Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Medicine, Wrocław, Poland

Studies on dressings for oral cavity mucosa

Part 5: Properties of xerogel stomatological dressings with one-side antiadhesive coating

K. MALECKA and A. A. KUBIS

The adhesion of xerogel dressings based on Eudragit (E), and methylcellulose (Mc) is in within the range of 143–270 g, and dissolution time of xerogel dressings in water is 3.4 h, and in artifical gastric juice 2.8 h. The 50% release time for Kunitz protease inhibitor ranges from 3.2–11.5 h.

1. Introduction

The encouraging results of preliminary clinical examinations of xerogel dressings prompted us to create formulations with prolonged activity of the Eudragit E.

2. Investigations and results

As it can be seen from the Table, adhesion of the dressings depends upon their qualitative and quantitative compositions. The lowest adhesion, (143 g) was given by the dressing without hydrophilizing agent, taken as the control. Addition of 30% and 50% of glycerol results in adhesion increased to 183 g and 223 g, respectively. Addition of the same percentages of 1,2-propylene glycol (PEG) resulted in adhesion increased to 230 g and 270 g, respectively. Similarly, the adhesion of dressings containing the same amounts of PEG rose to 197 g and 223 g, respectively.

It was noted that during washing out of the dressings in water the xerogel layer disappeared, whereas the antiadhesive coating remained intact. The washing out operations were continued until the dressings were fragmented into 1–2 mm pieces. As can be seen from the Table, the dressing fragmentation rate depends upon the qualitative composition of the preparation, not on quantitative relations of its components. The reference dressing was washed out within 1.7 h. Additions of 30% and 50% of glycerol resulted in a reduction of the time down to 1.3 h and 1.5 h, respectively. The dressings based on 1,2-propylene glycol or polyethylene glycol 400 (PEG 400) were characterized by longer washing out times, compared to the reference. With addition of 30% and 50% of 1,2-propylene glycol, the dressings were washed out within 1 h and 0.5 h, respectively. For PEG 400, the results were 1.66 h and 1.5 h, respectively.

Artificial gastric juice digested the dressings together with the antiadhesive coating. The dressings became thinner, became transparent, and disappeared. As can be seen from the Table, the digestion time depends upon the type of hydrophilizing agent, not on the percentage ratios of the components. The reference sample was washed out within 1.3 h. The dressings containing glycerol, or 1,2-propylene glycol, were washed out two times faster, and those with PEG 400 two times slower, compared to the reference.

Both the Table and the Fig. show that protease inhibitor liberation rate depends upon the concentration of hydrophilizing agent. The lowest liberation rate was given by the reference dressing, for which the 50% release time exceeded 11 h. In case of dressings containing 30% or 50% of glycerol, the inhibitor liberation rates were to 8 h and approx. 6 h, respectively. With 1,2-propylene glycol it exceeded 3 hours, irrespective of the concentration of hydrophilizing agent, whereas for the dressings containing 30%

Table: Influence of xerogel dressings composition on their pharmaceutical properties

Gel No.	MC/E ratio	Hydrophilizing agent content (%)	Adhesion (g)	Disintegration rate in vitro (h)		Release	
				H_2O	artif gastric juice	Rate constant (10^{-1} h^{-1})	$t_{50\%}$ (h)
0	1 : 0.3	0	143	1.7	1.3	0.59	11.54
1a	1 : 0.3	glycerol 30	183	1.3	0.8	0.83	8.34
1b	1 : 0.3	glycerol 50	223	1.5	0.75	1.19	5.82
2a	1 : 0.3	1,2-propylene glycol 30	230	2.7	0.75	1.86	3.72
2b	1 : 0.3	1,2-propylene glycol 50	270	2.2	0.8	2.14	3.24
3a	1 : 0.3	PEG 30	197	3.4	2.8	1.1	6.30
3b	1 : 0.3	PEG 50	233	3.2	2.8	2.0	3.46

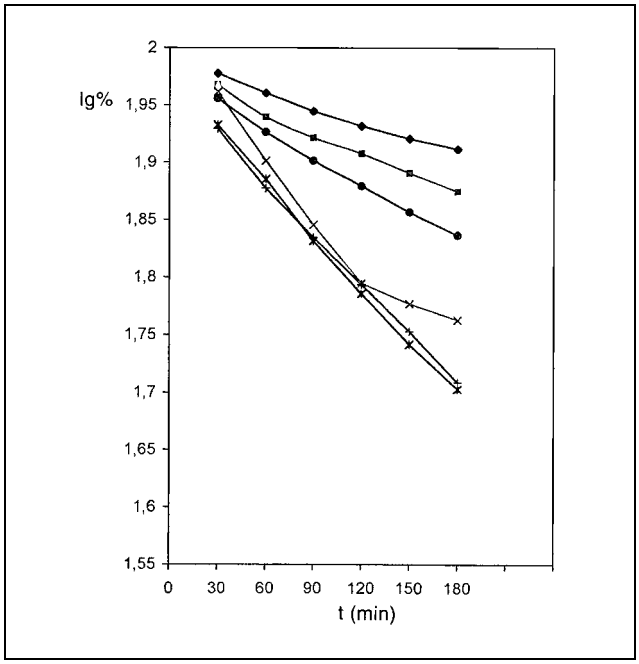

Fig.: Influence of the hydrophilizing agent on availability of the Kunitz type protease inhibitor. —◆— Without the hydrophilizing agent; —■— 30% glycerol, 50% glycerol; —×— 30% 1,2-propylene glycol; —✳— 50% 1,2-propylene glycol; —●— 30% PEG; —┼— 50% PEG

and 50% of PEG 400 the respective 50% release times were to 6.3 h and 3.46 h.

3. Discussion

The results of the measurements allow assessment of the pharmaceutical properties of the xerogel dressings containing the Kunitz' protease inhibitors. The xerogel dressings proved to be resistant to destruction in environments more aggressive than those in the oral cavity for 1.3–3.4 h. Therefore, it may be expected that dressings applied to sore paradontium tissue will remain intact for the period of time between consecutive meals. The xerogels are digested in gastric juice within 0.75–2.8 h, i.e. within the normal period of retention of food in the stomach, therefore there is no risk of their passing into the intestine.

4. Experimental

4.1. Materials

Methylcellulose (MC) (Loba Chemie Wien Fishamed Austria). Eudragit E 100 (E) (Röhm Pharma GmbH, Darmstadt). Glycerol AR grade, 1,2-propylene glycol, acetone, sodium chloride AR grade (Polish Chemical Reagents Gliwice). Polyethylene glycol 400 (PEG 400) (Loba Feinchemie). White wax (Wytwórnia Pszczelarska Poznań). Traskolan 5800 j.i.k./mg (Jelfa Jelenia Góra).

4.2. Apparatus

Apparatus for testing release of active substances from ointments, according to Olszewski and Kubis [1]. Apparatus for testing adhesion of ointments, according to Münzel. Spectrophotometer (Cecil Instruments Austria Chemist Handel).

4.3. Xerogel dressings

Xerogel dressings were prepared by mixing 5% methylcellulose solution and a 10% solution of Eudragit E in acetone. Then, the premix was mixed with a 10% aqueous solution of glycerol or 1,2-propylene glycol, or a 10% solution of polyethylene glycol 400 in acetone and poured on to a wax coated plate [2, 3]. After evaporation of solvent, xerogel dressings were obtained. Next, the dressings were uniformly coated with an acetone solution of Eudragit E and left to dry. For quantitive compositions of the dressings see Table.

4.4. Adhesion of the xerogel dressings

Adhesion was measured with the apparatus of Münzel. First, a 2.5×3.5 cm sample of the xerogel dressing was swollen in 0.5 cm^3 water and left for 10 min, then put into the apparatus. The plastic disc of the apparatus was put on the xerogel membrane for 5 min, then it was pulled off the membrane under an increasing load of scale weights. Each of the measurements was repeated three times.

4.5. Wash-out rate of xerogel dressing in vitro

Rates of washing out of the xerogel dressings were measured in the Farmex T apparatus, designed for measuring the rate of drug liberation from tablets. A 1×2 cm sample strip of xerogel dressing was put into a 1000 cm^3 beaker with 500 cm^3 distilled water, or 500 cm^3 simplified gastric juice. The measurement was carried out at 37 °C. The solutions were mixed with a mechanical paddle mixer at 60 rpm.

4.6. Release rate of Kunitz' protease inhibitor

The measurements were carried out with the apparatus of Olszewski and Kubis [1], designed for measuring the rate of drug liberation from ointments. For 180 min, 2 cm^3 portions of eluate were sampled at 30 min intervals. The amounts of inhibitor liberated were determined using a spectrophometric method, by measurement of the absorbance of particular eluates at 260 nm wavelength, with water as the reference.

References

1 Olszewski, Z.; Kubis, A.: Acta Polon. Pharm. **26**, 447 (1969)
2 Malecka, K.; Kubis, A.: Pharmazie **51**, 240 (1996)
3 Malecka, K.; Kubis, A.: Pharmazie **53**, 396 (1998)

Received July 22, 1999
Accepted July 9, 2000

Prof. Dr. A. A. Kubis
Dept. of Pharmamaceutical Technology
ul. Szewska 38
50-139 Wrocław
Poland