Effect of Different Water-Soluble Additives on Water Sorption into Silicone Rubber

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Received March 24, 1981, from the *Pharmaceutical Technology Laboratory, Institute of Pharmaceutical Chemistry, University of Pisa, 56100 Pisa, Italy.* Accepted for publication April 30, 1982.

Abstract □ The ability of ethylene glycol; glycerin; polyethylene glycols 200, 400, and 6000; polysorbate 80; and lactose dispersed in silicone rubber, to promote water sorption into the polymer was investigated in water and in isotonic (pH 7.4) phosphate buffer. Polyethylene glycols 200 and 400, lactose, and, especially, glycerin were effective water carriers. Marked differences in the kinetics of rubber swelling were observed, depending on the carrier. The swelling patterns relative to ethylene glycol, glycerin, and polyethylene glycol 200 showed a maximum due to significant leaching of these additives from the polymer. Steady swelling degrees were afforded by polyethylene glycols 400 and 6000 and by polysorbate 80. The interdependent processes of polymer imbibition and carrier release were speeded up without altering their kinetic patterns by increasing the initial surface-volume ratio of the devices. A proportionality resulted between maximal swelling and initial carrier concentration, although the swelling patterns were substantially unaffected by this variable.

Keyphrases □ Silicone rubber—effect of different water-soluble additives on water sorption □ Sorption—water, effect of different water-soluble additives on water sorption into silicone rubber □ Water-soluble additives—effect on water sorption into silicone rubber □ Swelling behavior—effect of different water-soluble additives on water sorption into silicone rubber

The advantages offered by the use of silicone rubber matrices as long-acting drug delivery systems are manifest in the literature (1–9). A number of water-soluble substances recently have been shown to promote water sorption into silicone rubber pellets containing morphine sulfate, thereby enhancing both *in vitro* and *in vivo* release of this drug (2, 3). In view of their potential use for control of drug release, other hydrophilic materials should be investigated with regard to their suitability to be dispersed in silicone rubber and to act as water carriers.

The present work is concerned with a study of the swelling behavior of silicone rubber devices containing different water-soluble additives: ethylene glycol; glycerin; polyethylene glycols 200, 400, and 6000; polysorbate 80; and lactose.

EXPERIMENTAL

Materials—Polydimethylsiloxane elastomer and silica filler[1]; stannous octoate[2]; ethylene glycol[3]; glycerin[3]; polyethylene glycols 200, 400, and 6000[4]; polysorbate 80[5]; monobasic sodium phosphate[3]; and dibasic sodium phosphate[3] were used as received. Lactose[3] was passed through a 140-mesh screen prior to use.

Preparation of Devices—The additive (ethylene glycol, glycerin, lactose, polyethylene glycol 200 or 400, or polysorbate 80) or a solution of the additive in chloroform (polyethylene glycol 6000) was dispersed in polydimethylsiloxane elastomer in the desired proportion by levigating for ~3 min. Five-gram amounts of the mixture generally were used. Stannous octoate catalyst (1 drop, ~20 mg; or 2 drops with polyethylene glycol 200) was levigated into 1 g of the above dispersion for ~0.5 min (after evaporation of chloroform in the case of polyethylene glycol 6000). The mixture then was added rapidly to a plastic mold, pressed with a plastic plate into a sheet of uniform thickness (0.2 or 0.05 cm), and allowed to cure overnight at room temperature. A cylinder (0.5-cm diameter, 0.2-cm thick) or a disk (1-cm diameter, 0.05-cm thick) was cut from the polymerized sheet and immediately used for the swelling experiments. The cylinders or the disks had dry weights which were between 46.2 and 54.4 mg or 49.1 and 53.5 mg, respectively, depending on the additive and its concentration.

Swelling Determinations—The sample being studied was flushed with distilled water and then rapidly placed between filter paper to remove clinging water. Its dry weight then was determined. Next, it was immersed in 20 ml of phosphate buffer (0.13 *N*, pH 7.4), or distilled water which was maintained at 37°. At measured intervals, the swollen sample was removed from the solvent, cleared of water with filter paper, weighed in a weighing bottle, and quickly immersed in 20 ml of fresh solvent prewarmed to 37° (time zero of the next interval). Each experiment was run in triplicate, and the data were averaged. The range of the measured values was not >±5% of the mean. Shaking had practically no effect on the swelling kinetics.

RESULTS AND DISCUSSION

The swelling kinetics of silicone rubber cylinders containing 12% (w/w) carrier, determined in isotonic phosphate buffer (pH 7.4) or in pure water, is presented in Figs. 1 and 2, respectively, where the ratio of the weights of swollen–dry sample, γ, defined as swelling degree, was plotted against time. The plots in Fig. 1 relative to ethylene glycol, glycerin, and polyethylene glycol 200 went through a maximum, thus, pointing to a change in the sign of the swelling pressure. Such a pattern was indicative of significant leaching of these substances from the silicone polymer. Much slower leaching, if any, of polyethylene glycols 400 and 6000 and polysorbate 80 was suggested by the respective swelling degrees which apparently attained steady equilibrium values. At any given swelling degree, a considerably higher swelling rate in pure water than in buffer was always observed. This was in accord with a higher osmotic pressure differential in the case of the pure water.

The swelling kinetics of silicone rubber disks (1-cm diameter and 0.05-cm thick), having the same volume and carrier concentration as the cylinders in Fig. 1, was followed to study the effect of varying the surface–volume ratio of the polymeric device. Disks filled with polyethylene glycol 6000 did not swell, and their weight decreased slightly upon hy-

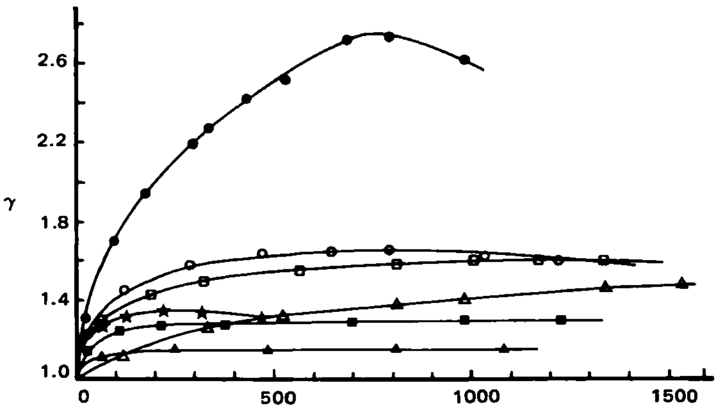

Figure 1—*Data on swelling in phosphate buffer (0.13* N, *pH 7.4) of silicone rubber cylinders (0.5-cm diameter, 0.2-cm thickness) containing various water carriers (12% w/w). Key: (●) glycerin; (○) polyethylene glycol 200; (□) polyethylene glycol 400; (★) ethylene glycol; (△) lactose; (■) polyethylene glycol 6000; (▲) polysorbate 80.*

[1] Silastic 382 medical grade elastomer, Dow Corning Corp., Midland, Mich.
[2] Catalyst M, Dow Corning Corp., Midland, Mich.
[3] Carlo Erba S.p.A., Milano, Italy.
[4] Merck-Schuchardt, München, West Germany.
[5] Tween 80, Atlas Chemie GmbH, Essen, West Germany.

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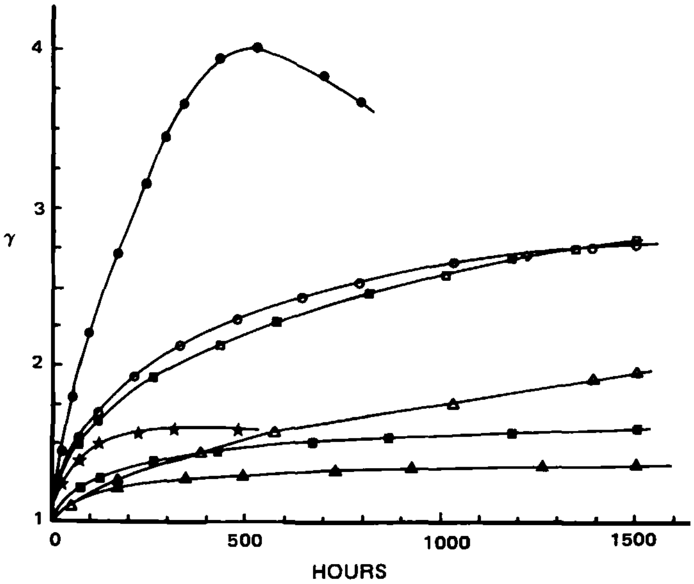

Figure 2—*Data on swelling in water of silicone rubber cylinders (0.5-cm diameter, 0.2-cm thickness) containing various water carriers (12% w/w). Key: (●) glycerin; (○) polyethylene glycol 200; (□) polyethylene glycol 400; (★) ethylene glycol; (△) lactose; (■) polyethylene glycol 6000; (▲) polysorbate 80.*

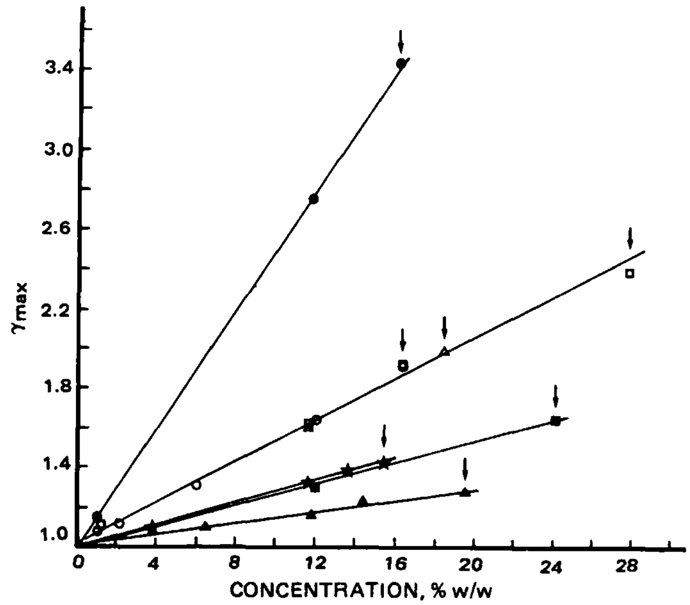

Figure 3—*Dependence of maximal swelling degree of cylinders in buffer on initial additive concentration. Key: (●) glycerin; (○) polyethylene glycol 200; (□) polyethylene glycol 400; (△) lactose; (★) ethylene glycol; (■) polyethylene glycol 6000; (▲) polysorbate 80. Concentrations substantially exceeding the values indicated for each additive by the arrows gave nonreproducible data.*

dration. The cause of this behavior could reside in an inadequate dispersion of this additive. Due to a comparatively high surface–volume ratio, the fraction of carrier undergoing a rapid dissolution from the disk surface predominated in this case over the carrier fraction in the disk core. The opposite occurred with the cylinders, which gave reproducible swelling data. The profile of the γ *versus* time plots, as well as the maximal swelling degrees of disks (not reported), remained unchanged with respect to the corresponding properties of cylinders, although the process was speeded up considerably in all cases with the disks. Since swelling was carrier driven, a similar effect of the surface–volume ratio on the release process of the leachable carriers could be inferred. The relevance of these findings to the release of water-soluble drugs embedded in silicone rubber is apparent.

Cylinders were used to study the effect of carrier concentration. Devices formulated with varying concentrations of the same additive all gave swelling plots similar in shape (not reported), although the magnitude of swelling was concentration dependent. Figure 3 shows the plots of the maximal swelling degree (γ_{max}) attained in buffer by the cylinders *versus* initial carrier concentration. Concentrations substantially exceeding the values indicated for each carrier in Fig. 3 did not yield reproducible results. A straight line with zero intercept was obtained with all of the additives studied. Such an apparent proportionality is intriguing, since the extent of swelling depended on numerous factors which in turn could be complex functions of initial carrier concentration. These are the osmotic activity of carrier (free or bound to the polymer through hydrogen or covalent bonding), the rate of carrier release from polymer, the polymer contractility, and the polymer plasticizing effect of the carrier. The slopes of the plots in Fig. 3, which can be referred to as the specific swelling power of the single carriers, appeared to be different for carriers of a similar physical and chemical nature, such as ethylene glycol and glycerin, or similar for additives of a different physical and chemical nature, such as polyethylene glycol 200 and lactose.

The variation range of all reported data was $\leq\pm5\%$. This reproducibility is indicative of an inherent ease in additive dispersal in polydimethylsiloxane, because of the simplicity of the mixing technique. With the liquid additives, especially with polyethylene glycol 200, higher than usual catalyst concentrations were needed to crosslink the polymer. Such an interference of these additives with the action of the initiator needs further investigation because of possibility that these compounds may be part of the crosslinking reaction. Shaking of the device–solvent systems did not affect the swelling data, suggesting the absence of boundary layer effects on the swelling kinetics.

In conclusion, polyethylene glycols 200 and 400, lactose, and especially glycerin were effective water carriers. Their actual role in drug release from silicone rubber will be assessed in future studies.

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ACKNOWLEDGMENTS

This work was supported in part by a grant from Consiglio Nazionale delle Ricerche.