APPLICATION OF CHITOSAN IN THE FORMULATION OF DERMATOLOGICAL HYDROGELS PREPARED ON THE BASIS OF MACROMOLECULAR COMPOUNDS

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Abstract

The effect of chitosan concentration on the properties of dermatological preparations prepared with 2% methylcellulose and 10% polyvinylpyrrolidone was studied. As the levels of chitosan, propylene glycol-1,2 and glycerol increased, the hardness, consistency and cohesiveness of the hydrophilic gels increased, while the dissipation capacity decreased. Gels based on methylcellulose and chitosan, compared to formulations containing polyvinylpyrrolidone, have a higher rate of loss of volatile compounds, higher pH values for 1,2-propylene glycol formulation and higher texture parameters. The tested hydrogels have good rheological properties, allowing extrusion from the tube and spreading on the skin.

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

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1. Introduction

Chitosan is a natural polysaccharide with haemostatic and antibacterial activity and has many beneficial properties such as biocompatibility and biodegradability. This allows it to be used in medicine as a component of dressings and drug carrier, among others [1-4]. Currently, a new generation of dressings are used, e.g. hydrogels. They are characterised by the ability to absorb large amounts of exudate, maintain proper moisture in the wound and facilitate the process of natural autolysis [5-6].

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

2. Materials and methods

2.1. Materials

Methylcellulose (Serva), polyvinylpyrrolidone k90 (Fluka AG), propylene glycol-1,2 (Sigma-Aldrich), glycerol (Chempur), chitosan (Sigma-Aldrich), hydrocortisone (Polfa Pabianice), purified water according to the Polish Pharmacopoeia XIth Ed, were used.

2.2. Preparation of hydrogels

Chitosan hydrogels at a concentration of 1% or 3% and 2% methylcellulose or 10% PVP containing 1% hydrocortisone, 1,2-propylene glycol or glycerol and distilled water were prepared ex tempore. The composition of the investigated gels is presented in Table1.

2.3. Consistency test

The texture profile analysis (TPA) test was performed with the Exponent Stable Micro Systems texture analyser TAXT plus. The texture of the gel was set by examining the hardness, consistency, and back extrusion method, which consists of the process of retracting extrusion. Test parameters were: force of 2g, speed of 2 mm/s, distance of 10 mm, diameter disc 40 mm [7,9].

2.4. Dynamic viscosity test

The dynamic viscosity test was carried out using a rotational viscosimeter Rheotest 2 (Medingen Dresden).

The determinations were performed in a range on a K-1 cone with the diameter of 36mm, at 37°C. The values of shear stress and viscosity were calculated from measurements [8,9].

3. Results and discussion

The study of the influence of 1% or 3% chitosan on the rheological properties of 2% methylcellulose hydrogels or 10% polyvinylpyrrolidone gel in the presence of the additives propylene glycol-1,2 and glycerol. Test formulations in the presence of propylene glycol-1,2 and glycerol should be characterised by viscosity and consistency, which will ensure good spreading and squeezing of the drug from the tube. Gels with a higher viscosity and hard consistency will ensure longer retention on the skin.

The texture determines the rheological and physical properties of the tested gels. The texture of the gel was set by examining the hardness, consistency and wheel field [9].

The gels with 2% methylcellulose and chitosan had a greater hardness and consistency than those made from polyvinylpyrrolidone; these are presented in Table 1.

Table 1. Texture parameters and the spread of hydrogels

The composition of the investigated gels	Hardness [g]	Consistency [g]	Wheel field [cm^2]
1% chitosan, 2% methylcellulose, 5% propylene glycol-1,2	69.01	285.34	20.63
1% chitosan, 2% methylcellulose, 5% glycerol	92.11	339.80	19.52
1% chitosan, 2% methylcellulose, 15% propylene glycol-1,2	148.23	558.78	19.44
1% chitosan, 2% methylcellulose, 15% glycerol	160.42	606.83	18.10
3% chitosan, 2% methylcellulose, 5% propylene glycol-1,2	366.47	1329.80	16.62
3% chitosan, 2% methylcellulose, 5% glycerol	394.08	1428.88	13.55
3% chitosan, 2% methylcellulose, 15% propylene glycol-1,2	1234.47	3910.70	12.81
3% chitosan, 2% methylcellulose, 15% glycerol	698.32	2362.89	13.36
1% chitosan	**14.09**	**72.52**	**21.24**
1% chitosan, 10% PVP, 5% propylene glycol-1,2	85.07	336.87	19.44
1% chitosan, 10% PVP, 5% glycerol	68.18	264.48	19.24
1% chitosan, 10% PVP, 15% propylene glycol-1,2	99.78	376.77	19.05
1% chitosan, 10% PVP, 15% glycerol	99.69	370.52	19.05
3% chitosan, 10% PVP, 5% propylene glycol-1,2	345.94	1251.19	16.26
3% chitosan, 10% PVP, 5% glycerol	350.85	1241.78	15.73
3% chitosan, 10% PVP, 15% propylene glycol-1,2	579.88	2010.01	14.35
3% chitosan, 10% PVP, 15% glycerol	384.40	1352.28	15.55
3% chitosan	**50.66**	**203.23**	**20.32**

Hardness gels with 1% chitosan and 2% methylcellulose, 5% or 15% propylene glycol-1,2 or glycerol, respectively, increased from 69.01 g to 160.42 g and from 14.09 g for reference gels. Hardness gels with 3% chitosan and 2% methylcellulose, propylene glycol-1,2 or glycerol, respectively, increased from 366.47 g to 1234.47 g and from 50.66 g for reference gels. Hardness gels with 1% or 3% chitosan and 10% polyvinylpyrrolidone, 5% or 15% propylene glycol-1,2 or glycerol, respectively, increased from 68.18 g to 99.78 g and from 345.94 g to 579.88 g.

The consistency of the gels with methylcellulose was from 285.34 g to 3910.70 g and 264.48 g to 2010.01 g for polyvinylpyrrolidone. The highest consistency was shown for gels containing 3% chitosan, 2% methylcellulose and 15% propylene glycol-1,2.
The spread of gels composed of PVP and chitosan is greater than in methylcellulose and chitosan. The addition of 1,2-propylene glycol and glycerol results in an increase in the spread of PVP gels and a decrease in methylcellulose gels [9].

Table 2. Viscosity parameters of hydrogels determined at 37°C and a shear rate of 4860.00 [s^{-1}]

The composition of the investigated gels	**Shear stress N/m^2**	**Viscosity mPa* s**
1% chitosan, 2% methylcellulose, 5% propylene glycol-1,2	1317.50	27.11
1% chitosan, 2% methylcellulose, 5% glycerol	2210.00	45.47
1% chitosan, 2% methylcellulose, 15% propylene glycol-1,2	1997.50	41.10
1% chitosan, 2% methylcellulose, 15% glycerol	2337.50	48.10
3% chitosan, 2% methylcellulose, 5% propylene glycol-1,2	2890.00	59.47
3% chitosan, 2% methylcellulose, 5% glycerol	2805.00	57.72
3% chitosan, 2% methylcellulose, 15% propylene glycol-1,2	3272.50	67.34
3% chitosan, 2% methylcellulose, 15% glycerol	2295.00	47.22
1% chitosan	**85.00**	**1.75**
1% chitosan, 10% PVP, 5% propylene glycol-1,2	1721.75	35.42
1% chitosan, 10% PVP, 5% glycerol	1360.00	27.98
1% chitosan, 10% PVP, 15% propylene glycol-1,2	1976.25	40.66
1% chitosan, 10.% PVP, 15% glycerol	2103.75	43.29
3% chitosan, 10% PVP, 5% propylene glycol-1,2	3825.00	78.70
3% chitosan, 10% PVP, 5% glycerol	3570.00	73.46
3% chitosan, 10% PVP, 15% propylene glycol-1,2	4122.50	84.83
3% chitosan, 10% PVP, 15% glycerol	3825.00	78.70
3% chitosan	**1041.25**	**21.42**

Methylcellulose, polyvinylpyrrolidone and propylene glycol-1,2 or glycerol have an influence by increasing the shear stress of gels with 1% chitosan, as presented in Table

2. Shear stress in the presence of methylcellulose gels with 1% chitosan increased from 1317.50 to 2337.50 N/m^2 and from 2295.00 to 3272.50 N/m^2 for 3% chitosan. The highest value of shear stress (3272.50 N/m^2) was found with the addition of 15% propylene glycol-1,2 and 3% chitosan and 2% methylcellulose [9].
Shear stress in the presence of PVP gels with 1% chitosan increased from 1360.00 N/m^2 to 2103.75 N/m^2 and from 3570.00 N/m^2 to 4122.50 N/m^2 for 3% chitosan. The highest value of shear stress (4122.50 N/m^2) was found with the addition of 15% propylene glycol-1,2, 3% chitosan and 10% polyvinylpyrrolidone. These tests have shown the beneficial properties of the application of the gel. Gels show thixotropic properties and belong to non-Newtonian systems.
The addition of chitosan, PVP or methylcellulose and propylene glycol or glycerol have a beneficial effect on the rheological properties of the gels, and ease the spreading of the drug on the skin, providing optimal application properties and appropriate application.

4. Conclusions

The gels with methylcellulose and chitosan have a greater hardness and consistency than those made from PVP. The highest hardness and consistency was shown by gels containing 3% chitosan, 2% methylcellulose and 15% propylene glycol-1,2 or 3% chitosan, 10% PVP and 15% propylene glycol-1,2.

The spread of gels composed of PVP and chitosan is greater than in methylcellulose and chitosan, respectively, from 14.35 cm^2 to 19.44 cm^2 for PVP and from 13.36 cm^2 to 20.63 cm^2 for methylcellulose.

PVP and chitosan gels containing propylene glycol-1,2 or glycerol have higher shear stress than those prepared on methylcellulose and chitosan.

The tested hydrogels have good rheological properties, allowing extrusion from the tube and spreading onto the skin.

5. References

[1] Orłowska J., Szcześniak P., Orszulak - Michalak D; (2011) Chitin derivatives – application in tissue engineering and design for active dressings. Farm. Pol. 67 (12), 867 – 872.
[2] Kumar A., Vimal A., Kumar A; (2016) Why Chitosan? From properties to perspective of mucosal drugdelivery. Int J Biol Macromol, 91, 615 – 622. **DOI**: 10.1016/j.ijbiomac.2016.05.054.
[3] Patrulea V., Ostafe V., Borchard G., Jordan O; (2015) Chitosan as a starting material for wound healing applications. Eur J Pharm Biopharm, 97, 417 – 426. **DOI**:10.1016/j.ejpb.2015.08.004
[4] Korytkowska-Wałach A., Emiga-Matuszowicz M., Łukaszczyk J; (2015) Polymeric in situ forming systems for biomedical applications. Part II. Injectable hydrogel systems. Polimery 60.7-8, 435-445. 435 **DOI**: dx.doi.org/10.14314/polimery
[5] Mazurek P., Kuliński S., Gosk J; (2013) The Possibilities of Using a Chitin and Chitosan in Wounds Treatment. Polim. Med.43, 43,297-302.
[6] Szcześniak M., Pluta J; (2012) Hydrożele. Farm. Pol. 7, 458-461.
[7] Szcześniak M., Pluta J; (2013) The effect of selected excipients on the properties hydro gels on the basis Carbopol 934 P. Polim Med 43, 29-34.
[8] Szcześniak M., Pluta J; (2011) Influence of polymers on hydrogels with hydrocortisone properties. Polim Med 41, 2, 43-48.
[9] Szcześniak M., Grimling B., Meler J., Karolewicz B; (2017) The influence of selected polymers on the rheological properties of hydrogels with chitosan applied

on the skin.. Progress on Chemistry and Application of Chitin and its Derivatives, Volume XXII, 201-206. **DOI**:10.15259/PCACD.2220