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An Analysis of Drug Dissolution Rates in the USP 24 Type 2 Apparatus

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This paper applies boundary layer theory to the process of drug dissolution in the USP 24, Type 2 Apparatus. The mass transfer rate from the top flat surface of a compact in various positions within the device is evaluated by means of a Pohlhausen integral method.

1 Introduction

The aim of this paper is to model dissolution testing in the USP 24 Type 2 Apparatus which is widely used to determine a drug's dissolution rate and, where possible, in vivo performance when an in vivo in vitro correlation has been established. The apparatus consists of a rotating paddle which lies 25mm above the hemispherical base of a container, as shown in figure 1. Cylindrical compacts of benzoic acid are fixed to the base of the container in one of three positions, referred to in this paper as the central position, position 1 and position 2. This work evaluates the rate of dissolution from the top flat surface of the compacts in each position.

The problem is set up as a boundary layer problem in which we have both a dissolution boundary layer and a momentum boundary layer. We first examine the top flat surface of the compacts in position 1 and 2 using a Pohlhausen integral method to solve the boundary layer equations. For position 1 and 2, the flow is treated as flat-plate flow for which an exact solution exists due to Lévêque[1]. The exact solution is used to verify the Pohlhausen method before it is applied to the compact in the central position, where a radial flow exists. The results of the analysis are then compared with those of experiment provided by D'Arcy et al[2] and Healy et al[3].

Fig. 1 The Paddle Apparatus

2 Initial Observations

One of the initial observations, which is central to our work, is that a drug dissolving into a liquid will diffuse much more slowly then momentum due to the tightly packed nature of the molecules. This leads to a dissolution boundary layer with thickness an order of magnitude less than the momentum boundary layer. For this reason, the dissolution layer only occupies the region of the momentum layer in which the velocity gradient is constant. The problem at hand is therefore analogous to that of heat transfer for large Prandtl numbers, for which an exact solution exists due to Lévêque[1], which provides a means of verifying our approximate method.

3 Analysis of a Compact in Position 1 and 2

The dissolution boundary layer equation is

$$u\frac{\partial c}{\partial x} + v\frac{\partial c}{\partial y} = D\frac{\partial^2 c}{\partial y^2} \tag{1}$$

where (u, v) are the velocity components in the (x, y) direction, D is the coefficient of diffusion and c is the concentration of drug.

The Pohlhausen method involves integrating the boundary layer equation with respect to y across the boundary layer. Applying the appropriate boundary conditions we arrive at the dissolution integral equation. In order to solve this equation we must substitute in appropriate velocity and dissolution profiles. For position 1 and 2 the Blasius velocity profile was used in conjunction with several different dissolution profiles. Using the exact solution of Lévêque[1] the most accurate dissolution
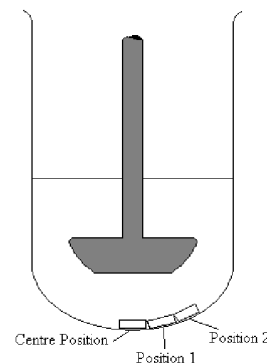
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profile was then chosen. The velocity and dissolution profiles are $u = 0.332yU_\infty\sqrt{\frac{U_\infty}{\nu x}}$ and $c = C_s[1 - \sin(\frac{y\pi}{2\delta_D})]$ respectively, where C_s is the concentration saturation, ν is the kinematic viscosity, U_∞ is the outer stream velocity and δ_D is the dissolution boundary layer thickness. Having obtained these profiles the method is applied to the top flat surface of the compacts by dividing the surface into strips. The outer stream velocity for each strip is obtained from FLUENT$_{TM}$ simulations.

The results for the dissolution rate from the top surface of a compact in position 1 and 2 are shown below in Table 1 along with experimental results.

Table 1 Dissolution Rates from Top Surface for Compact in Position 1 and 2

3mm Compact	Theoretical Results(g/sec)	Experimental Results(g/sec)
Position 1	1.22×10^{-5}	1.36×10^{-5}
Position 2	1.41×10^{-5}	1.40×10^{-5}

4   Analysis of a Compact in the Central Position

For the top flat surface of the compact in the central position we have a converging radial flow for which a new velocity profile was constructed using FLUENT$_{TM}$. The velocity profile is given by

$$u = \begin{cases} -\alpha y & \text{for} \quad r_1 \le r \le a \\ \frac{-\alpha y r}{r_1} & \text{for} \quad 0 \le r \le r_1 \end{cases}$$

where $r = a - x$, a is the compact radius, α is the velocity gradient and r_1 is the distance from the centre at which the velocity gradient begins to decrease toward zero. This velocity profile, along with the previously constructed dissolution profile were used to solve the dissolution integral equation.

To apply the method to the compact in the central position, the surface was divided into an outer annular area and an inner circular area. For the central position, a compact of height 8.5mm was also analyzed. The theoretical and experimental results for the dissolution rate from the top surface of a compact in the central position are shown below in Table 2.

Table 2 Dissolution Rates from Top Surface for Compacts in Central Position

Central Position	Theoretical Results(g/sec)	Experimental Results(g/sec)
8.5mm Compact	0.85×10^{-5}	0.902×10^{-5}
3mm Compact	0.998×10^{-5}	0.99×10^{-5}

5   Conclusion

The results obtained from our analysis are in good agreement with those of experiment. This paper has shown that the Pohlhausen method can be a powerful tool in predicting dissolution rates and that it can be applied to cases where an exact solution is not available, as is the case for a compact in the central position. It is proposed next to analyse the curved side surfaces of the compact using the methods we have established in this paper.

References

[1] M. A. Lévêque, Les lois de la transmission de chaleur par convection, Ann Mines **13**, page 201 (1928).
[2] D. M. D'Arcy, O. I. Corrigan and A. M. Healy, Hydrodynamic Simulation of Asymmetrically Positioned Tablets in the Paddle Apparatus: Impact on Dissolution Rates and Variability, Journal of Pharmacy and Pharmacology **Vol.57**, page 1243 (2005).
[3] A. M. Healy, L. G. McCarthy, K. M. Gallagher and O. I. Corrigan, Sensitivity of Dissolution Rate to Location in the Paddle Dissolution Apparatus, Journal of Pharmacy and Pharmacology **Vol.54**, page 441 (2002).