Formulation and optimization of mucoadhesive bilayer buccal tablets of atenolol using simplex design method

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Abstract

**Introduction:** In the present study, mucoadhesive buccal bilayer tablets of atenolol were fabricated with the objective of avoiding first pass metabolism and to improve its bioavailability with reduction in dosing frequency. Hence, the aim of this work was to design oral controlled release mucoadhesive tablets of atenolol and to optimize the drug release profile and bioadhesion. **Materials and Methods:** Bilayer buccal tablets of atenolol were prepared by direct compression method using simplex method of optimization to investigate the combined effect of hydroxypropyl methylcellulose 15 cps (X₁), Carbopol (X₂) and mannitol (X₃); the in vitro drug release (Y₁) and mucoadhesive strength (Y₂) were taken as responses. The designed tablets were evaluated for various physical and biological parameters like drug content uniformity, in vitro drug release, short-term stability, and drug-excipient interactions (FTIR). **Results:** The formulation containing hydroxypropyl methylcellulose 15 cps (10% w/w of matrix layer), Carbopol 934p (10% w/w of matrix layer) and mannitol (channeling agent, 40% w/w of matrix layer) was found to be promising. This formulation exhibited an in vitro drug release of 89.43% in 9 h along with satisfactory bioadhesion strength (7.20 g). Short-term stability studies on the promising formulation indicated that there are no significant changes in drug content and in vitro dissolution characteristics (P<0.05). IR spectroscopic studies indicated that there are no drug-excipient interactions.

**Key words:** Atenolol, bioadhesive strength, mucoadhesive buccal tablet, simplex method of optimization, swelling index

INTRODUCTION

The mucosa is considered as a potential site for drug administration. Transmucosal routes of drug delivery (i.e., the mucosal linings of the nasal, rectal, vagina, ocular and oral cavity) offer distinct advantages over peroral administration for systemic drug delivery. These advantages includes possible bypass of the first pass effect, avoidance of presystemic elimination of gastro intestinal tract (GIT).[11] Buccal delivery of drugs provides an attractive alternative to the oral route of drug administration, particularly in overcoming deficiencies associated with the latter mode of administration problems such as high first pass metabolism; drug degradation in gastro intestinal environment can be circumvented by administering a drug via buccal route.[2,3] Moreover, buccal drug absorption can be terminated promptly in case of toxicity by removing the dosage form from the buccal cavity. It is also possible to administer the drug to patients who cannot be dosed orally to prevent accidental swallowing. Therefore, mucoadhesive dosage forms were suggested for oral drug delivery, which includes adhesive tablets, adhesive gels, and adhesive patches.[4]

Atenolol [beta (β) blocker] has been widely used in the management of hypertension. The drug is well absorbed from the GIT but its bioavailability is low (54%) due to extensive first pass metabolism.[5,6] Since the buccal route bypasses first-pass effect, the dose of atenolol could be reduced by 50%. The physicochemical properties of atenolol, its suitable half-life (6-7 h), and low molecular weight (266.34) makes it a suitable candidate for administration by buccal route. The effective permeation of the drug through bovine buccal mucosa has already been reported.[7]

From the technological point of view, an ideal buccal dosage form must have three properties; it must maintain its position in the mouth for a few hours, release the drug in controlled fashion, and provide drug release in a unidirectional way towards mucosa.
In the present study, the mucoadhesive tablets were developed using hydrophilic polymers (Carbopol 934p, HPMC 15 cps) to get controlled and zero order drug release. The aim of this study was design, development, optimization, and characterization of a buccoadhesive controlled-release tablet of atenolol using some selective polymers like Carbopol 934p (CP) and hydroxypropylmethyl cellulose 15 cps (HPMC). Also, the interaction between polymers, drug-polymers, bioadhesion and in vitro release characteristics of atenolol from different buccoadhesive matrix tablets was evaluated to assess the suitability of such formulations.

**Optimization using simplex design method**

A simplex design was adopted to optimize the formulation variables. In this design, three factors were evaluated by changing their concentration simultaneously and keeping their total concentration constant. The simplex design for three component system was represented by an equilateral triangle Figure 1 in two dimensional space. Seven batches (A to ABC) were prepared; one at each vertex (A, B, C), one at half way between vertices (AB, BC, AC), and one at the center point (ABC). Each vertex represents a formulation containing the maximum amount of one component, with the other two components at a minimum level. The half way between the two vertices represents a formulation containing the average of the minimum and maximum amount of the two ingredients represented by two vertices. The center point represents a formulation containing one third of each ingredient. The amount of HPMC 15 cps, Carbopol 934p, and Mannitol were selected as independent variables and in vitro drug release and mucoadhesive strength was taken as dependent variables.

**MATERIALS AND METHODS**

**Materials**

Atenolol was gifted by Rajat Pharmachem Ltd, Ankaleshwar, Gujarat. Ethyl cellulose was gifted by Arihant Trading co., Mumbai, India; hydroxypropyl methylcellulose 15 cps and Carbopol 934p were gift samples from Colorcon Asia Pvt. Limited, Verna, India and ShinEtsu Chemical Co. Ltd Japan respectively. All other materials were of analytical or pharmacopoeial grade and used as received.

**Methods**

**Preparation of the buccal tablets**

**Preparation**

Direct compression method has been employed to prepare buccal tablets of atenolol using HPMC 15cps and Carbopol 934p as polymers.

**Procedure**

All the ingredients including drug, polymer, and excipients were weighed accurately according to the batch formula [Tables 1 and 2]. The drug is thoroughly mixed with mannitol on a butter paper with the help of a stainless steel spatula. Then all the ingredients except lubricant were mixed in the order of ascending weights and blended for 10 min in an inverted polyethylene pouch. After uniform mixing of ingredients, lubricant (sodium stearyl fumarate SSF) was added and again mixed for 2 min. The prepared blend (100 mg) of each formulation was pre-compressed, on a 10-station rotary tablet punching machine (Clt, Ahmedabad) at a pressure of 0.5 ton and turret speed of 2 rpm to form single layered flat-faced tablet of 8 mm diameter. Then, 50 mg of ethyl cellulose powder was added and final compression was done at a pressure of 3.5 tons and turret speed of 2 rpm to get bilayer tablet.

**Design of experiments**

Based on the results of preliminary trial formulations obtained...

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

| Ingredients                  | Amount (mg) |
|------------------------------|-------------|
| Atenolol                     | 25          |
| HPMC 15 cps                  | 10-40       |
| Carbopol 934p                | 10-40       |
| Mannitol                     | 10-40       |
| Aspartame                    | 3           |
| SSF                          | 3           |
| Spray dried flavoring agent  | 3           |
| Polyvinyl pyrrolidoneK-30    | 6           |
| Ethyl cellulose              | 50          |

Each tablet weight - 130 mg, HPMC- hydroxypropyl methylcellulose; PVP- polyvinyl pyrrolidone, SSF- Sodium Stearyl Fumarate

**Table 2: Combinations as per the chosen experimental design (Simplex design method)**

| Formulation code | X_1   | X_2   | X_3   |
|------------------|--------|-------|-------|
| A                | 40     | 10    | 10    |
| B                | 10     | 40    | 10    |
| C                | 10     | 10    | 40    |
| AB               | 25     | 25    | 10    |
| AC               | 25     | 10    | 25    |
| BC               | 10     | 25    | 25    |
| ABC              | 20     | 20    | 20    |

Coded level: X_1 - HPMC 15 cps, X_2 - Carbopol 934p, X_3 – Mannitol
from the batches of three mucoadhesive polymers (HPMC 15 cps, HPMC 50 cps, and HPMC K4M), the best mucoadhesive polymer screened was used for the final optimization of direct compression method, we have fixed the constraints for the level of independent variables (X₁, X₃, and X₅) i.e., HPMC 15 cps (X₁), carbopol 934p (X₃), and mannitol (X₅), as shown in Table 2. In this study, a simplex design was adopted to optimize the variables. In this design, two factors were evaluated and experiments were performed on all seven-possible combinations. The amount of HPMC 15 cps (X₁) and Carbopol 934p (X₃) were taken as independent variables since the total concentration of the three variations is constant, variation is the levels of X₁ and X₃ will automatically fix the levels of X₅ and in vitro drug release (Y₁) and mucoadhesive strength (Y₂) were taken as dependent variables [Table 3].

**Table 3: Formulation and evaluation of formulations in simplex design method**

| Formulation code | Transformed fractions | t₂₅% (h) | t₅₀% (h) | Mucoadhesive strength (g) |
|------------------|-----------------------|----------|----------|--------------------------|
| A                | 1 0 0                 | 0.57     | 02.20    | 07.4                     |
| B                | 0 1 0                 | 2.00     | 10.45    | 14.63                    |
| C                | 0 0 1                 | 0.39     | 03.90    | 07.2                     |
| AB               | 0.5 0.5 0             | 1.14     | 03.70    | 108.27                   |
| AC               | 0 0.5 0.5             | 0.61     | 03.08    | 105.33                   |
| BC               | 0.5 0 0.5             | 0.78     | 03.08    | 54.53                    |
| ABC              | 0.33 0.33 0.33        | -1.10    | 03.90    | 85.61                    |

X₁ = HPMC 15 cps, X₃ = Carbopol 934p, X₅ = mannitol, t₂₅% = time required to release 25% drug, t₅₀% = time required to release 50% drug

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 was passed through the filter to produce 50 ml. Aliquots of the solution were filtered through 0.45-µm membrane filter disc (Millipore Corporation) and analyzed for drug content by measuring the absorbance at 225.6 nm against solvent blank.

**Surface pH**

For the determination of surface pH of the buccal tablets, a combined glass electrode was used. The tablet was 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 index of the buccal tablet was evaluated by using pH 6.8 phosphate buffer. The initial weight of the tablet was 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°C and tablet was removed at different time intervals (0.5, 1.0, 2.0, 3.0, to 9.0 h), and re-weighed (w₂) [Figure 2]. The swelling index was calculated using the formula:

\[
\text{Swelling index} = 100 \left( \frac{w_2 - w_1}{w_1} \right)
\]

**Mucoadhesive strength**

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 al.,[20] 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, a clean 500-ml glass beaker was placed, 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 was excised, washed, and then 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 37°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 cyanoacrylate 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.

In vitro drug release study[21-23]
This was carried out in USP XXIII tablet dissolution test apparatus-II (Electrolab TDT-06N Mumbai, India), employing paddle stirrer at 50 rpm and 200 ml of p. 6.8 phosphate buffer as dissolution medium. The release study was performed at 37 ± 0.5°C. The backing layer of the buccal tablet was attached to glass disk with cyanoacrylate adhesive. The disk was placed at the bottom of the dissolution vessel. Samples of 5 ml were withdrawn at predetermined time intervals and were replaced with fresh medium. The samples were filtered through 0.45 µm Whatman filter paper and analyzed for atenolol after appropriate dilution by measuring the absorbance at 226.7 nm. The experiment was run in triplicate.

Stability studies
Accelerated stability studies were performed at a temperature of 40±2°C/75±5% RH over a period of three months (90 days) on the promising buccal tablets of atenolol (formulation C). Sufficient number of tablets (15) were packed in amber colored rubber stoppered vial and kept in a stability chamber maintained at 40±2°C/75±5% RH. Samples were taken at one month interval for drug content estimation. At the end of three months period, dissolution test was also performed to determine the drug release profiles.

Drug-excipient interaction studies
The IR spectra of atenolol, Carbopol 934p, HPMC 15cps, PVP K-30, SSF, and formulation (C) were obtained by KBr pellet method. (Perkin-Elmer series 1615 FTIR Spectrometer) [Figure 3].

RESULTS AND DISCUSSION
It has been proposed that mucoadhesion occurs in three stages. The first stage involves the formation of an intimate contact between the mucoadhesive and mucous. Second, the mucoadhesive macromolecules swell and interpenetrate the mucous macromolecules, becoming physically entangled. Third, these molecules interact with each other via secondary, non-covalent bonds such as hydrogen bonds.

The main goal of this work was to develop new buccoadhesive bilayer tablets of atenolol, an antihypertensive drug (beta blocker), consisting of drug free non-adhesive protective layer. The double layered structure design was expected to provide drug delivery in unidirectional fashion to the mucosa and to avoid loss of drug due to washout by saliva, release drug immediately to produce a prompt pharmacological action,
and remain in oral cavity and provide a sustained release of
enough drug over an extended period of time. A total of seven
formulations of buccoadhesive bilayer tablets of atenolol were
prepared and evaluated for biological, physical, and mechanical
parameters. The blends were also evaluated for various pre
compression parameters. These blends displayed angle of
repose values of about 35°; bulk density, tapped density and
Carr’s index values were found to be approximately 0.35 g/cc,
0.41 g/cc, and 14.63%, respectively. According to work plan, the
tablets were evaluated for their thickness, hardness, friability,
weight variation, swelling index, surface pH, drug content, and
mucoadhesive strength.

The appearance of buccoadhesive tablets was smooth and
uniform on physical examination. The hardness of prepared
tablets of atenolol was found to be 3.53 to 5.77 kg/cm²; hardness
increases with an increase in Carbopol 934p proportion in the
formulation. The thickness and weight variation were found to
be uniform as indicated by the low values of standard deviation
and were found to be in the range of 2.97 to 3.03 mm and 148.7
to 150.8 mg, respectively. Friability values less than 1% indicate
good mechanical strength to withstand the rigors of handling
and transportation. Results are given in Table 4. The drug
content of the tablets was quite uniform as seen in the above
mentioned table. The average drug content of the tablets was
found to be within the range of 95.35% to 102.61% and the low
values of standard deviation were found to be 0.39 to 1.45,
0.41 to 10.45 and 7.20 to 14.63 %, respectively. A ccording to work plan, the

| Formulation | Mean thickness* (mm) | Mean hardness* (kg/cm²) | Mean weight variation* (mg) | Friability (%) | Mean drug content* (%) | Mean surface PH* | Mean swelling index* (after 9 h) | Mucoadhesive strength* (g) |
|-------------|----------------------|-------------------------|-----------------------------|---------------|------------------------|----------------|-------------------------------|--------------------------|
| A           | 3.03±0.10            | 4.40±0.10               | 148.7±0.90                  | 0.46±0.0      | 100.40±1.31            | 6.73±0.11     | 73.43±3.37                    | 7.40±0.10                |
| B           | 3.03±0.15            | 5.77±0.15               | 150.3±1.10                  | 0.47±0.0      | 96.45±2.06             | 6.15±0.06     | 119.24±1.48                   | 14.63±0.35              |
| C           | 0.00±0.10            | 3.53±0.06               | 150.8±0.98                  | 0.27±0.0      | 100.67±2.85            | 7.64±0.06     | 50.03±4.14                    | 7.20±0.20               |
| AB          | 2.97±0.06            | 4.97±0.06               | 149.5±1.02                  | 0.46±0.0      | 99.77±2.03             | 5.89±0.04     | 103.95±4.96                   | 10.80±0.30              |
| AC          | 3.00±0.00            | 4.27±0.12               | 149.7±0.90                  | 0.34±0.0      | 95.35±2.22             | 5.96±0.03     | 54.65±4.19                    | 8.33±0.25               |
| BC          | 3.03±0.12            | 4.77±0.06               | 150.2±0.79                  | 0.39±0.0      | 99.84±0.36             | 6.68±0.11     | 93.02±2.33                    | 11.83±0.21              |
| ABC         | 3.03±0.12            | 4.63±0.06               | 149.5±1.36                  | 0.47±0.0      | 97.95±1.22             | 5.85±0.05     | 89.85±0.05                    | 8.20±0.10               |

*Average of three determinations, values shown in parenthesis are standard deviations. Formulation C was selected as the best and used for further studies.

The amounts of HPMC 15 cps (X₁), Carbopol 934p (X₂),
and mannitol (X₃) were selected as independent variables in
a simplex lattice design. The time required for 25% (t₂₅), 50%
drug dissolution (t₅₀), and mucoadhesive strength were taken
as responses. A statistical model incorporating seven interactive
terms was used to evaluate the responses,

\[ Y = b_1 X_1 + b_2 X_2 + b_3 X_3 + b_{12} X_1 X_2 + b_{13} X_1 X_3 + b_{23} X_2 X_3 + b_{123} X_1 X_2 X_3 \]  
\[ (1) \]

Where, \( Y \) is the dependent variable (response); \( X_1, X_2, X_3 \)
represent transformed percentage concentrations of A, B and
C respectively and \( b_1 \) = response at 100% A; \( b_2 \) = response at
100% B; \( b_3 \) = response at 100% C; \( b_{12} \) = response at 50-50
AB; \( b_{13} \) = response at 50-50 AC; \( b_{23} \) = response at 50-50 BC;
\( b_{123} \) = response at 1/3 A, 1/3 B and 1/3 C. The main effects (\( X_1 \)
and \( X_2 \)) represent the average result of changing 1 factor at a time
from its different concentration. The interaction terms (\( X_1 \)
\( X_2 \), \( X_1 \) \( X_3 \) and \( X_2 \) \( X_3 \)) show how the response changes when
two or more factors are simultaneously changed. The statistical
analysis of simplex design method batches was performed by
linear regression analysis using Microsoft Excel. The values
(Table 2) for t₂₅, %, t₅₀ % and mucoadhesive strength for all the
7 batches (A to ABC) showed a wide variation (i.e., 0.39 to 1.45,
1.40 to 10.45 and 7.20 to 14.63 g, respectively). The data clearly
indicate that the values of t₂₅, %, t₅₀ % and mucoadhesive strength are
strongly dependent on the selected independent variables. The
fitted equations relating the responses mucoadhesive strength,
t₂₅ and t₅₀ to the transformed factor are shown in Equation 2,
Equation 3, and Equation 4, respectively.

\[ \text{Mucoadhesive strength} = 7.40 X_1 + 14.63 X_2 + 7.20 X_3 + 388.99 X_1 X_2 + 183.92 X_1 X_3 + 377.70 X_2 X_3 + 1793.13 X_1 X_2 X_3 \]  
\[ (R² = 0.3942) \]  
\[ (2) \]

\[ t_{25} = 0.57 X_1 + 2.0 X_2 + 0.39 X_3 + 0.58 X_1 X_2 + 0.52 X_1 X_3 - 1.66 X_2 X_3 - 14.76 X_1 X_2 X_3 \]  
\[ (R² = 0.4955) \]  
\[ (3) \]
Shirsand, et al.: Optimization of mucoadhesive buccal tablets of atenolol by simplex design

\[ t_{50\%} = 2.20X_1 + 10.45X_2 + 1.40X_3 + 66.66X_1X_2 + 5.12X_1X_3 + 34.82X_2X_3 + 422.88X_1X_2X_3 \ (R^2 = 0.4334) \]  \(\text{(4)}\)

The relatively higher values (≥0.4) of correlation coefficients for \(t_{25\%}, t_{50\%}\), and mucoadhesive strength indicates a good fit, i.e., good agreement between the dependent and independent variables. The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries (i.e., positive or negative). The equation for mucoadhesive strength suggests that the factor \(X_1\) has more significant effect on mucoadhesive strength followed by factor \(X_2\) and \(X_3\). From the equations 3 and 4, it can be concluded that, factor \(X_2\) and \(X_3\) have more important role in prolonging both, \(t_{25\%}\) and \(t_{50\%}\). The magnitude of coefficients indicates that factor \(X_1\) and \(X_2\) have more favorable effect on both the dependent variables than factor \(X_3\) also the high value of \(X_1, X_2\) suggests that the interaction between \(X_1\) and \(X_2\) has a significant effect on \(t_{25\%}\) and \(t_{50\%}\). From the results of linear regression analysis, it can be concluded that the drug release pattern can be changed by appropriate selection of the \(X_1, X_2\) and \(X_3\) levels. The promising formulation was selected on the basis of the acceptance criteria for mucoadhesive strength, \(t_{25\%}\) and \(t_{50\%}\) as mentioned earlier. Results were as shown in Figure 4.

**In vitro drug release**

From dissolution data it is evident that the designed formulations have displayed more than 41.38% drug release in 9 h. The formulation C containing hydroxypropyl methylcellulose 15 cps (10% w/w of matrix layer), Carbopol 934p (10% w/w of matrix layer), and mannitol (channeling agent, 40% w/w of matrix layer) was found to be promising, which showed \(t_{25\%}, t_{50\%}, t_{60\%}, \text{and } t_{70\%}\) values of 0.39, 1.40, 3.00, and 6.36 h, respectively, and released 89.43% drug within 9 h. Results are shown in Table 5 and the drug release profiles depicted in Figure 5. A comparison of the release parameters is shown in Figure 6.
The formulation C containing hydroxypropyl methylcellulose mucoadhesive properties of tablets thereby controls the release of drug and improves the and delayed release pattern. This study concludes that the and ethyl cellulose as backing layer. It exhibited well controlled HPMC 15 cps and Carbopol 934p as mucoadhesive polymers successfully prepared by direct compression method using bilayer tablets of atenolol with controlled drug release can be.

CONCLUSIONS

Drug release kinetics

In vitro drug release data of all the buccoadhesive tablet formulations of atenolol was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetics, and according to Higuchi’s and Peppas models to ascertain mechanism of drug release. It was evident that all the formulations displayed zero-order release kinetics (after an initial burst release of 13-21% drug, with ‘r’ values from 0.847 to 0.943). Higuchi and Peppas data reveals that the drug is released by non-Fickian diffusion mechanism (‘r’ values from 0.469 to 0.999 and ‘n’ values from 0.803 to 0.981). The IR spectrum of the pure drug atenolol displayed characteristic peaks from 0.469 to 0.999 and ‘n’ values from 0.803 to 0.981). The IR spectrum of the pure drug atenolol displayed characteristic peaks at 1240.27 cm\(^{-1}\) and 1647.26 cm\(^{-1}\) are due to alkyl aryl ether linkage and alcoholic –OH groups respectively. All the above characteristic peaks were also found in the IR spectrum of the formulation BT1 (peaks at 3356.12 cm\(^{-1}\) and 1636.69 cm\(^{-1}\) due to N-H and C=O amide groups, respectively). The peaks of 1240.27 cm\(^{-1}\) and 2972.40 cm\(^{-1}\) are due to alkyl aryl ether linkage and alcoholic –OH groups respectively. All the above characteristic peaks were also found in the IR spectrum of the formulation BT1 (peaks at 3356.12 cm\(^{-1}\) and 1647.26 cm\(^{-1}\) due to N-H and C=O stretching, respectively, and peaks at 1240.27 cm\(^{-1}\) and 2972.40 cm\(^{-1}\) are due to alkyl aryl ether linkage and alcoholic –OH groups, respectively) as shown in Figure 3. The presence of above peaks confirms undisturbed structure of drug in the above formulation. Hence, there are no drug-excipient interactions. The stability studies data indicates that the drug content of formulation BT1 was not significantly affected at 40±2°C/75±5% RH after storage for three months. The ‘t’ value was found to be 1.03 against the table value of 4.3 (P<0.05).

CONCLUSIONS

The results of the present study indicate that buccoadhesive bilayer tablets of atenolol with controlled drug release can be successfully prepared by direct compression method using HPMC 15 cps and Carbopol 934p as mucoadhesive polymers and ethyl cellulose as backing layer. It exhibited well controlled and delayed release pattern. This study concludes that the addition of Carbopol 934p increases the viscosity and swelling of tablets there by controls the release of drug and improves the mucoadhesive properties.

The formulation C containing hydroxypropyl methylcellulose 15 cps (10% w/w of matrix layer), Carbopol 934p (10% w/w of matrix layer), and mannitol (channeling agent, 40% w/w of matrix layer) was found to be promising, which shows an in vitro drug release of 89.43% in 9 h along with satisfactory bioadhesion strength (7.20 g).

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