INFLUENCE OF POLOXAMER 407 ON THE PROPERTIES GYNECOLOGICAL POWDERS CONTAINING LACTIC ACID COMPLEXED WITH CHITOSAN

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Abstract

*Thermosensitive hydrophilic powders passing in gels containing lactic acid complexed with chitosan at a stoichiometric ratio 1:1 and 8:1 reveal pH ranged from 4.00 to 4.91 and 2.56 to 3.42. Rheological studies demonstrated that the investigated thermosensitive gels obtained from powders have the dynamic viscosity in the ranged from 269 mPa*s to 579 mPa*s for the 1:1 stoichiometric ratio and in the range from 220 mPa*s to 530 mPa*s for 8:1 ratio. As a result of the research preparations with different pH values including the physiological range were obtained. The thermosensitive gels obtained from the thermosensitive powders were characterized by the specific dynamic viscosity. The results proved that it is possible to produce a preparation with optimal pharmaceutical and application properties.*

Key words: *lactic acid complexed with chitosan, physiological environment of vagina, thermosensitive hydrophilic powders, vaginal mucosa, anti-inflammatory drugs, vaginal infections.*

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1. Introduction

The condition is most frequently associated with disturbed biocenosis resulting from bacterial vaginosis. Clinicians are still looking for effective solutions. The main problem in applied therapies is to maintain the continuity of treatment during 24 hours. The use of hydrophilic base for lactic acid complexation with alkaline polymers enabled production of gels with rheological properties of vaginal discharge. The gel remains at the site of application and provides proper pH of environment [1 - 12]. Aim of this study was to investigate the influence of 20%, 23% or 25% poloxamer 407 on the physico-chemical properties of powders for gynecological purposes. Powders with poloxamer 407 have been tested, to form the drug carriers containing vaginal lactic acid complexed with chitosan. Application of the powders passing applications in natural conditions in the gel is designed to obtain a physiological pH of the vaginal environment. The properties of powders containing poloxamer 407 and lactic acid complexed with chitosan passing were examined in presented research. In the study methylcellulose having a different viscosity was used as well rheological studies of gels prepared from powders were performed. As a result of the research thermosensitive preparations with different pH values including the physiological range were obtained. The gels obtained from the powders were characterized by the specific dynamic viscosity.

2. Materials and Methods

2.1. Materials

The following chemicals were used in experiments: lactic acid (P.Z.F. Cefarm (Wrocław, Poland), chitosan with deacetylation degree of 93.5% (Sea Fisheries Institute, Gdynia, Poland), methylcellulose (Aldrich Chemical Company Ltd. Gillingham – Dorest SP 84 SL, England), poloxamer 407 (Sigma – Aldrich Chemie GmbH, Germany) aqua purificata, acc. to FP X.

2.2. Methods

2.2.1. Preparation of hydrophilic intravaginal powder

The preparation of powder containing lactic acid complexed with chitosan consisted of the following stages:

1. Preparation of the lactic acid - chitosan complex.

The required amount of powdered chitosan was added to a known amount of lactic acid and was mixed. The mixture was left for 24h until a clear, thick fluid was formed that could be joined with methylcellulose [4].

2. Preparation of powder from methylcellulose and poloxamer 407.

The poloxamer 407, was mixed with a known amount of methylcellulose. Next the mixture was added to the lactic acid complexes with chitosan. The resulting powder was thoroughly pulverized. Homogenous powder was obtained sieved through a sieve having a mesh size of 0,16 mm.

3. Preparation of the tested gel.

A gel was obtained by mixing the powder with, known amount of distilled water and was cooled to 5 - 10 °C to enhance the process of gelation. The homogenous gel was weighed and additional amount of distilled water was added to obtain the initial mass.

2.2.2. Analytical methods

2.2.2.1. Dynamic viscosity measurement

Rheological investigations were performed using a rotational viscosimeter Rheotest 2 Medingen Dresden. 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. The values of the shear stress and viscosity were calculated from measurements at the temperature of 37°C.

2.2.2.2. pH-measurement

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. All gels were tested three times and the results reported as the average of three measurements at the temperature of 37°C.

3. Results and Discussion

Gels were prepared with powders, containing lactic acid complexed with chitosan in a stoichiometric ratio 1:1, 2;1, 3:1, 4:1 and 8:1. Depending on the content of methylcellulose and its viscosity, different properties of the gels were obtained. First the gel with addition of 4% of methylcellulose was investigated.

Table 1. Influence viscosity 4% methylcellulose on pH gels obtained from investigated powders

Stoichiometric ratio lactic acid to chitosan	pH gels with methyl-cellulose 4000 mPa*s	pH gels with methyl-cellulose 1500 mPa*s	pH gels with methyl-cellulose 400 mPa*s	pH gels with methyl-cellulose 25 mPa*s	pH gels with methyl-cellulose 15 mPa*s
1:1	3.92	3.96	4.17	4.25	4.44
2:1	3.48	3.82	4.04	4.19	4.25
3:1	3.17	3.25	3.44	3.65	3.90
4:1	2.75	2.87	2.90	2.95	3.09
8:1	2.36	2.58	2.65	2.78	2.84

The pH of the gels ranged from 3.92 to 4.44 for gels in ratio 1:1 and from 2.36 to 2.84 for gels with ratio 8:1.

The addition of 20% poloxamer 407 increases the pH ranged from 4.00 to 4.68 for gels 1:1 and from 2.56 to 3.20 for 8:1 ratio (Table 2).

Table 2. Influence viscosity 4% methylcellulose and 20% poloxamer 407 on pH gels obtained from investigated powders

Stoichiometric ratio lactic acid to chitosan	pH gels with methyl-cellulose 4000 mPa*s	pH gels with methyl-cellulose 1500 mPa*s	pH gels with methyl-cellulose 400 mPa*s	pH gels with methyl-cellulose 25 mPa*s	pH gels with methyl-cellulose 15 mPa*s
1:1	4.00	4.20	4.39	4.50	4.68
2:1	3.66	4.09	4.35	4.42	4.53
3:1	3.35	3.51	3.72	3.91	4.37
4:1	2.99	3.05	3.33	3.45	3.93
8:1	2.56	2.75	2.89	3.00	3.20

The addition of 23% poloxamer 407 increases the pH ranged from 4.15 to 4.76 for gels 1:1 and from 2.66 to 3.38 for 8:1 ratio (Table 3).

Table 3. Influence viscosity 4% methylcellulose and 23% poloxamer 407 on pH gels obtained from investigated powders

Stoichiometric ratio lactic acid to chitosan	pH gels with methyl-cellulose 4000 mPa*s	pH gels with methyl-cellulose 1500 mPa*s	pH gels with methyl-cellulose 400 mPa*s	pH gels with methyl-cellulose 25 mPa*s	pH gels with methyl-cellulose 15 mPa*s
1:1	4.15	4.29	4.45	4.62	4.76
2:1	3.72	4.15	4.38	4.54	4.68
3:1	3.46	3.63	3.80	3.99	4.49
4:1	3.06	3.21	3.47	3.53	4.00
8:1	2.66	2.83	3.10	3.17	3.38

The addition of 25% poloxamer 407 increases the pH ranged from 4.22 to 4.91 for gels 1:1 and from 2.73 to 3.42 for 8:1 ratio (Table 4).

Table 4. Influence viscosity 4% methylcellulose and 25% poloxamer 407 on pH gels obtained from investigated powders

Stoichiometric ratio lactic acid to chitosan	pH gels with methyl-cellulose 4000 mPa*s	pH gels with methyl-cellulose 1500 mPa*s	pH gels with methyl-cellulose 400 mPa*s	pH gels with methyl-cellulose 25 mPa*s	pH gels with methyl-cellulose 15 mPa*s
1:1	4.22	4.32	4.50	4.77	4.91
2:1	3.81	4.25	4.44	4.62	4.75
3:1	3.53	3.71	3.97	4.12	4.55
4:1	3.19	3.30	3.52	3.61	4.14
8:1	2.73	2.90	3.28	3.32	3.42

Rheological studies demonstrated that the investigated gels obtained from powders have the dynamic viscosity in the range from 53 mPa*s to 398 mPa*s for the 1:1 stoichiometric ratio chitosan to lactic acid in the complex and from 19 mPa*s to 242 mPa*s for 8:1 ratio (Table 5).

A modification of the composition of the tested powders containing 20%, 23% or 25% poloxamer 407 has increased the range of the dynamic viscosity of formulations suitably from 269 mPa*s to 579 mPa*s for gels 1:1 and from 220 mPa*s to 530 mPa*s for 8:1 ratio.

Presented studies have shown that it is possible to obtain thermosensitive gels with high adhesion properties to vaginal mucous membrane. The use of methylcellulose with different viscosity allows to obtain different formulations with a wide range of pH. Rheological investigations revealed an increase in the dynamic viscosity of thermosensitive preparations containing lactic acid complexed with chitosan in a stoichiometric ratio 1:1 in comparison to the gels with ratio 8:1.

Table 5. Influence of 4% methylcellulose on rheological properties (dynamic viscosity η[mPa*s]) of gels obtained from investigated powders

Stoichiometric ratio lactic acid to chitosan	η[mPa*s] gels with methyl-cellulose 4000 mPa*s	η[mPa*s] gels with methyl-cellulose 1500 mPa*s	η[mPa*s] gels with methyl-cellulose 400 mPa*s	η[mPa*s] gels with methyl-cellulose 25 mPa*s	η[mPa*s] gels with methyl-cellulose 15 mPa*s
1:1	398	254	165	110	53
2:1	356	232	159	98	44
3:1	305	221	143	87	38
4:1	286	204	136	71	24
8:1	242	198	129	62	19

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

4. Conclusions

1. The researches demonstrated that the methylcellulose with different values of the viscosity significantly affect the adhesive properties of thermosensitive hydrophilic gels obtained from thermosensitive powders, but at the same a wide range of pH.
2. The thermosensitive gels obtained from the powders were characterized by the specific dynamic viscosity.

5. References

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