THE EFFECT OF A POLYVINYL ALCOHOL AND DEXTRANE ON THE PROPERTIES OF THERMOSENSITIVE HYDROPHILIC GELS CONTAINING LACTIC ACID COMPLEXED WITH CHITOSAN

Katarzyna Małolepsza-Jarmołowska

Department of Pharmaceutical Technology, Faculty of Pharmacy
The “Silesian Piasts” memorial Medical University of Wrocław, ul. Szewska 38, 50-139 Wrocław, Poland.
e-mail: katarzynamj@poczta.onet.pl

Abstract
Gels containing lactic acid complexed with chitosan at a stoichiometric ratio 1:1 and 2:1 and 5 - 25% content of polyoxyethylene glycol 200 reveal pH from 2.5 to 4.6. The addition of 20 – 25% poloxamer 407 increases the pH to 4.55 to 5.30 for 1:1 gels and 4.00 to 4.85 for 2:1 gels. The addition of 0.5% polyvinyl alcohol decreases the pH of the investigated gels to 4.00 to 4.55 for 1:1 gels and 3.85 to 4.40 for 2:1 gels. The addition of 1.0% dextrane decreases the pH of investigated gels to 4.40 to 4.90 (1:1) and 4.00 to 4.48 (2:1). Rheological investigations revealed an increase in the dynamic viscosity of preparations containing poloxamer 407 with the addition of polyvinyl alcohol or dextrane in comparison to the reference gels. Results obtained in the experimental studies proved that it is possible to produce a preparation with optimal pharmaceutical and application properties.

Key words: lactic acid complexed with chitosan, thermosensitive polymer - poloxamer 407, polyvinyl alcohol, dextrane, vaginal infections, anti-inflammatory drugs.
1. Introduction

The condition is most frequently associated with disturbed biocenosis resulting from bacterial vaginosis. Clinicians are still looking for effective solutions. Numerous recurrences of the condition are widely discussed by clinicians. Traditional therapeutic schemes recommended by world treatment centres and health organizations do not bring satisfactory results. Numerous recurrences of the condition are widely discussed by clinicians. The main problem in applied therapies is to maintain the continuity of treatment during 24 hours [1 - 3].

The use of hydrophilic gels with high adhesion properties and ability to spread over the vaginal mucosa enable prolonged action of the drug [4 - 11]. The preparations, remaining at the site of application, produce adequate pH in the environment thanks to the content of lactic acid complexed with chitosan. The use of a thermosensitive polymer affects further adhesion of the investigated preparations [12].

The aim of the study was to investigate the effect of adjuvant substances on optimization properties of the vaginal gels containing lactic acid complexed with chitosan.

2. Materials and methods

2.1. Materials


2.2. Methods

2.2.1. Measurements of pH and viscosity

(see [11])

2.2.1.1. Determination of pH

For pH measurement of the investigated gels, the potentiometric method was used, in which a combined electrode integrated into a multifunctional computer meter, ELECTRON CX-742 was immersed into the investigated gel. Prior to the measurement the computer meter was calibrated by two buffer solutions with pH 7.00 and pH 4.00.

2.2.1.2. Rheological investigations

Rheological investigations were performed using a rotational viscosimeter. The determinations were performed in I a and II a range on a K-1 cone with the diameter of 36 mm and 0.917 fissure at 37 °C. The shear angle was measured using 12 shear rates in ascending direction and 11 rates in the descending direction. Viscosity and torque were calculated from appropriate formulas. The obtained results were used to plot the flow curves of the investigated gels.
2.2.2. Technology of manufacture of hydrophilic intravaginal gel

The production of gel containing lactic acid complexes with chitosan consisted of the following stages:

1. Obtaining the lactic acid - chitosan complex

Chitosan combines with organic acids by means of I-order amine groups. This property was used in the preparation of the complex. The required amount of powdered chitosan was poured onto a weighed amount of lactic acid. The mass was stirred until a homogenous suspension was obtained. The mixture was left for 24 h until a clear, thick fluid was formed that could be joined with methylcellulose [4].

2. Obtaining the excipient - preparation of gel from methylcellulose, polyvinyl alcohol or dextrane and poloxamer 407

A gel was obtained from methylcellulose, polyvinyl alcohol or dextrane and poloxamer 407 by adding a known amount of this compound to the solution of polyoxyethylene glycol 200 in water. In order to enhance the process of gelation, the mixture was cooled to 5 - 10 °C. The homogenous gel was weighed and enough distilled water was added to obtain the initial mass.

Lactic acid complexes with chitosan was added to methylcellulose, polyvinyl alcohol or dextrane and poloxamer 407 gel and stirred until an homogenous gel was obtained. Distilled water was added to obtain the initial mass.

3. Results and discussion

Gels containing lactic acid complexed with chitosan at a stoichiometric ratio 1:1 and 2:1 and 5 - 25% content of polyoxyethylene glycol 200 reveal pH from 2.5 to 4.6. The addition of 20 - 25% poloxamer 407 increases the pH to 4.55 to 5.30 for 1:1 gels and 4.00 to 4.85 for 2:1 gels.

The addition of 0.5% polyvinyl alcohol decreases the pH of the investigated gels to 4.00 to 4.55 for 1:1 gels and 3.85 to 4.40 for 2:1 gels.

The addition of 1.0% dextrane decreases the pH of investigated gels to 4.40 to 4.90 (1:1) and 4.00 to 4.48 (2:1).

The results obtained in the experimental are presented in Table 1.

Rheological studies demonstrated that the reference gels possess the dynamic viscosity from 159.16 to 354.41 for the 1:1 stoichiometric ratio in the complex and from 236.27 to 388.16 for 2:1 ratio. The addition of poloxamer 407 at concentrations of 20 to 25% increases the dynamic viscosity from 506.14 to 641.20 for 1:1 and 540.35 to 692.55 for 2:1 ratios.

The addition of 0.5% polyvinyl alcohol increases the dynamic viscosity from 590.20 to 720.63 for 1:1 and 560.90 to 698.82 for 2:1 ratios.
The addition of 1.0% dextrane increases the dynamic viscosity from 665.23 to 750.28 for 1:1 and 645.50 to 740.16 for 2:1 ratios. All the investigations were performed at 37 °C.

The results obtained in the experimental are presented in Table 2.

Table 1. Influence polyoxyethylene glycol 200 and polyvinyl alcohol or dextrane on pH investigated gels containing 4.0% methylcellulose and 25% poloxamer 407.

<table>
<thead>
<tr>
<th>Stoichiometric ratio lactic acid to chitosan</th>
<th>Concentration PEG-200, %</th>
<th>pH gels with addition PEG-200</th>
<th>pH gels with PEG-200 and addition 0.5% polyvinyl alcohol</th>
<th>pH gels with PEG-200 and addition 1.0% dextrane</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:1</td>
<td>5</td>
<td>4.84</td>
<td>4.00</td>
<td>4.40</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>4.88</td>
<td>4.25</td>
<td>4.48</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>4.90</td>
<td>4.36</td>
<td>4.62</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>4.98</td>
<td>4.40</td>
<td>4.85</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>5.30</td>
<td>4.55</td>
<td>4.90</td>
</tr>
<tr>
<td>2:1</td>
<td>5</td>
<td>4.30</td>
<td>3.85</td>
<td>4.00</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>4.38</td>
<td>3.90</td>
<td>4.25</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>4.50</td>
<td>4.10</td>
<td>4.38</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>4.65</td>
<td>4.25</td>
<td>4.45</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>4.85</td>
<td>4.40</td>
<td>4.48</td>
</tr>
</tbody>
</table>

Table 2. Influence polyoxyethylene glycol 200 and polyvinyl alcohol or dextrane on reological properties investigated gels containing 4.0% methylcellulose and 25% poloxamer 407.

<table>
<thead>
<tr>
<th>Stoichiometric ratio lactic acid to chitosan</th>
<th>Concentration PEG 200, %</th>
<th>Dynamic viscosity gels in mPa*s with addition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PEG-200</td>
</tr>
<tr>
<td>1:1</td>
<td>5</td>
<td>641.20</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>595.67</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>565.67</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>537.53</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>583.15</td>
</tr>
<tr>
<td>2:1</td>
<td>5</td>
<td>692.55</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>588.16</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>555.67</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>554.41</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>580.43</td>
</tr>
</tbody>
</table>

The investigations revealed that it is possible to obtain gels with high adhesion properties to vaginal mucous membrane.

The addition of polyvinyl alcohol or dextrane reduces the pH and maintains high adhesion. The use of polyvinyl alcohol and dextrane allowed to obtain physiological range pH.
Rheological investigations revealed an increase in the dynamic viscosity of preparations containing poloxamer 407 with the addition of polyvinyl alcohol or dextrane in comparison to the reference gels.

Results obtained in the experimental studies proved that it is possible to produce a preparation with optimal pharmaceutical and application properties.

4. Conclusions

1. In the performed experimental studies we obtained preparations with physiological pH and high adhesion properties.
2. Rheological investigations revealed an increase in the dynamic viscosity of preparations containing thermosensitive polymer - poloxamer 407 with the addition of polyvinyl alcohol or dextrane in comparison to the reference gels.
3. Results obtained in the experimental studies proved that it is possible to produce a preparation with optimal pharmaceutical and application properties.

5. References
