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Original Article

# Formulaion and Evaluation of Mucoadhesive Buccal Tablets of Atenolol by Using Natural Polymers

Satyabrata Bhanja[*], K Sravan Kumar [1], Muvvala Sudhakar[2], Chinmaya Keshari Sahoo[3], Bibhuti Bhusan Panigrahi [4]

[*,1&2] Department of Pharmaceutics, Malla Reddy College of Pharmacy (Affiliated to Osmania university),Maisammaguda, Dhulapally Secunderabad, Telangana state, India.
[4] Hi-Tech college of Pharmacy,Bhubaneswar,Odisha, India

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ABSTRACT

The main aim of the present work was to formulate and evaluate mucoadhesive buccal tablets of Atenolol an anti-hypertensive drug using natural polymers. Buccal mucosa is the preferred site for both systemic and local drug action. The mucosa has a rich blood supply and it relatively permeable. Buccal transmucosal delivery helps to bypass first-pass metabolism by allowing direct access to the systemic circulation through the internal jugular vein. Mucoadhesive polymers are used to improve drug delivery by enhancing the dosage forms contact time and residence time with the mucous membranes. Various natural polymers were be used in mucoadhesive buccal tablets are Xanthan Gum and guar gum. Buccal tablets were evaluated for different parameters such as weight uniformity, content uniformity, thickness, hardness, surface pH, swelling index,*ex-vivo* mucoadhesive strength, *ex-vivo* mucoadhesive time and *in-vitro* drug release. The formulations, F12 which shows an *in-vitro* drug release of 92.45% in 6h along with satisfactory bioadhesion strength 33 g. The swelling index of atenolol tablets was found to be 43.6 to 69.3.The surface pH of all tablets was found to be satisfactory (6.3±0.6 to7.3±0.4), close to neutral pH, hence buccal cavity irritation should not occur with these tablets. The drug release from optimum batch followed zero order kinetics with non-Fickian diffusion. Drug excipients compatibility study showed no interaction between drug and excipients. So it can be concluded that buccal mucoadhesive tablet is potential way of delivering Atenolol in order to prevent its extensive first pass metabolism and to improve its bioavailability.

**Key words:** *Ex-vivo* mucoadhesive strength, Muccoadhesive time, Surface pH and Swelling index.

## 1. INTRODUCTION

Patient and the clinician alike[1].Mucoadhesive polymers are able to interact with mucus, which is secreted by the underlying tissue [2]. The concept of mucoadhesive polymer has been accepted as a promising strategy to prolong the resident time and to improve the specific localization of drug delivery systems on various membranes[3].The buccal drug delivery systems have certain advantages such as it avoids

**Corresponding author ***
Dr Satyabrata Bhanja
Department of Pharmaceutics
Malla Reddy College of Pharmacy
(Affiliated to osmania university)
Maisammaguda Secunderabad.
Telangana state,
Email: satyabrata_bhanja@rediffmail.com

first pass effect, improves oral bioavailability, gives painless administration, possibility of easy drug withdrawal and have superior patient compliance. In addition, it releases the drug towards the mucosa in a controlled and predictable manner to elicit the required therapeutic response [4].Therefore; the oral mucosa may be potential site for the buccal controlled drug delivery[5].Atenolol cardio selective beta-adrenergic blocker possessing properties and potency similar to propranolol, but without a negative inotropic effect. It is mainly used in the treatment of high blood pressure. It has short biological half-life of 6-7 hours and rapidly eliminated from the body. It is a BCS class II compound and the bioavailability following oral administration is low (50%), BCS class II compounds are poorly soluble but highly permeable and they exhibit bioavailability that is limited by dissolution rate. Therefore, objective of the present study was the design and evaluation of mucoadhesive buccal tablets of atenolol by using natural polymers to overcome the bioavailability related problems, to reduce dose dependent side effects and frequency of administration.

## 2. MATERIALS AND METHODS

Atenolol was obtained gift sample from Gland Pharma Ltd, Hyderabad, India. Xanthan gum and Guar gum were obtained as gift samples from Central drug house Pvt. Ltd, New delhi. Microcrystalline cellulose Aspartame, magnesium stearate and talc were obtained S.D. Fine Chemicals, Mumbai, India .All others chemicals were used as analytical grades.

**Drug-Excipients Compatibility Studies by FTIR:**

Compatibility study was performed by preparing compatibility blends of drug, different ratios of different excipients with the drug based on tentative average weight.These blends were stored at accelerated condition of $40^0$C/75% RH. Control samples were stored at 400C.The ratio of drug to excipients varies from 1:1 to 1:10 depending on the purpose of use, and the samples were kept in double lined poly-bags. In the present study, the potassium bromide (Kbr) disc (pellet) method was employed.Chemical stability was confirmed by IR spectrometry.

**Formulation of buccal Tablets[6]**

All the formulations were prepared by direct compression. Atenolol and all other ingredients were individually passed through sieve no ≠ 60.All the ingredients were mixed thoroughly by triturating up to 15 min. The powder mixture was lubricated with talc. The tablets were prepared by using direct compression method. Total weight of the tablet was considered as 150mg.The compression of different formulations is given in Table 1.

**Table 1: Formulation composition for buccal tablets**

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Drug** | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| **Guar gum** | 10 | 20 | 30 | 40 | 50 | 60 | - | - | - | - | - | - |
| **Xanthan gum** | - | - | - | - | - | - | 10 | 20 | 30 | 40 | 50 | 60 |
| **MCC** | 95 | 85 | 75 | 65 | 55 | 45 | 95 | 85 | 75 | 65 | 55 | 45 |
| **Aspartame** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Mag. Stearate** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Talc** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Total wt** | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |

**Characterization of granular mixture[7]**

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested are as given below:

**Angle of repose:**

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$$\tan \theta = h / r \quad \text{Tan } \theta = \text{Angle of repose}$$

h = Height of the cone, r = Radius of the cone base

**Table 2 : Angle of Repose values**

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

**Bulk density:**

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm$^3$. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read. The bulk density was calculated using the formula:

Bulk Density = $M / V_o$

Where,M = weight of sample $V_o$ = apparent volume of powder

**Tapped density:**

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped

density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

Tap= M / V

Where, Tap= Tapped Density

M = Weight of sample, V= Tapped volume of powder

**Powder compressibility:**

In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

Carr's Index = [(tap - b) / tap] × 100

Where, b = Bulk Density Tap = Tapped Density

**Table 3: Carr's index value**

| 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 |

**Evaluation of post compression parameters for prepared Tablets[8,9,10&11]**

The designed compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

**Weight variation test:**

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined.The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

**Table 4 : Pharmacopoeial specifications for tablet weight variation**

| Average weight ofAverage weight tablet (mg) (I.P) | Average weight ofMaximum percentage tablet (mg) (U.S.P) | difference allowed |
|---|---|---|
| Less than 80 | Less than 130 | 10 |
| 80-250 | 130-324 | 7.5 |
| More than | More than 324 | 5 |

**Hardness:**

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation**.**

**Thickness:**

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

**Friability:**

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = [ ( W1-W2) / W] × 100

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

**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.

**Determination of drug content:**

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Atenolol were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

**Surface pH[12] :**

For the determination of surface pH of the buccal tablets, a combined glass electrode is used. The tablet is allowed to swell by keeping it in contact with 5 ml of distilled water (pH 6.8±0.05) for 2h at room temperature. The pH is identified by bringing the electrode into contact with the tablet surface and allowing to equilibrate for 1min.

**Swelling index[13]**:

The swelling index of the buccal tablet was evaluated by using pH 6.8 phosphate buffer. The initial weight of the tablet is determined (w1). The tablet was placed in pH 6.8 phosphate buffer (6 ml) in a petri-dish placed

in an incubator at 37±1$^0$C and tablet was removed at different time intervals (0.5, 1.0 to 6.0h) and reweighed (w2) . The swelling index was calculated using the formula:

Swelling index = 100 (w2-w1)/w1.

***In-vitro* mucoadhesion time (*in-vitro* residence time)[14]:**

The *in-vitro* residence time was determined using a locally modified disintegration apparatus (Disintegration tester).The disintegration medium was composed of 200 ml isotonic phosphate buffer pH 6.8 maintained at 37$^o$ C. A segment of bovine cheek pouch, 3 cm long, was glued to the surface of a glass slab, vertically attached to the apparatus. The mucoadhesive tablet was hydrated from one surface using ml of buffer and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to move up and down.The time necessary for complete erosion or detachment of the tablet from the mucosal surface was recorded.

**Mucoadhesion strength[15]**

The apparatus used for testing bioadhesion was assembled in the laboratory. Mucoadhesion strength of the tablet was measured on a modified physical balance employing the method described by Gupta et al17 using bovine cheek pouch as model mucosal membrane. (the buccal mucosa was collected from the local slaughterhouse). 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 g 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 g 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 isotonic phosphate buffer (pH 6.8) 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 5 g on right hand side is removed; this causes application of 5 g of pressure on buccal tablet overlying moist mucosa. The balance was kept in this position for 3 min and then slowly weights were increased on the right pan, till tablet separates from mucosal membrane. The total weight on right pan minus 5 g 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 min before reading a new tablet of same formulation to get reproducible multiple results for the formulation .

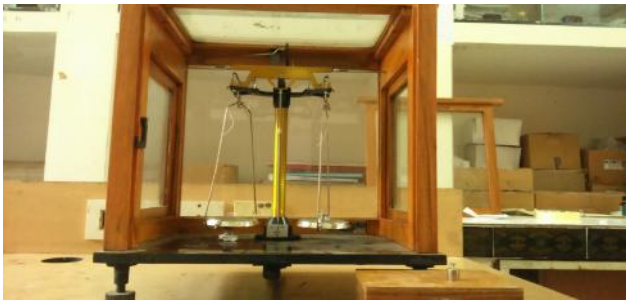

**Fig 1 : Measurement of bioadhesive strength by physical balance**

***In-vitro* drug release studies**

900ml 0f pH6.8 buffer solution was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c ± 0.5°c. Tablets were placed in the vessel and the vessel was covered the apparatus was operated for 6 hours at 50 rpm. At definite time intervals of 5 ml of the fluid was withdrawn, filtered and again 5ml fluid was replaced and analyzed by spectrophotometrically at 275 nm using UV-spectrophotometer.

***In-vitro* drug Release Kinetics**

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model. [16, 17, 18]

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data are fitted to the followingequation.**$F = K_o t$**

Where, 'F' is the drug release at time 't', and '$K_o$' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics**:**

The release rate data are fitted to the following equation

**Log (100-F) = kt**

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model:

To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

**F = k t1/2**

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation.The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t / M_\infty = K t^n$$

Where, $M_t / M_\infty$ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0;while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport),n=1; and for supercase II transport, n > 1.In this model, a plot of log ($M_t / M_\infty$) versus log (time) is linear.

Hixson-Crowell release model:

$$(100-Q_t)^{1/3} = 100^{1/3} - K_{HC}.t$$

Where, k is the Hixson-Crowell rate constant. Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. [19, 20, 21]

## 3. RESULTS AND DISCUSSIONS

### Drug–excipients compatibility study by FTIR

The individual pure drug and physical mixtures shows their intensity peaks. whereas, the characteristic peaks of Rutin shows the peak at 3341cm$^{-1}$ N – H Stretching, a peak at 2947 cm$^{-1}$ of $CH_3$ stretching, 2835 cm$^{-1}$ C-H stretching, 1651 cm$^{-1}$ C=O stretching, 1449cm$^{-1}$C-H stretching, 1408cm$^{-1}$ COO- Streching, 1113 cm$^{-1}$ C-O-C streching. The physical mixtures shows the wave numbers 3328 cm$^{-1}$ , 3315cm$^{-1}$ and 3321 cm$^{-1}$ N-H stretching, 2985 cm$^{-1}$ ,2984 cm$^{-1}$ and 2984 cm$^{-1}$ C-H stretching, 2524 cm$^{-1}$ ,2522 cm$^{-1}$ and 2522 cm$^{-1}$ O-H sharp peak, 1688.16cm$^{-1}$ , 1688.06 cm$^{-1}$ and1684 cm$^{-1}$ C=O stretching, 1414cm$^{-1}$ ,1411 cm$^{-1}$ and 1411.34 cm$^{-1}$ $CH_3$ stretching, 1018 cm$^{-1}$,1019 cm$^{-1}$ and 1019.78 cm$^{-1}$ C-O streching respectively. FTIR studies indicated that the drug is compatible with the polymers. So,there is no interaction between drug and polymers. The results are mentioned in Figure 02-05.

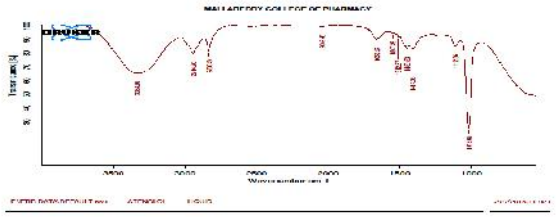

**Fig 2: FTIR study of Atenolol**

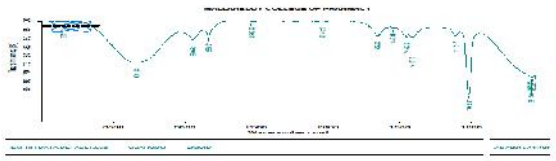

**Fig 3 : FTIR study of guar gum**

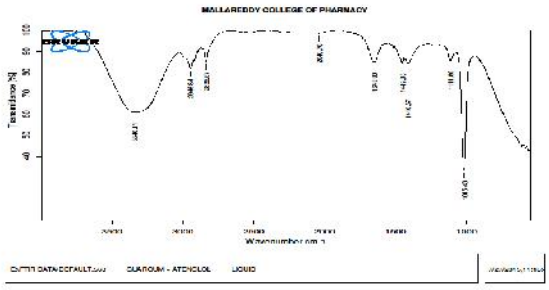

**Fig 4 : FTIR study of atenolol+Guargum**

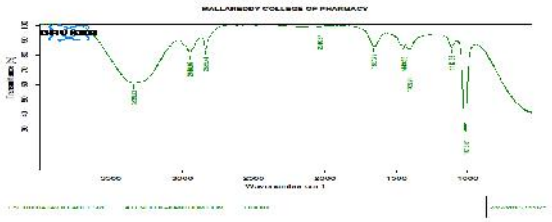

**Fig 5 : FTIR study of Atenolol+ Xanthan gum**

### Powder characterization

The powder mixtures of different formulations were evaluated for angle of repose, bulk density (apparent and tapped),carr's index and hausner's ratio. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.32±0.04 to 0.35±0.06 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.34±0.06 to 0.42±0.05showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 12.87±0.05 to 17.43±0.03 which show that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0.64±0.03 to 1.2±0.08 indicating the powder has good flow properties. The results are shown in Table 5.

**Table 5: Preformulation parameters of powder blend**

| Formulation Code | Angle of Repose | Bulk density (gm/cc) | Tapped density (gm/cc) | Carr's index (%) | Hausner's Ratio |
|---|---|---|---|---|---|
| F1 | 22.5 | 0.35±0.07 | 0.37±0.01 | 14.21±0.06 | 0.86±0.06 |
| F2 | 23.33 | 0.32±0.06 | 0.42±0.05 | 12.87±0.05 | 0.98±0.05 |
| F3 | 22.74 | 0.35±0.03 | 0.38±0.07 | 13.11±0.01 | 0.64±0.03 |
| F4 | 25.33 | 0.34±0.04 | 0.40±0.08 | 14.67±0.08 | 1.12±0.04 |
| F5 | 21.24 | 0.33±0.06 | 0.37±0.03 | 15.92±0.04 | 1.2±0.08 |
| F6 | 25.12 | 0.36±0.05 | 0.36±0.06 | 14.65±0.09 | 1.06±0.09 |
| F7 | 24.08 | 0.35±0.06 | 0.39±0.04 | 15.43±0.05 | 0.76±0.03 |
| F8 | 25.12 | 0.34±0.05 | 0.37±0.02 | 14.97±0.02 | 1.15±0.09 |
| F9 | 25.45 | 0.34±0.08 | 0.42±0.03 | 14.54±0.09 | 1.17±0.02 |
| F10 | 25.24 | 0.32±0.04 | 0.41±0.08 | 14.54±0.04 | 1.18±0.04 |
| F11 | 22.25 | 0.35±0.06 | 0.39±0.03 | 15.76±0.06 | 1.18±0.03 |
| F12 | 24.28 | 0.34±0.05 | 0.34±0.06 | 17.43±0.03 | 1.16±0.07 |

*Value expressed as mean±SD, n=3

**Evaluation of atenolol buccal tablets:**

Tablet quality control tests such as weight variation, hardness, friability, thickness, drug content , swelling index ,surface pH, mucoadhesive strength, mucoadhesive residence time, *in-vitro* drug release and stability studies in different media were performed on the tablets. Atenolol powder is compressed into tablets by direct compression method. The hardness of atenolol tablets was found between 3.0±0.4 to 4.4±0.5 kg/cm$^2$.The weight variation of atenolol tablets was found between 148±1to 150±.2 mg. The friability of atenolol tablets found to be 0.45±0.2%to 0.56±0.2%.The thickness of the tablets was found to be 2.7±0.1mm to 3.1±0.1mm.The mean percentage drug content of the atenolol tablets was found to be 99.12% to 99.87%. The swelling index of atenolol tablets was found to be 43.6 to 69.3. Surface pH of Atenolol tablets was found to be 6.3±0.6 to7.3±0.4. The formulation, F12 which shows satisfactory bioadhesion strength 33 g .All the parameters such as hardness, thickness, weight variation, friability, thickness, drug content and swelling index are within the limits. The results are shown in Table 6 and Figure 6 to 9.

**Table 6 : Evaluation parameters for buccal tablets**

| Formulation code | Weight variation (mg) | Hardness (kg/cm$^2$) | Friability (%loss) | Thickness (mm) | Drug content (%) | Swelling Index | Surface pH |
|---|---|---|---|---|---|---|---|
| F1 | 150±2 | 4.4±0.2 | 0.52±0.05 | 2.8±0.1 | 99.76 | 43.6 | 6.7±0.5 |
| F2 | 150±1 | 4.4±0.5 | 0.54±0.1 | 3.1±0.1 | 99.45 | 43.7 | 6.3±0.6 |
| F3 | 148±2 | 4.4±0.3 | 0.51±0.2 | 2.9±0.1 | 99.34 | 46.7 | 7.1±0.5 |
| F4 | 150±1 | 4.4±0.2 | 0.55±0.2 | 2.9±0.1 | 99.87 | 48.7 | 7.0±0.4 |
| F5 | 149±2 | 4.4±0.4 | 0.56±0.05 | 2.7±0.1 | 99.14 | 49.6 | 6.9±0.4 |
| F6 | 150±1 | 4.4±0.3 | 0.45±0.2 | 2.9±0.1 | 98.56 | 53.5 | 6.4±0.4 |
| F7 | 150±2 | 3.0±0.4 | 0.51±0.1 | 3.0±0.1 | 98.42 | 45.6 | 6.6±0.4 |
| F8 | 151±1 | 3.2±0.5 | 0.49±0.1 | 3.0±0.1 | 99.65 | 48.9 | 6.7±0.4 |
| F9 | 148±2 | 3.5±0.6 | 0.55±0.05 | 3.0±0.1 | 99.12 | 52.8 | 7.0±0.4 |
| F10 | 150±2 | 3.2±0.7 | 0.54±0.1 | 2.9±0.1 | 99.56 | 59.5 | 7.2±0.4 |
| F11 | 148±1 | 3.4±0.5 | 0.51±0.2 | 2.8±0.1 | 99.56 | 60 | 7.3±0.4 |
| F12 | 149±2 | 3.9±0.3 | 0.54±0.05 | 3.0±0.1 | 99.86 | 69.3 | 7.1±0.4 |

Value expressed as mean±SD, n=3.

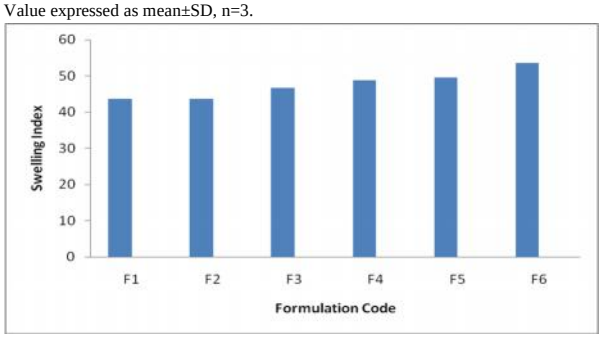


**Figure 6 : Swelling index of formulations F1-F6**

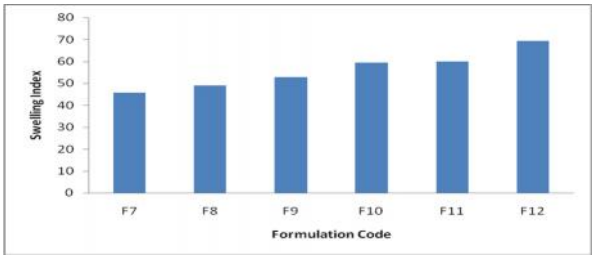


**Fig 7 : Swelling index of formualtions F7-F12**

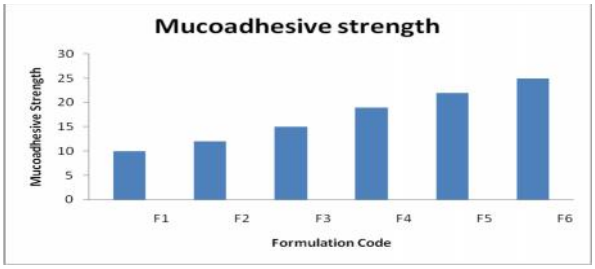


**Fig 8 : Mucoadhesive strength of formulations F1-F6**

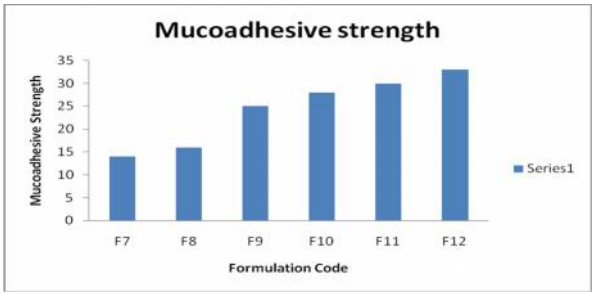


**Fig 9: Mucoadhesive strength of formulations F7-F12**

***In-Vitro* Drug Release Studies**

The *in-vitro* cumulative drug release profile of formulations (F1-F6) showed 69.35%, 74.81%, 78.02%, 80.45%, 86.88% and 87.05% respectively. Among these six formulations, F6 was found to be highest percentage drug release. During the study it was observed that the tablets were initially swell and non erodible over the period of 6 hrs. Similarly the *in-vitro* cumulative drug release profile of formulations (F7-F12) showed 79.98%, 82.18%, 84.37%, 86.66%, 89.57% and 92.45% respectively. Among these six formulations, F12 was found to be highest percentage drug release. During the study it was observed that the tablets were initially swell and non erodible over the period of 6 hrs. It was concluded that by increasing the concentration of xanthan gum as compared to guar gum in the formulations, the drug release rate from the tablets was found to be increased. This may be due to increased hydration (or) swelling characteristics of polymers with increased concentrations. From the overall data it was found that the formulation F12 showed the maximum percentage of drug release i.e. 92.45% at the end of 6 hrs. The results are shown in figures 10 &11.

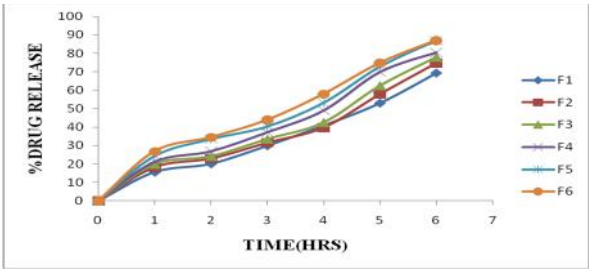


**Fig 10 : *in-vitro* percentage release of formulations F1-F6**

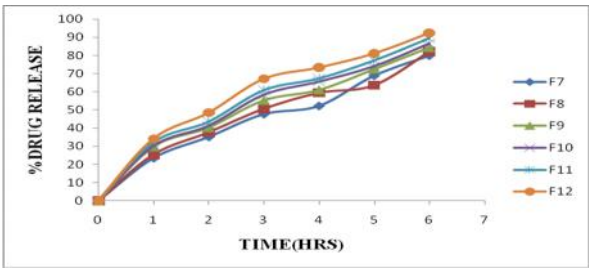


**Fig 11: *in-vitro* percentage release of formulations F7-F12**

### Drug release Kinetics

*In-vitro* drug release data for all the formulations F1 to F12 were subjected to release kinetic study according to zero order, first order, higuchi and korsemeyer-peppas equation to ascertain the mechanism of drug release. Among the zero-order and first-order, the $R^2$ values were found to be higher in zero-order.So all the formulations followed zero-order kinetics. But in case of mechanism of drug release, between higuchi and korsemeyer-peppas equation, the $R^2$ value were found to be higher in korsemeyer-peppas equation and release exponent "n" value less than 1 i.e. (n > 0.5). This indicates that all the formulations followed non-fickian diffusion. Hence it was concluded that all the formulations followed zero-order drug release with non-fickian diffusion.

## 4. CONCLUSION

The results of the present study indicate that mucoadhesive buccal tablets of atenolol with controlled drug release can be successfully prepared by direct compression method using xanthan gum as mucoadhesive polymers . It exhibited well controlled and delayed release pattern. This study concludes that, the addition of xanthan gum increases the viscosity and swelling of tablets there by controls the release of drug and improves the mucoadhesive properties. The formulations,F12 containing xanthan gum as polymers and aspartame(as sweetening agent )was found to be promising, which shows an *in-vitro* drug release of 92.45 % in 6h along with satisfactory bioadhesion strength 33gm.

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