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# FORMULATION AND INVITRO EVALUATION OF BUCCAL TABLETS OF PRAVASTATIN

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## ABSTRACT

In the present study, an attempt was made to prepare Buccal tablets of Pravastatin HCL (HMG-CoA reductase inhibitors), in order to overcome bioavailability problems, to reduce dose dependent side effects Buccal tablets containing the Pravastatin HCL were prepared by direct compression method using combinations of polymers (such as Sodium alginate, Guar gum & Xanthan gum). Estimation of Pravastatin HCL were carried out spectrophotometrically at 240 nm. The Buccal tablets were evaluated for various physical and biological parameters, drug content uniformity, *in-vitro* drug release, drug- excipient interactions (FTIR). IR spectroscopic studies indicated that there are no drug-excipient interactions. The formulations F9 (containing 40mg of Guar gum) were found to be promising, which showed maximum drug release within 8 h. These formulations have displayed good bioadhesion strength (4.72 gm respectively).

**KEYWORDS:** Pravastatin HCL, FTIR, Sodium alginate, Guar gum & Xanthan gum.

## INTRODUCTION

### Mucoadhesive drug delivery systems[1-3]

These may be defined as drug delivery systems, which utilize the property of bioadhesion of certain water soluble polymers which become adhesive on hydration and hence can be used for targeting of drug to particular regions of body for extended periods of time.

The mucosal layer lines of number of regions of the body including gastrointestinal tract, urogentital tract, airway, ear, nose and eye. These represent potential sites for attachment of any bioadhesive system and hence, the mucoadhesive drug delivery system includes following:

1. Buccal drug delivery system.
2. Oral delivery system.
3. Vaginal delivery system.
4. Rectal delivery system.
5. Nasal delivery system.
6. Ocular delivery system.

**Table 1: Comparison of some routes for systemic drug delivery available to the formulation scientist.**

| | Gastrointestinal | Dermal | Nasal | Oral | Vaginal |
|---|---|---|---|---|---|
| **Accessibility** | + | +++ | ++ | ++ | + |
| **Surface area** | +++ | +++ | + | ++ | +++ |
| **Surface** | + | ++ | + | +++ | + |
| **Permeability** | +++ | + | +++ | ++ | +++ |
| **Reactivity** | ++ | ++ | + | +++ | ++ |
| **Vascular** | +++ | + | +++ | ++ | +++ |
| **First pass** | + | +++ | +++ | +++ | + |
| **Patient** | ++ | +++ | ++ | +++ | ++ |

(+) poor, (++) good, (+++) excellent.

### Characteristics of an ideal mucoadhesive polymers.[28]

An ideal mucoadhesive polymer has the following characteristics.

1. The polymer and its degradation products should be nontoxic and should be nonabsorbent from the gastrointestinal tract.
2. It should be nonirritant to the mucous membrane.
3. It should preferably form a strong noncovalent bond

with the mucin- epithelial cell surface.
4. It should allow easy incorporation of the drug and offer no hindrance to its release.
5. It should adhere quickly to moist tissue and should possess some site specificity.
6. The polymer must not decompose on storage or during the shelf life of the dosage form.
7. The cost of polymer should not be high so that the prepared dosage form remains competitive

Pravastatin is the 6-alpha-hydroxy acid form of mevastatin. It is a statin medication, used preventing cardiovascular disease in those at high risk and treating abnormal lipids. Its oral bioavailability is low (17%) due to extensive first-pass metabolism. Since buccal route by passes first-pass effect. The Physico-chemical properties of Pravastatin, its suitable half-life (1.8 hours) make it suitable candidate for administration by buccal route. The structure was illustrated in Figure 1.

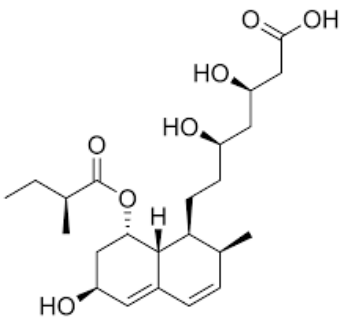


**Fig. 1: Structure of Pravastatin.**

**Experimental work**

Pravastatin API was purchased from the BMR Chemicals, Hyderabad, Sodium Alginate, Guar gum, Xanthan gum, Lactose, PVP K30, MCC, Magnesium stearate Talc purchased form lobachem and SD Fine chemicals limited

**Preformulation Studies[41]**

Preformulation testing is the initial phase in the improvement of dose types of a drug substance. It is one of the critical essential being developed of any drug delivery system. It tends to be characterized as an examination of physical and synthetic properties of a medicament substance alone and when joined with excipients.

Characterization of the medicament is an essential advance at the preformulation period of item improvement taken after by concentrate the properties of the excipients and their similarity. The general goal of preformulation testing is to produce data valuable to the formulator in creating steady and bioavailable measurements frames, which can be mass- produced. The following are the various preformulation studies.

**Solubility**

Solubility of Pravastatin was determined in water, methamol, ethanol and pH 6.8 phosphate buffers. Solubility studies were performed by taking excess amount of Pravastatin in different beakers containing the solvents. The mixtures were shaken for 48hrs in rotary shaker. The solutions were centrifuged for 10mins at 1000 rpm and supernatant were analyzed at suitable wavelength.

**Drug-Excipient Compatibility Studies**

In the tablet dosage form the drug is in intimate contact with one or more excipients; the latter could affect the stability of the drug. Knowledge of drug-excipient interactions is therefore very useful to the formulator in selecting appropriate excipients. This information may be present for known drugs. For new drugs or new excipients, the preformulation studies must generate the needed information.

**FT-IR Studies**

Physical compatibility studies were assured by FT-IR studies. The IR spectrums of the mixed powders were taken by preparing Potassium bromide pellets under dry condition by using pellet press. Spectra are superimposed. The transmission minimal (absorption maxima) in the spectra obtained with the sample corresponded in position and relative size to those in the spectrum obtained with the working/reference standards.

**Method of Preparation of Pravastatin Buccal tablets42**

Preparation: Direct compression method has been employed to prepare buccal tablets of Pravastatin using various polymers.

Procedure: All the ingredients including drug, polymer and excipients were weighed accurately. The drug is throughly mixed with Lactose on a butter paper with the help of a stainless steel spatula. Then all the ingredients except lubricants were mixed in the order of ascending weights and blended for 10 min. After uniform mixing of ingredients, lubricant was added and again mixed for 2 min. The prepared blend of each formulation was then compressed using an 8mm diameter die on a multi station tablet punching machine. Compositions of the designed buccal tablets are given Table-2.

**Table 2: Composition of Buccal tablets of Pravastatin.**

| Ingredients(mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Pravastatin | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| Xanthan gum | 20 | 30 | 40 | -- | -- | -- | -- | -- | -- |
| Sodium alginate | -- | -- | -- | 20 | 30 | 40 | -- | -- | -- |
| Guar gum | -- | -- | -- | -- | -- | -- | 20 | 30 | 40 |
| PVP K30 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| Lactose | 134 | 124 | 114 | 134 | 124 | 114 | 134 | 124 | 114 |
| Mg stearate | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Talc | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Total Weight | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |

**Post compression parameters of buccal tablets of Pravastatin:**[43-46]

**Hardness test:** The crushing strength (kg/cm2) of tablets was determined by using Pfizer hardness tester.

**Friability test:** This was determined by weighing 10 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25 rpm for 4 min. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated (% loss in weight).

**Uniformity of content:** The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation from the mean.

**Uniformity of drug content:** Five tablets were powdered in a glass mortar and the powder equivalent to 10 mg of drug is placed in a stoppered 100 ml conical flask. The drug is extracted with 25 ml water with vigorous shaking on a mechanical gyratory shaker (100 rpm) for 2 h and filtered into 50 ml volumetric flask through Whatman No.1 filter paper (Mean pore diameter 1.5 µm) and more solvent is passed through the filter to produce 50 ml. Aliquots of the solution are filtered through 0.22 µm membrane filter disc (Millipore corporation) and analyzed for drug content by measuring the absorbance at 240 wavelength against solvent blank.

**Surface pH study**: The surface pH of the buccal tablets is determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may irritate the buccal mucosa, we sought to keep the surface pH as close to neutral as possible. A combined glass electrode is used for this purpose. The tablet is allowed to swell by keeping it in contact with 1 ml of distilled water (pH 6.8 ± 0.05) for 2 h at room temperature. The pH is identified by bringing the electrode into contact with the tablet surface and allowing to equilibrate for 1 min.

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

The swelling index is calculated by the formula: Swelling index = 100 (w2-w1) / w1.

**Mucoadhesion strength:** The apparatus used for testing bioadhesion was assembled in the laboratory (fig.2). Mucoadhesion strength of the tablet was measured on a modified physical balance employing the method described by Gupta et al17, 69 using bovine cheek pouch as model mucosal membrane.

A double beam physical balance was taken, the left pan was removed. To left arm of balance a thick thread of suitable length was hanged. To the bottom side of thread a glass stopper with uniform surface was tied. A clean glass mortar was placed below hanging glass stopper. In this mortar was placed a clean 500 ml glass beaker, within which was placed another glass beaker of 50 ml capacity in inverted position and weighted with 50 gm to prevent floating. The temperature control system involves placing thermometer in 500 ml beaker and intermittently adding hot water in outer mortar filled with water. The balance was so adjusted that right hand-side was exactly 5 gm heavier than the left.

Method: The balance adjusted as described above was used for the study. The bovine cheek pouch, excised and washed was tied tightly with mucosal side upward using thread over the base of inverted 50 ml glass beaker. This beaker suitably weighted was lowered into 500 ml beaker, which was then filled with pH6.8 phosphate buffer kept at 37o C such that the buffer reaches the surface of mucosal membrane and keeps it moist. This was then kept below left hand side of balance. The buccal tablet was then stuck to glass stopper through its backing membrane using an adhesive (Feviquick). The 5gm on right hand side is removed, this causes application of 5 gm of pressure on buccal tablet overlying moist mucosa. The balance was kept in this position for 3 minutes and then slowly weights were increased on the right pan, till tablet separates from mucosal membrane. The total weight on right pan minus 5 gm gives the force required to separate tablet from

mucosa. This gives bioadhesive strength in grams. The mean value of three trials was taken for each set of formulations. After each measurement, the tissue was gently and thoroughly washed with isotonic phosphate buffer and left for 5 minutes before reading a new tablet of same formulation to get reproducible multiple results for the formulation.

***In vitro* drug release study**

The prepared buccal tablets were subjected to *in vitro* dissolution. Dissolution test was carried out using USP type 2 paddle method [apparatus 2]. The stirring rate was 50 rpm, pH 6.8 phosphate buffer was used as dissolution medium and dissolution medium was maintained at 37±0.5oC. Samples of 5 ml were withdrawn at regular intervals of time, filtered and replace with 5 ml of fresh dissolution medium, dilutions were made wherever necessary and were analyzed for Pravastatin at 240nm wavelength by using UV-visible spectrophotometer.

**Release Kinetics:** 47-48

In the present study, data of the in vitro release were fitted to different equations and kinetic models to explain the release kinetics of Pravastatin from the buccal tablets. The kinetic models used were Zero order equation, First order, Higuchi release and Korsmeyer-Peppas models.

**Kinetic Studies: Mathematical models**

Different release kinetic equations (zero-order, first-order, Higuchi's equation and Korsmeyer-peppas equation) were applied to interpret the release rate of the drug from matrix systems for the optimized formulation. The best fit with higher correlation (r2) was calculated.

**Zero-order model**

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be representedby the equation.

**Qt = Q0 + K0t**

Where Qt is the amount of drug dissolved in time t, Q0 is the initial amount of drug in the solution (most times, Q0 = 0) and K0 is the zero order release constant expressed in units of concentration/time. To study the release kinetics, data obtainedfrom in vitro drug release studies were plotted as cumulative amount of drug released versustime.

Application: It is used to describe the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems, as well as tablets with low soluble drugs in coated forms, osmotic systems, etc.

**First Order Model**

The first order equation describes the release from systems where the dissolution rate is dependent upon the concentration of the dissolving species.

Release behavior generally follows the following first order equation: Log C= Log Co-kt/2.303.

Where C is the amount of drug dissolved at time t,

Co is the amount of drug dissolved at t=0 and k is the first order rate constant.

A graph of log cumulative of % drug remaining vs time yields a straight line.

The pharmaceutical dosage forms following this dissolution profile, such as those containing water-soluble drugs in porous matrices, release the drugs in a way that is proportional to the amount of drug remaining in its interior, in such way, that the amount of drug released by unit of time diminishes.

**Higuchi model:** The first example of a mathematical model aimed to describe drug release from a system was proposed by Higuchi in 1961. Initially conceived for planar systems, it was then sustained to different geometrics and porous systems. This model is based on the hypothesis that.

- Initial drug concentration in the is much higher than drug solubility;
- Drug diffusion takes place only in one dimension (edge effect must be negligible);
- Drug particles are much smaller than system thickness;
- Swelling and dissolution are negligible;
- Drug diffusivity is constant; and
- Perfect sink conditions are always attained in the release environment.

In a general way the Higuchi model is simply expressed by following equation Q = KH - t1/2

Where, KH is the Higuchi dissolution constant.

The data obtained were plotted as cumulative percentage drug release versus square root of time.

Application: This relationship can be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems and tablets with water soluble drugs.

**Korsmeyer-Peppas model:** Korsmeyer et al.(1983) derived a simple relationshipwhich described drug release from a polymeric system equation. To find out the mechanism of drug release, first60% drug release data were fitted in Korsmeyer-Peppas model,

$Mt / M\infty = Ktn$

Where $Mt / M\infty$ is a fraction of drug released at time t, k is the release rate constant and n is the release exponent. The n value is used to characterize different release for cylindrical shaped matrices.

In this model, the value of n characterizes the release mechanism of drug as described in the following table.

**Table 3: Drug transport mechanisms suggested based on 'n' value.**

| S. No | Release exponent | Drug transport mechanism | Rate as a function of time |
|---|---|---|---|
| 1 | 0.5 | Fickian diffusion | t -0.5 |
| 2 | 0.45 < n = 0.89 | Non -Fickian transport | t n-1 |
| 3 | 0.89 | Case II transport | Zero order release |
| 4 | Higher than 0.89 | Super case II transport | t n-1 |

The results of *in vitro* release profiles obtained for the BDDS formulations were fitted into four models of data treatment as follows:

1. Cumulative percent drug released versus time (zero order kinetic model).
2. Log cumulative percent drug remaining versus time (first- order kinetic model).
3. Cumulative percent drug released versus square root of time (higuchi's model).
4. Log cumulative percent drug released versus log time (korsmeyer - Peppas equation)

## RESULTS AND DISCUSSION

**Solubility:** It was determined as per standard procedure. The results are given in Table 4.

**Table 4: Solubility of Pravastatin in various solvents.**

| Solvent | Solubility (µg/ml) |
|---|---|
| 0.1 N HCL | 0.234 |
| 6.8pH buffer | 0.521 |
| 7.4pH buffer | 0.468 |

**Drug-Excipient compatibility studies**

The IR spectrum of pure drug was found to be similar to the standard spectrum of Pravastatin. The spectrum of Pravastatin shows the following functional groups at their frequencies shown in Figure 3. From the spectra of Pravastatin, combination of Pravastatin with polymers, it was observed that all characteristic peaks of Pravastatin were not altered and present without alteration in the combination spectrum, thus indicating compatibility of the drug and excipients.

FTIR spectra of Pravastatin, and Optimized formulation are shown in Figures below.

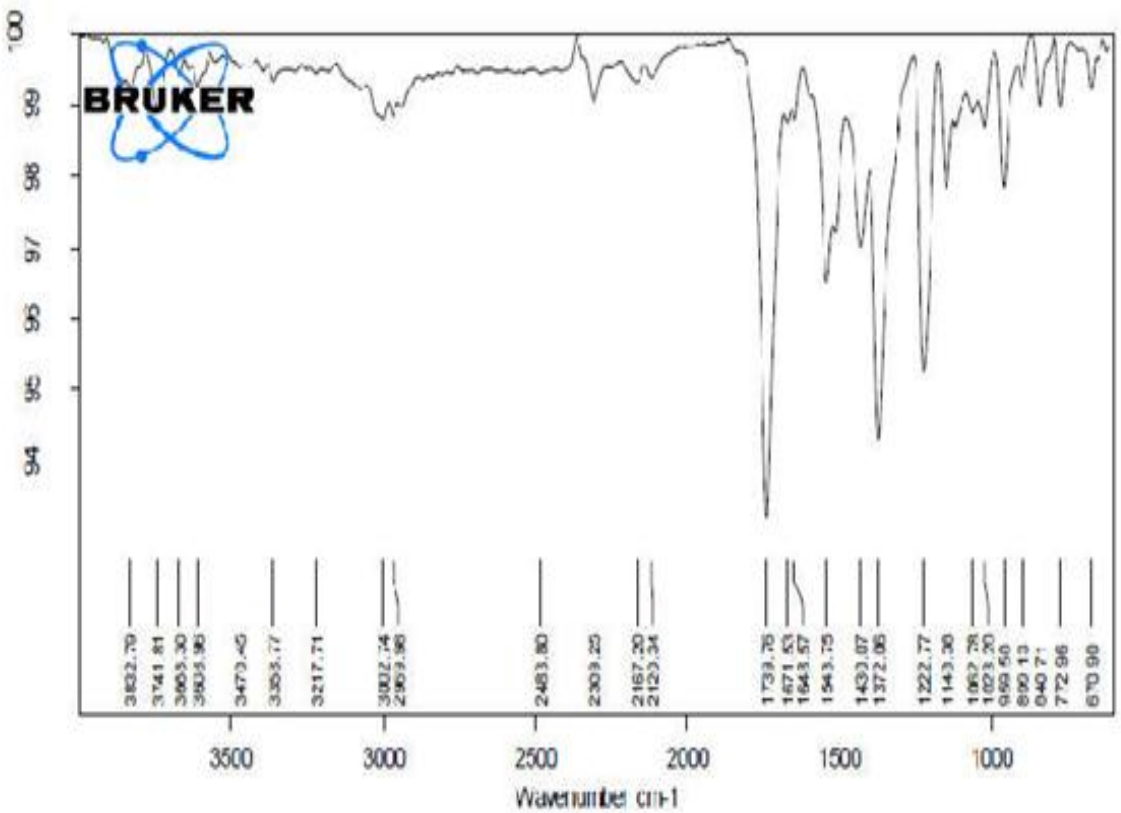


**Figure 3: FTIR spectrum of Pravastatin.**

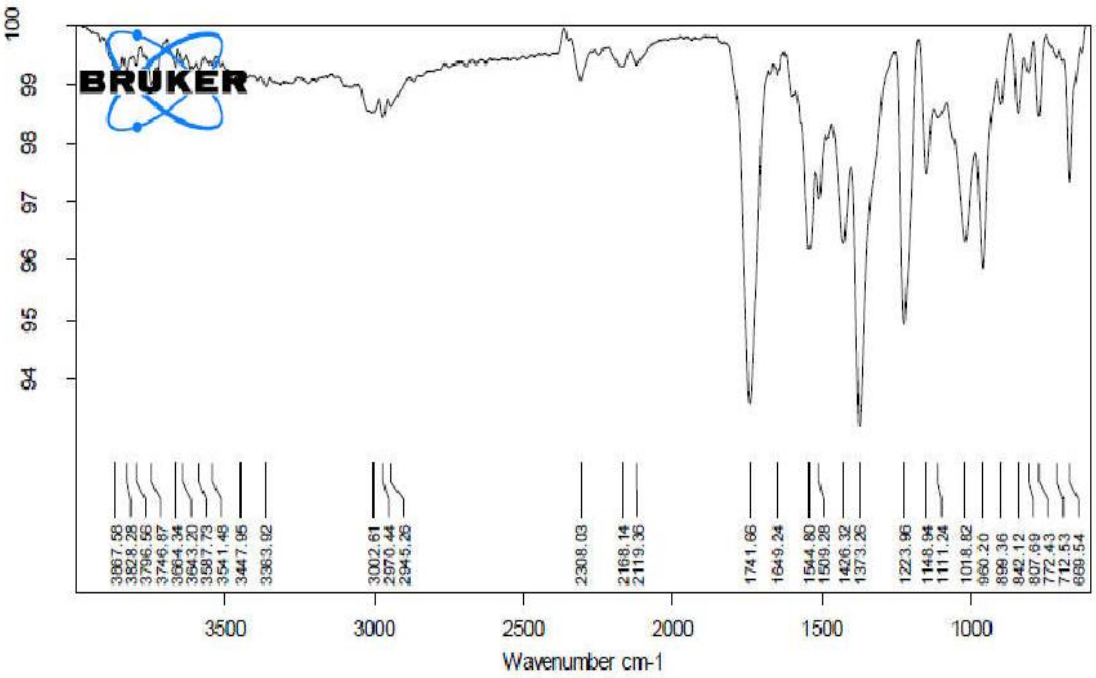


**Figure 4: FTIR Spectrum of drug and polymers.**

**UV Spectroscopy**

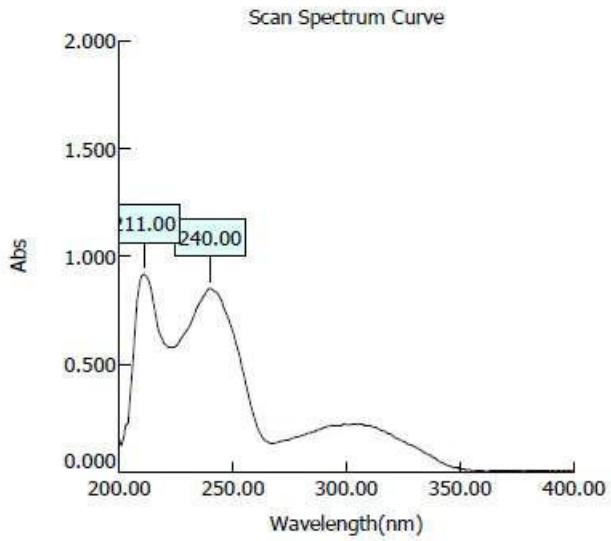


**Fig. 5: Uv spectrum of Pravastatin in 6.8pH buffer.**

**Standard graph**

The standard calibration curve of Pravastatin was developed in pH 6.8 phosphate buffer.

**a. Standard Calibration Curve in 6.8 pH phosphate buffer**

Standard graph of Pravastatin in pH 6.8 phosphate buffer shows linearity in the concentration range of 5-30µg/ml with correlation coefficient of 0.999. Table 5. gives data of the standard graph and Figure 6 shows the standard graph in pH 6.8 phosphate buffer.

**Table 5: Data for calibration curve of Pravastatin in pH 6.8 at 240nm.**

| Concentartion(µg/ml) | Absorbance |
|---|---|
| 0 | 0 |
| 5 | 0.164 |
| 10 | 0.297 |
| 15 | 0.476 |
| 20 | 0.637 |
| 25 | 0.798 |
| 30 | 0.958 |

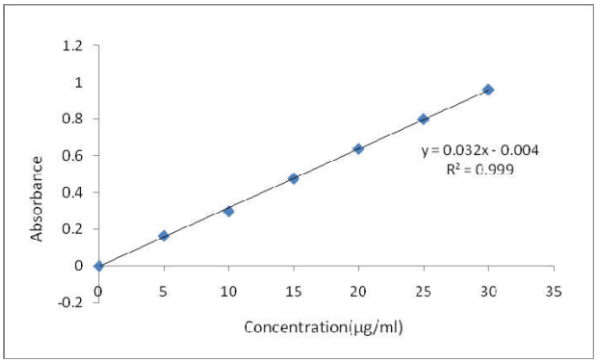


**Figure 6: Standard Calibration Curve of Pravastatin in pH 6.8 at 240 nm.**

**Flow properties of powder blend.**

**Table 6: Flow properties of powder blend.**

| Code | Angle of Repose±SD | Bulk Density (g/ml) | Tapped Density (g/ml) | Carr's Index. (%) | Hausner's ratio |
|---|---|---|---|---|---|
| F1 | 27.15±0.46 | 0.425±0.15 | 0.514±0.26 | 17.32±0.42 | 1.21±0.12 |
| F2 | 29.42±0.05 | 0.415±0.05 | 0.498±0.33 | 16.67±0.74 | 1.20±0.66 |
| F3 | 28.75±0.63 | 0.395±0.16 | 0.484±0.24 | 18.39±0.98 | 1.23±0.22 |
| F4 | 29.63±0.95 | 0.426±0.24 | 0.497±0.98 | 14.29±0.66 | 1.17±0.15 |
| F5 | 27.18±0.78 | 0.463±0.86 | 0.526±0.66 | 11.98±0.32 | 1.14±0.63 |
| F6 | 25.45±0.36 | 0.485±0.39 | 0.579±0.52 | 16.23±0.54 | 1.19±0.56 |
| F7 | 26.26±0.52 | 0.420±0.74 | 0.501±0.84 | 16.17±0.46 | 1.19±0.87 |
| F8 | 24.95±0.14 | 0.419±0.15 | 0.497±0.48 | 15.69±0.42 | 1.19±0.49 |
| F9 | 25.04±0.15 | 0.467±0.23 | 0.534±0.16 | 12.55±0.01 | 1.14±0.23 |

**Post compression parameters of Pravastatin buccal tablets:**

**Table 7: Post compression parameters of Pravastatin buccal tablets.**

| Formulation code | Hardness (kg/cm2) | Thickness (mm) | Weight variation | Friability(%) | % Drug content | Surface pH | SI (after8h) | Mucoadhesivsterngth |
|---|---|---|---|---|---|---|---|---|
| F1 | 4.5± 0.15 | 2.16± 0.04 | 199± 0.05 | 0.51±0.26 | 91.26±0.76 | 6.78±0.02 | 21.16±2.26 | 4.01±0.15 |
| F2 | 4.7± 0.26 | 2.45± 0.09 | 200± 0.15 | 0.12±0.14 | 96.14±0.86 | 6.83±0.16 | 35.02±1.52 | 4.06±0.25 |
| F3 | 5.1± 0.51 | 2.85± 0.13 | 198± 0.46 | 0.26±0.52 | 97.52±1.02 | 6.75±0.41 | 46.42±1.15 | 4.26±0.16 |
| F4 | 5.1± 0.89 | 2.46± 0.05 | 199± 0.04 | 0.16±0.65 | 95.63±1.46 | 6.39±0.15 | 35.15±1.23 | 4.15±0.02 |
| F5 | 5.0± 0.85 | 2.72± 0.06 | 200± 0.18 | 0.41±0.15 | 94.15±0.89 | 6.74±0.56 | 49.46±2.12 | 4.19±0.15 |
| F6 | 4.8± 0.49 | 2.24± 0.04 | 201± 0.96 | 0.52±0.41 | 99.45±1.10 | 6.76±0.47 | 57.85±1.15 | 4.24±0.41 |
| F7 | 4.9± 0.74 | 2.16± 0.08 | 197± 0.72 | 0.36±0.02 | 94.12±0.36 | 6.86±0.26 | 36.52±1.20 | 4.36±0.52 |
| F8 | 5.4± 0.89 | 2.32± 0.09 | 196± 0.31 | 0.14±0.06 | 98.16±0.52 | 6.43±0.89 | 44.16±1.23 | 4.51±0.26 |
| F9 | 4.7± 0.84 | 2.17± 0.04 | 199± 0.16 | 0.16±0.04 | 97.14±1.15 | 6.24±0.74 | 60.02±2.15 | 4.72±0.18 |

The appearance of buccal tablets was smooth and uniform on physical examination. The hardness of prepared buccal tablets of Pravastatin was found to be 4-5.4 kg/cm2.

The thickness and weight variation were found to be uniform as indicated by the low values of standard deviation. The thickness and weight of the prepared buccal tablets were found to be in the range of 2.16 to 2.85 mm and 196 to 201 mg respectively. Friability values less than 1% indicate good mechanical strength to withstand the rigors of handling and transportations.

The drug content of buccal tablets was quite uniform. The average drug content of the buccal tablets was found to be within the range of 91.26 to 99.45 % and the low

values of standard deviation and coefficient of variation (< 2) indicate uniform distribution of the drug within the prepared buccal tablets.

The surface pH was determined in order to investigate the possibility of any side effects, in the oral cavity as acidic or alkaline pH is bound to cause irritation to the buccal mucosa. Surface pH of all formulations was found to be in the range of 6.24 to 6.86. Hence it is assumed that these formulations cause no any irritation in the oral cavity.

The swelling profile of different batches of the tablets is shown in Table-7.4. These profiles indicate the uptake of water into the tablet matrix, producing an increase in weight. The swelling state of the polymer (in the formulation) was reported to be crucial for its bioadhesive behavior. Adhesion occurs shortly after the beginning of swelling but the bond formed between mucosal layer and polymer is not very strong. The adhesion will increase with the degree of hydration until a point where over-hydration leads to an abrupt drop in adhesive strength due to disentanglement at the polymer/tissue interface. In formulations maximum swelling was seen with the formulation containing higher concentration of Guar gum. Results indicate that as the concentration of polymers increases the swelling index increases.

The mucoadhesion of all the buccal tablets of varying ratios of polymers were tested and weight required to pull off the formulation from the mucous tissue is recorded as mucoadhesion strength in grams and results are given in Table-7. The mucoadhesivity of buccal tablets was found to be maximum in case of formulation F9 i.e. 40mg of Guar gum.

***Invitro* dissolution of Pravastatin buccal tablets F1 to F9**

**Table 8: *Invitro* dissolution data of formulations F1 to F6.**

| Time(hrs) | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.5 | 36.75±0.15 | 32.48±0.31 | 20.78±0.15 | 27.56±0.96 | 25.65±0.48 | 19.48±0.11 |
| 1 | 42.84±0.42 | 39.76±0.20 | 26.48±0.23 | 32.18±0.35 | 30.75±0.24 | 26.05±0.43 |
| 2 | 62.75±0.86 | 60.07±0.86 | 39.26±0.48 | 69.48±0.15 | 31.05±0.56 | 36.49±0.80 |
| 3 | 75.48±0.32 | 79.46±0.24 | 59.28±0.69 | 80.46±0.04 | 55.64±0.88 | 46.79±0.52 |
| 4 | 95.04±0.18 | 85.31±0.16 | 73.48±0.05 | 99.84±0.24 | 68.25±0.64 | 62.05±0.98 |
| 5 | | 98.04±0.48 | 86.18±0.32 | | 83.49±0.35 | 73.49±0.34 |
| 6 | | | 98.42±0.49 | | 95.48±0.21 | 80.45±0.21 |
| 7 | | | | | | 97.34±0.26 |

**Table 9: *Invitro* dissolution data of formulations F7 to F9.**

| Time(hrs) | F7 | F8 | F9 |
|---|---|---|---|
| 0 | 0 | 0 | 0 |
| 0.5 | 28.46±0.02 | 16.89±0.32 | 12.53±0.15 |
| 1 | 32.65±0.93 | 23.78±0.64 | 20.54±0.53 |
| 2 | 49.86±0.42 | 36.48±0.58 | 32.75±0.12 |
| 3 | 63.45±0.86 | 48.61±0.76 | 45.75±0.64 |
| 4 | 76.06±0.15 | 59.06±0.18 | 59.86±0.38 |
| 5 | 89.50±0.49 | 72.64±0.64 | 64.53±0.56 |
| 6 | 97.08±0.62 | 83.54±0.22 | 73.61±0.82 |
| 7 | | 97.12±0.43 | 85.48±0.44 |
| 8 | | | 97.85±0.15 |

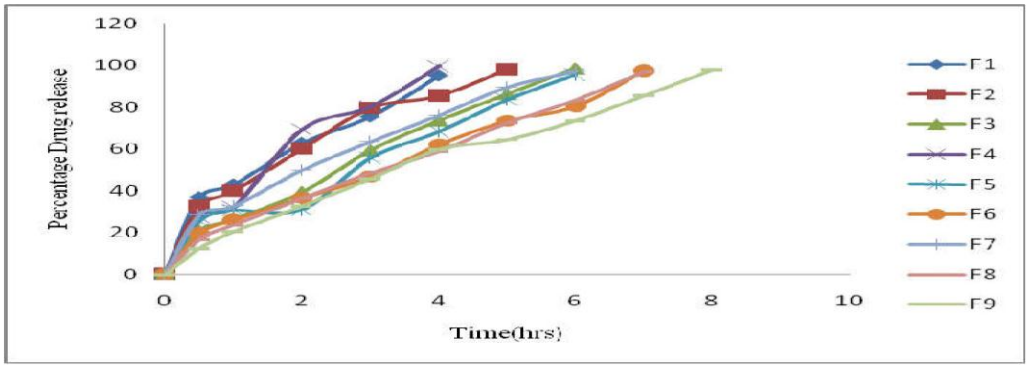


**Fig. 7: *in vitro* drug release profiles of F1-F9.**

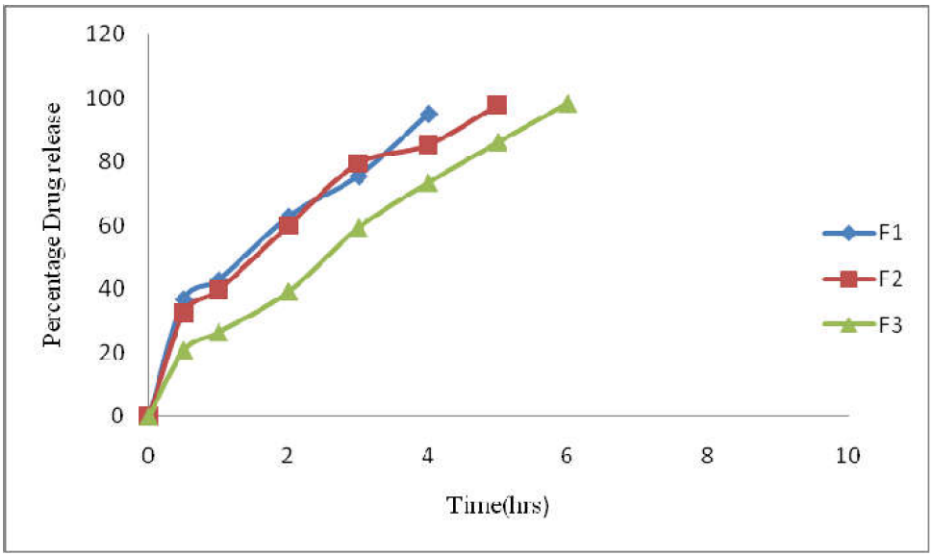


**Fig. 8: *In vitro* drug release profiles of F1-F3.**

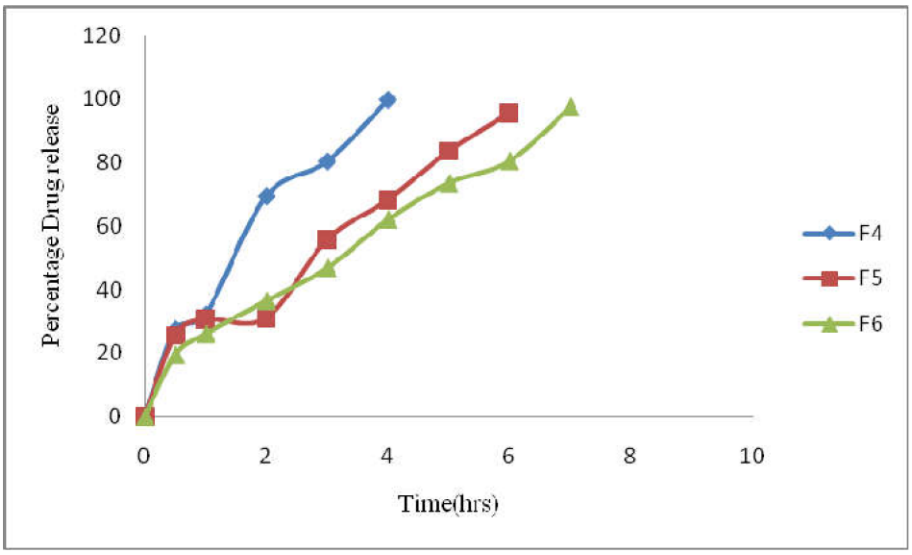


**Fig. 9: *In vitro* drug release profiles of F4-F6.**

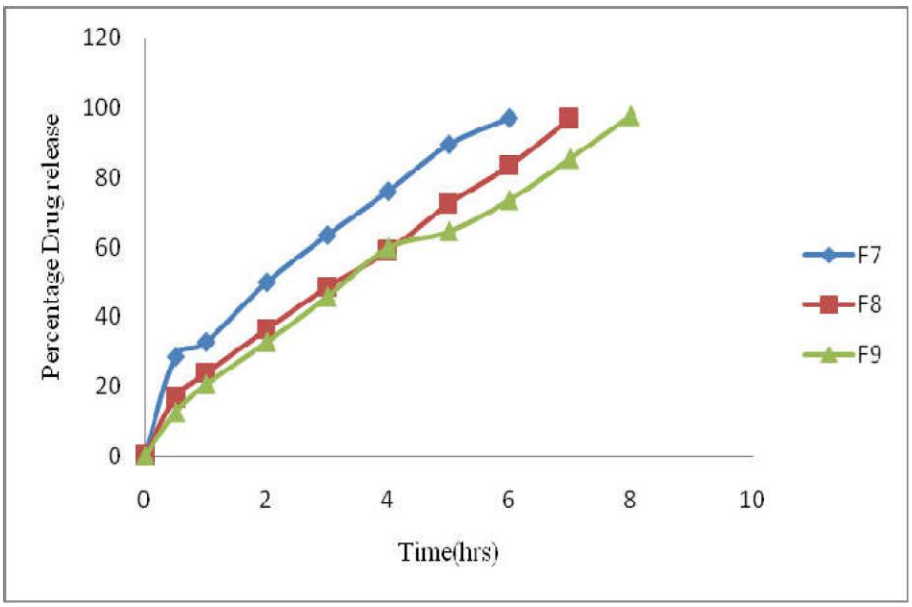


**Fig. 10: *In vitro* drug release profiles of F7-F9.**

## DISCUSSION

All the 9 formulations of Pravastatin buccal tablets were subjected to dissolution studies.

Formulations F1, F2, F3 containing the Xanthan gum as polymer. F1 formulation containing 20mg of xanthan gum shows 95.04% drug release at the end of 4hrs. Whereas F2 formulation containing 30mg of xanthan gum shows 98.14% drug release at the end of 5hrs. While the F3 formulation containing 40mg of xanthan gum shows 98.42% drug release at the end of 6hrs. As the concentration of polymer increasing release rate is slow down. So further trails were performed using Sodium alginate with same proportions.

Formulations F4, F5, F6 containing the Sodium alginate as polymer. F4 formulation containing 20mg of Sodium alginate shows 99.84% drug release at the end of 4hrs. Where as F2 formulation containing 30mg of Sodium alginate shows 95.48% drug release at the end of 6hrs. While the F3 formulation containing 40mg of Sodium alginate shows 97.34% drug release at the end of 7hrs. As the concentration of polymer increasing release rate is slow down. So further trails were performed using Guar gum with same proportions.

Formulations F7, F8, F9 containing the Guar gum as polymer. F4 formulation containing 20mg of Sodium alginate shows 97.08% drug release at the end of 6hrs. Where as F2 formulation containing 30mg of Sodium alginate shows 97.12% drug release at the end of 7hrs. While the F3 formulation containing 40mg of Sodium alginate shows 97.85% drug release at the end of 8hrs. As the concentration of polymer increasing release rate is slow down. So further trails were performed using Guar gum with same proportions.

Among all the 9 formulations F9 formulation is optimized, as it shows maximum drug release at the end of 8hrs which suits the buccal drug delivery system criteria as per our studies.

Further drug release kinetics were performed to F9 formulation.

**Drug Release Kinetics: Zero Order**

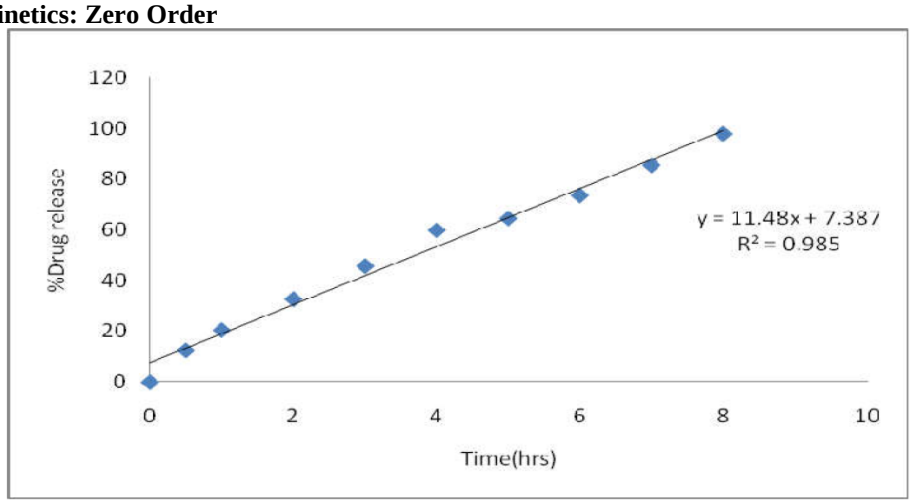


**Fig. 11: Zero order graph of F9 formulation.**

**First order**

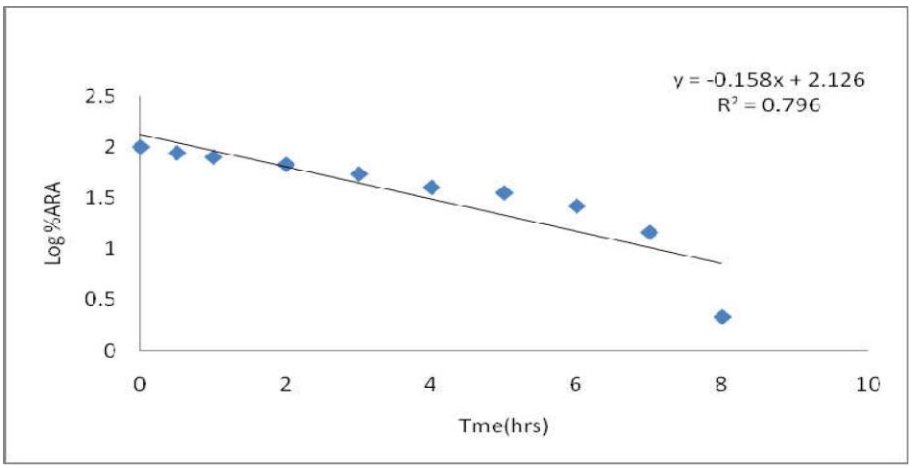


**Fig. 12: First order graph of F9 formulation.**

**Higuchi Plot**

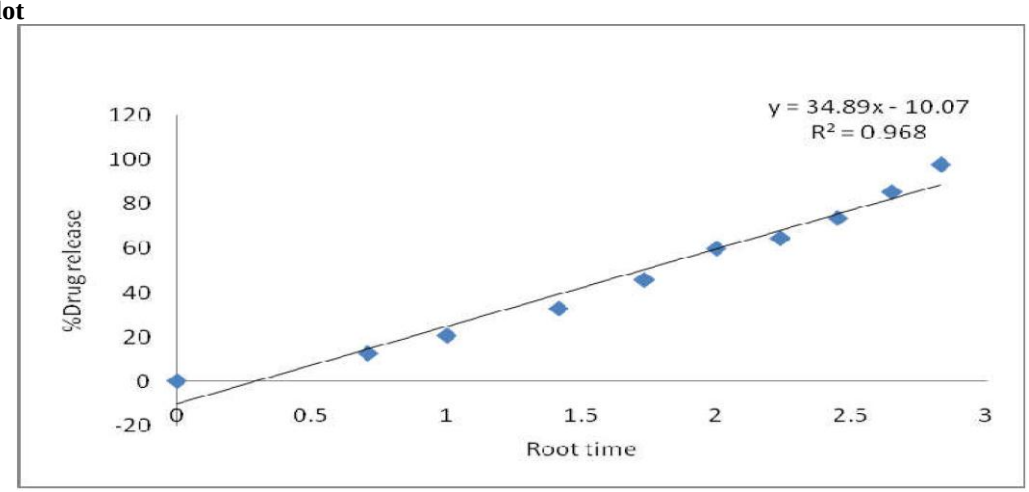


**Fig. 13: Higuchi plot of F9 formulation.**

**Peppas plot**

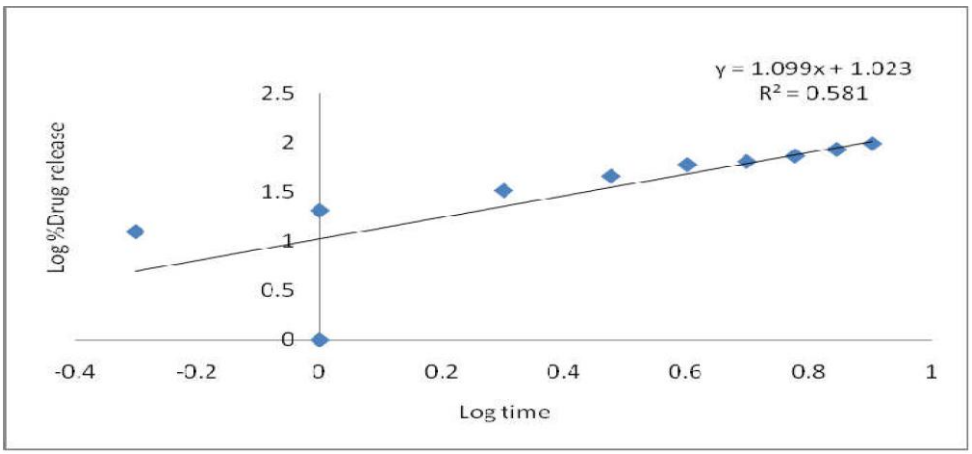


**Fig. 14: Peppas plot of F9 formulation.**

**Table 7.6: Drug release kinetics.**

| R2 values | | | | | n values |
|---|---|---|---|---|---|
| **Formulation** | **Zero order** | **First order** | **Higuchi** | **Korsmeyer - Peppas** | **Korsmeyer- Peppas (n)** |
| F9 | 0.985 | 0.796 | 0.968 | 0.581 | 1.099 |

The invitro dissolution data for best formulation F9 were fitted in different kinetic models i.e, zero order, first order, Higuchi and korsemeyer-peppas equation. Optimized formulation F9 shows R2 value 0.985. As its value nearer to the '1' it is conformed as it follows the zero orderrelease. The mechanism of drug release is further confirmed by the korsmeyer and peppas plot, if n = 0.45 it is called Case I or Fickian diffusion, 0.45 < n < 0.89 is for anomalous behavior or non-Fickian transport, n = 0.89 for case II transport and n > 0.89 for Super case II transport.

The 'n' value is 1.099 for the optimised formulation (F9) i.e., n value was n > 0.89 this indicates Super case II transport. The release kinetics for the optimized formula are shown in table.

## SUMMARY AND CONCLUSION

Buccal tablets containing drug was prepared by direct compression method by using combinations of polymers (Sodium alginate, Guar gum & Xanthan gum). Estimation of Pravastatin was carried out spectrophotometrically at 240 nm. The Buccal tablets were evaluated for physical parameters like appearance, hardness, thickness, weight variation, friability, swelling index, and surface pH; biological parameter-mucoadhesive strength; and other parameters such as drug content uniformity, *in- vitro* release, drug excipient interactions (FTIR).

The Buccal tablets prepared by direct compression were found to be of uniform thickness and weight, smooth appearance with uniform drug content, good hardness and mucoadhesive strength. An increase in polymer concentration brought in an increase in mucoadhesive

strength. The maximum mucoadhesive strength is shown by formulation F9 (40mg Guar gum) is approximately 4.72 gm.IR spectroscopic studies indicated that there are no drug- excipients interactions. Among all the 9 formulations F9 formulation is optimized, as it shows maximum drug release at the end of 8hrs which suits the buccal drug delivery system criteria as per our studies. Optimized formulation (F9) displayed that it follows zero order release kinetics and drug release follows super case II transport mechanism.

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