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Evaluation of a rotating filter apparatus: hydrodynamic characterization through modeling

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Summary

In this study a rotating filter was evaluated using a two-dimensional convective diffusion model. Experimental model testing involved analysis of dissolution rates from non-disintegrating salicylic acid discs. For each dissolution run the disc was positioned at the bottom of the dissolution container. The tablets were coated so only a single salicyclic acid face on the side facing the stirrer was exposed for dissolution. Experimental variables included stirring speed, tablet radius and the distance of the tablet from the center of the container. From the data and visualization studies liquid flow inside the dissolution fluid container was described. The single-faced salicylic acid tablets proved to be an excellent system with which to test the convective diffusion model. The results seem to support the proposed convective diffusion theory which indicates the numerical exponents for stirring speed and tablet radius are 0.5 and 1.5, respectively.

Introduction

The rotating filter device originally evaluated by Shah (1973) has found increasing use in pharmaceutical research (Grady, U.S.P.; Cabana and Prasad, 1976). In a previous report the rotating filter device was modified by removing the suspended basket in order to study the dissolution characteristics of suspensions (Howard et al., 1977, 1979). Another modification using the device involved replacement of the

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suspended basket with a magnetic basket, with the latter being placed on the bottom of the dissolution flask directly below the spinning filter (Vongvirat, 1981). This configuration was studied with capsule and tablet dissolution testing in mind.

Although a previous study (Mauger et al., 1979) reported on the hydrodynamic characteristics of the device when non-disintegrating salicylic acid tablets were suspended at the side of the rotating filter, no hydrodynamic characterization data are available when dissolution occurs from the bottom of the flask and underneath the rotating filter. With this in mind, the current study was designed to characterize the rotating filter device via a convective diffusion model when non-disintegrating tablets are placed at varying positions at the bottom of the dissolution flask.

Theory

A convective diffusion model for a transport-controlled dissolution rate process was derived by assuming the diffusion layer to be imbedded well within the hydrodynamic boundary layer (Shah, 1973) as shown in Fig. 1. The equation may be presented as:

$$j = 0.32\, D \cdot C(\nu/D)^{1/3}(U/\nu \cdot x)^{1/2} \qquad (1)$$

where j is the diffusional flux of solute, D is the diffusion coefficient (cm^2/sec), C is the saturation solubility (g/cm^3), ν is the kinematic viscosity (cm^2/sec), U is the free stream velocity (cm/sec) and x is the length (cm) of the solute surface in the same direction as the flow.

With the necessary integration in the flow direction over one surface of a tablet, Eqn. 1 can be written in general form as:

$$R = K \cdot D \cdot C \cdot (\nu/D)^{1/3}(U/\nu)^{1/2} r^{3/2} \qquad (2)$$

where R is the dissolution rate, K is a constant and r is the radius of a tablet. This equation expresses the physical situation where the dissolution rate increases in proportion to the square-root of the free stream velocity, which is assumed to be directly proportional to the stirring speed. The dissolution rate also increases in proportion to 3-halves the power of the radius of a tablet.

Limitations inherent in the strict application of this model to the rotating filter device relate to flow patterns assumed for the model. The physical picture of the free stream flow patterns inherent in the model is a unidirectional flow which is laminar and which will develop a well behaved boundary layer, while the flow actually developed from the rotating filter device is radial in nature.

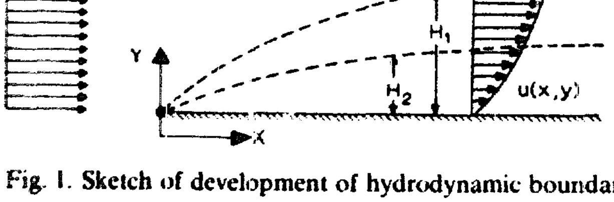

Fig. 1. Sketch of development of hydrodynamic boundary layer and diffusion layer.

TABLE 1

Experimental Design for the Convective Diffusion Model for Transport-Controlled Dissolution Rate Process Study

Tablet position	Diameter of the tablet	
	0.957 cm	1.300 cm
At the center of the bottom of the dissolution fluid container	200 rpm 300 rpm 400 rpm 500 rpm	200 rpm 300 rpm 400 4pm 500 rpm
At the side of the bottom, 3.5 cm from the center of the dissolution fluid container	200 rpm 300 rpm 400 rpm 500 rpm	200 rpm 300 rpm 400 rpm 500 rpm

Materials and methods

The convective diffusion model study was conducted with the rotating filter device described in a previous paper (Vongvirat et al., 1981) using the face-up exposure position (salycilic acid tablet face is up toward the stirrer) tablets at 4 different constant stirring speeds (200, 300, 400 and 500 rpm); two different sizes of tablets (0.957 cm diameter and 0.165 cm thickness tablets, and 1300 cm diameter and 0.165 cm thickness tablets); and two different positions in the dissolution fluid container (Fig. 2; (a) at the side of the bottom, 3.5 cm from the center of the dissolution fluid container; and (b) at the center bottom of the dissolution fluid container). It can be seen that $4 \cdot 2 \cdot 2 = 16$ experimental conditions, as shown in Table 1, were tested and each condition was replicated 3 times.

Standard U.S.P. hydrochloric acid buffer, pH 1.2 was selected as a dissolution medium. This medium suppresses ionization of salicylic acid and at the same time prevents excessive removal from the surface of a tablet during testing period which may enhance the convective diffusion pattern. Each experiment was conducted in 1400 ml of pH 1.2 buffer, at $37 \pm 0.5°C$ within the same dissolution container to avoid cell to cell variation. The spectrophotometric assay was conducted continuously at 237.5 nm.

In order to study a flow pattern, visualization studies were conducted using salicylic acid tablets containing 3% phenolphthalein. These tablets gave a pink coloration in a dissolution medium of 0.1 N sodium hydroxide solution upon dissolution.

Results and discussion

In order to test a particular convective diffusion model at the bottom of a dissolution fluid container, the standard hydrochloric acid buffer solution U.S.P., pH 1.2, was employed as a dissolution medium. The choice of positioning the tablet at the bottom of the dissolution fluid container related to an interest in testing the model in this region. The relationship between dissolution rate and stirring speed and also between dissolution rate and the radius of a tablet were determined. The dissolution profiles for face-up salicylic acid tablets with a diameter of 0.957 cm, positioned at the bottom and 3.5 cm from the center, are shown in Fig. 2. Data for face-up salicylic acid tablets with a diameter of 1.3 cm at the same position, tablets with a diameter of 0.957 cm positioned at the center of the bottom, and for tablets with a diameter of 1.3 cm at the same position were also obtained but not shown.

The experimental data show that mean of dissolution rates at the center are lower while the standard deviations are higher than the corresponding ones at 3.5 cm from the center. This difference indicates the different flow pattern across the surface of a tablet.

The ln–ln plot of means of dissolution rates from 3 replicates, with associated standard deviations versus stirring speeds for tablets at a position 3.5 cm from the center is shown in Fig. 3 and the plot for tablets at the center is shown in Fig. 4. According to the convective diffusion model, the expected slopes in Figs. 3 and 4 or the numerical coefficients relating dissolution rate with stirring speed should be 0.5 and the numerical coefficients relating dissolution rate with tablet radius should be 1.5.

The Student's t-test was employed to test the multiple linear regression for both tablet radii. For a position at the bottom, 3.5 cm from the center of a dissolution fluid container, we fail to reject the hypothesis that the numerical coefficient for stirring rate (slope in Fig. 3) = 0.5 at 0.05 level of significance for both tablet radii. We reject the hypothesis that the numerical coefficient for tablet radius (Table 4) = 1.5 at 0.05 level of significance, while we fail to reject the hypothesis that the numerical coefficient for tablet radius (Table 4) = 1.5 at 0.01 level of significance for

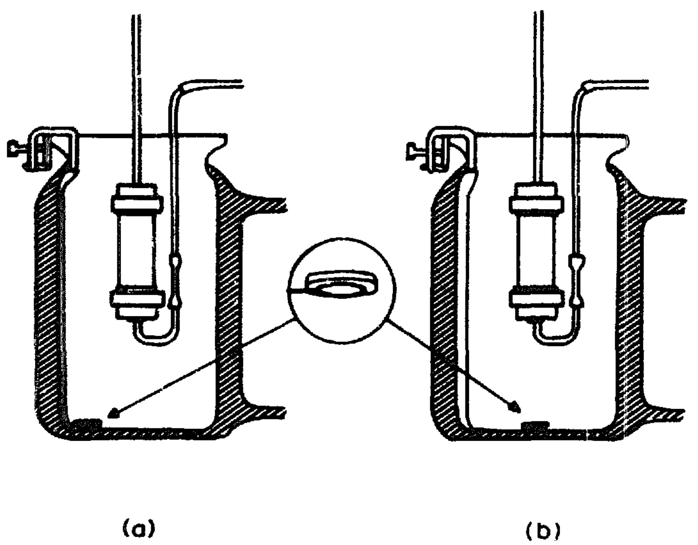

Fig. 2. Diagram of convective diffusion model study conditions.

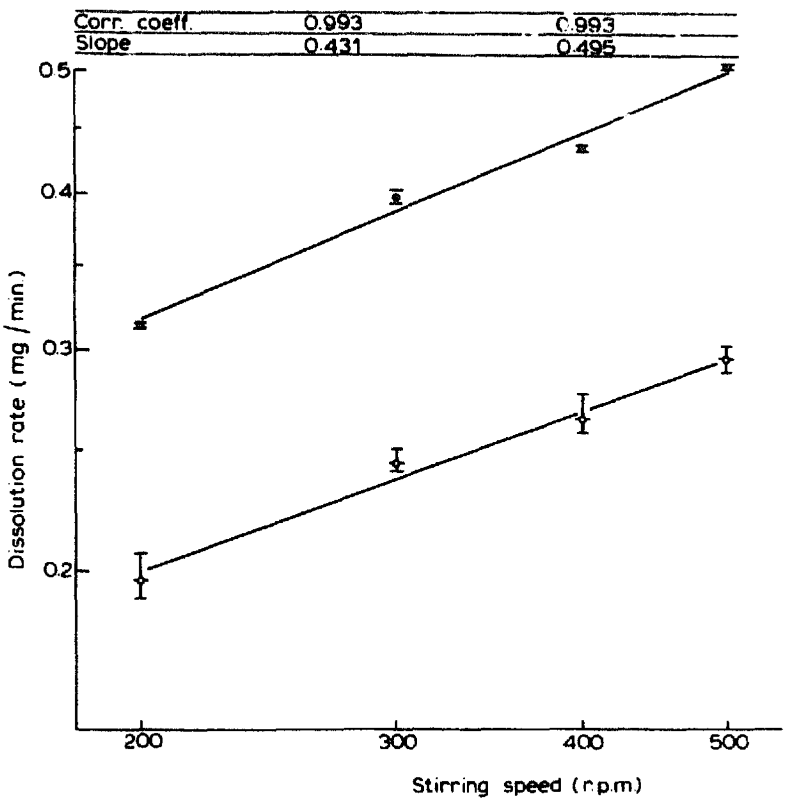

Fig. 3. ln–ln plot of dissolution rate versus stirring speed for faced-up salicylic acid tablet at the bottom, 3.5 cm from the center of a dissolution fluid container in standard hydrochloric acid buffer solution U.S.P., pH 1.2.

both tablet radii. In Table 2, a numerical coefficient relating dissolution rate with tablet radius for tablets at the side of the bottom of a dissolution fluid container seems to increase when the stirring speed is increased. This effect is caused by the interaction between stirring speed and tablet radius in the multiple linear regression

TABLE 2

Numerical Coefficient Relating Dissolution Rate with Tablet Radius for Faced-up Salicylic Acid Tablets at the Bottom, 3.5 cm from the Center of a Dissolution Fluid Container in Standard Hydrochloric Acid Buffer Solution U.S.P., pH 1.2

Stirring speed (rpm)	Dissolution rate (mg/min) for tablet radius		Numerical coefficient for tablet radius (0.4785/0.6500)
	0.4785 cm	0.6500 cm	
200	0.197 (±0.009)	0.314 (±0.001)	1.52 [a]
300	0.245 (±0.006)	0.397 (±0.005)	1.58
400	0.265 (±0.011)	0.434 (±0.001)	1.61
500	0.296 (±0.009)	0.503 (±0.001)	1.73
			average 1.61 (±0.088)

[a] Calculated using the relationship ln(0.197/0.314)/ln(0.4785/0.6500) = 1.52.

Corr coeff	0.988	0.999
Slope	0.471	0.509

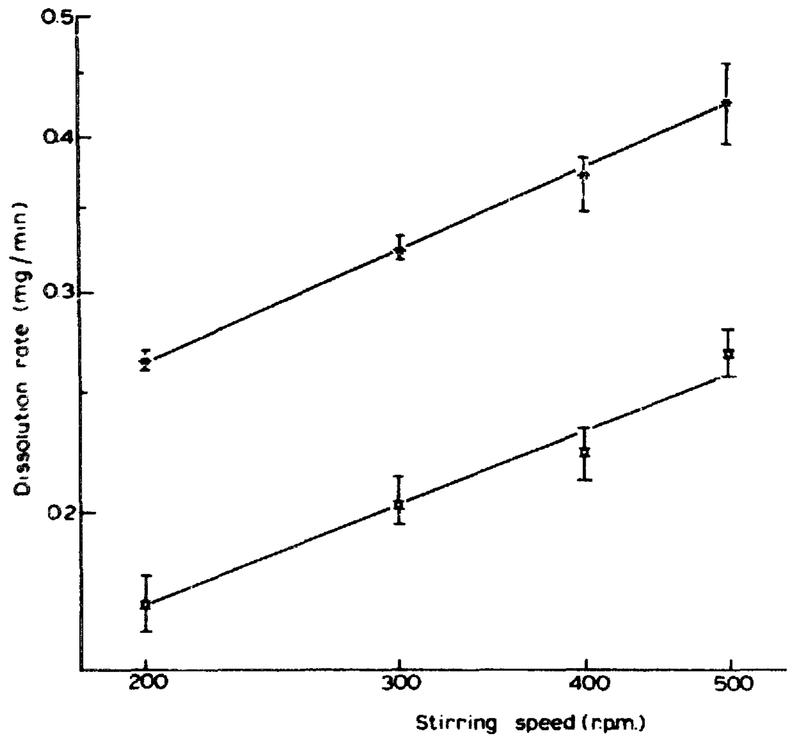

Fig. 4. ln–ln plot of dissolution rate versus stirring speed for faced-up salicylic acid tablet at the center of the bottom of a dissolution fluid container in standard hydrochloric acid buffer solution U.S.P., pH 1.2.

model and this effect may come from increasing undesirable turbulent flow at the edge of a smaller tablet. This effect is not observed from tablets at the center of the bottom of a dissolution fluid container shown in Table 3.

At the center of the bottom of a dissolution fluid container, from Student's t-test

TABLE 3

Numerical Coefficient Relating Dissolution Rate with Tablet Radius for Faced-up Salicylic Acid Tablets at the Center of the Bottom of a Dissolution Fluid Container in Standard Hydrochloric Acid Buffer Solution U.S.P., pH 1.2

Stirring speed (rpm)	Dissolution rate (mg/min) for tablet radius		Numerical coefficient for tablet radius (0.4785/0.6500)
	0.4785 cm	0.6500 cm	
200	0.170 (±0.009)	0.265 (±0.005)	1.45
300	0.202 (±0.010)	0.324 (±0.009)	1.54
400	0.224 (±0.011)	0.372 (±0.021)	1.65
500	0.267 (±0.012)	0.246 (±0.032)	1.53
			average 1.54 (±0.082)

of the multiple linear regression for both tablet radii, we fail to reject the hypothesis that the slopes from Fig. 4 = 0.5 and that the numerical coefficient from Table 3 = 1.5 at 0.05 level of significance, so we may assume that the proposed convective diffusion model is reasonable for our data.

Visualization studies of both tablet positions at the bottom of a dissolution fluid container were accomplished using 3% phenolphthalein in salicylic acid tablets and 0.1 N sodium hydroxide solution as described previously. The visualization studies confirmed that the liquid flow inside a dissolution fluid container was predominantly radially outward around the rotating filter assembly region, axially downward at the wall of a dissolution fluid container, radially inward at the bottom, and axially upward over the entire region below the rotating filter assembly. The flow pattern in any dissolution apparatus should be an important factor to determine sampling areas in order to avoid an unmixed stream of concentrated fluid.

Conclusion

A face-up salicylic tablet is considered to be an optimum model drug tablet to test the convective diffusion model. Our results seem to support the proposed convective diffusion theory which indicates the numerical exponents for stirring speed and tablet radius are 0.5 and 1.5, respectively.

A magnetic basket gives exact placement at the center of the bottom of a dissolution fluid container. The center of the bottom of a dissolution fluid container is considered to be an optimum place for basket positioning, giving a homogenous distribution of disintegrating particles on the bottom of a dissolution fluid container. A rotating filter assembly is a useful device providing mild and laminar-like liquid stirring which lends to the ability of this apparatus to correlate with convective diffusion theory, and which also functions as a microporous non-clogging filter. A motor-driven rotating filter assembly is suitable to incorporate into a motor-driven stirrer-type apparatus, such as the current official dissolution apparatus. A rotating filter–magnetic basket apparatus which combines a magnetic basket and a motor-driven rotating filter assembly is a potentially useful apparatus for dissolution testing of solid dosage forms.

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