Pharmaceutical Research, Vol. 5, No. 8, 1988

Research Article

Dissolution Rate Studies from a Stationary Disk/Rotating Fluid System

Nahla Khoury,[1,2] John W. Mauger,[1] and Stephen Howard[3]

Received September 28, 1987; accepted March 4, 1988

The dissolution rates for hydrocortisone alcohol and acetate were determined using a stationary disk/rotating fluid system. The hydrocortisone was compressed in a tablet die, and the die placed in a vessel above a rotating magnetic bar. Dissolution rates were evaluated in aqueous media under conditions involving the following independent variables: solubility (C_s), diffusion coefficient (D), viscosity (ν), rotational speed (ω), and tablet radius (r). A design equation which relates dissolution rate (R) to these variables was formulated for the system

$$R \alpha C_s D^{2/3} (\nu)^{-1/6} (\omega)^{1/2} (r)^{3/2}$$

This design equation adequately represents the system, which is related to fluid mechanics and convective diffusion models. The fluid mechanics model assumes that the fluid ideally rotates as solid-body rotation and the momentum layer is initiated at the outside radius of the tablet die. The convective diffusion model is based on the formation of a diffusion layer at the outside radius of the dissolving surface and a predictable relationship between the momentum and the mass transport quantities of bulk viscosity and diffusion coefficient. This configuration, like the rotating disk in a stationary fluid, offers the attractive attribute of being useful to study drug release mechanisms for systems of pharmaceutical interest.

KEY WORDS: stationary disk/rotating fluid; fluid mechanics; forced convection; design equation.

INTRODUCTION

Several methods have been utilized for studying the dissolution characteristics of solid dosage forms and have been reviewed by Dakkuri and Shah (1). Modifications of the beaker method are widely accepted for quality control, for product development, and for research. Most of the contemporary dissolution testing devices belong to this class, including the official apparatus. To date, characteristics which influence the performance of these devices have not been determined in the context of fluid mechanics models.

Another type of apparatus is the magnet-driven rotating filter dissolution device introduced by Shah and co-workers (2), which promotes stable flow of the dissolution medium near the dissolving surface. This device was characterized using a convective diffusion model which provides a basis for predicting performance characteristics (3). Vongvirat *et al.* (4) modified this apparatus using a motor-driven rotating filter and also found that this configuration could be characterized using a convective diffusion model. The rotating filter device leads to stable and potentially predictable flow properties since it represents a cylinder within a cylinder, which is a well-studied fluid mechanics model (5).

The rotating disk represents another commonly used apparatus. Wood *et al.* (6) described an assembly unit which can be attached to a rotor with only one surface exposed to the dissolution medium.

An important characteristic of the rotating disk is that mass transfer rates can potentially be calculated from relationships where the dissolution rate, R, is given by

$$R = f(\nu, \omega, D, C_s)$$

where ν is the kinematic viscosity of the fluid (cm^2/sec), ω is the angular velocity of the fluid (1/sec), D is the diffusion coefficient (cm^2/sec), and C_s is the solubility (g/cm^3) of the dissolving material.

Milosovich (7) showed the utility of an apparatus using a stationary dissolving surface in a stirred dissolution medium. Advantages related to this configuration are simplicity and ease of construction, elimination of the concern for misalignment, and wobble of a rotating shaft.

Of interest to this study is the investigation of a dissolution system having a stationary disk in a rotating fluid. Although the stationary disk/rotating fluid dissolution device has been studied (8,9), its fluid mechanical and mass transfer properties have not been evaluated using conditions applicable to pharmaceutical systems. An objective of this study was to characterize and evaluate this device, with the aim of formulating a design equation based on fluid mechanics and convective diffusion models. This equation, then, would be useful to predict dissolution performance and to study mass transfer mechanisms.

[1] School of Pharmacy, West Virginia University, Morgantown, West Virginia 26506.

[2] To whom correspondence should be addressed.

[3] Ortho Pharmaceutical Corp., Rariton, New Jersey 08869.

0724-8741/88/0800-0495$06.00/0

THEORY

Considerable effort has been given to provide a theoretical basis for understanding mass transfer in a moving fluid. As early as 1921, von Karman (10) studied the steady motion of an incompressible viscous fluid due to a rotating disk in a quiescent fluid. He obtained an approximate solution to the Navier–Stokes equations using the integral method, which he invented. Later, Cochran (11) calculated more accurate values for the velocity profiles using numerical integration. The physical picture of flow generated by a rotating disk is that of fluid being discharged radially outward from the center of the disk, therefore requiring an axial fluid motion toward the disk in order to preserve continuity. The momentum boundary layer, which forms in connection with friction at the surface of the disk, and the diffusion layer, which forms in connection with diffusional process, are initiated at the center of the disk. An important characteristic of this system is the uniform accessibility of the disk to mass transfer.

A method closely connected to the rotating disk is the stationary disk in a stirred fluid. In an idealized case, the fluid motion at a large distance from the stationary disk is in solid-body rotation. The rotating fluid approaches the stationary disk and travels inward and is discharged axially from the center, as shown in Fig. 1. Thus, the momentum and diffusion boundary layers are formed at the outermost edge of the disk, and in this case the disk is not uniformly accessible for mass transfer.

The experimental representation of the idealized flow is the development of a rotating fluid by a magnetic stirring bar.

The velocity profiles for this configuration are given by Schlichting (5) and expected mass transfer properties have been studied by Smith and Colton (8,9).

Assessment of the Momentum Boundary Layer Thickness ($h1$) for a Stationary Disk in a Rotating Fluid

The flux, J (g/sec cm^2), is related to the drug diffusion, solubility, and diffusion layer thickness by

$$J = \{D\,[C_s - C(\mathrm{b})]\}/h2 \tag{1}$$

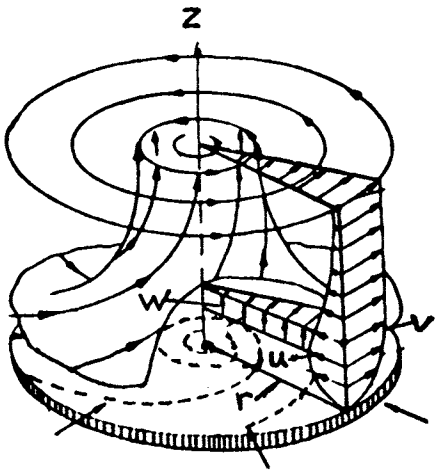

Fig. 1. Flow near a stationary disk in a rotating fluid. Velocity components: u, radial; v, circumferential; w, axial (5).

where C(b) is the concentration of dissolved solute in the bulk and $h2$ is the diffusion layer thickness (cm). An unfortunate aspect of this model is that the functional relationship between the diffusion layer thickness and other variables of interest, such as the viscosity, stirring rate, and momentum boundary layer ($h1$), is unknown. While dissolution rate studies have been interpreted in the context of Eq. (1), Nelson and Shah (3) have demonstrated that this model is inadequate for describing dissolution kinetics under convective conditions. Therefore, the use of this equation does not provide a characterization of a rotating fluid/stationary disk configuration, except in a general sense. A remedy for this situation is to use fluid mechanics principles, in order to generate a functional relationship which is useful in characterizing this system.

An estimate of the momentum boundary layer thickness, $h1$, can be made from an analysis of the Navier–Stokes equation and the physics of the system. At a large distance from the stationary disk the frictionless flow is characterized by solid-body rotation, where the radial pressure gradient is balanced by the centrifugal force and the radial velocity component vanishes. Thus

$$\partial p/\partial r = \omega^2 r \tag{2}$$

As the fluid approaches the disk, a frictional effect is encountered within the boundary layer thickness, $h1$. A fluid element in a rotating layer at a distance r from the center of the disk is acted on by the centrifugal force per unit volume. The same fluid element is acted on by the shearing stress at the wall, f_w, which points in the direction in which the fluid is slipping and forming an angle, θ, with the tangential velocity, V. The radial component of the shearing stress is given by

$$f_w\,(\sin\theta) = \rho\,\omega^2 r\,h1 \tag{3}$$

where ρ is the fluid density. The tangential component of the shearing stress is proportional to the velocity gradient where

$$f_w\,(\cos\theta) \propto \mu\,(\partial V/\partial z) \tag{4}$$

where μ is the fluid viscosity. Based on an order-of-magnitude analysis, the right-hand side of this expression can be approximated by

$$f_w\,(\cos\theta) \propto (\mu\omega r)h1 \tag{5}$$

Solving for $h1$ gives

$$h1 \propto [(\nu/\omega)(\tan\theta)]^{1/2} \tag{6}$$

This relationship among $h1$, ν, and ω is physically reasonable since the boundary layer thickness is expected to increase with increasing viscosity and decrease with increasing angular velocity.

Relationship Between the Diffusion Layer Thickness ($h2$) and the Momentum Boundary Layer Thickness ($h1$)

Levich (12) has discussed the relationship between the diffusion and the momentum layer thickness where

$$h2 \propto (D/\nu)^{1/3}(h1) \tag{7}$$

It is evident from this expression that when the transport quantities D and ν are comparable, a complete analogy

exists between the concentration and the momentum profiles.

For systems of pharmaceutical interest, the ratio of the diffusion coefficient to the kinematic viscosity is expected to be on the order of

$$D/\nu = 10^{-6}/10^{-2} = 10^{-4} \quad (8)$$

Therefore, the diffusion layer is well embedded in the momentum boundary layer.

Following the analysis of Rogers and Lance (13), Eq. (6) is rewritten in a form showing the dependency of $h1$ on the radial distance

$$h1 \propto (\nu/\omega)^{1/2}[f(r)] \quad (9)$$

which can be substituted in Eq. (7) to give

$$h2 \propto (D/\nu)^{1/3} (\nu/\omega)^{1/2} [f(r)] \quad (10)$$

An Expression for the Flux Under Conditions of a Stationary Disk in a Rotating Fluid

Having developed an expression for the diffusion layer thickness, it is possible to substitute Eq. (10) directly into Eq. (1) to give

$$J \propto D^{2/3}[C_s - C(b)](\nu)^{-1/6}(\omega)^{1/2} [f(r)]^{-1} \quad (11)$$

This expression is the presumed form useful for equating the flux with D, C_s, ν, and ω. In particular, when D and C_s can be determined independently, then values for J can be calculated and compared with experimental values for J.

Boundary equations of interest to this system are

(1) at $z = 0$, $C = C_s$; and
(2) at $z \gg h2$, $C \rightarrow 0$.

The first boundary condition is the solubility of the dissolving species at the surface and the second boundary condition is a statement of sink conditions.

Although the development of Eq. (11) as an expression which relates the flux to other physical chemical and fluid mechanics factors appears straightforward, several assumptions and constraints must be mentioned. The idealized solid-body rotation of the fluid far from the disk may not be attained under experimental conditions when using a smooth magnetic stirrer. However, evidence from studies where a color develops on the disk surface indicates that the diffusion layer is initiated at the leading edge of the disk and that flow in the boundary layer is directed radially inward and axially outward, which is consistent with the expected flow pattern (5).

Another assumption involves the uniformity of the disk surface for mass transfer. While the rotating disk in an unstirred fluid is uniformly accessible, a stationary disk in a rotating fluid is not (8). However, half the total transport takes place on the outer 15% of the disk, and only 10% on the inner 50% (8). Therefore, it is important to provide a well-developed momentum boundary layer. This can be accomplished by placing the mass transfer surface in a circular metal casing so that the fluid encounters a smooth nondissolving surface before reaching the leading edge of the dissolving surface. In this study, the dissolving material was compressed in a circular metal die and the die was placed in the stirred liquid medium.

Other assumptions concern the diffusion coefficient and the solubility term in Eq. (11). Due to the limited solubility of the compounds under study, their solutions are dilute and the diffusion coefficient is assumed to be independent of the concentration. Additionally, since C_s is $>>>$ $C(b)$, sink conditions are assumed.

MATERIALS AND METHODS

Preparation of Tablets for Dissolution Studies

Hydrocortisone alcohol tablets (The Upjohn Company, Kalamazoo, Mich., lot No. 471JR) were made in the following manner. Two hundred milligrams of hydrocortisone powder was weighed and transferred to a stainless-steel die having a 0.55-cm radius. A flat plate was used as a lower punch so that the tablet surface was flush with the die surface and the powder was compressed at 600-kg pressure for 20 sec using a Carver laboratory press (Model K, Fred S. Carver, Inc., Hydraulic Equipment, Summit, N.J.). The tablet was visually inspected to confirm that the tablet surface was flush with the surface of the die and free from lamination or capping.

Hydrocortisone acetate tablets (The Upjohn Company, Kalamazoo, Mich., lot No. 739 KU) were prepared using the same procedure. Hydrocortisone acetate was selected because its physicochemical properties are similar to those of hydrocortisone alcohol except for its solubility, which is 1/30 that of hydrocortisone alcohol (14).

In later phases of the study, dies of 0.65-cm radius were used to prepare tablets having a larger surface area. These tablets were prepared using the same procedure. All tablets were made 24 hr prior to the dissolution run and stored under dry conditions at room temperature.

Dissolution Testing

Apparatus. Figure 2 is a schematic of the dissolution apparatus, which consists of a 200-ml jacketed flask with two side openings that facilitate sample withdrawal and replacement. A holder for the tablet in its die allowed the tablet/die unit to be introduced through the neck of the flask. The tablet/die holder unit provided for a secure system

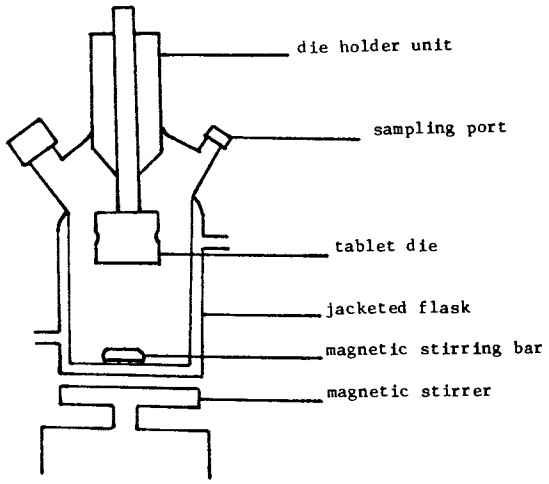

Fig. 2. Schematic of the dissolution apparatus.

which would not move during a run, for vertical alignment, and for holding the die at a consistent distance above a magnetic stirring bar. The temperature of the aqueous dissolution medium was maintained at 25°C using a circulatory water bath (Messgerate-Werk Lauda, West Germany, Type RM3S) and stirring was achieved using a magnetic stirrer (Nuova II stirrer, Syborn) and magnetic stirring bar. Care was taken to place the flask at exactly the same position on the magnetic stirrer to maintain consistency and reproducibility between runs. The 3-cm stirring bar was cylindrical in shape with a smooth surface which produced reproducible stirring conditions. A strobe lamp (Grass Medical Instruments Co., Quincy, Mass.) was used to calibrate stirring speeds and to check stirring speeds periodically.

Evaluation of h2 *Using Benzoic Acid.* The expression used to relate flat-faced tablet dissolution to other characteristics of the system is

$$R = (D\ C_s\ A)/h2$$

where R is the dissolution rate, D is the diffusion coefficient, C_s is the solute solubility, A is the area presented for dissolution, and $h2$ is the diffusion layer thickness. The diffusion layer thickness is a value expressing the fluid mechanical and convective diffusion characteristics of the system.

Benzoic acid, which has a known solubility and diffusion coefficient (15), was used as a prototype solute. From experimentally determined values for R and with known values for A, C_s, and D, a value for $h2 = 2.6 \times 10^{-3}$ cm was found under stirring conditions of 200 rpm and at 25°C. Thus, the stationary disk/rotating fluid system yields values for $h2$ which are of the same order of magnitude expected for a circular tablet rotated at 200 rpm in an unstirred aqueous system.

Dissolution Testing Procedure for Hydrocortisone Tablets. Prior to dissolution testing, tablets were prewetted for 2 min in a separate flask containing glass-distilled water held at 25°C. This conditioning procedure minimized tablet flaws such as rough edges, ensured the dissolution of any loose powder on the tablet surface, assisted in preventing air bubble formation on the tablet surface during the dissolution run, and improved the reproducibility of the dissolution data. The tablet was then air-dried for 5 min.

The dissolution run was initiated by gently lowering the tablet/die unit 4 cm above the bottom of the dissolution flask, which contained 180 ml of glass-distilled water held at 25°C.

An initial dissolution rate was determined by withdrawing 3-ml samples at 5-min intervals for the first 30 min of each run. Each volume of sample removed was immediately replaced by an equal volume of fresh solvent held at the same temperature. Samples were spectrophotometrically assayed at 248 nm (Perkin Elmer double-beam spectrophotometer, Coleman 124, Hitachi, Ltd., Tokyo). Absorbance values were converted to concentration units using a standard curve. Resulting dissolution curves were then corrected for the cumulative amount of drug lost through sampling. The dissolution rate, R, was obtained from the slope of the cumulative amount dissolved versus time curves.

Diffusion Coefficient Determination

Diffusion coefficients were determined using a non-steady-state method described by Fawcett and Caton (16) and characterized for pharmaceutical solutes by Stout *et al.* (17).

Equilibrium Solubility Studies

Equilibrium solubility values were determined at 25°C using the method described by Paruta *et al.* (18).

Viscosity Measurements

Viscosity of the dissolution media was determined at 25°C using a Ubbelohde capillary viscometer (Cannon N205).

RESULTS AND DISCUSSION

Basic objectives of this study included the evaluation of the dissolution kinetics of hydrocortisone from a stationary flat-faced tablet in a stirred fluid using a design equation which reflects the fluid mechanical properties of the system.

This was accomplished by determining dissolution rates/flux values while varying extrinsic factors such as tablet radius and stirring rate, as well as physicochemical variables such as drug solubility and viscosity. These experimentally determined dissolution rates can then be compared with the calculated values using the presumed form of the convective diffusion design equation [Eq. (11)] and the independently determined diffusion coefficient and solubility values.

Equation (11) can be expressed in terms of the dissolution rate, R, by multiplying the flux by the surface area of the dissolving surface. Thus, $R = J \times (\pi \times r^2)$.

According to Eq. (11), the flux or dissolution rate is directly proportional to the solubility of the dissolving substance under sink conditions where $C(b) \rightarrow 0$. Hydrocortisone alcohol and acetate were selected for study because of their similar physicochemical properties, except for solubility. Table I provides a summary of the solubility and diffusion coefficient data for hydrocortisone alcohol and acetate; dissolution rate and flux data for tablets of both forms of hydrocortisone having radii of 0.55 and 0.65 cm are shown in Table II. According to the proposed design equation, the ratio of flux or dissolution rate values of hydrocortisone alcohol to acetate should be equal to the ratio of their solubilities, when all the other variables are held constant. The ratio of solubilities is 327/11 = 29.7 and the ratio of flux values for the 0.55- and 0.65-cm tablets is 27.8 in both cases. Therefore, a stationary tablet in a rotating fluid gives a predictable relationship between flux and drug solubility.

Another relationship of interest is between the dissolution rate or flux and the stirring rate. According to the design equation, flux or dissolution rate values are propor-

Table I. Physiochemical Data for Hydrocortisone Alcohol and Acetate in Distilled Water[a] at 25°C

Drug	Solubility ($\mu g/cm^3$)	Diffusion coefficient (cm^2/sec)
Alcohol	327	4.50×10^{-6}
Acetate	11	4.21×10^{-6}

[a] Kinematic viscosity was 8.74×10^{-3} cm^2/sec.

Table II. Dissolution Rates and Flux Values for Hydrocortisone Alcohol and Acetate in Distilled Water at 25°C

Drug	Dissolution rate (μg/sec) for radius of		Flux[a] (μg/sec cm²) for radius of	
	0.55 cm	0.65 cm	0.55 cm	0.65 cm
Alcohol	0.458	0.590	0.483	0.445
Acetate	0.0165	0.0212	0.0174	0.0160

[a] Flux = [dissolution rate/π (radius)²].

tional to the stirring rate raised to the ½ power. Dissolution rate values for hydrocortisone alcohol dissolving in water at 25°C are given in Table III. The exponent determined from the experimental data is 0.48, which indicates that a design equation based on a convective diffusion model can be used to predict the effect of stirring on mass transfer.

Experiments were run to determine the influence of viscosity on flux values. The solubility, diffusion coefficient, and flux or dissolution rate values for hydrocortisone in 18% sucrose solutions are given in Table IV. Sucrose affects the flux or dissolution rate values, the solubility, and the diffusion coefficient for hydrocortisone alcohol when compared with similar values in aqueous systems not containing sucrose.

A question arises about whether the design equation accounts for the flux or dissolution rate values determined in water and in 18% sucrose solutions. According to the design equation, J or R is proportional to the quantity Z, where Z represents the diffusion coefficient to the ⅔ power times the kinematic viscosity to the $-1/6$ power times the solubility to the first power, when all other variables are kept constant. Data from Tables I, II, and IV were used to test this relationship via $R1/R2 = Z1/Z2$. In this case $R1$ represents the value determined in water and is 0.458, with the corresponding value for $Z1$ being 0.1964. A value for $Z2$ of 0.1311 was calculated for the sucrose system. Using values for $R1$, $Z1$, and $Z2$, a value of 0.306 was generated for $R2$, the value in the sucrose system. This value is within approximately 6% of the experimentally determined value of 0.290 and supports the relationship given by the design equation. These findings are consistent with those of Nelson and Shah (19), who also found that the influence of viscosity and the associated effects of viscosity on diffusivity were appropriately accounted for by convective diffusion theory.

An additional factor of interest in forced convection systems is the relationship between the dissolution rate and the surface area of the dissolving surface. Several authors (3,4) have demonstrated that when dissolution occurs from a circular disk under conditions of forced convection the dissolution rate, R, is related to r by

Table III. Dissolution Rates for Hydrocortisone Alcohol as a Function of Stirring Rate in Distilled Water at 25°C Using a 0.55-cm Disk

Stirring speed (rpm)	Dissolution rate (μg/sec)
100	0.323
200	0.458
300	0.548

Table IV. Solubility, Dissolution Rate, Flux, and Diffusion Coefficient Data for Hydrocortisone Alcohol in 18% Sucrose Solutions[a] at 25°C and 200 rpm Using a 0.55-cm Disk

Solubility (μg/cm³)	Dissolution rate (μg/sec)	Flux (μg/sec cm²)	Diffusion coefficient (cm²/sec)
363	0.290	0.305	2.29×10^{-6}

[a] Kinematic viscosity was 0.0124.

$$R \alpha r^n \tag{12}$$

As discussed by Nelson and Shah (3), the Nernst equation predicts an exponent of 2, while convective diffusion models typically yield exponents of less than 2 when the dissolving surface is not uniformly accessible.

Dissolution rates for hydrocortisone alcohol and acetate were determined at 25°C and 200 rpm using flat-faced tablets having radii of 0.55 and 0.65 cm. For hydrocortisone alcohol, dissolution rates of 0.458 and 0.590 μg/sec yield a numerical exponent of 1.51. Dissolution rates of 0.0165 and 0.0212 were determined for hydrocortisone acetate, giving a numerical exponent of 1.50.

These data relate well with the expectation that the exponent is less than 2 and justify the relationship given in Eq. (13), where

$$R \alpha D^{2/3} C_s (\nu)^{-1/6} (\omega)^{1/2} (r)^{1/2} \tag{13}$$

The proportionality constant, K, for Eq. (13) can be calculated using the physicochemical data from Table I and the dissolution rate data from Table IV. Four values for K were calculated using dissolution rate data for each form of hydrocortisone and for each radius. The average value for K for hydrocortisone alcohol was 1.25, and the average value for hydrocortisone acetate was 1.40, with an overall average value of 1.33. This average value incorporates the uncertainty in the experimentally determined dissolution rates as well as the uncertainty in the independently determined solubility values and diffusion coefficients.

This form of the design equation should be used with the underlying assumptions and constraints in mind. The stirring generated in the experimental system by a smooth magnetic stirrer yields flow patterns representative of the idealized flow of the fluid mechanics model. Therefore, effects due to the size of the stirrer, its distance from the dissolving surface, and perturbations from the idealized flow are incorporated in the numerical coefficient derived from experimental data. Mass transfer has been improved by using a system where the momentum boundary layer is well established before it reaches the dissolving surface by embedding the tablet in a metal die.

One additional attribute of a dissolution method is the reproducibility of the data. The average dissolution rate for hydrocortisone alcohol in distilled water is 0.458 ± 0.0272 μg/sec, based on 10 runs, using a 0.55-cm disk and a stirring rate of 200 rpm, giving a reasonable value for the coefficient of variation of slightly less than 6%. Care was taken to ensure that the disk was placed at the same distance above the magnetic stirrer for each run, that the stirring rate was reproducible, and that the magnetic stirrer was placed at the

same position for each run. Reproducibility was significantly enhanced by prewetting the disk, as described under Materials and Methods.

A rotating fluid/stationary tablet dissolution system is simple to construct, provides reproducible data, and yields predictable performance via a design equation based on fluid mechanics and forced convection principles. The latter characteristic is important since it links the flux or dissolution rate with transport quantities (diffusion coefficient and viscosity), with solubility, with surface area, and with stirring rate. This functional relationship offers the opportunity to predict dissolution performance and to evaluate mass transfer mechanisms in a systematic manner.

REFERENCES

1. A. Dakkuri and A. C. Shah. *Pharm. Technol.* June:28–86 (1986).
2. A. C. Shah, C. B. Poet, and J. F. Ochs. *J. Pharm. Sci.* **62**:671–677 (1973).
3. K. G. Nelson and A. C. Shah. *J. Pharm. Sci.* **64**:610–614 (1975).
4. B. Vongvirat, S. Howard, J. Mauger, and L. Luzzi. *Int. J. Pharm.* **9**:213–219 (1981).
5. H. Schlichting. *Boundary Layer Theory*, 6th ed., McGraw–Hill, New York, 1968.
6. J. H. Wood, J. E. Syarto, and H. Letterman. *J. Pharm. Sci.* **54**:1068 (1965).
7. G. Milosovich. *J. Pharm. Sci.* **53**:484–487 (1964).
8. K. A. Smith and C. K. Colton. *AICHE* **18**(5):949–958 (1972).
9. K. A. Smith and C. K. Colton. *AICHE* **18**(5):958–967 (1972).
10. T. von Karman. *Z. Angew Math. Mech.* **1**:244–247 (1921).
11. W. G. Cochran. *Proc. Cambr. Phil. Soc.* **30**:365–375 (1934).
12. V. Levich. *Physicochemical Hydrodynamics*, Prentice Hall, Englewood Cliffs, N.J., 1962.
13. M. H. Rogers and G. N. Lance. *Q. J. Mech. Appl. Math.* **17**:319–330 (1964).
14. P. Kabasakalian, E. Britt, and Y. Yudis. *J. Pharm. Sci.* **55**:642 (1966).
15. R. J. Braun and E. L. Parrot. *J. Pharm. Sci.* **61**:592–597 (1972).
16. N. C. Fawcett and R. Caton. *J. Anal. Chem.* **48**:600–604 (1979).
17. P. J. Stout, N. Khoury, J. Mauger, and S. Howard. *J. Pharm. Sci.* **75**:65–67 (1986).
18. A. Paruta, B. Sciarrone, and N. Lordi. *J. Pharm. Sci.* **58**:216–219 (1969).
19. K. G. Nelson and A. C. Shah. *J. Pharm. Sci.* **76**:799–802 (1987).