DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 20(10), 1753-1760 (1994)

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

DESIGN AND EVALUATION OF A ROTATING BASKET-PADDLE DISSOLUTION APPARATUS

Tarun K. Mandal[1], Charles S. Chiao[2], and Louis N. Ace
School of Pharmacy, Northeast Louisiana University, Monroe, LA 71209 (U.S.A).
[1] Present address: College of Pharmacy, Xavier University of Louisiana, New Orleans, LA 70125 (U.S.A).
[2] Present address: Columbia Research Laboratories, Madison, WI 53713 (U.S.A).

ABSTRACT

The rotating basket-paddle dissolution apparatus is a combination of the USP/NF rotating basket and rotating paddle. A comparative dissolution study was performed utilizing this new apparatus and the two USP/NF apparatus at various stirring speeds using non-disintegrating oxalic acid tablets and disintegrating aspirin tablets. The amount of drug released using the new apparatus was significantly higher than the rotating basket but significantly lower than the rotating paddle at each of the stirring speeds studied. The results obtained using this new apparatus were highly reproducible compared to the USP/NF apparatus.

INTRODUCTION

Reports on several *in vitro* dissolution apparatus, including the two official USP/NF methods (1), have appeared in the literature over the years. However, none have been accepted as universal because each apparatus is useful only for the dissolution testing of a specific group of drugs or dosage forms. The two official apparatus described in the USP/NF XXII, the rotating basket and the rotating paddle, produce different hydrodynamic conditions (2). The basic design of the rotating basket makes it suitable for dissolution testing of solid dosage forms containing poorly water soluble drugs, where dissolution is the rate limiting step (3). The rotating paddle provides greater agitation than the rotating basket (4,5) and makes it a suitable means of dissolution testing for solid dosage forms where disintegration is the key factor (3).

Recently, considerable attention has focused on the development of a single dissolution test apparatus to solve the problem of switching from one apparatus to another for routine dissolution testing of various drug products. For this project, a rotating basket-paddle dissolution apparatus was designed, constructed, and compared to the rotating basket and rotating paddle apparatus. Variation in percent dissolved and dissolution halftime, $DT_{50\%}$ (time required for 50% of the drug to dissolve) was compared.

Copyright © 1994 by Marcel Dekker, Inc.

RIGHTSLINK

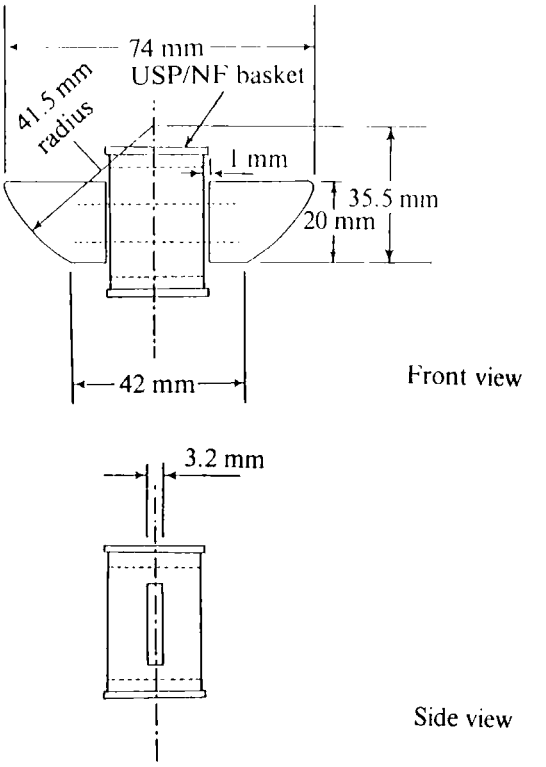

FIGURE 1

Diagram of the rotating basket-paddle dissolution apparatus.

MATERIALS AND METHODS

Apparatus Description

This rotating basket-paddle apparatus is essentially a combination of the USP/NF rotating basket and rotating paddle apparatus. Two small pieces of Teflon, which are nonreactive in both acidic and alkaline solutions, were used in the construction of the paddle. The paddle was then attached to the outer surface of a USP/NF basket using a stiff nichrome wire measuring 0.5 mm in diameter (Figure 1). The same motor shaft as used for the rotating basket method was fitted to hold the apparatus. For dissolution testing, the dosage unit is placed inside the basket of the apparatus.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

RIGHTSLINK

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

Model Dosage Forms

(1) Nondisintegrating oxalic acid dihydrate (J. T. Baker Chemical Co., NJ) tablets were used to compare hydrodynamic flow patterns. The tablets were prepared at 3000 lb force on a hydraulic press (Carver, Inc., NJ) using a flat-faced tablet punch and die with a flat steel plate as the lower retainer. The tablets weighed 120 mg, were 0.66 cm in diameter and 0.27 cm in thickness.

(2) The following dosage forms of aspirin were purchased from retail outlets:

(i) rapidly disintegrating sustained release tablets each containing 650 mg aspirin as microencapsulated particles (Glenbrook Laboratories, NY).

(ii) rapidly disintegrating buffered tablets each containing 325 mg aspirin and alkaline additives (Bristol-Myers, NY).

(iii) rapidly disintegrating plain tablets each containing 325 mg aspirin (Glenbrook Laboratories, NY).

Dissolution Rate Determination

In vitro dissolution rates were determined at 37^0 C by the rotating basket, the rotating paddle, and the rotating basket-paddle dissolution apparatus. The dissolution medium consisted of (i) 900 ml of 0.1 N HCl for oxalic acid tablets and (ii) 900 ml of 0.05 M acetate buffer for aspirin tablets. A Vankel dissolution apparatus utilizing six vessels was used for this study. The distance between the inside bottom of the vessels and the lower surface of the modified apparatus was maintained at 25 ± 2 mm during the test. After the introduction of the dosage form, one milliliter samples were collected at various times by means of a filter pipet.

Analysis

The amount of drug dissolved at any time t, reported as a cumulative percent dissolved, was determined at (i) 255 nm for oxalic acid and (ii) 265 nm for aspirin using a Response spectrophotometer (Gilford Systems, OH). Each dissolution profile is the average of six tablets.

RESULTS AND DISCUSSION

Nondisintegrating Tablets

The average cumulative percent of oxalic acid dissolved at different stirring speeds as a function of time are listed in Table 1. The data listed in this table indicate that the amount of drug released using the modified apparatus was significantly higher than the rotating basket but significantly lower than the rotating paddle at each of the rotating speeds studied (Table 1).

RIGHTSLINK

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

TABLE 1

Average Cumulative Percent of Oxalic Acid Dissolved at Various Sampling Times for the Different Apparatus at 50 and 100 rpm.

Stirring speed, rpm	Sampling time, min	Average percent dissolved			SNK[b] group
		rotating basket (A)	rotating paddle (B)	rotating basket-paddle (C)	
50	2	49.99 (2.68)[a]	58.53 (2.02)	55.41 (1.79)	A < C < B
50	3	63.97 (3.91)	74.65 (4.74)	68.11 (0.87)	A < C < B
50	4	72.89 (2.88)	86.21 (4.28)	79.07 (1.75)	A < C < B
100	2	65.50 (3.36)	81.16 (3.95)	75.45 (1.76)	A < C < B
100	3	80.07 (2.24)	93.13 (3.24)	85.16 (1.59)	A < C < B
100	4	90.38 (1.76)	98.44 (1.73)	93.23 (1.21)	A < C < B

[a] Coefficient of variation (CV%), n = 6
[b] Student-Newman-Keul's multiple range test ($\alpha = 0.05$)

The differences in drug release in the rotating basket-paddle apparatus and the rotating basket and rotating paddle apparatus were probably due to the differences in the basic design of these three apparatus. The paddle attached to the outer surface of the basket in the rotating basket-paddle apparatus makes it a better stirring device which leads to faster dissolution rates when compared to the rotating basket. However, the basket used in the rotating basket-paddle apparatus acts as a sample holder confining the dosage form in a relatively smooth flow of dissolution medium with minimal mechanical abrasion which leads to slower dissolution rates when compared to the rotating paddle. In order to evaluate the reproducibility of the different dissolution testing methods, six runs of each method were performed. From each series of six runs the coefficient of variation

RIGHTSLINK

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

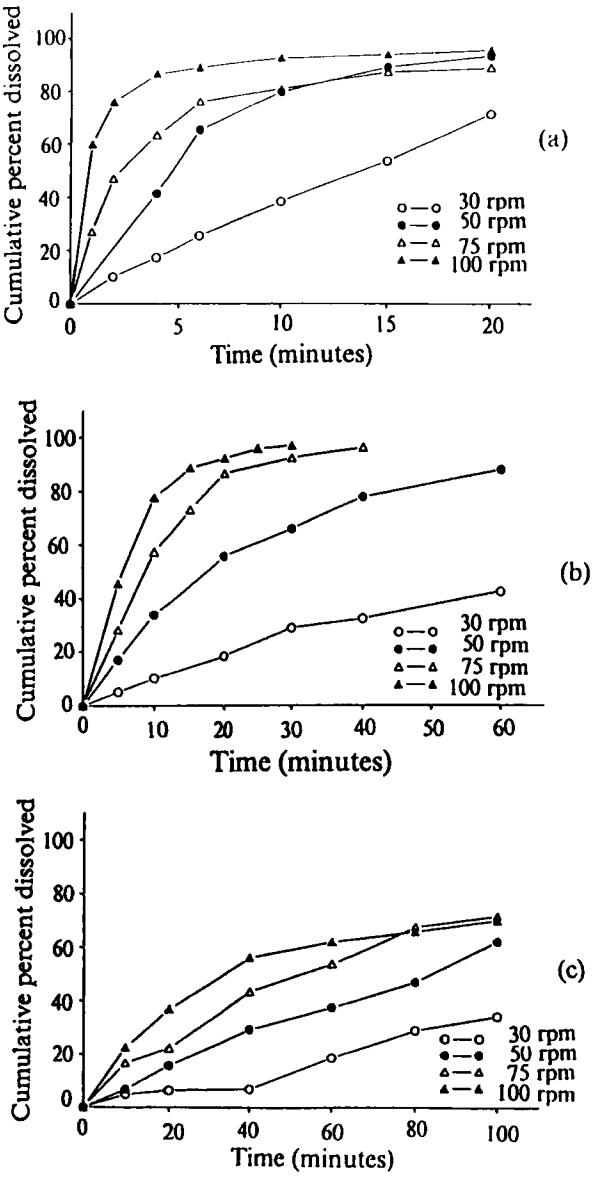

FIGURE 2

Dissolution profiles for aspirin tablets using the rotating basket-paddle apparatus with varying stirring speeds. (a) buffered aspirin tablets, (b) plain aspirin tablets, and (c) sustained release aspirin tablets. Each point represents the mean observation (n = 6).

RIGHTSLINK

TABLE 2

Average Aspirin Dissolution Halftimes for Commercial Dosage Forms Using the Rotating Basket-Paddle Apparatus and USP/NF Apparatus at the Same Stirring Speed.

Dosage forms	Dissolution halftime, $DT_{50\%}$, min			Results of t-test	Significance level
	rotating basket (A)	rotating paddle (B)	rotating basket-paddle (C)		
Buffered tablets		0.68 (41.19)[a]	2.51 (26.10)	C > B	$p < 0.0001$
Plain tablets	20.34 (8.51)		17.17 (6.29)	C < A	$p < 0.0100$
Sustained release tablets	37.62 (11.38)		32.85 (7.23)	C < A	$p < 0.0500$

[a] Coefficient of variation (CV%), n = 6

of the average percent dissolved was calculated at each of the sampling times. It is apparent from the coefficient of variations listed in Table 1 that the dissolution profiles obtained with the rotating basket-paddle apparatus are generally more reproducible than the rotating basket as well as rotating paddle apparatus.

Disintegrating Tablets

The dissolution rates of various disintegrating tablets of aspirin at different stirring speeds were compared by using the dissolution profiles and dissolution halftimes, $DT_{50\%}$. Dissolution profiles are shown in Figures 2a-c. Each of the dosage forms generated curves with one common character: the dissolution rate increased with increased stirring speed from 30 to 100 rpm. This observation indicates that the dissolution rates obtained using the rotating basket-paddle apparatus were sensitive to stirring speed.

Plain, buffered, and sustained release tablets of aspirin differ markedly in the mechanism involved for release of drug in the dissolution medium (6-9). Therefore, the USP/NF XXII formulary requires two different apparatus for the dissolution testing of aspirin: the rotating basket for plain and sustained release aspirin tablets,

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

RIGHTSLINK

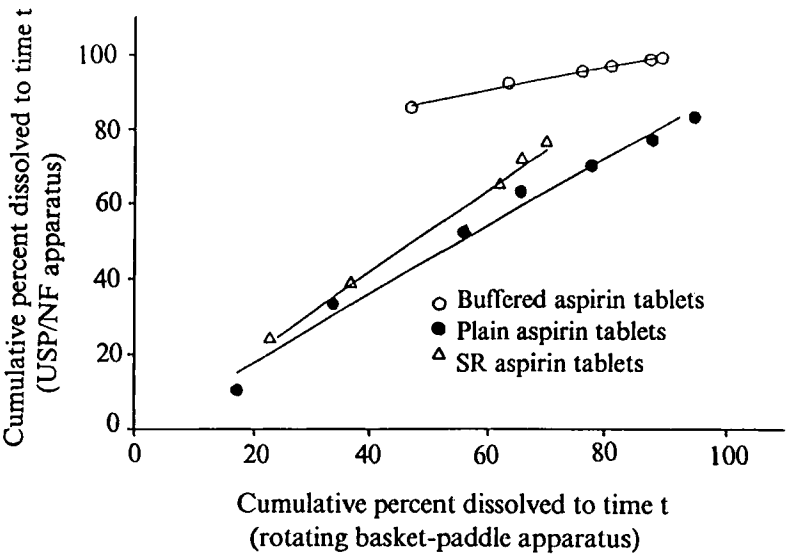

FIGURE 3

Relationship between percent dissolved, to the same time t, from various dosage forms of aspirin using the rotating basket-paddle apparatus and respective USP/NF apparatus. Each point represents the mean observation (n = 6).

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

and the rotating paddle for buffered aspirin tablets (1). The cumulative percent aspirin dissolved from various dosage forms over time using the rotating basket-paddle and the respective USP/NF apparatus was compared. The dissolution halftimes were calculated from the cumulative percent drug dissolved over time. Statistical comparisons were performed on dissolution halftimes using the independent t-test (Table 2). These comparisons indicate that the rotating basket-paddle apparatus produced significantly faster dissolution rates than the rotating basket apparatus and significantly slower dissolution rates than the rotating paddle apparatus. These observations affirm the results obtained with the nondisintegrating oxalic acid tablets (Table 1). The same rank order among these three dissolution apparatus indicates that the presence of various tablet additives does not affect the relative agitation intensities generated by different dissolution apparatus. Also, the coefficient of variation associated with the dissolution testing using different apparatus indicates that the rotating basket-paddle apparatus is more reproducible than the existing USP/NF methods.

Despite the significant differences found in dissolution rates between the rotating basket-paddle and respective USP/NF apparatus, excellent correlations, $r > 0.99$ ($p < 0.0001$), were observed between these apparatus in determining the cumulative percent of aspirin dissolved at various sampling times (Figure 3). These excellent

RIGHTSLINK

correlations suggest that the rotating basket-paddle apparatus can be used for the dissolution testing of plain, buffered, and sustained release aspirin tablets. As a result, instead of using two different official apparatus, the single rotating basket-paddle apparatus can be used for the dissolution testing of all three dosage forms of aspirin.

In conclusion, the rotating basket-paddle apparatus, which was developed during this investigation allows evaluation of dissolution from both nondisintegrating and disintegrating tablets with reproducible results. The apparatus is simple to use and inexpensive to construct. The use of this apparatus will alleviate the problem of switching from one apparatus to another during routine dissolution studies of aspirin from plain, buffered, and sustained release dosage forms.

REFERENCES

1. The United States Pharmacopoeia XXII/The National Formulary XVII. Maryland: The United States Pharmacopeial Convention, Inc (1990).

2. A.K. Singla and D.K. Mediratta, Drug Dev. Ind. Pharm., 14, 721 (1988).

3. J. Tingstad, E.Gropper, L. Lachman, and E.Shami, J. Pharm. Sci., 62, 293 (1973).

4. G.K. Bolhuis, C.F. Lerk, and K. Zuurman, Pharm. Weekbl., 108, 49 (1973).

5. E.A. Hardwidge, A.C. Sarapu, and W.C. Laughlin, J. Pharm. Sci., 67, 1732 (1978)

6. H. Weintrub and M. Gibaldi, J. Pharm. Sci., 59, 1792 (1970).

7. G. Levy, J.R. Leonards and J.A. Procknal, J. Pharm. Sci., 54, 1719 (1965).

8. W.L. Chiou and I. Onyemelukwe, J. Clin. Pharmacol., 14, 597 (1974).

9. W. Juhl and R.D. Kirchhoefer, J. Pharm. Sci., 69, 967 (1980).

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/29/12
For personal use only.

RIGHTSLINK