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A Simplified Model of Moisture Transport in Hydrophilic Porous Media With Applications to Pharmaceutical Tablets

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ABSTRACT

This work establishes a predictive model that explicitly recognizes microstructural parameters in the description of the overall mass uptake and local gradients of moisture into tablets. Model equations were formulated based on local tablet geometry to describe the transient uptake of moisture. An analytical solution to a simplified set of model equations was solved to predict the overall mass uptake and moisture gradients with the tablets. The analytical solution takes into account individual diffusion mechanisms in different scales of porosity and diffusion into the solid phase. The time constant of mass uptake was found to be a function of several key material properties, such as tablet relative density, pore tortuosity, and equilibrium moisture content of the material. The predictions of the model are in excellent agreement with experimental results for microcrystalline cellulose tablets without the need for parameter fitting. The model presented provides a new method to analyze the transient uptake of moisture into hydrophilic materials with the knowledge of only a few fundamental material and microstructural parameters. In addition, the model allows for quick and insightful predictions of moisture diffusion for a variety of practical applications including pharmaceutical tablets, porous polymer systems, or cementitious materials.

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Introduction

The importance of moisture transport into pharmaceutical materials is well recognized because of its effect on processing (flow[1] and tabletability[2]), properties (strength and tablet elegance[3]), and, perhaps most important, the efficacy of active ingredients.[4,5] The transport of moisture also plays a significant role in other nonpharmaceutical applications, such as cementitious materials, polymer systems, and the paper industry.[6-8] More contemporary problems related to the effect of moisture pickup during storage on the mechanical integrity of bilayer tablets highlight the importance of transients over equilibrium conditions.[9]

Early work examining the effect of environmental moisture on pharmaceutical tablets made of microcrystalline cellulose (MCC), saccharose, and sodium chloride showed that elevated humidity over a prolonged period of time, multiple days, resulted in a decrease in tablet strength.[10,11] Comparison of tablets produced at different compaction pressures showed that the kinetics of hydration was reduced at higher relative densities.[12] In Jerzewski and Lordi,[13,14] an experimental diffusion apparatus was constructed to examine moisture transport in high-density polyethylene (non-water absorbing) and lactose (water absorbing) tablets and probe the kinetics of water absorption in pharmaceutical materials. In all these cases, a single effective moisture diffusivity was calculated and used to study diffusion kinetics.

The current work aims to address moisture transport in porous media where porosity is present at 2 scales. For example, compacts made by granule compression contain both intragranular and intergranular porosity. The problem is not only highly applicable to pharmaceuticals but also related to other areas. Although the theoretical framework exists in the classic textbook,[15] no solutions have been applied to this particular problem to the best of our knowledge.

The goal of this study was to develop an approximate, yet, predictive model that explicitly recognizes microstructural

parameters in the description of the overall mass uptake and local gradients of moisture into tablets. Accounting for individual diffusion mechanisms, tablet material properties, and microstructure geometry are necessary to accomplish this goal. This work presents an analytical model, which accurately captures the mechanism of moisture diffusion through hydrophilic compacts with porosity at 2 length scales. The model uses material and geometric parameters to determine the time constant of the overall diffusion problem. The solution is generalized to be applicable to any highly adsorbing porous medium. With a known time constant expressed as a function of material properties, and microstructural geometry, the model provides a means to make design decisions without the need for excessive experimentation. Therefore, it provides a starting point for understanding local microscale mechanisms that dictate macroscale behavior related to moisture absorption, such as cracking and swelling.

Theory

The rate of water vapor diffusion through an absorbing porous medium is slower than that through air due to:

- the reduction of cross-sectional area by the presence of the solid,
- the effect of tortuosity recognized in Millington,[16]
- the geometric confinement effects, due to small pore diameter, that can be understood through the Knudsen number, Kn,[17] and
- the absorption of moisture by the solid.

The Knudsen number represents the ratio between the mean free path of water vapor in air to the diameter of a pore. For water vapor in air, the mean free path is approximately 0.1 μm at 30°C.[18] When Kn <1, typically 0.2 or smaller, molecule–molecule collisions occur more frequently than molecule–pore wall collisions. This situation justifies the use of classical molecular diffusion. When Kn >5, the interaction between diffusing species and the pore wall delays the effective diffusion (Knudsen diffusion), and an explicit dependence of the diffusivity D_K on the pore radius, r, must be included, for example[17]:

$$D_K = \left(\frac{8r}{3}\right)\left(\frac{RT}{2\pi m}\right)^{0.5} \tag{1}$$

where T is the temperature, m represents the molecular mass of the diffusing species, and R is the gas constant. A transitional regime exists around Kn = 1 and may be described by a diffusion coefficient that represents both mechanisms

$$\frac{1}{D_{trans}} = \frac{1}{D_K} + \frac{1}{D_o} \tag{2}$$

where D_{trans} is the transitional diffusion coefficient, D_o is the ordinary diffusion coefficient, and D_K is diffusion coefficient at high Kn numbers.[19]

In addition to molecular and pore wall interactions, the solid itself may allow for diffusion through the bulk. Diffusion of water vapor in a solid is drastically slower than the vapor phase through pores.[20,21] Similar to analyses in heat transfer, there exists a Biot number for mass transfer which is defined as

$$Bi = \frac{\beta k_m l}{D_S} \tag{3}$$

where k_m is the mass transfer coefficient from air to material, l is a characteristic length, β is the partition coefficient accounting for the

difference in the equilibrium quantity of moisture in each phase, and D_S is the diffusion coefficient of moisture within the bulk material. When Bi≪1, the diffusion is mass transfer limited, whereas for Bi ≫ 1, the process is limited by the diffusion through the bulk material.

A Diffusion Model

Most porous media inherently contain a wide distribution of pore sizes that may span several length scales from nanometers to microns. Materials made by powder consolidation typically contain 2 forms of porosity: pores between particles, also referred to as interparticle porosity, and pores within particles, or referred to as intraparticle porosity. Most often, both have continuous size distributions that may overlap partially. Dealing with continuous size distributions in numerical models is difficult. For most practical applications, 2 separate populations of pores can be identified corresponding to interparticle and intraparticle porosity.[22,23] Here, these 2 populations are assumed to be distinct so that each one can be represented with an average pore geometry. For pharmaceutical powders, intraparticle porosity is of the order of nanometers, whereas interparticle porosity is of the order of microns. Geometrically, these 2 types of pores can be idealized by a 2-scale periodic arrangement shown schematically in Figure 1, where the interparticle porosity is represented as the larger pores (unit cell 1) and the intraparticle porosity is represented as the smaller pores (unit cell 2). The interparticle pores are interconnected and percolate through the specimen. The intraparticle pores are interconnected and percolate throughout the particle representing porosity only within particles.

As mentioned earlier, the coupling of diffusion in the 2 scales is very difficult. Even if 1-dimensional diffusion is considered at the larger length scale, diffusion at the smaller scale may be 3 dimensional. To avoid such complexities, we develop an approximate model in 2 steps:

(a) First, we create a detailed model for the 2 scales by enforcing some rather strong assumptions for the diffusion at the smaller scale.
(b) Then we identify conditions that lead to a simplified set of equations in such a way that the assumptions enforced in the first step are no longer important.

We consider 1-dimensional (vertical, indicated by the arrow in Fig. 1) water vapor diffusion. We assume that vapor diffuses along the interparticle pore, whereas it also diffuses in the transverse direction into the intraparticle pores. Water vapor is also picked up by the solid material through adsorption as it diffuses along the intraparticle pore. At the same time, diffusion occurs within the solid.

Water vapor diffusion is dictated by concentration gradients in the vapor phase, whereas uptake into the material is governed by the difference in concentration between intraparticle pore and material itself. The diffusion of water through the material may occur both in the direction normal to the intraparticle pore and along the length of the particle.

Three mass balances describe the diffusion process through the interparticle pore, intraparticle pores, and solid, as shown through Equations 4-6, respectively.

$$\frac{\partial C_1}{\partial t} = \frac{D_1}{\phi}\frac{\partial^2 C_1}{\partial y^2} - \frac{k_{12}a_2}{V_1}(C_1 - C_2) \tag{4}$$

$$\frac{\partial C_2}{\partial t} = \frac{D_2}{\phi}\frac{\partial^2 C_2}{\partial x^2} - \frac{k_{2s}a_s}{V_2}(C_2 - \beta C_s) \tag{5}$$