# The influence of selected polymers on the rheological properties of hydrogels with chitosan applied on the skin

**Maria Szcześniak*, Bożena Grimling, Jan Meler, Bożena Karolewicz**

*Department of Pharmaceutical Technology,*
*Faculty of Pharmacy, Wrocław Medical University,*
*ul. Borowska 211 A, 50-556 Wrocław, Poland*
*e-mail: maria.szczesniak@umed.wroc.pl*

***Abstract***

*The aim of the study was to evaluate the effect of methylcellulose and carboxymethylcellulose on the rheological properties of hydrogels applied to skin on chitosan in the presence of the additives propylene glycol and glycerol. Rheological studies showed that the tested gels are non-newtonian systems, and have thixotropic properties. Substrates made of methylcellulose and chitosan are characterised by higher shear values than those obtained with carboxymethylcellulose. The addition of polymers had a positive influence on the dispersion of hydrogels, and the addition of excipients increased firmness, consistency and cohesiveness of the gels. Larger increases were observed with the addition of 10% of glycol propylene and glycerol contents for methylcellulose and of 20% of carboxymethylcellulose.*

***Key words****: hydrogels, chitosan, rheological parameters, pharmaceutical availability*

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# 1. Introduction

Hydrogels in the form of dressings are used on the skin for treatment of wounds, bed sores and burns. Modifications of properties may also allow the use of hydrogels in mucosal, oral or ocular medicine [1–3].

Cellulose derivatives used to make hydrogels facilitate the dispersion and suspension of a drug substance in the medium and increase the viscosity of the solutions. They are a component of substrates of various drug forms [4–11].

Chitosan has the ability to make films, hydrogels, nanoparticles and microspheres. It is used in the production of dressings, cosmetics, drug technology and tissue engineering [12].

The aim of the study was to evaluate the effect of methylcellulose and carboxymethylcellulose on the rheological properties of hydrogels to be applied to the skin on chitosan in the presence of the additives propylene glycol and glycerol.

# 2. Materials and methods

## 2.1. Materials

Methylcellulose (Serva), carboxymethylcellulose (Serva), propylene glycol-1,2 (Sigma-Aldrich), glycerol (Chempur), chitosan type 652 France, hydrocortisone (Polfa Pabianianice) and purified water to Polish Pharmacopoeia 10$^{th}$ Ed were used in the present study.

## 2.2. Preparation of hydrogels

Chitosan hydrogels at 1% concentration and 4% methylcellulose or 4% carboxymethlcellulose containing 1% hydrocortisone, 1,2-propylene glycol or glycerol and distilled water were prepared ex tempore. The compositions of the investigated gels are presented in Tables 1 and 2.

## 2.3. Consistency test

A texture profile analysis (TPA) test was performed using an Exponent Stable Micro Systems Texture Analyzer TAXT Plus. The texture of the gel was set by examining the hardness, consistency and density, using the back extrusion method, which consists of the process of retracting extrusion. Test parameters were as follows: force of 2 g, speed of 2 mm/s, distance of 20 mm and diameter disc of 35 mm [13].

## 2.4. Dynamic viscosity test

A dynamic viscosity test was carried out using a rotational viscosimeter Rheotest 2 Medingen Dresden.

The determinations were performed in I a range on K-1 cone with a diameter of 36 mm at 37°C. The values of shear stress and viscosity were calculated from measurements [14].

## 2.5. Examination of pharmaceutical availability of hydrocortisone

The process of hydrocortisone release from a hydrophilic base was carried out according to the Polish Pharmacopoeia 10$^{th}$ Ed. The concentration of hydrocortisone was determined with the Jasco V-650 spectrophotometer at a wavelength of 241 nm according to Polish Pharmacopoeia 10$^{th}$ Ed.

## 3. Results and discussion

The study investigated the influence of 1% chitosan on the physicochemical properties of hydrogels with 4% methylcellulose or carboxymethylcellulose in the presence of the additives propylene glycol-1,2 and glycerol.

The texture of the gel was set by examining the hardness, consistency and density.

The gels with methylcellulose and chitosan had greater hardness, consistency and density than gels made from carboxymethlcellulose (Tables 1 and 2).

**Table 1.** Texture parameters and the spread of hydrogels

| The composition of the investigated gels | Hardness [g] | Consistency [g] | Density [g*s] | Wheel field [cm$^2$] |
|---|---|---|---|---|
| 1% chitosan, 4% methylcellulose | 92.44 | 546.58 | 46.14 | 16.08 |
| 1% chitosan, 4 % methylcellulose, 10% propylene glycol-1,2 | 359.23 | 1553.11 | 109.24 | 18.49 |
| 1% chitosan, 4% methylcellulose, 20% propylene glycol-1,2 | 246.59 | 1480.89 | 126.08 | 19.02 |
| 1% chitosan, 4% methylcellulose, 10% glycerol | 344.22 | 2098.41 | 140.30 | 18.06 |
| 1% chitosan, 4% methylcellulose, 20% glycerol | 193.89 | 860.99 | 93.9 | 22.3 |
| 1% chitosan, 4% methylcellulose, 5% glycerol, 5% propylene glycol-1,2 | 468.77 | 2189.59 | 143.01 | 18.48 |
| 1% chitosan, 4% methylcellulose, 10% glycerol, 10% propylene glycol-1,2 | 201.44 | 1337.25 | 106.49 | 19.39 |

The hardness of gels with 1% chitosan and 4% methylcellulose and propylene glycol-1,2 or glycerol were from 193.89 to 468.77 g and was 92.44 g for the reference gels. However, the hardness of gels with 1% chitosan and 4% carboxymethylcellulose and propylene glycol-1,2 or glycerol were from 52.61 to 96.58 g and was 33.50 g for the reference gels. The consistency of the gels with methylcellulose was from 860.99 to 2189.59 g and 355.86 to 585.00 g for carboxymethylcellulose. The highest density was 143.01 g*s for the gel containing chitosan, 4% methylcellulose, 5% glycerol and 5% propylene glycol-1,2, and was 50.08 g*s for the formulation with carboxymethlcellulose and 20% propylene glycol-1,2.

The spread of gels composed of carboxymethylcellulose and chitosan was greater than for methylcellulose and chitosan. The addition of 1,2-propylene glycol and glycerol induced an increase in the spread of methylcellulose gels and a decrease for carboxymethylcellulose gels.

**Table 2.** Texture parameters and the spread of hydrogels

| The composition of the investigated gels | Hardness [g] | Consistency [g] | Density [g*s] | Wheel field [cm$^2$] |
|---|---|---|---|---|
| 1% chitosan, 4% carboxymethylcellulose | 33.50 | 245.76 | 14.89 | 21.83 |
| 1% chitosan, 4% carboxymethylcellulose, 10% propylene glycol-1,2 | 54.43 | 371.55 | 23.94 | 19.05 |
| 1% chitosan, 4% carboxymethylcellulose, 20% propylene glycol-1,2 | 96.58 | 585.00 | 50.08 | 21.03 |
| 1% chitosan, 4% carboxymethylcellulose, 10% glycerol | 95.73 | 515.74 | 40.83 | 21.65 |
| 1% chitosan, 4% carboxymethylcellulose, 20% glycerol | 86.82 | 414.55 | 29.63 | 18.47 |
| 1% chitosan, 4% carboxymethylcellulose, 5% glycerol, 5% propylene glycol-1,2 | 52.61 | 355.86 | 23.66 | 21.00 |
| 1% chitosan, 4% carboxymethylcellulose, 10% glycerol, 10% propylene glycol-1,2 | 90.45 | 582.85 | 45.17 | 20.03 |

Methylcellulose, carboxymethylcellulose and hydrophilising substances influencethe increasing shear stress of gels with 1% chitosan, with a shear rate from 11.10 to 4860.00 D [s$^{-1}$] (Table 3). Shear stress in the presence of methylcellulose gels with 1% chitosan was from 5376.25 to 9458.75 N/m$^2$. The highest value of shear stress (9458.75 N/m$^2$) was found with the addition of 5% propylene glycol-1,2 and 5% glycerol. Shear stress in the presence of carboxymethylcellulose gels with 1% chitosan was from 1298.25 to 2528.75 N/m$^2$, with the highest value being found for the addition of 10% propylene glycol-1,2 and 10% glycerol (2528.75 N/m$^2$).

The study of pharmaceutical availability was performed using the method from the Polish Pharmacopoeia 10$^{th}$ Ed. The release process of all formulations followed first order kinetics. The pharmaceutical availability of hydrocortisone from methylcellulose and chitosan-based gels increased with the addition of glycerol (K 0.03403 h$^{-1}$), and propylene glycol for CMC gels (K 0.0308 h$^{-1}$), as compared to reference gels (Table 4).


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**Table 3.** Viscosity parameters of hydrogels determined at 37°C and shear rates of 4860.00 [$s^{-1}$]

| The composition of the investigated gels | Shear stress $N/m^2$ | Viscosity mPa s | The composition of the investignated gels | Shear stress $N/m^2$ | Viscosity mPa s |
|---|---|---|---|---|---|
| 1% chitosan, 4% methylcellulose | 7392.00 | 152.1 | 1% chitosan, 4% carboxymethylcellulose | 722.50 | 14.87 |
| 1% chitosan, 4% methylcellulose, 10% propylene glycol-1,2 | 7416.25 | 152.6 | 1% chitosan, 4% carboxymethylcellulose, 10% propylene glycol-1,2 | 1615.00 | 33.24 |
| 1% chitosan, 4% methylcellulose, 20% propylene glycol-1,2 | 8420.00 | 173.25 | 1% chitosan, 4% carboxymethylcellulose, 20% propylene glycol-1,2 | 1976.25 | 40.66 |
| 1% chitosan, 4% methylcellulose, 10% glycerol | 8971.25 | 184.59 | 1% chitosan, 4% carboxymethylcellulose, 10% glycerol | 1636.25 | 33.67 |
| 1% chitosan, 4% methylcellulose, 20% glycerol | 5376.25 | 110.62 | 1% chitosan, 4% carboxymethylcellulose, 20% glycerol | 2507.50 | 51.59 |
| 1% chitosan, 4% methylcellulose, 5% glycerol, 5% propylene glycol-1,2 | 9458.75 | 194.62 | 1% chitosan, 4% carboxymethylcellulose, 5% glycerol, 5% propylene glycol-1,2 | 1298.25 | 26.76 |
| 1% chitosan, 4% methylcellulose, 10% glycerol, 10% propylene glycol-1,2 | 8330.00 | 171.40 | 1% chitosan, 4% carboxymethylcellulose, 10% glycerol, 10% propylene glycol-1,2 | 2528.75 | 52.03 |

**Table 4**. Release rate constant [K $h^{-1}$] of hydrocortisone from hydrogels on the basis of chitosan.

| The composition of the gels | Release rate constant [K $h^{-1}$] | Correlation coefficient R | The composition of the gels | Release rate constant [K $h^{-1}$] | Correlation coefficient R |
|---|---|---|---|---|---|
| 4% methylcellulose, 1% chitosan | 0.02637 | 0.9924 | 4% carboxymethylcellulose 1% chitosan | 0.02790 | 0.9957 |
| 4% methylcellulose, 1% chitosan, 20% propylene glycol-1,2 | 0.02643 | 0.9974 | 4% carboxymethylcellulose, 1% chitosan 20% propylene glycol-1,2 | 0.03080 | 0.9980 |
| 4% methylcellulose, 1% chitosan, 20% glycerol | 0.03403 | 0.9969 | 4% carboxymethylcellulose, 1% chitosan, 20% glycerol | 0.02747 | 0.9968 |


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Use of chitosan and methylcellulose or carboxymethylcellulose and hydrophilic substances have a beneficial effect on the physicochemical properties of the gels. This provides appropriate application, adhesion and ease of spreading the drug on the skin.

## 4. Conclusions

1. Rheological studies showed that tested gels are non-newtonian systems and have thixotropic properties. Substrates made of methylcellulose and chitosan are characterised by higher shear values than those obtained with carboxymethylcellulose. The addition of polymers had a positive influence on the dispersion of hydrogels.
2. The addition of excipients increased firmness, consistency and cohesiveness of gels. Greater increases were observed for 5% glycol propylene and 5% glycerol contents for methylcellulose and 20% glycol propylene for carboxymethylcellulose.

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