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Tablet Position and Basket Type Effects in Spin-Filter Dissolution Device

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Abstract □ The effects of stirring and basket placement on tablet dissolution using the previously developed Shah spin-filter device were investigated. Visualization of flow and dissolution patterns was possible by testing nondisintegrating colored tablets. Dissolution experiments were conducted on nondisintegrating double-layered tablets containing salicylic acid as the dissolving layer and ethylcellulose as an inert nondissolving layer. Visual observations revealed that color was drawn more rapidly from the tablet face resting on the bottom of the basket. Dissolution data from multilayered tablets revealed that when the salicylic acid face was resting on the bottom of the basket, the dissolution was appreciably more rapid than when it was facing up in the basket. This phenomenon was found for several stirring speeds.

Keyphrases □ Dissolution devices—spin filter, effects of tablet position and basket type, comparison to USP basket method □ Dissolution testing systems—spin filter compared to USP basket method, effects of tablet position and basket type □ Dosage forms—tablets, dissolution testing, spin filter compared to USP basket method, effects of tablet position and basket type

The dissolution profile of oral solid dosage forms is useful for controlling formulation and process variables that influence the bioavailability of the active ingredient.

An apparatus receiving acceptance by the scientific community is the spin-filter dissolution device developed by Shah *et al.* (1, 2). This apparatus provides a dynamic *in situ* microporous nonclogging rotating filter, which permits continuous and efficient filtration of the dissolution fluid. Furthermore, its relatively large filter area extends over most of the dissolution fluid, which permits representative sampling of the bulk dissolution medium. The smooth cylindrical surface of the rotating filter assembly without impeller blades and its agitation over a long vertical axis provide uniform, mild, laminar, nonturbulent, and reproducible stirring even at relatively high speeds.

In addition to a change in the stirring method from the USP apparatus (3), the basket mesh size was changed from the 40 mesh used in the USP basket to 12 mesh (1, 2). This change was made to prevent clogging of the basket pores by disintegrating tablets.

BACKGROUND

A study was undertaken to examine the spin-filter dissolution device hydrodynamically. Acceptance will probably increase since the spin filter was announced as acceptable for industrial dissolution testing by the Food and Drug Administration (4).

Several studies have been undertaken to examine dissolution devices hydrodynamically and to compare the spin-filter device to other dissolution devices (5–11). Skelly (12) and Grostic (13) highlighted the need for dissolution device standardization and suggested the use of nondisintegrating salicylic acid tablets as a calibrator to overcome device-to-device and laboratory-to-laboratory variations.

A carefully controlled study of the diffusion and hydrodynamic variables in the spin device seemed necessary. Nondisintegrating tablets were used so that hydrodynamic flow patterns rather than basket clogging or particle buildup would be the chief measurement parameter. Dye studies were initiated to measure visibly the large-scale flow patterns that would affect the dissolution of disintegrating as well as of nondisintegrating tablets. Nondisintegrating salicylic acid tablets were used (5) in this study, although special double-layered tablets were valuable for measuring position face as a variable. Direct correlation with nondisintegrating tablets may not be warranted, but such a study would provide valuable information in quantitating hydrodynamic effects and would apply directly to nondisintegrating dosage forms such as sustained-release products.

EXPERIMENTAL

All reported dissolution data were obtained using a device[1] reported by Shah *et al.* (1, 2) with the sample basket removed. The basic features

[1] Rotating filter dissolution device, courtesy of The Upjohn Co., Kalamazoo, Mich.

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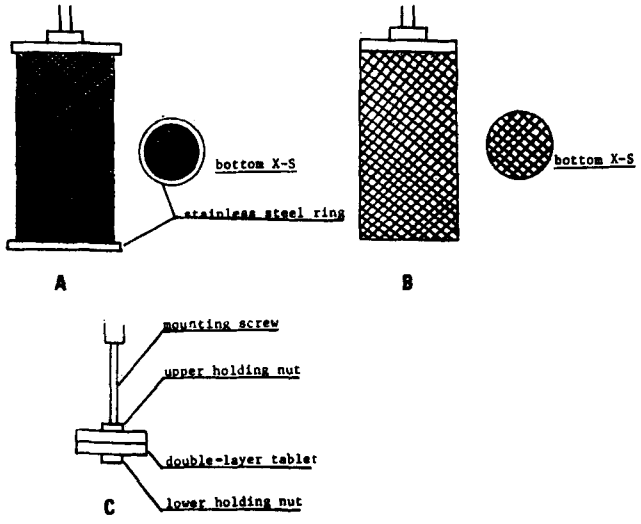

Figure 1—*Schematic diagram of the basket types and the suspended tablets used. Key: A, USP basket (40-mesh screen); B, Shah basket (12-mesh screen); and C, no basket, tablet suspended on the nut and bolt (used in System I).*

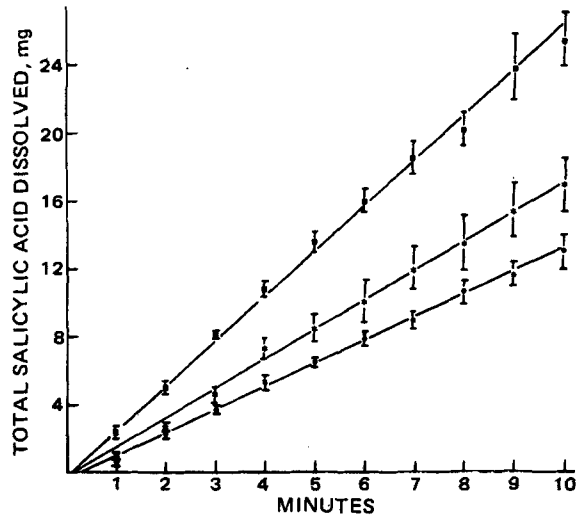

Figure 2—*Salicylic acid dissolution profiles demonstrating the effect of salicylic acid layer position on dissolution from the Shah basket at 300 rpm. Key (salicylic acid layer position): ●, faced up; *, faced down; and □, up–down.*

of this apparatus were a large volume fluid container, a rotating filter assembly, and an external, variable-speed magnetic stirrer. The rotating filter assembly provided a variable, mild, laminar liquid agitation and also functioned as an *in situ* nonclogging filter to permit efficient intermittent or continuous filtration of the dissolution fluid samples. A single dissolution cell with the temperature held at 37° was used for all studies.

The dissolution medium was an aqueous solution buffered at pH 7.2 with phosphate buffer USP (5). The assay was conducted spectrophotometrically at 296 nm using a flowcell with a sample flow rate of 100 ml/min. The tablet radius was 0.624 cm, and the average tablet thickness was 0.194 cm. Double-layered tablets of 0.624-cm radius consisted of 150 mg of salicylic acid and 150 mg of ethylcellulose. The ethylcellulose was compressed at 317 kg of pressure for 15 sec with a hydraulic press[2]. Salicylic acid powder was poured on the top of the compressed ethylcellulose in the die[3], and the two ingredients were compressed at 2268 kg for 15 sec. Single-layer, 300-mg salicylic acid tablets of 0.624-cm radius were compressed at 2268 kg for 15 sec. Nondisintegrating colored tablets made from polyethylene glycol 4000 USP and FD&C Red No. 3 were employed to demonstrate stirring effects and flow patterns for single-layer tablets in the dissolution medium.

Stirring speeds of 300 and 500 rpm were employed. The tablet was placed in the device using a 12-mesh basket (Shah basket), a 40-mesh screen basket (USP basket), or no basket (Fig. 1). When no basket was used, a nut and bolt assembly held the tablet in place (Fig. 1C); a hole was drilled in the tablet center, and a nut and bolt were used to connect the tablet to the holder assembly. All experiments were conducted in the same dissolution flask, thereby eliminating cell-to-cell variation.

Three tablet face positions were utilized. The "faced down" position utilized a double-layered tablet with the salicylic acid face resting on the bottom of the basket or on the bottom of the nut and bolt holder with no basket (Fig. 1). The "faced up" position utilized a double-layered tablet with the inert ethylcellulose layer resting on the bottom of the basket or on the nut and bolt holder (Fig. 1). In the "up–down" position, a single-layered pure salicylic acid tablet was utilized; thus, both tablet faces were active salicylic acid.

RESULTS AND DISCUSSION

An analytical methodology was developed to determine if the basket type, stirring speed, or tablet position in the basket would affect the dissolution rate of a nondisintegrating tablet. The systematic investigation of the tablet position effect on dissolution was begun with flow pattern visualization. Red polyethylene glycol tablets demonstrated that the color was drawn faster from the bottom than from the top of a tablet placed in the Shah basket. As a result of this demonstration and to show the quantitative effect of flow patterns on tablet dissolution in a basket, double-layered salicylic acid tablets were designed.

The salicylic acid dissolution profiles (Fig. 2) demonstrate the effect of the salicylic acid layer position on the salicylic acid dissolution rate from the Shah basket at 300 rpm. The y-axis in this plot is the total salicylic acid dissolved in milligrams, and the x-axis is the time in seconds. Each point is the average of three experiments, and the associated standard deviation is indicated by the vertical line. The slopes and intercepts are for least-squares lines for 10 min of data. In all three cases, the dissolution data were linear and highly reproducible, with correlation coefficients of ≥ 0.99. The dissolution profile for the up–down position was the most rapid, with the least-squares slope of 2.61. The dissolution rate for a double-layered salicylic acid tablet for the faced down position was much more rapid than for the faced up position.

To examine the differences among these three positions, an experiment with a 500-rpm stirring speed was performed. When compared with Fig. 2, Fig. 3 demonstrates that the dissolution profiles were affected more at 500 rpm than at 300 rpm. Again, the dissolution for the faced down

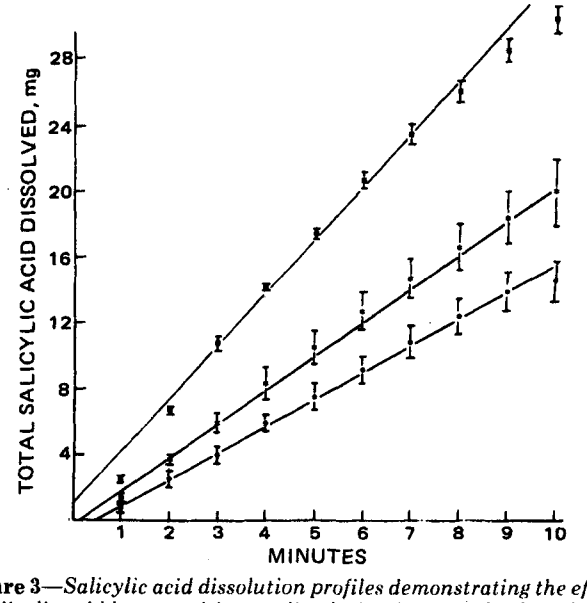

Figure 3—*Salicylic acid dissolution profiles demonstrating the effect of salicylic acid layer position on dissolution from the Shah basket at 500 rpm. Key (salicylic acid layer position): ●, faced up; *, faced down; and □, up–down.*

[2] Carver laboratory press model K, Fred S. Carver Inc., Summit, N.J.
[3] Beckman ACTA die model D-01, Beckman MIIC Ltd., Fife, Scotland.

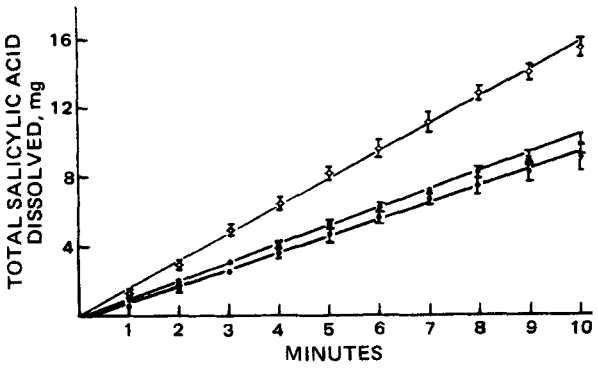

Figure 4—*Salicylic acid dissolution profiles demonstrating the effect of salicylic acid layer position on dissolution from the USP basket at 300 rpm. Key (salicylic acid layer position): ●, faced up; *, faced down; and O, up-down.*

position was much more rapid than for the faced up position. The dissolution profile for the up-down position was the most rapid, with a least-squares slope of 3.11, and was approximately equal to the summation of the faced up and faced down data. Therefore, the screening may interfere with the flow patterns around the salicylic acid layer tablet in the faced up position, increasing the effective diffusion layer. In contrast, the faced down tablet has a relatively higher dissolution rate because the salicylic acid layer in this position is in juxtaposition with the flow stream, which decreases the effective diffusion layer.

Since the USP dissolution basket is the most well known and commonly used, its effect on the dissolution rate was of interest. The dissolution medium flow pattern was visualized. The red color was being drawn again more from the bottom than from the top of the tablets but less dramatically than with the Shah basket.

The dissolution profile for the up-down position with the least-squares slope of 1.56 was the most rapid (Fig. 4). Even though the dissolution rate for the faced down position was slightly more rapid than the rate for the faced up position, the apparent difference between dissolution profiles was much less than for the Shah basket. The two dissolution profiles (Fig. 4) were close together, with least-squares slopes of 1.02 for the faced down and 0.95 for the faced up positions. The dissolution data for both positions at 500 rpm (Fig. 5) show that any apparent difference between the two positions was negligible. As expected, the dissolution profile for the up-down position was the most rapid.

One possible explanation for this phenomenon is that the USP basket has a stainless steel ring on the bottom, which is not present in the Shah basket. This ring should account for an increase in the stagnant layer at the bottom of the USP basket and for the decrease of salicylic acid dissolution in the faced down position.

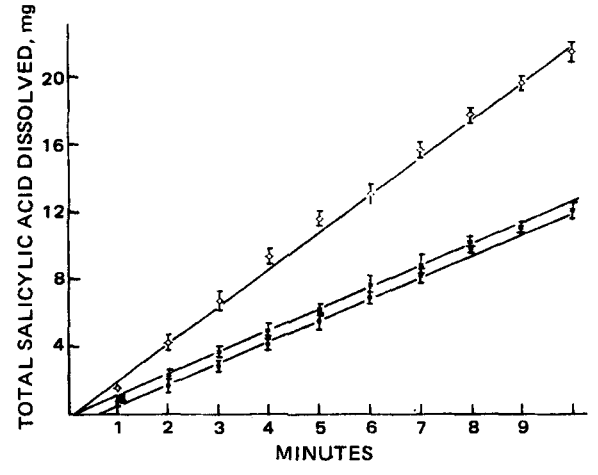

Figure 5—*Salicylic acid dissolution profiles demonstrating the effect of salicylic acid layer position on dissolution from the USP basket at 500 rpm. Key (salicylic acid layer position): ●, faced up; *, faced down; and O, up-down.*

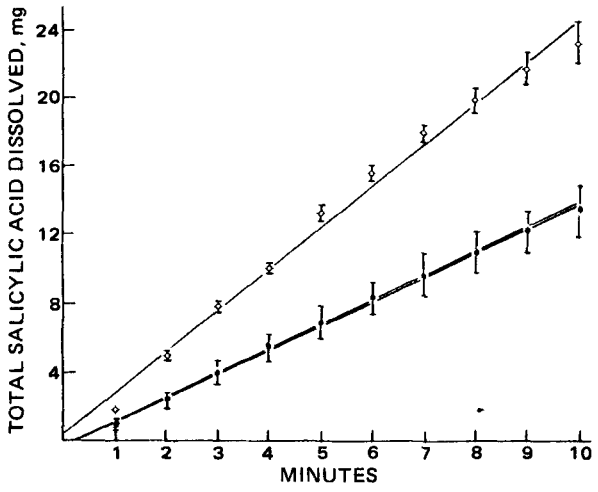

Figure 6—*Salicylic acid dissolution profiles demonstrating the effect of salicylic acid layer position on dissolution from the "no basket" system at 300 rpm. Key (salicylic acid layer position): ●, faced up; *, faced down; and O, up-down.*

All of the Shah basket dissolution rates were noticeably higher than the USP basket rates. Hence, the ratio of the Shah basket rates to those of the USP basket minus 1 was computed to show more clearly the differences in percentage.

According to the faced down comparison, the Shah basket was 76.5% faster at 300 rpm and 67.5% faster at 500 rpm than the USP basket. The faced up comparison shows that the Shah basket was 42.1% faster at 300 rpm and 27.5% faster at 500 rpm than the USP basket. With the faced down position, the dissolution data were affected more drastically by basket type. As mentioned, one possible explanation is that the stainless steel ring at the bottom of the USP basket yielded the significant dissolution rate decrease.

With the faced up position, this difference decreased 27.5% at 500 rpm. One possible explanation is that even though the wider screen size in the Shah basket seemed to yield more rapid dissolution than did the USP basket screen, at the faster stirring speed the flow stream is more capable of penetrating the USP basket screen than at lower speeds such as 300 rpm. The net result is a higher stirring speed effect with the USP basket.

The up-down data comparison shows differences of 67.3% at 300 rpm and 41.4% at 500 rpm. The resulting ratios were intermediate between the two other data sets. Although the slopes of the lines do not perfectly represent the rate, especially for the up-down dissolution data, they do excellently represent the effects of the baskets on the dissolution rate.

The stirring speed effect on the dissolution rate was determined by computing the ratio of the slopes at 500 to 300 rpm minus 1. The Shah basket dissolution data yielded percentages of 23.7% in the faced up position, 17.2% in the faced down position, and 19.1% in the up-down

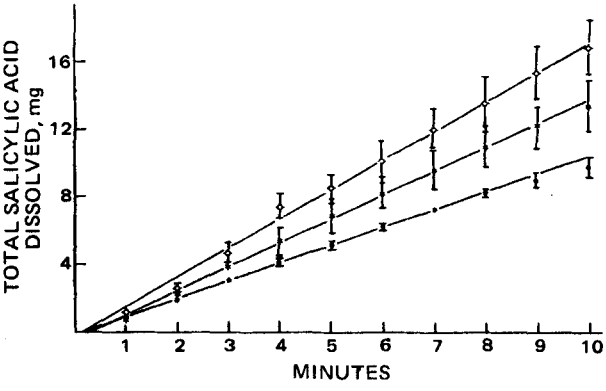

Figure 7—*Salicylic acid dissolution profiles demonstrating the effect of basket type on the dissolution of salicylic acid in the faced down position at 300 rpm. Key: O, Shah basket; ●, USP basket; and *, no basket.*

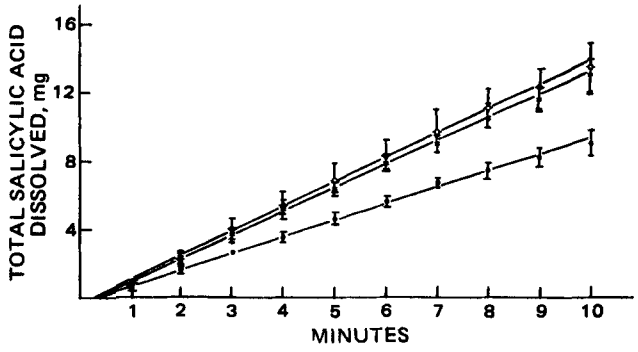

Figure 8—*Salicylic acid dissolution profiles demonstrating the effect of basket type on the dissolution of salicylic acid in the faced up position at 300 rpm. Key: *, Shah basket; ●, USP basket; and ○, no basket.*

position. With the USP basket, the dissolution rates yielded 37.9, 23.5, and 41.0%, respectively. These data suggest that the double-layered salicylic acid tablet was more affected by the stirring speed when placed in the USP basket than when placed in the Shah basket.

These experiments show that the basket screen, the stainless steel ring at the bottom of the USP basket, and the basket itself affected the dissolution rate of double-layered salicylic acid tablets. Therefore, to test the premise that the screen or the ring at the basket bottom in the direction of the flow stream caused the effect, the "no basket" condition was tested (Fig. 6).

The faced down and the faced up positions yielded almost identical dissolution profiles, with least-squares slopes of 1.42 and 1.43, respectively. When the tablet was suspended, there was no obstruction of the flow pattern, so the dissolution data for both positions were almost identical. The least-squares slope for the up–down position was 2.42 and was approximately equal to the summation of the two individual slopes.

The effects of position on dissolution rate were compared (Fig. 7). At 300 rpm, the faced down dissolution profile was faster for the Shah basket than for the no basket condition. The no basket dissolution was less rapid than expected. A possible explanation would be that the nut and bolt, present to suspend the tablet, took up ~10% of the total surface area and might have blocked the flow stream. As anticipated, the USP basket dissolution data were the slowest.

Figure 8 shows the faced up dissolution data at 300 rpm. The no basket dissolution rate was more rapid than the Shah basket dissolution rate. The no basket dissolution rate would have been expected to be much faster if the suspended tablet did not lose ~10% of the total surface area due to the nut and bolt. This figure seems to indicate that, in the faced up position, the mesh screen in the Shah basket interferes with the flow pattern, resulting in an increased stagnant layer and a decreased dissolution rate. The USP basket, with the finer mesh screen, had the slowest dissolution rate.

To demonstrate the effect of position on the dissolution rate, the ratio of slopes of the faced down to the faced up minus 1 were calculated. The percentage values were 33.3% at 300 rpm and 26.3% at 500 rpm for the Shah basket condition and 7.4% at 300 rpm and −3.8% at 500 rpm for the USP basket. The data indicate no significant position effect on dissolution from the USP basket. The effect was more drastic in the Shah basket. As expected for the no basket condition, position was not the important factor in determining tablet dissolution.

In summary, the dissolution data showed definite tablet position dependency effects when double-layered salicylic acid tablets were tested with a 12-mesh basket. This finding is potentially important in dissolution testing for tablets in general and for multilayered tablets in particular. Data from dissolution experiments with the finer 40-mesh USP basket compared with data with no basket present indicate that both screen size and basket design must be considered. Specifically, the support bar on the bottom of the USP basket appears to influence the measured dissolution rates.

The data support the idea that mechanical factors such as screen size and basket design play an important role in dissolution testing, especially with nondisintegrating tablets. Disintegrating tablets may yield different dependencies. Hydrodynamic characterization is important to tablet testing, to the establishment and understanding of procedures for optimum use of the device, and to the correct interpretation of test results.

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