EFFECT OF CHITOSAN ON THE RHEOLOGICAL PROPERTIES OF HYDROGELS BASED ON SODIUM CARBOXYMETHYLCELLULOSE

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Abstract

The aim of the study was to evaluate the effect of changing the concentrations of chitosan on the rheological properties of the obtained formulation. Hydrogels were prepared with 1% hydrocortisone containing 4% sodium carboxymethylcellulose with the addition of chitosan, propylene glycol-1,2 or polyethylene glycol 400 and glycerol or paraffin. The concentration of chitosan and excipients affects the rheological properties of gels and the pharmaceutical availability of hydrocortisone. Increasing the concentration of chitosan have influence on increasing the viscosity, hardness, and cohesiveness of the tested gels.

***Key words**: chitosan, sodium carboxymethylcellulose, pharmaceutical availability, rheological parameters*

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1. Intoduction

Sodium carboxymethylcellulose is widely used in pharmaceutical, cosmetic and food industries. In the pharmaceutical technology it is used for the production of gels, bioadhesive forms, emulsions, suspensions, granules, tablets. Hydrogels containing carmellose sodium are characterized by good release of the active substances [1-5].

Chitosan in various forms of pharmaceutical favourably affects the application properties and the pharmaceutical availability of many drugs [6-9].

The aim of the study was to evaluate the effect of changing the concentrations of chitosan on the rheological properties of the obtained formulation and pharmaceutical drug substance availability.

2. Materials and methods

2.1. Materials

Hydrocortisone (Polfa Pabianice, Poland), carboxymethylcellulose sodium (Sigma-Aldrich Gmbh Germany), propylene glycol-1,2 (Sigma-Aldrich Gmbh Germany), polyethylene glycol 400 (Loba Feinchemie, Fischamend), paraffin (Pharma Cosmetic Poland), glycerol (Chempur Poland), chitosan type 652 France, purified water to Polish Pharmacopoeia 9th Ed.

2.2. Preparation of hydrogels

Carboxymethylcellulose sodium hydrogels at 4% concentration and 1-5% chitosan containing 1% hydrocortisone were prepared ex tempore by mixing of solid and liquid components. The solid component was obtained by mixing of hydrocortisone, carboxymethylcellulose sodium and chitosan whereas the liquid component by mixing of 1,2-propylene glycol or polyethylene glycol 400 with paraffin, glycerol and distilled water.

2.3. Consistency test

TPA test was performed with Exponent Stable Micro Systems texture analyzer [10].

2.4. Dynamic viscosity test

Was carried out using the Rheotest 2. The values of the shear stress and viscosity were calculated from measurements [11].

2.5. Examination of pharmaceutical availability of hydrocortisone

The process of hydrocortisone release from hydrophilic base was carried out according to the method based on active substance diffusion through a semi-permeable membrane. Each of prepared hydrogels was placed in six Hanson diffusion chambers, which were next placed in a 6-position thermostated apparatus for determination active substance according to Polish Pharmacopeia 9thEd. Study was conducted at 37 °C and 7 pH. The concentration of

hydrocortisone was determined with the Jasco V-650 spectrophotometr at wavelength of 241 nm according to Polish Pharmacopoeia 9thEd.

3. Results and Discussion

The study on the effect of the chitosan addition to the gel prepared with 4% carboxymethylcellulose sodium and 15% propylene glycol-1,2 or 15% polyethylene glycol 400, 5% paraffin, 5% glycerol on rheological properties of gels and pharmaceutical availability of 1% hydrocortisone. Hydrocortisone release process is in accordance with first order kinetics. Logarithm from percentage of hydrocortisone as function of time is presented in Fig. 1. The obtained results were used to determine the release rate constants, which were presented in Table 1. The addition of 1-5% of chitosan and excipients influences on acceleration of hydrocortisone release. Gel containing 1 and 2% chitosan, 15% propylene glycol-1,2 and 5% paraffin is characterized by the highest pharmaceutical availability. Analysis of correlation and test NIR and Bown-Forsythe showed that the results are statistically significant.

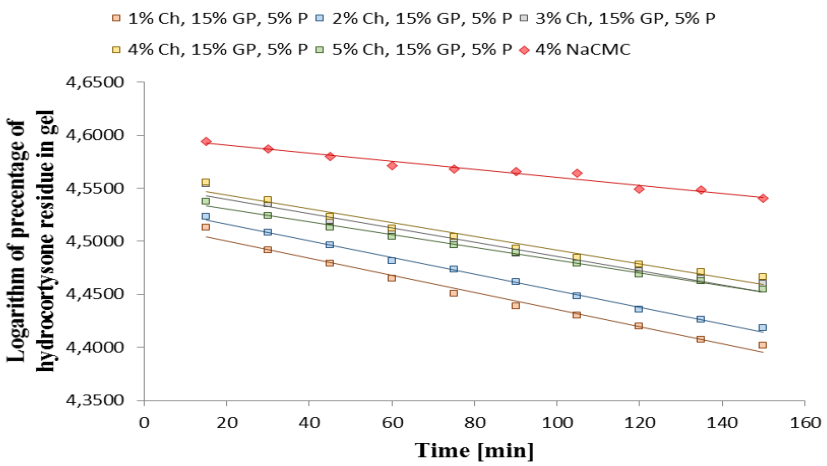

Figure 1. Influence of chitosan additive on hydrocortisone release from sodium carboxymethylcellulose hydrogels.

The addition of chitosan increases the hardness, cohesion and consistency of tested gels (Fig. 2). The highest hardness was found for the formulation containing 15% of 1,2-propylene glycol, 5% of glycerol and 4-5% of chitosan. Hydrogels with paraffin shows lower hardness difference (0,1258 to 0,1684 kg), gels with glycerol, shows respectively from 0,1255 to 0,3668 kg. The concentrations of chitosan gels influences on increasing of cohesiveness, with the exception of the formulation with 15% polyethylene glycol 400, 5% paraffin and 4-5% of the polymer. The highest increase of consistency was found for the

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gels with 15% of 1,2-propylene glycol and 5% glycerol. After 7 days of storage, the value of the studied parameters increased.

Table 1. The composition of the gels and the release rate constants of hydrocortisone

Hydrogels	**Release rate constants K [h^{-1}]**	**Correlation coefficient R**
1% Chitosan, 15%propylene glycol-1,2, 5% paraffin	0.04854	0.9924
2% Chitosan, 15% propylene glycol-1,2, 5% paraffin	0.04677	0.9980
3% Chitosan, 15% propylene glycol-1,2, 5% paraffin	0.04045	0.9854
4% Chitosan, 15% propylene glycol-1,2, 5% paraffin	0.03882	0.9848
5% Chitosan, 15% propylene glycol-1,2, 5% paraffin	0.03559	0.9974
1% Chitosan, 15% propylene glycol-1,2, 5% glycerol	0.03604	0.9936
2% Chitosan, 15% propylene glycol-1,2, 5% glycerol	0.03864	0.9876
3% Chitosan, 15% propylene glycol-1,2, 5% glycerol	0.04038	0.9968
4% Chitosan, 15% propylene glycol-1,2, 5% glycerol	0.03711	0.9953
5% Chitosan, 15% propylene glycol-1,2, 5% glycerol	0.03527	0.9914
1% Chitosan, 15% polyethylene glycol, 5% glycerol	0.03595	0.9957
2% Chitosan, 15% polyethylene glycol, 5% glycerol	0.03598	0.9956
3% Chitosan, 15% polyethylene glycol, 5% glycerol	0.03512	0.9942
4% Chitosan, 15% polyethylene glycol, 5% glycerol	0.03821	0.9968
5% Chitosan, 15% polyethylene glycol, 5% glycerol	0.03583	0.9969
4% sodium carboxymethylcellulose	0.02262	0.9858

Tested gels are non-Newtonian, thixotropic systems (Fig. 3). The addition of 1-5% of the chitosan influences on the increase in shear stress. The highest value of stress, from 2592,50 N/m^2 to 3803,75 N/m^2, was found for formulation containing 15% polyethylene glycol 400 and 5% glycerol. Mediums with 15% of

1,2-propylene glycol and 5% of paraffin or glycerol was characterized with stress in the range from 1742,50 N/m^2 to 3081,00 N/m^2.

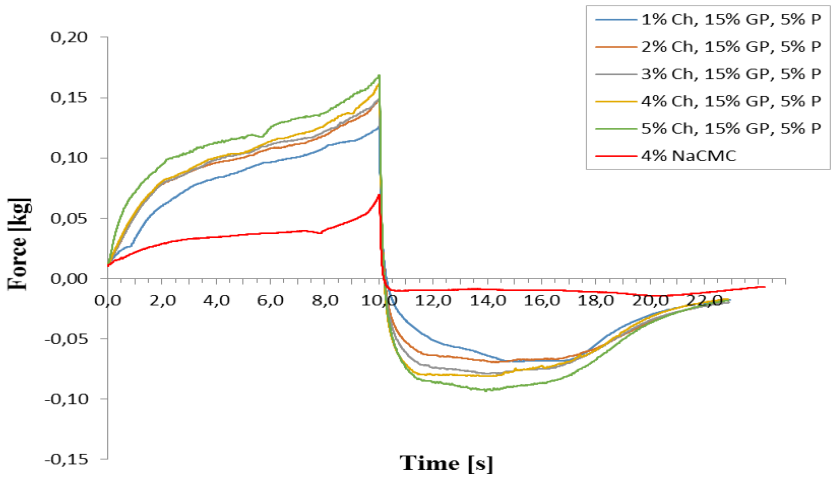

Figure 2. Influence of chitosan on consistency the sodium carboxymethylcellulose hydrogels.

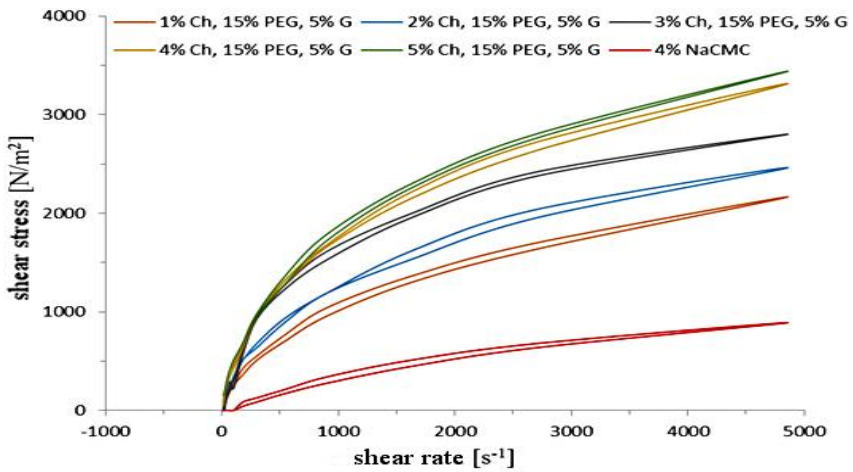

Figure 3. Flow curves of hydrogels on the basis 4% sodium carboxymethylcellulose containing chitosan**.**

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Depending on the qualitative and quantitative composition of the gels obtained of different release rates and physicochemical properties. Tested gels ensure adequate application properties and spreading on the skin.

4. Conclusions

1. Increasing the concentration of chitosan have influence on the viscosity, hardness, and cohesiveness of the tested gels.
2. Excipients and chitosan increases the rate of release of hydrocortisone. The largest pharmaceutical availability have preparations with 15% propylene glycol-1,2, 5% paraffin and 1-2% chitosan.

5. References

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