APPLICATION OF CHITOSAN IN THE FORMULATION OF HYDROGELS APPLIED ON SKIN

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Abstract
These studies concerned the effect of composition on the substrate physicochemical parameters of hydrogels for use on skin. Hydrogels containing 1% of hydrocortisone and 1% of chitosan addition was made on the basis of methylcellulose, sodium carboxymethylcellulose and Carbopol 934 P. The release proceeds according to first-order kinetics. Depending on the type and composition of the polymer gels were obtained with various pharmaceutical availability of hydrocortisone. Addition of 1% chitosan affects the acceleration of the release in any given case.

Key words: *hydrogels, chitosan, hydrocortisone, pharmaceutical availability.*

1. Introduction

Hydrogels as carriers of therapeutic substances to the skin in relation to conventional dermatological dosage forms, characterized by a favorable release profile and absorption, the effect on the skin and reduce the incidence of adverse events. Modifying the composition of the hydrogel surface and its properties makes it possible to prepare formulations administered by different routes [1].

The release and absorption of many active substances from hydrophilic base is more intensive than from lipophilic base. Beneficial effect was observed in case of morphine sulphate and hydrochloride, trebinafine, naproxen, ketoprofene, simvastatin, hydrocortisone and other active substances [2 - 10].

The aim of the study was to compare the pharmaceutical availability of hydrocortisone from hydrogels with addition of chitosan.

2.Materials and methods

2.1.Materials

Methylcellulose (Sigma-Aldrich Gmbh Germany), N,N-dimethylacetamide (Sigma-Aldrich Gmbh Germany), 1,2-propylene glycol-1,2 (Sigma-Aldrich Gmbh Germany), hydrocortisone (Polfa Pabianice, Poland), Carboxymethylcellulose Na-salt (Serva, Feinbiochemica, Heidelberg/New York), Carbopol 934P (BF Goodrich, Speciality Chemicals,Division, Ohio), chitosan type 652 food grade France, purified water to Polish Pharmacopoeia 9th Ed.

2.2. Preparation of hydrogels

Methylcellulose, carboxymethylcellulose Na-salt, Carbopol 934P hydrogels at 3% concentration and 1% cihtosane containing hydrocortisone were prepared ex tempore by mixing of solid and liquid components in a closed container. The solid component was obtained by mixing of hydrocortisone and methylcellulose, carboxymethylcellulose, Na-salt, Carbopol 934P, and chitosan whereas the liquid component-by mixing of hydrophilizing agent (1,2-propylene glycol) with dimethylacetamide, and distilled water.

2.3. 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. The hydrocortisone was released to 500 cm^3 of redistilled water, at 90 mixer revolections per minute. Samples were collected every 15 min. Study was conducted at 37 °C and 7 pH.

2.4. Quantitative determination of hydrocortisone

Concentration of hydrocortisone was determined with the CECIL INSTRUMENTS spectrophotometer of the CE 5501 type at wavelength of 241 nm according to Polish Pharmacopoeia 9th Ed.

3. Results and discussion

The process of release from the investigated hydrophilic gels containing hydrocortisone runs according to first order kinetics. Log from percentage of remaining active substance as function of time for selected preparation is presented in ***Figure 1, 2, 3***.

The obtained results were used to determine the release rate constants and half-release times, which were presented in ***Table 1***. Hydrocortisone half-release time from methylcellulose hydrogel was 11.34 h, containing propylene glycol-1,2, which is a reference preparation, was 15.60 h. The addition of 1% chitosane influenced in acceleration of the half-release process, and was 6.65 h.

A similar correlation was observed in case of hydrogels containing of sodium carboxymethylcellulose and Carbopol 934 P. Half-release times for the reference preparations were

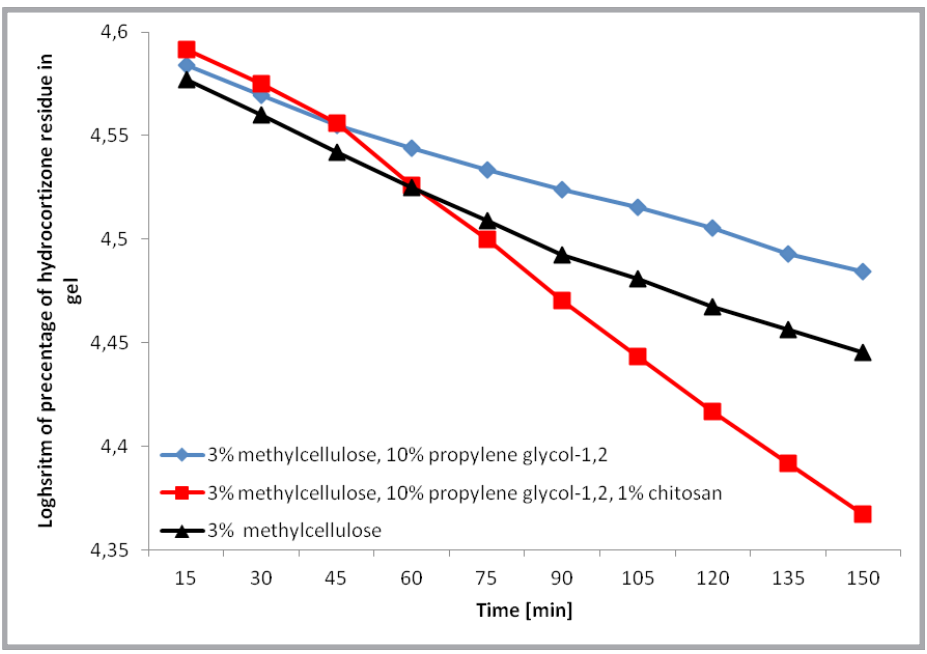

Figure 1. *Influence of 1% chitosan additive on hydrocortisone release from methylcellulose hydrogel.*

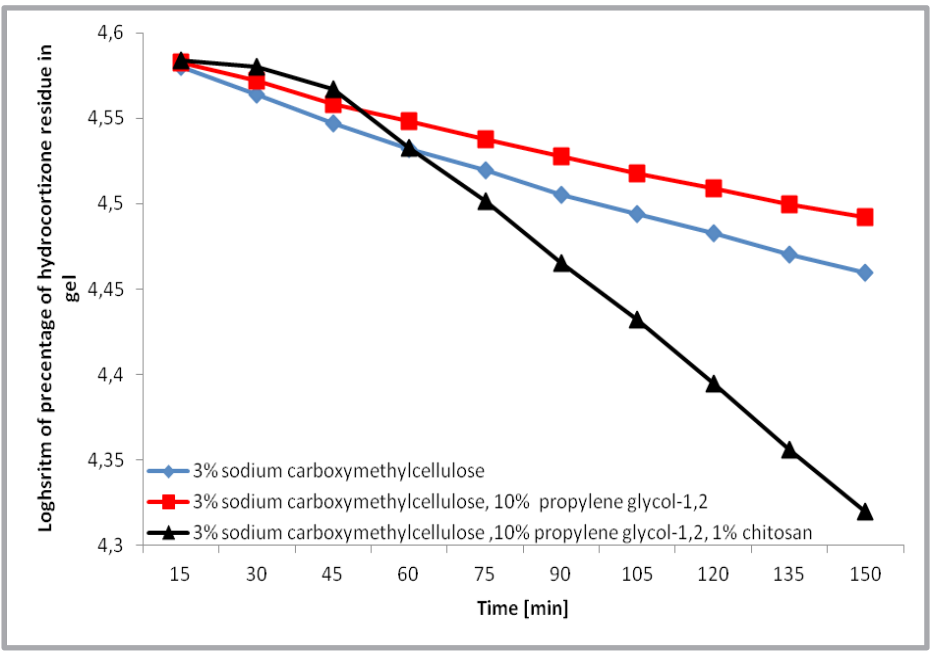

Figure 2. *Influence of 1% chitosan additive on hydrocortisone release from sodium carboxymethylcellulose hydrogel.*

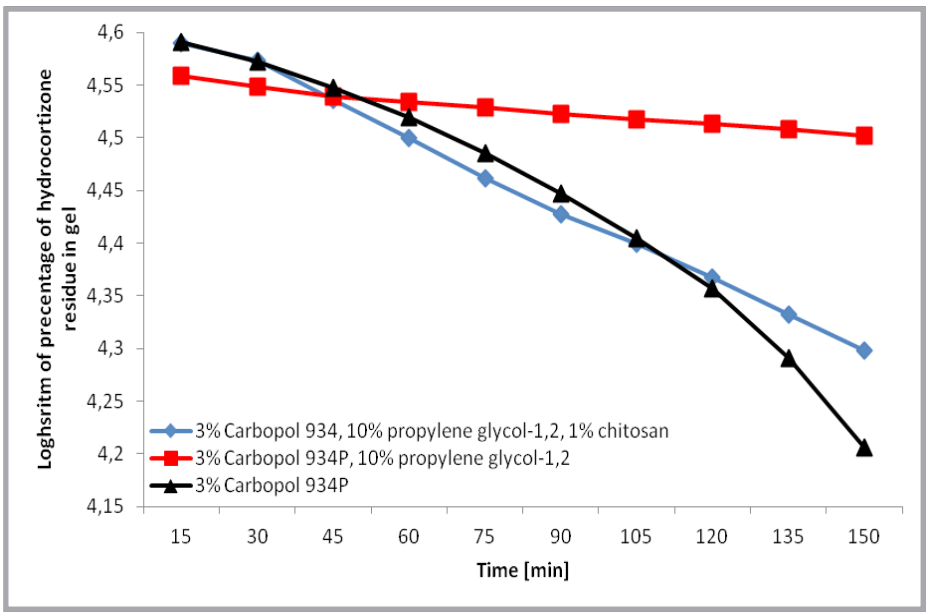

Figure 3. *Influence of 1% chitosan additive on hydrocortisone release from Carbopol hydrogel.*

Table 1. *Semiliberation rates of hydrocortisone from hydrogels.*

Gel no.	Hydrogels	half release period $t_{50\%}$, h	correlation coefficient r
1	3% methylcellulose	11.34	0.9847
2	3% methylcellulose, 10% propylene glycol-1,2	15.60	0.9902
3	3% methylcellulose, 10% propylene glycol-1,2, 1% chitosan	6.65	0.9875
4	3% sodium carboxymethylcellulose	12.37	0.9868
5	3% sodium carboxymethylcellulose, 10% propylene glycol-1,2	16.46	0.9923
6	3% sodium carboxymethylcellulose , 10% propylene glycol-1,2, 1% chitosan	5.64	0.9913
7	3% Carbopol 934P	14.05	0.9850
8	3% Carbopol 934P, 10% propylene glycol-1,2	15.06	0.9903
9	3% Carbopol 934, 10% propylene glycol-1,2, 1% chitosan	5.11	0.9895

12.37 h and 14.05 h respectively, while after the addition of 1% chitosane they were 5.64 h and 5.11 h respectively.

Prepared gels based on cellulose have a higher rate of diffusion than prepared with Carbopol 934P. Addition of 1% chitosan affects the acceleration of the release in any given case.

Rheological studies provide draft curves of changes in viscosity depending on shear rate. Progress of process is nonlinear, examined gels are non-Newtonian systems with thixotropic properties. Tested hydrogel dressings have a beneficial rheological properties ensure the appropriate application of product on the skin.

The use of 1% chitosan in hydrogels based of methylcellulose, cellulose and sodium carboxymethylcellulose and Carbopol 934 P affects the acceleration of the hydrocortisone release process and obtaining various pharmaceutical availability dressings.

4. Conclusions

1. Rheological studies provide draft curves of changes in viscosity depending on shear rate. Progress of process is nonlinear, examined gels are non-Newtonian systems with thixotropic properties.
2. The release proceeds according to first-order kinetics.
3. Prepared gels based on cellulose have a higher rate of diffusion than prepared with Carbopol 934 P.
4. Addition of 1% chitosan affects the acceleration of the release in any given case.

5. References

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