Comparative Evaluation of Various Dissolution Apparatus for Capsule Dosage Forms

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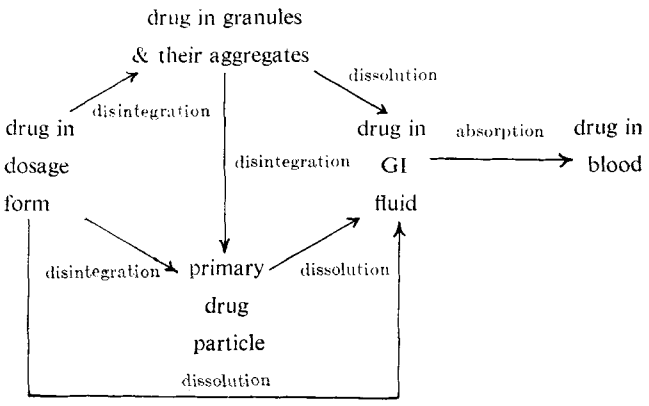
Abstract □ The dissolution profiles of experimental diuretic and antidiabetic compounds in capsules were investigated by bead, plate, blade, holder, basket, disintegration time, and proposed USP dissolution methods. The apparent initial dissolution rate and the extent of drug released within the testing period were used as parameters in comparative evaluation of these seven methods. The influence of the size of the stirrer, the volume of dissolution medium, and the size of screen cloths for making the basket on the dissolution profile was studied and discussed. The Reynolds number of the fluid is introduced to explain the influence of the size of the stirrer on the dissolution rate. Due to the small screen (40 mesh) employed in the proposed USP dissolution method, the visual observation of the behavior of the capsule is impaired, and the chance of clogging the screen by the granules is greater than the self-designed (8 mesh) basket used in the basket method. The dissolution profiles obtained with the disintegration time method provide the fastest rate and the greatest extent of dissolution for both experiemental diuretic and antidiabetic compounds.

Keyphrases □ Capsule dosage forms—dissolution apparatus □ Dissolution apparatus, comparison, evaluation—capsule dosage forms □ Stirring rate effect—capsule dissolution □ UV spectrophotometry—analysis

The majority of drugs today are formulated and marketed as tablets and capsules. For slightly and poorly water-soluble compounds, the effective absorption process is generally controlled by the disintegration time of the dosage form and the rate and extent of the subsequent dissolution at which the drug goes into and remains in the solution state. Thus, for a drug contained in a solid dosage form to be absorbed, the following illustrated sequence must occur (Scheme I):



Scheme I

The usefulness and importance of developing suitable dissolution apparatus and procedures in product research and development have been recognized for several years. In the product research area, dissolution testing is commonly employed as a means of evaluating and selecting the crystalline or amorphous forms, polymorphic or solvate forms, or the eutectic or complex forms of the compound. On the other hand, dissolution testing is generally accepted in the product development area for studying the drug-release patterns of the conceptual dosage forms, for investigating the formulation and process factors in the development of dosage forms, and for facilitating the selection of certain preliminary formulations for preclinical *in vivo* efficacy studies of the formulation. In general, when the correlations between the *in vitro* dissolution data and the *in vivo* clinical or pharmacokinetic evidence have been established, the dissolution method may be incorporated in the specification of the dosage form as a quality control tool. Therefore, the standardization of test apparatus and methodology is extremely important in the evolution of drug standards, and proper comparative evaluations play a significant role in such standardization.

Dissolution characteristics of solid dosage forms such as tablets or capsules may be determined by various apparatus employing various dissolution media, agitation intensities, and sampling methods for assaying the drug content in solution. Many *in vitro* techniques appear in the literature for the evaluation of drug-release patterns from solid dosage forms (1–24). The applicability and reliability of these apparatus and procedures are, in general, more suited for tablets than for capsules. It is the purpose of this article to evaluate comparatively the dissolution profiles attainable by various devices which are shown to be practical and reproducible for investigating the release pattern of the compound from the capsule.

EXPERIMENTAL

Materials—The diuretic compound was dried at 100° for 8 hr. The chemical identity was confirmed by elemental analysis and IR spectra. The moisture content, as determined by the Karl Fischer method, was about 1%. Analysis by a nonaqueous titrimetric method showed a purity of better than 99% which was substantiated by TLC analysis. The equilibrium solubility at 37° in phosphate buffer at pH 7.3 was about 1 mg./ml. Using U. S. standard sieves, the fraction of the diuretic compound passing through 40 mesh but retained in 100 mesh was collected and used throughout this investigation.

The antidiabetic compound was dried at 80° under vacuum for 12 hr. The moisture content, as determined by the Karl Fischer method, was negligible. The chemical purity was found to be better than 99.5%. The equilibrium solubility at 37° in double-distilled water was approximately 2%. The samples were sieved through U.S. standard sieves, and fractions of 20/100-mesh particles were collected for use in this investigation.

Determination of Dissolution Profile—Approximately 100 mg. of the sieved sample of the diuretic or antidiabetic compound was accurately weighed and carefully introduced into No. 1 clear gelatin capsules with as little compaction as possible. The capsule was then placed in one of the several devices, as depicted in Fig. 1, for obtaining the dissolution profile. The devices or apparatus employed are as follows: (*a*) The capsule is weighted down to the

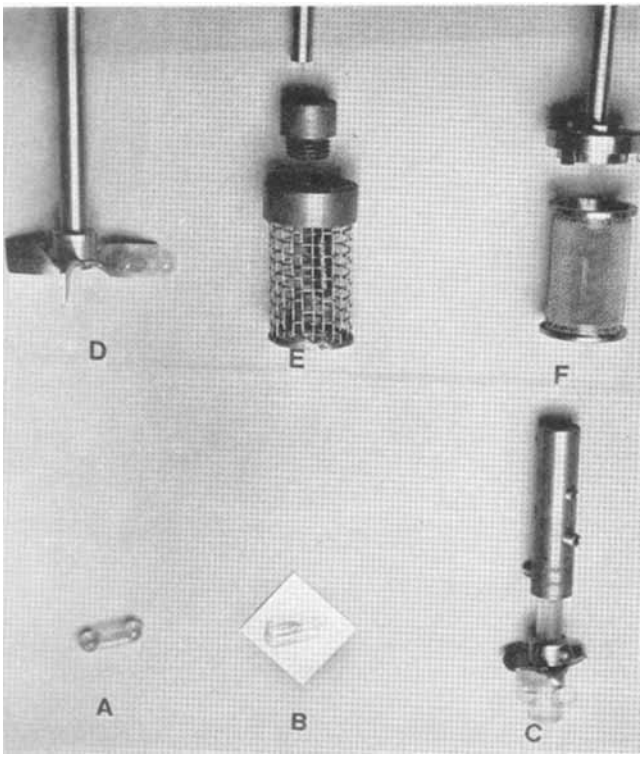


Figure 1—*Photograph illustrating the various devices employed for the investigation of capsule dissolution profile. Key: A, bead method; B, plate method; C, holder method with small stirrer; D, blade method with large stirrer; E, basket method with large stirrer; and F, proposed USP dissolution method.*

bottom of the dissolution flask by inserting two glass beads at both ends of the capsule (bead method) prior to the filling of the drug into the capsule. (*b*) The capsule sinks to the bottom of the dissolution flask by affixing the capsule to a 2 × 2-cm. stainless steel plate (plate method) with the aid of water-repellant glue. (*c*) The capsule is affixed to one of the three blades of the stirrer (blade method) with the same water-repellant glue. (*d*) The capsule is positioned into the orifice of a plastic capsule holder (holder method) specifically designed for a No. 1 gelatin capsule. (*e*) The capsule is placed in a self-fabricated basket (basket method) made from a stainless steel metal screen. (*f*) The capsule is placed in the USP proposed basket (proposed USP method) designed to be one of the official dissolution testing apparatus in the future.

The dissolution studies were performed using 300 ml. of dissolution medium at 37° in a pyrex beaker of 800-ml. capacity. The bottom face of the beaker was converted into a convex shape. The agitation of the dissolution medium was achieved by an overhead stirrer operated at 60 r.p.m. and placed at the center of the beaker. The agitation mechanism and the volume of dissolution fluid employed for each method are indicated in Table I. In all cases, the top surface of the agitation mechanism, such as the stirrer or basket, was immersed 2 cm. below the surface of the dissolution medium. The dissolution media employed for the diuretic and antidiabetic compounds were phosphate buffer at pH 7.3 and double-distilled water, respectively. At zero time, the capsule was introduced into the dissolution medium maintained at 37°. At prescribed time intervals, sample aliquots were withdrawn and replaced immediately with the same volume of fresh medium maintained at 37°. The aliquot was immediately filtered through 0.45-μ pore size Millipore filter paper. The clear filtrate was properly diluted with an appropriate solvent and assayed spectrophotometrically at 282 mμ for the diuretic compound and 347 mμ for the antidiabetic compound. Beer's law curves were constructed previously in the solvent systems employing 50% aqueous methanol and distilled water. A cumulative correction was made to account for the previously removed samples in determining the total amount of drug dissolved at any specific time. An average of at least three determinations was performed for each method investigated in this study. The gelatin capsule in the diluted sample aliquots was found not to interfere with the spectrophotometric assay at the aforementioned wavelengths.

RESULTS AND DISCUSSION

The experimental conditions employed to obtain dissolution profiles, together with their apparent agitation mechanism, are summarized in Table I. Numbers appearing in the first column of Table I correspond to the number designated for the curves in Figs. 2–6. Whenever the device investigated was suitable for studying the effect of the size of the stirrer on the release rate of drug from the capsule, two kinds of three-bladed stirrers were employed. The small stirrer used was 2.0 cm. in diameter and the angle of the blade to the horizontal plane was 45°, whereas the large stirrer employed was 4.3 cm. and the blade was perpendicular to the horizontal plane. It was suggested by Levy (15) that, using a stirring rate of 30 to 60 r.p.m., the agitation intensity is sufficient to obtain a homogeneous solution for sampling purposes yet low enough to preserve the microenvironment of the tablet being tested. Consequently, the constant stirring rate of 60 r.p.m. was employed throughout the study unless otherwise specified.

The plot in Fig. 2 depicts the dissolution profiles of the diuretic and antidiabetic compounds, using the bead method with the small and large stirrers. It is evident from the plot that a lag time does exist prior to the dissolution of drug from its encapsulated form into the dissolution medium. The existence of the lag time is explained by the dissolution of gelatin capsules prior to the leaching or releasing of the drug from the capsule. The lag time is about 5 min. for gelatin capsules under the experimental conditions employed. In general, the capsule breaks initially from both ends that are in contact with the glass beads, and this is soon followed by the melting of gelatin from the middle portion of the capsule. Comparison of the dissolution profiles of the two compounds investigated shows that the higher the aqueous solubility of the compound, the faster the initial rate of dissolution and the greater the extent of drug released. This finding is in accord with the Noyes-Whitney equation.

Although the stirring speed was kept constant at 60 r.p.m., it is conceivable that the larger the diameter of the stirrer, the greater the driving force and the better the efficiency of the dissolution fluid impacting on the capsule to release the drug. The increased dissolution rate could be correlated qualitatively to the Reynolds number, a dimensionless group of importance in fluid dynamics.

Table I—Experimental Conditions for the Dissolution Profile Study

Curve Ref.[a]	Method[b]	Agitation Mechanism	Volume of Dissolution Medium in ml.
1	Bead method	Small stirrer[c]	300
2	Bead method	Large stirrer[d]	300
3	Plate method	Small stirrer	300
4	Plate method	Large stirrer	300
5	Blade method	Small stirrer	300
6	Blade method	Large stirrer	300
7	Holder method	Small stirrer	300
8	Holder method	Large stirrer	300
9	Basket method	Basket alone	300
10	Basket method	Basket alone	600
11	Basket method	Basket & small stirrer	600
12	Basket method	Basket & large stirrer	600
13	D.T. method	D.T. rack assembly with disk	700
14	Proposed USP method	USP basket	300
15	Proposed USP method	USP basket	600
16	Proposed USP method	USP basket & large stirrer	600

[a] Numbers correspond to curves in Figs. 2–6. [b] See text for details. [c] The small stirrer employed is 2.0 cm. in diameter and the angle of the blade to the horizontal plane is 45°. [d] The larger stirrer employed is 4.3 cm. in diameter and the angle of the blade to the horizontal plane is 90°.

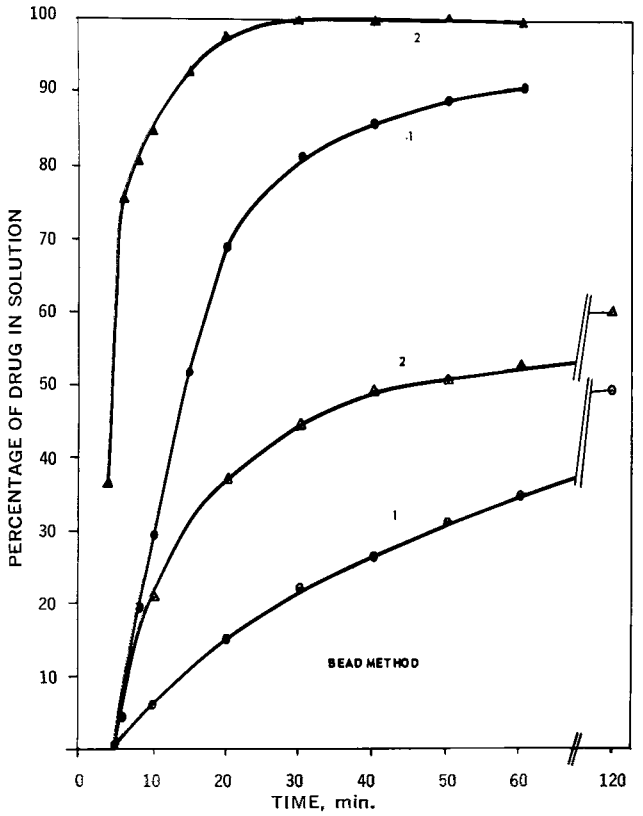


Figure 2—*Dissolution profiles of the diuretic (open symbols) and antidiabetic (solid symbols) compounds by bead method at 60 r.p.m. Key: 1, small stirrer; and 2, large stirrer.*

The Reynolds number (N_R) of the fluid having been agitated at constant speed (r) is related to the diameter of the stirrer (D) through the following equations:

$$N_R = kD^2 \qquad \text{(Eq. 1)}$$

$$k = \frac{r\rho}{\eta} \qquad \text{(Eq. 2)}$$

where ρ and η represent the density and viscosity of the fluid, respectively. Assuming that the ρ and η of the dissolution fluid are macroscopically independent of stirrer dimension, k will remain as a constant when the fluid is stirred at constant speed, r, Then, it follows from Eq. 1 that the ratio of Reynolds numbers obtained with larger *versus* smaller stirrers employed in this study are:

$$\frac{N_R^1}{N_R^s} = \frac{D_1^2}{D_s^2} = \frac{(4.3)^2}{(2.0)^2} = 4.6 \qquad \text{(Eq. 3)}$$

Therefore, as expected, the larger the stirrer size, the greater are the initial dissolution rate and the extent of the dissolution of the diuretic and antidiabetic compounds (Fig. 2). For the diuretic compound, the initial dissolution rate is increased about threefold, and the extent of dissolution within a 2-hr. period is approximately doubled when the smaller stirrer (Curve 1, open symbol, Fig. 1) is replaced with the large stirrer (Curve 2, open symbol, Fig. 1). Quantitative study of the effect of N_R on dissolution rate is in progress (25).

In the plate method, the capsule is affixed to a 2 × 2-cm. stainless steel plate in such a way that the contact area between the capsule and the metal plate is minimized by applying as little as possible of the water-repellant glue. The dissolution data obtained with the plate method are illustrated in Fig. 3 for the diuretic compound (open symbols) and the antidiabetic compound (solid symbols). It is clearly demonstrated again that the rate and extent of dissolution are increased with the intensity of agitation and the size of the stirrer. The general characteristics of these four curves of Fig. 3 are very similar to the corresponding curves illustrated in Fig. 2.

For the diuretic compounds (the lower two curves of Figs. 2 and 3), the apparent initial rate and the extent of dissolution are slightly greater for the bead method than for the plate method when small stirrers are employed; the similar apparent initial rate but a greater extent of dissolution is observed for the bead method than for the plate method when a large stirrer is used. The situation is somewhat different for the antidiabetic compound (the upper two curves of Fig. 3). Using a small stirrer, the identical apparent initial release rate is observed and the extent of dissolution is found to be slightly greater for the plate method than for the bead method when a larger stirrer is employed.

The data obtained with the blade method and the holder method are summarized together as depicted in Fig. 4. For the antidiabetic compound, the dissolution profiles obtained with either large or small stirrer using either blade or holder method are nearly superimposable. Therefore, the resulting dissolution profiles are illustrated representatively by the upper curve of Fig. 4. The effect of the size of the stirrer on the dissolution profile of the antidiabetic compound was not discernible for both the blade method and the holder method. This finding differs from that obtained with either the bead method or the plate method, in which the rate as well as the extent of dissolution is enhanced with increasing agitation intensity by replacing the small stirrer with the large stirrer.

The dissolution profile of the diuretic compound is not affected by the size of the stirrer used in the blade method (Curves 5 and 6, open symbol, Fig. 4) but is slightly altered in the holder method (Curves 7 and 8, open symbol, Fig. 4). Comparison of dissolution profiles of the diuretic compound in Figs. 2–4 indicated that, using a small stirrer, the apparent initial dissolution rate and the extent of drug release are decreased in the following order: blade method > holder method > bead method > plate method. However, no significant difference in the apparent initial dissolution rate is observed when the large stirrer is employed among the blade, holder, bead, and plate methods. It is interesting to note that the scattering of the dissolution profiles of the diuretic compound obtained among blade, holder, plate, and bead devices is greatly minimized by substituting the small stirrer with the large stirrer. It appears that the larger the stirrer operating at the same rotating

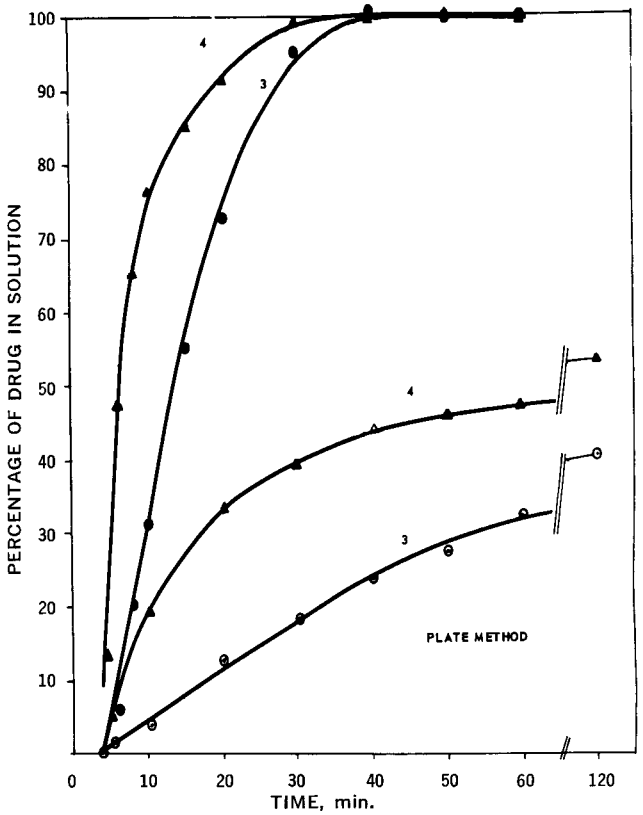


Figure 3—*Dissolution profiles of the diuretic (open symbols) and antidiabetic (solid symbols) compounds by plate method at 60 r.p.m. Key: 3, small stirrer; and 4, large stirrer.*

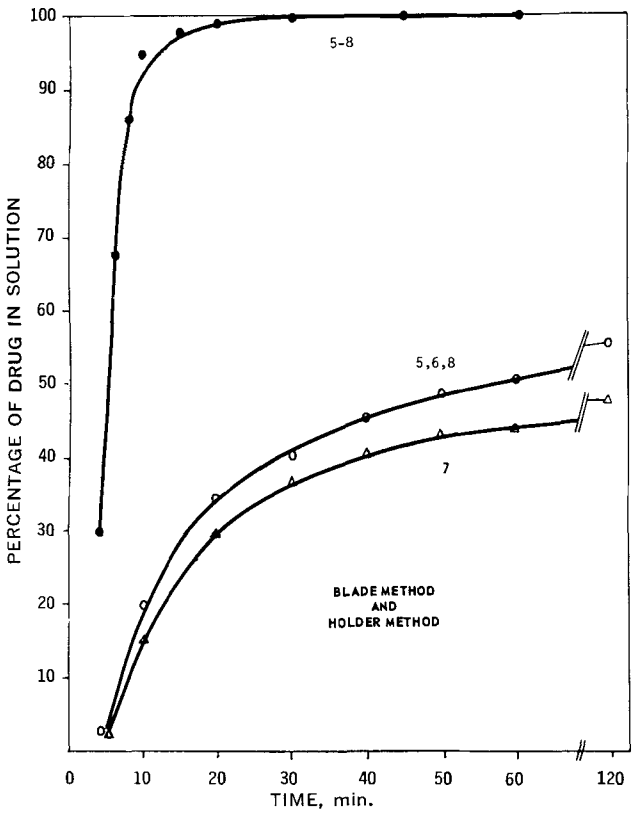


Figure 4—*Dissolution profiles of the diuretic (open symbols) and antidiabetic (solid symbols) compounds by blade (Curves 5 and 6) and holder (Curves 7 and 8) methods at 60 r.p.m. Key: 5 and 7, small stirrer; and 6 and 8, large stirrer.*

speed, the smaller variation of dissolution profiles is obtained among various devices. It was found in preliminary experiments with the blade methods that the difference in dissolution profiles of the diuretic compound is negligible when the capsule investigated is affixed at the bottom of the stirring shaft, at the face of the blade opposite to the direction of the flow, or at the face of the blade facing the same direction of the flow as shown in Fig. 1.

With blade or holder method, the majority of the drug is fairly well dispersed in the testing fluid at 60 r.p.m., although a small fraction of drug falls to the bottom of the dissolution vessel. The observation of the relative degree of drug dispersion in the dissolution fluid, together with the determination of dissolution profile, could be employed as a fast and useful means for screening the dosage forms. In general, if the large particulate agglomerates are visually observed to swell or sink in the dissolution flask, an unsatisfactory dissolution profile is expected. The poor dispersion effect may be taken as a possible early warning of drug-availability problems from the absorption viewpoint.

One common characteristic among the blade, holder, plate, and bead methods is that a certain segment of the capsule is physically in contact with supporting devices such as the stirring blade, plastic holder, metal plate, or glass bead, respectively. To prevent the physical contact and to alleviate the common problem of floating of the capsule on the surface of the dissolution medium, a self-designed basket was employed. The basket is labeled E in Fig. 1. The basket consists of a stainless steel cylinder 4.5 cm. in height and 2.3 cm. in diameter. The sides and bottom of the basket are No. 8 mesh stainless steel cloth. The bottom wire is welded together. The wire at the top of the cylinder is welded to a stainless steel ring which, in turn, is welded to an inverted T-shaped stainless steel attachment. The top of this cylindrical assembly has an orifice to be affixed to the bottom tip of the stirring shaft.

With this cylindrical basket, the dissolution profiles of the diuretic and the antidiabetic compounds were investigated. The results obtained are illustrated as Curves 9–12 in Fig. 5. When the agitation of dissolution fluid is provided by the rotational movement of the basket alone, the dissolution profile of the diuretic compound (Curve 9, open symbol, Fig. 5) closely resembles the profiles obtained with the plate—large stirrer (Curve 4, Fig. 3), holder—large stirrer (Curve 8, Fig. 3), and blade—small or large stirrer (Curves 5 and 6, Fig. 4) systems.

For evaluating the influence of the stirrer on the dissolution profile of the diuretic compound, it is necessary to increase the volume of dissolution fluid to accommodate the stirring assembly. As the volume is doubled from 300 to 600 ml. (Curves 9 and 10, Fig. 5), the rate and the extent of dissolution are enhanced when the basket alone is rotated at 60 r.p.m. to supply the agitation. By keeping the volume of dissolution fluid at 600 ml., the dissolution profiles (Curves 10–12, Fig. 5) show that the apparent initial dissolution rate and the extent of drug released are increased with the increase of the stirrer dimension.

Since the disintegration time (D.T.) apparatus, as described in USP XVII, is commonly employed in assessing the dissolution profile of a solid dosage form, this apparatus was incorporated in this investigation with the following slight modifications: a round-bottom dissolution flask of 800-ml. capacity was employed and one capsule was introduced to any one of the six compartments of the basket rack assembly. The assembly, agitated at 30 c.p.m., was allowed to descend to 1 cm. from the bottom of the dissolution flask on the downward stroke. The disk was used, and the volume of dissolution fluid was 700 ml. The data obtained for the diuretic compound are shown as Curve 13 (open symbol) in Figs. 5 and 6. The extent of the diuretic compound released within the testing period of 1 hr. is greatly enhanced with the D.T. method as compared with the basket, blade, holder, plate, or bead methods. This may be attributed to the stronger turbulent flow and the greater impacting force exerted on the capsule and the particulate aggregates by the D.T. method. Therefore, the percentages of drug released within 5 and 10 min. are already at the level of about 33 and 50%, respectively. However, the shape of the dissolution profile of the diuretic compound obtained by the D.T. method is similar to the following systems: (*a*) bead—large stirrer system (Curve 2, Fig. 2); (*b*) plate—large stirrer system (Curve 4, Fig. 3); (*c*) blade—small or large stirrer system (Curves 5 and 6, Fig. 4); (*d*) holder—large stirrer system (Curve 8, Fig. 4); and (*e*) basket—no stirrer system (Curve 9, Fig. 5).

The dissolution profiles obtained for the antidiabetic compound are depicted in Fig. 5 as circular and inverted-triangular solid symbols for basket and D.T. methods, respectively. It appears that the change of the volume of the dissolution fluid and the addition

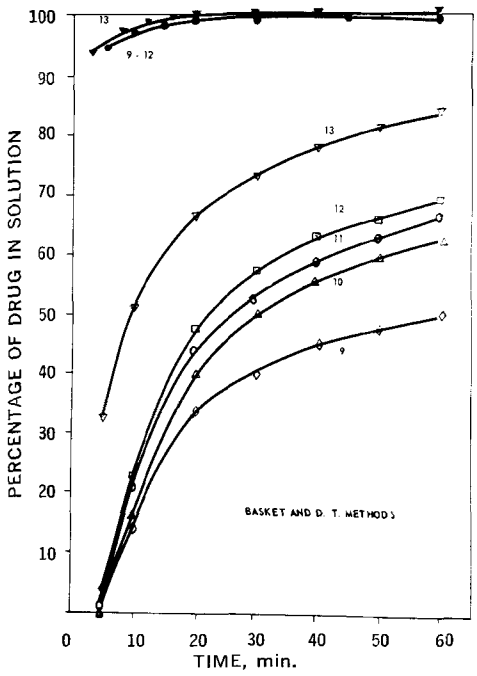


Figure 5—*Dissolution profiles of the diuretic (open symbols) and antidiabetic (solid symbols) compounds by basket (Curves 9–12) method at 60 r.p.m. and D.T. (Curve 13) method at 30 c.p.m. See Table I for detailed experimental conditions.*

of a small or large stirrer to the basket have not caused any detectable alteration in the dissolution profile of the antidiabetic compound. Consequently, the results are plotted collectively as solid circles of Curves 9–12 of Fig. 5. With the D.T. method, the dissolution profile is nearly superimposable to that obtained by the basket method.

Toward the completion of this investigation, a similar basket as was employed in this study was advocated by the USP as a tentative apparatus for investigating the dissolution of tablet and capsule dosage forms. Therefore, the suggested USP basket was purchased and incorporated in this study. The proposed USP apparatus (F in Fig. 1) consists of a stainless steel basket 3.6 cm. high and 2.5 cm. in diameter. The sides and bottom of the cylinder are 40 mesh stainless steel. The wire is welded to two stainless steel rings, top and bottom, and joined by welding at the seam. A stainless steel rod 30 cm. long with a 2.5-cm. plate and three spring clips are used to hold the basket (26). The results obtained with the proposed USP dissolution apparatus are shown in Fig. 6 for the diuretic (Curves 14–16, open symbols) and antidiabetic (Curves 14–16, closed symbols) compounds. For easy comparison, the dissolution profiles of both compounds obtained with the D.T. method are reproduced in Fig. 6.

For the diuretic compound, the initial dissolution rate and the extent of the drug released are enhanced by the increasing volume of dissolution medium (Curves 14 and 15) when the stirring mechanism is kept constant and by the use of additional stirrers (Curves 15 and 16) when the volume of dissolution medium is kept constant. This is in accord with the trend obtained with the basket method. The major difference between the basket method and USP dissolution apparatus is the stainless steel screen cloths used to fabricate the basket; USP apparatus uses 40-mesh screen, whereas 8-mesh screen is employed for the self-designed basket. When the basket method was replaced with the USP apparatus in determining the dissolution profile of the diuretic compound, no discernible difference was observed when the volume of dissolution medium was 300 ml. (Curve 14, Fig. 6, *versus* Curve 9, Fig. 5), whereas slight enhancement of the initial dissolution rate was observed when the volume was 600 ml. (Curve 15, Fig. 6, *versus* Curve 10, Fig. 5; and Curve 16, Fig. 6, *versus* Curve 12, Fig. 5).

The increase in the initial dissolution rate by substituting the basket method with the USP apparatus may be attributed to the higher agitation intensity of the smaller mesh screen used in the USP apparatus. With the larger screen used in the basket method, large drug particles and their agglomerates were observed to pass through the screen orifice and fall to the bottom of the dissolution flask after the dissolution of the capsule; the small screen employed in the USP method was observed to provide a mechanical sieve action which forced the drug particles and their aggregates through the small orifice of the screen as a fine dispersion, with lesser amounts of particulate matter swelling and remaining at the bottom of the dissolution vessel. However, due to the small orifice of the screen, the visual observation of the behavior of the capsule within the basket of the USP dissolution apparatus is impaired and not as convenient as when an 8-mesh screen was employed as in the basket method. It appears that a compromise lies in adopting a suitable screen cloth, between 8 and 40 mesh, to provide the convenience of visual observation of the capsule behavior in the basket as well as the prevention of the falling and accumulating of large drug particles and their aggregates at the bottom of the dissolution flask.

As shown in Figs. 5 and 6, the dissolution profiles obtained with the D.T. method provide the fastest rate and greatest extent of dissolution for both diuretic and antidiabetic compounds among the various devices employed in this investigation. It is sufficient to say that the turbulent flow created by D.T. apparatus operating vertically at 30 c.p.m. is stronger in agitation intensity than any other devices employing unidirectional convection and turbulence at 60 r.p.m. The disadvantage of the strong agitation intensity of the D.T. method is that the mild difference in the dissolution characteristics of several formulations to be screened may not be revealed explicitly.

SUMMARY AND CONCLUSION

The dissolution profiles of experimental antidiabetic and diuretic compounds in capsules were investigated by bead, plate, blade, holder, basket, disintegration time, and proposed USP dissolution methods. These methods are capable of preventing the common problem of the floating of capsules on the surface of dissolution fluid. The evaluation of drug-release patterns by these seven methods was compared from the standpoint of apparent initial dissolution rate, extent of dissolution, and reproducibility within the period of 1 to 2 hr. at 60 r.p.m.

At the constant stirring rate of 60 r.p.m., the initial rate and the extent of dissolution are enhanced with increasing stirrer dimension. It was found that the larger the size of the stirrer, the smaller was the variation of dissolution profiles obtained among various dissolution devices. The observation of the degree of the dispersion of drug in the dissolution media can be used as a visual method to predict the dissolution patterns during dosage form development work. For hydrophobic compounds, the better the dispersion and the lesser the amount of drug remaining or swelling in the bottom of the flask, the faster was the rate and the greater was the extent of dissolution.

For the easy visualization and comparison of the dissolution profiles obtained with the seven methods employed in this investigation, the time needed for dissolving the 25, 50, 75, and 90% of the total drug from the capsule was obtained from Figs. 2–6 and summarized in Table II. It is clearly indicated that the D.T. method provides the fastest rate and the greatest extent of dissolution for both diuretic and antidiabetic compounds among various devices employed in this investigation. This finding is attributed to the stronger turbulent flow and the greater impacting force exerted on the capsule and the particulate aggregates by D.T. apparatus operating vertically at 30 c.p.m. than that obtained by other devices employing unidirectional convection and turbulence at 60 r.p.m.

Although the reproducibility of the dissolution profiles obtained with the seven dissolution methods for capsules is satisfactory and comparable, the authors prefer the simplicity, convenience, and versatility of the basket method and the proposed USP method. However, due to the small screen (40 mesh) used in the basket of the USP method, the visual observation of the behavior of the capsule in the USP method is impaired and the chance of clogging the screen by the granules is greater than with the self-designed (8-mesh screen) basket used in the basket method. For providing the convenient visual observation of the behavior of the capsule in the basket and for preventing the fall and accumulation of large drug particles and their aggregates at the bottom of the dissolution flask,

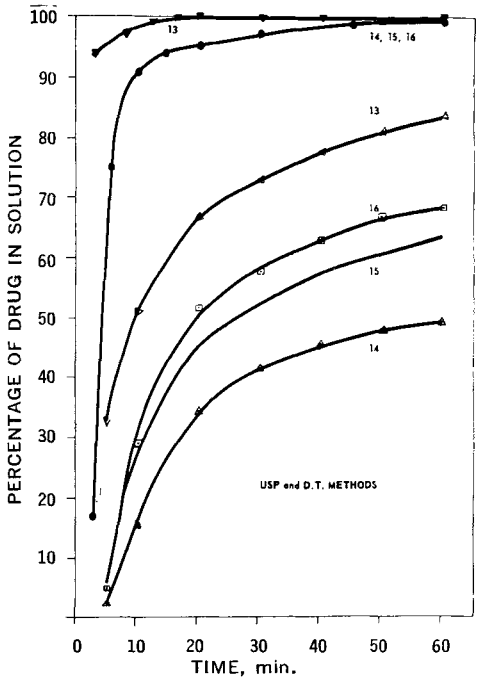


Figure 6—*Dissolution profiles of the diuretic (open symbols) and antidiabetic (solid symbols) compounds by proposed USP method (Curves 14–16) at 60 r.p.m. and D.T. (Curve 13) method at 30 c.p.m. See Table I for detailed experimental conditions.*

Table II—Dissolution Characteristics of Diuretic and Antidiabetic Compounds Investigated by Various Dissolution Apparatus

Expt. Cond.[a]	Time at Which the Indicated Fraction of Drug Dissolved, min. — Diuretic Compd. $t_{25\%}$	$t_{50\%}$	$t_{75\%}$	$t_{90\%}$	Antidiabetic Compd. $t_{25\%}$	$t_{50\%}$	$t_{75\%}$	$t_{90\%}$
1	36.5	120	—[b]	—	9	15	24	55
2	11.5	44	—	—	<4	4.5	6	12.5
3	42	—	—	—	9	13.5	18.5	27
4	14	50	—	—	5	6.5	9.0	18.5
5	13	57	—	—	<4	5	6	8.5
6	12.5	58	—	—	<4	5	6	8.5
7	16	135	—	—	<4	5	6	8.5
8	13	57	—	—	<4	5	6	8.5
9	15.5	60	—	—	<4	<5	<5	<5
10	13	30	—	—	<4	<5	<5	<5
11	11.5	26	—	—	<4	<5	<5	<5
12	10.5	22	—	—	<4	<5	<5	<5
13	4	10	33	88	<4	<5	<5	<5
14	14	60	—	—	<4	<5	5	10
15	9.5	27	—	—	<4	<5	5	10
16	8.5	20	—	—	<4	<5	5	10

[a] Numbers correspond to curve reference in Table I. [b] Not reached within experimental period of time.

the compromise should be made to employ a basket fabricated with the screen cloths of between 8 and 40 mesh.

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ACKNOWLEDGMENTS AND ADDRESSES

Received November 17, 1969, from *Pharmacy Research and Development Division, Development and Control Department, Ciba Pharmaceutical Co., Summit, NJ 07901*

Accepted for publication February 18, 1970.