INFLUENCE OF CHITOSAN ON THE PROPERTIES OF GELS PROTECTING OF THE ESOPHAGEAL MUCOSA

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Abstract

Gastro-esophageal reflux is a term that defines the reverse flow of acid gastric contents into the esophagus. On the other hand, alkaline reflux occurs in the case when alkaline intestinal contents enter the esophagus. The aim of the study was to examine the pharmaceutical properties of gels for the treatment of gastro-esophageal reflux, covering the mucosa, allowing prolonged contact with the esophageal mucosa. Formulations containing the PVP K-30 showed the lowest pH, which is an important feature and can be used in the treatment of advanced alkaline reflux. Gels containing PVP K-90 and chitosan can be used in the treatment of acid reflux. The addition of chitosan significantly increased the dynamic viscosity of the tested gels. The study of the work of adhesion showed the effect of PVP K-30 and PVP K-90 and their concentration on the value of the work of adhesion. The presented studies have shown that it is possible to obtain gels with high adhesion to the esophageal mucous membrane.

Key words: gastro-esophageal reflux, physiological environment of gastro-esophageal, hydrophilic gels, esophageal mucosa, anti-inflammatory drugs, esophageal infections.

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1. Introduction

Gastro-esophageal reflux disease is one of the more common gastroenterological diseases. It may lead to damage to the mucosa of the esophagus and, as a consequence, to serious complications that endanger health. Prevention of symptoms and treatment of the disease is the goal of current pharmacotherapy. Among the recommended drugs are causative agents that reduce the amount of secreted acid and preparations to alleviate the symptoms of the disease. Hydrogels have been designed to protect the mucosal membrane of the esophagus against damaging factors. Gastro-esophageal reflux is a term that defines the reverse flow of acid gastric contents into the esophagus. This symptom is a physiological reflex until the symptoms of disease or tissue damage occur as a result of prolonged exposure of the esophageal mucosa to the acid content of the stomach. The occurrence of these ailments more often than once a week is a prerequisite for naming the disease of gastro-esophageal reflux disease. Another criterion for the division is the reaction of the content causing the symptoms of the disease. If it is caused by acidic contents from the stomach, this form is called acid reflux. On the other hand, alkaline reflux occurs in the case when alkaline intestinal contents enter the esophagus. Damage to the mucous membrane in this case may be due to the action of bile salts or pancreatic enzymes [1-9].

The aim of the study was to examine the pharmaceutical properties of gels for the treatment of gastro-esophageal reflux, covering the mucosa, allowing prolonged contact with the esophageal mucosa.

The most important parameters influencing the properties of the examined gels were examined: pH, dynamic viscosity, adhesion and measurement of surface coverage in vitro with gel. The effect of chitosan on the properties of gels was investigated. Measurements were also made to illustrate the effect of the methylcellulose type on the adhesion strength of the prepared gels. The formulations were prepared with various pH and rheological properties. The tested gel is characterized by adhesive work. On the basis of the tests, the dynamic viscosity of gels was determined. The pH range of the gels allows the selection of the optimal preparation. Gels show the adhesion and the ability to cover the surface of the apparatus simulating the conditions in the esophagus. Gels were characterized by specific dynamic viscosity.

2. Materials and Methods

2.1. Materials

The following chemicals of analytical grade were used in the experiments: chitosan with a deacetylation degree of 93.5%, viscosity of 15 mPa*s, 1% in acetic acid (20°C) (Sea Fisheries Institute, Gdynia, Poland), methylcellulose viscosity of 4000 mPa*s, 2% in H2O (20°C) (Aldrich Chemical Company Ltd. Gillingham, England), polyoxyethylene glycol 200 [PEG-200] (Sigma-Aldrich Chemie GmbH, Germany), 1,2-propylene glycol (Sigma-Aldrich Chemie GmbH, Germany), glycerol (Sigma-Aldrich Chemie GmbH, Germany), polyvinylpyrrolidone K-30 (PVP K-30), Sigma – Aldrich Chemie GmbH, Germany), polyvinylpyrrolidone K-90 (PVP K-90), Sigma – Aldrich Chemie GmbH, Germany), aqua purificata as required by you FP XI.

2.2. Apparatus

- pH meter Elmetron - CX 742 (Elmetron Poland)
- Viscosimeter Rheotest - 2 MLW (Medingen Dresden Germany)
- Texturometer - TA.XT. Plus Texture Analyser (Stable Micro Systems England)
- Device simulating conditions in the esophagus
2.3. Methods
2.3.1. Preparation of hydrophilic gel
The preparation of gel consisted of the following stages:
1. Preparation of gel from methylcellulose and polyvinylpyrrolidone K-30 or K-90. Gels prepared from methylcellulose (4.0g), polyvinylpyrrolidone K-30 or K-90 (1.0g; 3.0g; 5.0g) were combined into a homogenous excipient and supplemented with distilled 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.
2. Preparation of gel with chitosan. Chitosan (1.0 g) was added to the homogeneous gel. The whole was mixed thoroughly and put back to temperature to 5 - 10 °C.

2.3.2. Analytical methods
2.3.2.1. 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. All gels were tested three times, and the results were reported as the average of three measurements at 37°C.

2.3.2.2. Dynamic viscosity measurement
Rheological investigations were performed using a rotational viscosimeter Rheotest 2 Medingen Dresden. The determinations were performed in Ia and II a range on a K-1 cone with a diameter of 36 mm and a 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. All gels were tested three times, and the results were reported as the average of three measurements. The values of the shear stress and viscosity were calculated from measurements at 37°C.

- shear stress for the range Ia: \[ \tau = c \cdot \alpha_{(1-12)} = 85.0 \cdot \alpha_{(1-12)} \]
- viscosity for the range Ia: \[ \eta = \frac{\tau}{D(1-12)} \cdot 100 = \frac{85.0 \cdot \alpha_{(1-12)}}{D(1-12)} \cdot 100 \]
- shear stress for the range IIa: \[ \tau = c \cdot \alpha_{(1-12)} = 820.2 \cdot \alpha_{(1-12)} \]
- viscosity for the range IIa: \[ \eta = \frac{\tau}{D(1-12)} \cdot 100 = \frac{820.2 \cdot \alpha_{(1-12)}}{D(1-12)} \cdot 100 \]

Where: \( \tau \) - shear stress [N/m²]; \( \eta \) – viscosity [mPa*s]; \( \alpha \) - shear angle [°]; \( D \) - shear rate [1/s].
2.3.2.3. Measurement of adhesion
A test for texture profile analysis (TPA) was performed with Exponent Stable Micro Systems Texture Analyzer TA.XT. Plus Texture Analyser Stable Micro Systems England.

To perform the measurements, a probe (P/1S) in the shape of a ball, built in stainless steel, with a diameter of 1 inch was used. The measurement parameters were as follows: speed of downward movement of the probe during the test was 0.5 mm/s, and the lifting speed of the probe was 10 mm/s, the maximum permissible force was 100 g, the dwell time of the probe in the gel was 10 s, and the height at which the probe was raised above the surface of the gel was 40 mm.

The measurement was started by placing the gel in a cylindrical vessel with a transparent plexiglass texturometer. Then, the probe was lowered just above the surface of the gel so that there was direct contact between them (the probe remained in this position for 10 seconds). After selecting the appropriate parameters of the program, the measurement started. The probe began to rise at a speed of 10 mm/s at a height of 40 mm above the surface of the gel after contact with the surface of the gel. All gels were tested three times, and the results were reported as the average of three measurements at 37°C.

2.3.2.4. Measurement of the ability to coat a surface with a gel
Due to the lack of a suitable measuring device, a model simulating conditions in the esophagus was constructed (Figure 1).

The model simulating the in vivo conditions of the esophagus (Figure 1) is a glass tube 25 cm long, modeled on a water cooler, with a double wall, finished on both sides with a wide opening. The model is connected to the thermostat, so that water, previously heated to 37 °C (body temperature), can constantly flow through the space between the inner and outer walls. The outer wall of the glass tube is provided with a measuring scale in millimeters. The model is placed in a vertical position using a tripod so that the measurement resembles physiological conditions the most. A plastic medical syringe with a scale in millimeters is also mounted vertically under the glass tube. It has no piston, the tip is closed, making it possible to collect in it, a hydrogel tube that flows down the walls. The correct measurement of the ability to move the preparation - the time of its flow begins with applying a uniform motion, using a separate medical syringe, 5 ml of hydrogel to the inner wall of the tube. Then it measures the time the hydrogel will flow towards the bottom of the glass instrument. It should also be noted, after what time the formulation will reach a segment of 5 cm, 10 cm, 15 cm, 20 cm and 25 cm. The hydrogel, which overcomes the entire length of the esophagus imitation, is collected into a syringe placed under the glass tube. The measurement time is 10 minutes. Next, the volume of hydrogel that has been drained into the syringe is read or the height on the scale of the glass tube at which the preparation has stopped has been recorded. The results of measurements are the average of three measurements.
3. Results and Discussion
3.1. pH measurement
Gels containing 4.0% methylcellulose (400 cp, 1500 cp, 4000 cp) - their pH ranged from 5.96 to 5.73. The addition of 1.0% chitosan increased the pH from 6.60 to 5.82 (Table 1).
The addition of 1.0%, 3.0%, 5.0% PVP K-30 decreased the pH from 4.37 to 3.80 the gels. A modification of the composition of the tested gels with of 1.0%, 3.0%, 5.0% PVP K-90 decreased the pH from 5.02 to 4.86 the gels (in compare to previous range from 5.96 to 5.73). Further addition of 1.0% chitosan increased the pH from 4.26 to 4.99 (for gels containing 1.0%, 3.0%, 5.0% PVP K-30) and increased the pH from 5.28 to 5.64 (for gels containing 1.0%, 3.0%, 5.0% PVP K-90) respectively (Table 1).
The use of methylcellulose and PVP K-30 or PVP K-90 allows various formulations with a wide range of pH to be obtained. The pH decreased with increasing concentration of PVP K-30 or PVP K-90 in gels (in compare to previous range from 5.96 to 5.73). All gels with the chitosan showed a pH in the physiological range of 4.0–7.0 at 37°C. The addition of chitosan allowed various formulations with a wide range of pH to be obtained. Formulations containing the PVP K-30 showed the lowest pH, which is an important feature and can be used in the treatment of advanced alkaline reflux. Gels containing PVP K-90 and chitosan can be used in the treatment of acid reflux.
Table 1. Influence of chitosan on the pH of gels containing 4.0% methylcellulose and PVP K-30 or PVP K-90

| Gels with 4.0% MC and addition PVP K-30 or PVP K-90 | pH of gels with 4.0% MC and addition PVP K-30 or PVP K-90 | pH of gels with 4.0% MC and addition PVP K-30 or PVP K-90 and with 1.0% chitosan |
|---------------------------------------------------|---------------------------------------------------|--------------------------------------------------|
| MC 400cp                                           | 5.96                                              | 6.60                                             |
| MC 1500cp                                          | 5.77                                              | 5.98                                             |
| MC 4000cp                                          | 5.73                                              | 5.82                                             |
| MC 400 cp + 1.0% PVP K-30                          | 4.37                                              | 4.99                                             |
| MC 1500 cp + 1.0% PVP K-30                         | 4.13                                              | 4.74                                             |
| MC 4000 cp + 1.0% PVP K-30                         | 4.04                                              | 4.56                                             |
| MC 400 cp + 3.0% PVP K-30                          | 3.99                                              | 4.45                                             |
| MC 1500 cp + 3.0% PVP K-30                         | 3.78                                              | 4.38                                             |
| MC 4000 cp + 3.0% PVP K-30                         | 3.77                                              | 4.29                                             |
| MC 400 cp + 5.0% PVP K-30                          | 3.93                                              | 4.47                                             |
| MC 1500 cp + 5.0% PVP K-30                         | 3.86                                              | 4.35                                             |
| MC 4000 cp + 5.0% PVP K-30                         | 3.80                                              | 4.26                                             |
| MC 400 cp + 1.0% PVP K-90                          | 5.02                                              | 5.64                                             |
| MC 1500 cp + 1.0% PVP K-90                         | 4.92                                              | 5.43                                             |
| MC 4000 cp + 1.0% PVP K-90                         | 4.68                                              | 5.28                                             |
| MC 400 cp + 3.0% PVP K-90                          | 5.31                                              | 5.90                                             |
| MC 1500 cp + 3.0% PVP K-90                         | 4.82                                              | 5.82                                             |
| MC 4000 cp + 3.0% PVP K-90                         | 4.60                                              | 5.64                                             |
| MC 400 cp + 5.0% PVP K-90                          | 5.22                                              | 5.52                                             |
| MC 1500 cp + 5.0% PVP K-90                         | 4.95                                              | 5.46                                             |
| MC 4000 cp + 5.0% PVP K-90                         | 4.86                                              | 5.28                                             |

MC-methylcellulose, PVP-polyvinylpyrrolidone

3.2. Rheological tests
Rheological studies demonstrated that the gels obtained from methylcellulose 400 cp, 1500 cp and 4000 cp possessed a dynamic viscosity of the formulation from 142 to 365 mPa*s. The addition of 1.0% chitosan increased the viscosity from 246 to 457 mPa*s (Table 2).

A modification of the composition of the tested gels with 1.0%, 3.0%, 5.0% PVP K-30 increased the viscosity from 180 to 486 mPa*s the gels. The addition of 1.0%, 3.0%, 5.0% PVP K-90 increased the dynamic viscosity of formulations from 250 to 499 mPa*s the gels (Table 2). The enrichment of the composition of the tested gels with 1.0% chitosan resulted in increased dynamic viscosity of the formulation from 298 to 510 mPa*s for PVP K-30 gels and from 370 to 591 mPa*s for PVP K-90 gels (Table 2).

Rheological investigations revealed an increase in the dynamic viscosity of preparations with PVP K-30 or PVP-90 in comparison to the gels without PVP K-30 or PVP-90. The dynamic viscosity increased with increasing concentration PVP K-30 or PVP K-90 of gels. Addition chitosan high increased dynamic viscosity tested gels.
### Table 2. Influence of chitosan on the viscosity of gels containing 4.0% methylcellulose and PVP K-30 or PVP K-90

| Gels with 4.0% MC and addition PVP K-30 or PVP K-90 | Dynamic viscosity of gels with 4.0% MC and addition PVP K-30 or PVP K-90 [mPa*s] | Dynamic viscosity of gels with 4.0% MC and addition PVP K-30 or PVP K-90 and with 1.0% chitosan [mPa*s] |
|--------------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| MC 400cp                                         | 142                                                                             | 246                                                                             |
| MC 1500cp                                        | 254                                                                             | 328                                                                             |
| MC 4000cp                                        | 365                                                                             | 457                                                                             |
| MC 400 cp + 1.0% PVP K-30                        | 180                                                                             | 298                                                                             |
| MC 1500 cp + 1.0% PVP K-30                        | 289                                                                             | 380                                                                             |
| MC 4000 cp + 1.0% PVP K-30                        | 399                                                                             | 462                                                                             |
| MC 400 cp + 3.0% PVP K-30                        | 210                                                                             | 340                                                                             |
| MC 1500 cp + 3.0% PVP K-30                        | 299                                                                             | 389                                                                             |
| MC 4000cp + 3.0% PVP K-30                        | 420                                                                             | 490                                                                             |
| MC 400cp + 5.0% PVP K-30                         | 300                                                                             | 410                                                                             |
| MC 1500cp + 5.0% PVP K-30                         | 365                                                                             | 486                                                                             |
| MC 4000cp + 5.0% PVP K-30                         | 486                                                                             | 510                                                                             |
| MC 400 cp + 1.0% PVP K-90                         | 250                                                                             | 370                                                                             |
| MC 1500cp + 1.0% PVP K-90                         | 365                                                                             | 430                                                                             |
| MC 4000cp + 1.0% PVP K-90                         | 470                                                                             | 578                                                                             |
| MC 400cp + 3.0% PVP K-90                         | 289                                                                             | 399                                                                             |
| MC 1500cp + 3.0% PVP K-90                         | 390                                                                             | 478                                                                             |
| MC 4000cp + 3.0% PVP K-90                         | 498                                                                             | 527                                                                             |
| MC 400cp + 5.0% PVP K-90                          | 320                                                                             | 410                                                                             |
| MC 1500cp + 5.0% PVP K-90                         | 465                                                                             | 550                                                                             |
| MC 4000cp + 5.0% PVP K-90                         | 499                                                                             | 591                                                                             |

MC - methylcellulose, PVP - polyvinylpyrrolidone

### 3.3. Adhesion tests

Tested gels possessed the work of adhesion - the adhesiveness at 37 °C. Work of adhesion studies demonstrated that the gels obtained from methylcellulose 400 cp, 1500 cp and 4000 cp possessed a value of work of adhesion of the formulation from 39.2 to 51.9 g/s. The addition of 1.0% chitosan increased the viscosity from 74.1 to 78.0 g/s (Table 3).

A modification of the composition of the tested gels with 1.0%, 3.0%, 5.0% PVP K-30 increased the viscosity from 42.8 to 48.3 g/s the gels. The addition of 1.0%, 3.0%, 5.0% PVP K-90 increased the dynamic viscosity of formulations from 60.9 to 65.4 g/s the gels (Table 3). The enrichment of the composition of the tested gels with 1.0% chitosan resulted in increased dynamic viscosity of the formulation from 76.2 to 86.0 g/s for PVP K-30 gels and from 80.0 to 96.0 g/s for PVP K-90 gels (Table 3).

Value the adhesiveness above 5.0g/s shows good adhesion. The presented studies have shown that it is possible to obtain gels with high adhesion to the esophageal mucous membrane. The study of the work of adhesion showed the effect of PVP K-30 and PVP K-90 and their concentration on the value of the work of adhesion. The gels showed...
good adhesion. The gels with 1.0% chitosan showed high adhesion in compare to gels without chitosan. The present study has shown that it is possible to obtain gels with high adhesion properties to esophageal mucous membrane, with a dynamic viscosity above 100 mPa*s.

Table 3. Influence of chitosan on the work of adhesion of gels containing 4.0% methylcellulose and PVP K-30 or PVP K-90

| Gels with 4.0% MC and addition PVP K-30 or PVP K-90 | Work of adhesion of gels with 4.0% MC and addition PVP K-30 or PVP K-90 [g/s] | Work of adhesion of gels with 4.0% MC and addition PVP K-30 or PVP K-90 and with 1.0 % chitosan [g/s] |
|-----------------------------------------------------|---------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| MC 400cp                                            | 39.2                                                                             | 74.1                                                                                           |
| MC 1500cp                                           | 48.3                                                                             | 76.0                                                                                           |
| MC 4000cp                                           | 51.9                                                                             | 78.0                                                                                           |
| MC 400 cp + 1.0% PVP K-30                           | 42.8                                                                             | 76.2                                                                                           |
| MC 1500 cp + 1.0% PVP K-30                          | 44.0                                                                             | 77.8                                                                                           |
| MC 4000 cp + 1.0% PVP K-30                          | 46.5                                                                             | 79.0                                                                                           |
| MC 400 cp + 3.0% PVP K-30                           | 43.9                                                                             | 74.3                                                                                           |
| MC 1500 cp + 3.0% PVP K-30                          | 45.6                                                                             | 76.9                                                                                           |
| MC 4000 cp + 3.0% PVP K-30                          | 47.3                                                                             | 79.8                                                                                           |
| MC 400 cp + 5.0% PVP K-30                           | 45.2                                                                             | 80.4                                                                                           |
| MC 1500 cp + 5.0% PVP K-30                          | 46.0                                                                             | 82.3                                                                                           |
| MC 4000 cp + 5.0% PVP K-30                          | 48.3                                                                             | 86.0                                                                                           |
| MC 400 cp + 1.0% PVP K-90                           | 60.9                                                                             | 80.0                                                                                           |
| MC 1500 cp + 1.0% PVP K-90                          | 61.8                                                                             | 86.1                                                                                           |
| MC 4000 cp + 1.0% PVP K-90                          | 63.5                                                                             | 89.0                                                                                           |
| MC 400 cp + 3.0% PVP K-90                           | 59.0                                                                             | 80.6                                                                                           |
| MC 1500 cp + 3.0% PVP K-90                          | 62.7                                                                             | 87.0                                                                                           |
| MC 4000 cp + 3.0% PVP K-90                          | 64.0                                                                             | 90.3                                                                                           |
| MC 400 cp + 5.0% PVP K-90                           | 60.9                                                                             | 82.5                                                                                           |
| MC 1500 cp + 5.0% PVP K-90                          | 63.6                                                                             | 89.2                                                                                           |
| MC 4000 cp + 5.0% PVP K-90                          | 65.4                                                                             | 96.0                                                                                           |

MC-methylcellulose, PVP-polyvinylpyrrolidone

3.4. Measurement of the ability to coat a surface with a gel

Tested gels possessed ability surface coating with gel at 37 °C.

The tests can be coated with a gel. The coating capacity depends on the initial methylcellulose viscosity (400 cp, 1500 cp, 4000 cp). At a viscosity of 400 cp, it flows out into the syringe 4.5 ml and at 4000 cp 4.0 ml. After the addition of 1.0 % chitosan, the values are 2.0 ml for methylcellulose gel 400 cp and 1.0 ml 4000cp (Table 4).

Modification of the composition of the tested gels with the addition of 1.0%, 3.0%, 5.0% PVP K-30 reduced the gel outflow to (4.3-2.9 ml for PVP K-30 and 3.4-2.0 ml for PVP K-90). The enrichment of the composition of the tested gels with 1.0 % chitosan reduced the gel outflow to (1.4-0.1 ml for PVP K-30 and 0.3-0.0 ml for PVP K-90) (Table 4).
The presented studies have shown that it is possible to obtain gels with high adhesion to the esophageal mucous membrane. Examination of the ability to coat the surface with gel showed that PVP K-30 and PVP K-90 and their concentration affect the ability of the gel to adhere to the surface. Gels with 1.0% chitosan showed high adhesion compared to gels without chitosan. Compositions containing methylcellulose 4000 cp, 1.0%, 3.0%, 5.0% PVP K-90 and 1500 cp, 3.0%, 5.0% PVP K-90 are maintained on the surface to be tested and do not flow out (Table 4).

Table 4. Influence of chitosan on ability of gel to coat a surface with a gel containing 4.0% methylcellulose and PVP K-30 or PVP K-90

| Gels with 4.0% MC and addition PVP K-30 or PVP K-90 | Surface coating with gel of gels with 4.0% MC and addition PVP K-30 or PVP K-90 [cm] after 10 min | Surface coating with gel of gels with 4.0% MC and addition PVP K-30 or PVP K-90 and with 1.0% chitosan [cm] after 10 min |
|--------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|
| MC 400cp                                         | 25.0 + 4.5 ml S                                                  | 25.0 + 2.0 ml S                                                 |
| MC 1500cp                                        | 25.0 + 4.1 ml S                                                 | 25.0 + 1.5 ml S                                                 |
| MC 4000cp                                        | 25.0 + 4.0 ml S                                                 | 25.0 + 1.0 ml S                                                 |
| MC 400 cp + 1.0% PVP K-30                       | 25.0 + 4.3 ml S                                                 | 25.0 + 1.4 ml S                                                 |
| MC 1500 cp + 1.0% PVP K-30                       | 25.0 + 3.9 ml S                                                 | 25.0 + 1.3 ml S                                                 |
| MC 4000 cp + 1.0% PVP K-30                       | 25.0 + 3.5 ml S                                                 | 25.0 + 1.0 ml S                                                 |
| MC 400 cp + 3.0% PVP K-30                       | 25.0 + 3.8 ml S                                                 | 25.0 + 1.2 ml S                                                 |
| MC 1500 cp + 3.0% PVP K-30                       | 25.0 + 3.6 ml S                                                 | 25.0 + 0.3 ml S                                                 |
| MC 4000 cp + 3.0% PVP K-30                       | 25.0 + 3.0 ml S                                                 | 25.0 + 0.2 ml S                                                 |
| MC 400 cp + 5.0% PVP K-30                       | 25.0 + 3.3 ml S                                                 | 25.0 + 0.3 ml S                                                 |
| MC 1500 cp + 5.0% PVP K-30                       | 25.0 + 3.1 ml S                                                 | 25.0 + 0.1 ml S                                                 |
| MC 4000 cp + 5.0% PVP K-30                       | 25.0 + 2.9 ml S                                                 | 25.0 + 0.1 ml S                                                 |
| MC 400 cp + 1.0% PVP K-90                       | 25.0 + 3.4 ml S                                                 | 25.0 + 0.3 ml S                                                 |
| MC 1500 cp + 1.0% PVP K-90                       | 25.0 + 3.2 ml S                                                 | 25.0 + 0.1 ml S                                                 |
| MC 4000 cp + 1.0% PVP K-90                       | 25.0 + 3.0 ml S                                                 | 25.0 + 0.0 ml S                                                 |
| MC 400 cp + 3.0% PVP K-90                       | 25.0 + 3.3 ml S                                                 | 25.0 + 0.2 ml S                                                 |
| MC 1500 cp + 3.0% PVP K-90                       | 25.0 + 3.1 ml S                                                 | 25.0 + 0.0 ml S                                                 |
| MC 4000 cp + 3.0% PVP K-90                       | 25.0 + 2.9 ml S                                                 | 25.0 + 0.0 ml S                                                 |
| MC 400 cp + 5.0% PVP K-90                       | 25.0 + 3.0 ml S                                                 | 25.0 + 0.1 ml S                                                 |
| MC 1500 cp + 5.0% PVP K-90                       | 25.0 + 2.6 ml S                                                 | 25.0 + 0.0 ml S                                                 |
| MC 4000 cp + 5.0% PVP K-90                       | 25.0 + 2.0 ml S                                                 | 25.0 + 0.0 ml S                                                 |

MC-methylcellulose, PVP-polyvinylpyrrolidone, S-syringe, 25.0 + 1.0 ml S means 25.0 cm coat gel + 1.0 ml in syringe.

This study shows the effect of the chitosan used on pH, dynamic viscosity and adhesiveness of gels. These gels have the ability to coat the in vitro surface. The results obtained in experimental studies have shown that it is possible to produce a formulation with optimal pharmaceutical and application properties. Due to the wide pH range, high dynamic viscosity, adhesion and the ability to cover the test surface, these gels can be adjusted to the individual needs of patients.
4. Conclusions
The studies have shown the effect of PVP K-30 and PVP K-90 and chitosan on pH, dynamic viscosity, adhesiveness and in vitro surface coverage of methylcellulose gel. The formulations obtained have a pH in the desired physiological range, high dynamic viscosity, adhesion and the ability to coat the surface to be tested. The results obtained in experimental studies have shown that it is possible to produce a formulation with optimal pharmaceutical and application properties. The test gels, due to their adhesive properties, should remain on the mucous membrane of the esophagus for a long time and protect it against adverse effects of stomach or bile content. The wide pH range of the tested gels enables the selection of the formulation with the optimal pH for the esophagus depending on the type of reflux. The presented assumptions and in vitro tests require verification in vivo, which is the goal of further research.

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6. References
[1] Raban M, Żak A, Litak J, Turska M, Grochowski C; (2017) Gastroesophageal reflux disease – unit description, diagnosis and treatment. J. of Education, Health and Sport 7, 215-225.
[2] Banks M; (2009) The modern investigation and management of gastro-oesophageal reflux disease (GERD). Clinical Medicine 1, 18-27.
[3] Vakil N, van Zanten SV, Kahrilas T; (2006) The Montreal definition and classification of gastroesophageal reflux disease: a global evidence – based consensus. Am. J. of Gastroenterology 101, 1900-1920.
[4] Katz PO, Gerson LB, Vela MF; (2013) Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am. J. of Gastroenterology 108, 308-328. DOI: 10.1038/ajg.2012.444.
[5] Numans ME, Lau J, de Wit NJ, Bonis PA; (2004) Short-term treatment with proton-pump inhibitors as a test for gastroesophageal reflux disease: a meta-analysis of diagnostic test characteristics. Annals of Internal Medicine 7, 518-527.
[6] Singh M, Lee J, Gupta N, Gaddam S, Smith BK, Wani SB; (2013) Weight loss can lead to resolution of gastroesophageal reflux disease symptoms: a prospective intervention trial. Obesity Silver Spring 21, 284-290. DOI: 10.1002/oby.20279.
[7] Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CAJ; (2006) Body-Mass Index and Symptoms of Gastroesophageal Reflux in Women. N Engl J Med 354, 2340-2348.
[8] Ze EY, Kim BJ, Kang H, Kim JG; (2017) Abdominal Visceral to Subcutaneous Adipose Tissue Ratio Is Associated with Increased Risk of Erosive Esophagitis. Dig Dis Sci. 62, 1265-1271. DOI: 10.1007/s10620-017-4467-4.
[9] Gao F, Gao Y, Chen X, Qian J, Zhang J; (2017) Comparison of oesophageal function tests between Chinese non-erosive reflux disease and reflux hypersensitivity patients. BMC Gastroenterol 67, 1-7. DOI: 10.1186/s12876-017-0624-7