Department of Pharmaceutical Technology, Wrocław Medical University, Wrocław, Poland

Influence of tensides on the release of medical agents from hydrophilic gels, part 2: The influence of selected tensides on hydrocortisone release from xerogels

M. Szcześniak, A. A. Kubis

Received April 28, 2003, accepted August 19, 2003

Dr. Maria Szcześniak, Department of Pharmaceutical Technology, Wrocław Medical University, Wrocław, Poland

Pharmazie 59: 198–199 (2004)

With the increase of polysorbates 20 and 21 concentration in xerogels, in the presence of 1,2-propylene glycol and PEG 200, hydrocortisone half-release periods from these preparations become longer while the half-release periods for polysorbate 80 and propylene glycol, and polysorbate 21 and PEG 200 are proportionally shortened. The concentration of tensides has no significant impact on the half-release periods of hydrocortisone with polysorbate 81 added to xerogels in the presence of propylene glycol and polysorbate 20 and 80 with PEG 200.

1. Introduction

In earlier publications it was claimed that the hydrocortisone release from hydrophilic substrates is influenced by hydrophilizing substances. In the presence of 1,2-propylene glycol and PEG 200 the release of therapeutic substances from hydrogels and xerogels becomes faster in comparison with the reference gel (Kubis et al. 1992; Szcześniak et al. 1992; Szcześniak et al. 1993). Because of the more intensive hydrocortisone release from xerogels a high concentration of hydrocortisone interacts with skin. In a recent publication (Kubis et al. 2000) it was revealed that hydrocortisone bound in micelles slows down the release of hydrocortisone from hydrogels.

The addition of surface active compounds establishes an equilibrium system between hydrocortisone bound in micelles and dissolved in the hydrophilic gel. This ensures a fixed, uniform effect of a lower concentration of hydrocortisone not bound in micelles on a pathologically changed place (Kubis et al. 2002).

The aim of this study was to investigate, how the above mentioned relations are reshaped in xerogels formed from hydrogels.

2. Investigations, results and discussion

The hydrocortisone release from xerogels with 1, 2 and 3% polysorbates 20, 80, 21 and 81 was analysed in accordance with the procedure accepted for the first order kinetic process. Half-release periods are compiled in Table 1 and 2. The data show that the xerogels containing 1,2-propylene glycol or PEG 200 can be divided into three groups depending on the applied tenside. Xerogels with hydrophilising substances without the addition of tensides are used as reference preparations.

In the first group there are preparations containing 1–3% of tenside. This has a directly proportional influence on the release rate. The group encompasses xerogels containing polysorbates 20 and 21 in the presence of propylene glycol which showed a prolonged release in comparison with reference gel of 17.4 h half-release time. In the examined P 21 concentration range half-release period is 18.5–43.7 h. In the presence of P 21 and PEG 200 a faster hydrocortisone release rate was observed in accordance with the same relations, at 1, 2 and 3% tenside concentration the process was slowed down in comparison with the reference preparation of half-release time of 9.6 h. Half-release period of the examined xerogels were in the range of 1.2–13.2 h.

The second group contains xerogels whose half-release develops inversely proportional to the emulsifier concentration. Preparations in this group contain polysorbate 80 and propylene glycol. The half-release period for these

Table 1: Semiliberation rates ($T_{0,5}$) of the hydrocortisone liberation for xerogels with tenside additives

Gel No	Concentrations (%) of:									
	H	MC	DMA	1,2-PG	P20	P80	P21	P81	r	$T_{50\%}$ (h)
1	1	4	10	10					0.9871	17.4
2	1	4	10	10	1				0.9933	23.7
3	1	4	10	10	2				0.9930	25.5
4	1	4	10	10	3				0.9916	42.9
5	1	4	10	10		1			0.9918	68.3
6	1	4	10	10		2			0.9937	25.2
7	1	4	10	10		3			0.9938	12.1
8	1	4	10	10			1		0.9915	18.5
9	1	4	10	10			2		0.9897	33.7
10	1	4	10	10			3		0.9907	43.7
11	1	4	10	10				1	0.9884	43.1
12	1	4	10	10				2	0.9916	36.6
13	1	4	10	10				3	0.9870	44.0

Note: H = hydrocortisone, MC = methylcellulose, DMA = dimethylacetamid, 1,2-PG = 1,2-propylene glycol, PEG 200 = polyoxytehylene glycol 200, P20 = polysorbate 20, P80 = polysorbate 80, P21 = polysorbate 21, P81 = polysorbate 81, $T_{50\%}$ = Half-release period, r = correlation coefficient

Table 2: Semiliberation rates ($T_{0,5}$) of the hydrocortisone liberation for xerogels with tenside additives

Gel No	Concentrations (%) of:									
	H	MC	DMA	PEG 200	P20	P80	P21	P81	r	$T_{50\%}$ (h)
1	1	4	10	10					0.9953	9.6
2	1	4	10	10	1				0.9907	22.2
3	1	4	10	10	2				0.9907	22.2
4	1	4	10	10	3				0.9857	18.2
5	1	4	10	10		1			0.9943	9.5
6	1	4	10	10		2			0.9965	9.0
7	1	4	10	10		3			0.9940	9.0
8	1	4	10	10			1		0.9943	1.2
9	1	4	10	10			2		0.9962	7.8
10	1	4	10	10			3		0.9873	13.8
11	1	4	10	10				1	0.9777	11.3
12	1	4	10	10				2	0.9949	6.4
13	1	4	10	10				3	0.9934	4.0

See: Table 1

preparations is between of 68.3 and 12.1 h. It was found that the release was prolonged at 1 and 2% tenside concentration, and at 3% it was shortened in comparison with the reference preparation of 17.4 h half-release time. The release from xerogels containing polysorbate 81 and PEG 200 also develops in an adversely proportional way. However, half-release periods are shorter in comparison with reference gel 17.4 h and fit in the range of 11.3–7.0 h, which confirms the acceleration of the process.

The third group contains xerogels which show that the addition of an emulsifier in the given concentration range slowed down the hydrocortisone release.

In the presence of polysorbate 81 and 1,2-propylene glycol half release times for the examined tenside concentrations made about 44 h and for polysorbate 20 in the presence of PEG 200 about 22 h. The periods for reference gels were 17.4 h and 9.6 h respectively. The addition of polysorbate 80 in increasing concentrations to gels containing PEG 200 had no significant impact on the hydrocortisone release. For the examined xerogels and reference gels the half-release period were about 9 h.

The diversification of the half-release periods depending on the composition of the examined xerogels makes it possible to select optimum hydrocortisone concentration to contact skin. Bound therapeutic substance in micelles leads to a decrease of free hydrocortisone concentration in xerogels. Only hydrocortisone not bound in micelles is released. The decrease of its concentration, resulting from the process, is compensated by diffusion from micelles based on the equilibrium between the concentration in micelles and in solution. Thanks to hydrocortisone bound in micelles and its prolonged release the skin would be in contact with a lower concentration of free steroid, which to some degree protects the skin from hydrocortisone side effects.

3. Experimental

3.1. Materials

Ethyl alcohol 96%, of analytical grade (POCH Gliwice, Poland), *N*,*N*-dimethyl acetamide (SIGMA), 1,2-propylene glycol (Laborchemie Apolda, Germany), polyoxyethylene glycol 200 (LOBA CHEMIE, Germany), water bidestilled and the deionised, semi-permeable membrane as used for dialyze in artificial kidney (Germany), hydrocortisone (Jelfa, Poland) methylcellulose (LOBA CHEMIE, Germany), polysorbate 20, 21, 80, 81 (Koch-Light Lab. Ltd., England).

3.2. Preparation of xerogels

Hydrogels from methyl-cellulose in 4% concentration, which were used to obtain xerogels, were prepared *ex tempore* by mixing solid and liquid components. The composition of the gels is presented in Table 1 and 2. The solid component was prepared by mixing hydrocortisone and methyl-cellulose, and the liquid component by mixing hydrophiliser in quantities given in charts (1,2-propylene glycol or PEG 200), with dimethyl acetamide, tenside and distilled water. The gel was prepared by scattering powder on the surface of the liquid component in a closed vessel. Everything was mixed for two minutes to obtain uniform consistence.

3.3. Determination of hydrocortisone release

The hydrocortisone release from gel substrates was measured by a method based on therapeutic substance diffusion through a semipermeable membrane (Olszewski et al. 1969).

A portion of gel containing the examined substance was placed on the semipermeable membrane of the apparatus by means of a syringe. When hydrogel turned into xerogel the apparatus was started after 24 h. Ten fractions of 5 cm^3 each were taken to calibrated test-tubes every 15 min.

3.4. Quantitative determination of hydrocortisone

Concentration of hydrocortisone was determined with the CECIL INSTRUMENTS spectophotometer of the CE 5501 type at wavelenght of 241 nm, according to European Pharmacopoeia 3rd Ed.

References

Kubis AA, Szcześniak M (1992) The influence of hydrophilizing agents on gel formation rate of cellulose derivatives. Part 1. Influence of 1,2-propylene glycol on homogeneity of methyl cellulose gel. Pharmazie 47: 362–364.

Kubis AA, Szcześniak M, Musiał W (2000) Influence of tensides on liberation of medical agents from hydrophilic gels effects of polysorbate 20 and polysorbate 80 on liberation of hydrocortisone from hydrophilic gels. Ars Pharmaceut. 41: 397–403.

Kubis AA, Musiał W, Szcześniak M (2002) Influence of some polysorbates on hydrocortisone release from hydrophilic gels considered as two compartment models. Pharmazie 57: 479–481.

Szcześniak M, Kubis AA, Grimling B (1992) Part 2 Influence of additional polymers on homogeneity of viscosity in methylcellulose gels ex tempore prepared in presence of hydrophilizing agents. Pharmazie 47: 150–151.

Szcześniak M, Kubis AA (1993) Part 3. Effect of hydrophilizing agents and of polymer type on the release rate of hydrocortisone from xerogel dressing. Pharmazie 48: 926–927.

Olszewski Z, Kubis AA (1969) A method for the determination of time course of the release of active substances from oiniment bases, by means of a self constructed device. Acta Pol Pharm 26: 447–454.