with the common excipients methyl paraben and sodium chloride in a buffer solution. Replicate analyses of these solutions are presented in Table I.

Several commercial samples were assayed by the proposed procedure (Tables II and III). Judging from the results, there appears to be a significant problem of epinephrine deterioration. Most samples over 6 months in age showed some decomposition. Samples containing 0.02 mg./ml. or less of epinephrine had higher and more severe incidences of decomposition. Additionally, samples that assayed less than 75% of the declared value often had wide variations from vial to vial; individual vial analyses of one sample ranged from 48 to 71%. This would indicate that the rate of decomposition is not constant. Several factors, including storage conditions, pH, substrate composition, and bisulfite concentration, may affect the rate of decomposition, but a discussion of these factors is not within the scope of this report. The cogent element of the method presented here is that it measures the stability of epinephrine in commercial preparations, whatever the factors affecting that stability may be.

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PHARMACEUTICAL TECHNOLOGY

Design and Evaluation of a Rotating Filter–Stationary Basket *In Vitro* Dissolution Test Apparatus I: Fixed Fluid Volume System

ASHOK C. SHAH[▲], CRAIG B. PEOT, and JOHN F. OCHS

Abstract ☐ The apparatus described in this report provides a reliable and convenient means for determining *in vitro* dissolution characteristics of tablets, capsules, powders, suspensions, and most other solid drug dosage forms. Basic components of the apparatus are a perforated stationary sample basket, a rotating filter-stirrer assembly, and a closed jacketed dissolution fluid container. Among major advantages of the apparatus are: (a) precision-controlled variable intensity of mild laminar liquid agitation; (b) continuous or intermittent filtration of representative dissolution fluid samples through a nonclogging, microporous, *in situ* filter for automated or manual dissolution rate determinations; (c) convenient means for introducing solid samples in a stationary basket and positioning at a set level in the fluid medium; (d) minimal mechanical impacts, abrasion, and wear of the solid sample, with the retainment of its microenvironment during the dissolution process; and (e) simultaneous determinations of disintegration-dissolution rates of tablets and capsules. Studies performed using this apparatus are described to demonstrate its reproducibility, reliability, and application versatility as a research, development, and quality control test apparatus. Dissolution rates of five different tablet lots of an antidiabetic drug evaluated by this apparatus correlated with their *in vivo* activity. A multiple-test system for the simultaneous automated determination of six dissolution rates is described.

Keyphrases ☐ Dissolution equipment—design and evaluation of a rotating filter–stationary basket apparatus, compared to compendial methods ☐ Rotating filter–stationary basket dissolution apparatus—design and evaluation, compared to compendial methods

It is now generally recognized that the dissolution rate of a drug from its solid dosage form can become the rate-limiting process in the physiological availability and *in vivo* absorption of the drug. In recent years, therefore, considerable interest has been focused on the development of a reliable *in vitro* dissolution test

method, which can positively characterize the *in vivo* dissolution rate-controlled absorption of drugs administered in solid dosage forms. One basic requirement to achieve this goal, however, seems to be the availability of a reliable and flexible dissolution test apparatus, which is not only suitable for characterizing *in vivo* dissolution behavior of essentially all types of solid drug dosage forms but is also convenient to use for research, development, and quality control. Such an apparatus should meet most of the following criteria:

1. The design, dimensions, and positioning of each individual component of the apparatus must be exactly specified. Prototype units can be economically fabricated from commercially available equipment.

2. The apparatus should be relatively simple in design, convenient to operate, flexible for use under a variety of test conditions, and give reproducible results upon repeated tests.

3. Dissolution rates evaluated by the apparatus under appropriate physiological test conditions should correlate with the *in vivo* dissolution rate-controlled drug absorption process.

4. The apparatus should permit controlled variable intensity of mild, uniform, nonturbulent liquid agitation.

5. It must provide a convenient means for introducing a test sample (tablet, capsule, *etc.*) into the dissolution medium and holding it at a set position such that the sample is completely immersed in the fluid medium. During the dissolution process, the test sample must be subjected to minimal mechanical impacts, abrasion, and wear in order to retain its microenvironment.

6. The dissolution fluid container must be closed to prevent solvent evaporation, thermostated to regulate fluid temperature, and preferably transparent to permit visual observation of the disintegration characteristics of the test sample and fluid flow conditions during dissolution. It should be possible to maintain solvent sink conditions by employing either a relatively large volume of dissolution fluid or other convenient means such as continuous flow dilution of the bulk fluid with fresh solvent.

7. Withdrawal of representative fluid samples of the bulk medium for analysis, either by manual or automated methods, must be possible without interrupting solution agitation. As an automated system it should be possible to conduct continuous filtration of the fluid samples efficiently without encountering any operational or analytical problems.

8. The apparatus must be applicable for the evaluation of disintegrating, nondisintegrating, dense, or "floating" tablets and capsules; finely powdered drugs; and all other types of solid drug forms.

Although numerous types of dissolution test apparatus are reported in the literature (1-14), many, including those recognized by the official compendia (15, 16), do not seem to meet all of the stated criteria desired. In addition, the nature and extent of solvent agitation, treatment of the test sample during the dissolution study, and liquid sampling techniques employed in some of these systems can yield unreliable dissolution rate results. For example, in NF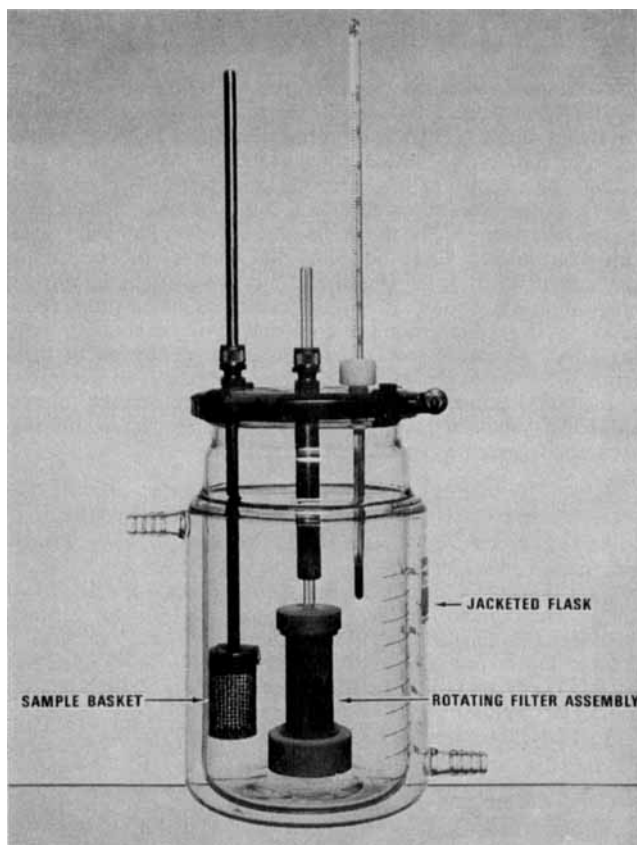 XIII Method II the fluid undergoes violent, turbulent agitation, while in both the official test methods (USP-NF Method I and NF Method II) the sample container itself serves as a liquid stirring device. Under these conditions, there can be excessive abrasion and wear of the sample due to its mechanical impacts with the container surface, thereby adversely influencing its microenvironment.

Another major problem present in most automated and continuous flow dissolution test apparatus is the difficulty in conducting continuous, efficient filtration of the dissolution fluid sample. Continuous monodirectional filtration through a conventional, static, coarse-filter element (stainless steel wire cloth screen, sintered glass, membrane, *etc.*) frequently clogs the filter with undissolved solid particles, which results in progressive diminution of the fluid flow rate (9, 17, 18). Liquid filtration through a relatively coarse-filter screen permits fine particles to escape and accumulate in the circulation tubing as well as in the spectrophotometer flow cell. These filtration problems not only create serious operational difficulties due to the diminishing fluid flow rates but may yield erroneous dissolution rate results due to: (*a*) continual passage of dissolution fluid through a filter covered with drug particles and (*b*) interference in the spectrophotometric analysis of the filtered fluid by solid particles collected in the spectrophotometer flow cell.

The design and evaluation of a reliable, rotating filter-stationary basket dissolution test apparatus[1],

Figure 1—*Photograph of the rotating filter-stationary basket apparatus.*
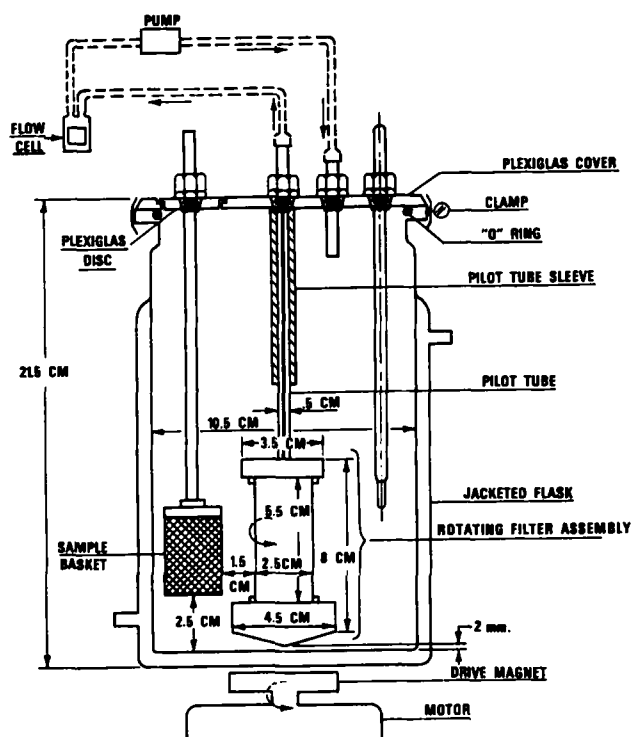

Figure 2—*Schematic diagram of the rotating filter–stationary basket apparatus. Broken lines represent setup for the automated spectro-photometric analysis.*

which eliminates these problems and meets essentially all of the above-mentioned criteria, are reported here. Essential features of the apparatus are a stationary sample basket, a large volume fluid container, and a rotating filter assembly. The rotating filter system, employed previously in the cultivation of mammalian cells (19), functions as a liquid agitation device as well as an efficient fluid sampling system.

APPARATUS DESCRIPTION

Single-Test Apparatus—The rotating filter–stationary basket single-test apparatus was constructed by incorporating necessary modifications into a commercially available microbial cell culture cultivation flask[a]. Basic features of the apparatus (Figs. 1 and 2) are a jacketed dissolution fluid container flask, a stationary sample basket, a rotating filter assembly, and an external variable speed magnetic stirrer[a]. Broken lines in Fig. 2 represent the optional setup for automated dissolution rate determinations, in which filtered fluid samples are cycled through a spectrophotometer flow cell by means of 2-mm. i.d. flexible polyethylene tubing and a peristaltic pump[a]. The description of individual parts of the apparatus follows.

Fluid Container Flask and Cover—The jacketed glass flask, suitable for holding up to 1.5 l. of dissolution fluid, has a removable Plexiglas cover secured firmly to the neck of the flask by means of an O-ring and a flexible metal belt. The cover serves as a support for the sample basket and the rotating filter assembly. A rabbeted edge circular opening in the cover, 3 cm. in diameter, provides an entrance pathway for the sample basket. There are three other ports in the cover: one in the center for a glass capillary pilot tube, another for a thermometer, and the third one for the return of the dissolution fluid from the spectrophotometer flow cell.

Sample Basket—The design features of the stationary sample basket are similar to the basket assembly employed in the official USP–NF Method I apparatus (15), with the exception of using 12-
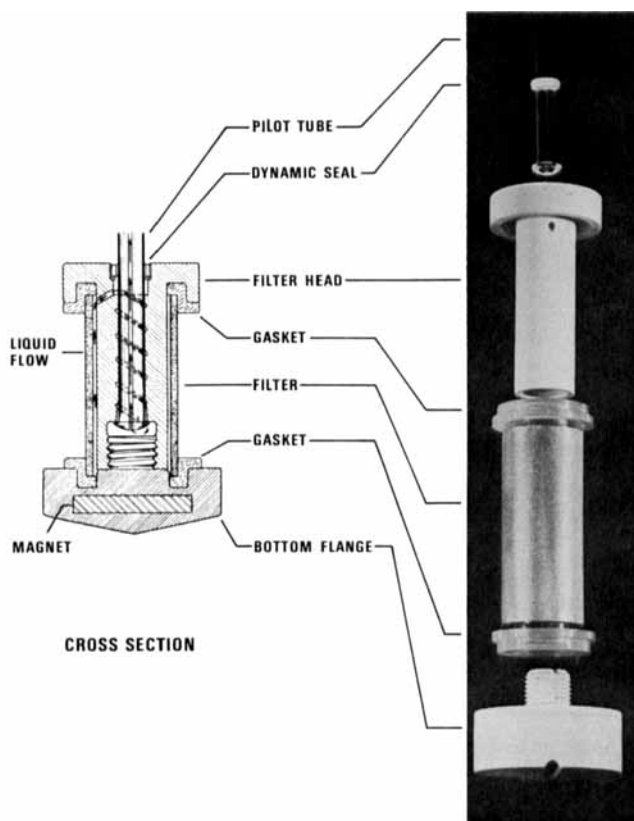
Figure 3—*Rotating filter assembly.*

mesh instead of 40-mesh wire cloth screen to facilitate fluid movement through the basket and prevent plugging of the basket screen with solid particles (4, 20, 21). A rabbeted edge circular Plexiglas disk is attached to the basket holding rod with a compression fitting, so that when the basket is introduced into the flask through the cover opening, this disk rests in the corresponding rabbeted edge opening and holds the basket at a preset level in stationary position. The basket level can be varied by moving the position of the disk along the holding rod. In all experiments, the basket was held 2.5 cm. from the flask bottom (Fig. 2).

Rotating Filter Assembly—The rotating filter assembly provides variable intensity of mild laminar liquid agitation and it also functions as an *in situ* nonclogging filter to permit intermittent or continuous filtration of the dissolution fluid samples efficiently during the dissolution process. The assembly is suspended in the center of the flask on the flared end of a glass capillary pilot tube. Since the pilot tube is secured firmly to the cover with a compression fitting,
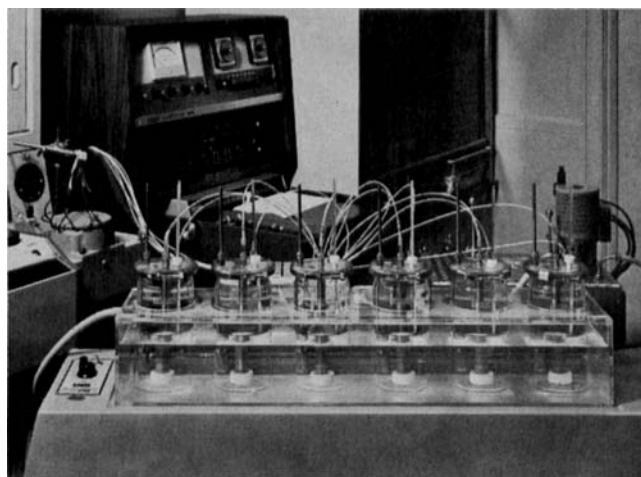

Figure 4—*Photograph of the multiple-test rotating filter–stationary basket apparatus.*
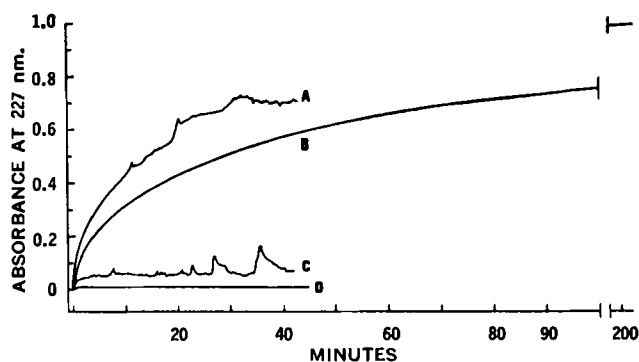
Figure 5—*Comparison of the rotating filter with the conventional wire mesh screen filter used in the automated spectrophotometric dissolution rate analysis of an active tablet sample (A and B) and placebo tablet sample (C and D). Key: A and C, screen filter; and B and D, rotating filter.*

it remains in a fixed position while the assembly can freely rotate on the flared end of the tube. The assembly rotates by means of a controlled, variable speed, external magnetic stirrer coupling with a magnetic bar embedded in the bottom part of the assembly. The level of the assembly in the flask can be varied simply by raising or lowering the pilot tube. A stainless steel pilot tube-sleeve provides support to the pilot tube and prevents subtle vibration of the assembly.

The design features of the assembly (Fig. 3) consist of a filter head, bottom flange, cylindrical filter, two flexible gaskets, and a dynamic seal. The filter head and bottom flange are fabricated from 20% glass-filled Teflon with a magnet embedded in the bottom flange. Cylindrical filters of glass fiber, Teflon, ceramic, or sintered stainless steel are available in the 0.2-3-μ porosity range. In the present studies, either a 0.5- or 1-μ porosity stainless steel filter was employed. In assembling these parts, first the filter head is suspended on the flared end of the pilot tube, then the cylindrical filter with one flexible gasket on each end is slipped over the filter head, and finally the bottom flange is screwed into the filter head threads. The spring-action dynamic seal slid over the pilot tube positions into the
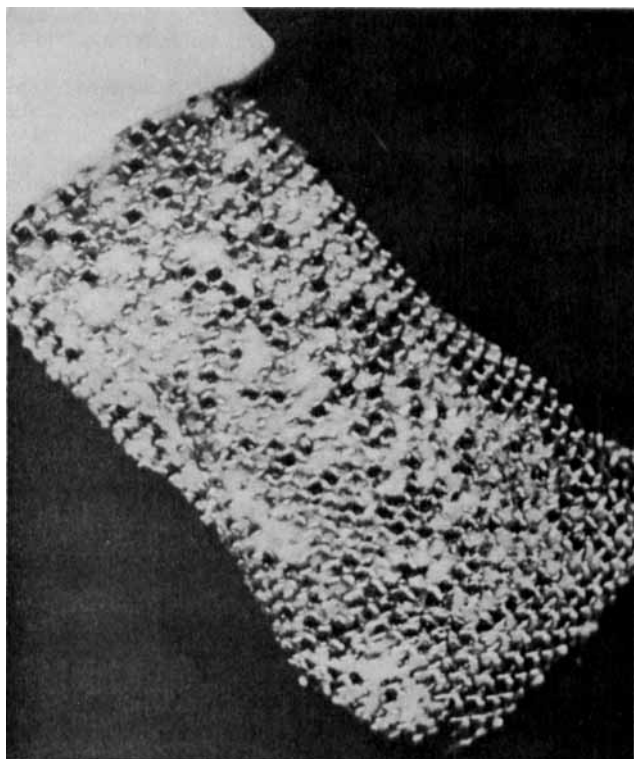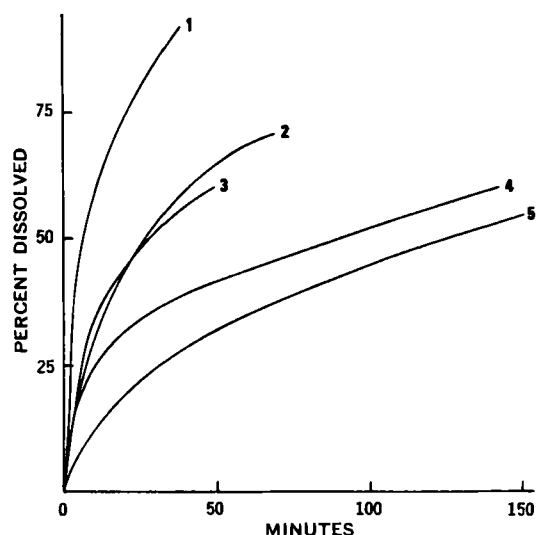

Figure 6—*Photograph of the clogged screen filter.*

Figure 7—*Dissolution profiles of five different tablet formulations of an antidiabetic drug measured by the automated rotating filter-stationary basket apparatus.*

filter head and prevents passage of liquid through the space between the pilot tube and the filter head. Arrows in the cross-sectional diagram of Fig. 3 show the liquid filtration system and flow through the assembly. Dissolution fluid upon filtration through the cylindrical filter flows through a hole in the filter head, channels through a helical path around the pilot tube, and then enters into the pilot tube capillary. Fluid samples can be withdrawn continuously or intermittently from the upper end of the pilot tube.

Multiple-Test Apparatus—An automated multiple-test rotating filter–stationary basket apparatus (Fig. 4) is capable of monitoring up to six dissolution tests simultaneously. The basic design of this apparatus is similar to the single-test unit, with the exception of using a Plexiglas water bath to thermostat all six units and a six-stage controlled variable speed magnetic stirrer operated by a single motor[4]. The upper panel of the stirrer housing is illuminated by a fluorescent light placed underneath the housing, which aids in visual observation of the test environment. Dissolution fluid samples from each flask are continuously cycled by a multichannel pump[3] through one of six flow cells located in the cell compartment of the spectrophotometer[5]. Dissolution rates are monitored by the spectral absorbance recording of the cycling fluid samples at programmed time intervals.

EXPERIMENTAL

Procedure—In a typical experiment, the sample basket is removed from the flask and a measured volume of dissolution fluid is transferred into the flask through the rabbeted edge opening in the cover. The fluid is allowed to equilibrate at 37° and is stirred by rotation of the filter assembly at set revolutions per minute. Filtered fluid samples are continuously withdrawn through the capillary pilot tube at a 40-ml./min. flow rate and are circulated through a spectrophotometer. When all the test conditions (*i.e.*, fluid temperature, stirring rate, cycling through the flow cell, and calibration of the spectrophotometer) are properly adjusted, the dissolution experiment is started by introducing the sample basket into the flask through the rabbeted edge opening in the cover.

For powdered drugs, a weighed amount of the sample is first dispersed into a small volume (5 ml.) of the dissolution medium and then immediately transferred into the bulk fluid medium. In the case of metastable drug–polyvinylpyrrolidone coprecipitates, the weighed powder sample was added directly into the fluid medium and was dispersed by a momentary rapid liquid agitation. In all powder dissolution studies, a 0.5-μ porosity filter was used,

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[4] Jar test machine model 7303, Coffman Industries, Kansas City, KS 66101
[5] Model DBG or Kintrac VII spectrophotometer, Beckman Instruments, Fullerton, CA 92634

Table I—Tablet Dissolution Rates $(T_{50}\%)^a$ Determined by the USP-NF Method I and Rotating Filter-Stationary Basket Method

| Apparatus | $T_{50}\%$, min. Experiment Number | | | | | | Mean | SD | Coefficient of Variation, % |
	1	2	3	4	5	6			
USP-NF Method I	23.6	44.7	44.9	53.6	15.6	57.0	39.9	16.6	41.7
Rotating filter-stationary basket method	34.0	34.0	31.3	34.0	33.0	33.0	33.4	1.09	3.28

a Time required for 50% of the drug to dissolve.

whereas in the tablet dissolution studies a 1-μ porosity filter was employed.

Upon completion of the dissolution run, the apparatus can be conveniently cleaned by discarding dissolution fluid through the opening in the cover and adding water through the same opening to clean the flask and the filter assembly. If necessary, however, the cover can be removed from the flask by loosening the metal belt and each component can be separately cleaned. The filter can be cleaned either by circulating water through it or by placing it in an ultrasonic cleaning bath.

Results—*Comparison of Static versus Dynamic Liquid Filter Systems*—The influence of filtration efficiency in the fluid sampling procedure upon the accuracy of dissolution rate results is demonstrated by comparing the dynamic rotating filter system described in this report with a conventional static filter consisting of a stainless steel 100-mesh wire cloth screen filter (3). Dissolution profiles of an active and a placebo tablet sample (Fig. 5) were determined by the automated spectrophotometric analysis of the fluid samples filtered continuously through the static screen filter (curves A and C) and the dynamic rotating filter system (curves B and D). Except for the difference in the filtration system, these studies were performed under identical experimental conditions.

Continuous filtration of the test fluid through the static screen filter resulted in clogging of the filter screen by accumulation of solid particles on the filter surface. Consequently, there was progressive diminution of the fluid flow rate from 40 ml./min. initially to only 2 ml./min. after about 45 min. A photograph of the clogged screen filter is illustrated in Fig. 6. A noticeable amount of fine particles escaped through the screen filter and accumulated in the flexible tubing and spectrophotometer flow cell. These apparent filtering problems encountered with the static filter system may account for the erratic spectral response evident in curves A and C

and a false absorbance reading recorded with the placebo tablet sample (curve C). Similar types of filter clogging problems were also observed with other static filter systems such as sintered-glass and Millipore filters.

The dynamic rotating filter system permitted continuous, efficient filtration of the test fluid for prolonged time periods (up to 200 min.) without any noticeable sign of filter clogging, change in the fluid flow rate, or escape of solid particles through the filter pores. The efficiency of the rotating filter system is reflected in the smooth spectral recording of the dissolution profiles (curves B and D, Fig. 5) and, as expected, the almost zero absorbance reading recorded upon dissolution of the placebo tablet (curve D).

Reproducibility of USP-NF Method I and Rotating Filter-Stationary Basket Apparatus—The dissolution rate results (Table I) were obtained upon six repeated runs for a tablet sample employing an automated USP-NF Method I apparatus (21), at 300-r.p.m. stirring, and the automated rotating filter-stationary basket apparatus, at 600-r.p.m. stirring. These stirring speeds were selected because of the comparable tablet dissolution rates $(T_{50}\%)$ obtained under these conditions in both apparatus. Other test conditions employed were one tablet sample per test, 900 ml. of simulated intestinal fluid without the enzyme, and 37°. It is apparent from the data listed in Table I that, for the tablet samples examined, the results obtained with the rotating filter-stationary basket apparatus are considerably more reproducible than with the USP-NF Method I apparatus.

In Vitro-In Vivo *Correlation*—Dissolution profiles for five different tablet lots of an antidiabetic drug (Fig. 7) were determined using the rotating filter-stationary basket apparatus. The test conditions employed for these studies were: one 2.5-mg. tablet sample, 1 l. of simulated intestinal fluid without the enzyme, 37°, and 400-r.p.m. stirring speed. Solvent sink conditions were maintained during the dissolution because the maximum drug concentration in solution reached upon complete dissolution was about 12% of the saturation concentration. The disintegration time for all of these tablet samples was less than 45 sec.
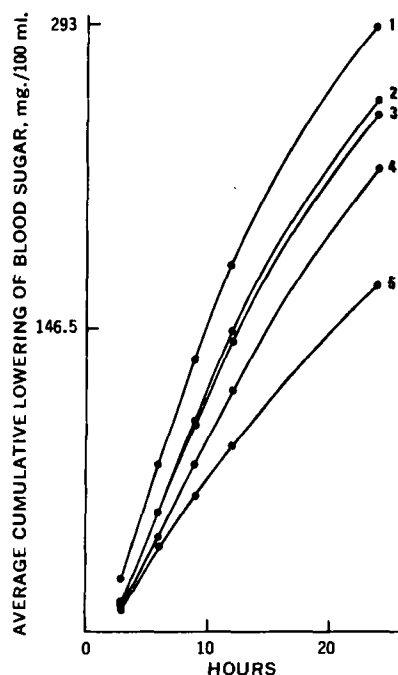

Figure 8—*Average cumulative blood sugar-lowering response in dogs after administration of the antidiabetic tablets.*
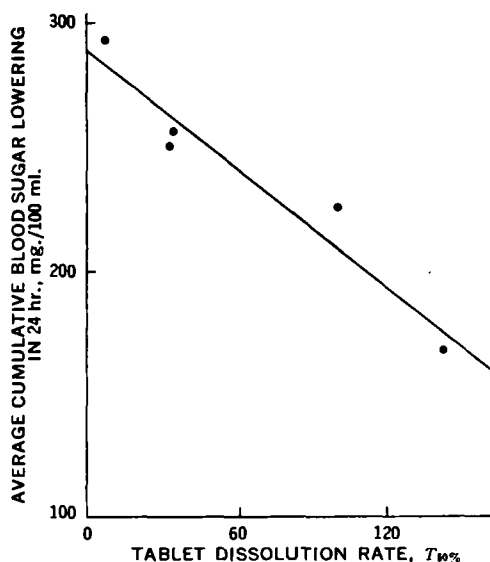

Figure 9—*Correlation between the* in vitro *dissolution rates* $(T_{50}\%)$ *and total* in vivo *response obtained with the antidiabetic tablets.*
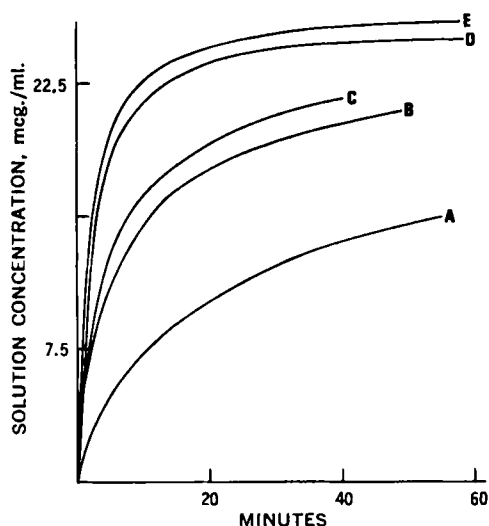
Figure 10—*Dissolution profiles of the powdered drug samples with varying particle size determined by the automated rotating filter–stationary basket apparatus. Key (surface area, m.²/g., of the powder samples): A, 0.87; B, 1.38; C, 1.54; D, 2.10; and E, 2.54.*

In a crossover study, these tablet samples were administered orally to mongrel female dogs, and their blood sugar concentrations were analyzed at various time intervals up to 24 hr. The average cumulative blood sugar-lowering response produced at various time intervals after administration is shown in Fig. 8. Comparison of these results with the dissolution profiles shown in Fig. 7 suggests a rank order *in vitro–in vivo* correlation. This correlation is further evident from a linear relationship (Fig. 9) obtained upon plotting the dissolution rate $T_{50\%}$ against the total 24-hr. blood sugar-lowering response (correlation coefficient = −0.9287).

Quality Control Dissolution Test for Powdered Bulk Drug Lots— During formulation development studies, it became apparent that the variation in the particle size among various milled bulk drug lots of a sparingly soluble drug seemed to have a noticeable effect upon the dissolution characteristics of tablets manufactured from these lots. Dissolution profiles of several bulk drug lots were, therefore, determined utilizing the rotating filter–stationary basket apparatus under the test conditions of 50 mg. of powdered drug suspended in 1 l. of 0.05 M phosphate buffer, pH 7.5, containing 0.05% polysorbate 80 as a wetting agent, 400 r.p.m., and 37°. From the dissolution profiles (Fig. 10), it is evident that the finer bulk drug with greater surface area showed faster dissolution than the coarse particle-size drug. Establishment of routine dissolution rate specifications for the bulk drug lots based on these results has
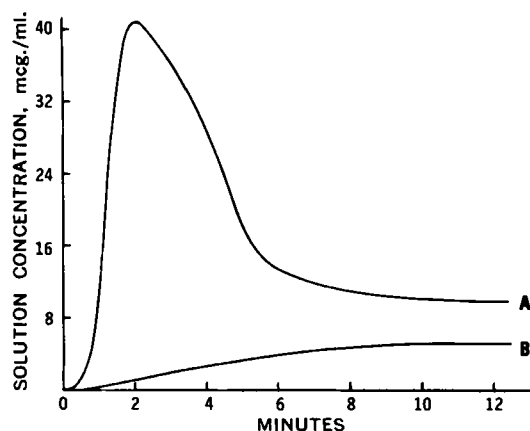

Figure 11—*Dissolution behavior of a metastable drug–polyvinyl-pyrrolidone coprecipitate (curve A) and the stable crystalline drug powder (curve B) evaluated by the automated rotating filter–stationary basket apparatus.*

Table II—Comparison of the Official Dissolution Test Apparatus with the Rotating Filter–Stationary Basket Apparatus[a]

Desired Features	Rotating Filter–Stationary Basket Apparatus	USP–NF Method I Apparatus	NF Method II Apparatus
Enclosed container	A	A	NA
Variable intensity of liquid agitation	A	A	NA
Definable (laminar) liquid flow	A	A	NA
Visibility of the test sample and fluid environments	A	?	?
Representative fluid sampling under mild agitation conditions	A	?	?
Automation with a continuous, efficient, clog-free fluid filtration system	A	NA	NA
Minimal mechanical impacts, abrasion, and wear of the test sample during dissolution	A	NA	NA

[a] A = available, NA = not available.

considerably improved the lot-to-lot uniformity of the tablet dissolution rate.

Dissolution Behavior of a Metastable Drug Form—The rotating filter–stationary basket apparatus was utilized as a preformulation research tool for the evaluation of dissolution and crystallization behavior of a drug in its metastable drug–polyvinylpyrrolidone (1:9) coprecipitate form. The coprecipitates were prepared by vacuum evaporation of a methanol solution of drug and polyvinylpyrrolidone. The test procedure employed was essentially similar to the previously described procedure for the powdered bulk drug dissolution studies. Rapid dissolution of the coprecipitates with the attainment of peak solution concentration, followed by the concentration decline due to precipitation of the drug, occurs within a few minutes (curve A, Fig. 11). Such a rapid transient dissolution behavior of the metastable drug form can be conveniently studied by the automated rotating filter–stationary basket apparatus. Curve B in Fig. 11 was obtained with the stable crystalline form of the drug.

In addition to these studies, the apparatus was utilized for dissolution rate determinations of capsules, granules, and timed-release dosage forms and also in evaluating solubility–solubilization of various drugs.

DISCUSSION

The rotating filter–stationary basket dissolution test apparatus was employed extensively by the authors over the past 18 months for testing various drugs and their dosage forms. The typical studies described here demonstrate its application as a preformulation research, formulation development, and quality control dissolution test apparatus. Its application as a quality control dissolution test system for both the active drug and the final dosage form offers a two-pronged approach to ensure drug quality from the standpoint of biological availability, a type of approach considered valuable by the NF Board (22).

Dissolution rates can be determined by either a manual or an automated test method. In the manual test method, filtered aliquots of the dissolution fluid are withdrawn at periodic time intervals and then assayed individually. This method is laborious and inconvenient for routine quality control testing of dissolution rates and unsuitable for evaluating very rapid dissolution processes; in addition, there is a human error involved in the accurate sampling and analysis.

Since the automated method overcomes these problems and provides a convenient means for monitoring dissolution rates, there have been increasing applications of the automated method in the pharmaceutical field. Aside from an automated titration tech-

nique (23), in most automated test methods a portion of the dissolution fluid is filtered continuously through a stainless steel wire cloth screen, sintered glass, membrane, or similar other static system and then cycled through a spectrophotometer flow cell or other analytical system for the continuous analysis of the circulating dissolution fluid (3, 5, 9, 11, 13, 20). However, use of such static filter elements for the continuous filtration of the dissolution fluid often presents filtration problems, such as clogging of the filter with solid particles and escape of solid particles through the filter element, which may yield erroneous dissolution rate results. The occurrence of these filtration problems has been acknowledged by other workers (9, 17, 18) and is demonstrated in the present study.

The rotating filter system employed in the present apparatus provides a dynamic *in situ* microporous filter element which, because of the boundary effect (centrifugal force), prevents the filter from becoming clogged with solid particles and permits continuous, efficient filtration of the dissolution fluid. Another advantage of the rotating filter system is its relatively large filter area extending over the greater portion of the dissolution fluid, which permits representative sampling of the bulk dissolution medium. From the dimensions of the rotating filter assembly, it may appear that there might be a considerable amount of liquid held inside the assembly, but, in fact, there is very little void space in the assembly so that the hold-up volume inside the assembly is less than 1 ml.

Dissolution rate determinations under solvent sink conditions can be performed by: (*a*) employing a relatively large fixed volume of dissolution fluid, (*b*) partitioning the dissolved drug into an organic solvent phase, (*c*) adsorbing the dissolved drug on a solid adsorbent, and (*d*) continuous flow replacement or dilution of the fluid with fresh solvent. In the adsorption and solvent partition methods, certain additional factors such as partition coefficient of the drug in the organic phase, rate of partitioning, and rate of adsorption are involved, which further complicate the dissolution rate determination. In a continuous flow system, replacement of dissolution fluid with fresh solvent medium necessitates continuous filtration of the fluid. Most of the existing continuous flow systems are, therefore, faced with the same types of filter clogging and other filtering problems as are the automated methods. Dissolution rate determination in a fixed fluid volume offers perhaps the simplest test method, provided it is possible to maintain a relatively dilute solution concentration by utilizing a large volume of the dissolution fluid. The present apparatus provides a relatively large size (1.5-l.) fluid container suitable for dissolution rate determinations under fixed fluid volume conditions. This apparatus can be employed as a continuous flow system by replacing a portion of the fluid with the fresh solvent medium, as described by Pernarowski *et al.* (11). However, achievement of rapid dilution of a large volume of the bulk fluid requires relatively fast fluid flow rates and consumption of appreciable amounts of fluid in a single dissolution test. For instance, to dilute 1-l. volume of the bulk fluid at a rate of 20%/min., one must replace 200 ml. of the bulk fluid per minute with the fresh solvent (*i.e.*, 200 ml./min. fluid flow rate); if the experiment is continued for 30 min., a total of 7 l. of dissolution fluid will be consumed. While these test conditions can be maintained, they obviously are not very convenient and practical for routine dissolution rate studies. A modification of the present apparatus capable of holding small volumes of the fluid, which is suitable as a continuous flow system, will be reported in a subsequent publication.

The importance of relatively mild agitation conditions for the determination of dissolution rates to reflect *in vivo* conditions was emphasized by Levy (24). Furthermore, the liquid agitation conditions must be reproducible upon repeated tests, and the hydrodynamics of the system must be quantitated to describe the dissolution process in terms of theoretical dissolution rate relationships. The agitation system employed in the present apparatus meets these criteria. The smooth cylindrical surface of the rotating filter assembly without impeller blades and its agitation action over a long vertical axis provide uniform, mild, laminar, nonturbulent, and reproducible liquid stirring even at relatively high revolutions per minute.

Retainment of the microenvironment of the test sample and accurate positioning of the sample are necessary requirements for reliable dissolution rate studies. These have been accomplished in the present apparatus by the use of a stationary sample basket held in position at a precise level. The sample can be conveniently introduced into the fluid after all other test conditions have been

adjusted. Visual observation of the test sample through the transparent flask and stationary basket permits simultaneous disintegration time–dissolution rate evaluation. A 12-mesh wire cloth screen basket was employed primarily to achieve unhindered liquid flow through the basket, to enable visual observation of the test sample, and to prevent plugging of the basket screen with the solid particles, as experienced by other workers with the official test method using a 40-mesh screen basket (4, 20, 21).

Recognition of the two dissolution test apparatus in the official compendia (15, 16) suggests wider use of these apparatus in the pharmaceutical field. Hence, a comparison of these two apparatus with the rotating filter–stationary basket apparatus is presented in Table II to illustrate the availability of some of the major features desired in a standard dissolution test apparatus.

SUMMARY

Requirements of a standard dissolution test apparatus suitable for all types of solid drug forms and applicable as a research, development, and quality control tool are discussed. The design of a rotating filter–stationary basket apparatus, which meets essentially all these criteria, is presented. Results are described to demonstrate its reproducibility and versatility of application in solubility and dissolution rate studies. *In vitro* dissolution rates of five different tablet samples of an antidiabetic drug determined by this apparatus are shown to correlate with the *in vivo* drug activity.

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