Evaluation of Dimethylpolysiloxane Fluids as Vehicles for Various Pharmaceuticals I: Effect on Stability and Dissolution of Aspirin

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Abstract □ The physicochemical effects of dimethylpolysiloxane fluids as vehicles for aspirin on its stability and release characteristics were evaluated. Aspirin was extraordinarily stable in the silicone fluids. No decomposition was noted during 8 weeks of storage at 4 and 26°, and less than 0.5% degradation was detected after 8 weeks of storage at 45°. Moreover, the dissolution patterns of aspirin suspensions in the silicone fluids appeared to be quite satisfactory as compared with that of plain aspirin powder.

Keyphrases □ Dimethylpolysiloxane vehicles—effect on stability and dissolution of aspirin □ Aspirin suspensions—effect of dimethylpolysiloxane vehicles on stability and dissolution □ Silicone fluids, dimethylpolysiloxane—effect on stability and dissolution of aspirin suspensions

In a previous study (1), it was found that aspirin decomposed rapidly when incorporated into various polyethylene glycol bases. The degradation was attributed, at least in part, to a transesterification reaction between aspirin and the polyethylene glycols. Reduction of the number of free hydroxy groups of the polyethylene glycols through the formation of acetylated glycols and methoxyglycols resulted in significant retardation of aspirin decomposition (2). However, while developing a stable and palatable liquid preparation of aspirin, the authors explored the potentiality of using dimethylpolysiloxane fluids as vehicles for aspirin because of their apparent inherent advantages over the commonly used nonaqueous vehicles.

Dimethylpolysiloxane fluids are odorless, colorless, tasteless, and strongly hydrophobic, and they possess very great chemical, thermal, and oxidative stability. They are superior to fixed oils in that they do not develop rancidity with aging. They have low viscosity–temperature coefficients, and their viscosity can be tailored to meet specific applications (3, 4). Dimethylpolysiloxane fluids have been reported to be very low in toxicity (5–9). Medical-grade silicones are widely used in tissue implants (10) and as inhalation sprays for the treatment of pulmonary edema involving frothing of fluid in the upper respiratory tract (11). They are pharmacologically inactive when given orally (12) and do not appear to possess any adverse effects when ingested (4). Their oral use as antiflatulents has been reported (11, 12). Silicones also have been used in tablet and capsule coatings and to fill in hypoplastic body areas for cosmetic purposes (11). In food processing, food-grade dimethylpolysiloxane is used for defoaming (13).

Turnbull and Avis (3) stated that the dimethylpolysiloxane fluids appear to possess most of the characteristics of an ideal nonaqueous solvent. The use of silicone fluids as vehicles for the intramuscular administration of drugs has been reported (3, 14, 15).

Apart from these properties of dimethylpolysiloxane fluids, their hydrophobic nature suggest that they may tend to retard the decomposition and enhance the absorption of drugs such as aspirin. Furthermore, in a recent study, dimethylpolysiloxane significantly protected rat gastric mucosa from the irritant effects of aspirin (12).

The objective of this study was to explore the physicochemical effects of dimethylpolysiloxane fluids, when utilized as vehicles for aspirin, on the stability and release characteristics of this drug.

EXPERIMENTAL

Materials—Dimethylpolysiloxane fluids[1] were used as received from the commercial source. Aspirin[2] and salicylic acid[3] were of USP quality. Chloroform[4] was spectrograde, and other ingredients were USP or analytical grades.

Stability Studies—Quantities of aspirin (0.3 g) were placed into 40-ml amber glass vials, each containing 9.7 g of the silicone fluid. The tightly screw-capped vials were divided into three groups for storage at 4, 26, and 45°, and the samples were assayed at various intervals.

Analytical Method—UV spectrophotometric analysis (2, 16, 17) was employed to measure aspirin and salicylic acid. The contents of each vial were transferred quantitatively into a 100-ml volumetric flask using chloroform containing 1% acetic acid and then diluted to volume with the chloroform–acetic acid mixture. Clear solutions were obtained since the silicone fluids used were miscible (1:10) in chloroform (4). Then 1 ml of this solution was pipeted into a 50-ml volumetric flask and diluted to volume with the chloroform–acetic acid mixture. The absorbance of this solution was read[5] at 280 nm for aspirin and 310 nm for salicylic acid using the appropriate blanks. The silicone fluids did not interfere with the assay. At the two wavelengths indicated, standard curves were prepared for aspirin and salicylic acid. The quantification of aspirin and salicylic acid was based on the standard method of simultaneous spectrophotometric determinations.

Dissolution Studies—A rotating-bottle apparatus, similar to that used by Asker and Becker (18), was used. Screw-capped centrifuge tubes, each of 50-ml capacity, were utilized. Into each tube, 0.1 g of aspirin (passed through a 100-mesh sieve) was dispersed in 3 g of the silicone fluid. Then 25 ml of 0.1 *N* HCl at 37° was introduced. The tubes were allowed to rotate at 45 rpm in a water bath maintained at 37°. Two tubes were removed at each time interval for duplicate determination of the quantity of aspirin released. One tube containing the silicone and hydrochloric acid but no drug served as a blank. Two other tubes containing the drug and the dissolution medium but without silicone were used as the control for comparison.

The contents of each tube were transferred to a small separator. An appropriate volume of the aqueous layer was separated, filtered, and subjected to the assay procedure described by Javaid and Cadwallader (19). The absorbance of the solution was read[5] at 303 nm.

[1] Trade-marketed by Dow Corning Corp. as DC 200 silicone fluid, 350 centistokes; DC 200 silicone fluid, food grade, 350 centistokes; DC 360 medical silicone fluid, 20 centistokes; and DC 360 medical silicone fluid, 50 centistokes.

[2] Merck and Co.

[3] Fisher Scientific Co.

[4] J. T. Baker Chemical Co.

[5] Cary model 118 spectrophotometer.

Table I—Mole Percent Decomposition of Aspirin[a] with Time in the Silicone Fluids

Weeks of Storage	Mole Percent of Salicylic Acid Formed	
	200 Fluid[b], 45°	200 Fluid, Food Grade[b], 45°
0	0	0
1	0	0
2	0	0
3	0	0
4	0	0
5	0.16	0.20
6	0.19	0.20
7	0.40	0.37
8	0.43	0.40

[a] Expressed as moles of salicylic acid formed per 100 moles of aspirin. [b] No salicylic acid formed at 4 and 26°.

RESULTS AND DISCUSSION

The use of nonaqueous vehicles to enhance the stability of aspirin liquid preparations has been reported (2, 16). Due to the outstanding advantages of the silicone fluids as nonaqueous vehicles, it was decided to explore their physicochemical effects on the stability and dissolution rate of aspirin incorporated into them.

Table I shows that aspirin was extraordinarily stable in the silicone 200 fluids. No decomposition was noted during 8 weeks of storage at 4 and 26°, and only less than 0.5% degradation was detected after 8 weeks of storage at 45°. This negligible amount of aspirin decomposition could have been caused by traces of moisture that contaminated the dry aspirin during weighing and preparing the samples. The results obtained support previous findings on the enhanced stability of aspirin in nonpolar vehicles (2, 17).

Figure 1 shows the overall dissolution profiles of aspirin suspended in the silicone 360 medical fluids of the viscosity grades 20 and 50 centistokes. The silicone 360 medical fluid is chemically identical to the 200 fluid but more refined, and the medical literature references to the 200 fluid also apply to the 360 medical fluid (4). The dissolution data indicate that more than 90% of the aspirin was released during the first 6 min when aspirin was suspended in either the 20- or the 50-centistokes viscosity-grade silicone fluids. Plain powder aspirin, on the other hand, demonstrated 100% release in 6 min. The difference can be attributed to the time required for the aqueous dissolution medium to extract the aspirin particles suspended in the highly hydrophobic silicone fluids. Incorporation of a surfactant in the dissolution medium to lower its surface tension to a value corresponding to gastric fluid would be expected to enhance the dissolution rate of aspirin from the silicone fluids. Such expectation is based on previous results (20–22). Further studies on the effect of surface tension of the dissolution medium on the release of aspirin from the silicone fluids would be necessary before drawing a final conclusion. However, the dissolution patterns of aspirin suspensions in the silicone fluids obtained in this study appear to be quite satisfactory as compared with that of plain aspirin. It appears also from Fig. 1 that the viscosity of the silicone fluid influenced the rate of aspirin dissolution. The higher the viscosity of the silicone fluid, the less amount of aspirin is released during the first 20 min. This is, of course, expected since higher viscosity values would retard effective extraction of the drug by the aqueous dissolution medium.

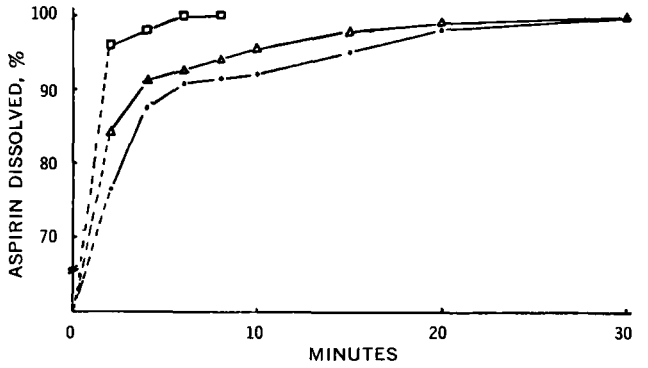

Figure 1—*Dissolution of aspirin in 0.1* N *HCl from aspirin suspensions in silicone fluids. Key:* △, *silicone fluid, 20 centistokes;* ●, *silicone fluid, 50 centistokes; and* □, *aspirin powder.*

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ACKNOWLEDGMENTS AND ADDRESSES

Received March 11, 1974, from the *School of Pharmacy, University of Georgia, Athens, GA 30602*

Accepted for publication May 22, 1974.

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