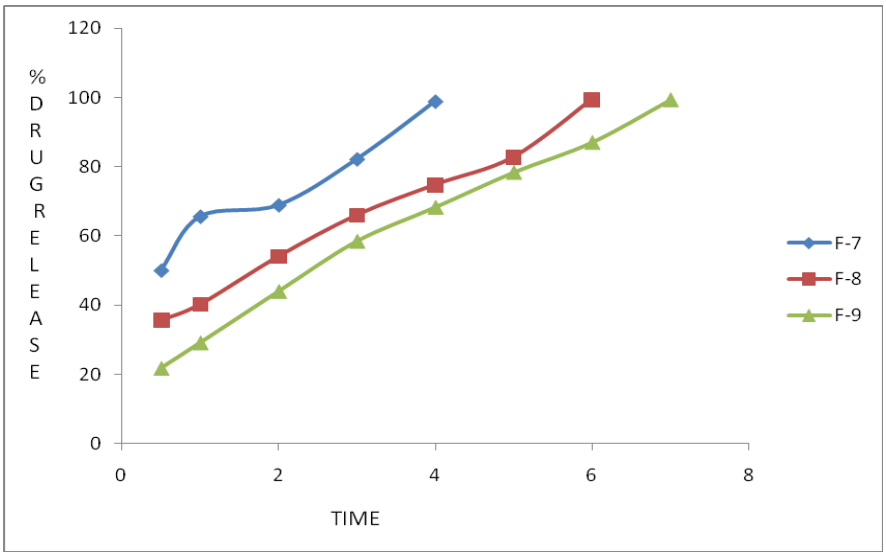

Fig 6: In Vitro Dissolution Graphs of Formulation (F7, F8 & F9)

Invitro drug release studies Venlafaxine HCl from different composition of matrix forming polymers. The release rate of Venlafaxine HCl decreased with rising concentration of the polymers. The Release rate of the tablets decreased from F1 to F3 when

tablets are ready with HPMC K15 in 1:1, 1:1.5 and 1:2 ratios.

The release rates were studied with concentrations of HPMC K100 and the release rate decrease with rising concentrations from F4 to F6 respectively. Release rates were studied with Carbopol 934 in rising concentrations i.e. 1:1, 1:1.5, and 1:2 and release rate was found to be decreased with all the three polymers when used in the ratio 1:2.

Among all Formulation F5 containing HPMC K100 M in the concentration of 1:1.5 was found to be excellent with better drug release i.e., 93.62% in 9 hours.

Several kinetic models describing drug release from immediate and modified released dosage forms. The replica release data by correlation coefficient (r). The correlation coefficient (r) value was used as criteria to choose the best model to explain the drug release from the buccoadhesive tablets. The 'r' values obtained for fitting the drug release data to first order, that the drug liberate follows first order kinetics. From Higuchi's equation, the high value of correlation coefficient 'r' suggesting that the drug liberate method from these tablets was diffusion controlled. The values of **'n'** in Pappas model indicate the drug liberates follows non-Fiction diffusion.

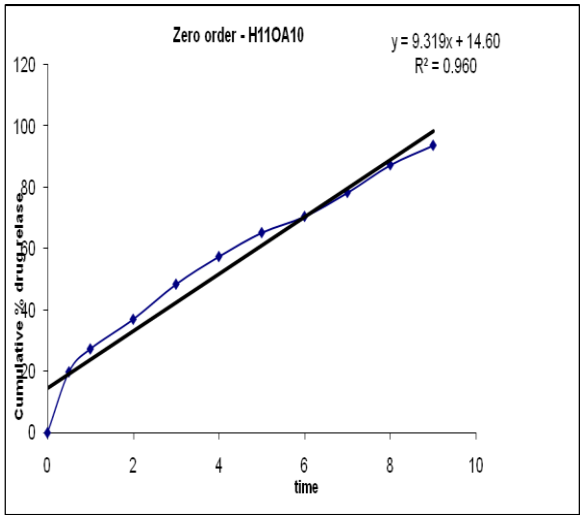

Fig 7: Zero Order Release Kinetics for F5

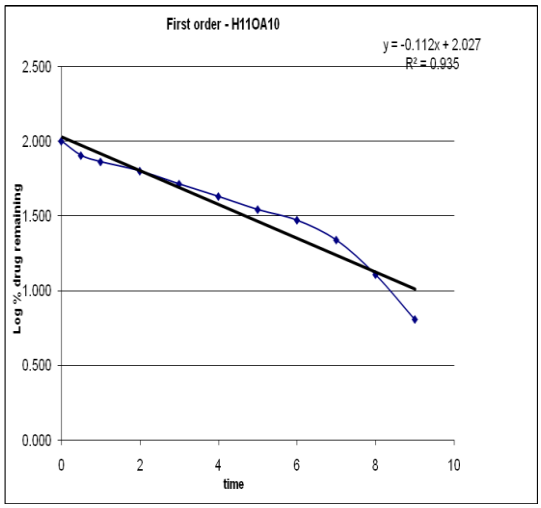

Fig 8: First Order Release Kinetics for F5

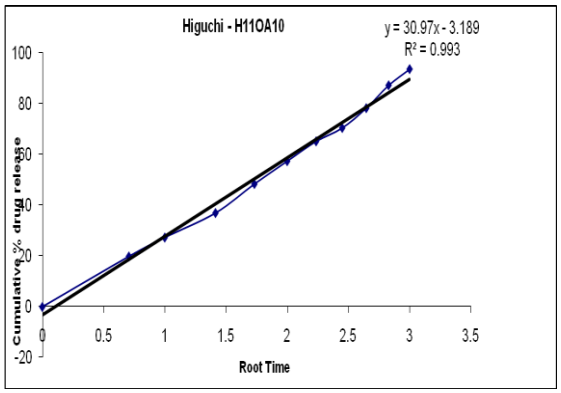

Fig 9: Higuchi Release Kinetics for F5

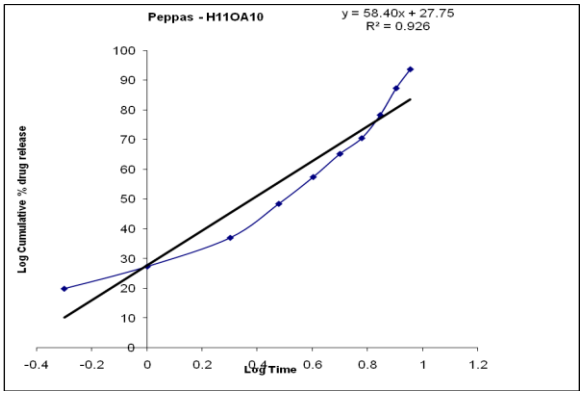

Fig 10: Korsmeyer Peppas Release Kinetics for F5

Table 10: Regression Analysis of the In Vitro Release Data According to Various Releases Kinetic Models:

Formulation code	Zero order	First order	Higuchi	Korsmeyer-Peppas
	r^2	r^2	r^2	r^2
F5	0.960	0.935	0.993	0.926

From the beyond consequences it is accomplished that the drug liberate from the formulate buccal adhesive tablets of Venlafaxine HCl follows Higuchi release kinetics and was diffusion controlled.

CONCLUSION:

The release rates were studied with concentrations of HPMC K100 and the release rate decrease with rising concentrations from F4 to F6 respectively. Release rates were studied with Carbopol 934 in rising concentrations i.e. 1:1, 1:1.5, and 1:2 and release rate was found to be decreased with all the three polymers when used in the ratio 1:2.

Among all Formulation F5 containing HPMC K100 M in the concentration of 1:1.5 was found to be excellent with better drug release i.e., 93.62% in 9 hours.

REFERENCES

1. Pandit JK, Vemuri NM, Wahi SP, Jayachandra Babu R. Mucosal Dosage Form of Ephedrine Hydrochloride using Gantrez-A 139. Eastern Pharmacist 1993; 36:169-170.
2. Gupta A, Garg S, Khar RK. Mucoadhesive Buccal Drug Delivery System: A Review. Indian Drugs 1992; 29(13):586-93.
3. Harris D, Robinson JR. Drug Delivery via Mucous Membrane of the Oral Cavity. J Pharm Sci 1992; 81:1-10.
4. Wong FC, Yuen KH, Peh KK. Formulation and Evaluation of Controlled Release Eudragit Bucccal Patches. Int J Pharm 1999; 178:11-2.
5. Marriott, C.and Gregory, N.P., 1990, Mucus physiology. In: V.Lenaerts and R.Gurny, Bioadhesive Drug Delivery Systems, CRC Press, Boca Raton, FL, pp.1-24
6. Marriott, C.and Hughes, D.R.L., 1990, Mucus physiology. In: R.Gurny and H.E.Junginger, Bioadhesion-possibilities and Future Trends, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, pp. 29-43
7. Langer, R.S. and Peppas, N.A., 1992, New Drug Delivery Systems. BMES Bull., 16:3-7
8. Peppas, N.A and Buri, p.a., Surface, interfacial and molecular aspects of polymer
9. bioadhesion on soft tissues. J. Controlled Release, 2: 257-275.
10. Nicholas A.Peppas, Mounica D.Little, and Yanbin Huang, Bioadhesive Controlled Released Systems pp-255-269.
11. Ponchel G, Irache J. Specific and non-specific bioadhesive particulate systems for oral delivery to the gastrointestinal tract. *Adv Drug Deliv Rev*. 1998; 34:191-219.
12. S. J.Hwang, H. Park and K. Park, "Gastric Retentive Drug-Delivery Systems", Crit. Rev. Ther. Drug Carrier Syst. 1998, 15 (3), 243–284.
13. L. Whitehead, J. T. Fell and J H Collett, "Development of a Gastroretentive Dosage Form", Eur. J. Pharma. Sci., 1996, 4 (1), 182.
14. P. Mojaverian, P. H. Vlasses, P. E. Kellner and M. . . Rocci, "Effects of gender, posture and age on gastric residence time of an indigestible solid: pharmaceutical considerations", Pharm. Res., 1988, 10, 639–644.
15. Singh B, Ahuja N. Response surface optimization of drug delivery system. In: Jain NK, ed. *Progress in Controlled and Novel Drug Delivery Systems.* New Delhi, India: CBS Publishers and Distributors; 2004, 20, 240.
16. .N. R. Jimenez-Castellanos, H. Zia and C. T. Rhodes, "Mucoadhesive drug Delivery Systems", Drug Dev. Ind. Pharm. 1993, 19, 143.
17. Vasir JK, Tambwekar K, Garg S.Bioadhesive microspheres as a controlled drug delivery. J Control Release 1998; 55:143-52.
18. Polymer profile Good R.J.Adhesion 8, 1.1976.
19. Choudary KPR., Srinivas L. Indian Drugs,37(9), 400.2000
20. S.B.Patil, R.S.R.Murthy, pharma times vol.38, No.4, Apr.2006.