FORMULATION AND EVALUATION OF MUCOADHESIVE BUCCAL PATCH OF ATORVASTATIN

Vadher Ravi kumar S.*

N.R.Vekaria Pharmacy College, Bilkha Road, Junagadh.

ABSTRACT
The aim of present work was to formulate Mucoadhesive buccal patches of Atorvastatin. The buccal region of the oral cavity is an attractive target for administration of the drug of choice for increase bioavailability and prevent first pass metabolism of drug. Mucoadhesive buccal patches were prepared by solvent casting technique. Nine formulations of Atorvastatin patches were prepared using HPMC E5, Carbopol 934. Formulations were prepared using $3^2$ Factorial design to explore the effect of HPMC E5, Carbopol 934 (as independent variable) on % drug release, Mucoadhesive strength, In vitro Residance time (as dependent variable). FTIR and DSC data revealed that there is no interaction between Atorvastatin and polymers. The patches were evaluated for their thickness, Uniformity content, folding endurance, weight uniformity, ex-vivo permeation study, Swelling index, tensile strength and surface pH. All the formulations exhibited satisfactory physicochemical characteristics. Cumulative percentage of the drug released of Atorvastatin-loaded patches in phosphate buffer (pH 6.8) exhibited drug release in the range of 89.32% to 99.38% in 140 min. Data of in vitro release from patches were fit in to different kinetic models to explain kinetics. The models used were zero and first-order equations, Hixon-crowell, Higuchi and Korsmeyer-peppas models. It was concluded that drug release from buccal patches followed zero order release model and the mechanism of the drug release was due to swelling of hydrophilic polymers. The results indicate that the mucoadhesive buccal patches of Atorvastatin may be good choice to bypass the extensive hepatic first pass metabolism with an improvement in the bioavailability of Atorvastatin through buccal mucosa. In conclusion, the present data confirm the feasibility of developing Mucoadhesive buccal patches of Atorvastatin for potential therapeutic use.

Keywords: Atorvastatin, Mucoadhesive, Buccal Patch, Hpmc E5, Carbopol 934, $3^2$ Factorial Design.

INTRODUCTION
Oral route is perhaps the most preferred for the patients. Within the oral mucosal cavity, the buccal region offers an attractive route of administration for systemic drug delivery. However, oral administration of drugs has disadvantages such as hepatic first pass
metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Buccal route of drug delivery is a good alternative, amongst the various routes of drug delivery. Buccal delivery is the administration of drug via the buccal mucosa (the lining of the cheek) to the systemic circulation. The buccal mucosa lines the inner cheek and buccal formulations are placed in the mouth between the upper gingival (gums) and cheek to treat local and systemic conditions. The buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotides and polysaccharides, as well as conventional small drug molecules[1].

Advantages of buccal drug delivery[1,2]

- Bypass of the gastrointestinal tract and hepatic portal system, increasing the bioavailability of orally administered drugs that otherwise undergo hepatic first-pass metabolism.
- avoidance of pre-systemic elimination within the GI tract, these factors make the oral mucosal cavity a very attractive and feasible site for systemic drug delivery. Considering the low patient compliance of rectal, vaginal, sublingual and nasal drug delivery for controlled release.
- Improved patient compliance due to the elimination of associated pain with injections.
- Sustained drug delivery.
- A relatively rapid onset of action can be achieved relative to the oral route and the formulation can be removed if therapy is required to be discontinued.
- Increased ease of drug administration.
- The large contact surface of the oral cavity contributes to rapid and extensive drug absorption.
- Extent of perfusion is more therefore quick and effective absorption.
- Nausea and vomiting are greatly avoided.
- Used in case of unconscious and less co-operative patients.
Drugs, which show poor bioavailability via the oral route, can be administered conveniently.

Ex: Drugs, which are unstable in the acidic environment of the stomach or are destroyed by the enzymatic or alkaline environment of the intestine\(^{2,3,4}\).

**Limitations of buccal drug delivery\(^{1,2}\)**

- Drugs which irritate oral mucosa or have bitter taste, or cause allergic reactions, discoloration of teeth cannot be formulated.
- If formulation contains antimicrobial agents, affects the natural microbes in the buccal cavity.
- The patient cannot eat/drink/speak.
- Only those drugs which are absorbed by passive diffusion can be administered by this route.
- Drugs which are unstable at buccal pH cannot be administered by this route.
- Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug.
- Low permeability of the buccal membrane, specifically when compared to the sublingual\(^{2,3,4}\).

**Basic components of buccal drug delivery system\(^{1,3}\)**

The basic components of buccal drug delivery system are

1) Drug substance
2) Bioadhesive polymers
3) Backing membrane
4) Permeation enhancers
5) Plasticizer
6) Solvents

**MATERIALS AND METHOD**

Materials:
Atorvastatin was received as gift sample from Mepro pharmaceutical pvt.ltd., India. Hydroxy propyl methyl cellulose E5, Carbopol 934, Polyethylene glycol 400, Aspartame were received from Yarrow chem. Ltd, Mumbai. All the other solvents and chemicals were of Laboratory Reagent grade.

Manufacturing methods of buccal patches

Solvent Casting Method:

Mucoadhesive buccal patches were prepared using solvent casting method. The formulation codes and their respective compositions are given in Table 1. An aqueous solution of polymers was prepared by dissolving in a fixed quantity of distilled water. To this polymeric solution measured quantities of PEG 400, Aspartame were added. Atorvastatin was dissolved in 2 ml of methanol and add into the polymeric solution. The suspension was stirred for 30 min. The thick viscous suspension was degassed to remove air entrapment by using ultrasonicator. Measured quantity of suspension was cast on a 47.75 cm² petri dish and dried in oven at 60°C. The patch was carefully removed from the petri dish. The films were stored in aluminium foil and place in air tight containers for further studies. The film samples were also stored for accelerated stability studies as per International Conference on Harmonization (ICH) guidelines.

**TABLE 1: FORMULATION TABLE OF MUCOADHESIVE BUCCAL PATCHES OF ATORVASTATIN**

<table>
<thead>
<tr>
<th>Ingredients</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>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin (mg)</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
</tr>
<tr>
<td>HPMC E5 (mg)</td>
<td>200</td>
<td>300</td>
<td>400</td>
<td>200</td>
<td>300</td>
<td>400</td>
<td>200</td>
<td>300</td>
<td>400</td>
</tr>
<tr>
<td>Carbopol 934 (mg)</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Aspartame (mg)</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>PEG-400 (%)</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Methanol (ml)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Water (ml)</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>
Evaluation of Mucoadhesive Buccal patch of Atorvastatin

- Weight uniformity
- Thickness
- Swelling index
- Surface pH
- In vitro Drug Release
- Drug content uniformity
- Moisture content
- Tensile strength
- Mucoadhesive strength
- Folding endurance
- Residence time

a) **Weight uniformity test**\(^5\)

For weight uniformity test each formulation were prepared in triplicate five Patch of 2×2 cm\(^2\) area were cut from each plate. Individually weigh all the patch using digital weighing balance and average weight was calculated.

b) **Thickness**\(^5,6\)

Thickness of tablet is important for uniformity of Patch size. Thickness was measured using Digital screw gauge. It was determined by checking five 2×2 cm\(^2\) patch from each petri plate.

c) **Swelling index**\(^7,8\)

Weight and area increase due to swelling were measured.

**Weight increase due to swelling:** A drug-loaded patch of 2×2 cm\(^2\)

was weighed on a preweighcover slip. It was kept in a petridish and 50 ml of phosphate buffer, pH 6.8 was added. Every five min, the cover slip was removed and weighed upto 30 min. The difference in weights gives the weight increase due to absorption of water and swelling of patch.
Area increase due to swelling: A drug loaded patch size of 2x2 cm$^2$ was cut and placed in petridish. A graph paper was placed beneath the petridish, to measure the increase in the area. 50 ml of phosphate buffer, pH 6.8, was poured into the petridish. An increase in the length a breadth of the patch was noted at five min intervals for 60 min and the area was calculated.

$$\text{Swelling Index} = \frac{W_2 - W_1}{W_1} \times 100$$

Where, $W_1$ is the weight of buccal patch before dipping into Beaker and $W_2$ is the weight of buccal patch after dipping in beaker and wiped.

d) Surface pH$^{[5]}$

The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible.

The method was used to determine the surface pH of the Patch A combined glass electrode was used for this purpose. The Patch was allowed to swell by keeping it in contact with 1 mL of distilled water (pH 6.8 ± 0.05) for 2 hours at room temperature. The pH was measured by bringing the electrode in contact with the surface of the patch and allowing it to equilibrate for 1 minute.

e) In vitro Drug release$^{[6,7,8]}$

In this study, sheep buccal mucosa was as a barrier membrane. Diffusion studies were carried out, to evaluate the drug relase across the sheep buccal mucosal membrane, by using Modified Franz diffusion cell. Sheep buccal mucosa was obtained from local slaughter house and used within 2 hrs of slaughter. The tissue was stored in phosphate buffer pH 6.8 solution upon collection. Sheep buccal mucosa was tide on surface of modified franz diffusion cell. Drug is dissolve in suitable solvent and make upto 10 ml with phosphate buffer 6.8 and pour into Modified franz diffusion cell. Modified franz diffusion cell dip in 250 ml beaker containing phosphate buffer 6.8. Put assembly on megnatic stirrer maintaining
speed at 50 rpm, Temp 37°C. Withdraw 5 ml of sample at interval of 15 min time. The withdrawn sample was diluted to 10 ml. The amount of Atorvastatin was determined by UV-VIS Spectrophotometer at 240 nm.

f) Drug content uniformity[^8,^9^]

The patches were tested for the content uniformity. A patch of size 2×2 cm² was cut and placed in a beaker. Ten ml of a Phosphate buffer 6.8 pH was added. The contents were stirred in a cyclo-mixer to dissolve the Patch. The contents were transferred to a volumetric flask (10 ml). The absorbance of the solution was measured against the corresponding blank solution at 240 nm.

g) Moisture content[^10^]

The polymer used for the formulation of mucoadhesive patches is hydrophilic polymer. The moisture absorption studies give an indication about the relative moisture absorption capacities of polymers and an idea whether the formulation maintains its integrity after absorption of moisture.

5% w/v agar in distilled water, in hot condition, was transferred into Petri plates and it was allowed to solidify. Three 2×2 cm² patches of each formulation were selected and weighed. They were placed in desiccator overnight prior to the study to remove moisture if any and laminated on one side with water impermeable backing membrane. They were placed on the surface of the agar and incubated at 37°C for one hour in incubator. The patches were removed and weighed again. The percentage of moisture content can be calculated using the formula.

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

h) Tensile strength[^9,^10^]

Area of the Patches and maximum load which film can tolerate were measured using a puncture test and texture analyzer (Instron® 3366-2716015, Germany) (n = 3). Patches specimens were mounted on a film holder. The puncture probe was driven through the film at a speed of 0.1 mm/s. Force vs. displacement curves were recorded with a 50 N load cell. Load versus displacement curves were
recorded until rupture of the patches and used to determine the tensile strength of Patches.

\[
\text{Tensile strength} = \frac{\text{Maximum force}}{\text{Area}}
\]

i) **Mucoadhesive strength**\[^{[6,7]}\]

Fresh sheep buccal mucosa was obtained from a local slaughter house and used within 2 h of slaughter. The mucosal membrane was separated by removing the underlying fat and loose tissues. The membrane was washed with distilled water and then with isotonic phosphate buffer pH 6.8 at 37 °C.

Bioadhesive strength of the patch was measured on a modified physical balance. The mucoadhesive patch was fixed to glass slide with cyanoacrylate glue on pan surface. And sheep buccal mucosa tied on 100 ml beaker containing IPB 6.8. Patch stick on beaker and put weight in another pan. The mass in (gm) required to detach the patch from the mucosal surface give the measure of mucoadhesive strength.

j) **Folding endurance**\[^{[8,10]}\]

Folding endurance of the patches was determined by repeatedly folding one patch at the same place till it broke or folded up to 300 times manually, which is considered satisfactory to reveal good patch properties. The number of times of patch could be folded at the same place without breaking gave the value of the folding endurance.

k) **Residence time**\[^{[7,8]}\]

The in-vitro residence time was determined using a locally modified USP disintegration apparatus. Disintegration medium was composed of 900 ml isotonic phosphate buffer pH 6.8 (IPB) maintained at 37°C. A segment of sheep buccal mucosa, 3 cm long, was glued to the surface of a glass slab, vertically attached to the apparatus. The mucoadhesive patch was hydrated from one surface using IPB 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 so that the patch was completely immersed in the buffer solution at the lowest point and was out at the highest point. The time necessary for complete erosion or detachment of the patch from the mucosal surface was recorded (mean of triplicate determinations).

Mathematical model of Mucoadhesive Buccal patch of Atorvastatin

The results obtaining in vitro release studies were plotted in different models of data treatment as follows:

a) Zero Order Kinetic

It describes the system in which the drug release rate is independent of its concentration.

\[ Q_t = Q_0 + K_0 t \]

Where

- \( Q_t \) = Amount of drug dissolved in time \( t \)
- \( Q_0 \) = Initial amount of drug in the solution, which is often zero and \( K_0 \) = zero order release constant.

If the zero order drug release kinetic is obeyed, then a plot of \( Q_t \) versus \( t \) will give a straight line with a slope of \( K_0 \) and an intercept at zero.

b) First Order Kinetic

It describes the drug release from the systems in which the release rate is concentration dependent.

\[ \log Q_t = \log Q_0 + kt/2.303 \]

Where,

- \( Q_t \) = amount of drug released in time \( t \).
- \( Q_0 \) = initial amount of drug in the solution
- \( k \) = first order release constant

If the first order drug release kinetic is obeyed, then a plot of \( \log (Q_0 - Q_t) \) versus \( t \) will be straight line with a slope of \( kt/2.303 \) and an intercept at \( t=0 \) of \( \log Q_0 \)

c) Higuchi Model
It describes the fraction of drug release from a matrix is proportional to square root of time.

\[
\frac{M_t}{M_\infty} = kH t^{1/2}
\]

Where,

- \( M_t \) and \( M_\infty \) are cumulative amounts of drug release at time \( t \) and infinite time, and
- \( kH \) = Higuchi dissolution constant reflection formulation characteristics.

If the Higuchi model of drug release (i.e. Fickian diffusion) is obeyed, then a plot of \( \frac{M_t}{M_\infty} \) versus \( t^{1/2} \) will be straight line with slope of \( kH \).

d) Korsmeyer-Peppas model (Power Law)

The power law describes the drug release from the polymeric system in which release deviates from Fickian diffusion, as expressed in following equation.

\[
\frac{M_t}{M_\infty} = k t^n
\]

\[
\log \left[ \frac{M_t}{M_\infty} \right] = \log k + n \log t
\]

Where,

- \( M_t \) and \( M_\infty \) are cumulative amounts of drug release at time \( t \) and infinite time (i.e. fraction of drug release at time \( t \)),
- \( k \) = constant incorporating structural and geometrical characteristics of CR device,
- \( n \) = diffusional release exponent indicative of the mechanism of drug release for drug dissolution.

To characterize the release mechanism, the dissolution data \( \{\frac{M_t}{M_\infty} < 0.6\} \) are evaluated. A plot of \( \log \left[ \frac{M_t}{M_\infty} \right] \) versus \( \log t \) will be linear with slope of \( n \) and intercept gives the value of \( \log k \). Antilog of \( \log k \) gives the value of \( k \).

Peepas used the \( n \) value in order to characterize different release mechanisms as shown in the table below

**TABLE 2: DIFFERENT RELEASE MECHANISMS**

<table>
<thead>
<tr>
<th>‘( n )’</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>Fickian diffusion</td>
</tr>
<tr>
<td>0.5 &lt; ( n ) &lt; 1</td>
<td>Non-Fickian diffusion</td>
</tr>
<tr>
<td>1</td>
<td>Class II transport</td>
</tr>
</tbody>
</table>
RESULT AND DISCUSSION
In the present study different formulations with variable concentration of polymers were prepared and evaluated for physico-chemical parameters; in vitro release and stability study and other evaluation parameter of mucoadhesive buccal patch.

Identification of Drug:
Preformulation Studies of Pure Drug Atorvastatin: It is one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the drug, which included melting point determination, solubility and standard curve.

a) Melting Point Determination
Melting point of Atorvastatin was determined by capillary method. The melting point of Atorvastatin was found to be in the range 159.2-160.7 ºC which compiled with BP standards, indicating purity of the drug sample.

b) Solubility
Atorvastatin solubility was slightly soluble in water. practical solubility of atorvastatin in water was 1.23 mg/ml.

c) Standard Calibration Curve of Atorvastatin
The scanning of drug solution in UV region (200-400 nm) to find out the wavelength of maximum absorption (λ_max). The λ_max was found to be at 240 nm for Atorvastatin. So the Standard calibration curve of Atorvastatin was developed at these wave length. The calibration curve was linear between 5 – 25µg/ml concentration ranges. The standard calibration curve of Atorvastatin was determined in phosphate buffer pH 6.8 by plotting absorbance against concentration at 240 nm, and it follows the Beer’s law. Results for Atorvastatin were tabulated in (Table No.4) Plotted in Fig. No (1) for Atorvastatin the r² and slope in phosphate buffer pH 6.8, 0.999 and 0.014 respectively.
### TABLE 3: STANDARD CALIBRATION CURVE OF ATORAVASTATIN IN PHOSPHATE BUFFER PH 6.8

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Concentration (µg/ml)</th>
<th>Absorbance in phosphate buffer (pH 6.8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>0.181</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>0.298</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>0.445</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>0.645</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>0.752</td>
</tr>
<tr>
<td>6</td>
<td>24</td>
<td>0.925</td>
</tr>
</tbody>
</table>

**Intercept**

**correlation coefficient**

\[ Y = 0.012 \]

\[ r^2 = 0.994 \]

![Standard Calibration Curve of Atoravastatin in Phosphate Buffer pH 6.8](image)

**Figure 1**

Standard Calibration Curve of Atoravastatin in Phosphate Buffer pH 6.8

Evaluation of Buccal Patch:
### TABLE 4: RESULTS OF EVALUATION OF ATORVASTATIN MUCOADHESIVE BUCCAL PATCH

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Patch thickness (mm)</th>
<th>Weight uniformity (gm)</th>
<th>Folding endurance</th>
<th>Moisture content (%)</th>
<th>Surface pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.14±0.016</td>
<td>0.088±0.002</td>
<td>254±2.44</td>
<td>2.69±0.72</td>
<td>6.71±0.024</td>
</tr>
<tr>
<td>F2</td>
<td>0.11±0.016</td>
<td>0.102±0.001</td>
<td>261±0.81</td>
<td>2.54±0.82</td>
<td>6.66±0.024</td>
</tr>
<tr>
<td>F3</td>
<td>0.18±0.012</td>
<td>0.086±0.001</td>
<td>274±2.82</td>
<td>3.87±0.05</td>
<td>6.72±0.032</td>
</tr>
<tr>
<td>F4</td>
<td>0.140±0.020</td>
<td>0.112±0.002</td>
<td>255±3.26</td>
<td>3.80±1.59</td>
<td>6.73±0.016</td>
</tr>
<tr>
<td>F5</td>
<td>0.12±0.012</td>
<td>0.084±0.002</td>
<td>284±2.44</td>
<td>5.43±2.25</td>
<td>6.63±0.033</td>
</tr>
<tr>
<td>F6</td>
<td>0.17±0.016</td>
<td>0.097±0.002</td>
<td>272±1.63</td>
<td>2.42±0.84</td>
<td>6.78±0.024</td>
</tr>
<tr>
<td>F7</td>
<td>0.19±0.016</td>
<td>0.105±0.001</td>
<td>297±1.63</td>
<td>3.79±1.60</td>
<td>6.53±0.028</td>
</tr>
<tr>
<td>F8</td>
<td>0.19±0.017</td>
<td>0.12±0.001</td>
<td>242±1.24</td>
<td>2.65±0.93</td>
<td>6.72±0.021</td>
</tr>
<tr>
<td>F9</td>
<td>0.16±0.016</td>
<td>0.126±0.001</td>
<td>257±2.08</td>
<td>2.69±0.72</td>
<td>6.76±0.020</td>
</tr>
</tbody>
</table>

### TABLE 5: RESULTS OF EVALUATION OF ATORVASTATIN MUCOADHESIVE BUCCAL PATCH

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>% swelling index</th>
<th>Retention time (min)</th>
<th>Drug content (%)</th>
<th>Mucoadhesive strength(gm)</th>
<th>Tensile strength (kg/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>78.2±3.28</td>
<td>60</td>
<td>96.69±0.21</td>
<td>3.8±0.2</td>
<td>64.16±4.54</td>
</tr>
<tr>
<td>F2</td>
<td>75.8±1.07</td>
<td>76</td>
<td>97.47±0.04</td>
<td>8.5±0.1</td>
<td>59.18±3.17</td>
</tr>
<tr>
<td>F3</td>
<td>69.2±3.78</td>
<td>92</td>
<td>98.19±0.07</td>
<td>13.2±0.1</td>
<td>57.35±4.15</td>
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<tr>
<td>F4</td>
<td>77.5±2.49</td>
<td>65</td>
<td>96.83±0.08</td>
<td>5.3±0.2</td>
<td>65.99±2.08</td>
</tr>
<tr>
<td>F5</td>
<td>73.6±1.30</td>
<td>81</td>
<td>95.95±0.02</td>
<td>9.6±0.2</td>
<td>58.92±2.36</td>
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<tr>
<td>F6</td>
<td>68.6±2.96</td>
<td>96</td>
<td>94.81±0.01</td>
<td>15.4±0.2</td>
<td>56.56±2.36</td>
</tr>
<tr>
<td>F7</td>
<td>76.5±3.78</td>
<td>72</td>
<td>97.17±0.08</td>
<td>6.2±0.1</td>
<td>62.06±4.16</td>
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<tr>
<td>F8</td>
<td>71.4±1.45</td>
<td>87</td>
<td>98.31±0.28</td>
<td>11.5±0.1</td>
<td>65.72±2.53</td>
</tr>
<tr>
<td>F9</td>
<td>67.1±2.76</td>
<td>105</td>
<td>96.47±0.01</td>
<td>18.6±0.1</td>
<td>63.89±1.63</td>
</tr>
</tbody>
</table>
In vitro Drug Release: In vitro Drug Release of all formulation was carried out and the results were shown in Table No.6.

**TABLE 6: IN VITRO DRUG RELEASE OF FORMULATION F1 TO F9**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>f1</th>
<th>f2</th>
<th>f3</th>
<th>f4</th>
<th>f5</th>
<th>f6</th>
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**Figure 2**

In vitro Drug Release of formulation f1 to f9 (%Cdr vs Time)
Mathematical-model of Mucoadhesive Buccal patch of Atorvastatin

For mathematical model in vitro drug release of the all formulation was carried out and the results were shown in Table No.7

**TABLE 7: MATHEMATICAL-MODEL OF MUCOADHESIVE BUCCAL PATCH OF ATORVASTATIN**

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**CONCLUSIONS**

It can be concluded that oral Mucoadhesive buccal patch of Atorvastatin, an anti hyperlipidemic agent can be formulated using HPMC E5 as a film forming material, Aspartame as a sweetener and PEG 400 as a plasticizer. Formulation variables like combination of different polymer with HPMC E5, were found to influence thickness, folding endurance, tensile strength, Mucoadhesive strength, and in vitro diffusion of the films. Prepared films were found to be thin and release drug with in 2 hr. from the result of in vitro drug release it was found that the release kinetics follows zero order drug
Therefore, Atorvastatin can be conveniently administered orally in the form of patches with lesser occurrence of its side effects and with improved bioavailability.

ACKNOWLEDGEMENTS

Authors thanks Mepro Pharma Pvt Ltd. Surendranagar Gujarat for providing a gift sample of Atorvastatin. HPMC E5, Carbopol 934, PEG 400, Aspartame, (Purchase from Yarrowchem ltd. Mumbai, India). The authors are thankful to Dr. S. Saisivam Principal, N.R Vekaria college of Pharmacy, Junagadh for his valuable support and providing facilities to carry out this research work and also for their valuable suggestions in carrying out this research work.

REFERENCES


For Correspondence:
Vadher Ravi kumar S
Email: ravi_vadher2007@yahoo.com