# Polymer-Induced Flocculation of Pharmaceutical Suspensions

ALVIN FELMEISTER▲, GALE M. KUCHTYAK, SUSAN KOZIOL, and CHARLES J. FELMEISTER

**Abstract** ☐ The effect of concentration of an anionic heteropolysaccharide on the sedimentation volume of sulfaguanidine, zinc oxide, talc, bismuth subcarbonate, and bismuth subnitrate aqueous suspensions was determined. All materials with the exception of sulfaguanidine showed a steady increase in sedimentation volume with increasing polymer concentration. Sulfaguanidine exhibited a maximum in the sedimentation volume–polymer concentration curve. All suspensions appeared uniform except for the bismuth subnitrate, which exhibited coarse, unsightly floccules. This effect was attributed to an interaction between the anionic polymer and the cationic bismuth subnitrate particles. Polymer bridging was postulated as the mechanism of flocculation in the other systems.

**Keyphrases** ☐ Flocculation, polymer induced—effect of polymer concentration on sedimentation volume of five pharmaceutical suspensions ☐ Polymers, anionic heteropolysaccharide—effect of concentration on induction of flocculation in pharmaceutical suspensions ☐ Suspensions—effect of polymer concentration on polymer-induced flocculation

Flocculation is recognized as an effective way of reducing the settling and subsequent caking of relatively coarse suspensions. Reduction of charge, chemical interaction, and polymer bridging have all been used to achieve this effect. Of these, polymer bridging appears to be the most efficient approach. The purpose of this study was to investigate the ability of an anionic heteropolysaccharide[1] to flocculate various pharmaceutical suspensions *via* polymer bridging.

## EXPERIMENTAL

**Materials**—The polymer used was an anionic heteropolysaccharide[1] produced by the action of the bacterium *Xanthomonas campestris* on carbohydrate. The other materials were sulfaguanidine NF XI[2], talc USP[3], zinc oxide USP[3], bismuth subcarbonate USP[3], bismuth subnitrate NF[3], and propylparaben USP[4]. Deionized water was used throughout this study.

**Procedure**—Five grams of drug was suspended in water, and the appropriate amount of a 5% aqueous dispersion of the polymer (preserved by 0.05% propylparaben) was added. The sedimentation volume was determined (1) in a 100-ml. glass-stoppered cylinder after 48 hr. Viscosity was determined using a rotational viscometer[5].

## RESULTS AND DISCUSSION

The viscosity of the suspending media at a relatively low shear rate (30 r.p.m.) ranged from 225 cps. for the maximum polymer concentration of 0.2% to 55 cps. for the 0.1% concentration.

**Sulfaguanidine Suspensions**—The sedimentation volume, $H_u/H_0$, increased with increasing polymer concentration up to 0.1% (Fig. 1). Beyond that level, the sedimentation volume decreased and appeared to level off only slightly above that observed in the absence of polymer. This effect is indicative of polymer adsorption and bridging, as postulated by LaMer and Healy (2); *i.e.*, maximum bridging occurs at some optimal polymer concentration and, consequently, a maximum in the sedimentation volume–polymer concentration is anticipated. Furthermore, the higher sedimentation volumes observed in this study, compared to those that resulted when sulfaguanidine was flocculated by a reduction in ζ-potential (3), are a further indication of polymer bridging.

**Zinc Oxide and Talc Suspensions**—As with sulfaguanidine, increasing the concentration of the polymer resulted in an increase in the sedimentation volume (Fig. 2). In the case of these two materials, however, the maximum sedimentation volume was much higher than with sulfaguanidine, reaching a value of 1 at a polymer concentration of 0.2%. At all sedimentation volumes, the suspension appeared to be uniform with no evidence of large separate floccules. This suggests that the suspension exists as a "single floc" extending throughout the vehicle as previously described (4).

Unfortunately, the effect of higher polymer concentrations on polymer–particle bridging and sedimentation volume could not be determined because of the polymer concentration required to achieve the maximum effect. Above this polymer concentration, the viscosity of the solution increased rapidly and there was evidence of a yield value, both of which tended to inhibit the settling almost completely over the observation period.

**Bismuth Suspensions**—The suspension of bismuth subcarbonate (Fig. 3) behaved essentially like the suspensions of zinc oxide and talc. However, the bismuth subnitrate formed very coarse, granular-appearing floccules which tended to settle rapidly to sedimentation volumes lower than those observed for the other materials at similar polymer concentrations. This effect apparently is the result of a chemical interaction between the negatively charged polymer and the positively charged bismuth subnitrate (5).

No attempt was made to quantify the redispersibility of the flocculated suspensions. However, qualitatively, it could be seen by gently inverting the cylinders containing the suspensions that all

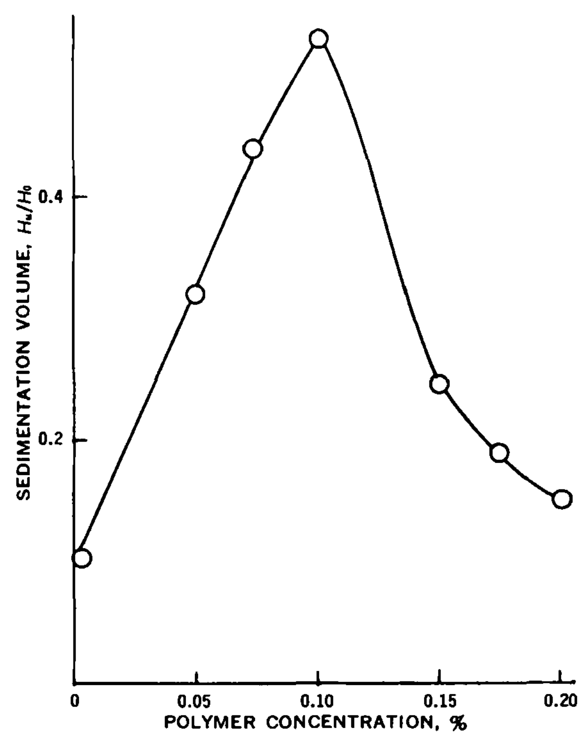


**Figure 1**—*Sedimentation volumes of 5% suspensions of sulfaguanidine in solutions of various concentrations of an anionic polysaccharide.*

[1] Biopolymer XB-23 xanthan gum, General Mills Chemicals, Inc., Minneapolis, Minn.
[2] American Cyanamid, Pearl River, N. J.
[3] Merck and Co., Rahway, N. J.
[4] Washine Chemical Corp, Lodi, N. J.
[5] Brookfield viscometer model LVT.

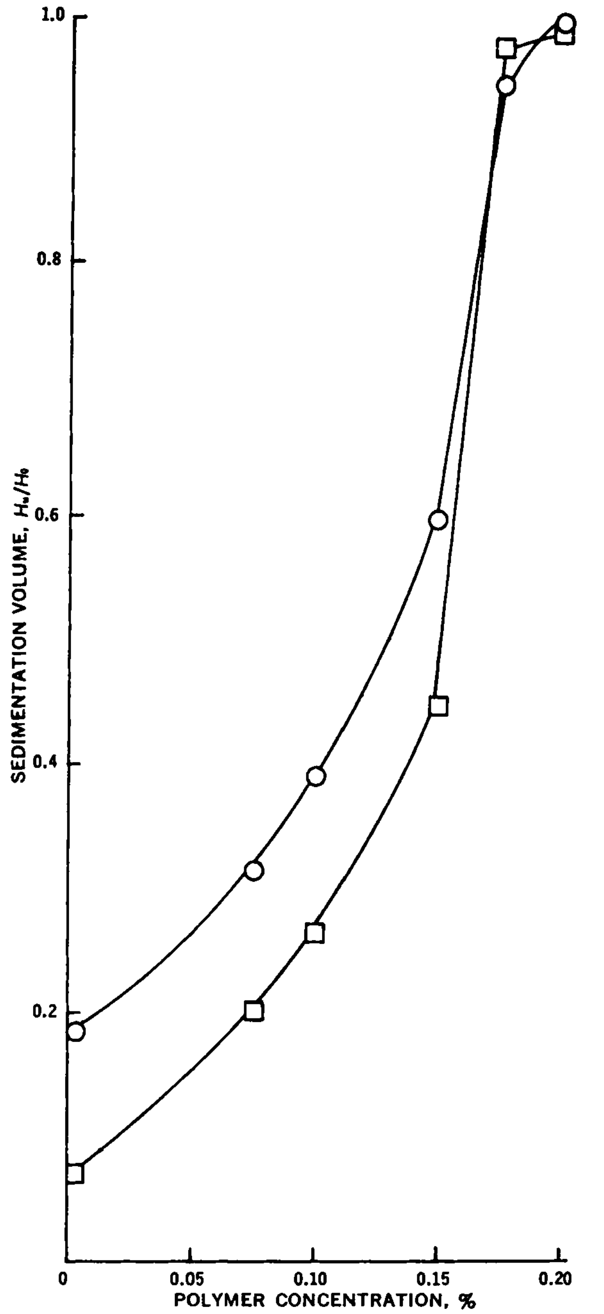


**Figure 2**—*Sedimentation volumes of 5% suspensions of zinc oxide (○) and talc (□) in solutions of various concentrations of an anionic polysaccharide.*

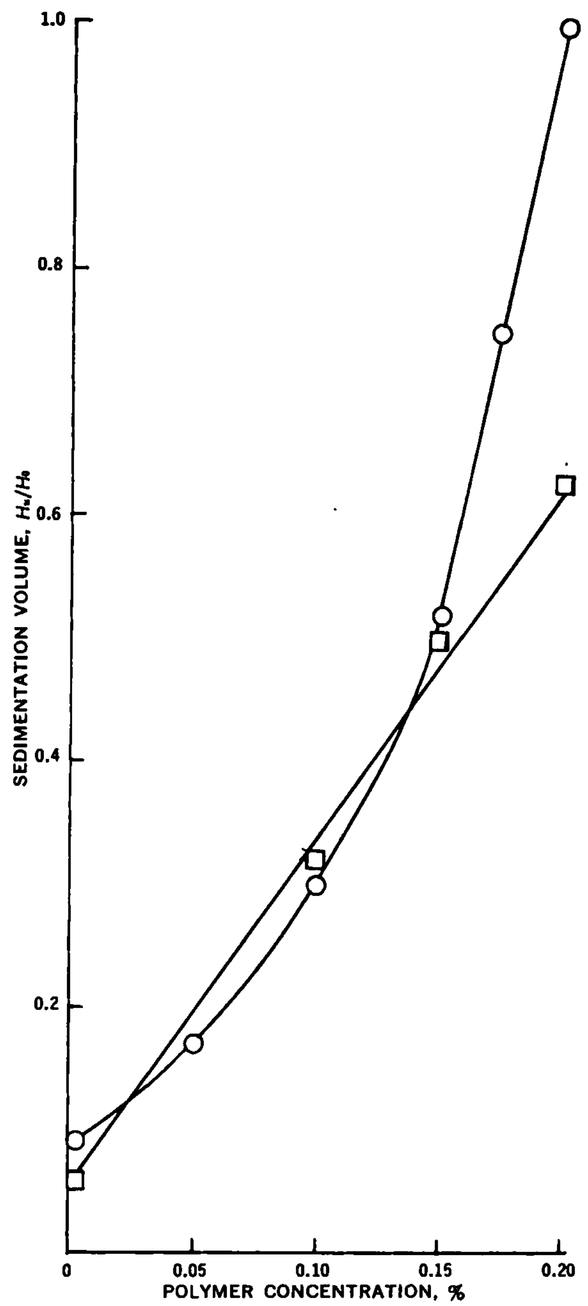


**Figure 3**—*Sedimentation volumes of 5% suspensions of bismuth subcarbonate (○) and bismuth subnitrate (□) in solutions of various concentrations of an anionic polysaccharide.*

the flocculated systems, with the exception of the bismuth subnitrate system, redispersed more easily than the deflocculated systems. Furthermore, with the same exception, all suspensions appeared smooth and could be readily poured from the cylinder after redispersion.

## CONCLUSIONS

The anionic polysaccharide polymer used in this study is an effective flocculating agent at relatively low concentrations for a wide variety of insoluble pharmaceutical materials. The high sedimentation volumes observed, in some instances apparently reaching the single floc condition (4), are indicative of polymer-particle bridging. The anionic charge on the polymer, however, interacts with the positive charge on the surface of bismuth subnitrate particles (and, probably, other positively charged particles) to yield an inelegant, and generally unacceptable, pharmaceutical suspension.

## REFERENCES


(1) H. T. Ward and K. Kammermeyer, *Ind. Eng. Chem.*, **32**, 622 (1940).

(2) V. K. LaMer and T. W. Healy, *J. Phys. Chem.*, **67**, 2417 (1963).

(3) R. D. C. Jones, B. A. Matthews, and C. T. Rhodes, *J. Pharm. Sci.*, **59**, 518(1970).

(4) E. N. Hiestand, *ibid.*, **61**, 268(1972).

(5) R. G. Wilson and B. Ecanow, *ibid.*, **53**, 913(1964).


## ACKNOWLEDGMENTS AND ADDRESSES


Received July 21, 1972, from the *College of Pharmacy, Rutgers—The State University, University Heights Campus, New Brunswick, NJ 08903*

Accepted for publication August 1, 1973.



▲ To whom inquiries should be directed.