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DESIGN, OPTIMIZATION AND EVALUATION OF MUCOADHESIVE BUCCAL TABLET OF VALSARTAN

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Keywords:

Valsartan, Mucoadhesive buccal tablets, Carbopol 934, Xanthan gum

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ABSTRACT: The main aim of this work was to formulate and study mucoadhesive buccal tablets of valsartan using various suitable bioadhesive polymers such as CP 934 and Xanthan gum. Nine formulations of valsartan were prepared by the direct compression method. The prepared tablets were characterized by swelling studies, % matrix erosion, surface pH, bioadhesive properties, *in-vitro* drug dissolution and *in-vitro* diffusion studies. It was found that CP 934 increases the swelling index also increased. The surface pH of all formulations was found to be satisfactory, and values were in between the range of 5-7 pH, hence no irritation to the buccal cavity is assumed. Tablets containing CP: Xanthan gum in the ratio 3:1 has shown the maximum percentage of *in-vitro* drug release through the buccal mucosa. The drug release was found to be zero-order release. The formulation F3 was considered as the optimized formulation based on satisfactory bioadhesive strength, *in-vitro* dissolution drug release of 96.72 ± 0.43%, for 12 h.

INTRODUCTION: Controlled drug delivery system is the one which delivers the drug at a predetermined rate, locally or systemically, for a specified period of time. The basic rationale of a controlled drug delivery system is to optimize biopharmaceutics, pharmacokinetic and pharma-codynamic properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug, administrated by most suitable route [1, 2, 3].

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These systems are actually controlling the drug concentration in the body, not just the release of the drug from the dosage form, as is the case in a sustained-release system. Another difference between sustained and controlled-release dosage forms is that the former is basically restricted to oral dosage form whilst controlled release systems are used in a variety of administration routes, including transdermal, oral and vaginal admini-stration. The main objective of developing these systems is to increase the safety of a product to extend its duration of action and decrease the side effects of drugs.

These systems have more flexibility in dosage design than conventional dosage forms. Drugs that are easily absorbed from the gastrointestinal tract (GIT) and have a short half life are eliminated quickly from the blood circulation.

To avoid this problem, the oral controlled-release (CR) formulation has been developed as these will release the drug slowly into the GIT and maintain a constant drug concentration in the serum for a longer period of time. Due to this other absorptive mucosa are considered as potential sites for drug administration. Transmucosal routes of drug delivery offer's distinct advantages over peroral administration for systemic drug delivery.

Permeation Barriers Across Buccal Mucosa: The main barriers that govern the permeation across the buccal mucosa are [22]

- Membrane coating granules
- Mucus
- Saliva
- Basement membrane

The Bioadhesive Dosage Forms: The bioadhesive dosage forms gave a new research field [24, 25]. These dosage formulations are mainly available for local therapeutic use for systemic therapeutic use. These forms have adhesion properties on a mucosa for a sufficient time to produce a therapeutic effect. Bioadhesion is the property of biological or synthetic material to adhere to a biological tissue for a given time. The bioadhesion mechanism is used to solve bioavailability problems resulting from a too-short stay of the pharmaceutical form at the absorption site. Bioadhesive tablets can adhere to the buccal mucosa and the drug is released upon hydration of the device, forming a hydrogel.

Bioadhesive tablets are usually prepared by direct compression. The two buccal adhesive tablets commercially available in the UK are "buccastem" (prochlorperazine maleate) and "suscard buccal" (glyceryl trinitrate).

MATERIALS: Valsartan was obtained as a gift sample from Ipca laboratory Ltd, Mumbai. Xanthan gum and Carbopol 934 p provide as gift samples from Bluecross laboratory Ltd., Nasik. Magnesium stearate, Mannitol, Talc purchased from Research lab fine chemical industry Mumbai. The entire chemicals were of analytical grade and double distilled water used throughout the experiment.

Ingredients used in Different Formulae of Mucoadhesive Buccal Tablet Formulation of Valsartan:

TABLE 1: INGREDIENTS USED IN DIFFERENT FORMULAE OF MUCOADHESIVE BUCCAL TABLET VALSARTAN

Ingredients	Formulation								
in (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Valsartan	80	80	80	80	80	80	80	80	80
Xanthan gum	20	20	20	40	40	40	60	60	60
Carbopol 934p	20	40	60	20	40	60	20	40	60
Mannitol	76	56	36	56	36	16	36	16	01
Talc	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2
Total weight					200				

METHODOLOGY:

Preformulation Studies: Preformulation studies on the obtained sample of a drug for identification and compatibility studies were performed [4, 5, 6, 7].

Characterization of the Drug:

Organoleptic Properties: The sample of valsartan was studied for organoleptic properties such as color, odor and appearance [26].

Melting Point: The melting points of valsartan were determined by the melting point apparatus. The observed value was compared with the reported value of [18].

Standard Plot of Valsartan in 6.8 pH: The U. V. spectrum of valsartan was obtained using UV Jasco V630 valsartan (10 mg) was accurately weighed and transferred to 100 ml volumetric flask. It was dissolved in 10 ml of methanol and diluted up to 100 ml with pH 6.8 phosphate buffer. The above-made solution was further diluted to obtain concentration ranging from 5-30 µg/ml. The resulting solution was recorded at 250 nm using a UV visible spectrometer. pH 6.8 phosphate buffer was taken as blank. The calibration plot was constructed and the linearity was established. A calibration curve was performed in triplicate [19].

Drug Excipient Compatibility Study: Drug excipient compatibility was performed by liquid fourier transform infrared. It was performed by mixing the drug with excipient in equal proportion and then the IR spectrum was noted for a mixture using NaCl cell. A small amount of the mixture was placed on the sample cell, the cell was then fitted in the sample holder, spectra were scanned over a frequency range 4000-400 cm^{-1} with FTIR instrument and the spectral analysis were done.

Preparation of Mucoadhesive Tablets:
Preparation of Mucoadhesive Buccal Tablet (By Direct Compression Method):

1. Weighing of ingredients
2. Milling of drug and excipients
3. Mixing of drug and excipients
4. Tablet compression

Mucoadhesive tablets were prepared by direct compression method. The blended powder was evaluated for its precompression characteristics and then compressed on a ten station pilot press using 8 mm flat-faced punches. Tablets were prepared by direct compression technique. The ingredients were accurately weighed and mixed in a glass mortar and pestle for 30 min to obtain a uniform mixture. The mixture was passed through sieve no. 120. Then the above blend was compressed on ten station pilot press at minimum compaction force in 8 mm punches of single stroke tableting machine [20].

Evaluation Parameters:
Bulk Density for Powder: Calculated based on the following formula: [8]

$$\text{Bulk density } (\rho\ 0) = m / v_0$$

Where, m = mass of powder taken, v_0 = apparent untapped volume

Tapped Density: Calculated based on the following formula: [9]

$$\text{Tapped density } (\rho\ t) = m / v_f$$

Where, m = weight of sample powder taken, v_f = tapped volume

Hardness: The hardness of five tablets was measured using Pfizer hardness tester. It is expressed in kg/cm^2.

Thickness and Diameter: Thickness and diameter of the prepared tablets were evaluated with the help of Vernier calipers and Screw gauge.

Friability: The friability of the tablets was determined 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. The friability was then calculated using the formula,

$$\text{Friability (\%)} = \text{Initial weight - Final weight / Initial weight} \times 100$$

Weight Variation: Ten tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 10 tablets were calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weights deviate from the average weight by more than the percentage and none deviate by more than twice the percentage ± 7.5.

Drug Content Estimation: Three tablets were crushed into powder, the quantity of powder equivalent to the average weight of formulation was weighed and taken in a volumetric flask dissolved in 15 ml of methanol, the solution is filtered through Whatman filter paper, from this 1 ml of solution is withdrawn and diluted to 10 ml. Again from this, 1 ml of solution is withdrawn and diluted to 10 ml, absorbance is taken at 250 nm and % drug content is, calculated by the formula [21].

$$\text{Drug content} = \text{absorbance / slope} \times \text{dose} \times \text{dilution factor} \times 1 / 1000$$

$$\text{\% Drug content} = \text{Drug content / Dose of the formulation} \times 100$$

% Swelling Study: One tablet from each formulation was randomly selected, weighed individually (W_1) and placed separately in petridish containing simulated saliva fluid (pH 6.8) for predetermined times (15 min, 30 min, 1 h, 2 h, up to 8 h). After immersion tablets were wiped off by the excess surface water by the use of filter paper. The swollen tablets were reweighed (W_2) and the swelling index of each tablet was calculated using the below equation [10, 11] (n=3).

$$\text{\% Swelling index} = W_2 - W_1 / W_1 \times 100$$

Surface pH Study: Surface pH studies were carried out in order to investigate the possibility of any side effects. This has to be studied as the alkaline or acidic pH irritates buccal mucosa. The tablet was allowed to swell by keeping in contact with 1 ml distilled water in a petridish for 2 h at room temperature. The pH was identified by bringing the electrode into contact with the tablet surface and allowing the surface to equilibrate time [15].

***Ex-vivo* Mucoadhesive Strength:** A modified balance method was used for determining the mucoadhesion strength [13, 14]. Fresh sheep buccal mucosa was obtained from the local slaughterhouse and used within 2 h of slaughter. The buccal mucosa was separated by removing the underlying fat and loose tissues. The membrane was washed with distilled water and then with phosphate buffer pH 6.8. The fresh buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. A piece of buccal mucosa was attached to flat end of beaker with the help of cyanoacrylate gum, a watch glass attached to thin chains at equal distance forms the left-hand pan. To the lower side of the watch glass, the tablet adhered just above the mucosa.

The right pan consists of an empty beaker, both the pans are balanced by adding suitable weights, then a 5 gm weight is removed from the right-hand pan, which lowered the left-hand pan making tablet to come in contact with buccal mucosa. The balance was allowed in this position for 3 min. Then water was gradually added to the right-hand pan until tablet detaches from the buccal mucosa. The weight required to detach the tablet from the mucosal surface gave the measure of mucoadhesive strength. Experiments were carried out triplicate and the averages of them are noted down.

***In-vitro* Drug Release:** The USP type II dissolution apparatus was used to study the release of drug from buccal Tablets. The dissolution medium consists of 500 ml of phosphate buffer pH 6.8. The release was performed at 37 ± 0.5 °C, at a rotating speed of 50 rpm. The impermeable layer of the Tablet was attached to a glass slide with instant adhesive. The slide was put in the bottom of the dissolution vessel so that the tablet remained on the upper side of the slide. Dissolution was carried out and samples of 5 ml, at each time intervals were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through Whatman filter paper and were analyzed spectrophotometrically at 250 nm against phosphate buffer pH 6.8 as blank [17, 23].

Pharmacokinetic Modelling of Drug Dissolution Profile: In order to examine the release mechanism of a drug from the tablets, the *in-vitro* drug release data of best buccoadhesive tablet formulation of valsartan were subjected to following release models [12].

- Zero-order
- First-order
- Higuchi
- Peppas models

Optimization by 3^2 Factorial Designs: Optimization is the key parameter in the development of any product factorial designs used to evaluate two or more factors simultaneously interactions can be determined in the factorial design [1, 3]. A study in which two factors and three levels are involved is called 3^2 factorial design. For the present work, 3^2 factorial design selected and 2 factors were evaluated at three possible levels by formulating all possible 9 formulation combinations, which are shown in **Table 2**.

Formulation code assigned to the batches

X1 = Carbopol 934p

X2 = Xanthan gum

TABLE 2: DESIGN SUMMARY

Factor	Name	Unit	Type	Min	Max	-1 actual	±1 actual	Mean	Std. dev
A	Carbopol 934p	Mg	Numeric	-1.000	±1.000	20	60	40	16.330
B	Xanthum Gum	Mg	Numeric	-1.000	±1.000	20	60	40	16.330

Xanthan gum and Carbopol 934p are independent variables used in the formulation. They are mucoadhesive polymer to increase the residence time of formulation in the oral cavity and also show their effect on mucoadhesive strength, swelling index, *in-vitro* drug release.

Independent Variable:
X2 = Xanthan gum
X1 = Carbopol 934p

Dependent Variable:
Y1 = Drug release
Y2 = Swelling index
Y3 = Mucoadhesive strength

Stability Studies: Stability studies for 3 months were carried out for the best formulation; the best formulation is kept under two different conditions like at 30 ± 2 °C & 65 ± 5% Rh and other at 40 ± 2 °C & 75 ± 5% Rh. After 30 days first-month stability studies were carried out for important parameters like diameter, thickness, drug content *etc*. The same study is repeated after completion of 60 and 90 days [16].

RESULTS AND DISCUSSION:

Preformulation:

Organoleptic Properties: Organoleptic properties of valsartan were found crystalline appearance, white to pale yellow color and odorlessodour.

The Valsartan solubility in methanol 0.7783 mg/ml and methanol: pH 6.8 phosphate buffer 1.7 mg/ml .

Melting Point: Melting point 117.55 °C that complying with the standard report.

UV Spectroscopic Study and Beer-Lambert's Plot:

UV Spectroscopic Study and Beer-Lambert's Plot in Methanol: It was found that the drug shows absorbance at 250 nm when the solution is prepared in Methanol is shown in **Fig. 1** solution of valsartan prepared in methanol and scanned between 200-400 nm using UV spectrometer which showed a peak at 250 nm.

UV Spectroscopic Study and Beer-Lambert's Plot in Phosphate Buffer: It was found that drug shows absorbance at 250 nm when solution is prepared in pH 6.8 Phosphate buffer is shown in **Fig. 2** solutions of valsartan prepared in pH 6.8 phosphate buffer: methanol and scanned between 200-400 nm using UV spectrometer which showed peak at 250 nm

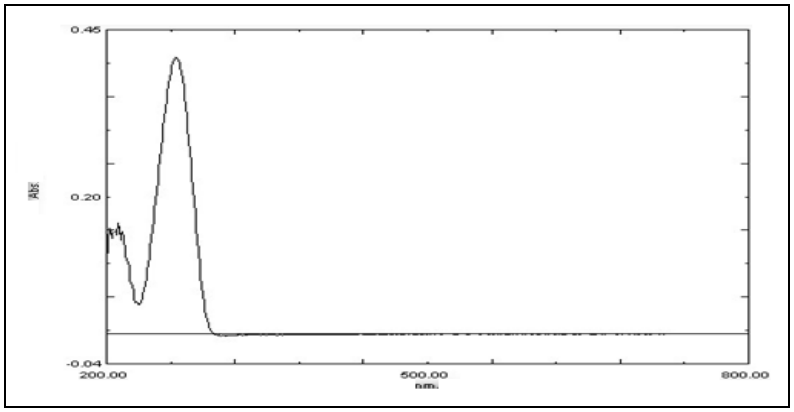

FIG. 1: UV SPECTRUM OF VALSARTAN IN METHANOL UV SPECTROSCOPIC STUDY AND BEER-LAMBERT'S PLOT IN METHANOL: pH 6.8

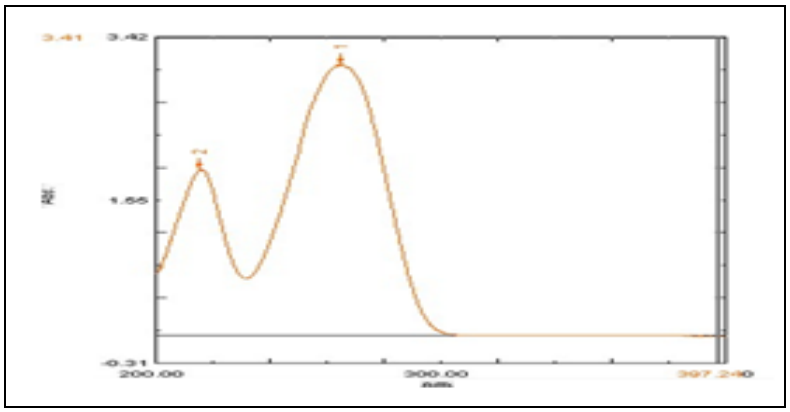

FIG. 2: UV SPECTRUM OF VALSARTAN IN PHOSPHATE BUFFER. UV SPECTROSCOPIC STUDY AND BEER-LAMBERT'S PLOT IN PHOSPHATE BUFFER: pH 6.8

Drug and Excipients Compatibility Studies:

Compatibility Study by FTIR Spectroscopy: FTIR spectra of drug-drug and drug-excipient mixtures retained the characteristic functional peaks of the drug as shown in **Fig. 3** & **4** below. From the observation of the FTIR spectra of valsartan for and its interpretation data.

It was concluded that the polymer and drug did not interact with each other and are compatible.

FTIR of Valsartan and Xanthan Gum:

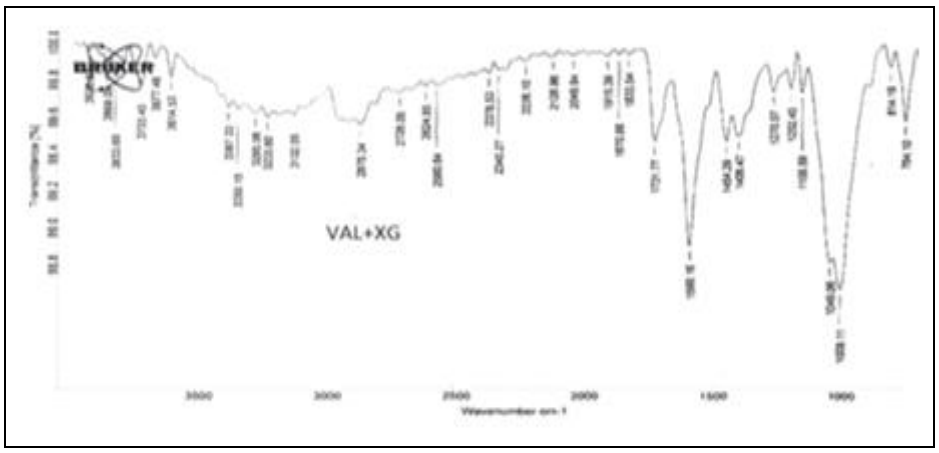

FIG. 3: FTIR OF VALSARTAN AND XANTHAN GUM

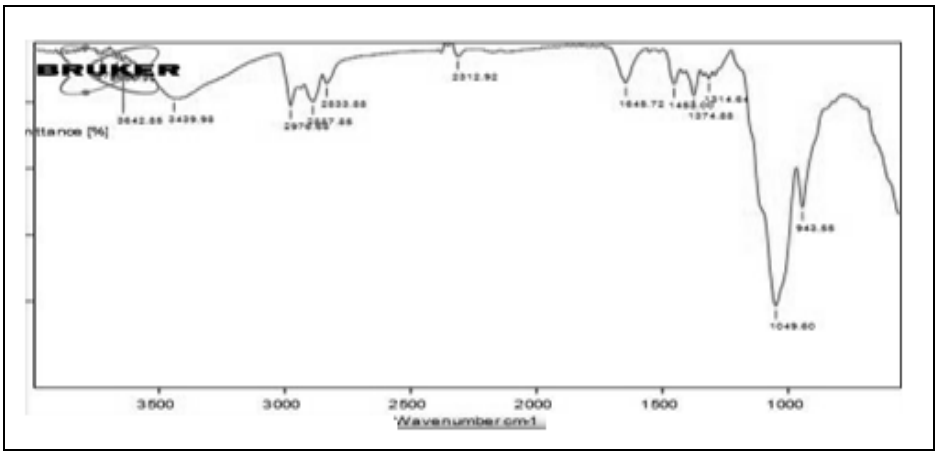

FIG. 4: FTIR OF VALSARTAN AND CARBOPOL 934P

Evaluation of Pre-compressional Characteristics of all Mucoadhesive Formulations: The Valsartan mucoadhesive buccal tablets were prepared by direct compression. Ingredients were accurately weighed, grounded and passed through mesh # 120 and then thoroughly blended with talc and magnesium stearate before compression. The powder blend was studied for rheological characteristics. The uniformly blend of powder was then compressed in a 10 station tablet punching machine using 8 mm flat-faced punches. Before the compression powder bed of all formulations was studied for various rheological characteristics bulk density, true density, compressibility index, Hausner's ratio and angle of repose. The results of the studies indicated that the powder bed is easily compressible and hence can be compressed into a compact mass of tablets. The angle of repose is an indicative parameter of powder flowability from hopper to die cavity. A repose angle between 20° to 30° indicates the good flowability of the powder bed. In this work, the angle of repose was found to be varying between 20.11° and 22.88° when glidants were incorporated. These studies indicated that the powder beds of all formulations are easily flowable.

Powder Characteristics: High angle of repose and compressibility index of a blending mixture showed that mixtures have good flowability. Hence, the powder characterization concludes that drug is a suitable candidate for direct compression.

TABLE 3: PRE-COMPRESSIONAL CHARACTERISTICS OF ALL MUCOADHESIVE FORMULATIONS

Formulation code	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose (°□)	Compressibility index (%)	Hausner's ratio
F1	0.3335 ± 0.0064	0.3734 ± 0.004	22.14	11.96	1.119
F2	0.3422 ± 0.0055	0.3821 ± 0.009	20.23	11.65	1.116
F3	0.3385 ± 0.0061	0.3788 ± 0.0053	20.11	12.00	1.119
F4	0.3328 ± 0.0064	0.3371 ± 0.0028	20.23	12.92	1.012
F5	0.3234 ± 0.0019	0.3633 ± 0.0016	21.12	12.33	1.123
F6	0.3407 ± 0.0034	0.3757 ± 0.001	20.13	10.27	1.102
F7	0.3331 ± 0.0059	0.3684 ± 0.002	22.88	10.59	1.105
F8	0.3401 ± 0.0058	0.3791 ± 0.006	21.25	11.46	1.114
F9	0.3406 ± 0.0071	0.3751 ± 0.0023	20.33	10.12	1.101

Evaluation of Compressional Characteristics of all Mucoadhesive Formulations: Hardness of tablets varied between 3.5 ± 0.04 and 4.5 ± 0.12 indicating good binding and satisfactory strength of tablets to withstand stress during transportation and also offer good adhesion to the mucosa. The % friability was found in the range of 0.195 ± 0.001% and 0.396 ± 0.0013%. The drug content of formulation f1 to f9 was found to be in between 97.65 ± 0.718 and 102.67 ± 0.55 the surface pH of all the mucoadhesive tablet formulations was found to be uniform, consistent between 6.20 ± 0.38 to 6.80 ± 0.46 indicating that all the formulation provide an acceptable pH in the range of salivary pH (5.5 to 7.0).

TABLE 4: EVALUATION OF PHYSICAL CHARACTERISTICS OF MUCOADHESIVE TABLETS CONTAINING VALSARTAN

Formulation Code	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Weight variation (mg)	% Drug content	Surface pH
F1	4.0 ± 0.26	0.197 ± 0.009	2.64 ± 0.083	202.40 ± 0.22	97.65 ± 0.718	6.30 ± 0.48
F2	3.5 ± 0.12	0.198 ± 0.0005	2.66 ± 0.052	202.0 ± 0.58	99.56 ± 1.982	6.34 ± 0.05
F3	3.5 ± 0.10	0.297 ± 0.0032	2.74 ± 0.118	201.80 ± 0.69	100.66 ± 0.76	6.20 ± 0.38
F4	4.5 ± 0.12	0.199 ± 0.004	2.68 ± 0.034	200.20 ± 0.98	100.74 ± 1.13	6.51 ± 0.46
F5	4.5 ± 0.03	0.195 ± 0.001	2.72 ± 0.117	204.60 ± 0.11	99.66 ± 1.762	6.78 ± 0.34
F6	4.0 ± 0.02	0.296 ± 0.008	2.77 ± 0.068	202.60 ± 0.33	101.33 ± 1.34	6.29 ± 0.78
F7	3.5 ± 0.04	0.197 ± 0.006	2.79 ± 0.032	202.20 ± 0.17	100.7 ± 0.99	6.32 ± 0.42
F8	4.5 ± 0.01	0.197 ± 0.003	2.78 ± 0.043	202.60 ± 0.48	102.67 ± 0.55	6.47 ± 0.06
F9	4.0 ± 0.10	0.396 ± 0.0013	2.77 ± 0.042	201.80 ± 0.79	100.76 ± 0.52	6.80 ± 0.46

Swelling Study: The % swelling index of the valsartan mucoadhesive tablet for a period of 8 h is shown in **Fig. 5**. The water uptake nature of the polymer is one of the important properties that affect the onset of swelling. The swelling has been increased with increases in the amount of Xanthan gum or Carbopol 934p. The maximum swelling was attained in 8 h. the formulation containing Xanthan gum show maximum swelling.

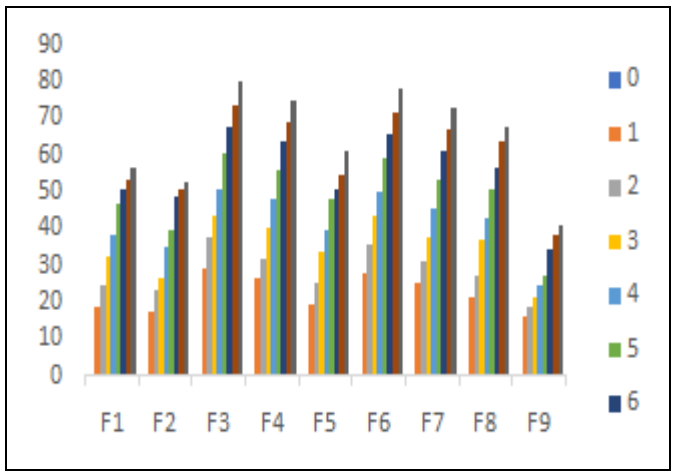

FIG. 5: GRAPH OF SWELLING INDEX

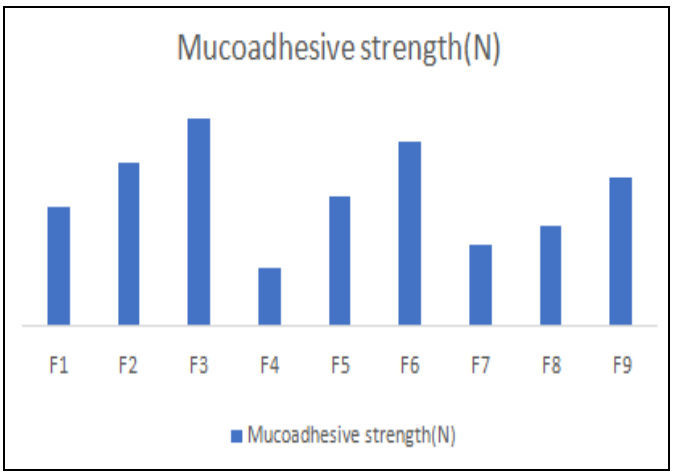

FIG. 6: GRAPH OF MUCOADHESIVE STRENGTH

Mucoadhesive Strength: The bioadhesive property of mucoadhesive tablets of the valsartan-containing varying proportions of polymers was determined with an insight to develop the tablets with adequate bioadhesion.

It was found that all tablet formulations possess adequate bioadhesion. Mucoadhesive strength has been increased with increases in the amount of Carbopol Carbopol 934p as shown in **Fig. 6**.

***In-vitro* Dissolution Study % Cumulative Drug Release:**

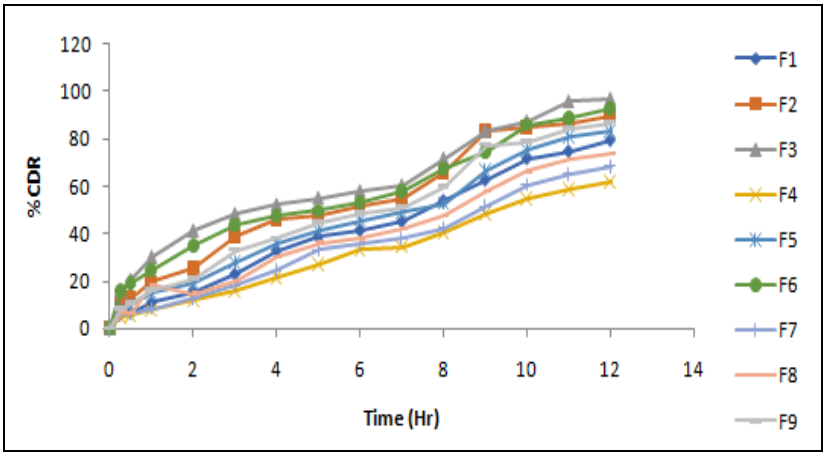

FIG. 7: GRAPH OF % CUMULATIVE DRUG RELEASE

Kinetic Study:

TABLE 5: KINETIC STUDY

Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9
R^2 value for Zero order	0.9933	0.9696	0.9452	0.9952	0.9875	09612	0.9915	0.9821	0.9828
R^2 value for First order	0.7529	0.6283	0.5116	0.7996	0.6978	0.5385	0.7766	0.6283	0.6814
R^2 value for Higuchi order	0.9461	0.9634	0.9731	0.9316	0.9495	0.9706	0.9305	0.9323	0.9561
R^2 value for Korsemayer order	0.8344	0.6297	0.4597	0.8766	0.7307	0.5189	0.8437	0.8957	0.7143

Optimization: A 3^2 full factorial design was selected and 2 factors were evaluated at 3 levels respectively.

The percentage of Carbopol 934p (x_1) and Xanthan gum (x_2) were selected as the independent variable and dependent variable was % drug release, swelling index and mucoadhesive strength.

The data obtained were treated using design expert version 7.0.0 software and analysed statistically using analysis of variance (Anova).

The data were also subjected to 3d response surface methodology to study the effect of Carbopol 934p (x_1) and Xanthan gum (x_2) independent variable parameter and other statistical parameter for the dependent variable % drug release, swelling index and mucoadhesive strength.

The value of x_1 and x_2 were found to be significant at $p<0.5$, hence confirmed the significant effect of both the variable on the selected responses.

From the data optimum concentration of Carbopol 934p 60 mg and 20 mg Xanthan gum was found in F3 formulation.

Multiple regression analysis of 3^2 full factorial design batches for *in-vitro* drug release and mucoadhesive strength and swelling index is shown in the below figures respectively.

The response % drug release, swelling index and mucoadhesive strength and model was found to be linear as shown in **Fig. 8, 9, 10** respectively.

As well ascounter plot effect on % drug release, mucoadhesive strength and swelling index as shown in **Fig. 11, 12, 13** respectively.

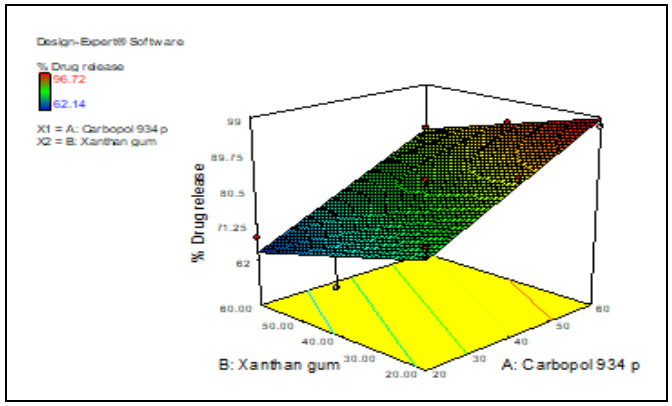

FIG. 8: SURFACE RESPONSE PLOT SHOWING EFFECT OF CARBOPOL 934P AND XANTHAN GUM ON % DR

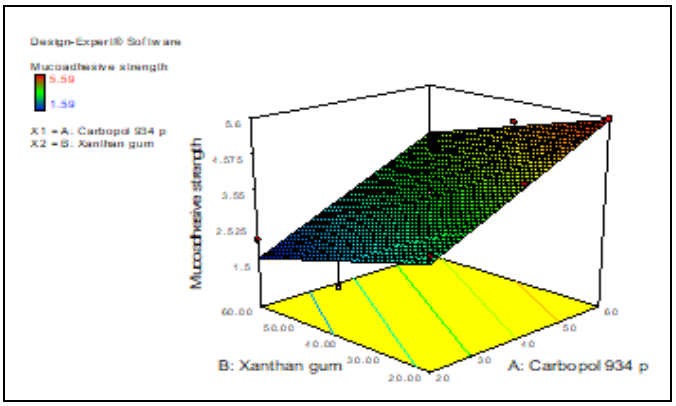

FIG. 9: SURFACE RESPONSE PLOT SHOWING EFFECT OF CARBOPOL 934P AND XANTHAN GUM ON MUCOADHESIVE STRENGTH

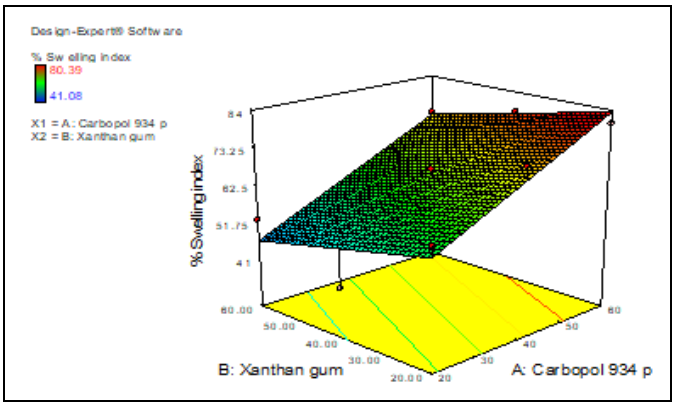

FIG. 10: SURFACE RESPONSE PLOT SHOWING EFFECT OF CARBOPOL 934P AND XANTHAN GUM ON % SWELLING INDEX

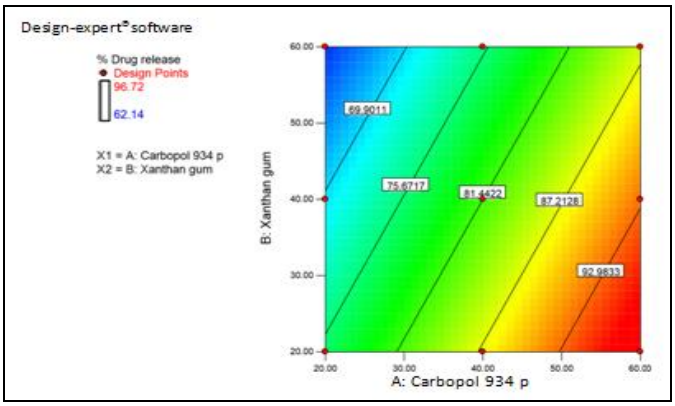

FIG. 11: CONTOUR PLOT SHOWING EFFECT OF CARBOPOL 934P AND XANTHAN GUM ON % DR

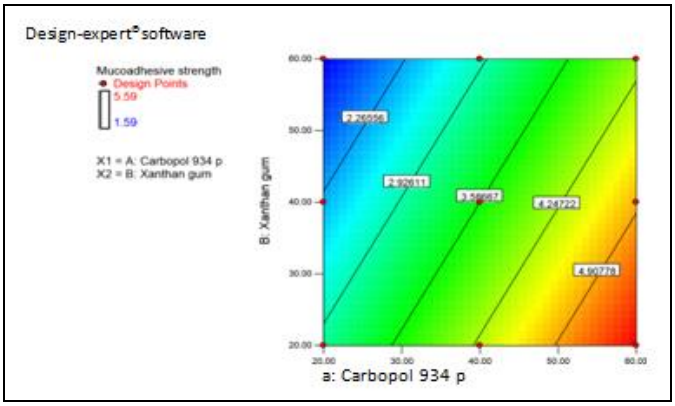

FIG. 12: CONTOUR PLOT SHOWING EFFECT OF CARBOPOL 934P AND XANTHAN GUM ON MUCOADHESIVE STRENGTH

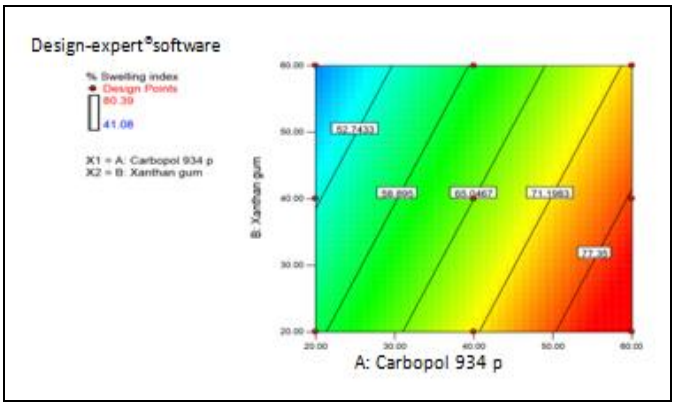

FIG. 13: CONTOUR PLOT SHOWING EFFECT OF CARBOPOL 934P AND XANTHAN GUM ON SWELLING INDEX

Stability Study: The accelerated stability study was carried out on optimized formulation F3 the tablets were wrapped in aluminum foil and stored at 40 ± 2 °C & 75 ± 5% Rh for three months. After three months samples were withdrawn and tested for physical parameters, thickness, hardness, % friability, % drug content and surface pH studies. **Table 6** showed that there are no considerable changes in parameters, thickness, hardness, % friability, % drug content and surface pH of formulation F3 before and after accelerated stability study.

Hence, mucoadhesive buccal tablet prepared was found to be stable and not such affected by elevated humidity and temperature conditions.

TABLE 6: PARAMETERS STUDIED OF F3 FORMULATION BEFORE AND AFTER STABILITY STUDY

Parameters	Before stability study	After 1 month	After 2 month	After 3 month
Colour	White	White	White	White
Thickness	2.74 ± 0.116	2.74 ± 0.112	2.74 ± 0.110	2.74 ± 0.102
Hardness	3.5 ± 0.10	3.5 ± 0.15	3.5 ± 0.21	3.5 ± 0.33
Friability	0.297 ± 0.002	0.297 ± 0.032	0.298 ± 0.044	0.299 ± 0.002
% Drug content	100.66 ± 0.10	100.08 ± 0.33	100.00 ± 0.12	99.58 ± 0.10
Surface pH	6.20 ± 0.34	6.18 ± 0.34	6.34 ± 0.38	6.52 ± 0.34

CONCLUSION: The best polymer composite was selected from the various ratios of the polymers. The best polymer ratio was found to be Carbopol 934p, Xanthan gum in the ratio 3:1. The mucoadhesive strength of buccal tablets increases as the concentration of secondary polymer increases. The above polymer composite had shown satisfactory results in the parameters such as thickness, hardness, drug content, swelling index, matrix erosion, mucoadhesive strength, *in-vitro* dissolution and *in-vitro* diffusion.

The satisfactory formulation shows a zero-order drug release profile depending on the regression value and show a satisfactory dissolution profile. Slow, controlled and maximum release of valsartan over a period of 8 h was obtained from buccal tablets F3 formulation containing Carbopol 934p, Xanthan gum. F3 batch formulation was found to be optimized as per 3^2 factorial design. Stability data indicates that there is no decrease in the drug content was observed for a period of 3 months. Therefore, it was ascertained that the mucoadhesive tablets of valsartan could be stored for a period of at least 2 years.

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REFERENCES:

1. Raja N, Raghunandan N, Chamundeswari D and Shamunganathan S: Quality by design approach for optimization of Repaglinide buccal tablets using box-behnken design. Future Journal of Pharmaceutical Science 2018; 4: 265-72.
2. Joe M and Jan GS: Formulation and evaluation of selected transmucosal dosage forms containing a double fixed-dose of Acyclovir and Ketaconazole. European Journal of Pharmaceutical Sciences 2018; 111: 503-13.
3. Burak C: Resperidone mucoadhesive buccal tablet: formulation design optimization and evaluation. Dove Press Journal Drug Design, Development and Therapy 2017; 11: 3355-65.
4. Sandhya P, Spoorthy V, Susmitha A, Safooratalat, Ashwin K and Kumar G: Formulation and evaluation of mucoadhesive buccal tablet of Losartan by using natural polymers. International Journal of Pharmacy and Analytical Research 2016; 5(2): 239-44.
5. Vinay C and Ahmed M: Formulation and evaluation of mucoadhesive buccal tablets of Candesartan. Journal of Drug Delivery and Tics 2015; 5(5): 56-63.
6. Singh S, Shrivastava G and Singh P: Formulation and evaluation of mucoadhesive buccal tablets of Zolmpitriptan. World Journal Pharmacy Pharmaceutical Science 2016; 5(7): 1402-19.
7. Bhikshapathi D: Formulation and development of muco-adhesive tablets of Captopril. International Journal of Pharmacy and Analytical Research 2015; 4(2): 144-54.
8. Krishna M, Uppala P, Kumar K and Patro S: Formulation and evaluation of mucoadhesive tablets of Linagliptin. International Journal of Pharmacy and Pharmaceutical Research 2015; 4(2): 141-58.
9. Gowtham N, Debnath S and Babu M: Formulation and evaluation of mucoadhesive bilayer buccal tablets of Amphotericin-B hydrocarbon. International Journal of Novel Trends in Pharmaceutical Sciences 2015; 5(4): 107-13.
10. Milind GM, Yogesh G and Yadav A: Formulation and evaluation of mucoadhesive buccal tablets of Propranolol prepared using natural polymer. International Journal Pharm Science & Research 2018; 9(7): 2905-13.
11. NagarajanP,GopinathS, Peter Christoper GV andPreethy AJ: Formulation development and *in-vitro* evaluation of mucoadhesivebuccal tablet containing Mucolytic agent. Pelagia Research Library Der Chemica Sinica, 2018, 9(2): 649-61.
12. Sriram N and Katakam P: Formulation and evaluation of mucoadhesive microspheres of Pioglitazone Hydrochloride prepared by ionotropic external gelation technique. Journal of Encapsulation and Adsorption Sciences 2016; 6: 22-34.
13. Biswal B, Nabin K and Bhavesh B: Formulation and evaluation of Repaglinide buccal tablet: *ex-vivo* bioadhesion study and *ex-vivo* permeability study. Journal of Applied Pharmaceutical Science 2014; 4(5): 096-03.
14. Reddy VB and Reddy RKV: Formulation and evaluation of buccal mucoadhesive tablet of Glipizide. World Journal of Pharmacy and Pharmaceutical Sciences 2015; 4(07): 1804-21.
15. Pethe AM and Salunkhe SP: Formulation and evaluation of mucoadhesive buccal tablet of Simvastatin. International Journal of Pharma and Bio Sciences 2014; 5(03): 268-78.
16. Gite SS, Shinkar DM and Saudagar RB: Development and evaluation of mucoadhesive tablets of Atenolol and its β-cyclodextrin complex. Asian Journal of Biomedical and Pharmaceutical Sciences 2014; 4(37): 25-32.
17. Reddy PD, Balanjineyulu R, Swarnalatha D, Badarinath AV and Gopinath C: Design, development and *in-vitro*

characterization of Felodipine mucoadhesive buccal tablets. Journal of Pharmacy Research 2015; 9(02): 170-76.
18. Indian Pharmacopoeia: The Indian Pharmacopoeia Composition Dehli 2007; 73-34.
19. United States Pharmacopeia: Port City Press, Baltimore Twenty sixth Edition 2008; 231-32.
20. Lachman L, Libberman HA and Kaing JI: The Theory and Practice of Industrial Pharmacy. Varghese Publishing House Mumbai Third Edition 1990; 296-02.
21. Dhake AS, Shinkar DM, Shayle S, Patil SB and Setty CM: Development and evaluation of mucoadhesive tablets of Clotrimazole and its β-cyclodextrin complex for the treatment of candidiasis. International Journal of Pharmacy and Pharmaceutical Sciences 2011; 3(3): 159-64.
22. Shinkar DM, Dhake AS and Setty CM: Drug delivery from the oral cavity: A focus on mucoadhesive buccal drug delivery systems. PDA Journal of Pharmaceutical Science and Technology 2012; 66: 466-00.
23. Birari AE and Khairanar DA: Formulation and *in-vitro* evaluation of chitosan based omeprazole mucoadhesive buccal tablets. International Journal of Pharma Sciences and Research 2014; 5: 630-38.
24. Gilhotraa RM, Ikrama M, Srivastavaa S and Gilhotrab N: A clinical perspective on mucoadhesive buccal drug delivery systems. The Journal of Biomedical Research 2014, 28(2): 81-97.
25. Kianfar F, Antonijevic MD, Chowdhry BZ and Boateng JS: Formulation development of a carrageenan based delivery system for buccal drug delivery using ibuprofen as a model drug. J of Biomater Nano 2011; 2: 582-92.
26. Jain CP and Naruka PS: Formulation and evaluation of fast dissolving tablets of valsartan. International Journal of Pharmaceutical Sciences 2009; 1(1): 219-26.

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