FORMULATION AND EVALUATION OF CHLORPHENERAMINE MALEATE
BILAYERED BUCCAL TABLETS

Ravali Vainala* & K. Rajitha

1 Department of pharmaceutics, St.Peter’s College of pharmacy, Hyderabad road,
Madikonda, Andhra Pradesh, India, 506142
*Corresponding Author Email: vainalaravali@gmail.com

ABSTRACT
The aim of the study was to prepare bilayered buccal tablets of Chlorpheneramine maleate using Carbopol 934 as primary polymer with secondary polymers like HPMC K4M and HPMC K15M by direct compression technology. The Preformulation study using FTIR and DSC spectroscopy revealed that there was no drug-polymer and polymer-polymer interaction. The tablets were evaluated for weight variation, thickness, hardness, friability, uniformity of drug content and surface pH concluded that all these parameters were in acceptable range of pharmacopoeial specification. The tablets were studied for swelling index, in vitro drug release and also the effect of Carbopol concentration on these parameters was studied. The buccal tablet showed good swelling of >80% up to 6 hrs maintaining the integrity of polymers. As the concentration of Carbopol 934 increased there was significantly increase in viscosity and swelling index. The optimized formulations F4 and F8 showed 88.7% and 91.2% release in 6 hr in vitro dissolution studies. The in vitro release obeyed First order kinetic with mechanism of release was erosion followed by non fickian diffusion. Hence Carbopol 934 and other polymers can be used to prepare bilayered buccal tablets of Chlorpheneramine maleate having prolonged therapeutic effect with enhanced bioavailability.

KEY WORDS
CPM, Carbopol, swelling index, in vitro drug release, Bilayered buccal tablets.

INTRODUCTION
For many decades, treatment of an acute disease or a chronic illness has been mostly accomplished by delivering drugs using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, creams, ointments, liquids, aerosols and injectables as carriers. Amongst various routes of drug delivery oral route is perhaps the most preferred to the patient and the clinician alike. However this route presents some problems for a few drugs. The enzymes in the GI fluids, GIT-pH conditions and the enzymes bound to GIT membranes are a few factors responsible for the bioavailability problems. The blood that drains the GIT carries the drug directly to the liver leading to first-pass metabolism resulting in poor bioavailability.

The inherent problems associated with the drug in some cases can be solved by modifying the formulation or by changing the routes of administration. Parenteral, mucosal and transdermal routes circumvent hepatic first-pass metabolism and offer alternative routes for the systemic delivery of drugs.

In recent years, the interest in novel routes of drug administration occurs from their ability to enhance the bioavailability of drugs. Drug delivery via the buccal route using bioadhesive dosage forms offers such a novel route of drug administration. Extensive first-pass metabolism and drug degradation in the harsh gastrointestinal environment can be circumvented by administering the drug via buccal
route. Buccal delivery involves administration of desired drug through the buccal mucosal membrane lining of oral cavity. The mucosal lining of oral cavity offers some distinct advantages. It is richly vascularized and more accessible for the administration and removal of a dosage form. Additionally, buccal drug delivery has high patient acceptability compared to other non-oral routes of drug administration. Drug absorption through buccal mucosa is mainly by passive diffusion into the lipoidal membrane. After absorption the drug is transported through facial vein which then drains into the general circulation via jugular vein bypassing the liver and thereby sparing the drug from first pass metabolism.

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. The oral cavity can be used for local and systemic therapy. Examples of local therapy would be the treatment of oral infections, dental caries, mouth ulcers and stomatitis. The buccal route is of particular interest with regard to the systemic delivery of small molecules that are subjected to first pass metabolism or for the administration of proteins and peptides.

From the technological point of view, an ideal buccal dosage form must have three properties; It must maintain its position in mouth for few hours, releasing the drug in controlled manner and provide drug release in a unidirectional way towards mucosa. Chlorpheniramine maleate (CPM) is a first generation alkyl amine anti histamine used in the prevention of the symptoms of allergic conditions such as asthma, hay fever, rhinitis and urticarial. The drug is well absorbed from gastrointestinal tract but its bioavailability is low due to extensive first pass metabolism. The physicochemical properties of CPM, its suitable half-life 21-27 hours and low molecular weight makes it suitable candidate for administration by buccal route. In present study, an attempt was made to design efficacious and prolonged release bilayered tablets of CPM by using various polymers to avoid first pass metabolism and to improve patient compliance with improved bioavailability.

MATERIALS AND METHODS

CPM was gifted by Elite Pharma Pvt. Limited Ahmadabad. Ethyl cellulose was gifted by (S.D Fine Chemicals Pvt Limited.) and Carbopol 934p were gifted by (S.D Fine Chemicals Pvt Limited.). All other materials were of analytical or pharmacopoeial grade and used as received.

Preparation of Buccal tablets:

Preparation:

Direct compression method has been employed to prepare buccal tablets of CPM using Carbopol 934 as primary polymer along with HPMCK4M and HPMCK15M as secondary polymers.

Procedure:

Direct compression method was employed to prepare buccal tablets of CPM using Carbopol934 as primary polymer and HPMC K4M & HPMC K15M as secondary polymers. All the ingredients including drug, polymer and excipients were weighed accurately according to the batch formula (Table 1). The drug and all the ingredients except lubricants were taken on a butter paper with the help of a stainless steel spatula and the ingredients were mixed in the order of ascending weights and blended for 10 min in an inflated polyethylene pouch. After uniform mixing of ingredients, lubricant was added and again mixed for 2 min. The prepared blend of each formulation was pre-compressed by using different punches (6mm) according to their weights on a single stroke tablet punching machine (Rimek Press Minipress II MT, Ahmadabad) to form a tablet. Then 50 mg of ethyl cellulose powder was added and final compression was done to get bilayered buccal tablet.

Evaluation of Bilayered buccal tablets of CPM:

1) Uniformity of weight:

The weight variation test was performed as per procedure of IP. The weight (mg) of each of 20 individual tablets, selected randomly from each formulation was determined by dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation.
2) Thickness:
The thickness of three randomly selected tablets from each formulation was determined in mm using vernier calipers.

3) Hardness test:
Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm². Tablets were randomly picked from each formulation and the mean and standard deviation values were calculated.

4) Friability test:
It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablet was determined by using Roche Friabilator as per IP procedure of friability. It is expressed in percentage (%). Twenty tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again ($W_{final}$). The percentage friability was then calculated by,

$$F = \frac{(W_{initial} - W_{final})}{W_{initial}} \times 100$$

% Friability of tablets less than 1% is considered acceptable.

5) Swelling Index:
The swelling index of the buccal tablet was evaluated in phosphate buffer pH 6.8. The initial weight of the tablet was determined and then tablet was placed in 6 ml phosphate buffer pH 6.8 in a Petri dish and then was incubated at 37 ± 1°C. The tablet was removed at different time intervals (1.0, 2.0, 3.0, 4.0, 5.0, and 6.0 h) blotted with filter paper and reweighed ($W_2$). The swelling index is calculated by the formula:

Swelling index = 100 ($W_2 - W_1$) / $W_1$.

Where, $W_1$ = Initial weight of the tablet.
$W_2$ = Final weight of tablet.

6) Uniformity of drug content:
Five tablets were powdered in a glass mortar and the powder equivalent to 14 mg of drug was placed in a stoppered 100 ml conical flask. The drug was extracted with 40 ml of distilled water with vigorous shaking on a mechanical shaker (100 rpm) for 1 hour. Then heated on water bath with occasional shaking for 30 minutes and filtered into 50 ml volumetric flask through cotton wool and filtrate was made up to the mark by passing more distilled water through filter, further appropriate dilution were made and absorbance was measured at 265 nm against blank (distilled water).

7) Surface pH study:
The surface pH of the buccal tablets is determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may irritate the buccal mucosa, we sought to keep the surface pH as close to neutral as possible. A combined glass electrode is used for this purpose. The tablet is allowed to swell by keeping it in contact with 1 ml of phosphate buffer pH 6.8 for 2 h at room temperature. The pH is identified by bringing the electrode into contact with the tablet surface and allowing equilibrating for 1 min.

8) In vitro drug release study:
The study was carried out in USP type-II tablet dissolution test apparatus (Electrolab TDT-06), employing paddle stirrer at 50 rpm and 250 ml of phosphate buffer pH 6.8 as dissolution medium maintained at 37± 0.5°C. The tablet was supposed to release drug from one side only hence a one side of tablet was fixed to glass disk with cyano acrylate adhesive. The disk was placed at the bottom of the dissolution vessel. At different time interval 5 ml of sample was withdrawn and replaced with fresh medium. The samples were filtered through 0.25 µm membrane filter paper and analyzed for CPM after appropriate dilution at 265 nm using Elico-150 UV-Visible spectrophotometer.

9) Short Term Stability studies:
Short-term stability study was performed at a temperature of 40 ±2°C over a period of three months (90 days) on the promising buccal tablets of
CPM. Sufficient numbers of tablets (10) were individually wrapped using aluminium foil and packed in amber colour screw cap bottle and kept in stability chamber for 3 months. Samples were taken at each month interval for evaluation of drug content, surface pH and in vitro drug release study.

RESULTS AND DISCUSSION
Buccal drug delivery system is a promising tool for the drugs with low oral bioavailability due to extensive first pass effect and also this route provides an easy termination of drug effect. Chlorpheniramine maleate is a first generation alkyl amine anti histamine used in the prevention of the symptoms of allergic conditions such as asthma, hay fever, rhinitis and urticarial.

In the present work, bilayered buccal tablets of CPM were prepared using Carbopol-934 along with sodium alginate, Guar gum, HPMC K4M and HPMC K15M and as polymers by direct compression method. All other polymers and chemicals obtained were used as supplied by the standard manufacturers.

Pre compressional parameters:
The granulation characteristics are the most important interest to formulation scientist and therefore most universally measured. These basic measurements of the granulation have been used to develop and monitor the manufacture of many successful pharmaceutical dosage forms. Table 2 depicts the Pre compressional parameters CPM buccal tablets.

Bulk density may influence compressibility, tablet porosity, dissolution and other properties and depends on the particle size, shape and tendency of particles to adhere together. The bulk density and tapped density of powder blend of CPM with Carbopol 934, HPMC K4M and HPMC K15M was found to be between 0.39 ± 0.09 to 0.47 ± 1.52 g/cm³ and 0.48 ± 1.22 to 0.56 ± 1.34 g/cm³. This indicates good packing capacity of powder blend. Carr’s index evaluated interparticulate cohesive properties with angle of repose measurements and studied the effects of packing geometry of solids with bulk and tapped density. Carr’s index was found to be between 13.46 to 22. Hausner’s ratio is simple method to evaluate stability of powder column and to estimate flow properties. Hausner’s ratio was found 1.15 to 1.30. Low range was observed of Hausner’s ratio that indicates good flow ability. The angle of repose of all the formulations were observed within the range of 30.44 ± 0.35 to 32.49 ± 0.31 i.e. powders were of good flow properties.

Post compressional parameters:
All the prepared bilayered buccal tablets of CPM were evaluated for thickness, hardness, friability, weight variation, swelling index, drug content, surface pH and are represented in Table 3. The hardness of prepared mucoadhesive buccal tablets were from 4.13 ± 0.41 kg/cm² to 5.47 ± 0.26 kg/cm² and increased due to increasing weight of the tablet for each category of secondary polymer used. As the concentration of Carbopol was decreased, the hardness of the tablet was increased. The thickness of the tablets was from 2.56 ± 0.13 to 3.27 ± 0.75 mm. All the prepared tablets complies the Indian Pharmacopoeia standard for weight variation and friability.

The swelling studies of prepared buccal tablets were performed in phosphate buffer at the pH of 6.8 and the results are presented as percentage weight change with respect to time in hrs. The swelling behaviour of a buccal tablet is an important property for uniform and prolonged release of drug. The swelling behaviour depends upon nature of polymer, concentration of polymer and pH of the medium. The swelling of all the tablets were increased as the time proceeds because the polymer gradually absorbs water due to hydrophilicity of the polymer. The outermost hydrophilic polymer layer hydrates/swells first and as the hydrated layer progressively dissolves or disperse, the hydration swelling process will continuous towards new expose surfaces thus maintaining the integrity of dosage form. The swelling index of tablets was 30.15% ± 0.46 to 82.71% ± 0.85. The Carbopolar934 is insoluble in aqueous media of pH 6.8 but absorbs large quantity of water and hence gets swelled. The swelling index was affected by the concentration of Carbopol, as the concentration of the Carbopol increases the viscosity and swelling index of tablets increases.
Drug content was in the range of 97.95% ± 0.38 to 101.36% ± 0.83 indicating good content uniformity in the all formulations. The reading complies as per IP that indicates drug was uniformly distributed throughout the tablet. The surface pH was in the range of 6.89 ± 0.17 to 7.04 ± 0.06 which was nearer to salivary pH (6.5-7.5) suggesting that the prepared buccal tablets can be used without the risk of mucosal irritation and discomfort.

**In vitro release study data:**
The in vitro release of CPM was performed in phosphate buffer at the pH of 6.8 and the data was represented in Table 4 and illustrated in fig.1-2. The in vitro release of CPM was mainly affected by drug polymer ratio, nature and amount of polymer and the dissolution medium. The addition of secondary polymers like HPMC K4M and HPMC K15M along with Carbopol as primary polymers in formulations prolonged the release of CPM up to 6hrs. The buccal tablets containing HPMC K4M (F1-F5) and HPMC K15M (F6-F10) showed a maximum release of 88.76% and 91.27% respectively because HPMC with a grade of K4M and K15M has a hydrophilic gel forming matrix which was used as a release retardant.

**Drug release kinetics:**
Finally the in vitro study was subjected to Zero order, first order, Higuchi, Korsmeyer Peppas and Hixson Crowell. Release kinetics of CPM for all the formulations seems to follow First order and from Korsmeyer-Peppas equation the n-values were found to be 0.5 < n < 1 for all the buccal tablet formulations. Therefore it shows that the release mechanism was Non-Fickian diffusion.

**CONCLUSION**
The Formulation and evaluation of bilayered buccal tablets of CPM reveals following. The bilayered buccal tablets of CPM could be successfully prepared by using Carbopol-934 as primary polymer and in combination of secondary polymers like HPMC K4M and HPMC K15M by direct compression method. The buccal tablets showed good swelling up to 6 hrs in phosphate buffer at the pH of 6.8 maintaining the integrity of formulation which is required for uniform and prolonged release of drug. As the concentration of Carbopol increases, the swelling index of tablets increased. The in vitro release of CPM with Carbopol 934 and HPMC K15M in the ratio of (10:40) (F9) shows better drug release (78.85%) within 6 hrs and it is considered as optimized.
Figure 2: FTIR spectra of CPM with HPMC K4M.

Figure 3: FTIR spectra of CPM with HPMC K15M.
Figure 4: DSC Spectra of CPM with HPMC K4M and HPMC K15M:

![DSC Spectra](image)

Figure 5: *In vitro* release data of CPM from bilayered buccal tablets containing Carbopol-934 and HPMC K4M (F1-F5):

![Cumulative Drug Release](image)
Figure 6: *In vitro* release data of CPM from bilayered buccal tablets containing Carbopol-934 and HPMC K15M (F6-F10):

![Graph showing cumulative drug release over time for different formulations.]

Table 1: Composition of bilayered buccal tablets of CPM

<table>
<thead>
<tr>
<th>Ingredients (mg)</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>
</tr>
</thead>
<tbody>
<tr>
<td>CPM</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Carbopol 934</td>
<td>40</td>
<td>30</td>
<td>20</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>40</td>
<td>30</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>HPMC K4M</td>
<td>10</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HPMC K15M</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td>PVP-k-30</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Sodium saccharine</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>PEG-6000</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Talc</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Ethyl cellulose</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>
Table 2: Pre compression parameters of Formulations:

<table>
<thead>
<tr>
<th>Sl.No</th>
<th>Parameters</th>
<th>Formulation code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>1.</td>
<td>Bulk density (g/cm³)</td>
<td>0.42</td>
</tr>
<tr>
<td>2.</td>
<td>Tapped Density (g/cm³)</td>
<td>0.51</td>
</tr>
<tr>
<td>3.</td>
<td>Carr's Index</td>
<td>17.64</td>
</tr>
<tr>
<td>4.</td>
<td>Hausner's Ratio</td>
<td>1.30</td>
</tr>
<tr>
<td>5.</td>
<td>Angle of Repose (θ)</td>
<td>32.41</td>
</tr>
</tbody>
</table>

Table 3: Post compression parameters of Formulations:

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Weight variation (mg)±SD</th>
<th>Mean Thickness (mm)±SD</th>
<th>Mean Hardness (kg/cm²)±SD</th>
<th>Friability (%)±SD</th>
<th>Mean Swelling index±SD</th>
<th>Mean Drug content (%)±SD</th>
<th>Drug Surface pH±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>149.6±0.99</td>
<td>2.80±0.00</td>
<td>4.82±0.02</td>
<td>0.79±0.01</td>
<td>38.06±0.05</td>
<td>100.09±0.56</td>
<td>6.95±0.09</td>
</tr>
<tr>
<td>F2</td>
<td>148.8±0.38</td>
<td>2.83±0.06</td>
<td>4.60±0.07</td>
<td>0.67±0.15</td>
<td>41.01±0.26</td>
<td>100.73±0.46</td>
<td>7.01±0.17</td>
</tr>
<tr>
<td>F3</td>
<td>149.8±0.45</td>
<td>2.87±0.05</td>
<td>4.32±0.05</td>
<td>0.57±0.42</td>
<td>54.42±0.14</td>
<td>98.75±0.88</td>
<td>6.95±0.79</td>
</tr>
<tr>
<td>F4</td>
<td>150.7±0.21</td>
<td>2.86±0.26</td>
<td>5.45±0.03</td>
<td>0.55±0.12</td>
<td>66.88±0.49</td>
<td>99.70±0.34</td>
<td>6.89±0.17</td>
</tr>
<tr>
<td>F5</td>
<td>149.8±0.45</td>
<td>2.84±0.45</td>
<td>5.37±0.02</td>
<td>0.51±0.42</td>
<td>82.71±0.85</td>
<td>97.95±0.38</td>
<td>6.94±0.12</td>
</tr>
<tr>
<td>F6</td>
<td>150.1±0.75</td>
<td>2.90±0.15</td>
<td>4.25±0.14</td>
<td>0.87±0.32</td>
<td>30.15±0.46</td>
<td>98.75±0.88</td>
<td>6.98±0.11</td>
</tr>
<tr>
<td>F7</td>
<td>1506±0.11</td>
<td>2.56±0.13</td>
<td>4.35±0.53</td>
<td>0.46±0.25</td>
<td>44.84±0.37</td>
<td>101.36±0.83</td>
<td>7.04±0.06</td>
</tr>
<tr>
<td>F8</td>
<td>149.3±0.56</td>
<td>2.97±0.35</td>
<td>4.13±0.41</td>
<td>0.72±0.34</td>
<td>53.08±0.00</td>
<td>101.09±4.0</td>
<td>7.00±0.10</td>
</tr>
<tr>
<td>F9</td>
<td>149.6±0.34</td>
<td>3.27±0.75</td>
<td>5.47±0.26</td>
<td>0.56±0.37</td>
<td>68.38±0.06</td>
<td>99.75±0.38</td>
<td>6.94±0.09</td>
</tr>
<tr>
<td>F10</td>
<td>149.8±0.85</td>
<td>2.57±0.63</td>
<td>5.22±0.15</td>
<td>0.40±0.15</td>
<td>79.07±0.75</td>
<td>99.22±0.29</td>
<td>6.89±0.17</td>
</tr>
</tbody>
</table>
Table 4: In-vitro release data of bilayered buccal tablets of CPM

<table>
<thead>
<tr>
<th>Time in hrs</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>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>12.73</td>
<td>13.81</td>
<td>16.68</td>
<td>26.01</td>
<td>37.74</td>
<td>13.7</td>
<td>15.5</td>
<td>19.31</td>
<td>26.55</td>
<td>33.4</td>
</tr>
<tr>
<td>2</td>
<td>16.20</td>
<td>17.77</td>
<td>26.3</td>
<td>36.25</td>
<td>46.68</td>
<td>18.6</td>
<td>19.33</td>
<td>26.84</td>
<td>37.46</td>
<td>47.81</td>
</tr>
<tr>
<td>3</td>
<td>21.06</td>
<td>22.2</td>
<td>35.77</td>
<td>46.12</td>
<td>57.11</td>
<td>24.6</td>
<td>26.63</td>
<td>37.43</td>
<td>43.43</td>
<td>58.35</td>
</tr>
<tr>
<td>4</td>
<td>25.8</td>
<td>28.07</td>
<td>43.88</td>
<td>54.46</td>
<td>67.76</td>
<td>31.63</td>
<td>34.16</td>
<td>48.16</td>
<td>55.7</td>
<td>69.72</td>
</tr>
<tr>
<td>5</td>
<td>31.67</td>
<td>36.79</td>
<td>50.96</td>
<td>62.39</td>
<td>76.36</td>
<td>35.36</td>
<td>40.96</td>
<td>53.46</td>
<td>66.15</td>
<td>79.88</td>
</tr>
<tr>
<td>6</td>
<td>38.16</td>
<td>42.06</td>
<td>56.23</td>
<td>74.32</td>
<td>88.76</td>
<td>41.1</td>
<td>45.16</td>
<td>64.09</td>
<td>78.85</td>
<td>91.27</td>
</tr>
</tbody>
</table>

REFERENCES

International Journal of Pharmacy and Biological Sciences (e-ISSN: 2230-7605)
*Corresponding Author:
**Ravali Vainala**
St. Peter’s College Of Pharmacy,
Hyd-Road, Madikonda,
Warangal - 506 142. (A.P.), INDIA.
Email: vainalaravali@gmail.com