약제학회지 (1986), 제16권 제 3 호
J. Kor. Pharm. Sci., Vol. 16, No. 3, 101~105 (1986)

Effect of Water-Soluble Carriers on Water-Absorption and Swelling of Polydimethylsiloxane-5-Fluorouracil Devices

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(Received April 18, 1986)

The changes of water absorption and surface area of polydimethylsiloxane-5-fluorouracil devices containing different water soluble additives such as sodium chloride, glycerine, polypropylene glycol(PPG 400), and polyethylene oxide(PEO 400, 400 and 2000) were investigated. It was confirmed that carriers controlled water absorption and swelling of the devices in the aqueous solutions. The water absorption and the swelling were affected by the osmotic pressure and ionic strength of the aqueous solutions.

Polydimethylsiloxanes (silicone rubbers) are biocompatible, non-biodegradable and chemically inert polymers which are ideal for use in controlled drug delivery systems. Polydimethylsiloxanes are employed as rate controlling membranes and matrices for both human and veterinary pharmaceutical implant and transdermal dosage forms.

Delivery of drugs from hydrophobic polydimethylsiloxanes has been limited to lipophilic and non-ionic drugs. It has been reported that the release of hydrophilic drugs such as heparin,[1] melatonin,[2] morphine sulphate,[3] sulfanilamide,[4] or progesterone[5] can be enhanced by polydimethylsiloxanes which are blended with water soluble materials such as glycerine, polyethylene oxide (PEO 400 and 20000), polypropylene glycol, sodium chloride, azone, lactose and sodium alginate.

In order to explore the potential use of water-soluble additives for controlled drug release, hydrophilic materials should be investigated with regard to their suitability for blending with polydimethylsiloxanes, and the action as water-carriers.

This study was concerned with the water absorption and the swelling of polydimethylsiloxane-5-fluorouracil devices containing various water soluble additives such as sodium chloride, glycerine, polypropylene glycol (PPG 400), and polyethylene oxides.

EXPERIMENTAL

Materials

Polydimethylsiloxane and stannous octoate (Dow Corning Corp., Co.), polypropylene glycol 400 (Polyscience Co.), polyethylene oxide (PEO 400, 4000, 20000) (Sigma Co.) glycerine and sodium chloride (Wako Pure Chem. Ind. Co.), and 5-fluorouracil (Roche Korea Co.) were used as received. Sodium chloride and 5-fluorouracil were passed through a 200 mesh screen prior to use.

Preparation of Devices

The additive such as sodium chloride, glycerine, PEO 400 or the chloroform solution of PEO 4000 and 20000 was blended with silicone rubber in the desired proportion.

The mixture containing chloroform was dried in a vacuum dry oven at room temperature. The 5-fluorouracil was dispersed homogeneously into silicone rubber containing the additive. Stannous octoate catalyst (20mg or 40mg for polyethylene oxide 400, glycerine, and polypropylene glycol 400) was dispersed into 5g of the above dispersion. The mixtures were applied rapidly to polyethylene plates and degassed in a high vacuum oven (20 μm Hg). Next those samples were allowed to vulcanize overnight at room temperature. Disk devices (0.615 cm diameter, 0.210 cm thickness) were cut from the vulcanized sheets and immediately used for the swelling experiments.

Determination of Swelling

The samples were immersed in 10 ml of double distilled water, normal saline solution 0.2 M phosphate buffer (pH 7.4), and maintained at room temperature. At appropriate time intervals, the swollen samples were removed from the solutions, cleared of water with tissue paper, weighed and quickly immersed in fresh solvent. Each experiment was run in triplicate, and the data were averaged. Stirring had practically no effect on the swelling kinetics.

RESULTS AND DISCUSSION

The swelling kinetics of the device composed of silicone rubber (90%w/w), 5-fluorouracil (5% w/w) and water carriers (5% w/w), in double distilled water, normal saline solution and 0.2 M phosphate buffer (pH 7.4) are presented in

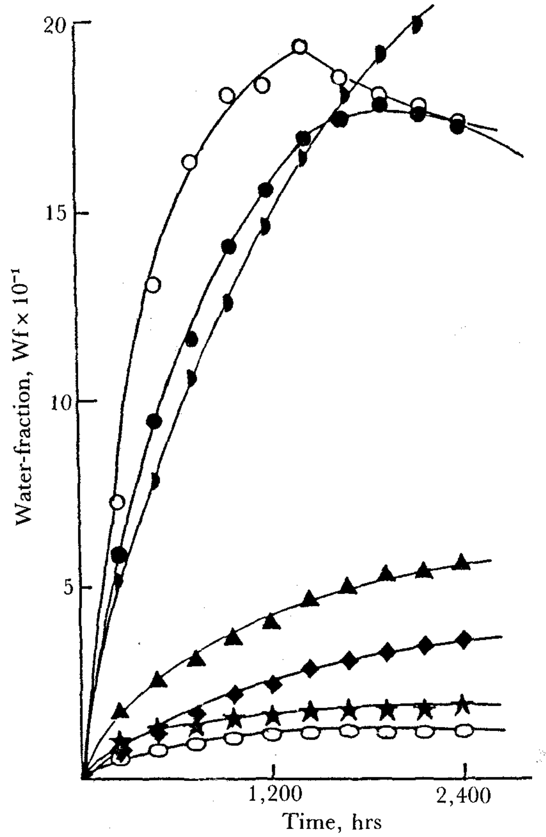

Figure 1 — Data on water-fraction in water of silicone rubber devices (0.21-cm thickness, 0.62-cm diameter) having 5-fluorouracil (5% w/w) and various water carriers (5% w/w).
Key: (O), sodium chloride; (●), glycerine; (◗), PEO 400; (▲), PEO 4000; (◆), PPG 400; (★), PEO 20000; (○), none

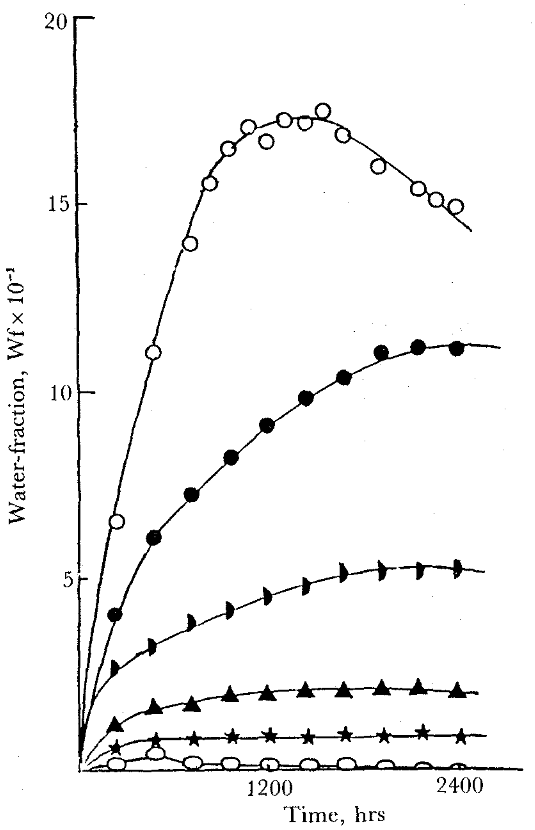

Figure 2 — Data on water-fraction in 0.2M phosphate buffer (pH 7.4) of silicone rubber devices (0.21-cm thickness, 0.62-cm diameter) having 5-fluorouracil (5% w/w) and various water carriers (5% w/w).
Key: (O), sodium chloride; (●), glycerine; (◗), PEO 400; (▲), PEO 4000; (★), PEO 20000; (○), none

Figs. 1, 2, 3 and Table I. The ratio of weight increase after swelling, Wf, defined as water absorption degree was plotted against time. As seen in Fig. 1, sodium chloride and glycerine increased the water absorption of device quickly to the maximum level and then the water absorption decreased with time. Such a pattern suggested that the water absorption was different with additives used in silicone rubber-5-fluorouracil devices.

As the molecular weight of polyethylene oxide derivatives increased, water absorption decreased. However overall water absorption increased very slowly over time.

At any given degree of swelling, a faster swelling rate was observed in double distilled water

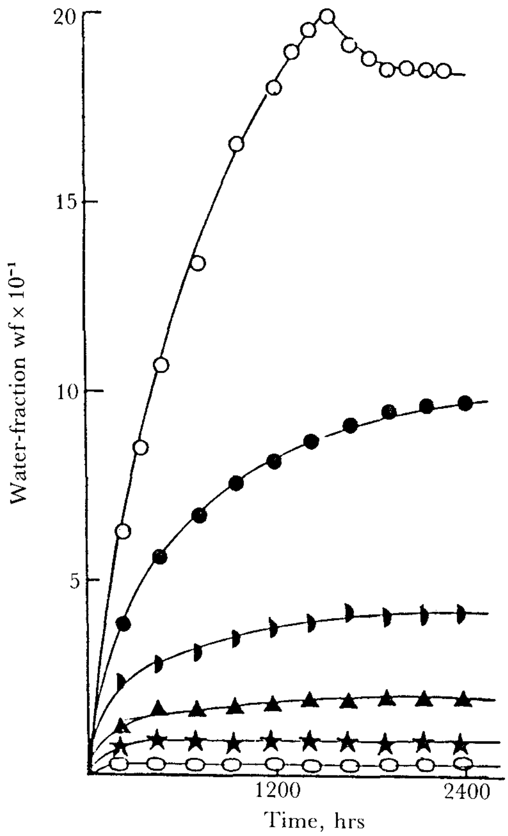

Figure 3 — Data on water-fraction in saline solution of silicone rubber devices (0.21-cm thickness, 0.62-cm diameter) having 5-fluorouracil (5% w/w) and various water carriers (5% w/w).
Key: (○), sodium chloride; (●), glycerine, (◗), PEO 400; (▲), PEO 4000; (★), PEO 20000; (◯), none

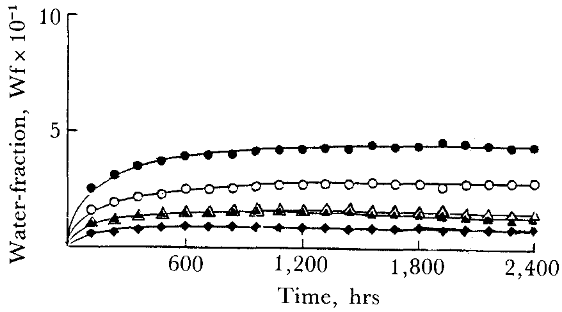

Figure 4 — Data on water-fraction in saline of silicone rubber devices (0.21-cm thickness, 0.65-cm diameter) having various water carriers and 5-fluorouracil.
Key: (●), 15% w/w PEO 20000 — 5% w/w 5-fluorouracil; (○), 10% w/w PEO 20000—5% w/w 5-fluorouracil; (▲), 5% w/w PEO 20000 — 10% w/w 5-fluorouracil; (△), 5% w/w PEO 20000 — 15% w/w 5-fluorouracil; (◆), 5% w/w PEO 20000 — 5% w/w 5-fluorouracil

than in normal saline solution and 0.2 M phosphate buffer (Compare Figs. 2 and 3 with Fig. 1). This was considered to be due to the lower ionic strength and osmotic pressure of double distilled water, comparing with those of saline solution and 0.2 M phosphate butter.

When the effect of additive concentration was

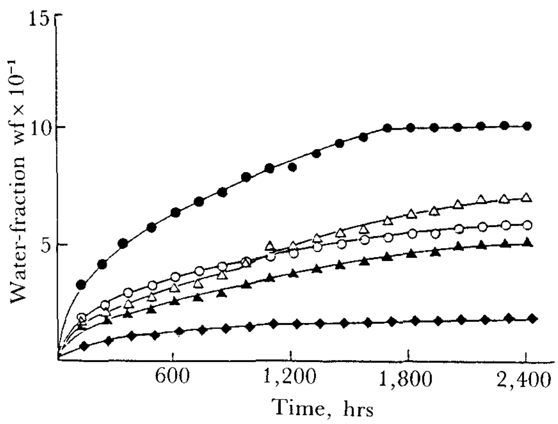

Figure 5 — Data on water-fraction in water of silicone rubber devices (0.21-cm thickness, 0.65-cm diameter) having various water carriers and 5-fluorouracil.
Key: (●), 15% w/w PEO 20000 — 5% w/w 5-fluorouracil; (○), 10% w/w PEO 20000 — 5% w/w 5-fluorouracil; (▲), 5% w/w PEO 20000 — 10% w/w 5-fluorouracil; (△), 5% w/w PEO 20000 — 15% w/w 5-fluorouracil; (◆), 5% w/w PEO 20000 — 5% w/w 5-fluorouracil

examined, all devices formulated with various concentrations of the same additives and 5-fluorouracil produced the similar swelling patterns one another, but the degree of the swelling was concentration dependent. When the water absorption by adding the water-carrier reached its maximum degree, the swelling degree of the devices having various water-carriers was the same. It was suggested that when water was not in complete contact with the water-carrier in the devices, the devices did not absorb water.

The water absorption and the swelling of silicone rubber-5% w/w 5-fluorouracil devices containing various concentrations of PEO 20000 are shown in Figs. 4, 5 and 6, and in Table II. The magnitude of water absorption and swelling of the devices having PEO 20000 was concentration dependent. The profile of the water absorption versus time, as well as the water absorption fraction versus time, followed the first order kinetics. On the other hand, the water absorption fraction and the fraction of swelling of the devices showed different values with various aqueous solutions. This was considered to be due to the different osmotic presure and ionic strength of media.

The effect of 5-fluorouracil on the swelling and the water absorption of the devices was demonstrated. Although the magnitude of tne water absorption fraction and fraction of swelling was related to 5-fluorouracil concentration, the extent of swelling and water absorption

Table I – *The Changes in the Surface Area and the Weight of Silicone Rubber Devices (0. 21 cm Thickness, 0. 62 cm Diameter) Having 5%w/w Various Water-Carriers and 5% w/w 5-Fluorouracil in Various Aqueous Solutions.*

Water carrier	Water		Saline-solution		0.2M Phosphate buffer(pH 7.4)	
	Sf[a]$\times 10^{-1}$	Wf[b]$\times 10^{-1}$	Sf$\times 10^{-1}$	Wf$\times 10^{-1}$	Sf$\times 10^{-1}$	Wf$\times 10^{-1}$
None	0. 961*	1. 217	0. 321	0. 279	0. 101	0. 159
Sodium chloride	11. 560	17. 310	10. 480	18. 500	10. 160	15. 550
Glycerine	12. 240	17. 320	6. 461	9. 817	7. 342	11. 400
PEO 400	11. 920	20. 770	2. 031	4. 571	2. 751	5. 479
PEO 4000	4. 451	5. 562	0. 961	1. 905	1. 331	2. 121
PEO 20000	1. 172	1. 850	1. 091	0. 851	0. 821	0. 925
PPG 400	2. 940	3. 507	–	–	–	–

*The devices were soaked for 2, 400 hrs.

$^{a)}Sf = \dfrac{\text{surface area after soaking} - \text{initial surface area}}{\text{initial surface area}}$

$^{b)}Wf = \dfrac{\text{weight after soaking} - \text{initial weight}}{\text{initial weight}}$

Table II – *The Changes in the Surface Area and the Weight of Silicone Rubber Devices(0. 21 cm Thickness, 0. 62 cm Diameter) Having 5% w/w 5-Fluorouracil and Various Concentrations of PEO 20000 in Various Aqueous Solutions.*

PEO 20000	Water		Saline solution		0.2M Phosphate buffer(pH 7.4)	
	Sf[a]$\times 10^{-1}$	Wf[b]$\times 10^{-1}$	Sf$\times 10^{-1}$	Wf$\times 10^{-1}$	Sf$\times 10^{-1}$	Wf$\times 10^{-1}$
None	0. 961*	1. 217	0. 321	0. 279	0. 101	0. 159
5%	1. 172	1. 860	1. 091	0. 851	0. 821	0. 925
10%	5. 951	5. 868	4. 101	2. 966	3. 891	3. 253
15%	6. 821	11. 300	4. 741	4. 695	4. 791	4. 791

*The devices was soaked for 2, 400 hrs. [a)]Sf and [b)]Wf are the same as seen in Table I.

Table Ⅲ – *The Changes in the Surface Area and the Weight of Silicone Rubber Devices (0.21 cm Thickness, 0.62 cm Diameter) Having 5% w/w PEO 20000 and Various Concentrations of 5-Fluorouracil in Various Aqueous Solutions.*

5-Fluorouracil	Water		Saline solution		0.2M Phosphate buffer (pH 7.4)	
	Sf[a] × 10^{-1}	Wf[b] × 10^{-1}	Sf × 10^{-1}	Wf × 10^{-1}	Sf × 10^{-1}	Wf × 10^{-1}
5%	1.172*	1.850	1.091	0.851	0.821	0.921
10%	3.631	5.087	1.261	1.631	1.861	1.642
15%	5.231	6.898	1.301	1.667	1.921	1.657

*The devices was soaked for 2,400 hrs. [a]Sf and [b]Wf are the same as seen in Table I.

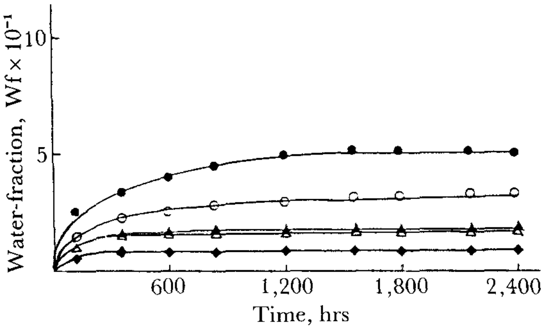

Figure 6 — Data on water-fraction in 0.2M phosphate buffer (pH 7.4) of silicone rubber devices (0.21-cm thickness, 0.65-cm diameter) having various water carriers and 5-fluorouracil.
Key: (●), 15% w/w PEO 20000 — 5% w/w 5-fluorouracil; (○), 10% w/w PEO 20000 — 5% w/w 5-fluorouracil; (▲), 5% w/w PEO 20000 — 10% w/w 5-fluorouracil; (△), 5% w/w PEO 20000 — 15% w/w 5-fluorouracil; (◆), 5% w/w PEO 20000 — 5% w/w 5-fluorouracil.

depended on some factors which might be the function of the initial water carrier concentration (Table III).

Devices containing polypropylene glycol (PPG 400) showed slightly increased water absorption and swelling of the device in water. With liquid additives such as polypropylene glycol 400 and glycerine, high concentrations of the catalyst than the usual were required to crosslink the polymer. Such an interference of these additives with the action of the initiator needs further investigation because of the possibility that these compounds may be a part of the crosslinking reaction. In conclusion, sodium chloride, glycerine, PPG 400 and PEO 400 were effective water carriers but PEO 4000 and 20000 sustained the water absorption. The devices containing PEO 4000 and 20000 swelled very slightly. The drug release characteristics from silicone rubber should be further studied.

CONCLUSIONS

Water carriers such as sodium chloride, glycerine, PPG 400, and PEO 400, 4000, and 20000 controlled the water absorption and the swelling of polydimethylsiloxane-5-fluorouracil devices.

1. The values of the water absorption and the swelling varied with the soaking solution.
2. The water absorption and the swelling were affected by the osmotic pressure and ionic strength of the aqueous solutions.

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