

APPLICATION OF CHITOSAN IN THE FORMULATION OF METHYL CELLULOSE-BASED HYDROGELS

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Abstract

The aim of this work was to study the properties of methylcellulose hydrogels with supplements containing chitosan and 1% hydrocortisone. Depending on the composition of the substrate, gels are characterised by a variety of pharmaceutical availabilities. Increasing the concentration of chitosan has an influence on increasing the viscosity, hardness, and cohesiveness of the tested gels.

Key words: *methylcellulose, chitosan, rheological parameters, pharmaceutical availability.*

1. Introduction

Hydrogels are more commonly being used in pharmaceutical technology. When applied on the skin, these have a favourable effect on the course of treatment [1, 2]. Another advantage of hydrogels is the possibility of controlling the pharmaceutical availability. Methylcellulose is used as a carrier for medicinal substances in hydrogel formulations for administration to the skin, in transdermal systems, and on the oral mucosa in dental dressings. It can be used as a drug coating and a disintegrant, and it increases the viscosity of suspensions, ointments, and eye drops [1 - 4].

Chitosan is used in medication with controlled release, for the nose and eye dosage forms, dermatological drugs and cosmetics [5 - 9].

The aim of this work was to study the properties of methylcellulose hydrogels with supplements containing chitosan and 1% hydrocortisone.

2. Materials and methods

2.1. Materials

Methylcellulose (Sigma-Aldrich GmbH Germany), chitosan type 652 food grade France, hydrocortisone (Polfa Pabianice, Poland), N,N-dimethylacetamide (Sigma-Aldrich GmbH Germany), 1,2-propylene glycol-1,2 (Sigma-Aldrich GmbH Germany), purified water to Polish Pharmacopoeia 9th Ed were all used.

2.2. Preparation of hydrogels

Methylcellulose hydrogels at 3% concentration and 1% chitosan containing hydrocortisone were prepared *ex tempore*. Hydrocortisone, methylcellulose and chitosan were used by mixing 1,2-propylene glycol with N,N-dimethylacetamide and distilled water. The composition of the investigated gels is presented in **Table 1**.

2.3. Examination of the pharmaceutical availability of hydrocortisone

The process of hydrocortisone release from hydrophilic base was carried out according to the Polish Pharmacopoeia 9th Ed. The study was conducted at 37 °C and pH 7. The concentration of hydrocortisone was determined with the Jasco V-650 at wavelength of 241 nm according to the Polish Pharmacopoeia 9th Ed.

2.4. Dynamic viscosity test

This was carried out using the Rheotest 2. The values of the shear stress and viscosity were calculated from measurements.

2.5. Consistency test

The TPA test was performed with the Exponent Stable Micro Systems texture analyser.

3. Results and discussion

Studies of the influence of gel compositions on their properties and pharmaceutical availability were conducted for 3% methylcellulose gel with the addition of propylene glycol-1,2, DMA, and 1 to 4% of chitosan.

The study of pharmaceutical availability was performed using the method from the Polish Pharmacopoeia 9th Ed. The release process is in accordance with first order kinetics. Logarithm from the percentage of hydrocortisone as a function of time is presented in **Figure 1**.

The addition of chitosan affects the acceleration of hydrocortisone $T_{0.5}$ release process from 17.61 h to 15.21 h, respectively for 1% to 4% of the polymer content in the gel, which were presented in **Table 1**.

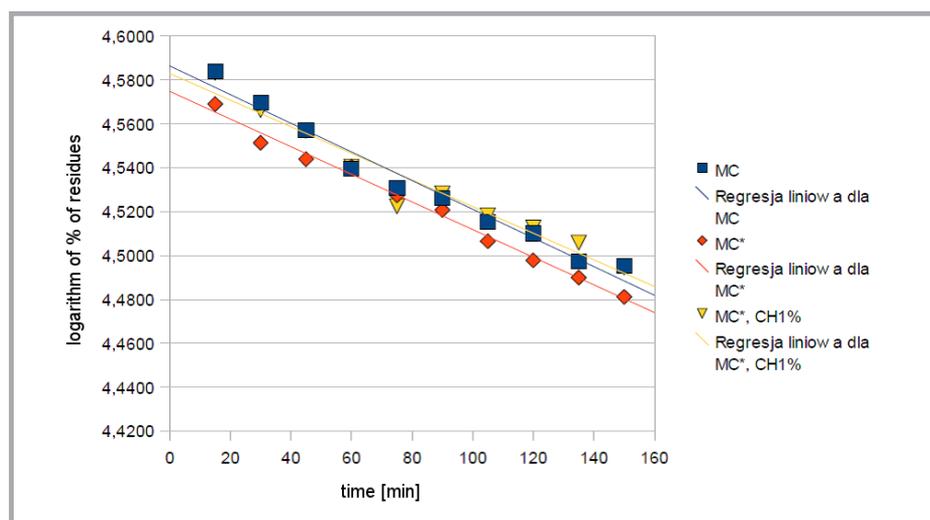


Figure 1. Influence of 1% chitosan additive on hydrocortisone release from methylcellulose hydrogels.

Table 1. Semi-liberation rates of hydrocortisone from hydrogels.

Hydrogels	half release period $t_{1/2}$ [h]	Standard deviation
3% methylcellulose, 10% propylene glycol-1,2, 5% N,N-dimethylacetamide	17.80	0.001900
3% methylcellulose, 1% chitosan, 10% propylene glycol-1,2, 5% N,N- dimethylacetamide	17.61	0.002120
3% methylcellulose, 2% chitosan, 10% propylene glycol-1,2 5%N,Ndimethylacetamide	16.44	0.003615
3% methylcellulose, 3% chitosan, 10% propylene glycol-1,2, 5% N,N- dimethylacetamide	15.31	0.001952
3% methylcellulose, 4% chitosan, 10% propylene glycol-1,2, 5% N,N- dimethylacetamide	15.21	0.000530

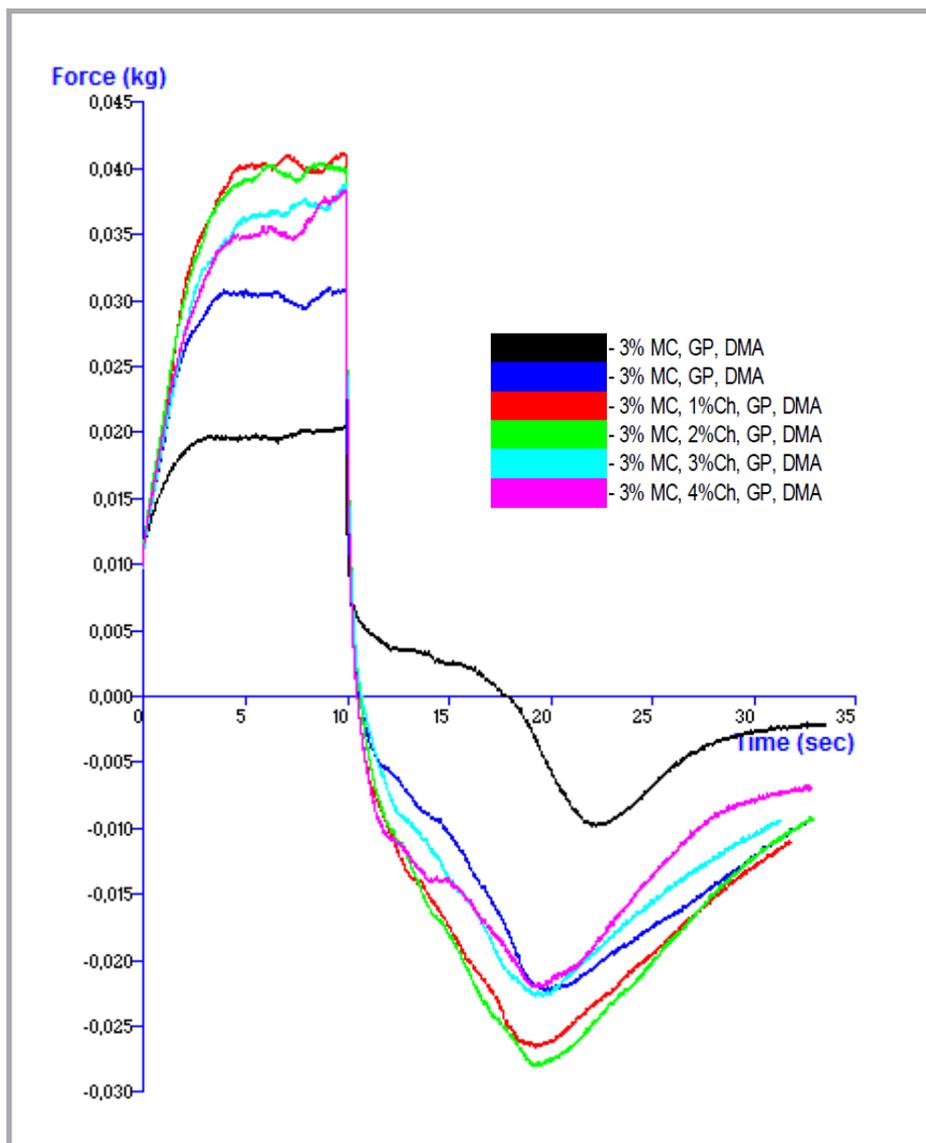


Figure 2. Influence of chitosan on consistency of the methylcellulose hydrogels.

The texture of the gel was set by examining the hardness, consistency and density; results are presented in **Figure 2**. Chitosan used in the gel, in the presence of 10% 1,2-propylene glycol and 5% N,N-dimethylacetamide, increases the hardness texture and cohesion of the investigated formulations. Gels with 1 and 2% chitosan, from 4.63 to 41.27 g, and 18.01 to 26.61 g for reference gels, were characterised by the highest hardness value. Tenacity value for these gels ranges from 356.32 to 359.67 gs, and 155.72 to 283.3 gs for reference

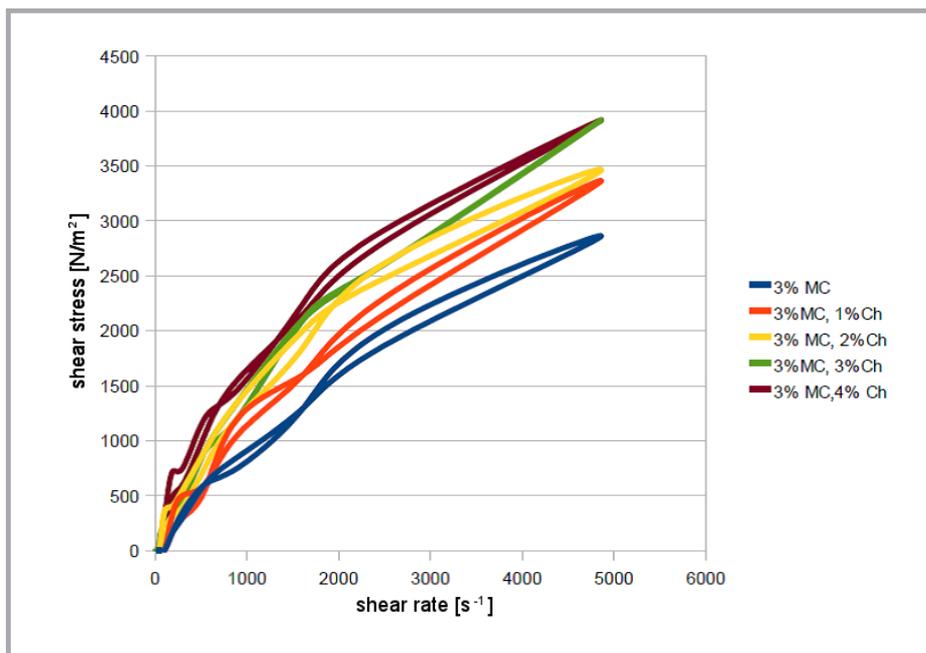


Figure 3. Flow curves of hydrogels containing chitosan.

gels. Hydrogels containing 10% propylene glycol-1,2, and 5% DMA were more compact than the reference gels.

Tested gels are non-Newtonian, pseudoplastic systems (**Figure 3**). With the increase in the concentration of chitosan gels, shear stress value increases from 2863.3 N/m² for a gel without polymer, to 3466.1 N/m² for 4% polymers. The addition of propylene glycol-1,2 and DMA results in the increase in shear stress from 5024.3 N/m² to 6630.8 N/m² for 1% to 4% of chitosan.

The addition of chitosan gels based on methylcellulose affects the time diversity of the half-release of drug substances, and profitably on the rheological properties which facilitates the preparation, squeezing from a tube and spread on the skin.

4. Conclusions

1. Rheological studies have shown that the process is nonlinear, and gels show thixotropic properties. Increasing the concentration of chitosan has an influence on increasing the viscosity, hardness, and cohesiveness of the tested gels.
2. Depending on the composition of the substrate, gels are characterised by a variety of pharmaceutical availability. The addition of increasing concentrations of chitosan has an influence on the increased rate of the release process.

5. References

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