FORMULATION AND EVALUATION OF CHLORHEXIDINE GLUCONATE DENTAL GELS

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ABSTRACT
Chlorhexidine used to reduce oral bacteria and dental plaque also it has bactericidal and bacteriostatic properties. The gel was formulated by using different polymers with different concentration. Ten different formulae were prepared and characterized physically in term of color, syneresis, spreadability, pH, drug content and rheological properties. F2 composition formulation were found to be good and can be used for the preparation of Chlorhexidine gluconate dental gels.

KEYWORDS: Chlorhexidine Gluconate, Periodontal disease, Formulation, Gels.

INTRODUCTION
Periodontal disease such as chronic periodontitis, aggressive periodontitis, systemic disease-associated periodontitis and necrotizing periodontitis. It is a general term which cover several pathological conditions affecting the tooth supporting structures [1]. These conditions are characterized by a destruction of the periodontal ligament, a resorption of the alveolar bone and the migration of the junctional epithelium along the tooth surface. It is a localised inflammatory response caused by bacterial infection of a periodontal pocket associated with subgingival plaque [2]. Although bacteria are the primary cause of periodontal disease, the expression of microbial pathogenic factors alone may not be sufficient to cause periodontitis. Periodontal pathogens produce harmful by-products and enzymes that break extracellular matrices as well as host cell membranes to produce nutrients for their growth. In doing so, they initiate damage directly or indirectly by triggering host-mediated responses that lead to self-injury. In the early phase of the disease (gingivitis), inflammation is confined to the gingiva but extends to deeper tissues in periodontitis, leading to gingival swelling, bleeding. In the late phase of the disease, the supporting collagen of the periodontium is degenerated, alveolar bone begins to resorb and gingival epithelium migrates along the tooth surface forming a ‘periodontal pocket’ [3]. This periodontal pocket provides ideal conditions for the proliferation of microorganisms. The
microflora found in periodontitis is complex and composed mainly of Gram negative anaerobic bacteria [4]. The disease may then require extensive treatment, failing which the teeth may be lost. Therefore, clearance of the subgingival infection and elimination of the periodontal pocket are considered a priority in the treatment of periodontitis.

In mouthwash chlorhexidine used as an active ingredient, which reduce oral bacteria and dental plaque. It has bactericidal and bacteriostatic properties [5]. Also it has longer effect than any other drug when used in the mouthwashes, hence used for the treatment of the gingivitis [6] and to treat periodontal pockets equal or greater than 5 mm, chlorhexidine is also available in high concentration (36%) in a gelatin chip.

There are oral pathologic conditions in which the maintenance of oral hygiene with the twice-daily use with 0.12% chlorhexidine gluconate solution (in which a salt of chlorhexidine and gluconic acid has been dissolved) is required for healing and regeneration of the oral tissues. These conditions included gingivitis, periodontitis, dental traumas [7] (such as subluxation), oral cysts [8] and after wisdom tooth extraction.

The major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations [9].

Gels found to have high drug release, which is not dependent on the solubility of water, when compared with the ointment and cream [10]. Also have less risk for adverse reactions, with ease of applying [11].

**MATERIALS AND METHODS**

**Materials** Chlorhexidine gluconate(Loba Chemicals), Carbopol 934P, Carbopol 940, Hydroxy propyl methyl cellulose K4M, Hydroxy propyl methyl cellulose 100, Hydroxy methyl cellulose, Hydroxy propyl cellulose, Sodium carboxy methyl cellulose, Methyl cellulose, Propylene glycol, Methyl paraben, Propyl paraben, Chitosan, Dialysis membrane, Triethanolamine, Menthol, Aspartame, Buffers, Glycerol, Ethanol, Tween 80, Ethyl cellulose, Xanthan gum, N-octyl alcohol, Sodium phosphate monobasic, Sodium phosphate dibasic, all materials were purchased from Loba Chemicals, Robin Chemicals, Rolex Laboratory, Sisco Research Lab, Spectrochem, and Himedia.

**Methods**

General procedure for formulation of gels:

Gels were prepared by continuous stirring with agitation of different concentrations of polymer (selected) in water for a period of 1-2 hours. Then solution of Chlorhexidine gluconate in propylene glycol was added dropwise under continuous stirring using magnetic stirrer about
1600rpm. After complete addition the mixture is stirred till the homogeneous gel obtained and stored in the wide mouthed bottles. The air bubbles entrapped was removed by placing a gel in vacuum oven for 2 hours. All the samples were allowed to equilibrate at room temperature prior to calculating the Physical properties [12].

Table 1: Composition of Chlorhexidine Gluconate medicated dental gels (%w/w)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ingredients</th>
<th>Formulation Code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>1</td>
<td>CHX</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Carbopol 934</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Carbopol 940</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Sodium CMC</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>HPMC</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Chitosan</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>Mannitol</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>Menthol</td>
<td>0.1</td>
</tr>
<tr>
<td>9</td>
<td>Methyl Paraben</td>
<td>0.04</td>
</tr>
<tr>
<td>10</td>
<td>Propyl Paraben</td>
<td>0.02</td>
</tr>
<tr>
<td>11</td>
<td>Triethanolamine</td>
<td>0.1</td>
</tr>
<tr>
<td>12</td>
<td>Purified Water</td>
<td>Qs100ml</td>
</tr>
</tbody>
</table>

Carbopol 940 gel
Methyl paraben and propyl paraben were dissolved in water at 80°C. Then accurately weighed quantity of carbopol 940 as shown in Table 1 was dispersed in water at 40°C with constant stirring using mechanical stirrer at 1200 rpm for 30 min. The extracts were dissolved in PEG 400 and added to the base and mixed well. The pH was then adjusted to pH 6 using triethanolamine and stirred slowly until a clear gel was obtained.

Sodium CMC gel
Methyl paraben and propyl paraben were dissolved in water at 80°C, and then accurately weighed quantity of sodium CMC as shown in Table 1 was dispersed in water at 50°C with constant stirring using a mechanical stirrer at 2000 rpm for 30 min. The extracts were dissolved in PEG 400 and added to the gel base and mixed well to get a homogenous gel.

HPMC gel
Methyl paraben and propyl paraben were dissolved in water at 80°C [13]. Accurately weighed quantity of HPMC as shown in Table 1 was dispersed in a portion of hot water (about one third of the total volume) heated at 80°C with constant stirring using a mechanical stirrer. Stirring was continued until a thin hazy dispersion was formed, then the remaining amount of water was added on cold and mixing was continued till smooth homogenous gel is formed. The gel was left
overnight in the refrigerator (hot/cold technique). The drug solution in PEG 400 was added to the gel base and mixed well to get a homogenous gel.

**Carbopol 940 and sodium CMC gel**

Methyl paraben and propyl paraben were dissolved in water 80°C. Accurately weighed quantity of carbopol 940 and sodium CMC as shown in Table 1 were dispersed in water separately as explained above and were mixed well. The extracts were dissolved in PEG 400 and added to the gel base and mixed well.

**Evaluation of Chlorhexidine gluconate dental gels:**

**Determination of pH:**

The pH of 20% w/v concentration of chlorhexidine gluconate solution was found to be 7.2 ± 0.5773 (average of three readings)*.

**Physical appearance of gel formulation:**

Ten formulations were evaluated for physical appearance, homogeneity and consistency of all formulations (F1-F10) was good. No precipitation occurred. Hence, all these formulations other tests were performed on them.

**pH measurement of gel formulation:**

pH was measured in each gel, using a pH meter, which was calibrated before each use with standard buffer solutions. The measurement of pH was performed at initial, 1 month, 2 months, 3 months after preparation to detect any pH fluctuation with time. The data is reported in Table 2.

**Viscosity:**

Viscosity measurements of the prepared gels were recorded at controlled temperature of 30 ± 2°C. Viscosities (in cps) of the prepared gels were recorded and reported in Table 2. The viscosities of the formulations were in the range of 49143.76 to 51986.62 cps and were found to be satisfactory. Viscosity increases as the polymer concentration increases. All the formulations showed non-Newtonian flow and exhibited pseudoplastic behavior, suggesting that gels do not flow at low shear stress and room temperature.
Table 2: Physical Properties of Chlorhexidine Gluconate dental gels

<table>
<thead>
<tr>
<th>Formulation</th>
<th>pH±SD, n=3</th>
<th>Viscosity (cps)</th>
<th>Tube Extrudability (%) ±SD, n=3</th>
<th>Spreadability (cm)±SD, n=3</th>
<th>Syringeability</th>
<th>Drug Content (%)±SD, n=3</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>7.11±0.02</td>
<td>49143.76</td>
<td>96±1.2</td>
<td>8.20±0.10</td>
<td>+</td>
<td>98.14±1.16</td>
</tr>
<tr>
<td>F2</td>
<td>7.12±0.02</td>
<td>49556.54</td>
<td>96±1.6</td>
<td>8.15±0.10</td>
<td>+</td>
<td>99.67±0.15</td>
</tr>
<tr>
<td>F3</td>
<td>7.12±0.03</td>
<td>48785.45</td>
<td>95±1.2</td>
<td>8.40±0.10</td>
<td>+</td>
<td>98.03±0.47</td>
</tr>
<tr>
<td>F4</td>
<td>7.12±0.04</td>
<td>48583.65</td>
<td>95±1.0</td>
<td>7.35±0.10</td>
<td>+</td>
<td>99.16±0.37</td>
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<tr>
<td>F5</td>
<td>7.14±0.02</td>
<td>48857.68</td>
<td>93±0.6</td>
<td>6.50±0.10</td>
<td>+</td>
<td>98.84±0.87</td>
</tr>
<tr>
<td>F6</td>
<td>7.14±0.05</td>
<td>50385.97</td>
<td>93±0.4</td>
<td>6.45±0.10</td>
<td>+</td>
<td>98.52±0.91</td>
</tr>
<tr>
<td>F7</td>
<td>7.11±0.03</td>
<td>51986.62</td>
<td>94±1.3</td>
<td>7.20±0.10</td>
<td>+</td>
<td>97.03±0.21</td>
</tr>
<tr>
<td>F8</td>
<td>7.11±0.02</td>
<td>51641.52</td>
<td>94±1.4</td>
<td>7.50±0.10</td>
<td>+</td>
<td>99.48±0.12</td>
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<tr>
<td>F9</td>
<td>7.12±0.02</td>
<td>48593.49</td>
<td>93±1.3</td>
<td>7.80±0.10</td>
<td>+</td>
<td>98.52±0.49</td>
</tr>
<tr>
<td>F10</td>
<td>7.11±0.04</td>
<td>48863.76</td>
<td>93±1.6</td>
<td>7.85±0.10</td>
<td>+</td>
<td>99.48±0.07</td>
</tr>
</tbody>
</table>

**Spreadability:**

Medicated dental gels were evaluated by placing the gel at the centre of glass plate and another glass plate placed over it, 2kg weight placed at centre of plate and care taken to avoid sliding. After 30 min diameter of gel measured and results were tabulated in Table 2. The range was from 6.45 – 8.40 and all the formulations were in the desirable range. Spreadability of the gels was not much influenced by the type of hydrocolloids. However, spreadability values of the gels decreased as the concentration of the polymer increased in the formulations. The decrease in the spreadability was relative to that of changes in the viscosity of the gels.

**Tube extrudability**

Tube extrudability is determined by filling the gel in a tube with a nasal tip of 5 mm opening. Tube extrudability is determined by measuring the amount of gels extruded through the tip and the results were tabulated in Table 2. The range was from 93-96 as it is more then 90% it is acceptable. However, tube extrudability values of the gels decreased as the concentration of the polymer increased in the formulations. The decreases in the tube extrudability values were relative to that of changes in the viscosity of the gels.

**Syringeability study**

Syringeability of gel formulations was done with the help of 21 G needle and findings were tabulated in Table 2. All the formulations passes through the syringe no blockage was observed in a normal pressure hence passes the test.
CONCLUSION

On the basis of the results we can conclude that: Gels were successfully incorporated with Chlorhexidine gluconate. From among all the developed formulation the formula F2 shows good spreadability, Tube Extrudability, viscosity and drug content. Thus, it was accomplished that F2 composition can be used for the preparation of Chlorhexidine gluconate dental gels. However, further evaluation of the studies is required to be further taken.

REFERENCES


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