“Fundamentals of Heat and Mass Transfer”, Incropera ve DeWitt 6. Baskısından çözümlü örnekler (Türkçe çeviride olmayan örnekler):

EXAMPLE 14.3

The efficacy of pharmaceutical products is reduced by prolonged exposure to high temperature, light, and humidity. For water vapor–sensitive consumer products that are in tablet or capsule form, and might be stored in humid environments such as bathroom medicine cabinets, *blister packaging* is used to limit the direct exposure of the medicine to humid conditions until immediately before their use.

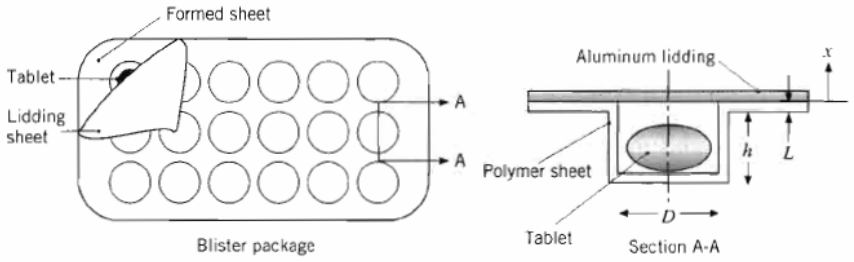
Consider tablets that are contained in a blister package composed of a flat *lidding sheet* and a second, *formed sheet* that includes troughs to hold each tablet. The formed sheet is $L = 50\ \mu m$ thick and is fabricated of a polymer material. Each trough is of diameter $D = 5$ mm and depth $h = 3$ mm. The lidding sheet is fabricated of aluminum foil. The binary diffusion coefficient for water vapor in the polymer is $D_{AB} = 6 \times 10^{-14}$ m^2/s while the aluminum may be assumed to be impermeable to water vapor. For molar concentrations of water vapor in the polymer at the outer and inner surfaces of $C_{A,s1} = 4.5 \times 10^{-3}$ kmol/m^3 and $C_{A,s2} = 0.5 \times 10^{-3}$ kmol/m^3, respectively, determine the rate at which water vapor is transferred through the trough wall to the tablet.

SOLUTION

Known: Molar concentrations of water vapor at the inner and outer surfaces of a polymer sheet and trough geometry.

Find: Rate of water vapor molar diffusive transfer through the trough wall.

Schematic:



Assumptions:

1. Steady-state, one-dimensional conditions.
2. Stationary medium.
3. No chemical reactions.
4. Polymer sheet is thin relative to the dimensions of the trough, and diffusion may be analyzed as though it occurs through a plane wall.

Analysis:

The total water vapor transfer rate is the summation of the transfer rate through the cylindrical walls of the trough and the bottom, circular surface of the trough. From Equation 14.54 we may write

$$N_{A,x} = \frac{D_{AB}A}{L}(C_{A,s1} - C_{A,s2}) = \frac{D_{AB}}{L}\left(\frac{\pi D^2}{4} + \pi Dh\right)(C_{A,s1} - C_{A,s2})$$

Hence

$$N_{A,x} = \frac{6 \times 10^{-14}\ \text{m}^2/\text{s}}{50 \times 10^{-6}\ \text{m}}\left(\frac{\pi(5 \times 10^{-3}\ \text{m})^2}{4} + \pi(5 \times 10^{-3}\ \text{m})(3 \times 10^{-3}\ \text{m})\right)$$
$$\times (4.5 \times 10^{-3} - 0.5 \times 10^{-3})\ \text{kmol/m}^3$$
$$= 0.32 \times 10^{-15}\ \text{kmol/s}$$

Comments:

1. The mass diffusion rate of water vapor is $n_{A,x} = \mathcal{M}_A N_{A,x} = 18\ \text{kg/kmol} \times 0.32 \times 10^{-15}\ \text{kmol/s} = 5.8 \times 10^{-15}\ \text{kg/s}$.
2. The *shelf life* of the medicine is inversely proportional to the rate at which water vapor is transferred through the polymer sheet. Shelf life may be extended by increasing the thickness of the sheet, resulting in increased cost of the package. Specification of materials for use in blister packaging involves tradeoffs between shelf life, cost, formability, and recyclability of the polymer material.

14.6
Mass Diffusion with Homogeneous Chemical Reactions

EXAMPLE 14.6

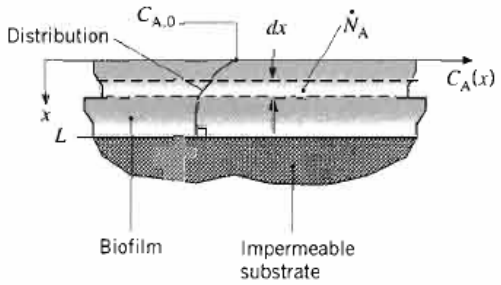
Biofilms, which are colonies of bacteria that can cling to living or inert surfaces, can cause a wide array of human infections. Infections caused by bacteria living within biofilms are often chronic because antibiotics that are applied to the surface of a biofilm have difficulty penetrating through the film thickness. Consider a biofilm that is associated with a skin infection. An antibiotic (species A) is applied to the top layer of a biofilm (species B) so that a fixed concentration of medication, $C_{A,0} = 4 \times 10^{-3}$ kmol/m^3, exists at the upper surface of the biofilm. The diffusion coefficient of the medication within the biofilm is $D_{AB} = 2 \times 10^{-12}$ m^2/s. The antibiotic is consumed by biochemical reactions within the film, and the consumption rate depends on the local concentration of medication expressed as $\dot{N}_A = -k_1 C_A$ where $k_1 = 0.1\ \text{s}^{-1}$. To eradicate the bacteria, the antibiotic must be consumed at a rate of at least 0.2×10^{-3} kmol/s $\cdot$ m^3 ($\dot{N}_A \leq -0.2 \times 10^{-3}$ kmol/s $\cdot$ m^3) since, at smaller absolute consumption rates, the bacteria will be able to grow back faster than it is destroyed. Determine the maximum thickness of a biofilm, L, that may be treated successfully by the antibiotic.

SOLUTION

Known: Topical antibiotic and biofilm properties, surface concentration of the medication, and required minimum consumption rate of antibiotic.

Find: Maximum thickness of a bacteria-laden biofilm, L, that may be successfully treated.

Schematic:



Assumptions:

1. Steady-state, one-dimensional conditions.
2. Stationary, homogeneous medium.
3. Constant properties.
4. Impermeable bottom of the biofilm.

Analysis: The absolute antibiotic consumption rate will be smallest at $x = L$, where the antibiotic concentration is smallest. Thus, we require $\dot{N}_A(L) = -0.2 \times 10^{-3}$ kmol/s $\cdot$ m^3. The expression for the first-order reaction may be combined with Equation 14.74 to write

$$\dot{N}_A(L) = -k_1 C_A(L) = -k_1 \frac{C_{A,0}}{\cosh mL} \tag{1}$$

where

$$m = (k_1/D_{AB})^{1/2} = \left(\frac{0.1\ \text{s}^{-1}}{2 \times 10^{-12}\ \text{m}^2/\text{s}}\right)^{1/2} = 2.24 \times 10^5\ \text{m}^{-1}$$

Equation 1 may be solved for the maximum allowable thickness:

$$L = m^{-1} \cosh^{-1}[-k_1 C_{A,0}/\dot{N}_A(L)] \tag{2}$$

Substituting values into Equation 2 yields

$$\begin{aligned} L &= (2.24 \times 10^5\ \text{m}^{-1})^{-1} \cosh^{-1}[-0.1\ \text{s}^{-1} \times 4 \times 10^{-3}\ \text{kmol/m}^3/ \\ &\quad (-0.2 \times 10^{-3}\ \text{kmol/s} \cdot \text{m}^3)] \\ &= 5.9 \times 10^{-6}\ \text{m} = 5.9\ \mu\text{m} \end{aligned}$$ ◁

Comment: The ability of the antibiotic agent to kill bacteria in thicker biofilms is hampered by the high rate at which the agent is consumed and the slow rate at which it can be diffused through the complex, polymeric matrix of the biofilm [6].

EXAMPLE 14.7

Transdermal drug delivery involves the controlled time-release of medication through the skin to the bloodstream, usually from a *patch* that is adhered to the body. Advantages include steady and mild drug delivery rates that reduce shock to the system as might occur with intravenous infusions, the ability to deliver medication to nauseated or unconscious patients that would be otherwise delivered in oral form, and ease of use.

Consider a square patch of length and width $L = 50$ mm that consists of a host medium containing an initial, uniform density of medication, $\rho_{A,p,i} = 100$ kg/m^3. The patch is applied to the skin, which contains an initial drug concentration of $\rho_{A,s,i} = 0$. At the patch–skin interface located at $x = 0$, the ratio of the medication density on the patch side to the medication density on the patient side is described by a *partition coefficient* of $K = 0.5$.

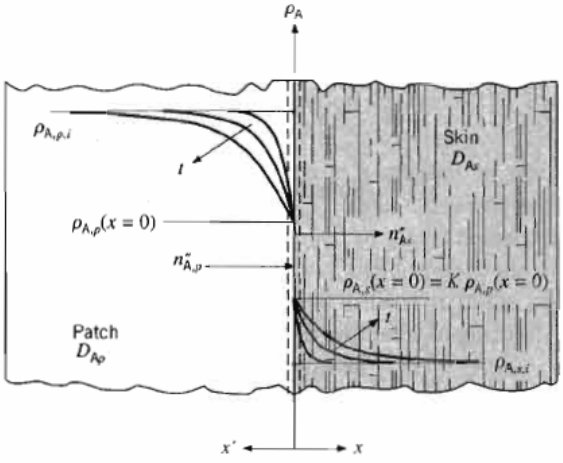
1. Determine the total amount of medication (dosage) delivered to the patient over a treatment period of one week. Nominal values of the diffusion coefficients of the medication within the patch and skin are $D_{Ap} = 0.1 \times 10^{-12}$ m^2/s and $D_{As} = 0.2 \times 10^{-12}$ m^2/s, respectively.
2. Investigate the sensitivity of the total dosage delivered to the patient to the mass diffusivity of the patch, D_{Ap}, and the mass diffusivity of the patient's skin, D_{As}.

SOLUTION

Known: Initial densities of a drug within a transdermal patch, size of the patch, partition coefficient, and mass diffusivities.

Find: Total dosage of medicine delivered to the patient over a one-week time period, sensitivity of the dosage to the mass diffusivity of the patch and skin.

Schematic:



Assumptions:

1. One-dimensional conditions with constant properties.
2. Semi-infinite patch and skin.
3. No chemical reactions.
4. Stationary media.

Analysis:

1. The conservation of species equation applies to both the patch and skin. With the foregoing assumptions, Equation 14.47b becomes

$$\frac{\partial^2 \rho_A}{\partial x^2} = \frac{1}{D_{AB}} \frac{\partial \rho_A}{\partial t}$$

which is analogous to Equation 5.26. Moreover, the initial conditions

$$\rho_A(x < 0,\ t = 0) = \rho_{A,p,i}; \quad \rho_A(x > 0,\ t = 0) = \rho_{A,s,i}$$

boundary conditions

$$\rho_{A,p}(x \to -\infty) = \rho_{A,p,i}; \quad \rho_{A,s}(x \to +\infty) = \rho_{A,s,i} \tag{1a}$$

and interface condition

$$n''_{A,x,p}(x = 0) = n''_{A,x,s}(x = 0) \tag{1b}$$

are analogous to the situation in Figure 5.9 and Equation 5.61 where two semi-infinite solids are brought into thermal contact. In this problem, the partitioning of the species must also be accounted for. That is,

$$\rho_{A,s}(x = 0) = K \cdot \rho_{A,p}(x = 0) \tag{1c}$$

By analogy to Equation 5.62, we have

$$\frac{-D_{Ap}(\rho_{A,p}(x = 0) - \rho_{A,p,i})}{\sqrt{\pi D_{Ap} t}} = \frac{D_{As}(\rho_{A,s}(x = 0) - \rho_{A,s,i})}{\sqrt{\pi D_{As} t}}$$

which, after noting that $\rho_{A,s,i} = 0$, may be solved to yield

$$\rho_{A,s}(x = 0) = \rho_{A,p,i}\left(\frac{\sqrt{D_{Ap}}}{\sqrt{D_{As}} + \sqrt{D_{Ap}}/K}\right) \tag{2}$$

The instantaneous flux of medication to the patient may be determined by noting the analogy with Equation 5.58:

$$n''_A(x = 0,t) = \frac{D_{As}\rho_{A,s}(x = 0)}{\sqrt{\pi D_{As} t}} \tag{3}$$

Substituting Equation 2 into Equation 3 yields

$$n''_A(x = 0,t) = \frac{\rho_{A,p,i}}{\sqrt{\pi t}} \cdot \frac{\sqrt{D_{As}D_{Ap}}}{\sqrt{D_{As}} + \sqrt{D_{Ap}}/K}$$

The dosage, D, delivered to the patient from $t = 0$ to a treatment time of t_t may be expressed as

$$D = L^2 \int_{t=0}^{t_t} n''_A(x = 0,t)dt$$

$$D = \frac{\rho_{A,p,i}L^2}{\sqrt{\pi}} \cdot \frac{\sqrt{D_{As}D_{Ap}}}{\sqrt{D_{As}} + \sqrt{D_{Ap}}/K} \int_{t=0}^{t_t} t^{-1/2}dt$$

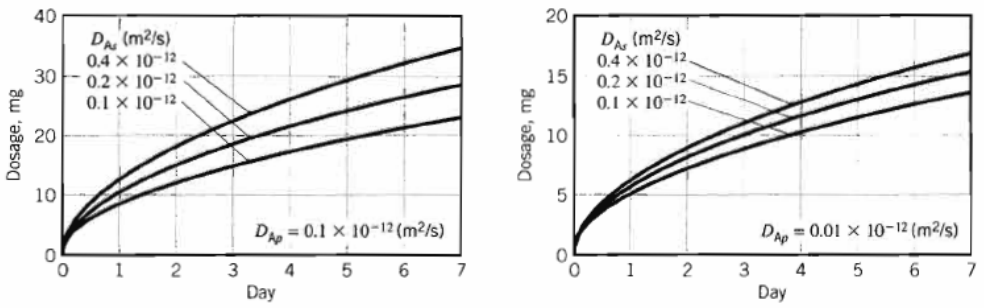
$$= \frac{2\rho_{A,p,i}L^2}{\sqrt{\pi}} \cdot \frac{\sqrt{D_{As}D_{Ap}}}{\sqrt{D_{As}} + \sqrt{D_{Ap}}/K} \sqrt{t_t} \tag{4}$$

For a total treatment time of $t_t = 7$ days $\times$ 24 h/day $\times$ 3600 s/h $= 605 \times 10^3$ s, the dosage is

$$D = \frac{2 \times 100 \text{ kg/m}^3 \times (50 \times 10^{-3} \text{ m})^2}{\sqrt{\pi}} \times \frac{\sqrt{0.2 \times 10^{-12} \text{ m}^2/\text{s} \times 0.1 \times 10^{-12} \text{ m}^2/\text{s}}}{\sqrt{0.2 \times 10^{-12} \text{ m}^2/\text{s}} + \sqrt{0.1 \times 10^{-12} \text{ m}^2/\text{s}}/0.5} \sqrt{605 \times 10^3 \text{ s}}$$

$$= 29 \times 10^{-6} \text{ kg} = 29 \text{ mg} \quad \triangleleft$$

2. The sensitivity of the dosage to the patch and skin mass diffusivities may be evaluated by solving Equation 4 for different combinations of D_{A_p} and D_{A_s}. Results are shown in the following graphs for $D_{A_p} = 0.1 \times 10^{-12}$ m^2/s and 0.01×10^{-12} m^2/s and for $D_{A_s} = 0.1 \times 10^{-12}$ m^2/s, 0.2×10^{-12} m^2/s, and 0.4×10^{-12} m^2/s. Note that as either mass diffusivity is increased, the dosage increases.



Comments:

1. The function of the outer layer of the skin, the *epidermis,* is to protect the body from external contamination. Transdermal drug delivery is feasible only for medications characterized by extremely small molecules that can diffuse through the relatively impenetrable epidermis. Mass transfer considerations restrict the number of drugs that can be delivered transdermally. The skin diffusivity is variable from location to location on the body, and the patient is instructed where to apply the patch.

2. It is desirable to desensitize the dosage to variations in the skin diffusivity, since this parameter varies from patient to patient. Therefore, the host medium of the patch (called the *vehicle*) is designed so that it is the rate-limiting factor in controlling the dosage. The sensitivity of the dosage to the patient's skin diffusivity is reduced by decreasing the mass diffusivity in the vehicle, as evident by comparing the results of part 2 of the problem. In general, it is desirable to design the vehicle so that $D_{A_p}/D_{A_s} \ll 1$.

3. The patch is designed to deliver medication as though it is a semi-infinite medium. The required patch thickness for this assumption to be valid may be estimated by calculating the location where the density of the medication in the vehicle is reduced to 95% of the difference between $\rho_{A,p,i}$ and $\rho_{A,p}(x = 0)$ over the treatment time. By analogy to Equation 5.57, the *species penetration depth,* x_S, associated with 5% depletion of the drug may be determined from

$$\frac{\rho_{A,p}(x') - \rho_{A,p}(x' = 0)}{\rho_{A,p,i} - \rho_{A,p}(x' = 0)} = 0.95 = \text{erf} \frac{x_S}{\sqrt{4 D_{A_p} t_t}}$$

Evaluating this expression yields a species penetration depth of 690×10^{-6} m = 0.69 mm. The assumption of a semi-infinite patch is valid for a vehicle thickness greater than 0.69 mm.

4. If the vehicle is much thinner than the species penetration depth calculated in Comment 3, the actual dosage will fall below the desired dosage prior to the end of the one-week treatment period. Therefore, a tradeoff in the design of the patch involves (a) loading enough medication to assure semi-infinite behavior and (b) minimizing the cost of the patch. In practice, more than 95% of the medication remains in the vehicle after the treatment period, necessitating careful disposal of the patch after its use.