

Moisture Sorption Kinetics for Water-Soluble Substances I: Theoretical Considerations of Heat Transport Control

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Abstract □ A model based on heat transport control was developed to describe the uptake of water on a deliquescent solid in an atmosphere of pure water vapor. The model assumes the presence of a saturated liquid film on the surface of the solid. The decrease in the vapor pressure of water over the surface, brought about by the colligative effect of solid dissolved in the liquid film, is effectively offset by the increase in temperature of the film (and the solid) caused by the heat released on condensation of the water vapor. The thermal transients die out quickly and a steady-state analysis is valid. At steady state the temperature of the liquid film (and solid) is that temperature at which the vapor pressure of water above the saturated solution is equal to the chamber pressure. Consequently, water uptake occurs at a rate that depends on the heat flux away from the surface. The water uptake rate, W_h , is constant at a given relative humidity and is described by an equation of the form $W_h = (C + F) \ln(RH_i/RH_o)$, where C and F are conductive and radiative coefficients, RH_i the chamber relative humidity, and RH_o the relative humidity at and above which continuous water uptake (deliquescence) occurs. The model contains no adjustable parameters and can thus be directly tested against experimental results.

Keyphrases □ Sorption—moisture, water-soluble substances, kinetics, heat transport control, theoretical model with water vapor atmosphere □ Kinetics—moisture sorption of water-soluble substances, heat transport control, theoretical model with water vapor atmosphere □ Deliquescence—water-soluble substances, sorption kinetics, heat transport control, theoretical model with water vapor atmosphere

The interaction of water with pharmaceutical materials plays a fundamental role in many aspects of drug product development, from synthetic design and dosage form selection to effective product packaging and drug bioavailability. The affinity that a substance has for sorbing water from its vapor state is generally referred to as hygroscopicity. Since adsorption or condensation is not an entropically favored process, the water-solid interaction must provide a sufficient enthalpic driving force if such sorption is to occur. Even the relatively weak binding of physisorption, for which the heat of adsorption is comparable to the heat of condensation, can provide this driving force over a large range in relative humidity. At higher relative humidities, multilayer adsorption can occur (1). For water-soluble substances, dissolution of the molecules at the solid surface can occur once such multilayer adsorption is established. Chikazawa, Kanazawa, and others have shown that as few as two layers of adsorbed water can effect hydrated ion formation at relative humidities 30–40% below that humidity associated with the equilibrium water vapor pressure over a saturated solution of the solid (2, 3). This critical relative humidity, or RH_o, characteristic of the solid is that point above which the adsorbed water assumes the character of bulk solution or condensate. Water activity of the condensate is depressed as a result

of the solute present, and the phenomenon of deliquescence is thereby triggered.

Figure 1 shows a schematic representation of the deliquescent process for a soluble drug particle. Suppose that water vapor at a bulk atmosphere relative humidity, RH_i, adsorbs onto the solid surface of the particle. If this humidity is above the RH_o of the drug, further adsorption will occur spontaneously and the thickness of the condensate film will grow. Solid will continue to dissolve and saturate the film, maintaining the relative humidity at the surface at RH_o. To reach equilibrium with the atmosphere at RH_i, total dissolution and some degree of solution dilution must occur. To predict deliquescent behavior *a priori* requires an understanding of what fundamental factors, chemical and environmental, control the kinetics of the process. Despite the practical consequences of deliquescent hygroscopic behavior, only limited investigations of sorption kinetics above RH_o have appeared in the literature (4–8), all using an empirical expression to describe the phenomenon. The purpose of the present study, therefore, was to gain a more quantitative understanding of deliquescence.

BACKGROUND

Consider the overall picture of what processes are operating to control deliquescence in the presence of an inert atmosphere such as air, where adsorption of vapor onto any solid surface involves the simultaneous transport of both mass and heat (9–16). While there may exist additional heat effects, these two processes are at least coupled by the heat of water condensation released per unit mass transported from the vapor to the condensed phase. This is expressed by:

$$W' \cdot \Delta H = Q \quad (\text{Eq. 1})$$

where $W' = dW/dt$ = rate of mass transport (vapor condensation), W is the sample weight at time t , ΔH is the heat generated per unit mass condensed, and Q is the heat flux from the surface at which condensation occurs. The extent to which either process limits or controls the rate of condensation depends on the molecular diffusivities and thermal prop-

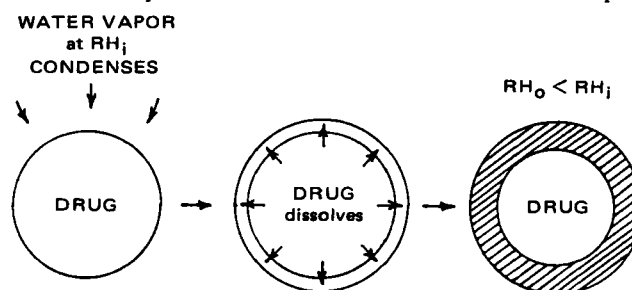


Figure 1—Deliquescent sorption by a water-soluble solid particle.

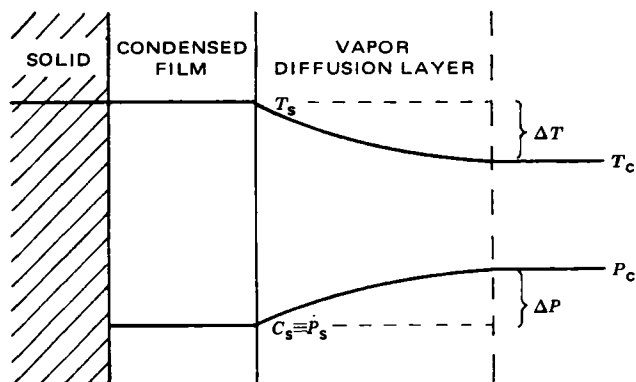


Figure 2—Thermal and pressure gradients existing at a soluble solid surface covered with condensed water.

erties of all phases in the condensing system. For hygroscopic moisture uptake by a solid exhibiting substantial water solubility, such as that illustrated in Fig. 1, this system consists of three phases: pure, undissolved solid; a liquid film of condensate in which solid has dissolved; and water vapor in an atmosphere of inert gas. It follows then that there exist two interfaces over which transport must occur: solid-liquid and liquid-vapor. A closer examination of this condensation system is given in Fig. 2, in which:

$$P_c = RH_i \left(\frac{P_0}{100} \right) \quad (\text{Eq. 2})$$

where P_c is equal to the bulk water vapor pressure in the atmosphere, and

$$P_s = RH_o \left(\frac{P_0}{100} \right) \quad (\text{Eq. 3})$$

where P_s is equal to the water vapor pressure in equilibrium over a saturated solution of the solid; P_0 represents the pressure of pure water vapor at bulk atmosphere temperature, T_c , and C_s and T_s represent the water vapor concentration and the temperature at the surface, respectively. Possible steady-state thermal and pressure gradients are indicated in Fig. 2. Steady-state sorption implies that the driving force for uptake, whether thermal or diffusive, has reached a constant value, *i.e.*, W' is constant.

The zero pressure (or concentration) gradient shown within the liquid film in Fig. 2 is consistent with the assumption that film saturation is maintained throughout steady-state moisture uptake. The likelihood of a zero gradient in temperature within the solid and liquid phases will be substantiated shortly in the discussion of non-steady-state heat transport.

The thermodynamic basis for hygroscopic uptake lies in the difference between P_s and P_c in the vicinity of the saturated film surface. Water vapor will condense progressively on the surface as long as $P_s < P_c$. Three general cases exist when sorption occurs, each implying a different extent to which heat or mass transport controls uptake.

Case i: Mass Transport Control (Isothermal), $\Delta T = 0$, $\Delta P = \Delta P_{\max}$ —Heat generated upon condensation is rapidly transported away from the liquid-vapor interface so as to render the system effectively isothermal throughout the course of steady-state uptake. The pressure difference, ΔP , is maximized since P_s at T_c is less than P_s at T_s for any $T_s > T_c$. The rate of uptake, W' , is then proportional to ΔP and the surface area over which uptake occurs.

Case ii: Heat Transport Control (Isobaric), $\Delta T = \Delta T_{\max}$, $\Delta P = 0$ —Heat generated upon condensation is sufficient to maintain the liquid-vapor interface at a temperature T_s , elevated above that of the bulk atmosphere maintained externally at T_c . The temperature difference, $\Delta T = T_s - T_c$, is exactly that necessary to raise P_s at T_c to P_s at T_s such that P_s at T_s equals P_c at T_c . In this case, W' is proportional to ΔT by virtue of its explicit dependence on the heat flux as given in Eq. 1.

Case iii: Mass-Heat Transport in Balance, $0 < \Delta T < \Delta T_{\max}$, $0 < \Delta P < \Delta P_{\max}$ —The gradients depicted in Fig. 2 exemplify this intermediate situation. Because neither ΔP nor ΔT is constrained to zero, there exists no unique ΔP - ΔT combination which can be predicted *a priori* to satisfy the requirements of steady-state condensation without knowledge of both the thermal and diffusive characteristics of the system.

In considering the three cases given above, it is apparent that for water uptake from an atmosphere of pure water vapor, diffusion barriers to

transport in the vapor phase cannot exist. In the absence of a second gas component, resistance to transport can arise only from the collision of water molecules against one another, which in itself would not generate a measurable gradient in water vapor pressure, *i.e.*, "nature abhors a vacuum." Consequently, the role of heat transport can be tested explicitly by deriving appropriate equations for case *ii* and testing the model with experimental studies using an atmosphere of pure water vapor. The present paper, therefore, reports a theoretical model for case *ii*; the second paper of this series (17) presents a test of this model with experimental studies, and the third paper describes water uptake in an inert atmosphere such as air (18).

THEORETICAL

The sample undergoing sorption is considered to be a compressed circular disk situated symmetrically near the hemispherical base of a cylindrical chamber, a configuration chosen for its experimental feasibility. Figure 3 illustrates the geometry that must be considered in discussing the transport of heat within this system. Regarding the development of a local temperature gradient within the sample disk itself, the disk may be considered to behave as a planar slab if its diameter far exceeds its thickness. With respect to any transport external to the sample or the surface of its developing film, a hollow-sphere geometry will be assumed, consistent with the radial nature of the transport occurring between the disk and the surrounding chamber. Here the sample is represented by a hypothetical inner sphere of radius $r = a$ such that it is equivalent in surface area to that of the sample itself; the chamber then behaves as an outer sphere of radius $r = b$ at which surface the temperature is maintained at T_c . Presuming the disk and chamber to behave as concentric spheres allows a more manageable mathematical treatment of transport occurring in the system. The more rigorous approach of using disk-to-sphere or disk-to-hemisphere transport geometries is unnecessarily complex for two reasons. First, the isotherm surfaces that exist during steady-state heat transport from a disk to a surrounding sphere take on spherical shape as distance from the disk increases, behaving much like a hollow-sphere system when the disk diameter is small relative to the outside sphere. Second, and more practically, the errors associated with predicting transport as if within a closed sphere should have a constant effect for any sample tested in this configuration. Thus, the legitimate theoretical comparison of the hygroscopic behavior of different materials can be made despite these approximations.

Upon condensation, heat is generated at the film surface by two primary sources (in the absence of auxiliary reactions, *e.g.*, hydration, *etc.*): heat of condensation, releasing $\Delta H_v = 0.58$ cal/mg of water condensed; and heat of dissolution, approximately equal to the product of the solubility, C_{sat} , and the heat of solution, ΔH_{soln} . For a number of nonhydrating alkali halide salts, $C_{\text{sat}} \Delta H_{\text{soln}}$ is unlikely to exceed an approximate value of 0.04 cal/mg of water; for such compounds the contribution of the heat of dissolution to the heat generated on condensation can be considered negligible, such that $\Delta H = -\Delta H_v$ in Eq. 1.

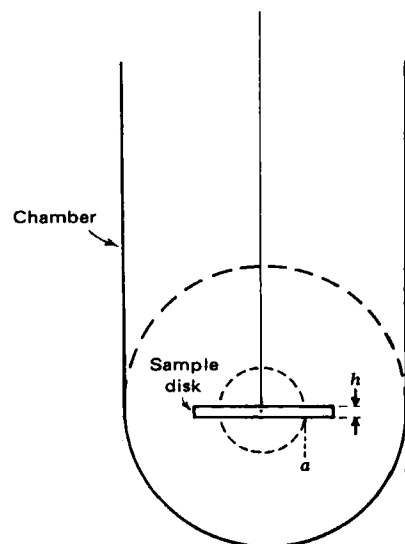


Figure 3—Chamber and sample geometry; slab and hollow-sphere model.

Table I—Physical Constants for the Transport Model in an Atmosphere of Pure Water Vapor

Symbols	Constants
a , cm	0.5 ^a
b , cm	2.0 ^a
M_w , mg/mole	1.8×10^4
k , cal/cm-sec-deg	4.26×10^{-5}
α , cm ² /sec	4.13
ΔH , cal/mole	-10,500 ^b
ΔH_v , cal/mole	10,500
R , cal/deg-mole	1.987
T_c , °K	298
σ , cal/cm ² -sec-deg ⁴	1.36×10^{-12}
e	0.95 ^c

^a Theoretically arbitrary in value; these particular values have been assigned in this case for their consistency with an available experimental apparatus. ^b The assumption is made here that the heat of condensation predominates over all other possible heat effects such that the latter are neglected. ^c Film surface emissivity approximated by value given for pure water (20).

Heat transport away from the surface limits the rate of condensation; thus, uptake depends on the thermal properties of the system. There exist two primary heat sinks in the system described in Fig. 3: the atmosphere surrounding the sample and the sample itself. Heat transport to and through these media can occur *via* three basic mechanisms: conduction inward through the sample or radially outward through the atmosphere; convection, a term used here (in the absence of forced convection) to designate the extra heat transport that occurs as a result of the radially inward bulk flow of water vapor that feeds the condensation process; and radiation from the hypothetical surface $r = a$ to surface $r = b$.

A general expression for heat flux, Q , reflecting the three mechanisms of heat transport (19) is:

$$Q = q_{\text{cond}} + q_{\text{conv}} + q_{\text{rad}} \quad (\text{Eq. 4})$$

where

$$q_{\text{cond}} = -4\pi r^2 \cdot k \frac{dT}{dr} \quad (\text{Eq. 5})$$

$$q_{\text{conv}} = WC_p(T_s - T) \quad (\text{Eq. 6})$$

$$q_{\text{rad}} = A\sigma e(T_s^4 - T_c^4) \quad (\text{Eq. 7})$$

and k is the thermal conductivity of the medium, C_p is the specific heat capacity of the medium, A is the sample surface area = $4\pi a^2$, σ is the Stefan-Boltzmann constant, and e is the emissivity of the sample surface. Table I contains the physical constants of interest.

Before discussing the quantitative implications of steady-state uptake for heat transport-controlled condensation, it is necessary to estimate the time required to establish steady-state thermal gradients within the system, *i.e.*, within both the solid disk and the surrounding atmosphere. In doing so the assumption is made that thermal conductivity, thermal diffusivity, and specific heat values are independent of water vapor concentration and temperature.

Non-Steady-State Heat Transport—Sample Disk—Only conduction need be considered for heat transport within the sample disk. The time-dependent temperature distribution for a slab of thickness, h , whose parallel surfaces are subjected to a sudden change in temperature has already been determined in the literature (21, 22). The sample disk can be assumed to behave according to this model if edge effects are neglected. Specifically, the disk region bounded by $-h/2 < z < +h/2$ is subjected to the boundary conditions that $T = T_c$ for all z at $t = 0$ and $T = T_s$ at $z = \pm h/2$ for $t > 0$. The temperature profile describing one-half of the (symmetrical) slab for $z = 0$ to $z = h/2$ is given by (21):

$$T = T_s + \frac{4}{h} \sum_{n=0}^{\infty} \exp[-\alpha(2n+1)^2\pi^2t/h^2] \cos \frac{(2n+1)\pi z}{h} \cdot \left[\frac{h(-1)^{n+1}T_s + T_c}{(2n+1)\pi} + T_c \int_0^{h/2} \cos \frac{(2n+1)\pi z'}{h} dz' \right] \quad (\text{Eq. 8})$$

where α is the thermal diffusivity of the solid slab. In dimensionless terms this can be written (21, 22):

$$T^* = 1 - \frac{4}{\pi} \sum_{n=0}^{\infty} \frac{(-1)^n}{2n+1} \cdot \exp[-(2n+1)^2\pi^2t^*/4] \cos \frac{(2n+1)\pi z^*}{2} \quad (\text{Eq. 9})$$

in which:

$$T^* = \frac{T - T_c}{T_s - T_c} \quad (\text{Eq. 10})$$

$$z^* = \frac{z}{h/2} \quad (\text{Eq. 11})$$

$$t^* = \frac{\alpha t}{(h/2)^2} \quad (\text{Eq. 12})$$

From Eq. 9 it can be shown (21, 22) that the center ($z = 0$) of such a slab reaches 97% of its equilibrium value by dimensionless time, $t^* = 1.5$, from which real time can be calculated. For example, the center portion of a (relatively) thin solid disk of potassium chloride crystal of $\alpha = 0.056$ cm²/sec and a thickness $h = 0.06$ cm should attain ~97% of its final temperature change, ΔT , within 0.03 sec. Thus, one could predict that thermal equilibrium should be rapidly established within such materials as the alkali halide salts. Furthermore, the heat required to raise, for example, a 150-mg sample of potassium chloride ($C_p = 0.162$ cal/g-deg) by a $\Delta T = 5^\circ$ is 0.12 cal. Since heat is released at the disk surface at the rate of 0.58 cal/mg of water vapor condensed, the role of such a disk as a significant heat sink over the course of substantial steady-state uptake can be considered negligible.

Atmosphere—The time required to establish a steady-state temperature gradient external to the disk surface depends on the non-steady-state component of heat transport radially outward from the sample. Such heat transport through the atmosphere can occur *via* all three mechanisms identified earlier, and indeed they all contribute to maintaining the steady-state gradient. If the water vapor atmosphere is considered transparent to radiation, however, only conduction and convection will contribute to the establishment of the gradient. Since the effect of convection on maintaining the steady state will be shown to be negligible in the following discussion, only conductive flux will be considered in the non-steady-state gradient development.

The solution for the time-dependent temperature distribution in the atmosphere is readily accessible from the non-steady-state mass and heat transport equations developed in Appendix I. In terms of dimensionless variables where T^* is defined in Eq. 10 and the analogous distance and time variables are defined as:

$$r^* = \frac{r - a}{b - a} \quad (\text{Eq. 13})$$

and

$$t^* = \frac{\alpha t}{(b - a)^2} \quad (\text{Eq. 14})$$

the expression for T^* , as taken from Eq. A8, becomes:

$$T^* = \left[\frac{1}{r^*(b/a - 1) + 1} \right] \cdot \left[1 - r^* - \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{1}{n} \sin n\pi r^* \cdot \exp(-n^2\pi^2 t^*) \right] \quad (\text{Eq. 15})$$

This function is described in Fig. 4 where $\Pi^* = T^*$. For condensation in vacuum (where $b - a = 1.5$ cm) the time required to reach $t^* = 0.5$ is only 0.28 sec. If air were present, steady-state gradients would essentially be attained within 5.6 sec given an estimated value of $\alpha = 0.214$ cm²/sec for humid air¹. As apparent earlier for the disk, it can be concluded that a steady thermal state is rapidly established within the atmosphere relative to the time scale of extended uptake.

The time required for the conductive heat flux, and therefore uptake rate, to reach a steady-state level at surface $r = a$ can be calculated using Eq. A21. For the example above, these lag times equal (-)0.047 sec and (-)0.94 sec in vacuum and in air, respectively. These times are consistent with the development of the temperature gradients as established in Fig. 4. At surface $r = b$, lag times are calculated using Eq. A25, and for the vacuum and air systems equal 0.94 sec and 1.9 sec, respectively.

Steady-State Heat Transport—Steady-state moisture uptake requires a constant heat flux, by virtue of the coupling in Eq. 1; this, in turn, implies the maintenance of a constant ΔT . The ΔT necessary to raise P_s at T_c to P_s at T_s such that it equals P_c at T_c , as implied by heat transport control, can by first approximation be estimated by the Clausius-Clau-

¹ Since heat transfer will also contribute to sorption kinetics in air, and since the effect of air will be discussed in the third paper in this series (18), lag times in reaching steady state both in vacuum and air are included at this point for comparison purposes, as developed in Appendix I. This value for humid air was estimated using C_p values of water vapor and air weighted by mole fraction and thermal conductivity (k) values for water vapor and air, as taken from Table I and as calculated using the Lindsay and Bromley modification of the Wassiljewa equation (23), respectively.

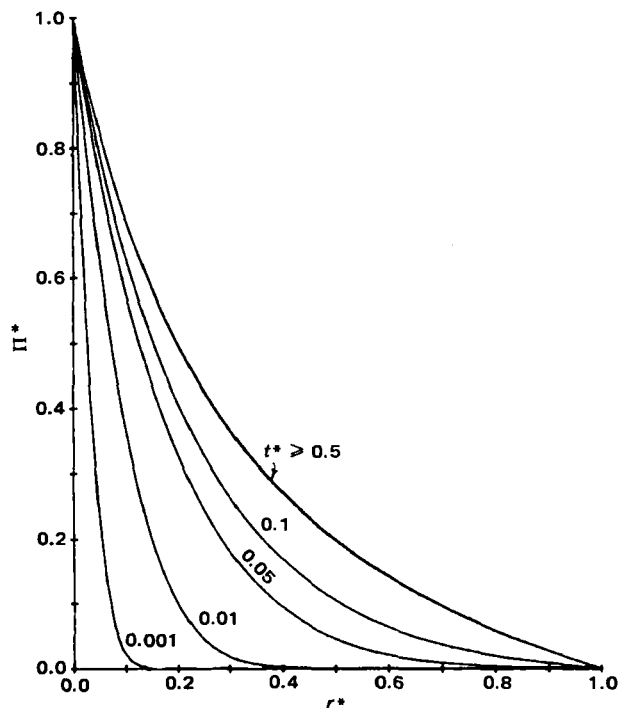


Figure 4—Gradient in Π^* at various t^* values for a hollow sphere, $a < r < b$, where $b/a = 4$.

peyron equation as developed below:

$$\ln \frac{P_s(T_s)}{P_s(T_c)} = \ln \frac{P_c(T_c)}{P_s(T_c)} \quad (\text{Eq. 16})$$

$$= \ln \frac{RH_i}{RH_o} \quad (\text{Eq. 17})$$

such that:

$$\ln \frac{RH_i}{RH_o} = \frac{\Delta H_v}{RT_s T_c} (T_s - T_c) \quad (\text{Eq. 18})$$

where ΔH_v is the heat of vaporization and R is the gas constant. Solving for ΔT , one obtains:

$$T_s - T_c = \frac{RT_c^2 \ln \frac{RH_i}{RH_o}}{\Delta H_v - RT_c \ln \frac{RH_i}{RH_o}} \quad (\text{Eq. 19})$$

For several nonhydrating alkali halide salts whose solubility and RH_o dependence on temperature are known (24, 25), ΔT as defined above is observed to vary from 0–15°, depending on the ratio of $RH_i(T_c)$ to $RH_o(T_c)$. Use of the Clausius-Clapeyron equation to estimate these ΔT values for saturated salt solutions is subject to two sources of error: the small temperature dependence of the heat of vaporization of pure water and, more significantly, the effect of the salt and its (temperature-dependent) solubility on water activity and the heat of vaporization. Despite these errors, Eq. 19 predicts ΔT values equal to 100–110% of those actually observed (24, 25) for saturated solutions of the alkali halides.

The evaluation of transient-state heat flux within and heat capacity of the sample disk suggests that the disk has a negligible effect on the maintenance of ΔT . Of primary importance, then, is the radial heat flow within the hollow-sphere system. From Eqs. 4–7 this steady-state flux can be expressed as:

$$Q = -4\pi r^2 \cdot k \frac{dT}{dr} + W'C_p(T_s - T) + A\sigma e(T_s^4 - T_c^4) \quad (\text{Eq. 20})$$

During steady-state flux:

$$\frac{dQ}{dr} = 0 \quad (\text{Eq. 21})$$

Therefore:

$$0 = 4\pi k \frac{d}{dr} \left(r^2 \frac{dT}{dr} \right) + W'C_p \frac{dT}{dr} \quad (\text{Eq. 22})$$

where the derivative of the radiation term vanishes under the assumption that the atmosphere is transparent to radiative flux. Differentiating the product term and rearranging leads to:

$$\frac{d^2 T}{dr^2} + \left(\frac{2}{r} + \frac{W'C_p}{4\pi k r^2} \right) \frac{dT}{dr} = 0 \quad (\text{Eq. 23})$$

Solving the equation by reduction of order and then applying the boundary conditions, $T = T_s$ at $r = a$ and $T = T_c$ at $r = b$, one arrives at the expression:

$$T = \frac{T_s \left[\exp \left(\frac{W'C_p}{4\pi k r} \right) - \exp \left(\frac{W'C_p}{4\pi k b} \right) \right] - T_c \left[\exp \left(\frac{W'C_p}{4\pi k r} \right) - \exp \left(\frac{W'C_p}{4\pi k a} \right) \right]}{\left[\exp \left(\frac{W'C_p}{4\pi k a} \right) - \exp \left(\frac{W'C_p}{4\pi k b} \right) \right]} \quad (\text{Eq. 24})$$

Expressed in terms of T^* as defined in Eq. 10:

$$T^* = \frac{1 - \exp \left[\frac{W'C_p}{4\pi k} \left(\frac{1}{r} - \frac{1}{b} \right) \right]}{1 - \exp \left[\frac{W'C_p}{4\pi k} \left(\frac{1}{a} - \frac{1}{b} \right) \right]} \quad (\text{Eq. 25})$$

The above expressions describe the steady-state temperature gradient within the hollow sphere as maintained by both conduction and convection. Convection is used here to denote the heat transport that occurs in raising the temperature of the water vapor surrounding the sample to T_s just prior to its condensation. It will be shown that this convective component of the flux has essentially no effect on the temperature gradient given W' values of experimental magnitude. Neglecting the convective term, Eq. 22 becomes:

$$0 = 4\pi k \frac{d}{dr} \left(r^2 \frac{dT}{dr} \right) \quad (\text{Eq. 26})$$

This leads to a second-order differential equation whose solution over the same boundary conditions is:

$$T = (T_s - T_c) \frac{a}{r} \left(\frac{b-r}{b-a} \right) \quad (\text{Eq. 27})$$

or

$$T^* = \frac{a}{r} \left(\frac{b-r}{b-a} \right) \quad (\text{Eq. 28})$$

As expected, this is the same gradient described by Eq. (A4) as $t \rightarrow \infty$. As the term $W'C_p/4\pi k$ increases, convection is more likely to influence the temperature profile. Yet even at a relatively high uptake rate of $W' = 2 \text{ mg/min}$ in the vacuum system, for which the value of $C_p/4\pi k = 837 \text{ cm-sec/g}$, the temperature gradient remains effectively indistinguishable from the steady-state profile exhibited in Fig. 4, in which convection was neglected. Consistent with this result, it has been shown (26) that convection contributes negligibly (<2%) to the overall steady-state heat flux from the surface $r = a$. This flux is then given by:

$$Q \Big|_{r=a} = -4\pi k a^2 \frac{dT}{dr} \Big|_{r=a} + q_{\text{rad}} \quad (\text{Eq. 29})$$

$$= -4\pi k a^2 (T_s - T_c) \frac{dT^*}{dr} \Big|_{r=a} + q_{\text{rad}} \quad (\text{Eq. 30})$$

which on substituting Eqs. 7 and 28 yields:

$$Q \Big|_{r=a} = \frac{4\pi k a b}{b-a} (T_s - T_c) + 4\pi a^2 \sigma e (T_s^4 - T_c^4) \quad (\text{Eq. 31})$$

Recalling Eq. 1, the uptake rate may easily be expressed in terms of T_s by utilizing the above equation. It is of greater interest, however, to determine the direct dependence of W' , the dependent experimental variable, on RH_i , the independent variable. An expression relating ΔT to RH_i is given by Eq. 19. A comparable expression for $\Delta(T^4)$ is required for substitution into the radiation term. From Eq. 19 the solution for T_s can be raised to the fourth power and simplified by dropping all terms contributing <2% (for RH_i/RH_o ratios <2.7) to the resulting overall polynomial. This leads to an approximate expression for $\Delta(T^4)$ similar in form to that for ΔT :

$$T_s^4 - T_c^4 = \frac{4RT_c^5 \ln \frac{RH_i}{RH_o}}{\Delta H_v - 4RT_c \ln \frac{RH_i}{RH_o}} \quad (\text{Eq. 32})$$

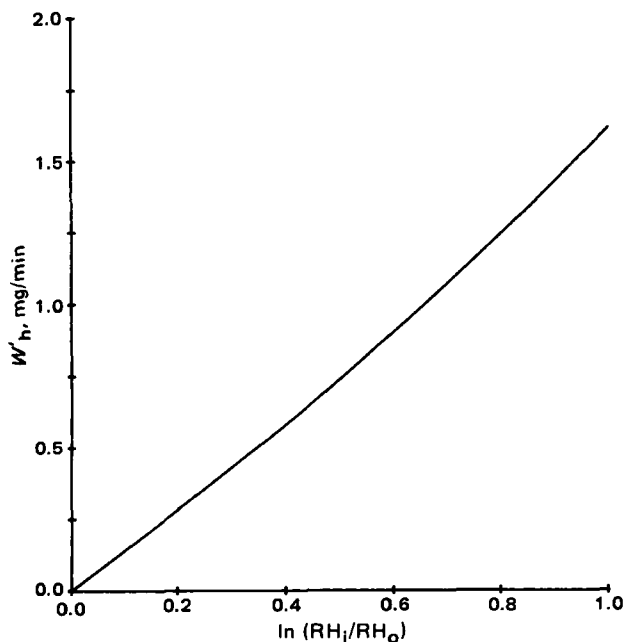


Figure 5—Theoretical W'_h versus $\ln(RH_i/RH_o)$ as predicted by Eq. 33.

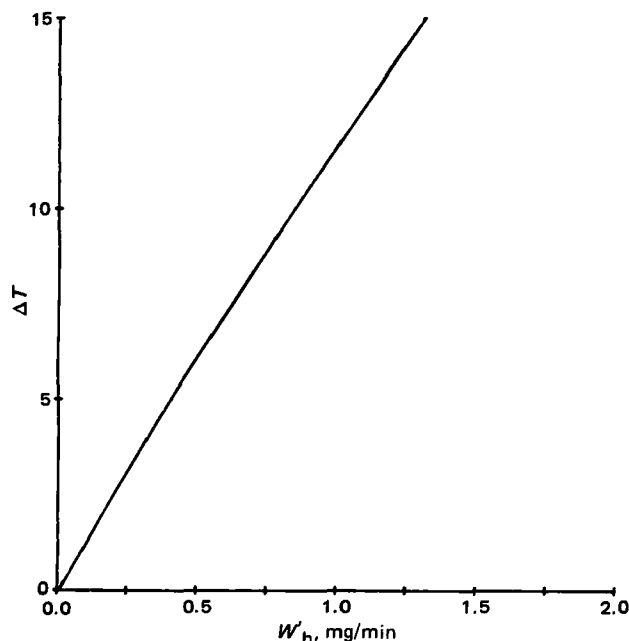


Figure 6—Relationship between ΔT and W'_h for heat transport-controlled sorption (see Table I).

Substituting Eqs. 19 and 32 into Eq. 31, then combining with Eq. 1, one arrives at a final equation for the dependence of W' , or W'_h to indicate heat transport control, on RH_i :

$$W' = W'_h = \left[\frac{60M_w \cdot 4\pi kab}{\Delta H(b-a)} \left(\frac{RT_c^2}{\Delta H_v - RT_c \ln \frac{RH_i}{RH_o}} \right) + \frac{60M_w \cdot 4\pi a^2 \sigma \epsilon}{\Delta H} \left(\frac{4RT_c^5}{\Delta H_v - 4RT_c \ln \frac{RH_i}{RH_o}} \right) \right] \cdot \ln \frac{RH_i}{RH_o} \quad (\text{Eq. 33})$$

where the factor $60M_w$ simply converts W'_h from mole/sec to mg/min. More simply:

$$W'_h = (C + F) \ln \frac{RH_i}{RH_o} \quad (\text{Eq. 34})$$

where C and F represent the conduction and radiative terms, respectively, in Eq. 33 and are themselves weakly dependent on $\ln(RH_i/RH_o)$. Interestingly, C and F , *i.e.*, conduction and radiation, contribute almost equally to heat transport in an atmosphere of pure water vapor.

Eq. 33 allows *a priori* prediction of heat transport-controlled uptake rates for condensation systems whose geometry is well defined and whose physical properties are known. Furthermore, the curve so predicted and shown in Fig. 5 represents a unique curve for W'_h as a function of $\ln(RH_i/RH_o)$ that should be common to all materials, regardless of their RH_o values, given the same sample and chamber geometry.

Since ΔT is a unique function of $\ln(RH_i/RH_o)$ by virtue of the Clausius-Clapeyron relation and W'_h is also a unique function of $\ln(RH_i/RH_o)$, ΔT and W'_h should be interdependent if condensation is indeed proceeding under thermal control. Again using the parameters listed in Table I, the predicted graph of ΔT versus W'_h is given in Fig. 6.

SUMMARY

A heat transport control model for water uptake by solids has been developed for the case of a water-soluble solid immersed in an atmosphere of pure water vapor. The model is based on the fact that the heat of condensation of water released during water uptake must be transported to the surroundings. In an atmosphere of pure water vapor, where diffusion does not occur, this heat flux limits the rate of condensation.

Development of a non-steady-state model indicates that the non-steady time period is very short. Thus, a steady-state model is appropriate for time periods of pharmaceutical interest. The equations for heat transport (conduction, convection, and radiation) when combined with the Clausius-Clapeyron equation lead to an equation which predicts the water uptake rate with no adjustable parameters (Eq. 33). The results of the analysis indicate that the convection term is of minor importance and that conduction and radiation control heat flux to comparable degrees.

APPENDIX I: NON-STEADY STATE

The non-steady-state solution referred to previously is developed herein. Since non-steady-state considerations are of interest both here and in subsequent papers, which include mass transport considerations, a general solution is developed for both heat and mass transport. Because of the analogous behavior of mass diffusion and (conductive) heat flow, the general parameter, Π , will be used to represent either concentration (C) or temperature (T). Similarly, the symbol, τ , will be used to represent a general diffusivity in place of D or α .

The general equation for radial diffusion with a constant diffusion coefficient is:

$$\frac{\partial \Pi}{\partial t} = \tau \left[\frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial \Pi}{\partial r} \right) \right] \quad (\text{Eq. A1})$$

The solution to this equation describes the time dependence of either the concentration distribution for mass diffusion or the temperature distribution for conductive heat flux in which all velocity gradients associated with convection and viscous dissipation have been assumed to be equal to zero (27). For the hollow-sphere system in which $a < r < b$, subjected to the boundary conditions $\Pi = \Pi_c$ for all r at $t = 0$, $\Pi = \Pi_s$ at $r = a$, and $\Pi = \Pi_c$ at $r = b$ for $t > 0$, Π is described by the function (28):

$$\begin{aligned} \Pi = & \frac{a\Pi_s}{r} + \frac{(b\Pi_c - a\Pi_s)(r-a)}{r(b-a)} \\ & + \frac{2}{\pi r} \sum_{n=1}^{\infty} \left\{ \frac{b\Pi_c \cos n\pi - a\Pi_s}{n} \right. \\ & \cdot \sin \frac{n\pi(r-a)}{b-a} \cdot \exp[-\tau n^2 \pi^2 t / (b-a)^2] \left. \right\} \\ & + \frac{2\Pi_c}{r(b-a)} \sum_{n=1}^{\infty} \left\{ \sin \frac{n\pi(r-a)}{b-a} \cdot \exp[-\tau n^2 \pi^2 t / (b-a)^2] \right. \\ & \cdot \left. \int_a^b r' \sin \frac{n\pi(r'-a)}{b-a} dr' \right\} \quad (\text{Eq. A2}) \end{aligned}$$

Given that Π^* is defined as:

$$\Pi^* = \frac{\Pi - \Pi_c}{\Pi_s - \Pi_c} \quad (\text{Eq. A3})$$

it can be shown that the nature of Eq. A1 does not change if expressed in dimensionless terms, *i.e.*, Π^* can be substituted for Π in Eq. A1. Thus, the solution expressed by Eq. A2 for Π is readily adapted to a solution for Π^* according to Eq. A3. Because the boundary conditions are redefined as $\Pi^* = 1$ at $r = a$ ($\Pi = \Pi_s$) and $\Pi^* = 0$ at $r = b$ ($\Pi = \Pi_c$), however, the solution for Π^* simplifies to:

$$\begin{aligned} \Pi^* = & \frac{a}{r} + \frac{(-a)(r-a)}{r(b-a)} \\ & + \frac{2}{\pi r} \sum_{n=1}^{\infty} \left\{ \frac{-a}{n} \sin \frac{n\pi(r-a)}{b-a} \cdot \exp[-\tau n^2 \pi^2 t / (b-a)^2] \right\} \quad (\text{Eq. A4}) \end{aligned}$$

where the fourth term vanishes when expressed in dimensionless form. Then, allowing:

$$t^* = \frac{\tau t}{(b-a)^2} \quad (\text{Eq. A5})$$

and

$$r^* = \frac{r-a}{b-a} \quad (\text{Eq. A6})$$

where then

$$\frac{a}{r} = \frac{1}{r^*(b/a - 1) + 1} \quad (\text{Eq. A7})$$

and substituting these new variables into Eq. A4, the expression for Π^* further simplifies to:

$$\begin{aligned} \Pi^* = & \left[\frac{1}{r^*(b/a - 1) + 1} \right] \left[1 - r^* - \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{1}{n} \sin n\pi r^* \right. \\ & \cdot \left. \exp(-n^2 \pi^2 t^*) \right] \quad (\text{Eq. A8}) \end{aligned}$$

The time course to developing a steady-state Π^* gradient over r^* can then be plotted for various t^* values at a given ratio of b/a . Figure 4 presents such a plot for $b/a = 4$, where the incremented value of n was truncated at $n = 20$. Discontinuities observed in the $t^* = 0.001$ plot at $\Pi^* \sim 0$ would not have appeared if n were to have been truncated at an even higher value. It is clear from Fig. 4 that the gradient at $t^* = 0.5$ is virtually indistinguishable from the $t^* = \infty$ curve.

To determine the time required for the actual flux, and hence uptake rate, to reach a steady-state level, the time

dependence of the flux must be evaluated. Total mass flux from the surface $r = a$ over time t is given by:

$$W_t \Big|_{r=a} = \int_0^t -D \frac{\partial C}{\partial r} \Big|_{r=a} dt' \quad (\text{Eq. A9})$$

The term ρC_p must be introduced into the analogous expression for heat flux:

$$Q_t \Big|_{r=a} = \int_0^t -\rho C_p \cdot \alpha \frac{\partial T}{\partial r} \Big|_{r=a} dt' \quad (\text{Eq. A10})$$

or

$$Q_t \Big|_{r=a} = \int_0^t -k \frac{\partial T}{\partial r} \Big|_{r=a} dt' \quad (\text{Eq. A11})$$

where k is the thermal conductivity of the medium in the hollow sphere. Because of the introduction of the additional parameter k and the potential confusion of its appearance with α in the solution to Eq. A11, the flux associated with heat conduction, rather than mass diffusion, will be solved for in the following development.

In terms of T^* , r , and t , where T^* is defined by Eq. 10 and is consistent with the definition of Π^* :

$$Q_t \Big|_{r=a} = -k(T_s - T_c) \int_0^t \frac{\partial T^*}{\partial r} \Big|_{r=a} dt' \quad (\text{Eq. A12})$$

Allowing S to represent the summation term in Eq. A8 in which $\Pi^* = T^*$,

$$\frac{\partial T^*}{\partial r} \Big|_{r=a} = -\frac{1}{a} - \frac{1}{b-a} + \frac{\partial S}{\partial r} \Big|_{r=a} \quad (\text{Eq. A13})$$

where:

$$\begin{aligned} \frac{\partial S}{\partial r} \Big|_{r=a} = & -\frac{2a}{\pi r} \Big|_{r=a} \frac{\partial}{\partial r} \sum_{n=1}^{\infty} \left\{ \frac{1}{n} \sin \frac{n\pi(r-a)}{b-a} \right. \\ & \cdot \left. \exp[-\alpha n^2 \pi^2 t / (b-a)^2] \right\} \Big|_{r=a} \\ & + \frac{2a}{\pi r^2} \sum_{n=1}^{\infty} \left\{ \frac{1}{n} \sin \frac{n\pi(r-a)}{b-a} \cdot \exp[-\alpha n^2 \pi^2 t / (b-a)^2] \right\} \Big|_{r=a} \quad (\text{Eq. A14}) \end{aligned}$$

$$= -\frac{2}{b-a} \sum_{n=1}^{\infty} \exp[-\alpha n^2 \pi^2 t / (b-a)^2] \quad (\text{Eq. A15})$$

Then:

$$\begin{aligned} \int_0^t \frac{\partial T^*}{\partial r} \Big|_{r=a} dt' = & -\frac{bt}{a(b-a)} - \frac{2}{b-a} \\ & \cdot \int_0^t \sum_{n=1}^{\infty} \exp[-\alpha n^2 \pi^2 t' / (b-a)^2] dt' \quad (\text{Eq. A16}) \end{aligned}$$

$$\begin{aligned} = & -\frac{bt}{a(b-a)} - \frac{2(b-a)}{\alpha \pi^2} \left\{ \sum_{n=1}^{\infty} \frac{1}{n^2} \right. \\ & \left. - \sum_{n=1}^{\infty} \frac{1}{n^2} \cdot \exp[-\alpha n^2 \pi^2 t / (b-a)^2] \right\} \quad (\text{Eq. A17}) \end{aligned}$$

Since:

$$\sum_{n=1}^{\infty} \frac{1}{n^2} = \frac{\pi^2}{6} \quad (\text{Eq. A18})$$

then

$$Q_t \Big|_{r=a} = k(T_s - T_c) \left\{ \frac{bt}{a(b-a)} + \frac{b-a}{3\alpha} - \frac{2(b-a)}{\alpha\pi^2} \cdot \sum_{n=1}^{\infty} \frac{1}{n^2} \cdot \exp[-\alpha n^2 \pi^2 t / (b-a)^2] \right\} \quad (\text{Eq. A19})$$

As $t \rightarrow \infty$, the total conductive flux from surface $r = a$ becomes:

$$Q_{t\infty} \Big|_{r=a} = k(T_s - T_c) \left[\frac{b}{a(b-a)} \right] \left[t + \frac{a(b-a)^2}{3\alpha b} \right] \quad (\text{Eq. A20})$$

revealing a lag time to steady-state flux of:

$$t_{\text{lag},r=a} = - \frac{a(b-a)^2}{3\alpha b} \quad (\text{Eq. A21})$$

The total heat flux at the surface $r = b$ over time t can be similarly evaluated. In this case:

$$\frac{\partial T^*}{\partial r} \Big|_{r=b} = - \frac{a}{b(b-a)} + \frac{\partial S}{\partial r} \Big|_{r=b} \quad (\text{Eq. A22})$$

which leads to:

$$Q_t \Big|_{r=b} = k(T_s - T_c) \left\{ \frac{at}{b(b-a)} - \frac{a(b-a)}{6\alpha b} - \frac{2a(b-a)}{b\alpha\pi^2} \cdot \sum_{n=1}^{\infty} \frac{(-1)^n}{n^2} \cdot \exp[-\alpha n^2 \pi^2 t / (b-a)^2] \right\} \quad (\text{Eq. A23})$$

As $t \rightarrow \infty$, the total conductive flux to surface $r = b$ becomes:

$$Q_{t\infty} \Big|_{r=b} = k(T_s - T_c) \left[\frac{a}{b(b-a)} \right] \left[t - \frac{(b-a)^2}{6\alpha} \right] \quad (\text{Eq. A24})$$

revealing a lag time to steady-state flux at the outside surface of:

$$t_{\text{lag},r=b} = \frac{(b-a)^2}{6\alpha} \quad (\text{Eq. A25})$$

Note that the final equations given above for total heat flux and the lag times to steady state at either surface $r = a$ or $r = b$ (Eqs. A19, A21, A23, and A25) can be readily converted to the analogous expressions in time-dependent mass flux by replacing Q_t and T by W_t and C , respectively, and by replacing both α and k by D .

APPENDIX II: GLOSSARY

a	effective sample radius, radius of hypothetical inner sphere
A	surface area
b	chamber radius
c	subscript, chamber
C	concentration
C	conduction term
C_p	heat capacity
C_s	surface concentration
C_{sat}	saturation solubility
D	(vapor) diffusion coefficient
e	emissivity
F	radiation term
h	thickness of sample disk
ΔH	heat generated or consumed per unit moisture condensed

ΔH_{soln}	heat of solution
ΔH_v	heat of vaporization
k	thermal conductivity
M_w	molecular weight of water
P	water vapor pressure
P_c	pressure in atmosphere (chamber)
P_0	pressure of pure water vapor at given temperature
P_s	pressure at sample surface
ΔP	pressure difference
ΔP_{max}	maximum pressure difference, taken as $P_c - P_s$
q_{cond}	conductive heat flux
q_{conv}	convective heat flux
q_{rad}	radiative heat flux
Q	heat flux
Q_t	quantity of heat flow in time t
r	radius
r^*	dimensionless radius
R	gas constant
RH _i	relative humidity in atmosphere
RH _o	critical relative humidity of a substance associated with the relative humidity in equilibrium over a saturated solution of the substance
s	subscript, at the sample surface
S	series term
t	time
t^*	dimensionless time variable
$t_{\text{lag},r=a}$	lag time to steady-state flux at surface $r = a$
T	temperature
T_c	temperature in chamber, i.e., at temperature-controlled wall of chamber
T_s	temperature at sample surface
T^*	dimensionless temperature variable
ΔT	temperature difference
ΔT_{max}	maximum temperature difference, taken as $T_s - T_c$
W	sample weight
W'	sorption rate
W_h	sorption rate associated with heat transport control
z	slab thickness
z^*	dimensionless slab thickness
α	thermal diffusivity
Π	general mass or heat quantity, non-steady state
Π^*	dimensionless non-steady-state general mass on heat quantity variable
σ	Stefan-Boltzmann constant
τ	diffusivity

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ACKNOWLEDGMENTS

Submitted by L. Van Campen to the University of Wisconsin-Madison in 1981, in partial fulfillment of the doctor of philosophy degree requirements.

L. V. C. expresses appreciation for graduate fellowship support to the American Foundation for Pharmaceutical Education and Merck Sharp and Dohme Research Laboratories.

Moisture Sorption Kinetics for Water-Soluble Substances II: Experimental Verification of Heat Transport Control

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Abstract □ The rates of water sorption as a function of relative humidity for water-soluble substances exhibiting deliquescence have been measured in an atmosphere of pure water vapor. The substances studied included a series of alkali halides, choline halides, and sugars. The results were compared with a theoretical model, previously described, which relates the rate of water uptake to the transport of heat produced during the process away from the surface. Taking into account the heat of water vapor condensation, heat of solution, and heat of hydration, when hydration occurs, the model allows excellent *a priori* prediction of water uptake rates as a function of relative humidity.

Keyphrases □ Sorption—kinetics, alkali halides, choline halides, and sugars in a water vapor atmosphere, application of theoretical model □ Kinetics—moisture sorption, alkali halides, choline halides, and sugars in a water vapor atmosphere, application of theoretical model □ Deliquescence—sorption kinetics, alkali halides, choline halides, and sugars in a water vapor atmosphere, application of theoretical model

A quantitative treatment for the kinetics of water vapor sorption onto water-soluble solids which exhibit deliquescence has been developed in the preceding paper (1). The treatment was confined to situations where the rate is determined solely by the kinetics of heat transfer away from the surface to the atmosphere surrounding the solid. It was assumed that the resultant film of aqueous solution is saturated with respect to the dissolved solid throughout the process.

The model essentially says that heat generated upon condensation of water vapor, and any other heat change

occurring during sorption, maintains the liquid-vapor interface at a temperature, T_s , elevated above that of the bulk atmosphere, externally maintained at T_c . The water vapor pressure over the saturated film, therefore, rises with temperature until the pressure difference between surface and atmosphere becomes infinitesimal, and remains so during steady-state uptake. The ability of the system to transfer heat away from the surface is assumed to limit the sorption rate. This sorption rate, W_h' , was shown to depend on the relative humidity of the atmosphere, RH_i , and that in equilibrium with the saturated aqueous film around the solid, RH_o , as described by the equation:

$$W_h' = \left[\frac{60M_w \cdot 4\pi k a b}{\Delta H(b-a)} \left(\frac{RT_c^2}{\Delta H_v - RT_c \ln \frac{RH_i}{RH_o}} \right) + \frac{60M_w \cdot 4\pi a^2 \sigma e}{\Delta H} \times \left(\frac{4RT_c^5}{\Delta H_v - 4RT_c \ln \frac{RH_i}{RH_o}} \right) \right] \cdot \ln \frac{RH_i}{RH_o} \quad (\text{Eq. 1})$$

0022-3549/83/1200-1388\$01.00/0
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