FORMULATION AND DEVELOPMENT OF METOPROLOL TARTRATE BUCCO-ADHESIVE FILMS

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Abstract

The buccal drug delivery system of Metoprolol tartrate were prepared by the film casting on a mercury substrate and characterized in-vitro by drug release studies, skin permeation studies and drug-excipients interaction analysis. The various formulations of buccal films were developed for Metoprolol tartrate, dose in given area of 3.14 cm² was 12.5 mg using various polymers. Various formulations were developed by using controlled release rate and bioadhesive polymers like Carbopol 934 P, Eudragit RL100, PVP, HPMC K15M and Na CMC in single and combinations by solvent casting method with incorporations of different penetration enhancers like DMSO, Tween 60 and Castor oil using propylene glycol as a plasticizer. The formulations were made unidirectional by casting impermeable layer of ethyl cellulose (10% w/v) on the films of the formulations F1 to F12. The release of Metoprolol tartrate from the buccal films varied according to types of buccal film forming polymers. From among all the developed formulations, since formulation F2 retarded the drug release for prolong period, also proved DMSO effect on penetration of drug through mucosa. They were selected as best formulation. The drug release mechanism of all formulations followed zero order kinetics and release mechanism was found to be anomalous diffusion which confirmed by scanning electron microscopy from the 3.14 cm² area of the film. The most satisfactory formulation had showed no significant (p<0.05) change in physicochemical properties, drug content, bioadhesion properties, in-vitro dissolution pattern or ex-vivo diffusion pattern after storage at 30°C ± 2 °C (65% RH) and at 40 ± 2 °C (75% RH) during stability studies for 2 months as per ICH guidelines Q1C.

Keywords: Buccal drug delivery, matrix system, metoprolol tartrate, in-vitro release, in-vitro permeation.

1. Introduction

The present paper deals with the planning and realization of mucoadhesive polymeric films containing a β-adrenoreceptors blocking agent (Metoprolol tartrate) for the topical administration in the oral cavity. Buccal drug delivery has many advantages over conventional modes of drug administration; it avoids hepatic first pass metabolism and improves patient compliance1, 2. One particular problem that is common to many drug delivery systems, aimed to the treatment of the
oral cavity diseases, is the short residence time at the site of application. This problem may be resolved by using bioadhesive polymers, i.e. polymers that exhibit characteristic adhesive interactions with biological membranes.

During the last decade, bioadhesive polymers received considerable attention as platforms for buccal controlled delivery due to their ability to localize the dosage form in specific regions to enhance drug bioavailability.

Metoprolol tartrate is a β-adrenoreceptors drug used in the treatment of mild to moderate essential hypertension. It acts by blocking the β-adrenoreceptors and is almost completely absorbed after oral administration, although the systemic bioavailability varies widely owing to extensive presystemic metabolism. Peak plasma concentrations are achieved after 2–3 h. The plasma half-life is about 3 h, which makes frequent dosing necessary to maintain the therapeutic blood levels of the drug for a long-term treatment. Therefore, Metoprolol tartrate is an ideal drug candidate for buccal drug delivery.

In the present studies, various formulations were developed by using release rate controlling and bioadhesive polymers like Carbopol 934 P, Eudragit RL100, PVP, HPMC K15M and Na CMC in single and combinations by solvent casting methods with incorporations of different penetration enhancers like DMSO, Tween 60 and Castor oil using propylene glycol as a plasticizer. The main emphasis in the present investigation is concerned with the development of buccal films, which after oral administration were designed to prolong adhesion time, thus to increase the bioavailability of the drug and its half-life.

2. Materials and method

Metoprolol tartrate and Eudragit RL 100 were received as a gift sample from Aurubindo Pharma Ltd, Hyderabad, India, and Sun Pharmaceuticals, Baroda, India, respectively. Carbopol 934 P, HPMC K15M and Na CMC were received from Central Drug House (P) Ltd, Delhi. PVP, DMSO and Propylene glycol from Karnataka fine chemicals were used.

2.1 Preparation of drug loaded buccoadhesive films

Buccal films were prepared by solvent casting technique. The polymers were dissolved in solvent mixture of acetone and isopropanol (3:2) by simultaneous addition of polymers. After the neutralization of Carbopol, plasticizer were added and mixed. The drug was then dispersed uniformly in the viscous solution with continuous stirring. The resulting mass was poured into glass mould of 3 cm in diameter. The moulds were left undisturbed at room temperature for one day. The films could be retrieved intact by slowly lifting from the moulds.

Ethyl cellulose 10% w/v was dissolved in ethanol and propylene glycol as a plasticizer was added to formulate backing layer by casting 0.5 ml of the solution on dry films.

3. Evaluation of physical parameters of Metoprolol tartrate buccal films:

3.1. Surface pH

The surface pH was determined by a combined glass electrode. The films were kept in contact with 0.5 ml of distilled water for 1 h. pH was noted by bringing the electrode near the surface of the
formulations and allowing it to equilibrate for 1 min.

3.2. Swelling studies
The swelling studies were done by taking 5% w/v agar in hot water. It was transferred into Petri plates and it was solidify. Three drug loaded films from each formulation were selected and weighed. They were placed in vacuum oven overnight to remove moisture then incubated at 37°C for 1 h, removed and reweighed. The percentage moisture absorption was calculated by using the formula:

\[
\% \text{ Moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100
\]

3.3. Weight uniformity
Three samples of films from each batch were randomly taken and weighed individually each film. The data were analyzed for mean weight and standard deviation.

3.4. Film thickness
Five samples from each batch were taken and thickness of each film was determined using “Dial Caliper”. The data were analyzed for mean film thickness and standard deviation.

3.5. Folding endurance
Folding endurance of the film was determined by repeatedly folding a small strip of film at the same place until it broke. The number of times, the film could be folded at the same place, without breaking, gave the value of folding endurance.

3.6. Determination of residence time
The in-vitro residence time was determined using a locally modified U.S.P disintegration apparatus. The disintegration medium was 800 ml isotonic phosphate buffer solution pH 6.8, maintains at 37°C ± 1°C.

3.7. Test for drug content uniformity of active ingredient
A 2 cm² film was cut into small pieces, dissolved into 10 ml of methanol and diluted upto 100 ml with the phosphate buffer (pH 6.8), and shaken continuously. Then filtered the solution, the drug was estimated spectrophotometrically at 275 nm after dilution.

3.8. In-vitro bioadhesive studies
Bioadhesive strength of the buccal films were measured on the “Modified Physical Balance method”.

3.9. In-vitro release studies by using dissolution apparatus
The drug release was determined using U.S.P. dissolution test apparatus (paddle over disk type method) thermo stated at 37 ± 1°C and stirred at a rate of 50 rpm. Sink condition was maintained throughout the study.

Each film was fixed on glass slide with the help of cyanoacrylate adhesive, so that the drug could be released only from upper face. The slide was immersed in the vessel containing 250 ml of phosphate buffer pH 6.8. Aliquots of 5 ml of sample were withdrawn with graduated pipette at every 1 h time intervals up to 12 h with equal volume of phosphate buffer and analyzed spectrophotometrically at 275 nm.

3.10. Ex-vivo diffusion studies by using Keshary-Chien diffusion cell
The diffusion studies were carried out by using a K-C diffusion Cell and analyzed spectrophotometrically at 275 nm.
3.11. Analysis of release mechanism \textsuperscript{18}

The kinetic models were used a zero order equations, first order equations, Higuchi release, Korsemeyer and Peppas models.

3.12. Temperature dependent stability studies \textsuperscript{19}

To assess the drug and formulation stability, stability studies were performed according to ICH guidelines Q1C. The most satisfactory formulation stored in sealed in aluminum foil. These were stored at 30\degree C ± 2\degree C, 65\% ± 5\% RH and 40\degree C ± 2\degree C, 75\% ± 5\% RH for 2 months.

4. Results

Buccal delivery of drugs provides an attractive alternate to the route of drug administration, particularly in over coming disadvantages associated with latter mode of dosing. Problems such as high first-pass metabolism, less bioavailability up to 12\%, short half-life time up to 3 h, can be circumvented by administering the drug via the buccal route.

Metoprolol tartrate is a \(\beta\)-adrenoreceptors drug used in the treatment of mild to moderate essential hypertension. It acts by blocking the \(\beta\)-adrenoreceptors and is almost completely absorbed (95\%) after oral administration, although the systemic bioavailability varies widely owing to extensive presystemic metabolism. Hence, Metoprolol tartrate was selected as a model drug for the present investigation.

4.1 Formulation studies

Various formulations of buccal films were developed for Metoprolol tartrate, dose in given area of 3.14 cm\(^2\) was 12.5 mg using various bioadhesive polymers like PVP, HPMC K15M, Na CMC, Carbopol 934 P and Eudragit RL100. Buccal films were prepared by solvent casting technique by using a solvent Acetone: Isopropanol (3:2) with and without incorporated different penetration enhancers like DMSO, Tween-60 and Castor oil. For making the films unidirectional release of drug, the backing membrane was casted on films by making solution of ethyl cellulose (10\%w/v) in alcohol with propylene glycol as a plasticizer as shown in Table i (a, b).

<table>
<thead>
<tr>
<th>Ingredients (mg)</th>
<th>Formulation Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>F1</td>
</tr>
<tr>
<td>225</td>
<td></td>
</tr>
<tr>
<td>Carbopol 934 P</td>
<td>150</td>
</tr>
<tr>
<td>P. V. P.</td>
<td>1250</td>
</tr>
<tr>
<td>HPMC K15M</td>
<td>750</td>
</tr>
<tr>
<td>Na CMC</td>
<td>--</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>0.6</td>
</tr>
<tr>
<td>DMSO</td>
<td>--</td>
</tr>
<tr>
<td>Tween 60</td>
<td>--</td>
</tr>
<tr>
<td>Castor oil</td>
<td>--</td>
</tr>
<tr>
<td>Solvent (q.s.)</td>
<td>25</td>
</tr>
<tr>
<td>Solvent * (q.s.)</td>
<td>--</td>
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</tbody>
</table>
An acidic or alkaline formulation is bound to cause irritation on the mucosal membrane and hence this parameter assumes significance while developing a mucoadhesive formulation. The results revealed that all the formulations provide an acceptable pH in the range of 5.5 to 7.0 (salivary pH). Hence, they may not produce any local irritation to the mucosa as shown in Table II (a, b).

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
<th>F10</th>
<th>F11</th>
<th>F12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface pH *</td>
<td>6.21 ±0.01</td>
<td>6.20 ±0.02</td>
<td>6.27 ±0.03</td>
<td>6.61 ±0.1</td>
<td>5.88 ±0.22</td>
<td>5.88 ±0.19</td>
<td>6.12 ±0.10</td>
<td>5.84 ±0.07</td>
<td>6.15 ±0.14</td>
<td>5.97 ±0.05</td>
<td>6.28 ±0.01</td>
<td>6.59 ±0.1</td>
</tr>
<tr>
<td>% Moisture absorbed*</td>
<td>34.6 ±3.7</td>
<td>37.13 ±1.8</td>
<td>35.38 ±3.5</td>
<td>27.07 ±1.1</td>
<td>52.34 ±1.3</td>
<td>64.46±1.6</td>
<td>72.42 ±1.3</td>
<td>71.65 ±1.4</td>
<td>40.00 ±5.5</td>
<td>43.32 ±3.8</td>
<td>32.31 ±1.2</td>
<td>39.05 ±0.82</td>
</tr>
<tr>
<td>Weight Uniformity (mg)**</td>
<td>86.0 ±0.6</td>
<td>85.3 ±1.2</td>
<td>91.3 ±0.9</td>
<td>98.6 ±2.1</td>
<td>101.1 ±5.0</td>
<td>92.0 ±4.0</td>
<td>105.7 ±6.4</td>
<td>100.5 ±2.7</td>
<td>93.2 ±1.3</td>
<td>86.06 ±1.4</td>
<td>96.0 ±1.9</td>
<td>105.5 ±4.2</td>
</tr>
<tr>
<td>Thickness (mm)*</td>
<td>0.21 ±0.002</td>
<td>0.185 ±0.004</td>
<td>0.236 ±0.024</td>
<td>0.183 ±0.008</td>
<td>0.206 ±0.020</td>
<td>0.21 ±0.018</td>
<td>0.242 ±0.002</td>
<td>0.281 ±0.005</td>
<td>0.157 ±0.008</td>
<td>0.166 ±0.011</td>
<td>0.200 ±0.021</td>
<td>0.208 ±0.012</td>
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<tr>
<td>Folding Endurance*</td>
<td>143 ±3.5</td>
<td>138.8 ±2.3</td>
<td>136.8 ±2.6</td>
<td>104.6 ±4.2</td>
<td>161.8 ±4.1</td>
<td>156.6 ±2.7</td>
<td>157.4 ±6.3</td>
<td>144.6 ±3</td>
<td>169.4 ±3</td>
<td>164.8 ±3.7</td>
<td>154.8 ±6</td>
<td>146 ±5</td>
</tr>
<tr>
<td>Mucoadhesion time (h)*</td>
<td>11.73 ±0.06</td>
<td>12.86 ±0.26</td>
<td>10.98 ±0.24</td>
<td>9.7 ±0.05</td>
<td>10.56 ±1.22</td>
<td>11.86±1.5</td>
<td>11.33 ±1.95</td>
<td>10.13 ±0.15</td>
<td>9.08 ±0.07</td>
<td>10.36 ±0.34</td>
<td>11.03 ±0.20</td>
<td>11.48 ±0.53</td>
</tr>
<tr>
<td>Bioadhesion Strength (g)*</td>
<td>7.75 ±0.12</td>
<td>8.00 ±0.09</td>
<td>7.72 ±0.25</td>
<td>7.00 ±0.01</td>
<td>9.7 ±0.05</td>
<td>9.82 ±0.14</td>
<td>9.06 ±0.05</td>
<td>8.73 ±0.03</td>
<td>6.68 ±0.05</td>
<td>6.71 ±0.06</td>
<td>6.29 ±0.06</td>
<td>5.50 ±0.14</td>
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</table>
Among all the formulations Eudragit RL100 and PVP based formulations F1, F2, F3 and F4 showed less amount of percentage moisture absorbed as compared to other formulations. Which could be due to percentage swelling property of Carbopol 934 P was reduced by addition of Eudragit RL 100.

Weight uniformity, folding endurance and thickness are in acceptable range as shown in table ii (a, b). Mucoadhesion time of the Eudragit RL 100 and PVP based formulation F1, F2, F3 and F4 varied from, 9.07 ± 0.05 h to 12.86 ± 0.26 h. Mucoadhesion time of the HPMC K15M based formulations F5, F6, F7 and F8 varied from 10.13 ± 0.15 to 11.86 ± 1.15 h. Mucoadhesion time of Na CMC based formulation s F9, F10, F11 and F12 varied from 9.08 ± 0.07 h to 11.48 ± 0.53 h. It may be due to the presence of PVP in the formulations, which would increase adhesive property as shown in Table ii (a, b).

Bioadhesion strength of Eudragit RL 100 and PVP based formulations F1, F2, F3 and F4 varied from 7.0 ± 0.01 g to 8.00 ± 0.09 g. Bioadhesion strength of HPMC K15M based formulations F5, F6, F7 and F8 varied from 8.73 ± 0.03 g to 10.03 ± 0.06 g. Bioadhesion strength of Na CMC based formulations F9, F10, F11 and F12 varied from 5.50 ± 0.14 g to 6.71 ± 0.06 g which conforms with the results of mucoadhesion time. Drug content of the developed formulations F1 to F12 varied from 11.91±0.56 to 12.39±0.11 mg that was within the official requirements as shown in Table ii (a, b).

The release of Metoprolol tartrate from buccal films contained 12.5 mg in 3.14 cm² area varied according to the types and combination of film forming polymers. HPMC K15M based formulations F5, F6, F7 & F8 and Na CMC based formulations F9, F10, F11, & F12 were showed higher drug release ranged from 84.98± 2.30% to 93.05± 1.07% compared to F1, F2, F3 & F4 formulations which could due to rapid hydration of gelling polymer which leads to faster erosion of film. It could be due to that during dissolution Na CMC and HPMC K15M containing films swelled forming a gel layer on the exposed film surfaces. The loosely bound polymer molecules were easily eroded, allowing the release of Metoprolol tartrate easily as compared to Eudragit RL100 and PVP films. Eudragit RL100 and PVP based formulations F1, F2, F3 & F4 showed lowest drug release 73.95± 1.41%, 75.04± 0.52%, 76.01± 0.45% & 75.13± 1.42% respectively at the end of 12 h. The decreased in the amount of drug release from formulation F1, F2, F3 & F4 attributed to Eudragit RL100 and PVP content as well as Carbopol 934 P as a bioadhesive polymer as shown in Figure i, ii, iii.
It may be due to the percentage swelling property of Carbopol 934 P was reduced by increasing ratio of Eudragit RL100 with PVP. The decrease in swelling causes a decrease in drug release from the matrix. The polymer erosion was rate-controlling step in the drug release. When swellable polymer matrix was made by incorporating Eudragit RL100 with the polymer solution, delay in dissolution of polymer occurs. This leads to controlled release of drugs from mucoadhesive films. The order of drug release from the selected polymer combinations was found to decrease in the following order. Na CMC and Carbopol 934 P>HPMC K15M & Carbopol 934 P>Carbopol 934 P, Eudragit RL100 & PVP.

The in-vitro permeation studies were performed using Keshary-Chien diffusion cell. It was found that only 61.00 ± 0.74%, 56.00 ± 0.60% and 58.00± 0.60% from F1, F5 and F9 formulation respectively of the drug permeated through mucosa at the end of 12 h. These formulations contained no penetration enhancers. The buccal films F2, F6 and F10 containing DMSO as penetration enhancer showed highest drug diffusion 78.53± 0.6%, 72.00± 1.41% and 54.25± 2.73% respectively. Formulation F3, F7 and F11 with Tween 60 as penetration enhancers were found 75.00± 1.41%, 66.00± 1.0 % and 67.57± 0.60% drug diffused. Formulation F4, F8 and F12 with Castor oil as penetration enhancers were found 65.00± 1.0%, 68.00± 0.74% and 69.00± 1.41% respectively. It has been concluded that formulation F2 gave lowest drug release profile for prolonged period and showed highest diffusion profile. Therefore, F2 formulation selected as most satisfactory formulation. It has been concluded that the synergistic effect may be due to functioning of glycol in combination with DMSO to produce saturated or nearly saturated solution of active medicament in the formulation, thereby maximizing the thermodynamic activity of penetrant. It was concluded that permeation promoting activity of Non-ionic surfactant like Tween 60 and Castor oil might be due to the reduction in surface tension, improvement in the wetting of skin and enhanced distribution of the drug. From physicochemical evaluation, it was concluded that the formulation developed by using Tween 60 and Castor
oil showed decrease folding endurance or increased brittleness and also found less bioadhesion strength compared to other formulations as shown in Figure iv, v, vi.

However, formulations F6 contained HPMC K15M and F10 contained Na CMC showed maximum drug released but they exhibited poor residence time as they dislodges early from the mucosal surface. From among all developed formulations, since F2 formulation prolonged drug release for longer period upto 12 h.

The in-vitro release data was fitted to various equations like Higuchi, First order, zero order and Korsemeyer. The best fitted with the highest correlation r and determination r² coefficients were shown by plot of cumulative percentage drug released verses time. The zero order plots were found to be linear to the formulations. The n values for formulation F2, n> 0.5
was obtained as 0.7888 by this equation which indicated that the drug released by anomalous mechanism confirmed by scanning electron microscopy as shown in Figure vii.

Figure vii: Scanning electron micrographs of surfaces of drug-containing buccal films during the release studies

The stability studies were carried out on the most satisfactory formulations F2 at 30 ± 2°C/ 65± 5% RH and 40°C ± 2°C/ 75± 5% RH for two months to assess their long term stability as per ICH guidelines Q1C as shown in Table iii, iv.

At various time intervals of 30 days and 60 days samples were evaluated. There was no significant difference(p<0.05) in the physicochemical parameters, *in-vitro* drug release profiles and *ex- vivo* diffusion profiles were found to be super impossible with the initial readings at zero days results as shown in Figure viii, ix.

Table iii:

<table>
<thead>
<tr>
<th>Time(Days)</th>
<th>Surface pH* Surface pH±S.D.</th>
<th>% Moisture Absorbed</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>30±2°C 65±5% RH</td>
<td>6.18±1.03</td>
</tr>
<tr>
<td></td>
<td>40±2°C 75±5% RH</td>
<td>6.21±0.51</td>
</tr>
<tr>
<td>30</td>
<td>30±2°C 65±5% RH</td>
<td>6.19±0.13</td>
</tr>
</tbody>
</table>
### Table iv: Evaluation of physico-chemical characterization of most satisfactory formulation during stability studies

<table>
<thead>
<tr>
<th>Time (Days)</th>
<th>30±2°C 65±5% RH</th>
<th>40±2°C 75±5% RH</th>
<th>30±2°C 65±5% RH</th>
<th>40±2°C 75±5% RH</th>
<th>30±2°C 65±5% RH</th>
<th>40±2°C 75±5% RH</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>141±3.12</td>
<td>143±2.13</td>
<td>139±3.05</td>
<td>141±3.85</td>
<td>141±3.85</td>
<td>137±2.05</td>
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<tr>
<td>30</td>
<td>139±3.05</td>
<td>145±3.05</td>
<td>145±3.05</td>
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</tr>
<tr>
<td>60</td>
<td>141±3.85</td>
<td>141±3.85</td>
<td>141±3.85</td>
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<td>141±3.85</td>
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</table>

<table>
<thead>
<tr>
<th>Content Uniformity* (mg)</th>
<th>12.03±0.18</th>
<th>12.38±0.17</th>
<th>12.05±0.10</th>
<th>12.37±0.29</th>
<th>12.56±0.07</th>
<th>12.47±1.31</th>
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</thead>
<tbody>
<tr>
<td>Bio adhesion Strength * (g)</td>
<td>8.12±0.5</td>
<td>7.85±0.09</td>
<td>8.31±0.51</td>
<td>8.03±0.23</td>
<td>7.99±0.10</td>
<td>7.87±0.17</td>
</tr>
<tr>
<td>Mucoadhesion Time* (h)</td>
<td>6.75±0.31</td>
<td>6.85±0.21</td>
<td>7.13±0.31</td>
<td>7.21±0.15</td>
<td>6.83±1.51</td>
<td>6.69±0.25</td>
</tr>
</tbody>
</table>

* Average of 3 reading
5. Discussion
Metoprolol tartrate is one of the drugs, which is used for the management of hypertension and angina pectoris. It has only a short half-life of 3 h and oral bioavailability is 12%. Therefore, the present investigation is concern with the development of the unidirectional buccal films, which after administration were designed to prolong adhesion to buccal cavity and thus to increase the bioavailability of the drug and its half-life.

A suitable method of analysis of drug by UV Spectroscopy was developed. Metoprolol tartrate showed maximum absorption at wave length 275nm in isotonic phosphate buffer (pH6.8). Various formulations were developed by using release rate controlling and bioadhesive polymers like Carbopol 934 P, Eudragit RL100, PVP, HPMC K15M and Na CMC in single and combinations by solvent casting methods with incorporations of different penetration enhancers like DMSO, Tween 60 and Castor oil using propylene glycol as a plasticizer. The formulations were made unidirectional by casting impermeable layer of ethyl cellulose (10% w/v) on the films.

Developed buccal films possessed the required physicochemical properties such as surface pH, percentage moisture absorption, folding endurance, weight variation, bioadhesion time and bioadhesion strength. All the developed matrix films showed the bioadhesion time in the range of 9.07 ± 0.05 h to 12.86 ± 0.26 h. Percentage moisture absorption studies indicated significant moisture absorption and contributed in drug release ranged from 73.95±1.41% to 93.05 ±1.07%.

The higher viscosity film forming polymers like Eudragit RL100 and PVP had seemed to inhibit the initial burst release of Metoprolol tartrate from the buccal films. However, out of HPMC K15M based formulations F6 and Na CMC based formulations F10 showed maximum drug released but they
exhibited poor residence time as they dislodges early from the mucosal surface. The most satisfactory formulation had showed no significant (p<0.05) change in physicochemical properties at stability studies.

Thus, the objective of the present work of formulating a bucco-adhesive dosage form of Metoprolol tartrate by using different bioadhesive and film forming polymers had been achieved with success.

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