and that comparable precision is obtained. In comparison with the colorimetric method, the TCE method is faster and simpler. Once the sample solutions were prepared, between 25 and 30 determinations could be run each hour. The reproducibility of the TCE, as determined by repeatedly assaying a single sample dilution, is indicated by a deviation of the mean ±0.90% for six determinations.

Figure 3 shows the current–time curve for the dissolution study. Once the tablet was placed in the beaker, no further manipulative steps were required to record continuously the tablet dissolution. Although not included here, the dissolution could be determined as a function of pH using the same analytical procedure.

In summary, it is concluded that the electrochemical method for the determination of dopa presented in this paper is more convenient, faster, and simpler to use than previously available methods without any significant loss in precision and accuracy. Although automation was not employed in this study, the method may readily be incorporated into automated or semiautomated systems because it employs continuous analysis on a flowing stream of sample. And, finally, the applicability of the analytical method in the direct and continuous monitoring of tablet dissolution is demonstrated.

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PHARMACEUTICAL TECHNOLOGY

Soft Gelatin Capsules I: Factors Affecting Capsule Shell Dissolution Rate

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Abstract □ A method to study the relationship between various factors influencing the dissolution rate of the soft gelatin capsule shell is reported. The gelatin disk method makes use of the current USP rotating-basket dissolution apparatus. The effects of agitation, temperature, dissolution medium, and shell composition on the capsule shell dissolution rate are illustrated and discussed. A knowledge of these factors and their influence on dissolution should be of assistance in the formulation of soft gelatin capsule shells for various purposes.

Keyphrases □ Dissolution rate of soft gelatin capsules—effects of agitation, temperature, dissolution medium, and shell composition □ Capsules, soft gelatin—effects of agitation, temperature, dissolution medium, and shell composition on dissolution rate □ Gelatin capsules, soft—effects of agitation, temperature, dissolution medium, and shell composition on dissolution rate

Although soft gelatin capsules have been in mass production (1) since the introduction of the rotary die process (2), little or no work has been reported on the relationship between formulation design and dissolution rate of the capsule shell. Nevertheless, several formulations designed for specific uses have been patented (3–8) in this country. Recently, studies on comparisons of dissolution rates of drugs from soft gelatin capsules and tablets were reported (9, 10). The present report deals with a method to study the relationship between various factors influencing the dissolution rate of the soft gelatin capsule shell.

In the design and formulation of soft gelatin capsule dosage forms, one should consider the effects of components and other parameters on the dissolution rate of the capsule shell. A method that is simple, fast, able to differentiate minor but meaningful changes in dissolution rate, and readily reproducible is of great utility. Eckert *et al.* (11), concerned with drug availability, advocated the use of the *in vitro* initial-release rate to reflect this factor in the monitoring of soft gelatin capsule manufacture. The initial-release rate is adequate for such a purpose, but it lacks the sensitivity and simplicity based on the criteria of the present proposal. A more appropriate method was developed in this laboratory.

Many factors that influence the dissolution rate of the soft gelatin capsule shell may be adequately studied by the use of the Nelson (12) modification of the Noyes–Whitney equation. Using the Noyes–Whitney equation, one may write:

$$\frac{dW}{dt} = KS(C_s - C) \qquad \text{(Eq. 1)}$$

where W is the amount dissolved, t is the time, K is the solution rate constant with dimensions of distance/

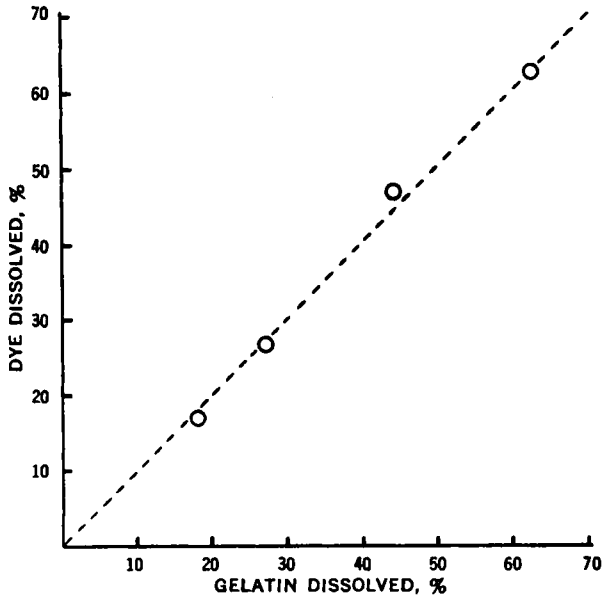

Figure 1—*Plot showing the correlation of the percent dye and gelatin dissolved in simulated gastric fluid without pepsin at 37° and 100 r.p.m. for a given dissolution time in the gelatin disk method. The dashed line is drawn for a theoretically perfect correlation.*

time, S is the surface area of the dissolving solid, C_s is the concentration of dissolving solid at the liquid–solid interface, and C is the concentration in the dissolution medium. At very low percent saturations of dissolving substance in dissolution medium, Nelson (12) showed that the C term may be ignored so Eq. 1 reduces to:

$$\frac{dW}{dt} = KSC_s \qquad \text{(Eq. 2)}$$

Integration, with S considered a constant, yields:

$$W = KSC_s t \qquad \text{(Eq. 3)}$$

By dividing both sides of Eq. 3 with S and setting $KC_s = k$, one then has:

$$\frac{W}{S} = kt \qquad \text{(Eq. 4)}$$

A plot of W/S *versus* t yields a straight line going through the origin. The slope of the line equals k. Equation 4 is valid for initial dissolution rates and at dilute solutions, which is the case in the beginning of each dissolution experiment.

EXPERIMENTAL

Materials—Gelatins used were Type A USP and Type B USP, with gel strength in Bloom grams of 264 ± 4[1], 195 ± 3[2], 27 ± 1[3], and 77 ± 2. The last was a blend of a higher and of a lower gel strength gelatin. The gelatins were sieved to obtain a particle size between U. S. Standard 20- and 40-mesh screens. The following were also used: glycerin USP[4], sorbitol solution USP[5], hexaglycerol[6], FD&C certified Blue No. 1[7], lysine hydrochloride[8], and analytical reagent grade urea[9] and chemicals. Commercial grades of additives were used where reagent grades were not available.

[1] Kind and Knox Gelatin Co.
[2] Rousselot Corp.
[3] B. Young and Co. of America, Ltd.
[4] Dow Chemical Co.
[5] Atlas Chemical Ind.
[6] Stokely-Van Camp.
[7] Hilton-Davis Chemical Co.
[8] Merck and Co.
[9] Mallinckrodt Chemical Works.

Table I—Repetitive Determinations of Dissolution Rate Constants of Gelatin A and B Type Soft Gelatin Capsule Shell Samples in Simulated Gastric Fluid T.S. without Pepsin at 37° and 100 r.p.m.

	Gelatin Type A Shell, mg./cm.² min.	Gelatin Type B Shell, mg./cm.² min.
	1.83	2.74
	2.07	2.76
	2.03	2.65
	1.98	2.81
	2.09	2.84
Average ± *SD*	2.00 ± 0.12	2.76 ± 0.08

Gel Strength—Gelatin gel strengths, measured in Bloom grams by the use of a Bloom gelometer (13), are averages of duplicate runs.

Dissolution Medium—The aqueous solution pH values were as follows: pH 1.2 simulated gastric fluid T.S. with or without pepsin (14), pH 1.2–2.0 USP standard buffer solutions (14), pH 7.5 simulated intestinal fluid T.S. without pancreatin (14), pH 2.2–5.0 McIlvaine's standard buffer solution (15), and pH 9.9 carbonate buffer solution (16).

Preparation of Sample—Soft gelatin capsule shell disks, containing about 0.25% on dry basis of FD&C Blue No. 1 with either Type A or B gelatin and varying amounts of plasticizer such as glycerin, may be made in the following manner. As an example, mix 60.25 g. gelatin with 31.50 g. glycerin in a 500-ml. filtering flask fitted with a stopcock. Add 33 ml. cold, aqueous solution of 250 mg. FD&C Blue No. 1 dye and additive, if any, and mix well. Reduce pressure of system to deaerate contents, and close off stopcock to maintain a reduced pressure. Heat system on a steam bath to dissolve contents and to obtain a flowable mass. Mix well by swirling flask contents without creating bubbles in the molten mass. Vent flask and pour flask contents on a clean glass plate. Immediately level mass with a constant-thickness doctor blade. The formed film should be homogeneous and free of bubbles. Allow film to set at room temperature for 1 hr., and then mount film between two plastic brackets to keep it flat along edges. Allow film to equilibrate for at least 2 weeks in a desiccator containing solid calcium chloride in equilibrium with a saturated solution of calcium chloride. Just before a dissolution run, cut a disk of the gelatin film with a No. 13

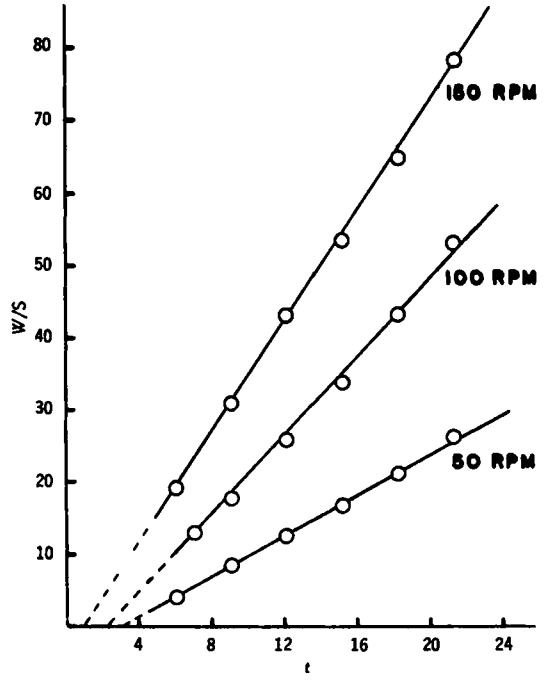

Figure 2—*Plot of the amount dissolved (mg./cm.²) versus time (minutes), showing the dissolution of soft capsule shells made from a Type B gelatin in simulated gastric fluid at 37° and three rates of agitation.*

Table II—Salt Effects on the Dissolution Rate Constants of Gelatin A and B Type Soft Gelatin Capsule Shells at 37° and 100 r.p.m.

Sodium Chloride, *M*	pH 1.2	
	Gelatin Type A, mg./cm.² min.	Gelatin Type B, mg./cm.² min.
0.00	2.09	—
0.034	2.00	2.76
0.171	1.46	2.55
0.342	1.00	2.48

Potassium Chloride, *M*	pH 1.2	pH 5.0	
	Gelatin Type B, mg./cm.² min.	Gelatin Type A, mg./cm.² min.	Gelatin Type B, mg./cm.² min.
0.00	2.78	1.08	1.45
0.05	2.84	—	—
0.15	2.39	1.24	1.38
0.30	2.35	1.13	1.44

cork borer. Determine the weight of the disk on an analytical balance, and calculate the surface area from measurements of diameter and thickness.

Dissolution Apparatus—The USP XVIII rotating-basket dissolution apparatus (14) is used. A modification of this method was described recently (17) which facilitates faster determinations of dissolution rates. Throughout this study, the temperature of the dissolution medium was kept constant at the indicated temperature ±0.1° by use of a constant-temperature circulator[10].

Dissolution Procedure—Place a weighed soft gelatin disk sample flat on the bottom of the stainless steel basket, and secure with fine stainless steel wires inserted crosswise immediately above the sample. Assemble to stirring motor and raise dissolution vessel to predetermined height by use of a laboratory jack. The temperature of the vessel and its contents is kept constant at the desired temperature ±0.1°. Add 500 ml. simulated gastric fluid T.S. (with or without pepsin as the case may be) maintained at the same desired temperature. To start dissolution, turn on stirring motor set at a predetermined revolutions per minute. At suitable time intervals, determine the absorbance of the dissolution medium at 630 nm. *versus* water in a suitable spectrophometer. A 3-ml. aliquot may be withdrawn for this purpose. However, absorbance is best determined by continuous analysis in a spectrophotometer flow cell assembly. The amount of soft gelatin film dissolved in time t, W_t, is equal to that fraction of the disk dissolved in time t. One may write:

$$W_t = \frac{A_t M}{A_\infty} \qquad \text{(Eq. 5)}$$

where M is the weight of the plug in milligrams, and A_t and A_∞ are the absorbance values at 630 nm. for time t and infinity (completed dissolution), respectively. In this manner, the term W/S may be determined for corresponding values of time. The dissolution constant, k, is obtained from the slope of the straight line in a plot of W/S *versus* t and will have the dimensions of mg./cm.² min., where S is measured in cm.² and t in minutes. The results are averages of at least duplicate runs.

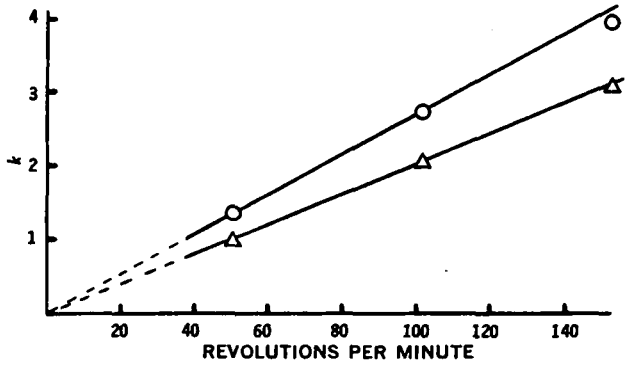

Figure 3—*Effect of agitation (r.p.m.) on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from gelatin Types A (Δ) and B (○) in simulated gastric fluid at 37°.*

[10] Bronwill model 20, VWR Scientific.

Table III—Effect of Pepsin in Simulated Gastric Fluid T.S. on the Dissolution Rate Constants of Slow Dissolving Type A Soft Gelatin Capsule Shell Samples at 37° and 100 r.p.m.

	2-Week-Old Sample, mg./cm.² min.	2-Year-Old Sample, mg./cm.² min.
With pepsin	2.22 ± 0.13	2.01 ± 0.13
Without pepsin	2.29 ± 0.08	1.50 ± 0.19

Validity of Method—The use of soft gelatin capsule shell disks in the method ensures that each test sample presents uniform and constant surface to the dissolving medium. The sample disk has the additional advantage in being relatively simple to prepare. Since it is difficult to prepare soft gelatin capsule shell films containing the same amount of water, the conditioning of the film in a constant relative humidity atmosphere before a dissolution rate determination is important because an unconditioned, freshly made sample has a relatively higher initial dissolution rate and this rate decreases to a constant value under controlled humidity storage condition. The incorporation of the water-soluble dye permits ready appraisal of dissolution of the gelatin. The relatively simple absorbance measurement of the dye in the dissolution medium renders the method amenable to the use of the present USP XVIII rotating-basket dissolution apparatus.

Apparently the water-soluble dye is distributed uniformly throughout the gelatin shell, and there is no indication that the dye diffuses from the matrix at a rate greater than the dissolution of gelatin. The diffusion of the dye out of the gelatin matrix is measurable only with nearly insoluble samples, where dissolution is extremely slow or at low temperatures and low agitations. Nevertheless, this rate is considerably less than normal dissolution and does not contribute significantly to the measurements discussed. Furthermore, visual observations indicate that the amount of dye dissolved is proportional to the amount of the gelatin mass dissolved. This was confirmed by analyses of both dye and gelatin dissolved for a given dissolution time. The percent gelatin dissolved was calculated from the relative amounts of nitrogen in solution as determined by a slightly modified USP XVIII Method II (14). The described dissolution procedure was used with the exception that 100 ml. instead of the 500 ml. of simulated gastric fluid made without pepsin was used. Figure 1 shows that the results fall on top of the theoretical, perfect correlation line.

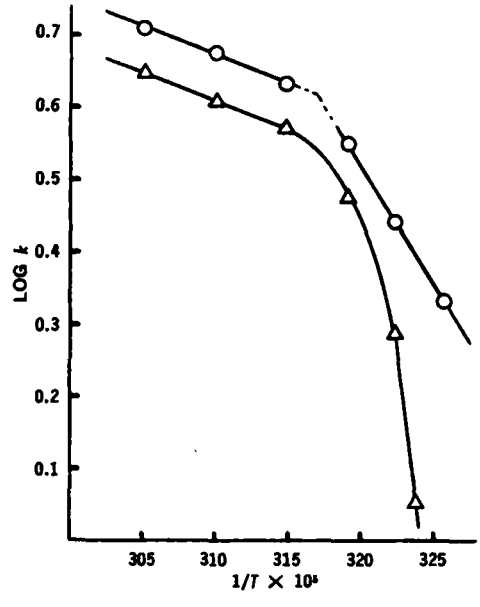

Figure 4—*Arrhenius plot showing the effect of temperature on the dissolution rate constant, k, of soft capsule shells made from gelatin types A (Δ) and B (○) in simulated gastric fluid at 100 r.p.m.*

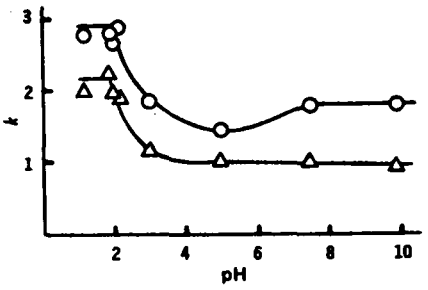

Figure 5—*Effect of pH of the medium on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from gelatin Types A (△) and B (○) at 100 r.p.m. and 37°.*

In separate experiments, the blue soft gelatin film, when dissolved in an acid dissolution medium at the concentrations of the dissolution experiments, obeyed Beer's law at the wavelength of 630 nm. The FD&C Blue No. 1 was chosen for its high absorptivity and water solubility. Although it is not the only dye that can be used in the method, the present report is limited to its use.

Gas bubbles clogging the dissolution basket wire screen were observed to slow the dissolution rate measurably, but this source of error was eliminated by the removal of dissolved gas. The addition of a small piece of stainless steel screen or a piece of boiling stone helped the dissolved gas to nucleate and to grow into larger gas bubbles. Gentle agitation under reduced pressure removed the gas bubbles. This treatment, before each dissolution rate determination, produced results that were reproducible and typical of those shown in Table I.

RESULTS AND DISCUSSION

Stirring Rate—Figure 2 shows plots of *W/S versus* time in minutes at 50, 100, and 150 r.p.m. of the rotating basket for gelatin Type B soft gelatin capsule shells in simulated gastric fluid T.S. without pepsin at 37°. It can be seen that the lines are straight, but they do not seem to extrapolate linearly to the origin as predicted by Eq. 4. These observed differences or apparent lag times may be explained by the inefficiency of mixing at lower stirring rates. This postulation is supported by the smaller apparent lag times at higher revolutions per minute values. However, these apparent initial lag times seem to have little or no effect on the values of the dissolution rate constants as shown in Fig. 3. The linear relationship as depicted in the plot of dissolution rate constant, *k*, *versus* revolutions per minute is in accord with a diffusion-controlled dissolution process (18). Both Figs. 2 and 3 show the importance of agitation on the dissolution rate of the soft gelatin capsule shell. Withey and Mainville (19) came to a similar conclusion after they tested a soft gelatin capsule sample.

Temperature—Because of the abilities of gelatin to form thermally reversible rigid gels and to hydrogen bond, temperature may be expected to have a marked effect on the dissolution rate of soft gelatin capsule shells. Indeed, this is the case, especially below about 42°, as shown by the Arrhenius plots in Fig. 4 of log *k versus* the reciprocal of the absolute temperature. In the regions of the curves below 42°, the activation energy varies from 71 to 15 kcal./mole for the gelatin Type A and Type B soft gelatin capsule shell. By contrast, the activation energy above 42° is relatively constant at 3.6–3.7 kcal./mole. Unfortunately, most of the dissolution rate determinations are at 37°. Consequently, the temperature of the medium during a dissolution rate determination must be kept precisely constant.

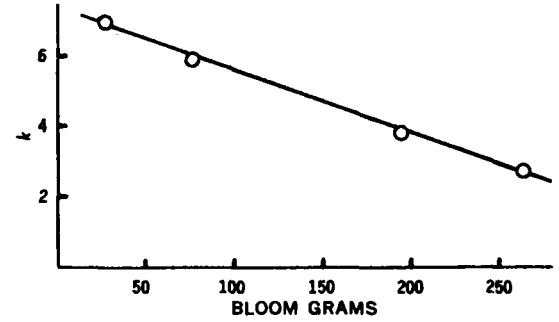

Figure 6—*Effect of gelatin gel strength in Bloom grams on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from Type B gelatins in simulated gastric fluid at 37° and 100 r.p.m.*

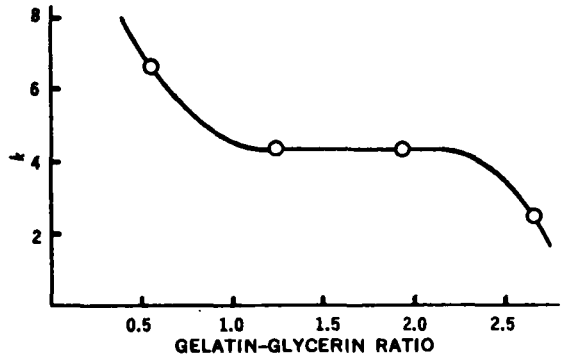

Figure 7—*Effect of gelatin-glycerin ratio in a capsule formulation on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from a Type B gelatin in simulated gastric fluid at 37° and 100 r.p.m.*

Dissolution Medium—The influence of pH of the medium on the dissolution rate constant for gelatin Type A and Type B soft gelatin capsule shells is shown in Fig. 5. The pH seems to have little effect above a value of 3 on dissolution rate constants of both types of soft gelatin capsule shells. Also, there appears to be a minimum at pH 5 for the Type B gelatin in the pH dissolution profile. The pH of the minimum seems to coincide with the isoelectric point (pH 4.7–5.1) of gelatin Type B. As the pH values decrease from 3 to 1, the dissolution rate constants seem to approach a higher plateau. This increase in dissolution rate may be due to the protonation of amino groups that have pKa values in this pH range.

Small amounts of salts such as sodium or potassium chloride may or may not have an effect on the dissolution rate constants of soft gelatin capsule shells, depending on the type of gelatin used and the pH of the medium. Both sodium and potassium chloride at concentrations from 0 to 0.30 *M* and a pH value of 5.0 seem to have no effect on the dissolution rate constant of both Types A and B soft gelatin capsule shells. However, at a pH value of 1.2, both salts seem to have a small negative effect on the dissolution rate constants of both types of gelatin shells (Table II).

In most instances the use of pepsin in the simulated gastric fluid T.S. has little or no effect on the dissolution rate constant of the soft gelatin capsule shell. This is particularly true for relatively unaged and fast dissolving samples. However, in certain aged and relatively slow dissolving samples, the use of enzyme may increase the dissolution rate. This is illustrated by the results listed in Table III for a 2-year-old sample and a relatively slow dissolving Type A soft gelatin capsule shell sample. It can be seen that in this instance there is no significant difference between the dissolution rate of a slow

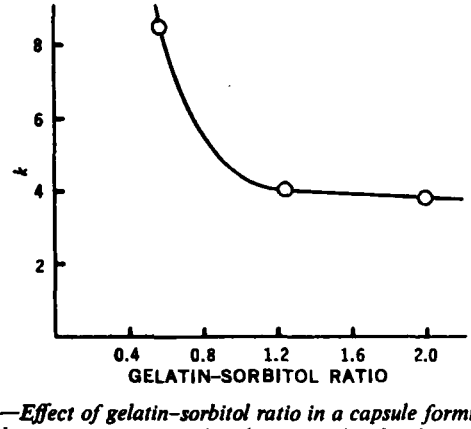

Figure 8—*Effect of gelatin-sorbitol ratio in a capsule formulation on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from a Type B gelatin in simulated gastric fluid at 37° and 100 r.p.m.*

Table IV—Normal Gelatin–Glycerin Ratio Values for Several Different Capsule Shell Formulations and Their Suggested Uses

Gelatin–Glycerin Ratio	Suggested Uses
1.5–3.0	Oral products with oil vehicles
1.0–2.0	Oral products with oil vehicles plus surfactant
1.0–2.2	Water-miscible vehicles
0.8–2.0	Organic solvents having a hardening effect on the gelatin shell
0.5–1.5	Squeeze-out-type capsules
0.4–1.0	Suppositories

dissolving sample in simulated gastric fluid T.S. with or without the use of pepsin. However, there is a small difference in the dissolution rate of the aged sample. In a case of an aged soft gelatin capsule where dissolution rate was a problem, pellicle formation was observed. A thin membrane on the inner side of the capsule shell seemed to be responsible for the delay in dissolution time. Apparently the pepsin in the simulated gastric fluid helped to accelerate the dissolution of the pellicle and the subsequent liberation of the encapsulated drug. Pellicle formation in gelatin capsules has been encountered with aldehydes and/or aldehyde-containing liquids, such as in perfumes and flavors. The use of aldehyde, *e.g.*, formaldehyde, to render gelatin less water soluble is the basis of a technique (3) to produce delayed-release soft gelatin capsules.

Gelatin Gel Strength—For a given soft gelatin capsule, there is an optimum gelatin Bloom strength to use when all factors are taken into account. One of these factors is the dissolution rate of the capsule shell. The effect of Bloom strength on the dissolution rate constant of the Type B gelatin capsule shell in simulated gastric fluid without pepsin at 37° and 100 r.p.m. is shown in Fig. 6. It is not surprising to observe a linear relationship, since the same types of gelatin may be blended to obtain a desired property, such as Bloom strength. The straight line with a negative slope indicates a reverse linear relationship: the lower the Bloom the higher the dissolution rate and the higher the Bloom the lower the dissolution rate. This relationship holds true provided other factors are constant. For example, gelatins with higher Bloom values have greater physical strength; therefore, thinner films or ribbons may be made from them. Capsules made with thinner ribbons have faster apparent dissolution. In most instances, soft gelatin capsules are made with Type B gelatin having Bloom strength values between 150 and 200 g.

Plasticizer—The plasticizer is an important part of the soft gelatin capsule shell formulation. Not too many compounds may be used to replace glycerin as the plasticizer of gelatin. Glycerin is relatively pure, commercially available in large quantities, relatively inexpensive, and nontoxic. Propylene glycol and polyethylene glycol 400 can be used, but they have no advantage over glycerin. Sorbitol has limited uses as a plasticizer for gelatin. Usually it is used to replace part of the glycerin in cases where a low glycerin content is desirable in a particular formulation. Hexaglycerol and its family of polymers are not commercially available at present. They have properties similar to glycerin as plasticizers for gelatin. The plasticizer in a

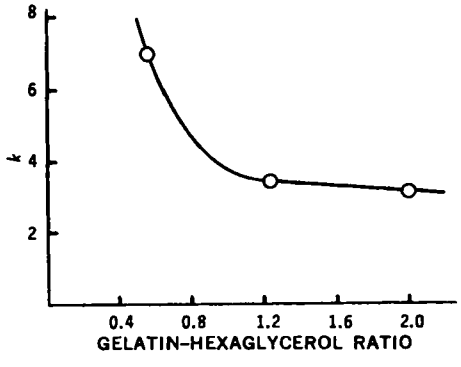

Figure 9—*Effect of gelatin–hexaglycerol ratio in a capsule formulation on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from a Type B gelatin in simulated gastric fluid at 37° and 100 r.p.m.*

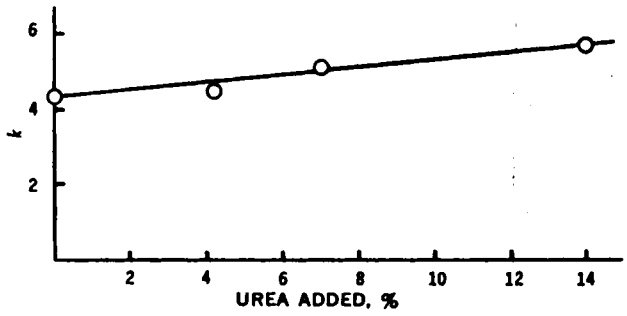

Figure 10—*Effect of percent urea added to a capsule formulation on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from a Type B gelatin in simulated gastric fluid at 37° and 100 r.p.m.*

formulation, expressed as the gelatin–plasticizer ratio, controls the consistency of the soft gelatin capsule. Hence, the gelatin–plasticizer ratio reflects the projected use of the capsule. Figures 7–9 show the influence of the gelatin–plasticizer ratio on the dissolution rate constant of the Type B gelatin capsule shell. It is surprising to see that the gelatin–plasticizer ratios for glycerin, sorbitol, and hexaglycerol have similar effects on the dissolution rate constant, in particular in the region between 1.2 and 2.0 ratios where the plasticizer seems to have little influence on dissolution. Table IV shows a tabulated list of normal gelatin–glycerin ratio values for several different capsule shell formulations and their suggested uses.

Additives—The influence of certain additives on the dissolution rate constant of the soft gelatin capsule shell in simulated gastric fluid without pepsin at 37° at 100 r.p.m. has been investigated. Figure 10 reflects the increased dissolution rate, which may be attributable to the hydrogen bond breaking effect of urea in a plot of dissolution rate constant *versus* percent urea added to the capsule shell. The increase in dissolution rate is small for the amount of urea added. A somewhat greater increase with lysine hydrochloride, probably due to acidity, is illustrated in Fig. 11. For ease of comparison, a list of additives tabulating the changes in the dissolution rate constant realized through the addition of 1% of each to a standard soft gelatin capsule shell formulation is compiled in Table V. Most of the compounds caused only a slight change in the dissolution rate constant. Acid salts and mineral and organic acids seem to cause the largest change in dissolution rate, probably due to acid hydrolysis of the polypeptide in the gelatin.

SUMMARY AND CONCLUSIONS

A simple method is described to study the effects of various factors on the dissolution rates of soft gelatin capsule shells. The method involves the use of the current USP XVIII dissolution apparatus and the spectrophotometric determination of the amount of dye dissolved from a blue, soft gelatin capsule shell disk placed in the rotating basket. The validity of the gelatin disk method was confirmed by a correlation study of the percent dye and gelatin dissolved for any given dissolution time. Dissolution rate constants may be obtained from a plot of the amount of the soft gelatin

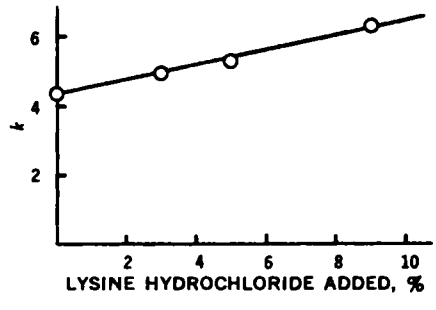

Figure 11—*Effect of percent lysine hydrochloride added to a capsule formulation on the dissolution rate constant (mg./cm.² min.) of soft capsule shells made from a Type B gelatin in simulated gastric fluid at 37° and 100 r.p.m.*

Table V—Effects of Some Additives on the Dissolution Rate of a Typical Soft Gelatin Capsule Shell

Compound Added	Change in Dissolution Rate/1% Added, mg./min. cm.[2]
Acacia	0.044
Ammonium citrate	0.030
Ammonium nitrate	0.044
Fumaric acid	0.778
Glycine	0.140
Hydrochloric acid	7.320
Lysine hydrochloride	0.215
Maleic acid	0.550
Poloxalene L44[a]	0.050
Poloxalene L64[a]	0.150
Polysorbate 80	0.460
Polyvinylpyrrolidone	0.025
Sodium acetate	0.110
Sodium carbamate	0.147
Starch, potato	0.086
Tartaric acid	0.443
Thiourea	0.155
Urea	0.096

[a] Pluronic (brand of poloxamer), BASF Wyandotte Corp.

capsule shell dissolved, which is directly proportional to the dye dissolved, divided by the dissolving solid surface area *versus* time.

The use of the gelatin disk method has permitted the present investigation of the influence of agitation, temperature, dissolution medium, gelatin gel strength, plasticizer, and certain additives on the dissolution rate of the capsule shell. Gelatin gel strength, when measured in Bloom grams, appeared to have an inverse linear relationship with dissolution rate. The plasticizer plays an important role, and its effect on dissolution rate seems to depend on the gelatin–plasticizer ratio in a particular formulation. Acid salts and mineral and organic acids seem to cause a greater change in dissolution rate, probably due to acid hydrolysis of gelatin.

In conclusion, various factors have been demonstrated to influence soft gelatin capsule shell dissolution rates. A knowledge of these relationships is helpful in the formulation of soft gelatin capsule shells for various purposes.

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