

doses. The depressor effect of the esters was similar in cats and rabbits. It could not be blocked by atropine, and it could be reversed by epinephrine. This was indicative that the effect was due to direct smooth muscle relaxation or to the cardiac depression which was quite apparent.

To show that the depressor effect was primarily due to cardiac inhibition, the esters were tested on the isolated rabbit heart after the method of Langendorff (11). As can be seen in Fig. 4, all of the compounds brought about a sharp decline in both rate and amplitude of the heart beat. If given in carefully controlled doses, the heart returned to normal, but higher doses resulted in complete heart arrest. Coronary flow was also markedly diminished, precluding the possibility of significant direct smooth muscle relaxation.

SUMMARY AND CONCLUSIONS

The results of this study indicate that the four citric acid esters used as plasticizers have well defined and marked pharmacological activity when administered parenterally. All four have local anesthetic action and can block neural transmission when they come in direct contact with a nerve trunk. All of them diffuse from the blood stream into the cord in sufficient concentration to depress cord function. At the same time they apparently stimulate the higher centers. Although they vary widely in potency, both the ethyl esters and the butyl esters depress cardiac activity sufficiently to produce cardiovascular collapse. Chronic administration of three of them (TEC, ATEC, and TBC)

does not appear to have an effect on the blood picture, but there are indications that ATBC may inhibit production or increase destruction of red blood cells. No species variation was observed throughout the investigation.

One must take care not to extrapolate the results reported in this paper to actual polyvinyl chloride devices which might contain plasticizers as reported here, since the biological activity will be elicited only when the plasticizer is released into the body fluids and, further, that the magnitude of the response shall have a direct relation to the concentration released. The biological responses reported here for a group of plasticizers should, however, alert those manufacturing plastic devices to learn more about the ingredients they employ in their plastic formulation if these items are to be introduced into medical practice.

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Rheology of Gelatin Films

By ROBERT A. CASTELLO* and JERE E. GOYAN†

A procedure has been developed for the evaluation of the viscoelastic properties of gelatin films employed in soft gelatin capsule formulations. It involves the measurement of the tensile relaxation modulus of the film and the fitting of the resultant curve on an analog computer to obtain the appropriate constants. A theory was proposed for the mechanism of stress relaxation in gelatin films. Based upon this theory, an equation for the tensile relaxation modulus was derived. This equation was of the same form as the empirical equation which fit the stress relaxation curves of the gelatin films.

ALTHOUGH MUCH INFORMATION has been gathered concerning changes in the rheological properties of gelatin solutions upon thermal aging, little is known of the characteristics

of gelatin films. Since the rheological behavior of gelatin films influences the properties of capsules molded from them, information concerning changes in this behavior might be helpful in evaluating technological problems encountered in the encapsulation process.

The viscoelastic properties of gelatin have been investigated by several authors. Among them, Ferry (1, 2) has studied the concentration effect on gel rigidities, and Tobolsky (3, 4) has studied stress relaxation as a tool in the investigation of gelation mechanisms. In this study the stress relaxation model has been

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adapted for the investigation of soft gelatin capsule formulations.

The field of viscoelasticity is intimately concerned with two basic physical laws. The first of these is Newton's law of viscosity which states that the stress on a perfectly viscous body is directly proportional to the rate of strain and is independent of the strain, giving

$$\sigma = \eta d\epsilon/dt \quad (\text{Eq. 1})$$

where σ = stress, $d\epsilon/dt$ = rate of strain, and η = coefficient of viscosity. The second is Hooke's law which states that the stress on a perfectly elastic body is proportional to the strain and is independent of the rate of strain, giving in the case of simple extension

$$\sigma = E\epsilon \quad (\text{Eq. 2})$$

where σ = stress, ϵ = strain, and E = Young's modulus of elasticity.

The basic viscoelastic equations may be derived from these two equations; Reiner (5) has done this for the stress relaxation modulus. Stress relaxation may be defined as the change in stress with time of a viscoelastic body under constant strain. Upon differentiating Eq. 2 with respect to time

$$d\sigma/dt = E d\epsilon/dt \quad (\text{Eq. 3})$$

Then, combination of this with Newton's equation gives

$$2d\epsilon/dt = (1/E) d\sigma/dt + (1/\eta)\sigma \quad (\text{Eq. 4})$$

Under the conditions of stress relaxation, the strain is constant. Therefore, $d\epsilon/dt$ is equal to zero and the equation becomes

$$d\sigma/dt = (E/\eta)\sigma \quad (\text{Eq. 5})$$

By separating the variables and integrating

$$\sigma(t) = \sigma_0 \exp - (E/\eta)t \quad (\text{Eq. 6})$$

This then describes the change in stress with time of a viscoelastic system under constant strain.

A very wide class of substances exhibit mechanical behavior in which elastic and viscous behavior are superposed. Much interest has been generated in this complex mechanical behavior and several authors (6-8) have employed mechanical models depicting these phenomena.

Nearly a century ago, Maxwell first postulated the stress relaxation equation. This equation corresponds to a mechanical model consisting of a spring and dashpot in series (see Fig. 1) which is therefore called a Maxwell element. In this model, the spring obeys Hooke's law,

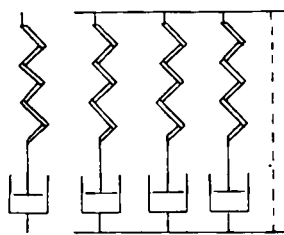


Fig. 1.—Maxwell and Wiechert mechanical models for stress relaxation.

and the resistance to flow in the dashpot is supplied by a Newtonian viscous oil.

The Maxwell equation is

$$\sigma(t) = \sigma_0 \exp - (t/\tau) \quad (\text{Eq. 7})$$

where τ = the Maxwell relaxation time (the time required for the stress to equal $1/e$ times its initial value). In terms of the Maxwell model, the spring would have a Young's modulus of E , and the oil a viscosity of η . Therefore

$$\tau = \eta/E \quad (\text{Eq. 8})$$

The Maxwell model describes adequately the stress relaxation of a single polymer chain, but polymeric systems such as gelatin solutions are described as being composed of n polymer chains. A theory that accounts for the presence of a number of chains was proposed by Wiechert. The mechanical model suggested by Wiechert is simply a large number of Maxwell elements placed in parallel as shown in Fig. 1. The equation for stress relaxation of the Wiechert model is

$$\sigma(t) = \sum_{i=1}^n \sigma_i \exp(-t/\tau_i) \quad (\text{Eq. 9})$$

where σ_i = partial stress contributed by the i th element ($\sigma_0 = \sum \sigma_i$) and τ_i = Maxwell relaxation time of the i th element. A similar analogy can be made as with the Maxwell model so that

$$\tau_i = \eta_i/E_i \quad (\text{Eq. 10})$$

where η_i and E_i are the coefficient of viscosity and Young's modulus of the i th elements, respectively.

EXPERIMENTAL

Several different types of gelatin were employed in this study. Specifications for these samples appear in Table I. The formulation used consisted of:

Gelatin (on an anhydrous basis) . . .	43%
Glycerin U.S.P.	18%
Distilled water	39%

In the preparation of the sample, the gelatin was weighed and placed in a 2-L. resin reaction flask equipped with a Gerald K. Heller model GT-21 motor and controller.¹ The stirrer shaft was inserted through the center part of the resin flask

¹ G. K. Heller Co., Las Vegas, Nev.

TABLE I.—SPECIFICATIONS OF GELATIN SAMPLES^a

Sample	Source	Viscosity, Millipoise	Bloom	pH	Raw Material	Process	% Moisture
33-59A	Amer. Agr. Chem. Co.	44.5	250	5.7	Porkskin	Acid	9.8
33-59B	Amer. Agr. Chem. Co.	47.1	225	5.55	Ossien	Lime	9.4
33-59C	Amer. Agr. Chem. Co.	51.3	281	5.8	Porkskin	Acid	9.3
33-59D	Amer. Agr. Chem. Co.	50.5	290	5.55	Porkskin	Acid	9.5
33-59E	Amer. Agr. Chem. Co.	44.7	203	5.45	Calfskin	Lime	13.1
33-59F	Amer. Agr. Chem. Co.	47.1	150	5.6	Calfskin	Lime	10.3
33-59G	Amer. Agr. Chem. Co.	29.5	165	4.95	Porkskin	Acid	10.6
33-59H	Amer. Agr. Chem. Co.	25.6	177	5.65	Porkskin	Acid	8.9
33-59I	Amer. Agr. Chem. Co.	29.8	177	5.15	Porkskin	Acid	10.1
33-59J	Amer. Agr. Chem. Co.	35.8	161	5.5	Ossien	Lime	8.6
33-59K	Swift	37 to 43	195 to 205	4.4 to 4.8	Porkskin	...	10.0
33-59L	Vyse	37 to 43	120 to 130	5.5 to 7.0	Calfskin	...	10.4
33-59N	Riches Nelson	30	200	5.0	Ossien	Acid	12.9

^a The authors thank the Lederle Division of American Cyanamid Corp. for supplying gelatins 33-59K and 33-59L.

with a ball and socket joint. The flask was immersed in a water bath at 90°. The glycerin and water were mixed and heated to 90°, then added to the gelatin. The age of the melt was calculated from the time of this addition. The gelatin was allowed to melt, and the sample was then stirred for 30 minutes to insure homogeneity. After stirring, the sample was transferred to a 1-L. round bottomed flask which was immersed in a water bath at 60° ± 0.1°. Transfer was accomplished by a vacuum supplied by a water aspirator. This transfer also served to deaerate the gelatin melt.

Film strips were cast on the apparatus shown in Fig. 2. The brass hopper was equipped with a semi-circular valve to control the flow of gelatin. It was inserted through a port in the top of the drum assembly and was adjusted with set screws at the four corners of the hopper assembly to a position 0.010 in. above the drum surface. The casting thickness of the film was set at 0.025 in. with an adjustable gate in front of the hopper. The temperature of the hopper was controlled by a Glas-col heating mantle which was made to hopper dimensions. It was adjusted to maintain a 60° temperature in the sample. The films were cast on an 8-in. diameter chrome plated drum which was driven by a 1/8 h.p. Boston gear ratio motor² having a gear reduction of 1600 to 1. At the time of the casting, the valve was opened and the motor turned on. The film was cast at a rate of 1 r.p.m. The films were stripped from the casting drum and placed on stainless steel sheets to be cut into test strips. Test strips were cut with a razor blade using a template. The dimensions of the test portion were 1 × 5 cm. The actual film thickness was measured with a micrometer at the time of tensile measurements.

Film strips were aged in a blue M vapor-temp humidity chamber model VP-100 which had been modified.³ The solenoid valve was bypassed, and a water-alcohol mixture was circulated through the cooling coils by means of a centrifugal pump. The cooling mixture was contained in a refrigerated water bath and was kept at a temperature of -2°. The centrifugal pump was connected through an electrical relay which was controlled by a resistor whose resistance varied with humidity. The dry bulb temperature was adjusted as normally in the humidity cabinet. The relay was then adjusted

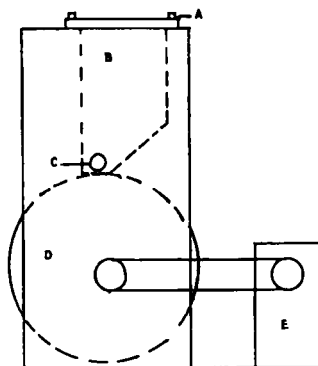


Fig. 2.—Film casting apparatus.

- A, Set screw
B, Hopper
C, Valve
D, Drum
E, Motor

so that the pump would shut off when the proper wet bulb depression was obtained on a wet bulb thermometer mounted inside the cabinet. The cover for the humidity cabinet which was originally an inverted bell jar was changed to a Plexiglas cabinet which would accommodate the tensile strength apparatus. Access to the inside of the cabinet was gained through an 8 × 12-in. door which was held in place by wing nuts at each of the corners. The edges of the door and the bottom of the Plexiglas cover were sealed with sponge rubber to prevent transfer of moisture from the atmosphere to the controlled humidity air inside the cabinet. A circulating fan was placed in the cabinet to insure that variations in the humidity at various levels in the cabinet would be negligible.

Tensile measurements of the films were made on a Gardner Laboratories tensile strength apparatus⁴ mounted inside the humidity cabinet. This apparatus was modified in the following manner. The spring for recording the force was replaced by a Statham Laboratories model G-1 transducer,⁵ and the output voltage was recorded on a model G-10 Varian Associates recorder.⁶ A Starret dial indicator⁷ was mounted on the apparatus to measure film elongation. The indicator had a range of 0.25 in. and was graduated in 0.001 in. At the time of measurement, the sample was instantaneously placed under a small strain by turning the handle on the worm gear at the top of the apparatus. The stress was followed with time and was recorded on

⁴ Gardner Laboratories, Bethesda, Md.

⁵ Statham Instruments, Hato Rey, Puerto Rico.

⁶ Varian Associates, Palo Alto, Calif.

⁷ Marwedel, San Francisco, Calif.

¹ Marwedel, San Francisco, Calif.

² Fisher Scientific Co., Pittsburgh, Pa.

TABLE II.—COMPUTER CONSTANTS OF GELATIN FILM 33-59B DURING THERMAL AGING OF MELT AT 60°C.

Melt Age, Hr.	Pre-exponentials $\times 10^{-8}$ (dynes cm. ⁻²)				Exponentials (sec. ⁻¹)		
	A	B	C	D	α	β	γ
7	4.30	4.68	4.38	3.26	0.922	0.261	0.046
24	4.04	4.66	3.80	2.72	0.922	0.261	0.046
48	5.58	4.82	3.24	2.74	0.922	0.261	0.046
72	5.28	3.80	3.78	2.66	0.922	0.261	0.046

the Varian recorder at a chart speed of 16 in. per minute. The elongation was measured to the nearest 1/1000 in. on the dial indicator, and the film thickness was measured with a micrometer for the calculation of the cross-sectional area.

Effect of Thermal Aging of the Melt.—A sample was prepared and hydrolyzed at 60° for 96 hours measured from the time of addition of the glycerin-water mixture to the dry gelatin. Film strips were cast at 24-hour intervals. These strips were aged in a humidity cabinet at 30° and 49% relative humidity for 3 hours. It had previously been determined that the film moisture content equilibrated during this aging period. Stress-time plots were recorded and the tensile relaxation moduli were calculated. Duplicate test strips were run for all measurements and agreed within 5% error. The stress relaxation curves were fitted on an analog computer and the constants determined. All of the curves fit

$$E(t) = Ae^{-at} + Be^{-bt} + Ce^{-\gamma t} + D \quad (\text{Eq. 11})$$

A typical set of constants is shown in Table II.

Film Storage at Constant Relative Humidity.—A gelatin melt was prepared and cast at 24, 48, and 72 hours. Several test strips were cut from each casting and aged in a humidity cabinet at 30° and 49% relative humidity. Tensile relaxation measurements were made at 48-hour intervals for 336 hours after casting. The stress relaxation curves were again fitted on the computer. Sample constants are shown in Table III.

Refrigerator Storage of Melt.—A sample was prepared and maintained at 60° for 30 hours. At 28 hours, a sample was cast and aged in the humidity cabinet at 30° and 43% relative humidity for 3 hours. The tensile relaxation modulus was determined. At the end of the 30-hour period, the sample was placed in a refrigerator at 3° for 15 days. The sample was removed from the refrigerator and heated an additional 5 hours at 60° to melt it. At this time, additional test strips were prepared in the same manner and the tensile relaxation moduli determined.

RESULTS AND DISCUSSION

All of the stress relaxation curves for a given gelatin melt were fitted using the same set of decay

constants regardless of the time of thermal aging. This was true not only for samples cast at various times from the same melt but also for samples cast from subsequent melts containing the same gelatin. These exponential decay constants could then be used as parameters to identify a specific gelatin.

As the gelatin was aged, the values of the initial modulus, E_0 , and the equilibrium modulus, E_e , decreased indicating that the number of cross links in the network was decreasing. These values did not decay in a regular fashion as did the viscosity values of the diluted gelatin melt (see Fig. 3). In most cases there appeared to be an induction period with little change in the tensile properties of the film and then a marked decrease usually appearing in the 48-hour sample. Therefore, the decay in the modulus could not be adequately explained by a scission of the polymer chain and subsequent loss of cross-linking sites from the molecule. If this were so, the decay would be expected to parallel the loss in viscosity.

Another cause for the tensile modulus decay may be proposed based on the concept of crystallinity in polymer systems. As the time of thermal aging increased, the polymer chains would contract and become more amorphous. When the gelatin temperature was lowered to the gel point during film casting, there would be fewer bonding sites oriented for cross-linking and the tensile modulus of the film would be lower. If this were the case, it would be expected that after extended periods at low temperatures the gelatin molecules could reorient and the modulus would increase.

This type of behavior was demonstrated during humidity cabinet storage of the gelatin films. The moduli increased with time of storage in the humidity cabinet indicating an increase in the number of cross-links and an increase in the crystallinity of the films. Since the increase of the tensile properties was a rate process, a treatment similar to Bisschop's for crystalline polymers was employed (9, 10). The equilibrium modulus of the film was plotted *versus* time of storage in the humidity cabinet. These plots for the 48-hour casting and 72-hour casting are shown in Fig. 4. As reported in the literature, these plots yielded straight lines whose slopes could be used as an estimation of the gel rate. It was interesting to note that the rate

TABLE III.—COMPUTER CONSTANTS OF GELATIN FILM 33-59J DURING HUMIDITY CABINET AGING 48-HOUR CASTING

Film Age, Hr.	Pre-exponentials $\times 10^{-8}$ (dynes cm. ⁻²)				Exponentials (sec. ⁻¹)		
	A	B	C	D	α	β	γ
48	4.22	1.54	1.54	0.85	0.874	0.252	0.043
96	4.50	1.28	1.28	0.79	0.874	0.252	0.043
144	4.14	1.45	1.94	1.25	0.874	0.252	0.043
192	3.70	2.16	2.36	1.55	0.874	0.252	0.043
240	3.63	1.81	1.65	1.24	0.874	0.252	0.043
288	3.61	2.60	2.46	2.02	0.874	0.252	0.043
336	3.15	3.38	2.83	2.00	0.874	0.252	0.043

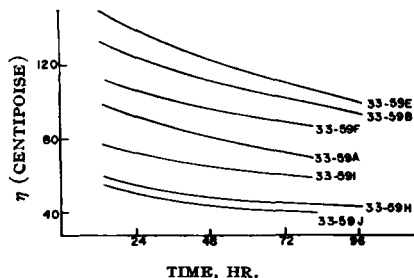
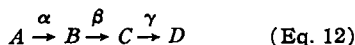


Fig. 3.—Viscosity of gelatin melts vs. time of thermal aging.

for the 48-hour casting was greater than that for the 72-hour casting. Thus, it appears that one of the effects of thermal aging of the melt is a decrease in the rate of gelation after casting.

Samples stored in the refrigerator for extended periods showed increased tensile properties over the thermally degraded melts which had previously been cast. This held true even though the samples had to be reheated at 60° for an additional 5 hours to reach casting consistency. These results again support the proposition that an orientation mechanism may account for the decay of tensile properties in gelatin films. At the refrigerator temperature the sample could reorient and increase its crystallinity allowing for a greater number of cross-links to be formed upon remelting and casting.

Experimental evidence favors the concept of crystalline-amorphous transitions in gelatin films. Assuming this concept to be true, the films would be expected to become more amorphous during thermal aging. This should result in a shift of the cross-link distribution to increase the number of short relaxation time cross-links. The phenomenon of stress relaxation could then be explained on the basis of an entropy change in the system which had been induced by the elongation of the polymer chains forcing them into a more oriented and more highly crystalline form. This concept may be investigated from a theoretical viewpoint to determine what type of equation for stress relaxation would be predicted. The film, as cast, may be considered to consist of polymer chains of varying degrees of crystallinity. During stress relaxation there is crystal growth, and these chains are transformed to the crystalline state. A series of reactions would be occurring during this process corresponding to the model



where *A* corresponds to the amorphous chains, *B* and *C* to intermediate degrees of crystallinity, and *D* to the crystalline chains. The rate constants for the transformations of these chains to more crystalline forms are α , β , and γ .

Assuming that these are all first-order transformations, a series of differential equations for the change in concentration of these cross-links with time may be

$$\frac{d[A]}{dt} = -\alpha[A] \quad (\text{Eq. 13})$$

$$\frac{d[B]}{dt} = \alpha[A] - \beta[B] \quad (\text{Eq. 14})$$

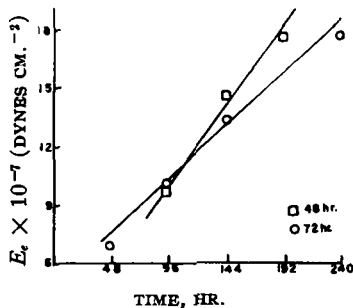


Fig. 4.—Equilibrium modulus gelatin film 33-59J vs. time of humidity cabinet aging.

$$\frac{d[C]}{dt} = \beta[B] - \gamma[C] \quad (\text{Eq. 15})$$

$$\frac{d[D]}{dt} = \gamma[C] \quad (\text{Eq. 16})$$

These equations may then be solved for the concentration of the cross-links.

The tensile modulus of the film should be proportional to the concentration of the cross-links and may be

$$E(t) = k_1[A] + k_2[B] + k_3[C] + k_4[D] \quad (\text{Eq. 17})$$

By substitution of the values for the concentration of the cross-links into the above equation one may obtain the equation for the tensile relaxation modulus, which on rearrangement yields

$$E(t) = k_4(A_0 + B_0 + C_0 + D_0) + \left[\frac{k_1(\alpha - \beta)(\alpha - \gamma) + k_2(\alpha - \gamma) + k_3\alpha\beta - k_4\beta\gamma}{(\alpha - \beta)(\alpha - \gamma)} \right] A_0 e^{-\alpha t} + \left[\frac{k_3\alpha\beta - k_2\alpha(\beta - \gamma) + k_4\alpha\gamma}{(\alpha - \beta)(\beta - \gamma)} \right] A_0 e^{-\beta t} + \left[\frac{k_2(\beta - \gamma) + k_3\beta + k_4\gamma}{(\beta - \gamma)} \right] B_0 e^{-\beta t} + \left[\frac{k_4\alpha\beta - k_3\alpha\beta}{(\gamma - \alpha)(\gamma - \beta)} \right] A_0 e^{-\gamma t} + \left[\frac{k_3\beta + k_4\beta}{(\gamma - \beta)} \right] B_0 e^{-\gamma t} + (k_3 - k_4) C_0 e^{-\gamma t} \quad (\text{Eq. 18})$$

This predicts for the tensile relaxation modulus an equation which would fit the Wiechert mechanical model with the following boundary conditions

$$\text{at } t = 0 \quad E_0 = k_1 A_0 + k_2 B_0 + k_3 C_0 + k_4 D_0 \quad (\text{Eq. 19})$$

$$\text{at } t = \infty \quad E_\infty = k_4(A_0 + B_0 + C_0 + D_0) \quad (\text{Eq. 20})$$

Since the experimental curves also fit this model, it may be proposed that the stress decay can be attributed to a change in the crystalline-amorphous ratio in gelatin films.

SUMMARY

Information gathered to this point from stress relaxation measurements seems to support the theory of crystallite formation in gelatin films. Results of humidity cabinet aging studies indicate that the increase in the tensile properties of the films is a kinetic process whose rate is influenced

by the degree of thermal aging of the melt. The decrease in the rate of gelation may be explained on the basis of dissolution of the smaller crystallites at elevated temperatures. At the time of casting, these crystallites are not present to serve as nuclei, and the rate of crystallization would be decreased. The crystallites reappear after an induction period at low temperatures. This may be demonstrated by storage of the thermally aged melt in a refrigerator for a period of time. Subsequent measurement of the tensile relaxation modulus of films cast from this melt show an increase in its value. This reversal of the thermal degradation of the melt lends support to the crystalline-amorphous concept.

Viscosity studies of the melt proved ineffectual in describing changes occurring in the tensile properties of films cast from the melt. Results indicated an orderly decrease in molecular weight with thermal aging. Changes in the tensile properties could not be reconciled with changes in molecular weight. Not only were these changes not parallel with the decrease in viscosity but also there was no way to explain the reversal of thermal changes during low temperature storage of the melt. Although some changes in the tensile properties may result from a scission of the polymer chain

during hydrolysis, it does not appear to be the major contributing factor.

To obtain a complete picture of the changes occurring in the rheological properties of gelatin films, it seems that, in addition to viscometric studies, one must measure some viscoelastic property whereby one may obtain information about the cross-linking processes occurring during gelation. It is felt that these changes may be responsible for some of the technological problems arising in the use of gelatin systems in the pharmaceutical industry.

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Powdered Particle Interactions: Suspension Flocculation and Caking III

By ROBERT G. WILSON* and BERNARD ECANOW

The chemistry of bismuth subnitrate in aqueous suspension has been investigated and explained in terms of coordination theory. Particular attention has been given to the reaction that occurs between phosphate ions and the surface of the bismuth subnitrate particles. Flocculation and caking phenomena are reviewed and interpreted in the light of these new findings.

IN A PREVIOUS paper (1) flocculation phenomena for bismuth subnitrate suspension systems were reported in terms of microscopic data and the relative suspension heights obtained from a series of controlled flocculation experiments. Strong bonds were seen to form between the particles while in the suspended state. The particles were held in fixed relative positions as they settled and were unable to shift and slide past one another to squeeze out the suspension medium and form a dense, compact sediment. Instead, the flocculated particles settled into the framework of a bulky sediment.

In this prior work (1) some effort was made to suggest the probable nature of the reacting

groups, but only tentative conclusions could be drawn. The work has continued with a closer inspection of the reactions of bismuth subnitrate in aqueous suspension in the hope that such information could provide a better insight into the mechanics of flocculation.

The literature (2-7) contains little detailed information on bismuth subnitrate or its reactions. A number of empirical formulas have been assigned to the compound. It is evident that the composition and properties of the crystalline material will vary, depending upon the method of preparation and the nature of changes that may occur when the material is subjected to further processing. The structure of the commercial product cannot be reduced to lattice formulas that describe an exact crystal geometry.

MATERIALS AND METHODS

Materials.—Bismuth subnitrate N.F. from the same lot, supplied by Mallinckrodt Chemical Works,

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