DESIGN AND DEVELOPMENT OF CLINDAMYCIN FILM FOR PERIODONTAL DISEASE.

Aniket Janku Pulate1, Dr.Raosaheb Sopanrao Shendge2, Shubham Rameshrao Pandit3, Pooja Sonyabapu Shinde4, Vaishnavi Pathare5

1,3,4,5 Research Scholar, Department of Pharmaceutics
Sanjivani College of Pharmaceutical Education and Research, Kopargaon.
2 Associate Professor, (Pharmaceutics Department),
Sanjivani College of Pharmaceutical Education and Research, Kopargaon.
Email: shendgerajan@gmail.com

ABSTRACT

Clindamycin is lincosamide antibiotic. Which is used to treat periodontal disease including gingivitis and periodontitis, are serious bacterial infection that left untreated can lead to tooth loss. Clindamycin film local delivery against infecting microorganism in the periodontal pocket.

Material and Method: Clindamycin film prepared by using solvent casting method. There after evaluation parameter to be evaluated like Weight, Thickness, Drug content, Dissolution study, FTIR, DSC, Tensile strength.

Result and Discussion: Clindamycin film prepared by using two polymer such as sodium alginate and sodium carboxy methyl cellulose and evaluated so it was observed that batch 1 shows maximum drug content 98.49 and shows 98.16% drug release.

Conclusion: Clindamycin film prepared and evaluated so it was found that batch 1 shows maximum drug release as compare to other batches.

Keyword: Clindamycin film, sodium alginate, SCMC, Periodontal disease.

I. INTRODUCTION

Periodontal is a chronic infection and inflammatory disease that damages the supporting tissue of teeth caused by microorganism or group of microorganism resulting in progressive destruction of the teeth to loosen or lead to tooth loss and without treatment can destroy the bone that support your teeth. (1, 2, 3). The treatment of periodontitis is aimed at controlling the population of microorganisms which require sustained delivery of antibacterial agents. The local delivery of drug in periodontal pocket film improving patient compliance during the periodontitis treatment (4, 6).

It is drug delivery system applied biodegradable periodontal pocket and easy to place on mucosa as well as Drug produced with polymers providing increased contact between mucosa and dosage forms (4). The drug in periodontal pocket for local delivery systems, including strips, tablet, films, gels, fiber, gel, insitu gel, implants (5, 6, 7). The polymer used in film are gelatin, alginate, chitosan and cellulose derived polymer such as sodium carboxymethyl cellulose, ethyl cellulose, hydroxyl propyl methylcellulose have been used in medical application or medical studies (8, 9, 10, 11).

The local drug delivery application of an antibiotic on periodontal disease is an appropriate treatment due to local drug concentration is high and minimum adverse effects (12, 13). The appropriate effectiveness periodontal disease treatment depends on the prolong drug release rate. The control drug release rate has significant place among film forming technique (12).
Clindamycin is a broad spectrum antibiotics it used in treatment of dental and periodontal therapies. It has a molecular formula is C18H33CIN2O5S and its molecular weight is 424.98 g/mol. It is water soluble drug and biological half life is 2.9 h (14, 15).

The aim of study is to prepare of clindamycin loaded sodium alginate-sodium carboxy methyl cellulose film for periodontal disease and examine the effect of concentration of films in mucosa and evaluate different parameter of films for treatment of periodontal application.

**Mechanism of Action**

Clindamycin has bacteriostatic effect. It is bacterial protein synthesis inhibitor by inhibiting ribosomal translocation (16). It binds to 50 rRNA of bacterial ribosome subunit. It also inhibit binding of amino-acyl transfer RNA or the translocation of mRNA. Clindamycin contains basic pyrrolidine ring attached to sugar group though amide bond. The replacement of hydroxyl group in lincomycin to chloride atom increase the lipophiicity and clindamycin shows a better absorption and penetration into bacterial cells.

![Mechanism pathway of clindamycin hydrochloride](image_url)

**Fig No 1:** Mechanism pathway of clindamycin hydrochloride (17, 18).

**EXPERIMENTAL**

**Materials**
Clindamycin was obtained gift sample from AurbindoPharma limited (Hyderabad), sodium alginate (Bharat Heavy Chemicals Mumbai), sodium carboxymethyl cellulose high viscosity grade (Delta Chemsol Mumbai).

**Preparation of clindamycin film**

The clindamycin prepared using a solvent casting method, sodium alginate and sodium carboxy methyl cellulose (SCMC) were used as a polymers. A certain amount of polymer was dissolved in 20ml distilled water and 150 mg clindamycin was added to this solution with continuous stirring, until a homogenised solution formed. The desired quantity of glycerol (2% w/v) was added to the homogenised Drug-Polymer solution as a plasticizer. Then the polymer solution was transferred to a petri plate and kept at room temperature for drying. The dried film was cut to the desired size and wrapped in aluminium foil and kept in a desiccator until used.

**Dose Calculation**

Dose of Clindamycin is 200 mg, therefore therefore the dose required in the 2*2 cm² films is 200 mg

Area of Circle = \( \pi r^2 \)

Therefore Area = \( 3.14 \times (3.75)^2 \)

\[ = 44.15 \text{ cm}^2 \]

Area of film 2*2 cm² = 4 cm²

Dose Required for 4 cm² is 200 mg

Therefore dose for 44.15 cm² is 2.2 gm. (20).

<table>
<thead>
<tr>
<th>SR NO</th>
<th>Ingredient</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Clindamycin (gm)</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>2.</td>
<td>SCMC (mg)</td>
<td>750</td>
<td>500</td>
<td>250</td>
<td>900</td>
<td>100</td>
</tr>
<tr>
<td>3.</td>
<td>Sodium Alginate (mg)</td>
<td>250</td>
<td>500</td>
<td>750</td>
<td>100</td>
<td>900</td>
</tr>
<tr>
<td>4.</td>
<td>Glycerol</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>5.</td>
<td>Sodium Saccharin (mg)</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>6.</td>
<td>Pineapple Flavour (mg)</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>7.</td>
<td>Distilled water</td>
<td>20ml</td>
<td>20ml</td>
<td>20ml</td>
<td>20ml</td>
<td>20ml</td>
</tr>
</tbody>
</table>

SCMC (Sodium carboxymethyl cellulose)

**Preformulation study**

1 **DSC**

The DSC thermogram of clindamycin is characterised by sharp endothermic peak at 144. Which corresponding to melting point of clindamycin. The DSC scan of physical mixture also showed melting point at 144. It is clear that there is no change in position of the characteristics peak of the drug in the physical mixture. (DSC graph given in Fig No 4 & 5) (25)

2 **FTIR**

FTIR study used to determine chemical structure of drug molecule as well as to check compatibility of formulation. If any functional group shows interaction with drug molecules then changes in peak. So in this formulation all peak of drug molecules same as it is in complex formulation so it indicate that no interaction between drug molecules and excipient. (FTIR graph given in Fig No 6, 7, 8 & 9) (19, 25, 27).
II. MELTING POINT DETERMINATION

Melting point determination is a qualitative test for determination of drug molecule. Thiel tube method were used to determine melting of clindamycin and it was found that 143.

So it was confirm that given drug sample is clindamycin.

Evaluation

1 Appearance Size Shape and Thickness

Thickness of film decide the dissolution rate, if the film thick then dissolution rate will be less and vice versa. Thickness of determine 5 different location of film and then calculate the mean. Thickness of film check by using Digital Vernier Caliper Micrometer Screw Guage and Dial Guage Tester. (19, 20, 21, 22)

2 Folding endurance

Initially film were cut then film fold into repeated time at same point until break. The number of time film folding until break is called folding endurance. Typical value for folding endurance up to 300. Folding endurance given in table no 2. (19, 20, 21)

3 Tensile strength

This test is used to determine mechanical properties of film. Tensile strength basically depends on the concentration of polymer used in the formulation. It can be determine using texture analyser and digital tensile tester. Tensile strength means maximum stress applied at which film break. It can be calculate by using following formula tensile strength graph of the formulation given in Fig no 11. (22)

\[
\text{Tensile Strength} = \frac{\text{Load at Failure}}{\text{Strip Thikness} \times \text{Strip Width}} \times 100
\]

4 pH determination

Cut film into 2*2 cm², add film into petri dish containing 5 ml distilled water. After completely dissolved film check pH of solution by using digital pH meter. PH of film given in table no 2. (19, 22, 24)

5 Swelling study

Film were weighed individually (W1) and placed separately in petri dishes containing 5 ml of phosphate buffer pH 6.8 solution. The dishes were stored at room temperature. Then, films were removed and excess surface water was removed carefully using the filter paper after specified time intervals. The swollen films were then again weighted (W2) and swelling index calculated using formula, (19, 22, 24, 25)

\[
\text{SI} \,(\%) = \frac{\text{W2} - \text{W1}}{\text{W1}} \times 100
\]

6 Drug content uniformity

The film (2x2) was dissolved in 100ml of 6.8 phosphate buffer solutionin a beaker. The dispersion was kept in dark place for overnight after completely dissolved film then filtered. The 1ml of filtered solution was diluted in 10ml of 6.8 phosphate buffer in 10ml volumetric flask. To determine the amount of drug content by taking 3 readings using UV visible spectrophotometer at 210. Drug content of formulation given in table no 2. (19, 20, 21, 24)

7 In vitro drug release study

The pH of gingival fluid lies between 6.5-6.8, thus phosphate buffer pH 6.8 was used as simulated gingival fluid. Films of known weight and dimension (2x2) were placed separately in small test tube containing 10 ml of pH 6.8 phosphate buffer. The test tube were sealed with aluminium foil and kept at 37°C. The sample was withdrawn and replaced with fresh 1 ml of 6.8 pH for every 1 hour up to 7 hours. The concentration of drug in the buffer was measured at 210 nm by using a UV-spectrophotometer. Drug release data shows in table no 3 and drug release graph shows in fig no 2. (20, 21)

8 Ex vivo drug release studies

www.turkjphysiotherrehabil.org
The ex vivo release was performed using Franz Diffusion cell. Phosphate buffer pH6.8 was used as a receptor solution as a dissolution medium. The volume of diffusion cell was 10 ml. The prepared periodontal film (2x2 mm) was firmly pressed onto the centre of semi permeable membrane and the membrane was mounted in the donor compartment. The donor compartment was then placed in a position such that the surface of membrane just touches the receptor fluid surface. The whole assembly was fixed on a hot plate magnetic stirrer and the solution in the receptor compartment was continuously stirred at 100 rpm using magnetic beads and the temperature was maintained at 37±1°C. The diffusion was carried out for 24 h and 1 ml of the receptor fluid was withdrawn at predetermined time interval and replaced immediately with the same volume of fresh dissolution media to maintain risk conditions. The samples were analysed for drug release at 210 nm using ultraviolet visible spectrophotometer after suitable dilution with diffusion media.(24, 26)

9 Scanning electron microscopy

The SEM photograph showed smooth surfaces without any scratches so it indicating that clindamycin is uniformly distributed. Some crystal images shown in photograph but does not effect on dissolution study. SEM images of formulation given in fig no 10. (27)

10 Stability:

Optimized medicated films were subjected to stability testing. Films were placed in a glass beaker lined with aluminium foil and kept in a humidity chamber maintained at 40 +2°C and 75 + 5% RH for 1 month. Changes in the appearance and drug content of the stored films were investigated after storage. The data presented were the mean of 3 determinations. Stability study data shows in table no 4. (19, 23)

III. CONCLUSION:

Clindamycin film was prepared by using solvent casting method. Sodium alginate and sodium carboxy methyl cellulose, glycerine were involve in this formulation. By changing the concentration of two polymer film were prepared and evaluated. So it was found batch 1 given outstanding result of all evaluation. Film drug content in 98.49 and shows 98.16% drug release.

ACKNOWLEDGEMENT:

The Authors thanks for giving support and proper direction for making successful research work and also help to find new and innovative information for making research article. We would also like to thanks Sanjivani College of Pharmaceutical Education and Research Kopargaon, Maharashtra-423603, India. For providing required facilities to carry out this Research work.

IV. RESULT AND DISCUSSION

Table No 2. Result of parameter

<table>
<thead>
<tr>
<th>SR NO</th>
<th>Films</th>
<th>Thickness (mm)</th>
<th>Surface pH</th>
<th>Folding endurance</th>
<th>Swelling % (3hrs)</th>
<th>Drug content(%)</th>
<th>% CDR at 7th Hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Batch 1</td>
<td>0.23</td>
<td>7</td>
<td>310</td>
<td>41.21</td>
<td>98.49</td>
<td>98.16</td>
</tr>
<tr>
<td>2</td>
<td>Batch 2</td>
<td>0.24</td>
<td>6.9</td>
<td>290</td>
<td>49.24</td>
<td>96.88</td>
<td>93.81</td>
</tr>
<tr>
<td>3</td>
<td>Batch 3</td>
<td>0.22</td>
<td>6.8</td>
<td>305</td>
<td>51.09</td>
<td>96.14</td>
<td>92.93</td>
</tr>
<tr>
<td>4</td>
<td>Batch 4</td>
<td>0.25</td>
<td>7.1</td>
<td>300</td>
<td>54.42</td>
<td>97.66</td>
<td>95.37</td>
</tr>
<tr>
<td>5</td>
<td>Batch 5</td>
<td>0.23</td>
<td>7</td>
<td>295</td>
<td>38.20</td>
<td>94.43</td>
<td>89.54</td>
</tr>
</tbody>
</table>
Table No 3. Drug release of film

<table>
<thead>
<tr>
<th>Time (hrs)</th>
<th>Batch 1</th>
<th>Batch 2</th>
<th>Batch 3</th>
<th>Batch 4</th>
<th>Batch 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.04</td>
<td>11.60</td>
<td>11.75</td>
<td>13.07</td>
<td>11.46</td>
</tr>
<tr>
<td>2</td>
<td>26.90</td>
<td>22.49</td>
<td>22.34</td>
<td>26.75</td>
<td>17.93</td>
</tr>
<tr>
<td>3</td>
<td>38.66</td>
<td>34.40</td>
<td>35.13</td>
<td>38.96</td>
<td>30.28</td>
</tr>
<tr>
<td>4</td>
<td>54.10</td>
<td>47.63</td>
<td>49.40</td>
<td>50.13</td>
<td>48.22</td>
</tr>
<tr>
<td>5</td>
<td>67.04</td>
<td>63.52</td>
<td>62.63</td>
<td>66.02</td>
<td>68.96</td>
</tr>
<tr>
<td>6</td>
<td>84.16</td>
<td>81.75</td>
<td>76.31</td>
<td>81.40</td>
<td>80.57</td>
</tr>
<tr>
<td>7</td>
<td>98.16</td>
<td>93.81</td>
<td>92.93</td>
<td>95.37</td>
<td>89.54</td>
</tr>
</tbody>
</table>

Fig No 2. % Drug Release graph of all batches
Fig no 3. Franz Diffusion Study of optimized Batch

Fig no 4. Stability study of film

Table No 4. Stability study data

<table>
<thead>
<tr>
<th>SR.NO</th>
<th>Time (Day)</th>
<th>Drug content</th>
<th>%Drug Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>98.46</td>
<td>98.16</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>97.03</td>
<td>97.94</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>95.89</td>
<td>97.11</td>
</tr>
</tbody>
</table>

DSC
Fig no 5. DSC of Clindamycin

Fig no 6. DSC of Clindamycin and polymer mixture

Fig no 7. FTIR of Clindamycin
Fig no 8. FTIR of Polymer

Fig no 9. FTIR of Clindamycin + Sodium CMC

Fig no 10. FTIR of Clindamycin + Sodium Alginate
REFERENCE
23 Srilatha K S. Formulation and evaluation of norfloxacin periodontal film for local delivery. IJNDD, 11 (5), Jul-Sep, 2019, 158-166.