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# Design and evaluation of a rotating filter–magnetic basket apparatus: tablet and basket position

Boonpuck Vongvirat **, Stephen A. Howard *, John W. Mauger and Louis A. Luzzi ***

*School of Pharmacy, West Virginia University, Morgantown, WV 26506; *** College of Pharmacy, University of Rhode Island, Kingston, RI 02881 (U.S.A.); and ** 629 New Road, Samyek, Bangkok 1 (Thailand)*

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## Summary

The authors have designed a dissolution device which combines the properties of a rotating filter device developed by Shah and a magnetic basket designed by Shepard et al. The effects of stirring, tablet and basket placement were investigated. Visualization of flow and dissolution patterns was possible by testing non-disintegrating salicylic acid tablets containing 3% phenolphthalein in 0.1 N sodium hydroxide solution. Dissolution experiments were conducted on non-disintegrating salicylic acid in pH 7.4 U.S.P. phosphate buffer at 37°C. For the tablet placement experiments one tablet face and the tablet land was coated so that only a single tablet face was available for dissolution. The data for the same size tablets placed at the side of the bottom and at the center of the bottom of the dissolution fluid container indicated the importance of exact placement of a tablet in a dissolution fluid container. The differences in face position of the tablet either with or without a magnetic basket present indicates the importance of face position which must be accounted for especially in the testing of double-layer sustained release products. Through the dissolution data and the visualization studies the authors have characterized the hydrodynamics of this device.

## Introduction

Many dissolution rate testing apparati for oral dosage forms have been developed and reported (Hersey, 1969; Wagner, 1971; Cooper and Rees, 1972; Pernarowski,

* To whom reprint requests should be addressed.

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1974) during the last two decades. To be useful for research, development and quality control purposes, an apparatus should meet certain criteria. The apparatus should be economical, relatively simple, convenient to operate, flexible for use under a variety of test conditions, capable of being fashioned from standard laboratory equipment or modified from an available apparatus. It should be reliable, able to give reproducible results and able to be standarized by simple methods when its geometry is different from others. It was hoped that the construction of a rotating filter–magnetic basket would provide such a device. This apparatus combines the simplicity of the magnetic basket (Sheperd et al., 1972) and the advantage of the non-clogging rotating filter (Shah et al., 1973; Shah and Ochs, 1974) which makes it more useful than the magnetic basket apparatus, more economical and more easily constructed from standard laboratory equipment.

The magnetic basket dissolution apparatus was introduced by Shepherd et al. (1972). The magnetic basket serves as a stationary sample container. The basket is supported by a stiff nichrome wire above the internal magnet and held at the center of the bottom of a dissolution container by an external magnet, attached at the outside of the container by resin glue. This apparatus is simple and easy to construct either by altering the official apparatus (Shah et al., 1972, 1973; Shah and Ochs, 1974; Grady, U.S.P.) or from ordinary laboratory equipment.

The rotating filter–stationary basket apparatus was introduced by Shah et al. (1973, 1974) and utilized the rotating filter device which provides a most promising, non-clogging micropourous, and automated sampling method. This apparatus has been studied and evaluated by the U.S.P.–A.Ph.A. Committee on Dissolution Methodology and has been recognized by the F.D.A. as a dissolution testing device (Cabara and Prasad, 1976).

The authors have modified the device to use a motor-driven rotating filter instead of a magnetic-driven rotating filter. This modification provides for easier incorporation with the U.S.P. apparatus. Either a jacketed flask or a standard water bath may be used to control temperature.

The magnetic basket (Shepherd et al., 1972; Needham et al., 1973, 1974; Luzzi and Needham, 1973; Needham and Luzzi, 1974) was chosen in order to ensure a normally required reproducible placement of the sample in its dissolution media and in order to minimize the effect of non-uniform distribution or accumulation of disintegrated particles about a vortex at the center bottom of a dissolution container.

The purpose of this study was to hydrodynamically characterize this potentially useful device. Khwangsopha (1978) has shown that tablet position and basket type and position have a marked effect on dissolution rate in the rotating filter device. It was the purpose of this study to quantify the effects of these variables in the magnetic basket device.

## Materials and methods

Dissolution rates of non-disintegrating salicylic acid [1] tablets were employed for comparison, evaluation and hydrodynamic studies. The dissolution rates were determined by using a rotating filter–magnetic basket apparatus.

[1] Fisher Scientific, Fair Lawn, NJ.

*Apparatus description*

Basic features of the rotating filter–magnetic basket apparatus (Fig. 1) are dissolution fluid container flask, a magnetic basket with inner and outer magnets and a motor-driven rotating filter assembly [2]. The broken lines in Fig. 1 represent the set-up for automated dissolution rate determination. The description of individual parts of the apparatus follows.

*Fluid container flask.*

Although an ordinary beaker or an official vessel (U.S.P., 1970, 1975; N.F., 1970, 1975) can be employed, a jacketed flask [3] suitable for holding up to 1.5 liters of dissolution fluid was selected for visualization purposes. Liquid was pumped from an external constant temperature regulatory bath [4] through the external cavity of the flask to maintain the temperature at 37 ± 0.5°C.

*Sample basket.*

The magnetic basket was constructed of 8-mesh screen in a cylindrical shape, equipped with an 8-mesh hinged door opening at one end of the cylinder. The basket was held in place by a stiff nichrome wire above the internal magnet from the bottom of the cage. Exact placement of the basket was ensured by attaching an outer magnet to the center of the outer bottom of the beaker.

*Rotating filter assembly.*

The rotating filter assembly (Fig. 2) provided variable intensity mild laminar-like liquid agitation and it also functioned as a microporous non-clogging filter to permit either intermittent or efficient continuous filtration of the dissolution filter samples during the dissolution process (Shah et al., 1973). The upper head of the assembly was connected to a stainless steel shaft that was connected to a variable constant speed motor [5] and the lower head was connected with the U-shaped glass pilot tube that was attached to a stainless steel pilot tube by a polyethylene tube. The upper and lower heads were synthetic rubber and the filter was 0.5 μm porosity sintered stainless steel filter with polyethylene gaskets at both ends. The spring action dynamic seal slid over the U-shaped glass pilot tube into the lower filter head and prevented passage of liquid through the space between the pilot tube and the lower filter head. The dissolution fluid, upon filtration through the cylindrical filter flowed through a hole between the core of filter assembly and the filter head, then entered into the U-shaped glass pilot tube, and then went to the stainless steel pilot tube. Fluid samples can be withdrawn continuously or intermittently from the upper end of the stainless steel pilot tube.

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[2] The VirTis Company, Gardiner, NY 12525.

[3] The VirTis Company, Gardiner, NY 12525.

[4] Forma-Temp Jr. Bath and Circulator, forma Scientific, Marietta, OH.

[5] Electronic Controller GT Laboratory Mixer, Gerald K. Heller, Las Vegas, NV.

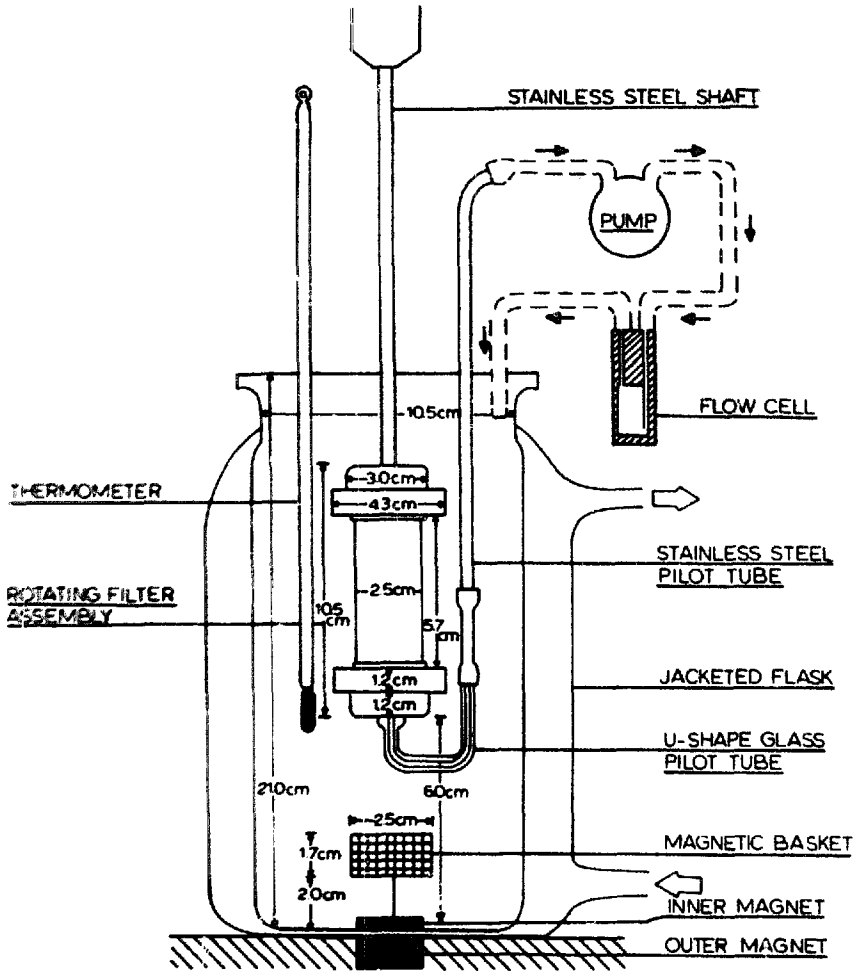


Fig. 1. Schematic diagram of the rotating filter-magnetic basket apparatus. Broken line represents the automated spectrophotometric analysis.

## *Materials*

### *Model drug tablets.*

Non-disintegrating salicylic acid tablets were chosen as the model drug tablets for dissolution rate testing.

### *Preparation of tablets.*

Tablets were prepared with the following dimensions: 0.957 cm diameter, 0.305 cm thickness and 300 mg weight. They were prepared by directly compressing the weighed ground salicylic acid powder in a die using flat-face punches on a hydraulic press [6] at a pressure of 50,000 lbs./in. $^2$. After removal from the die, the tablets were coated on their sides for up-down exposure position and in some cases were further

[6] Carver Laboratory Press Model K, Fred S. Carver, Hydraulic Equipment, 1 Chatham Road, Summit, NJ.

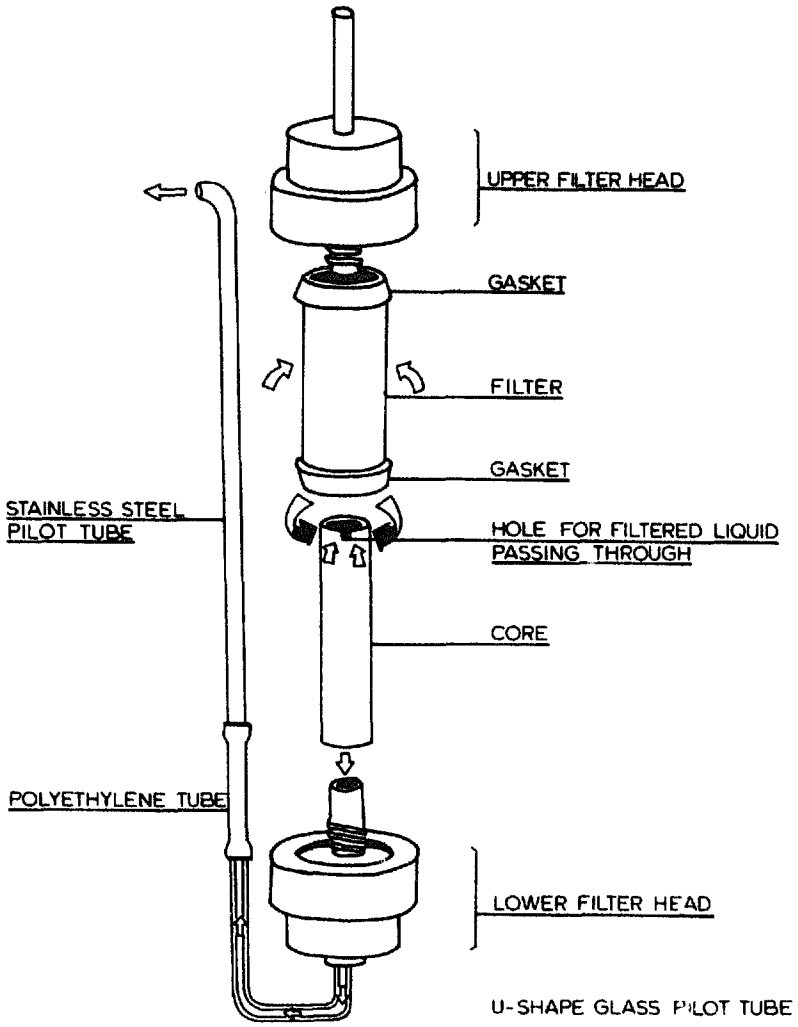


Fig. 2. Rotating filter assembly (dismantled). Arrows show liquid flow.

coated on one face for either face-up or face-down exposure position, as shown in Fig. 3d, e and f. Epoxy resin was selected as the coating material because of its toughness, non-reactive properties and imperviousness to the dissolution medium.

*Dissolution media.*

The standard U.S.P. phosphate buffer solution pH 7.4 was employed for the comparison and evaluation studies.

*Procedure*

The experiment conditions relating to tablet placement within the dissolution container are presented in Fig. 3. The studies were conducted under 2 different stirring conditions (100 and 300 rpm) and 3 different exposure positions of tablets (Fig. 3; face-up (d), up-down (e), and face-down (f) exposure positions). As shown in Fig. 3, the face-up exposure position indicates that the coated surface points to the bottom of the dissolution fluid container and the face-down exposure position

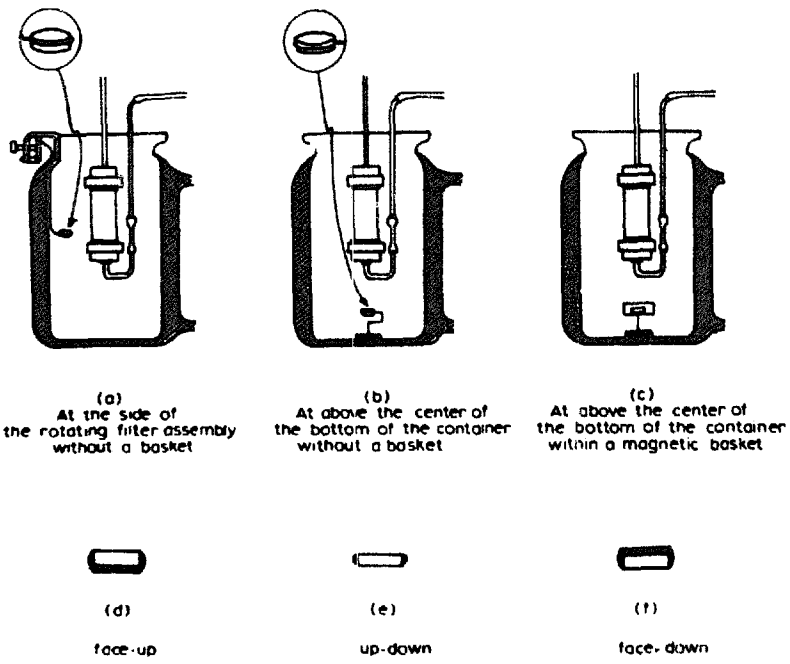


Fig. 3. Diagram of comparison and evaluation study conditions.

indicates the converse. The up-down exposure position indicates that both faces were exposed and only the circular edge was coated. These were studies with 3.2.2. = 18 experimental conditions as in Table 1 and each condition required 3 replicates.

Each experiment was conducted with a salicylic acid tablet than had 0.957 cm diameter and 0.305 cm thickness. The tablet was supported by a nichrome wire ring with ethylcellulose glue (ethylcellulose in chloroform) in 1400 ml standard U.S.P. phosphate buffer, pH 7.4 at $37 \pm 0.5$°C. The spectrophotometrical assay was conducted continuously at 231 nm by pumping dissolution sample with a peristaltic pump [7] through a flow cell [8] and a spectrophotometer [9]. The stirring speeds were calibrated and monitored from time to time by a strobe lamp [10].

In addition to the comparison and evaluation studies, extended experiments were conducted using the face-up tablets at the side of the rotating filter assembly without a basket. Stirring speeds of the rotating filter assembly used were 100, 200, 300, 400 and 500 r.p.m.

## Results and discussion

The importance of relatively mild agitation conditions for the determination of dissolution rates to reflect in vivo conditions was emphasized by Levy (1963).

[7] Cole Palmer Instruments, Chicago, IL.
[8] Micro Flow Cell, Fisher Scientific, Fair Lawn, NJ.
[9] Cary Model 118, Varian Instrument Division, 611 Hansen Way, Palo Alto, CA 94303.
[10] Glass PS 22 Photo Stimulator, Glass Medical Instruments, Quincy MA.

TABLE I

Experimental Design for the Comparison and Evaluation of the Dissolution Rate Studies

| Tablet position | Exposure position | | |
|---|---|---|---|
| | Face-up | Face-down | Up-down |
| At the side of the rotating filter assembly without a basket | 100 rpm<br>300 rpm | 100 rpm<br>300 rpm | 100 rpm<br>300 rpm |
| At above the center of the bottom of the container without a basket | 100 rpm<br>300 rpm | 100 rpm<br>300 rpm | 100 rpm<br>300 rpm |
| At above the center of the bottom of the container within a magnetic basket | 100 rpm<br>300 rpm | 100 rpm<br>300 rpm | 100 rpm<br>300 rpm |

Furthermore, liquid agitation conditions should be reproducible upon repeated tests, and the hydrodynamics of the system should correlate with hydrodynamic theory that provides for standardization among dimensionally different apparati. A rotating filter type assembly seems to meet this criteria (Shah et al., 1973) and provides mild laminar-like reproducible liquid stirring.

Since the disintegration time is an important factor in a dissolution test, excessive mechanical impact should be avoided during the disintegration process. A basket should be placed at the position that has less shearing force and provides a uniform distribution of disintegrating particles while the stirring speed is high enough to ensure reproducible results and a well-mixed process. A preliminary question of interest was related to the placement of the basket in the dissolution vessel which would provide these characteristics.

An analytical methodology was developed by comparing dissolution rates of non-disintegrating tablets between the position at the side of a rotating filter assembly and at the center of the bottom of a dissolution fluid container, and between the position at the center of the bottom of a dissolution fluid container with and without a magnetic basket.

Typical dissolution data shown in Fig. 4 demonstrate dissolution profiles of salicylic and tablets at 3 different exposure positions. Similar data was obtained for each of the experimental conditions described in the experimental section. The x-axis in this plot represents time in minutes. Each point is the average of 3 replicates and the associated standard deviation is indicated by the vertical line. Each line is the least-squares line and a value of slope or a dissolution rate is shown above the graph. In all cases, linearity was demonstrated with a correlation coefficient above 0.99. This indicates that the accuracy of an employed analytical method was high and variation of dissolution rate of each tablet from time to time was small. All average dissolution rates or slopes of least-square lines and standard deviations are shown in Tables 2 and 3.

In all cases, as expected, the dissolution rates of an up-down exposure position were the most rapid since the most exposure area was available. Ideally the dissolution rate of an up-down position should be approximately equal to the summation of dissolution rates of the face-up and face-down exposure positions, but

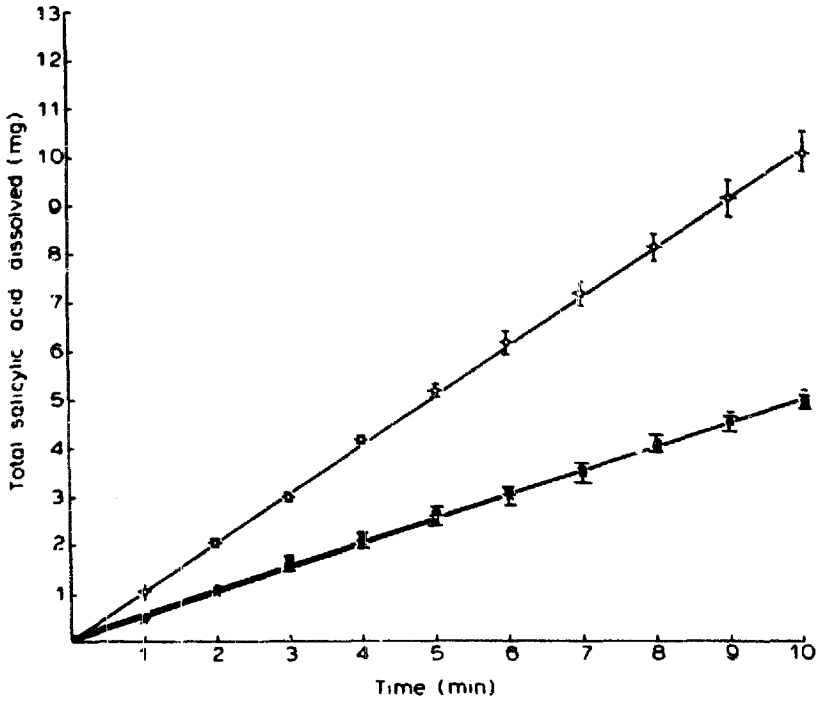


Fig. 4. Salicylic acid dissolution profiles of 3 exposure positions at 4 cm from the center of a rotating filter assembly without a basket at 100 rpm. Symbols relate to exposure position (followed by dissolution rate in mg/min)—●, faced-up (0.482±0.021); ★, faced-down (0.489±0.025); -○-, up-down (0.999±0.051).

many of our experimental data were found to be somewhat less than expected. One possible explanation is that the dissolution process on one exposure surface interfered with the dissolution on the other exposure surface due to axial flow (this possibility will be explored later when visualization is discussed).

TABLE 2

Means of Dissolution Rates of Salicylic Acid Tablets from 3 Replicates in Various Exposure Positions and Conditions at 100 rpm

| Condition | Exposure position | | |
|---|---|---|---|
| | Face-up | Face-down | Up-down |
| At 4 cm from the center of a rotating filter assembly without a basket | 0.482 (±0.021) | 0.489 (±0.025) | 0.999 (±0.051) |
| At 2.5 cm above the center of the bottom of a container without a basket | 0.301 (±0.005) | 0.415 (±0.085) | 0.774 (±0.028) |
| At 2.5 cm above the center of the bottom of a container within a magnetic basket | 0.232 (±0.045) | 0.403 (±0.117) | 0.509 (±0.097) |

TABLE 3

Means of Dissolution Rates of Salicylic Acid Tablets from 3 Replicates in Various Exposure Positions and Conditions at 300 rpm

| Condition | Exposure position | | |
|---|---|---|---|
| | Face-up | Face-down | Up-down |
| At 4 cm from the center of a rotating filter assembly without a basket | 0.691 (±0.008) | 0.735 (±0.001) | 1.232 (±0.042) |
| At 2.5 cm above the center of the bottom of a container without a basket | 0.523 (±0.032) | 0.514 (±0.025) | 0.872 (±0.035) |
| At 2.5 cm above the center of the bottom of a container within a magnetic basket | 0.443 (±0.050) | 0.455 (±0.038) | 0.709 (±0.006) |

Experimental data from Tables 2 and 3 clearly show that under the same conditions, dissolution rates for a tablet at the side of a rotating filter assembly is the highest and dissolution rates for a tablet within a magnetic basket is the lowest. As expected, dissolution rates at 100 r.p.m. are lower than dissolution rates at 300 rpm.

The data presented in Tables 2 and 3 can be more easily understood and interpreted in combination with visualization studies. By using salicylic acid tablets containing 3% phenophthalein and 0.1 N sodium hydroxide solution, it was observed that visualized boundary layers of both face-up and face-down exposure positions of a tablet positioned 4 cm from the center of a rotating filter assembly moved horizontally at a rotating speed of 100 rpm. At 300 rpm it moved downward from horizontal by approximately 10° and turned back to move horizontally at 500 rpm. This effect is caused by a change of the axial flow region as fluid flowed radially outward from the rotating filter assembly, axially downward near the wall of the dissolution fluid container, and axially upward over the entire region below the rotating filter assembly. These visualization results correlate well with the noticeable difference between dissolution rates of the face-up and face-down exposure positions at 300 rpm as shown in Fig. 5. A final point to be made is that the dissolution rates for the side position are essentially equal for the face-up and face-down exposure position at 100 rpm but diverse at 300 rpm suggesting the possibility of changing hydrodynamic conditions with increasing stirring rate.

For a tablet positioned at the center of the bottom, the natural convection due to a difference in density of a concentration layer, played an important role that was observed via visualization studies. Without stirring, the concentrated fluid from a tablet moved freely downward to the bottom of the dissolution container. When the rotating filter assembly began to rotate, the concentrated fluid started to flow radially inward and axially upwards. As the stirring speed increased, one could

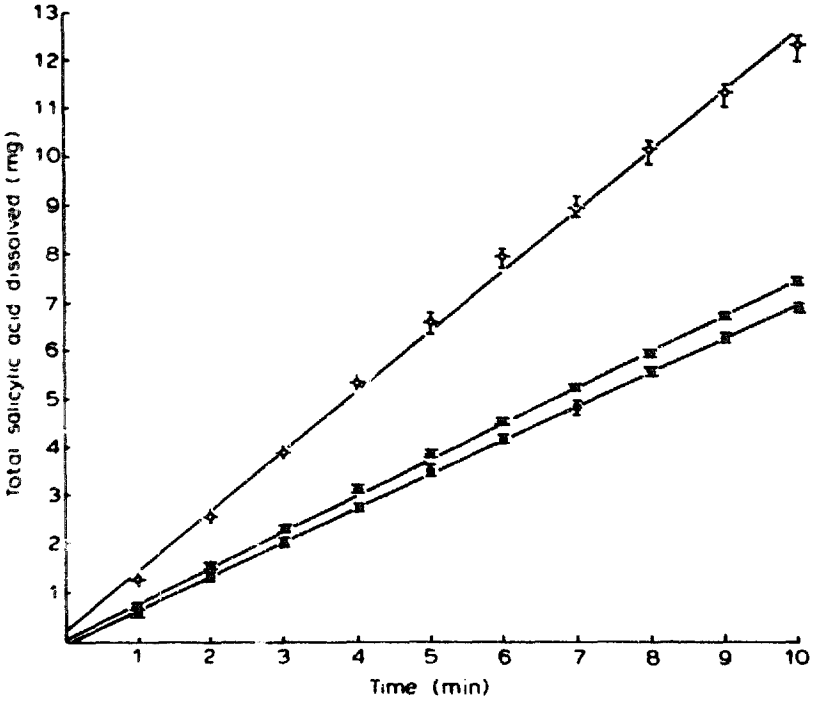


Fig. 5. Salicylic acid dissolution profiles of 3 exposure positions at 4 cm from the center of a rotating filter assembly without a basket at 300 rpm. Symbols relate to exposure position (followed by dissolution rate in mg/min)—●, faced-up (0.691 ± 0.008); ★, faced-down (0.735 ± 0.001); -O-, up-down (1.232 ± 0.042).

visualize a competitive effect between natural connection and an axial upflow. At 100 rpm, the concentrated dissolution fluid still fell downward from a tablet to some extent by natural convection before moving upward by stirring-induced axial upflow. The data in Fig. 6 show that the face-up and face-down dissolution rates are considerably different and that the variation in the data points, as shown by the associated standard deviation for each data point and the dissolution rate, is large for the face-down position. At 300 rpm, natural convection was no longer observed and a visualized boundary layer for a tablet was seen to be spirally moving upward. The dissolution data shown in Table 3 show that the dissolution rates are equivalent and the associated standard deviation for the face-down position is approximately equal to that for the face-up position. For the stirring rates studied, it seems that increasing stirring rates stabilize the system insofar as providing for equivalent dissolution rates for the face-up and face-down positions and decreasing dissolution variability for the face-down position.

A similar effect was observed from a tablet within a basket, but at 100 rpm the concentrated dissolution fluid seemed to remain for a moment before being transported out. This resulted in a noticeable difference between the dissolution rates for the face-up and face-down position as well as increased variability in the dissolution rate at the face-down position. Increasing the stirring speed from 100 rpm to 300 rpm provided for hydrodynamic conditions which maintained equivalent dissolution rates for the face-up and face-down positions. Increasing the stirring also decreased the variability associated with the dissolution rate for the face-down position.

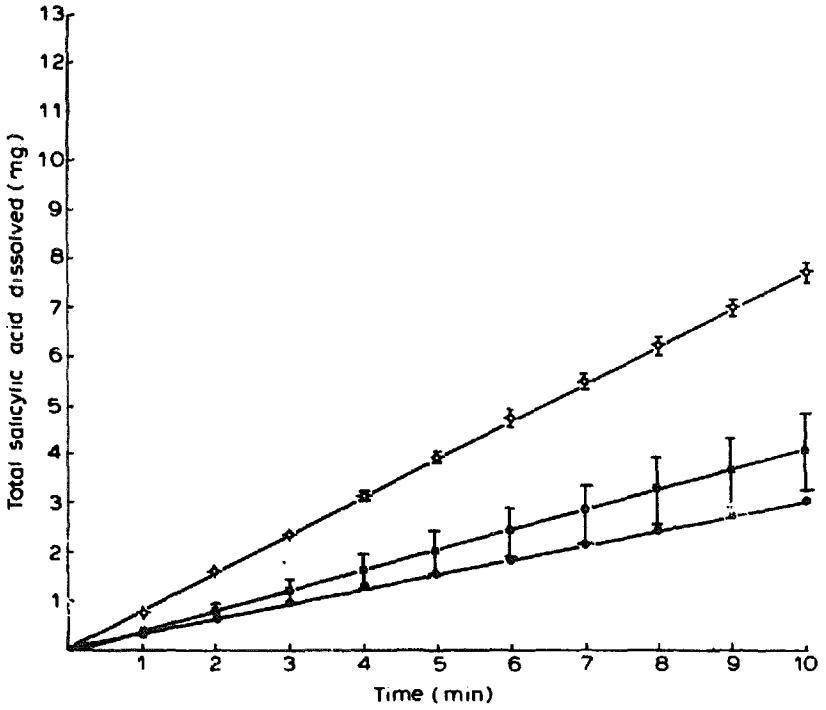


Fig. 6. Salicylic acid dissolution profiles of 3 exposure positions at 2.5 cm above the Center of the bottom of a dissolution fluid container without a basket at 100 rpm. Symbols relate to exposure position (followed by dissolution rate in mg/min)—●, faced-up (0.301 ± 0.005); ★, faced-down (0.415 ± 0.085); -O-, up-down (0.774 ± 0.028).

One further comparison is related to the ratio of the dissolution rate for the up-down position to the sum of the face-up and face-down positions at each stirring speed and at each tablet position. Ratios are summarized in Table 4, and show that a ratio of unity is found at 100 rpm for a tablet positioned at the side of the filter assembly and at the bottom of the assembly without a basket.

On one hand, a ratio of unity may be interpreted as ideal and desirable. On the other hand, stability coupled with consistent performance at different stirring speeds

TABLE 4

Dissolution rate ratios for Salycilic acid tablets for the Face-Up/Face-up + Face-down positions

| Condition | 100 rpm | 300 rpm |
|---|---|---|
| At 4 cm from the center of a rotating filter assembly without a basket | 1.03 | 0.86 |
| At 2.5 cm above the center of the bottom of a container without a basket | 1.08 | 0.84 |
| At 2.4 cm above the center of the bottom of a container within a magnetic basket | 0.80 | 0.78 |

may be equally important. Neither case where a ratio of unity is found is completely satisfactory since a ratio of less than unity is found with increasing stirring rate. Only with a tablet positioned at the bottom of the assembly with a basket is the ratio invariant with stirring speed, although the ratio is less than unity.

## Conclusions

The data from these experiments suggest that a tablet placed at the bottom of a rotating assembly in a basket will give equal dissolution rates from the face-up and face-down position when the stirring rate is increased in order to overcome naturally occurring downward convection tendencies. Converging dissolution rates with increasing stirring speed for the face-up and face-down tablet position coupled with diminished variability in the dissolution rate of the face-down position for a tablet in a basket are interpreted as desirable attributes. The ratio for the dissolution rate of the up-down position to the sum of the dissolution rates for the face-up and face-down positions was found to be less than unity. However, this ratio seems to be of less value than other factors related to hydrodynamic stability and variability in characterizing a dissolution device.

The effect of tablet placement with both a side- or center-placed basket is very important and should certainly be considered especially when non-disintegrating layered tablets are to be tested.

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