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Research Article

## Formulation Development and *In Vitro* Evaluation of Alendronate Buccal Tablets

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### ABSTRACT

The aim of this work was to develop a mucoadhesive buccal tablet for the buccal delivery of the alendronate via buccal mucosa. Buccal tablets of alendronate are designed to release drug at mucosal site for extended period of time without wash out of drug by saliva. Alendronate sodium is a bisphosphonates which has antiresorptive effect which is implicated in the prophylaxis and treatment of osteoporosis. Sodium alginate, ethyl cellulose and carbopol were selected as mucoadhesive polymers on the basis of their matrix forming properties. The objective of the study is to improve the bioavailability of alendronate buccal tablets. Extensive literature survey was done for the collection of theoretical and technical data. The methodology part includes the explanation of implemented methods in the present study. In present study, an attempt was made to design mucoadhesive buccal tablets containing alendronate, sodium alginate, ethyl cellulose and carbopol using as polymers. The tablets were prepared by direct compression method. The formulations were evaluated for hardness, thickness, friability, weight variation, drug content estimation, surface pH determination, swelling index, in vitro drug release. *In vitro* bioadhesive strength & *in vitro* release studies showed that formulation F11 showed optimum bioadhesive & exhibited optimum drug release 97.6% in 7hr. Kinetics results reveals that the F11 formulation follows zero order kinetics as correlation coefficient ( $r^2$ ) values are higher than that of first-order release kinetics. Optimized formula F11 show drug is released by non-Fickian diffusion mechanism. The stability studies of formulation F11 prepared mucoadhesive buccal tablets of alendronate were stable. Overall evaluations of the mucoadhesive of tablets show good mucoadhesive properties.

**Keyword:** mucoadhesive buccal tablet, alendronate, extended release, carbopol, sodium alginate

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### INTRODUCTION:

#### Mucoadhesive drug delivery systems:

Since the early 1980s, the concept of mucoadhesion has gained considerable interest in pharmaceutical technology [1]. Adhesion can be defined as the bond produced by contact between a pressure sensitive adhesive and a surface. The American society of testing and materials has defined it as the state in which two surfaces are held together by interfacial forces, which may consist of valence forces, interlocking action or both. Mucoadhesive drug delivery systems prolong the residence time of the dosage form at the site of application or absorption. They facilitate an intimate contact of the dosage form with the underlying absorption surface and thus improve the therapeutic performance of the drug [2-3]. In recent years, many such mucoadhesive drug delivery systems have been developed for oral, buccal, nasal, rectal and vaginal routes for both systemic and local

effects.[4] The mucoadhesive drug delivery system includes the following: [5] .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

Alendronate has a positive influence on all symptoms of osteoporosis by increasing bone mineral density and patient mobility, reducing the risk of osteoporotic fractures in all vulnerabilities (vertebrae, hip, arm and femoral neck) and having an analgesic effect in bone pain. Alendronate sodium is a bisphosphonates which has anti resorptive effect which is implicated in the prophylaxis and treatment of osteoporosis. Alendronate sodium is a BCS class III bisphosphonate, which acts as a potent, specific inhibitor of osteoclast-mediated bone resorption. However, low oral bioavailability (under 1%) is the most important disadvantage of alendronate sodium. It is caused by several factors such as: low permeability due to its negatively

charged molecules (belongs to the III class of biopharmaceutical classification system); short plasma half-time ( $T_{1/2} = 0.5-2$  h); its chelation by  $Ca^{2+}$  ions resulting in non-absorbable complexes. Research in bisphosphonates in general aims to increase the bioavailability of these substances, to decrease side effects, to increase adherence to treatment especially for elderly patients[6-8].

In this study we have investigated the possibility of improving the oral bioavailability of alendronate by buccal tablet containing sodium alginate, ethyl cellulose and carbopol using as polymer.

## MATERIALS AND METHODS:

**Materials:** Materials used for this formulation obtained from different sources. Alendronate is provided by Chandra labs, hydroxyl propyl methyl cellulose (HPMC), Micro crystalline cellulose, Guar gum procured from NRchem, Mumbai. Sodium alginate procured from Karnataka fine chem., Bangalore. Ethyl Cellulose (EC), Talk, PVP K-30 procured from S.D. Fine Chem. Ltd, Mumbai, India.

## METHODS:

### Pre formulation studies:

Pre-formulation is defined as study of physical and chemical properties of a drug substance alone prior to formulation. The overall objective of pre-formulation studies is to generate information useful to the formulator in developing stable dosage forms. The results of Preformulation are given table no-02

### Formulation of mucoadhesive tablets of alendronate:

In this work, direct compression method has been employed to prepare buccal tablet with different polymers because with the dry granulation and wet granulation the hardness of tablets has increased because of which rate of drug release got decreased. For one tablet accurately weighed 300 mg was used in the formulation. All the ingredients were accurately weighed and passed through mesh # 60. In order to mix all ingredients thoroughly drug, polymers, micro crystalline cellulose, aspartame were blended geometrically in mortar and pestle for 10 minutes then magnesium stearate and talc were mixed for 1-2 min. The powder blends of various proportions were evaluated for angle of repose, carr's compressibility index and compressed into tablets of diameter 9mm on cadmach press16 Station machine. Using stainless steel flat surface dies and punches by maintaining individual tablet weight constant at 300 mg [9-10].

**Table 1: Composition of alendronate buccal tablets**

| Ingredients (mg) | F1  | F2  | F3  | F4   | F5   | F6  | F7  | F8   | F9   | F10 | F11 | F12 |
|------------------|-----|-----|-----|------|------|-----|-----|------|------|-----|-----|-----|
| Alendronate      | 40  | 40  | 40  | 40   | 40   | 40  | 40  | 40   | 40   | 40  | 40  | 40  |
| Sodium alginate  | 15  | -   | -   | -    | -    | -   | -   | -    | -    | -   | -   | -   |
| Carbopol         | -   | 15  | -   | 22.5 | -    | 15  | 7.5 | 22.5 | 7.5  | 30  | -   | 15  |
| EC               | -   | -   | 15  | -    | 22.5 | 7.5 | 15  | 7.5  | 22.5 | -   | 30  | 15  |
| Talc             | 7.5 | 7.5 | 7.5 | 7.5  | 7.5  | 7.5 | 7.5 | 7.5  | 7.5  | 7.5 | 7.5 | 7.5 |
| PVP k-30         | 7.5 | 7.5 | 7.5 | 7.5  | 7.5  | 7.5 | 7.5 | 7.5  | 7.5  | 7.5 | 7.5 | 7.5 |
| MS               | 7.5 | 7.5 | 7.5 | 7.5  | 7.5  | 7.5 | 7.5 | 7.5  | 7.5  | 7.5 | 7.5 | 7.5 |
| MCC              | q.s | q.s | q.s | q.s  | q.s  | q.s | q.s | q.s  | q.s  | q.s | q.s | q.s |
| Aspartame        | 3   | 3   | 3   | 3    | 3    | 3   | 3   | 3    | 3    | 3   | 3   | 3   |
| Total weight     | 300 | 300 | 300 | 300  | 300  | 300 | 300 | 300  | 300  | 300 | 300 | 300 |

### Micrometrics properties:

The blends for buccoadhesive tablets were characterized with respect to angle of repose, bulk density, tapped density, carr's index, and hausner's ratio. Angle of repose was less than  $30^\circ$  and Carr's index values were less than 20 for the blend of all the batches indicating excellent to good flowability and compressibility. Hausner's ratio was less than 1.25 for all the batches indicating excellent flow properties [11]. The outcome are given table no-03.

### Compatibility studies:

To investigate any possible interactions between the drug and excipients used, the FT-IR spectra of pure drug alendronate and physical mixture of optimized formulation F 11 by using thermo electron corporation (Nicolet IR 200 FTIR) spectrophotometer. The samples were prepared by 1 mg of drug is mixed with the 100 mg of spectroscopic grade of KBr and triturated for uniform mixing. The thin and transparent pellet is prepared by applying 150 lbs pressure.

The prepared pellet is exposed to IR beam and spectra are recorded by using FTIR scanned between  $450-4000\text{cm}^{-1}$ [12-13].

### Thickness:

The thickness of the tablets is measured by vernier calipers and it is expressed in mm. The outcomes are given in the table no.04

### Hardness:

Tablets require strength or hardness to withstand mechanical shocks of handling in manufacture, packing and shipping. Tablet hardness was measured by Monsanto hardness tester and results are expressed in  $\text{Kg/cm}^2$ . The outcomes are given in the table no.04

### Weight variation test:

20 tablets were weighed individually. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The

percentage difference in the weight variation should be within the permissible limits ( $\pm 7.5\%$ ). The percent deviation was calculated using the following formula. The acceptance limits are as per Indian pharmacopoeia (IP) [14-15].

$$\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

#### Friability:

It was performed in Roche friabilator where the tablets were subjected to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of six inches with each revolution in chamber. Pre weighted samples of 20 tablets were placed in the Friabilator, which is then operated for 100 revolutions. The tablets are then dusted and reweighed [16]. Permitted friability limit is 1.0%. The percent friability was determined using the following formula. The outcomes are given in the table no.04

$$\% \text{ Friability} = (\text{initial weight} - \text{final weight} / \text{initial weight}) \times 100$$

#### Determination of drug content

Twenty tablets were taken and triturated well. The quantity equivalent to 100mg of Alendronate was dissolved in 100ml of phosphate buffer pH 6.8 solutions on rotary shaker overnight. The solution was centrifuged and supernatant was collected. The absorbance was measured using UV-Visible spectrophotometer at 238nm [17]. The outcomes are given in the table no.04

#### Microenvironment pH study

The microenvironment pH of the tablets was determined by the method proposed by Bottenberg, et al, 1991. The tablets were allowed to swell for 2 hours in 2ml of pH 6.8 phosphate buffer (pH  $6.8 \pm 0.05$ ) in specially fabricated glass tubes and microenvironment pH was measured by placing the pH electrode in contact with the surface of the tablet and allowing it to equilibrate for 1 minute [18-19]. The outcomes are given in the table no.05

#### Swelling index

It is evaluated by determination of percent of swelling. Each tablet was weighed (W1) and placed in petri dish with 5ml of phosphate buffer pH6.8 and incubated at  $37^\circ\text{C}$  for predetermined times. After placing the formulation for specified time, the tablets were wiped off to remove excess of surface water by using filter paper and again reweighed (W2) [20]. The result outcomes are given in the table no.05

$$\% \text{ swelling index} = \frac{(W2) - (W1)}{W1} \times 100$$

Where,

W 1=Initial weight of the tablet.

W2= Weight of tablet after swelling time interval

#### Determination of the *In vivo* residence time

The *In vivo* residence time was found using a locally modified USP disintegration apparatus. The disintegration medium was composed of 800 ml pH 6.8 phosphate buffer maintained at  $37^\circ\text{C}$ . The sheep buccal tissue was tied with thread to the central stand. The buccal tablet was hydrated with 0.5ml of pH 6.8 phosphate buffer and then the hydrated surface was brought in contact with the mucosal membrane

[21-22]. The tissue was allowed to run in such way that the tablet completely immersed in the buffer solution at the lowest point and was out at the highest point. The time taken for complete erosion or dislodgment of the tablet from the mucosal surface was noted.

#### *In Vitro* drug release study:

*In vitro* drug release study of mucoadhesive tablets were performed using standard USP dissolution apparatus type II (lab india USP XXII). The bowls of the dissolution apparatus was filled with 500ml of phosphate buffer pH 6.8 and maintained at a temperature of  $37 \pm 0.5^\circ\text{C}$ . For each time interval 5ml sample withdrawal and replacement of fresh media at predetermined time interval. The collected samples were filtered through the  $0.45\mu\text{m}$  pore filter [23-24]. The samples were analyzed for drug content using double beam UV spectrophotometer at 238nm.

#### Drug Release Kinetics

To examine the release mechanism of alendronate from the prepared buccoadhesive tablets, the results were analyzed according to the following equation:

$$f_t = M_t / M_\infty = Kt^n$$

Where  $M_t / M_\infty$  is the fractional drug released at time  $t$ ,  $k$  is a kinetic constant incorporating structural and geometrical characteristics of drug / polymer system [device], and  $n$  is the diffusion exponent that characterizes the mechanism of drug release. Drug release is generally expressed by Fickian diffusion mechanism. For non-fickian release, the  $n$  value falls between 0.5 and 1.0 ( $0.5 < n < 0.89$ ) whereas in the case super case II transport  $n > 0.89$  [25]. Data of the *in-vitro* release was fit in to different equations and kinetic models to explain the release kinetics of drug from buccal tablets. The kinetic models used were zero-order equation, first order equation, Higuchi equation and Korsmeyer-Peppas equation.

**Stability studies:** Stability studies were performed at a temperature of  $25 \pm 2^\circ\text{C}$  and  $65 \pm 5\% \text{RH}$  and  $40 \pm 2^\circ\text{C}$  and  $75 \pm 5\% \text{RH}$ , over a period of three months (90 days) for the optimized buccal tablet i.e., formulation F11. Sufficient number of tablets were packed in amber colored screw capped bottles and kept in stability chamber maintained at  $40 \pm 1^\circ\text{C}$  &  $75\% \text{RH}$ . Samples were taken at monthly intervals for drug content estimation [26-27]. At the end of three months period, dissolution test and drug content studies were performed to determine the drug release profiles and drug content.

## RESULTS AND DISCUSSION:

#### Preformulation Study:

Table 02. Results of identification tests of drug

| S.No | Parameter     | Drug                |
|------|---------------|---------------------|
| 1    | Colour        | Fine White powder   |
| 2    | Odor          | Odorless            |
| 3    | Taste         | Tasteless           |
| 4    | Appearance    | Crystalline powder  |
| 5    | Melting Point | $234^\circ\text{C}$ |

#### Compatibility studies

The FTIR spectroscopy is used for identifying both organic and inorganic chemicals which utilized to quantify some components of an unknown mixture and can be used to analyze liquids, solids and gases. The FT-IR spectrum didn't showed presence of any additional peaks for new functional

groups in optimize formulation F11 indicating there is no chemical interaction between drug and the used polymers.

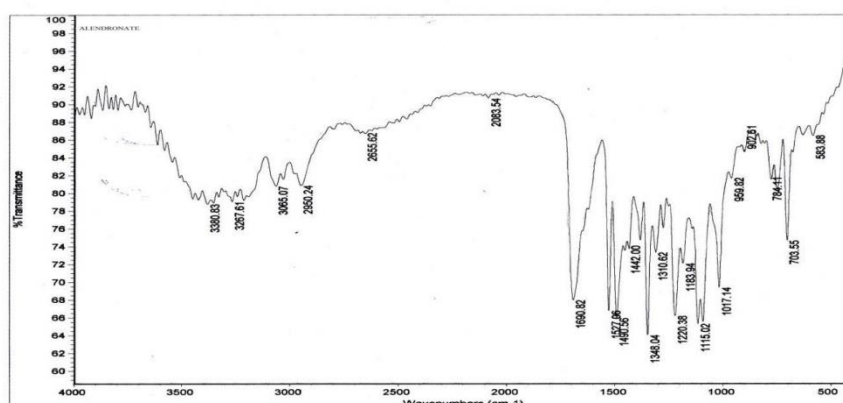


Fig 1: FTIR Spectra of alendronate pure drug

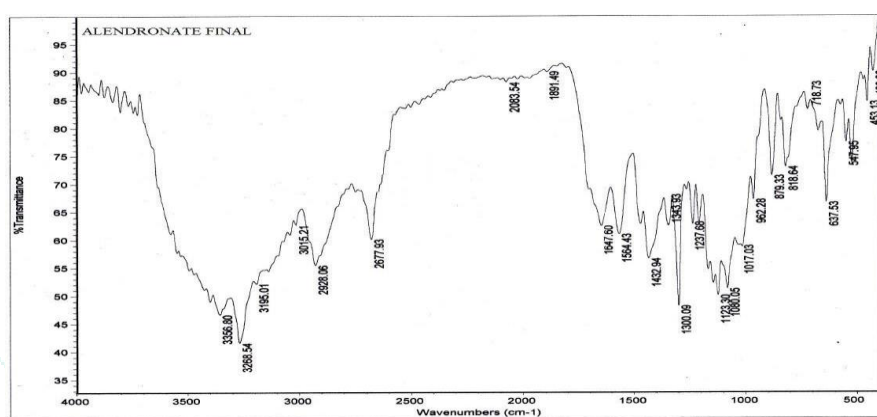


Fig 2: FTIR spectra of alendronate sodium optimized formulation

#### Characterization of blend:

The blends for buccoadhesive tablets were characterized with respect to angle of repose, bulk density, tapped density, carr's index, and hausner's ratio. Angle of repose was less

than 30° and Carr's index values were less than 20 for the blend of all the batches indicating excellent to good flowability and compressibility. Hausner's ratio was less than 1.25 for all the batches indicating excellent flow properties.

Table 03: Physical properties of Pre-compression blend

| Formulations Code | Angle of repose | Bulk Density (g/mL) | Tapped Density (g/mL) | Carr's Index (%) | Hausner's ratio |
|-------------------|-----------------|---------------------|-----------------------|------------------|-----------------|
| F1                | 25.90±0.29      | 0.35±0.045          | 0.41±0.025            | 14.63±1.44       | 1.17±0.034      |
| F2                | 27.20±0.75      | 0.32±0.025          | 0.38±0.071            | 15.79±1.21       | 1.19±0.022      |
| F3                | 29.50±0.69      | 0.31±0.012          | 0.36±0.045            | 16.67±1.38       | 1.20±0.041      |
| F4                | 26.40±0.87      | 0.38±0.038          | 0.37±0.042            | 16.22±0.87       | 1.19±0.055      |
| F5                | 30.20±1.27      | 0.44±0.018          | 0.46±0.024            | 15.25±1.67       | 1.15±0.028      |
| F6                | 27.40±0.43      | 0.43±0.055          | 0.51±0.027            | 15.69±1.12       | 1.19±0.061      |
| F7                | 28.60±0.29      | 0.34±0.041          | 0.41±0.034            | 17.07±1.56       | 1.21±0.074      |
| F8                | 29.30±0.41      | 0.37±0.023          | 0.44±0.027            | 15.91±1.33       | 1.19±0.034      |
| F9                | 30.50±1.38      | 0.42±0.22           | 0.51±0.017            | 16.00±1.41       | 1.19±0.021      |
| F10               | 27.90±0.77      | 0.36±0.044          | 0.43±0.034            | 16.28±0.87       | 1.19±0.037      |
| F11               | 26.50±0.44      | 0.46±0.027          | 0.54±0.037            | 14.81±0.92       | 1.17±0.047      |
| F12               | 27.30±0.52      | 0.44±0.031          | 0.51±0.083            | 13.73±1.85       | 1.16±0.012      |

\*Average of three observations (n=3)

\*All the values are expressed as mean ± SD

#### Physical evaluation of buccoadhesive tablets:

The results of physical evaluation of buccoadhesive tablets are given in below table. All the tablets of different batches complied with the official requirements of uniformity of weight as their weights varied between 297 and 310 mg. The hardness of the tablets ranged from 4.0-4.4 kg/cm<sup>2</sup> and the friability values were less than 0.5% indicating that the

buccoadhesive tablets were compact and hard. The thickness of the tablets ranged from 3.70-3.78 mm. All the formulations satisfied the content of the drug as they contained 98 to 101 % of alendronate and good uniformity in drug content was observed. Thus all the physical attributes of the prepared tablets were found to be practically within control.

Table 04: Post formulation parameters of alendronate sodium buccoadhesive tablets

| Formulation. Code | Hardness (kg/cm <sup>2</sup> ) | Thickness (mm) | Weight (mg) | Friability (%) | Drug content (%) |
|-------------------|--------------------------------|----------------|-------------|----------------|------------------|
| F1                | 4.3±0.31                       | 3.71±0.26      | 304±1.45    | 0.40±0.08      | 99.2±0.45        |
| F2                | 4.2±0.64                       | 3.75±0.61      | 310±1.15    | 0.39±0.11      | 100.3±0.72       |
| F3                | 4.1±0.26                       | 3.72±0.17      | 308±1.86    | 0.20±0.02      | 98.63±0.27       |
| F4                | 4.2±0.24                       | 3.70±0.25      | 297±1.84    | 0.22±0.07      | 99.02±0.37       |
| F5                | 4.4±0.46                       | 3.74±0.31      | 298±1.98    | 0.21±0.04      | 99.24±1.54       |
| F6                | 4.5±0.41                       | 3.76±0.22      | 301±0.87    | 0.26±0.14      | 98.56±2.35       |
| F7                | 4.4±0.31                       | 3.73±0.34      | 300±1.12    | 0.31±0.11      | 100.3±0.74       |
| F8                | 4.3±0.54                       | 3.72±0.12      | 306±1.76    | 0.38±0.06      | 101.6±0.58       |
| F9                | 4.2±0.27                       | 3.75±0.51      | 305±1.48    | 0.32±0.07      | 98.6±0.32        |
| F10               | 4.0±0.45                       | 3.72±0.33      | 304±1.67    | 0.36±0.12      | 97.4±0.84        |
| F11               | 4.0±0.28                       | 3.78±0.41      | 299±1.38    | 0.21±0.08      | 99.64±0.46       |
| F12               | 4.3±0.18                       | 3.74±0.24      | 303±1.95    | 0.26±0.04      | 100.1±1.17       |

\*Average of three observations (n=3)

\*All the values are expressed as mean ± SD

**Microenvironment pH study:**

The surface pH of all formulations was found to be within ±1 units of neutral pH. The values are tabulated in the table no 05. As the pH is neutral it would not cause any irritation in buccal cavity.

**Swelling Index:**

The swelling behavior of a buccal adhesive system is an important properties uniform and prolonged release and effective mucoadhesion. The swelling index study indicated that the rate of swelling was directly proportional to Sodium alginate and polymer content. Swelling index was calculated with respect to time. The swelling index gives an indication

of the relative moisture absorption capacities of polymers and whether the formulations maintain their integrity after moisture absorption. The results of present formulation were tabulated in the table no. 05.

**Mucoadhesion time:**

*In vivo* residence time was determined by using sheep buccal mucosa. The mucoadhesion time is important to know how long the tablet could able to stick to the buccal mucosa. This adhesion time relates to the release rate of drug. The bioadhesive tablet is important for good mucoadhesion. bioadhesion characteristics are affected by the type and ratios of bioadhesive polymers The results were tabulated in the table no. 05.

Table 05: Surface pH, swelling index and mucoadhesion time

| Formulation Code | Surface pH | Swelling Index | Mucoadhesion time |
|------------------|------------|----------------|-------------------|
| F1               | 6.4±0.31   | 140            | 1hrs 32min        |
| F2               | 7.2±0.24   | 120            | 2hrs 03min        |
| F3               | 6.5±0.76   | 145            | 1hrs 45min        |
| F4               | 7.1±0.33   | 130            | 3hrs 40min        |
| F5               | 6.6±0.18   | 160            | 3hrs 50min        |
| F6               | 6.5±0.61   | 150            | 3hrs 35 min       |
| F7               | 6.8±0.38   | 165            | 4hrs 02min        |
| F8               | 6.4±0.24   | 150            | 5hrs 39min        |
| F9               | 6.1±0.85   | 120            | 4hrs 30min        |
| F10              | 6.4±0.21   | 155            | 4hrs 47min        |
| F11              | 6.6±0.41   | 165            | 6hrs 45min        |
| F12              | 6.2±0.37   | 150            | 5hrs 55min        |

**In-vitro drug release study:**

The In-vitro drug release study has been done for various formulations (F1-F12). The different ratios of polymers were

used. The results shown that as the proportion of polymers in the formulation increases, cumulative percent drug released was found to be reduced.

Table 06: *In-vitro* release of formulation F1-F6

| Time(Hrs.) | % Drug release |      |      |       |       |      |
|------------|----------------|------|------|-------|-------|------|
|            | F1             | F2   | F3   | F4    | F5    | F6   |
| 0          | 0              | 0    | 0    | 0     | 0     | 0    |
| 0.5        | 32.1           | 21.1 | 23.8 | 25.1  | 29.2  | 22.6 |
| 1          | 57.2           | 48.3 | 46.4 | 50.8  | 46.8  | 43.1 |
| 2          | 98.6           | 71.2 | 70.8 | 73.4  | 70.6  | 68.1 |
| 4          |                | 99.7 | 98.6 | 84.3  | 85.1  | 87.2 |
| 5          |                |      |      | 100.1 | 100.8 | 99.8 |

Table 07: *In-vitro* release of formulation F7-F12

| % Drug release |      |       |       |      |      |      |
|----------------|------|-------|-------|------|------|------|
| Time (Hrs)     | F7   | F8    | F9    | F10  | F11  | F12  |
| 0              | 0    | 0     | 0     | 0    | 0    | 0    |
| 0.5            | 28.3 | 18.6  | 19.8  | 20.8 | 16.2 | 18.1 |
| 1              | 51.7 | 30.9  | 29.1  | 33.1 | 27.1 | 31.2 |
| 2              | 63.2 | 48.6  | 44.3  | 49.2 | 38.3 | 45.4 |
| 3              | 86.4 | 59.3  | 63.4  | 69.4 | 56.1 | 60.6 |
| 4              | 97.4 | 76.3  | 80.3  | 78.1 | 64.8 | 71.8 |
| 5              |      | 83.4  | 100.1 | 99.8 | 73.1 | 85.6 |
| 6              |      | 100.7 |       |      | 84.3 | 99.5 |
| 7              |      |       |       |      | 97.6 |      |

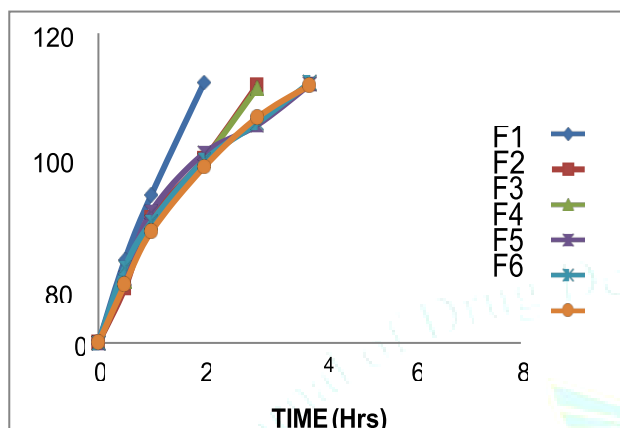


Fig 3: Dissolution graph for formulations F1-F6

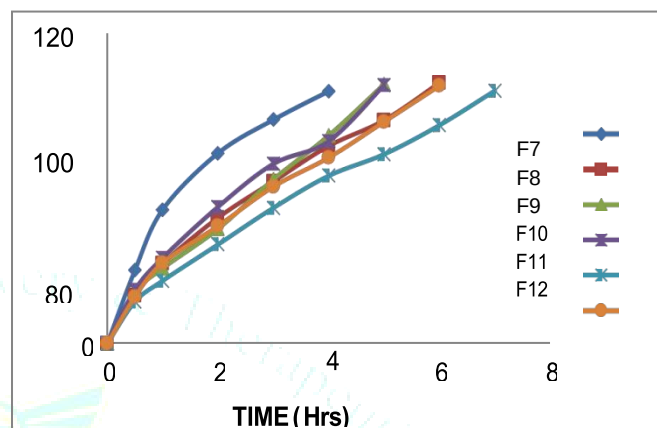


Fig 4: Dissolution graph for formulations F7-F12

**Release kinetics:**

For analyzing the release mechanism, the data obtained were fitted to various kinetic equations of zero order, first order, Higuchi model and Korsmeyer-Peppas model. The regression coefficient was calculated. From the data, it can be

seen the formulation, F11 have displayed zero order release kinetics. From Peppas model it is evident that the drug is released by non-Fickian diffusion mechanism. The data of regression coefficient of different kinetic models were summarized in table no.08.

Table 08: Release kinetics for the optimized formulation F11

|                | ZERO         | FIRST               | HIGUCHI             | PEPPAS         |
|----------------|--------------|---------------------|---------------------|----------------|
|                | (% CDT Vs T) | (Log % remain Vs T) | % CDT Vs $\sqrt{T}$ | Log C Vs Log T |
| Slope          | 12.901       | -0.18208893         | 36.88339627         | 1.076787696    |
| Intercept      | 9.980166667  | 2.106740204         | -7.29768667         | 1.100314385    |
| R <sup>2</sup> | 0.975636613  | 0.824537248         | 0.971885439         | 0.490727483    |

**Stability studies:**

Results from stability studies indicate that the formulated Alendronate bucoadhesive tablet are stable for a period of 3

months under 2 different conditions at 25  $\pm$  2°C and 65  $\pm$  5% RH and 40  $\pm$  2°C and 75  $\pm$  5% RH. There were no remarkable changes were observed during the period of storage.

Table 09: Release kinetics for the optimized formulation F11

|         |        | Assay                       |                                |                                |                                |
|---------|--------|-----------------------------|--------------------------------|--------------------------------|--------------------------------|
|         |        | Cumulative % drug release   |                                |                                |                                |
| Time    | Colour | $\pm$ 2°C and 65 $\pm$ 5%RH | 40 $\pm$ 2°C and 75 $\pm$ 5%RH | 25 $\pm$ 2°C and 65 $\pm$ 5%RH | 40 $\pm$ 2°C and 75 $\pm$ 5%RH |
| 0 days  | White  | 99.64                       | 99.64                          | 97.60                          | 97.60                          |
| 30 days | White  | 99.06                       | 99.42                          | 97.02                          | 97.01                          |
| 60 days | White  | 98.51                       | 98.00                          | 97.01                          | 96.89                          |
| 90 days | White  | 98.46                       | 97.41                          | 96.88                          | 96.77                          |

## CONCLUSION:

The study performed on "Development and evaluation of mucoadhesive buccal tablets of alendronate" reveals following conclusion. The mucoadhesive buccal tablets of alendronate could be prepared using ethyl cellulose and carbopol by direct compression method. The prepared mucoadhesive buccal tablets subjected to FTIR study suggested that there was no drug-polymer and polymer-polymer interaction. The formulation F11 show the tablets were in acceptable range in all factors like friability, hardness, pH. The formulation F11 showed good swelling up to 6hr 45min in phosphate buffer pH6.8 maintaining the integrity of formulation which is required for bioadhesion. *In vitro* bioadhesive strength & *in vitro* release studies showed that formulation F11 showed optimum bioadhesive & exhibited optimum drug release 97.6% in 7hr. Kinetics results shown in table no-08 reveals that the F11 formulation follows zero order kinetics as correlation coefficient ( $r^2$ ) values are higher than that of first-order release kinetics. The optimized formulation F11 show drugs released by non-Fickian diffusion mechanism. The stability studies of formulation F11 prepared mucoadhesive buccal tablets of alendronate were stable. Hence the mucoadhesive buccal tablets of alendronate can be prepared with enhanced bioavailability and prolonged therapeutic effect for the better management of hypercholesterolemia patients. The study conducted so far reveals a promising result suggesting scope for pharmacodynamics and pharmacokinetic evaluation.

## AUTHORS CONTRIBUTIONS

All the author have contributed equally

## CONFLICTS OF INTERESTS:

The author of this study declared no conflict of interest

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