Development of Oral Mucoadhesive Tablets of Losartan Potassium using Natural Gum from *Manilkara Zapota* Seeds

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**ABSTRACT**

The present investigation reports the isolation of mucilage from *Manilkara zapota* seeds as per AOAC guideline and evaluating it as mucoadhesive agent. *Manilkara zapota* (Linn.) P. Royen syn. a small tree belonging to family sapotaceae. Physiochemical characteristics of mucilage, such as swelling index, microbial count, viscosity, hydration capacity, flow property, and pH were studied. The mucilage was evaluated for its mucoadhesive properties in compressed tablet, using losartan potassium as model drug. Granules were prepared by wet granulation process using polyvinylpirrolidone as binding agent. Mucilage was used in four different concentrations i.e. 20, 40 and 60 % w/w. The tablet were prepared and evaluated for its physical property. Further in vitro dissolution and swelling index was determined. The property of bioadhesive strength of isolated mucilage was compared with guar gum and HPMC E5LV, which was used as standard mucoadhesive agent concentration. Bioadhesive strength of the tablet was measured on the modified physical balance. Result revealed that mucilage had good micromeritics properties and prepared tablets showed good physical properties, further drug release was retarded as concentration of mucilage was increased. The force of adhesion was obtained 0.2337N, 0.4664N, 0.6210N, 0.8679N and 0.3983N respectively for F1, F2, F3, F4 and F5. Formulations were subjected for study of effect of intensity of agitation at different rpm and electrolyte, formulation showed relative effect on release of drug from formulation. All the formulations were subjected to stability studies for three months all formulation showed stability with respect to release pattern. It is concluded that the seed mucilage of *Manilkara zapota* can be used as a mucoadhesive excipient in oral mucoadhesive drug delivery systems.

**KEYWORDS:** *Manilkara zapota*; Mucoadhesive agent; Effect of Electrolytes and Agitations on dissolution.

**Introduction**

Since the early 1980s, the concept of mucoadhesion has gained considerable interest in pharmaceutical technology (Chickering, 1999). Mucoadhesive substance/polymer are synthetic, semi-synthetic or natural agent which interact with the mucin molecules which form a major part of the mucus layer covering the mucosal epithelial surface and help in releasing the drug in a controlled manner at the site of action. The adhesive firmly sticks to the mucosal surface and prolongs its gastric residential time.

Mucoadhesive drug delivery system utilizes the property of bioadhesion of certain water-soluble polymer which become adhesives on hydration and hence can be used for targeting a drug to a particular region of the body for extended periods of time. Mucoadhesion is provided by the formation of non-covalent bond such as hydrogen bonds and ionic interactions or physical entanglement between the mucus gel layer and polymer (Andreas, 2005).

Natural polysaccharides are extensively used for the development of solid dosage forms. These polymers of monosaccharide's (sugars) are inexpensive and available in a variety of structures with a variety of properties. They are highly stable, safe, non-toxic, hydrophilic and gel forming in nature. Pectin's, chitosan, starch, guar gum, amylase and Karaya gum are a few polysaccharides commonly used in controlled release dosage forms. Non-starch, linear polysaccharides remain intact in the physiological environment of the stomach and the small intestine, but are degraded by the bacterial inhabitants of the human colon which make them potentially useful in targeted delivery systems to the colon (Patel and Patel, 2009).

*Manilkara zapota* (Linn) P. Royen syn. is a large, evergreen, forest tree more than 30 m in height a tree belonging to family from Sapotaceae. The plants were used since Vedic age. However, it was not attempted for physiochemical property, micromeritics characterization and mucoadhesive characterization. Even as some literature is available on the phytochemical study and medicinal properties of all the plants. But information on mucoadhesive study of isolated mucilage from seed is still not reported.
In the present study, we isolated, formulated and evaluated natural excipient for oral mucoadhesive drug delivery system. These studies have promising potential to identify mucoadhesive excipients for the pharmaceutical aspects in the formulation of microsphere and nanoparticles of various drugs in variety of dosage forms.

**Materials and Methods**

**Materials**

*Manilkara zapota* spreng seeds were procured from the forest of Rajigamar, District-Korba, State Chhattisgarh, India. Losartan Potassium was obtained as gift sample from Alembic Pharmaceutical Pvt. Ltd, Baroda. All other ingredients used are of analytical grade and procured from Loba Chemie, Mumbai.

**Methods**

**Plant collection and authentication**

The fruits were collected from the plant and seed was separated from the fruit. The plant material was identified and authenticated from Dr. H. B. Singh, Professor and Head of Raw Herb and Material Dept., NISCAIR, New Delhi, India.

**Isolation of Mucilage**

The seeds were dried and coarsed powder then extracted with water and methanol by heating under reflux. The extracts were concentrated under reduced pressure to a semisolid mass and it was made free from solvent as per AOAC guideline (AOAC,1990).

**Physicochemical properties of dried mucilage**

The physicochemical properties such as appearance, solubility, swelling index, microbial count, melting point, loss on drying, charring, viscosity, hydration capacity, flow property, hausner ratio, bulk density, tapped density, and pH were studied (Martin, 2010).

**Interference studies**

Excipient(s) are believed to be as inert substance but they can have considerable impact on the ultimate pharmacological availability of a drug substance when added to a formulation. The magnitude of this effect depends on the physiochemical characteristics of the drug and on the quantity and properties of the excipients (Kimberley, 2000).

IR spectra of drug, drug and polymers were obtained using Thermo scientific FTIR. Thermal analysis was performed on the mixture of drug and the selected formulation using a Differential scanning calorimeter (DSC) and Differential thermal analysis (DTA).

**Formulation of losartan oral mucoadhesive tablets**

Literature review suggested that studies were conducted on Losartan Potassium as a drug for mucoadhesive delivery system, hence Losartan Potassium was selected as model drug for the formulation and evaluation of oral mucoadhesive delivery system (Marina et al, 2010; Chandrasekara et al, 2011; Jain et al, 2012; Achanta 2012).

Oral mucoadhesive tablets containing Losartan Potassium were prepared by wet granulation techniques using variable concentration of mucilage obtained from seeds of *Manilkara zapota* as test material, Guar Gum and HPMC E5LV were used as standard mucoadhesive agent. In all case, the amount of the active ingredient was kept 50 mg. All the ingredients except Aerosil were blended in blender uniformly. Granulation was done with sufficient binding solution of PVP with isopropyl alcohol. The lubricated granules were compressed into tablet using 6 mm standard punch on rotary (Clit Jemkay) machine and keeping average weight 120 mg. All Losartan Potassium loaded mucoadhesive tablet were stored in airtight container at room temperature for further study. Compositions of various formulations are shown in Table 1.

**TABLE 1**

<table>
<thead>
<tr>
<th>Formulations Code of Losartan Oral Mucoadhesive tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingredient</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>MMZ</td>
</tr>
<tr>
<td>GG</td>
</tr>
<tr>
<td>HPMC E5LV</td>
</tr>
<tr>
<td>PVP</td>
</tr>
<tr>
<td>Lactose</td>
</tr>
<tr>
<td>Aerosil</td>
</tr>
<tr>
<td>Avg. Wt.</td>
</tr>
</tbody>
</table>

**Evaluation of the mucoadhesive tablet**

Mucoadhesive tablets prepared were evaluated for the following official parameters: Hardness, Friability (Banker and Rhodes 2009), Weight variation, Thickness and drug content as per official procedures (USP, 2008).

**In-vitro dissolution study**

The *in vitro* drug release studies of the mucoadhesive tablets were conducted in USP type II dissolution apparatus equilibrated (TDT–08L, USP ETC-11LFC–12 Electro lab) at temperature 37 ± 0.5 °C and 100 rpm speed. The dissolution studies were carried out in triplicate for 8 hours in 900 ml of phosphate buffer 6.8 pH. The dissolution samples were collected at specific interval and replaced with an equal volume of gastric fluid to maintain the volume constant. The sample solution was diluted sufficiently and analyzed at 250 nm as mentioned in IP by a UV spectrophotometer (shimadzu, Kyoto, Japan). The amount of drug present in the sample was calculated with the help of appropriate calibration curves constructed from reference standard of the respective drug.

**Effect of intensity of agitation on *in-vitro* release rate**

The tablets of all batches were studied to observe the effect of agitation on dissolution which was carried out at 50, 100 and 150 rpm.
Effect of electrolytes on in-vitro release rate

The tablets of all batches were studied to observe the effect of electrolyte on in vitro dissolution. Two classes of release modulating agents were incorporated into the dissolution media (phosphate buffer 6.8 pH), these are NaCl and CaCl2 (Ishrat et al., 2005).

Mass degree of swelling

The method reported by Atul et al., (2006) and Owen et al., (2004) was followed to measure the mass degree of swelling. Six tablets from each formulation batch were weighed and placed in petri dish containing the standard set of condition as specified for dissolution. The tablets were removed and change in weight of each tablet was determined after 5 h using following formula.

\[
\text{Swelling index (S.I)} = \frac{W_t - W_o}{W_o} \times 100
\]

Whereas, SI is swelling index, \( W_t \) is Weight of tablet at time t; \( W_o \) is Weight of tablet before placing in beaker.

Radial and axial swelling of the tablet

The initial diameter and height of the tablet were measured, and the tablet was stored in distilled water. The increase in diameter and height were measured at selected time interval up to 5 h by digital vernier caliper (HI-Mezar). The equilibrium degree of swelling (Q) was calculated from the radial and axial swelling ratio using the following equation (Owen et al., 2004).

\[
Q = \frac{V_t}{V_o} = \left( \frac{R_t}{R_o} \right)^2 = \left( \frac{t}{I_o} \right)
\]

Were \( V_t \) and \( V_o \) are the tablet volume, \( R_t \) and \( R_o \) is the radius and \( I_t \) and \( I_o \) are the height at the time zero, respectively.

In vitro mucoadhesive strength

Mucoadhesive strength of the tablet was measured on the modified physical balance (Figure 1). The apparatus consist of a modified double beam physical balance in which the right and left pan has been replaced by lighter pans. The left side of the balance was made 5 g heavier than the right side by placing a 5 g weight on left side pan. Another Teflon block of 3.8 cm diameter and 2 cm height was fabricated with an upward portion of 2 cm height and 1.5 cm diameter on one side. This was kept in beaker, which was then placed below the left hand set of the balance.

The goat intestine mucosa was used as the model membrane and pH 6.8 was used as the moistening fluid. The goat intestine was kept in Tyrode solution at 37 °C for 2 h. The underlying mucus membrane was separated and washed thoroughly with a pH 6.8 solution. It was then tied to Teflon-coated glass slide and this slide was fixed over the protrusion in Teflon block using a thread. The block was then kept in beaker containing pH 6.8 buffer solution at the level that just touches the membrane. By keeping a 5 g weight on the right pan, the two sides of the balance were made equal. The beaker with the Teflon block was kept below the left hand set up of the balances. The tablets of each batch were struck on to the lower side of the left hand side pan. The 5 g weight from the right pan was then removed. This lowered the left pan along with the tablet over the membrane with a weight of 5 g. This was kept undisturbed for 3 minute. Then, the weight on the right hand side was slowly added in an increment of 0.5 g till the tablet just separated from the membrane surface. The excess weight on right pan i.e., total weight minus 5 g was taken as a measure of the mucoadhesive strength (Ranga and Buri, 1989; Achar and Pepass, 1994). From the mucoadhesive strength, the force of adhesion was calculated using the following formula:

\[
\text{Force of adhesion (N)} = \frac{\text{Bioadhesive strength} \times 9.81}{1000}
\]

\[
\text{Bon strength (N/m)} = \frac{\text{Force of adhesion (N)}}{\text{Surface area of tablet (m²)}}
\]

Surface area of tablet = 2 \( \pi r (r + t) \); Where \( r \) is the radius of the tablet and \( t \) is the thickness of the tablet.

Data analysis

To study the mechanism of drug release from the matrix tablets, the in vitro drug release data were fitted to various kinetic models like zero-order, First order, Higuchi, Peppas, Hixsoncrowell, and Webull equation and coefficient of correlation (r) values were calculated for linear curves by regression analysis of the above plot. These models used to explain drug release mechanism due to swelling (upon hydration) along with gradual erosion of the matrix (Paulo and Jose, 2001).

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile. Losartan Potassium mucoadhesive tablets were placed on plastic tubes containing desiccant and stored at conditions, such as at room temperature, oven temperature (40 ± 2 °C and 75 ± 5 %) for a period of 3 month for stability studies. The tablets were evaluated for Physical properties and in vitro drug release after 1, 2 and 3 months (Amin and Kohli 2003; Kulkarni et al, 2004; ICH, 2005).
Results

Mucoadhesive drug delivery of Losartan Potassium was formulated, using mucilage obtained from seeds of *Manilkara zapota* (Linn.) P. Royen syn. Losartan Potassium mucoadhesive tablets were prepared by wet granulation techniques.

The mucilage was isolated from the seeds of *Manilkara zapota* (Linn.) P. Royen syn. (MMZ) following AOAC guide line which yield 6.2 % w/w.

Physicochemical properties of dried mucilage

The result of physicochemical evaluation of isolated mucilage is shown in Table 2. The appearance of mucilage was reddish in color. The isolated natural mucilages from all seed were soluble only in warm water. The swelling index study showed that mucilage swells well in distilled water than in acid or alkaline media. The water absorption (swelling index) capacity of the polymers was inversely related to the pH of the medium. The viscosity studies of 1% w/v solution for isolated mucilage (MMZ) showed decrease in viscosity with increase of temperature. The microbial count in MMZ was found 64 CFU/g. The result of microbial property obtained was within official limits [Less than 100 colony-forming units (CFU/g)] as per the prescribe range by British Pharmacopeia, 1993. The pH was found to be neutral. Melting point was obtained as 138.5 °C. Charring was obtained as 159.2 °C which indicated the mucilage is thermally stable. The true density was obtained as 1.2 g/mL. The result of bulk and tapped density indicated that mucilage is porous in nature. The micromeritics study showed that the flow property was good for MMZ as per standard flow range (Subramanyam, 2008).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MMZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Brown</td>
</tr>
<tr>
<td>Solubility</td>
<td>Water</td>
</tr>
<tr>
<td>Swelling index (after 3 h)</td>
<td></td>
</tr>
<tr>
<td>At, Distilled water</td>
<td>67.20</td>
</tr>
<tr>
<td>pH-1.2</td>
<td>52.07</td>
</tr>
<tr>
<td>pH-7.4</td>
<td>64.97</td>
</tr>
<tr>
<td>Viscosity (1% w/v) (cP)</td>
<td></td>
</tr>
<tr>
<td>At, 37 °C</td>
<td>234.6</td>
</tr>
<tr>
<td>45 °C</td>
<td>91.17</td>
</tr>
<tr>
<td>60 °C</td>
<td>1.660</td>
</tr>
<tr>
<td>Microbial count(CFU/g)</td>
<td>Bacteria: -ve</td>
</tr>
<tr>
<td></td>
<td>Fungi: -ve</td>
</tr>
<tr>
<td>pH</td>
<td>6.8</td>
</tr>
<tr>
<td>Melting Point (°C)</td>
<td>138.5</td>
</tr>
<tr>
<td>Charring (°C)</td>
<td>159.2</td>
</tr>
<tr>
<td>Loss on drying (%)</td>
<td>2.88</td>
</tr>
<tr>
<td>True density (g/mL)</td>
<td>1.212</td>
</tr>
<tr>
<td>Bulk density (g/mL)</td>
<td>0.85</td>
</tr>
<tr>
<td>Tapped density (g/mL)</td>
<td>0.95</td>
</tr>
<tr>
<td>Hausner’s Ratio</td>
<td>1.123</td>
</tr>
<tr>
<td>Compressibility index</td>
<td>11.11</td>
</tr>
<tr>
<td>Angle of Repose</td>
<td>36.79</td>
</tr>
</tbody>
</table>

Interference studies

The FTIR spectral analysis showed that there was no appearance or disappearance of any characteristic peaks of pure drug Losartan Potassium in the optimized formulation of drug and polymer (Figure 2 and 3), which confirms the absence of chemical interaction between drug and polymers. Further, it was also confirmed by DSC and DTA analysis (Figure 4, 5 and 6).
Fig. 3. FTIR Spectra of physical mixture of losartan potassium and MMZ.

Fig. 4. DSC spectra of losartan potassium.

Fig. 5. DSC spectra of physical mixture of losartan potassium and MMZ.
TABLE 3
Micromeritics Characterization of Granules Ready for Compression

<table>
<thead>
<tr>
<th>Material</th>
<th>Angle of repose</th>
<th>Bulk density (gm/mL)</th>
<th>Tapped density (gm/mL)</th>
<th>Compressibility Index</th>
<th>Hausner ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losartan</td>
<td>29°.24 ± 0.601</td>
<td>0.485 ± 0.057</td>
<td>0.555 ± 0.010</td>
<td>44.70 ± 0.019</td>
<td>1.19 ± 0.024</td>
</tr>
<tr>
<td>F1</td>
<td>27°.41 ± 0.331</td>
<td>0.499 ± 0.018</td>
<td>0.564 ± 0.016</td>
<td>11.52 ± 0.024</td>
<td>1.13 ± 0.022</td>
</tr>
<tr>
<td>F2</td>
<td>28°.29 ± 0.326</td>
<td>0.523 ± 0.021</td>
<td>0.602 ± 0.017</td>
<td>13.12 ± 0.021</td>
<td>1.15 ± 0.017</td>
</tr>
<tr>
<td>F3</td>
<td>27°.17 ± 0.235</td>
<td>0.493 ± 0.004</td>
<td>0.552 ± 0.028</td>
<td>10.68 ± 0.019</td>
<td>1.11 ± 0.039</td>
</tr>
<tr>
<td>F4</td>
<td>26°.26 ± 0.331</td>
<td>0.557 ± 0.051</td>
<td>0.616 ± 0.015</td>
<td>09.50 ± 0.021</td>
<td>1.10 ± 0.021</td>
</tr>
<tr>
<td>F5</td>
<td>28°.33 ± 0.226</td>
<td>0.498 ± 0.042</td>
<td>0.597 ± 0.039</td>
<td>16.58 ± 0.021</td>
<td>1.19 ± 0.014</td>
</tr>
</tbody>
</table>

Note: values are mean of 6 observation (N=6) and values in parenthesis are standard deviation (± SD)

TABLE 4
Physical Evaluation of Uncoated Mucoadhesive Tablets after Compression

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Weight variation in mg</th>
<th>Thickness in mm</th>
<th>Diameter in mm</th>
<th>Hardness in Kg/cm²</th>
<th>Friability (%)</th>
<th>Drug content</th>
<th>Force of adhesion (N)</th>
<th>Bond Strength (N/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>121.1 ± 0.22</td>
<td>2.41 ± 0.029</td>
<td>6.70 ± 0.019</td>
<td>4.68 ± 0.19</td>
<td>0.17 ± 0.030</td>
<td>101.01</td>
<td>0.2337 ± 0.003</td>
<td>0.0017 ± 0.0021</td>
</tr>
<tr>
<td>F2</td>
<td>123.4 ± 0.31</td>
<td>2.81 ± 0.014</td>
<td>6.74 ± 0.026</td>
<td>4.21 ± 0.20</td>
<td>0.20 ± 0.019</td>
<td>101.38</td>
<td>0.4664 ± 0.001</td>
<td>0.0035 ± 0.0003</td>
</tr>
<tr>
<td>F3</td>
<td>124.1 ± 0.29</td>
<td>3.05 ± 0.026</td>
<td>6.63 ± 0.015</td>
<td>4.59 ± 0.11</td>
<td>0.17 ± 0.011</td>
<td>100.21</td>
<td>0.6210 ± 0.002</td>
<td>0.0047 ± 0.0036</td>
</tr>
<tr>
<td>F4</td>
<td>120.6 ± 0.16</td>
<td>3.09 ± 0.034</td>
<td>6.61 ± 0.038</td>
<td>4.42 ± 0.19</td>
<td>0.15 ± 0.022</td>
<td>101.29</td>
<td>0.8679 ± 0.003</td>
<td>0.0066 ± 0.0012</td>
</tr>
<tr>
<td>F5</td>
<td>118.9 ± 0.11</td>
<td>2.60 ± 0.029</td>
<td>6.56 ± 0.021</td>
<td>4.63 ± 0.22</td>
<td>0.24 ± 0.009</td>
<td>101.18</td>
<td>0.3983 ± 0.002</td>
<td>0.0030 ± 0.0039</td>
</tr>
</tbody>
</table>

Note: values are mean of 6 observation (N=6) and values in parenthesis are standard deviation (± SD)

**Micromeritics and post compressional evaluation**

The result of micromeritics study for granules ready for compression is tabulated in Table 3. Result indicated that granules possess good flow property as compare to mucilage. All the formulated batches were evaluated for the physical properties such as hardness which was obtained in the range of 4.5 to 4.6 (kg/cm²). Percentage weight loss in the friability test was less than 1% in all batches and all the batches contained Losartan Potassium within 100 ± 5 % of labeled content. Overall, the prepared tablet batches were of good quality with regards to hardness, friability and drug content. The result of physical evaluation of all the tablets is tabulated in Table 4.

**In vitro mucoadhesive strength**

The in vitro mucoadhesive strength study was performed on the modified physical balance to measure the force (N) required for detaching the tablet. The result of in vitro mucoadhesive strength analysis is tabulated in...
Table 4. The bioadhesive characteristics were affected by the concentration of the mucoadhesive polymer. Viscosity of the polymer also affects the mucoadhesive strength of the tablet.

**Mass degree of swelling and radial & axial swelling**

The result of mass degree of swelling and radial swelling for formulations F1 to F5 is tabulated in Table 5. The result suggested that on increasing or decreasing the concentration of natural polymer increases both the phenomena i.e. radial and axial swelling of tablet.

**In vitro dissolution study**

The result of in vitro dissolution study is tabulated in Table 6. From the overall dissolution profile, it was concluded that the drug release rate decreased as the polymer increased, which was also attributed to different diffusion and swelling behavior of the polymer.

**Effect of intensity of agitation and electrolytes on in-vitro release rate**

The result of intensity of agitation and electrolytes on in-vitro release rate is tabulated in Table 7. The result suggested that on increasing the concentration of natural polymer increases both the phenomena i.e. radial and axial swelling of tablet.

**Data analysis**

The result of data analysis is tabulated in Table 11. From the result of the dissolution data, the Korsmeyer and Peppas model found to be best fitted in all dissolution profile having a higher correlation coefficient. Thus, it was concluded that the drug release occurred via a diffusion mechanism and due to affinity of hydrophilic polymers towards water.

**Stability studies**

The stability study showed that there was no change in the appearance and on drug release pattern of the tablet.
Discussion

Physicochemical properties of dried mucilage

The physicochemical evaluation was performed for to get primary idea on physical property of mucilage. The pH of MMZ was neutral indicating that mucilage may not irritate the mucus mucosal drug delivery systems. The swelling index showed that mucilage swollen slowly in water at neutral pH which can be considered highly beneficial as similar study on Guar gum showed premature swelling cause obstruction of, or damage to, the esophagus and due to such reason appetite suppressants containing guar gum in tablet form have been banned in the UK (Uusitupa, 1990).

Melting point is also one of the physical constant for given material and is depending on structure/physiochemical properties. The weight loss on drying indicates the fine amount of moisture present available in the material. In one of the study mucilage from Anogeissus latifolia exhibited good physical properties like swelling index and compressibility which led for better acceptability as an excipient (Jani et al., 2007).

Interferences study

Compatibility study between drug and polymer was performed in order to check whether there is any interaction available between isolated mucilage and drug. The result of interference study showed that there is no change in FTIR spectrum peak, endotherm peaks of DSC and DTA. The present study indicated similar result of interference study by Zaki et al., (2009) for Bora rice starch from Assam as pharmaceutical excipient.

Micromeritics and post compressional evaluation

The mucoadhesive tablets of Losartan Potassium were prepared by wet granulation using mucilage (MMZ), Guar gum and HPMC E5LV as mucoadhesive agent. The granules for mucoadhesive tablet were prepared according to the formula given in related table and characterized with respect to pre-compressional evaluation such as angle of reposes, bulk density, compressibility index, Hausner ratio and drug content. Micromeritics study was performed to check the suitability of compressional method as well correlation between polymers. The angle of reposes was less than 29° for all batches of granules indicating satisfactory flow behavior. Other parameters for granules were also found in acceptable range. The result of micromeritics study showed that some physical modification can improve more efficacies in the property of excipient. Dhiren and Jani (2009) reported similar studies indicating only physical modification was carried out on Gellan gum by microwave oven showed excellent micromeritics property.

Little significant difference was observed in the weight of individual tablets form the average weight. Tablet weights of all batches were found with in recommended USP limits. The data of uniformity of content which was performed using UV spectrophotometer indicated that tablets of all batches had drug content within USP limits. The hardness of tablets of all batch are in range of 4-5 Kg/cm² which is acceptable for mucoadhesive tablets. Formulation (F1-F5) showed percentage friability less than 1 % that indicates ability of tablets to withstand shocks even in transportation. Little significant difference was observed in the thickness of individual tablet from the average value.

In vitro mucoadhesive strength

The in vitro mucoadhesive strength study showed that the bioadhesion characteristics of test and standard mucoadhesive polymer were affected by type and concentration of polymer. Viscosity of polymer also affects the bioadhesive strength of tablet as reported earlier by Deshmukh and colleagues (Deshmukh et al., 2009).

Mass degree of swelling and radial and axial swelling

The Important physical properties of mucilage depend on the precise structure of the polymer network. Of key importance is mass degree swelling capacity (Hussein et al., 1994). Mass degree of swelling and equilibrium degree of swelling of all the formulation batches showed that the batch which contain hydrophilic polymer Guar gum and MMZ have higher degree of both and remaining other mucilage are having relatively less degree of swelling similar manner. During mucoadhesive formulation development, tablet hydration capacity (swelling) is very important to be considered because the water penetration is responsible for drug release. However, since swelling and gel formation can make tablets erodible, it is very important to know if and when the formulation loses its integrity (Perioli et al., 2004). For this reason formulations were investigated by comparing the initial and final tablet weight after immersion in water.

In-vitro dissolution study

Addition of either water-soluble or insoluble diluents in large quantities can markedly increase or decrease the
release of active principles (Vazquaz et al., 1992). The in vitro release of Losartan Potassium from mucoadhesive tablet of formulation (F1-F5) varied according to the amount and grade of mucoadhesive polymer used. The tablets contain Guar gum as mucoadhesive agent controls the release of medicament up to 8 h and had initial high burst of 33.17% in 1 h. The total amount was released in 7 h in the same manner which had used HPMC E5LV and MMZ as a polymer.

**Effect of intensity of agitation and electrolytes on in-vitro release rate**

The effect of agitation on dissolution showed proportional changes in release profile. The effect of salts on in vitro dissolution study of formulation showed variation in release profile which was obtained may be due to common ion effect. Ishrat et al., (2005) reported earlier that the incorporation of mono and divalent metal salt increased the release rate of drug.

**Data analysis**

The drug release data were explored for the type of release mechanism followed. The in vitro release profile data of Losartan Potassium mucoadhesive tablet were fitted to various kinetic model such as Zero order, First order, Higuchi, Korsmeyer-peppa’s, Hixoncrowell and Weibull. The interpretation of release exponent values (n) indicated the all the formulation follows zero order of release pattern with anomalous drug transport.

**Stability studies**

The short term stability studies (as per ICH guide line) show the formulation are stable and confirm the suitability of mucilage as mucoadhesive agent. The similar result of stability studies was reported by Shah et al., (2009) for seed mucilage of *Blepharis edulis* as disintigrant in tablet which indicated that isolated mucilage from seed is stable with different solid dosage form.

**Conclusions**

We successfully formulated and evaluated effect of mucilage isolated from the seed of *Manilkara zapota* (Linn.) P. Royen syn on release rate of mucoadhesive tablet. Mucoadhesive tablet were formulated using standard polymers in varying concentrations. Tablets were subjected to various evaluation parameters such as hardness, friability, drug content, mucoadhesive strength study and in vitro drug release study. It was revealed that all batches had acceptable physical parameters. Formulation (F3) has good mucoadhesion along with in vitro drug release in compression of standard HPMC E5LV but lower than the tablet which was prepared using guar gum. It was observed that all batches followed the equation of zero order drug release profiles. The release exponent value indicated that drug is releasing from the dosage form following diffusion mechanism. Stability studies revealed that there was no significant change in the hardness, friability, drug content and in vitro dissolution profile of all formulation.

Thus all formulations were stable at different condition of temperature. It is concluded that there is sufficient mucoadhesive strength for isolated mucilage from the seeds of *Manilkara zapota* (Linn.) P. Royen syn.

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