Variation on the USP–NF Rotating-Basket Dissolution Apparatus and a New Device for Dissolution Rate Studies of Solid Dosage Forms

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Abstract □ Tablet dissolution studies were conducted comparing three devices: the USP–NF rotating basket, a modification of this called the bent basket, and a newly designed L-shaped Teflon holder/stirrer. In these studies, the latter two devices were superior to the official device.

Keyphrases □ Dissolution equipment—modified compendial rotating basket, new rotating assembly □ Tablet dissolution—modified compendial rotating basket, new rotating assembly

The USP XVIII and NF XIII include a description of a rotating-basket dissolution apparatus, the purpose of which is to provide: "an objective means of determining the dissolution characteristics of a solid dosage form" (1). The intent of this apparatus is to determine compliance with the limits on dissolution where stated in the individual (USP) monograph for a tablet or capsule form (1). The USP monograph for prednisolone tablets, for instance, states that the time required for 60% of the labeled amount of $C_{21}H_{28}O_5$ to dissolve is not more than 20 min., deaerated water being used as the dissolution medium and the basket being rotated at 100 r.p.m. (2). Similar time limits are cited for five other tablets in USP XVIII. While the designated use of the USP–NF dissolution apparatus is quite limited, its official status ensures that it will be extensively used for many solid drug products, both new and old. To date, only a very limited quantity of published data exists relating to the use of the USP–NF rotating-basket apparatus. In short, its utility for characterizing the dissolution properties of the large number of drugs marketed as tablets or capsules remains unproven. This preliminary report describes some difficulties encountered in our laboratories with the official apparatus and describes a variation on this apparatus that subsequently led to the design of a new rotating device which may offer certain advantages.

EXPERIMENTAL

Dissolution studies, using the USP–NF rotating-basket device (Fig. 1*b*), were conducted on two batches of an experimental tablet formulation. The active ingredient was a steroid (chlormadinone acetate) having a water solubility of 1.7 mcg./ml. at 37°. Pertinent physical characteristics of two lots of the same formulation, differing appreciably in their dissolution behavior, are shown in Table I. A volume of boiled (deaerated) water sufficient to provide sink conditions (1500 ml.) was employed, and all experiments were conducted at 37°. The basket was rotated at 80 r.p.m. Samples were taken by filtering the entire volume of dissolution fluid through a 0.45-μ membrane[1] and using 250 ml. of the filtrate for chloroform extraction. The extract was evaporated to dryness, and the residue was redissolved in an accurately measured volume of chloroform. The absorbance of this solution was recorded at 286 nm. on a spectrophotometer[2], and the quantity of steroid dissolved at various time points was determined. At a later date, USP–NF rotating baskets made with 24-mesh stainless steel screen, rather than the 40-mesh screen, were used in an attempt to get better dispersion of the tablet particles into the dissolution fluid as disintegration occurred.

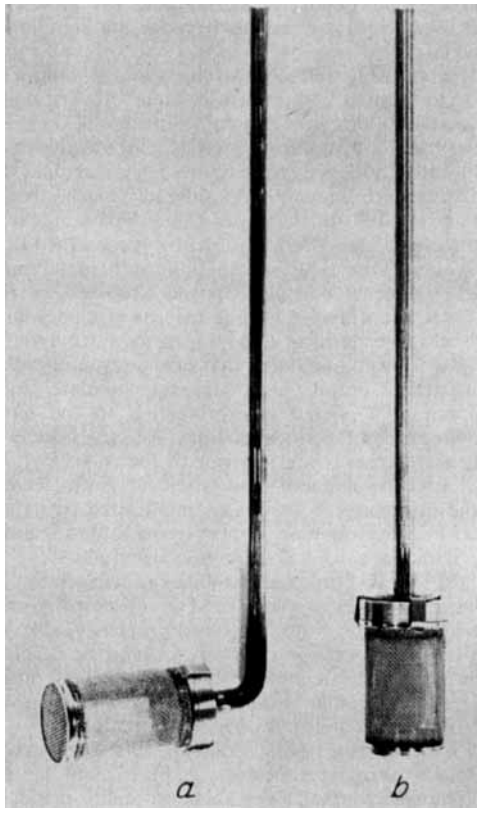

Figure 1—(a) *Bent basket, and* (b) *USP NF rotating basket.*

The USP–NF basket, with 40-mesh screen, was further modified by bending the stainless steel stirring rod of the apparatus at a 90° angle just above the basket to yield an L-shaped configuration (Fig. 1*a*). This device provided a greater flow of dissolution fluid over the tablet.

As a consequence of the experience with the bent basket, a third device was designed and constructed in this laboratory. The tablet holder/stirrer (Fig. 2) consisted of a piece of Teflon rod which was attached at a 90° angle to a stainless steel stirring rod, and a cylinder of stainless steel screen (24 mesh) was seam-welded to fit tightly over the Teflon holder. This device ensured that the tablet (or capsule) was held at a fixed distance from the center of rotation during the disintegration phase of the dissolution experiment. The agitation intensity could be varied by changing either the stirring rate or the length of the Teflon rod.

[1] Metricel.

[2] Beckman DB.

Table I—Drug and Tablet Characteristics

Active ingredient	Chlormadinone acetate, 0.5 mg./tablet	
Total tablet weight	80 mg.	
Drug solubility	1.7 mcg./ml. (37°)	
	—Batch A—	—Batch B—
Hardness (S–C units)	3–4	5–6
Disintegration time:		
With disk	3–5 min.	4–5 min.
Without disk	11–14 min.	11–13 min.

When highly acidic solutions, such as artificial gastric fluid (pH 1.2), are employed as the dissolution medium, the stainless steel used in components of the apparatus may be subject to corrosion. For such experiments the stainless steel rod and screen can be replaced with a glass rod and nylon mesh.

RESULTS AND DISCUSSION

Dissolution data obtained for the two tablet batches with the USP–NF rotating basket are shown in Fig. 3*a*. These data indicate that significant *in vitro* differences exist between the dissolution rates of the two different batches. With Batch A, the substitution of 24-mesh screen for 40-mesh screen had no effect on the dissolution except at the 15-min. time point. With Batch B, the dissolution rate did increase with the 24-mesh screen but not as much as expected.

It was obvious from subsequent observation of tablet remains that the slow dissolution rates shown in Fig. 3*a* were the result of slow and incomplete *disintegration* of the tablets using the USP–NF apparatus. Tablets from both batches disintegrated poorly in the official dissolution device, and disintegration was incomplete after several hours at stirring speeds up to 100 r.p.m. Whether the difference between batches was primarily due to different disintegration characteristics was uncertain at this point. Disintegration tests conducted with the official disintegration apparatus, both with and without disks (Table I), indicated no significant differences between Batches A and B.

The use of deaerated water was essential for all of the dissolution studies. If there is dissolved air in the dissolution fluid, bubbles collect on the screen and hamper the flow of fluid over the tablet. This can lead to low values and extensive scatter in the data.

The purpose of the basket in the USP–NF apparatus presumably is to hold the tablet or capsule in a fixed position during the disintegration process. In essence, the distance of the tablet from the center of rotation is fixed within small limits. However, the position and orientation of a tablet in the bottom of the basket may vary somewhat from experiment to experiment unless the stirring speed is sufficient to hold the tablet against the outer perimeter of the screen by centrifugal force.

As a tablet disintegrates during the dissolution test, the flow of solvent through the basket must be sufficient to disperse the tablet components and sweep them through the openings in the basket screen. If not, disintegration may be impeded and unusually slow dissolution of the active ingredient will result. Experiments conducted during these studies suggested that the basket of the USP–NF apparatus provided what might be described as a protective envelope around the tablet. This was indicated by the relatively minor effect on dissolution rates produced by changes in the stirring rate or the mesh size of the screen. In addition, installation of a 12.7-cm. (5-in.) stirring blade on the stirring shaft directly above the basket produced no appreciable effect on the dissolution rate, although a considerable increase in the agitation in the bulk dissolution medium was observed. Beyer and Smith (3) indicated that the degree of vibration in the USP–NF dissolution apparatus has a marked effect on the dissolution rate of tolbutamide tablets at rotation speeds below 150 r.p.m. They noted that vibration at lower stirring speeds caused particles of disintegrating tablets to escape from the basket, producing a higher rate of dissolution.

A configurational change in the standard USP–NF rotating-basket apparatus, which ensured better flow of the solvent through the basket, radically changed the results obtained with this device in the present study. The stainless steel stirring rod of the apparatus was bent at a 90° angle just above the basket to yield an L-shaped configuration (Fig. 1*a*). This modification gave a

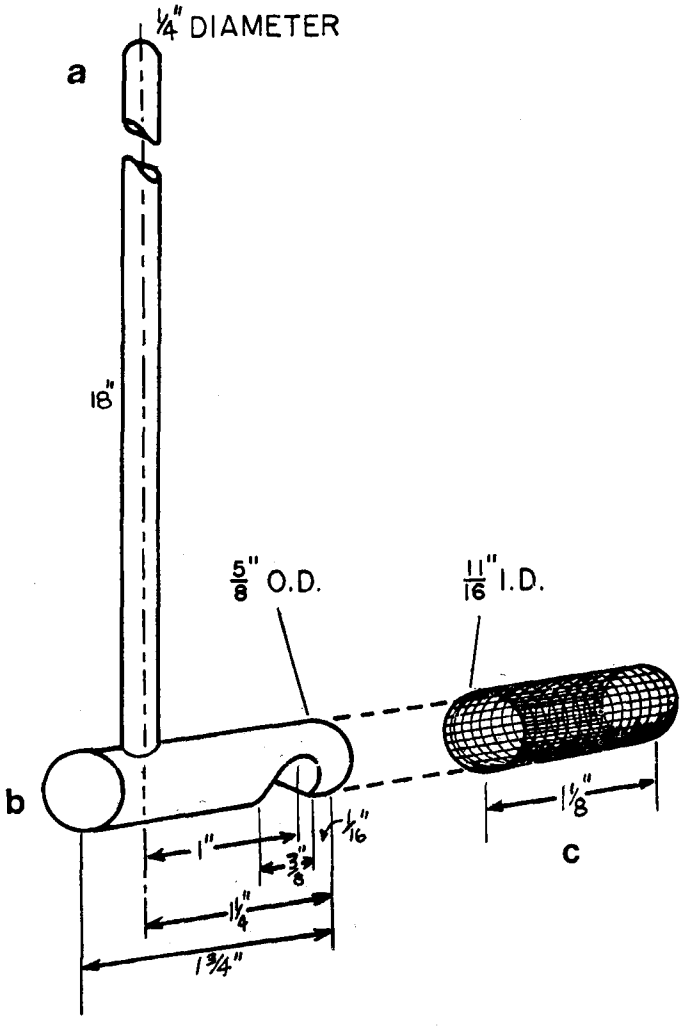

Figure 2—*Diagram of Teflon stirrer/holder. Key: a, stainless steel rod; b, Teflon tablet holder; and c, stainless steel screen.*

maximum stirring radius of 6.1 cm. (2.4 in.) for the tablet. The dissolution data for Batches A and B obtained with this bent basket are shown in Fig. 3*b*. With the bent basket the dissolution increased considerably over that obtained with the straight USP–NF rotating basket—from 30 to 55% for Batch B and from 75 to 95% for Batch A at 60 min. For Batch A the bent basket with 40-mesh screen gave a better dissolution rate than that with 24-mesh screen. The authors have no explanation for this[3]. There was essentially no difference for Batch B.

Dissolution data obtained using the L-shaped Teflon device are shown in Fig. 3*c*. With this device, as with the bent basket, complete disintegration of both batches occurred in approximately 30 min. Nonetheless, a distinct difference in dissolution rates between the two batches was found, as noted previously with both the bent and straight baskets. The data obtained with the Teflon device were lower—by 1–20%—than those obtained with the bent basket. This was undoubtedly due to the much greater stirring radius obtained with the bent basket, 6.1 cm. (2.4 in.) *versus* 2.54 cm. (1.0 in.). A disadvantage of the modified or bent USP–NF basket is that at low stirring speeds (<60 r.p.m.) a tablet tends to wander within the basket, so greater variability in the data may be obtained.

As recently noted by Mattok *et al.* (4), highly acidic media can be very detrimental to the stainless steel rotating-basket device. The new device described here can be constructed entirely of non-

[3] The reviewer observed in his laboratory, in a similar situation, "heavy excipients with the drug settling to the bottom of the vessel and remaining there undisturbed." In his opinion, the smaller mesh basket prevents this.

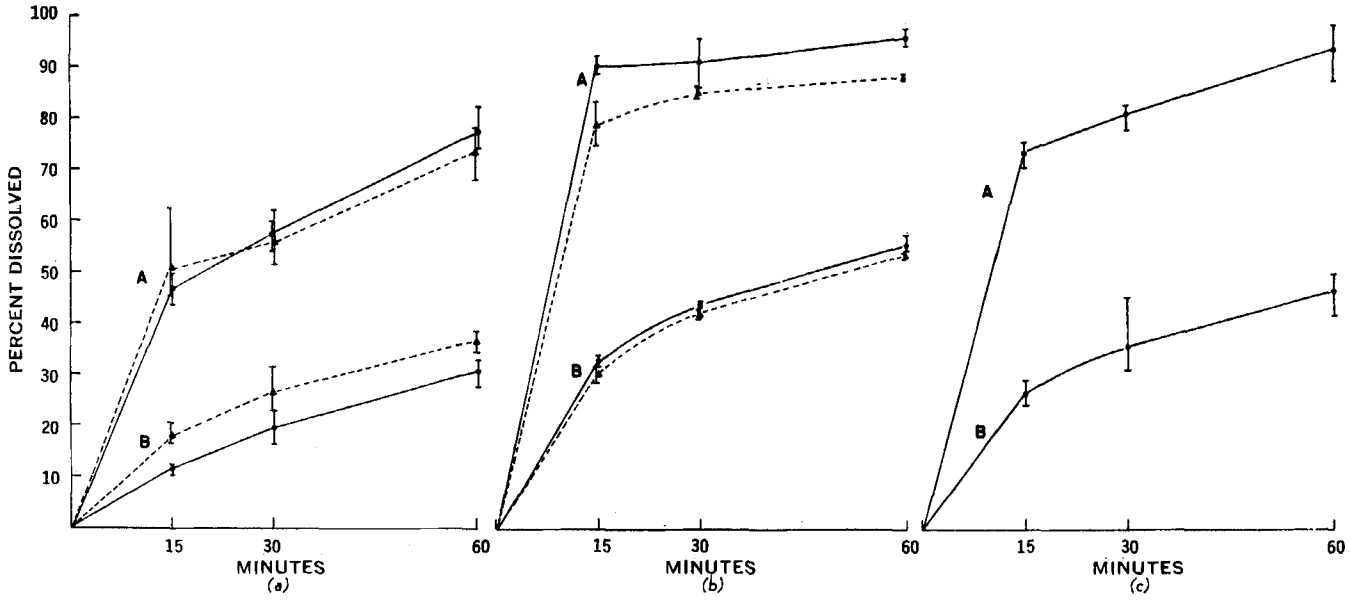

Figure 3—*Dissolution profiles of chlormadinone acetate (0.5-mg.) tablets (Batches A and B) determined at 80 r.p.m. Key:* (a), *USP–NF rotating basket;* (b), *bent basket (modified USP–NF basket);* (c), *Teflon device;* ——, *40-mesh screen; and* - - -, *24-mesh screen.*

corroding materials: a glass rod, a Teflon tablet holder, and nylon screening.

Although the Teflon device was not originally designed for capsule studies, it will accommodate up to a number 3 hard gelatin capsule. For larger sizes, the cavity of the device can be appropriately enlarged.

The Teflon holder/stirrer described in this report has the following features:

1. The tablet is held at a fixed distance from the center of rotation regardless of the stirring speed.
2. The configuration of the device ensures that particles of the disintegrating tablet are swept from the tablet holder into the bulk dissolution medium. The holder also functions effectively as a stirring blade to provide sufficient agitation to keep tablet particles dispersed in the dissolution medium.
3. The stainless steel components can be replaced with glass and nylon for use in highly acidic media. In addition, the device is simple in design and inexpensive to construct.

As a final point, it must be emphasized that *in vitro* dissolution rate differences observed in the *in vitro* test are of limited value in the estimation of relative bioavailability. Such conclusions can be arrived at only following appropriate *in vivo* experiments.

REFERENCES

(1) "The U. S. Pharmacopeia," 18th rev., Mack Publishing Co., Easton, Pa., 1970, p. 934.

(2) *Ibid.*, p. 530.

(3) W. F. Beyer and D. L. Smith, *J. Pharm. Sci.*, **60**, 496(1971).

(4) G. L. Mattok, I. J. McGilveray, and R. D. Hossie, *ibid.*, **61**, 460(1972).

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