

Research Article

Psychrometric Analysis of the Environmental Equivalency Factor for Aqueous Tablet Coating

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Abstract. Process control of aqueous tablet coating depends on a number of thermodynamic and psychrometric variables. Since many of these variables are interdependent, the choice of parameters by which to control the process or designate a design space is not necessarily obvious. Several mass or heat conservation models for aqueous tablet coating can be found in the literature, varying in approach and proposed method for controlling the coating process. A commonly used first-principles model built upon the coupled heat and mass transfer in evaporative mass transfer derives an “Environmental Equivalency” (EE) factor as an indicator of the relative rate of water evaporation from the tablet bed surface and as a relevant scaling factor for aqueous coating. The EE factor is expressed by an equation involving ten individual parameters; however, if the derivation of EE is extended further under the context of an adiabatic process, a much-simplified yet equivalent expression for EE emerges consisting of only three parameters, each directly measurable or obtainable from a psychrometric chart and which bear direct significance to the gross thermodynamic conditions of the coating. The psychrometric model herein is presented as a more physically evocative description of the coating process, enhancing process understanding and potentially playing a key role in a Quality by Design approach to defining an aqueous coating design space.

KEY WORDS: aqueous tablet coating; environmental equivalency; psychrometric chart; scale up; thermodynamics.

INTRODUCTION

Aqueous tablet film coating has become a ubiquitous part of pharmaceutical manufacturing since Abbott marketed the first film-coated tablet in 1953. Tablet film coatings are used for aesthetic reasons (color), taste masking, controlling drug release, or for applying an active pharmaceutical

ingredient to a core tablet. For environmental and economic reasons, aqueous coating has become preferred over solvent-based coating.

The ability to predict the performance of a tablet coater, specifically in regards to the parameters that impact the film coating quality, is essential for efficient and effective scale-up where processing conditions may vary greatly. This is especially true in the case of functional coatings that require a contiguous, homogeneous film in order to impart the functional properties of the coating. Some potential problems encountered in tablet coating as a result of poor control of the thermodynamic conditions are sticking defects from operating at too wet of a tablet bed, while conditions that are too dry can result in spray-drying and a porous, “orange-peel” film coating.

Since the coating process involves a large number of parameters not independent of each other, an empirical Design of Experiments (DoE) approach alone is insufficient to achieve the process understanding needed to accomplish robust process design and scale-up. The coating process involves a large number of parameters convoluted with each other, and without a theoretical framework in which to understand these parameters, a purely empirical approach would tend to be cumbersome, laborious, and ultimately unreliable. A number of first-principles thermodynamic coating models have been reported in the literature as being useful for understanding and predicting the performance and scale-up of aqueous tablet coating and the key parameters

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NOMENCLATURE: A , surface area (m^2); c_p , constant pressure specific heat ($J/kg \cdot K$); h , enthalpy of moist air (J/kg); h_{fg} , latent heat of evaporation (J/kg); H_{loss} , heat loss (J/s); k , mass transfer coefficient ($kg/m^2 \cdot s$) or heat transfer coefficient ($J/m^2 \cdot K \cdot s$); K , empirical heat loss coefficient ($J/K \cdot s$); \dot{m} , rate of mass transfer (kg/s); M , molecular weight (mol/kg); p , pressure (Pa); q , rate of heat transfer (J/s); RH, relative humidity (%); R , ideal gas constant ($J/mol \cdot K$); T , temperature ($^{\circ}C$ or K); Y , mass fraction in vapor phase. **Greek:** ρ , density (kg/m^3); ω , humidity ratio (kg water per kg dry air). **Subscripts:** 1, point 1; 2, point 2; ∞ , free stream; a , dry air; $a+w$, moist air; amb , ambient; B , tablet bed; ex , exhaust conditions; $film$, film conditions; h , heat transfer; i , species i ; in , inlet conditions; m , mass transfer; na , nozzle air; pa , process air; w , water; wb , wet bulb conditions.

which impact the quality of the film coating (1–5). It has been reported (5) that the Environmental Equivalency (EE) model proposed by Ebey (6) is the most widely used aqueous coating model and has also been incorporated into the TAAC computer program published by Thomas Engineering (7). The EE model has been frequently cited in recent papers and texts on aqueous tablet coating (1–11).

The EE factor is a measure of the predicted drying rate occurring in the wetted tablet bed, and if EE is kept constant, it is proposed that equivalent film coating quality can be obtained upon scale-up or changes in operating parameters. While the equation for EE is arrived at via a coupled heat and mass transfer analysis, the aim of this work is to show that EE is equivalently expressed by relating the internal thermodynamic conditions to the saturation conditions (i.e., where the exhaust is fully saturated or 100% relative humidity (RH)) along a constant enthalpy line on a psychrometric chart. This model, by using a few reasonable approximations, reduces the published equation for EE to a greatly simplified expression. The benefits of this approach will be discussed in relation to process understanding, process design and scale-up, as well as the Quality by Design concept of design space.

Pan-coating or fluidized bed coating process is a batch process and as such consists of both a transient period related to the start-up of the process and a steady-state period comprising the rest of the coating process. This analysis applies to the steady-state operation of the coater.

THEORY

Coating Process Heat and Mass Balance

A basic diagram of a pan coater is shown in Fig. 1, where the process airflow is shown to enter the inlet plenum (IN), flow into rotating perforated pan containing the tablet bed, enter the tablet bed (1), exit the bed (2), and flow out the exhaust plenum (EX). Additional air inlet streams are the spray nozzle atomization and pattern air (not shown). The following analysis applies equally well to a fluidized bed coater.

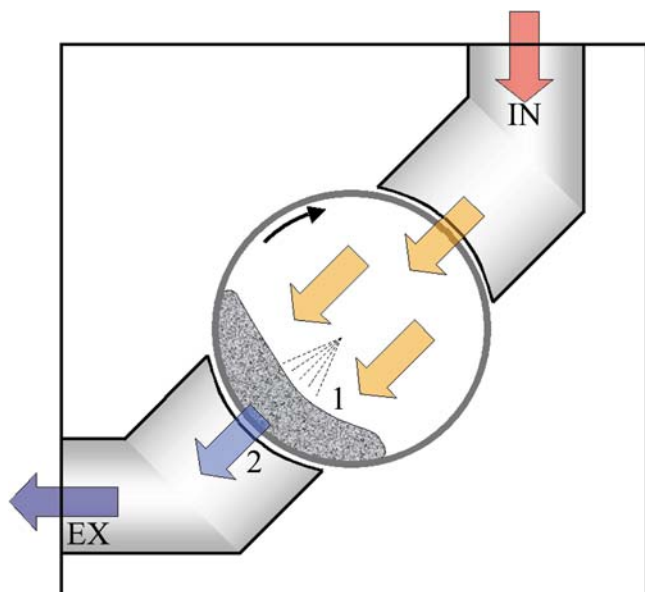


Fig. 1. Pan coater diagram

An accounting of inlet and exhaust heat and mass flows is a straightforward exercise. The total specific enthalpy at Point 1 is the sum of the enthalpies associated with the inlet air flow, the nozzle air flow, and the spray solution, minus heat loss occurring between the point of inlet temperature measurement and Point 1:

$$h_1 = (\dot{m}_{pa}h_{in} + \dot{m}_{na}h_{na} + \dot{m}_w h_w - H_{loss,in}) / (\dot{m}_{pa} + \dot{m}_{na}) \quad (1)$$

If the evaporation of the spray solution is assumed to occur in the tablet bed without heat loss to the external environment, enthalpy is conserved, and the evaporation occurring between Points 1 and 2 is an adiabatic process:

$$h_2 = h_1 \quad (2)$$

Again, if heat loss is occurring post-bed, the exhaust specific enthalpy will be equal to the specific enthalpy at Point 2 after heat loss is accounted for.

$$h_{ex} = h_2 - H_{loss,ex} / (\dot{m}_{pa} + \dot{m}_{na}) \quad (3)$$

The mass balance for water is equally straightforward:

$$\omega_2 = (\dot{m}_{pa}\omega_1 + \dot{m}_{na}\omega_{na} + \dot{m}_w) / (\dot{m}_{pa} + \dot{m}_{na}) \quad (4)$$

$$\omega_{in} = \omega_1$$

$$\omega_{ex} = \omega_2$$

Since $\dot{m}_{pa} \gg \dot{m}_{na}$ for typical aqueous coating and the enthalpy contribution of the liquid spray solution is negligible compared to that of an equivalent mass of water vapor, Eqs. 1, 3, and 4 respectively can usually be simplified without incurring significant error:

$$h_2 = h_1 = h_{in} - H_{loss,in} / \dot{m}_{pa} \quad (5)$$

$$h_{ex} = h_2 - H_{loss,ex} / \dot{m}_{pa} \quad (6)$$

$$\omega_2 = \omega_1 + \dot{m}_w / \dot{m}_{pa} \quad (7)$$

Psychrometric Interpretation of Coater Operation

This process can be graphically represented on a psychrometric chart (see Fig. 2), where contours of constant relative humidity, specific volume and specific enthalpy are plotted against dry bulb temperature and humidity ratio ω . Psychrometric charts are readily available for a range of temperatures and pressures and can also be generated by commercial software programs. The psychrometric charts shown here were generated by a custom macro-driven MS Excel® spreadsheet, solving for moist air enthalpy and volume using virial equations of state and relative humidity from psychrometric relationships (12). For the purpose of illustration, an example of a coating “operating line” is shown where the inlet conditions are $T_{in}=68^\circ\text{C}$ and $\omega_{in}=0.006$. The heat loss from the Inlet to Point 1 is a constant absolute humidity cooling process resulting in $T_1=60^\circ\text{C}$, followed by an adiabatic (constant enthalpy) evaporation process from Point 1 to Point 2 where $T_2=37^\circ\text{C}$ and $\omega_2=0.015$, and then another constant absolute humidity cooling process depicting

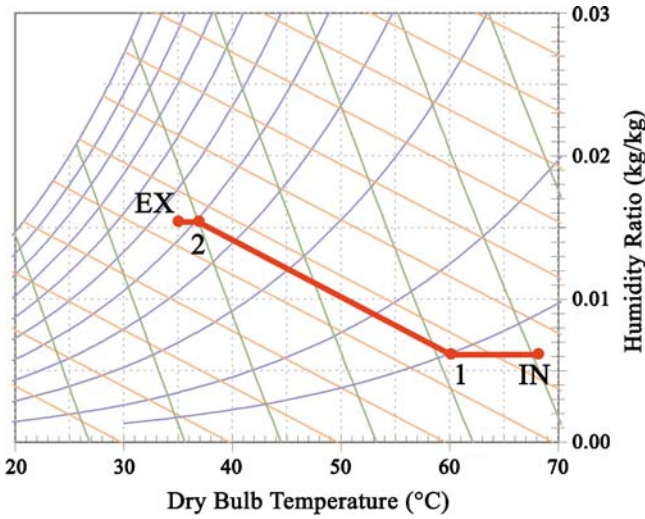


Fig. 2. Example of a non-adiabatic coating process on psychrometric chart. *Orange* specific enthalpy (kJ/kg); *blue* relative humidity (%); *green* specific volume (m^3/kg)

the heat loss from Point 2 to the Exhaust at temperature $T_{\text{ex}} = 35^\circ\text{C}$.

It is usually the case that coater installations include both temperature and humidity measurements at both the Inlet and Exhaust points. Point 1 may be determined empirically if the process air temperature can be reliably measured near the bed so that the effect of heat loss can be avoided. Alternatively, Point 1 can be estimated from the inlet temperature if a heat loss coefficient has been determined, for example, using an empirical expression as shown in Eq. 8:

$$T_1 = T_{\text{in}} - \frac{K}{\dot{m}_{\text{pa}} c_p} (T_{\text{in}} - T_{\text{amb}}) \quad (8)$$

If these empirical determinations are not deemed reliable, it is usually the case that temperature T_2 and the bed temperature closely coincide so that an infrared thermometer can accurately estimate T_2 . With measured inlet and exhaust absolute humidity, Point 1 can be found by the intersection of the horizontal inlet absolute humidity line with the constant enthalpy line through Point 2. Alternatively, Eq. 7 can be employed to estimate either the inlet or exhaust absolute humidity based on the other since the spray rate is a known quantity. In general, only three quantities are needed to specify the adiabatic operating line since the slope of the adiabatic operating line is constant for an air/water system.

Original Derivation of EE Factor

The original derivation for the EE factor is clarified below, beginning with Newton's law of cooling for the heat transfer between two points shown in Eq. 9, here labeled with "∞" to indicate the relatively hot, dry air stream and "B" to indicate the relatively cooler, moist tablet bed.

$$q = k_h A_h (T_\infty - T_B) \quad (9)$$

Since evaporation is an endothermic process, the evaporation rate is proportional to the heat supplied where the proportionality constant is the latent heat of vaporization, h_{fg} .

Although h_{fg} does vary with temperature, it is treated as a constant in accordance with the original derivation of Ebey.

$$\dot{m}_w = \frac{q}{h_{fg}} \quad (10)$$

Analogously to Eq. 9, the rate of mass transfer of a species i across an interface may be expressed as a function of a mass transfer driving force, which according to mass transfer theory is the difference in mass fraction of the species across the interface.

$$\dot{m} = k_m A_m (Y_{w,B} - Y_{w,\infty}) \quad (11)$$

The mass fraction of a species i in a gas mixture can be defined as the ratio of the mass of species i over the total mass of the mixture, or equivalently as the ratio of the density ρ_i over the total density of the mixture. In addition, the equation of state for an ideal gas is given by Eq. 12:

$$p_i = \frac{\rho_i R T}{M_i} \quad (12)$$

Incorporating the definition of mass fraction along with the ideal gas equation of state into Eq. 11 yields the following expression for rate of mass transfer:

$$\dot{m}_w = k_m A_m \left[\frac{M_w p_{w,wb}}{R T_{wb}} - \frac{M_w p_{w,\infty}}{R T_\infty} \right] \quad (13)$$

Here, it is implied that the evaporative mass transfer is occurring in the wetted part of the bed that is assumed to be at the wet-bulb temperature, hence the change in subscript from "B" to "wb" (to be precise, since tablet coating in the absence of heat loss to the surroundings is an adiabatic cooling process, the adiabatic saturation temperature should be used instead of the wet-bulb temperature. However, for air-water mixtures, the two coincide so closely that they are often used interchangeably). Since \dot{m}_w is common to Eqs. 10 and 13, they can be combined together as shown:

$$\frac{A_h}{A_m} = \frac{\left[\frac{M_w p_{w,wb}}{R T_{wb}} - \frac{M_w p_{w,\infty}}{R T_\infty} \right]}{k_h (T_\infty - T_B)} k_m h_{fg} \quad (14)$$

The ratio of k_m over k_h can be estimated by applying the Chilton-Colburn analogy (13) that expresses this ratio in terms of the dimensionless Lewis number:

$$\frac{k_h}{k_m \rho_{\text{film}} c_p} = Le^{2/3} \quad (15)$$

The Lewis number relates the thermal diffusion rate from a wet surface to the mass diffusion rate, and for air-water systems, the Lewis number is close to unity for a wide range of temperature and pressure (14), indicating that evaporation mass transfer and heat transfer are strongly coupled. This fact is also why the wet-bulb temperature for air-water systems coincides very closely with the adiabatic saturation temperature. Assuming $Le=1$, Eq. 14 becomes:

$$\frac{A_h}{A_m} = \frac{\left[\frac{M_w p_{w,wb}}{R T_{wb}} - \frac{M_w p_{w,\infty}}{R T_\infty} \right] h_{fg}}{\rho_{\text{film}} c_p (T_\infty - T_B)} \quad (16)$$

Finally, the theory is practically applied to a tablet coater by the approximations $T_2 = T_B$ and $T_1 = T_\infty$, resulting in Eq. 17.

$$EE = \frac{A_h}{A_m} = \frac{\left[\frac{M_w p_{w,wb}}{RT_{wb}} - \frac{M_w p_{w,1}}{RT_1} \right] h_{fg}}{\rho_{\text{film}} c_p (T_1 - T_2)} \quad (17)$$

In Ebey's analysis, the density of moist air in the denominator of Eq. 17 is evaluated at a film temperature $T_{\text{film}} = (T_1 + T_2)/2$, although it is not clear that $(T_1 + T_{wb})/2$ is not more appropriate. Evaporative mass transfer would be associated with wetted tablets having a surface temperature closer to the wet-bulb temperature while the bulk bed temperature is an average over the entire bed. Further, a value of 2,502 kJ/kg (corresponding to 0°C) was used for h_{fg} in the original derivation, most likely because this is a standard value. However, as previously mentioned, h_{fg} is a function of temperature and a difference in EE as large as 5% or more might result by evaluating h_{fg} at, say, a $T_{\text{film}} = 60^\circ\text{C}$ instead of at 0°C. The dry air specific heat c_p is only a very weak function of temperature and here is treated as a constant.

As described by Ebey, one can vary individual coating parameters such as spray rate, inlet or exhaust temperatures or inlet humidity, but as long as the EE factor is held constant, one should expect to observe a consistent film-coating quality.

Psychrometric Analysis of EE Derivation

Equation 17 can be further simplified. Hereafter, the nomenclature EE' is used to indicate the EE factor under the new derivation. Returning to Eqs. 11 and 12, the two mass fraction terms in Eq. 11 can be expressed in terms of density ratios instead of pressures and following a similar development as before the following equation can be written:

$$EE' = \frac{\left[\frac{\rho_{w,wb}}{\rho_{a+w,wb}} - \frac{\rho_{w,1}}{\rho_{a+w,1}} \right] h_{fg}}{c_p (T_1 - T_2)} \quad (18)$$

The following psychrometric relation for humidity ratio ω , the mass ratio of water vapor to air of an air–water mixture, can now be employed:

$$\omega = \frac{M_w p_w}{M_a P_a} = \frac{M_w \rho_w RT / M_w}{M_a \rho_a RT / M_a} = \frac{\rho_w}{\rho_a} \quad (19)$$

Since $\rho_{a+w} = \rho_a + \rho_w$ and $\rho_w \ll \rho_a$ for moist air typical of coating conditions,

$$EE' = \frac{(\omega_{wb} - \omega_1) h_{fg}}{(T_1 - T_2) c_p} \quad (20)$$

If an overall heat balance is determined for the coater, the evaporation rate can be determined as a function of the inlet and exhaust temperatures as shown in Eq. 21. In addition, the evaporation rate can be expressed in terms of the mass flow rate of dry air and the difference in inlet and outlet humidity ratios as shown in Eq. 22:

$$\dot{m}_w = \frac{\dot{m}_a (h_{a,1} - h_{a,2})}{h_{fg}} = \frac{\dot{m}_a c_p (T_1 - T_2)}{h_{fg}} \quad (21)$$

$$\dot{m}_w = \dot{m}_a (\omega_2 - \omega_1) \quad (22)$$

Solving Eqs. 20 and 22 for h_{fg} , and substitution of this result into Eq. 19 yields a simple expression for EE' :

$$EE' = \frac{(\omega_{wb} - \omega_1)}{(\omega_2 - \omega_1)} \quad (23)$$

The inverse of this expression for EE' is identical to that obtained in the mass balance derivation for the vaporization efficiency parameter E for aqueous coating developed earlier by Reiland and coworkers (15), although the relevance of this result to the drying kinetics of a wetted tablet was not specifically noted in that analysis. Vaporization efficiency as defined in Eq. 23 has traditionally been employed in industrial drying and has recently been described as a means of characterizing spray drying processes such as microencapsulation in the food industry (3). That the coupled heat and mass transfer approach of Ebey yields a result that is thermodynamically equivalent to the vaporization efficiency E is notable. Examination of Eq. 23 reveals that as the solution spray rate approaches zero, the denominator would also approach zero (i.e., no evaporation), resulting in an infinite EE' . As the outlet conditions approach saturation, the coater evaporation rate approaches the maximum possible where $\omega_2 = \omega_{wb}$, hence EE' approaches unity.

Since Eq. 23 is expressed entirely in terms of humidity ratio, it may be illuminating to examine this result on a psychrometric chart as shown in Fig. 3. An operating line indicating the gross internal thermodynamic conditions of the coater is plotted similar to the previous example in Fig. 2 but as a purely adiabatic process (the adiabatic operating line of an actual coater can be determined as described in the "INTRODUCTION" section). The dotted extension of the adiabatic operating line terminates at the saturation line where the air–water mixture attains 100% RH, also known as

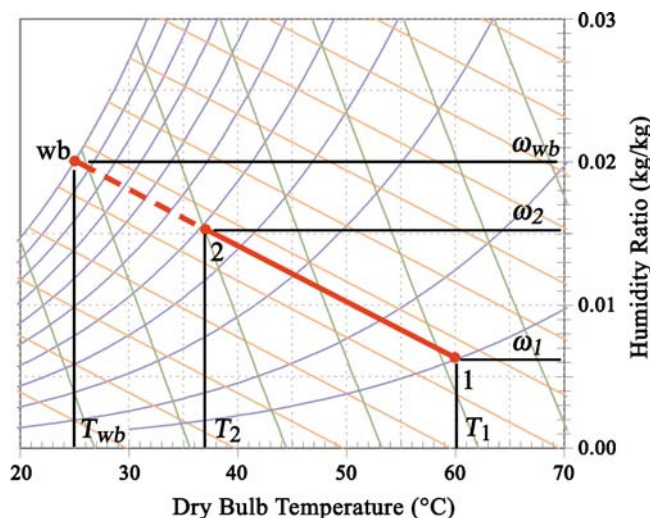


Fig. 3. Psychrometric chart with adiabatic coating operating line

the adiabatic saturation temperature. For brevity, the following shorthand nomenclature is used:

$$\begin{aligned}\Delta \omega &\equiv \omega_2 - \omega_1 \\ \Delta \omega_{wb} &\equiv \omega_{wb} - \omega_1 \\ \Delta T &\equiv T_2 - T_1 \\ \Delta T_{wb} &\equiv T_{wb} - T_1\end{aligned}$$

In Fig. 3, ω_1 , ω_2 , and ω_{wb} are the y-axis coordinates of Point 1, Point 2, and wet-bulb points of the operating line, respectively. Similarly, T_1 , T_2 , and T_{wb} are x-axis coordinates of the same points of the operating line, respectively. Because the adiabatic operating line is linear, the following equality is valid:

$$EE' = \frac{1}{E} = \frac{\Delta \omega_{wb}}{\Delta \omega} = \frac{\Delta T_{wb}}{\Delta T} \quad (24)$$

Finally, because E (or the inverse of EE') has a finite range of $[0, 1]$, it would seem to be a more mathematically amenable expression than EE' . Therefore, in this work, the vaporization efficiency E , as determined by employing the ΔT approach described herein, is proposed as a superior alternative.

$$E = \frac{\Delta T}{\Delta T_{wb}} \quad (25)$$

Although it has been shown that the Ebey EE factor and the vaporization efficiency E , determined either by the $\Delta \omega$ or the ΔT method, both embody the same thermodynamic information for an aqueous coating system (neglecting minor approximations in the respective derivations), the benefit of the ΔT method for determining E is that it combines both a first-principles understanding of the evaporation process with a resulting parameter that is easily determined yet theoretically rigorous. The use of direct temperature measurements and the psychrometric chart allows ready calculation of E represented by the simplified Eqs. 5–7, though a comprehensive thermodynamic balance represented by Eqs. 1–4 can also be employed by interpolation on a psychrometric chart or via calculations that can be easily automated in a software spreadsheet using numerical estimates to thermodynamic and psychrometric data (12).

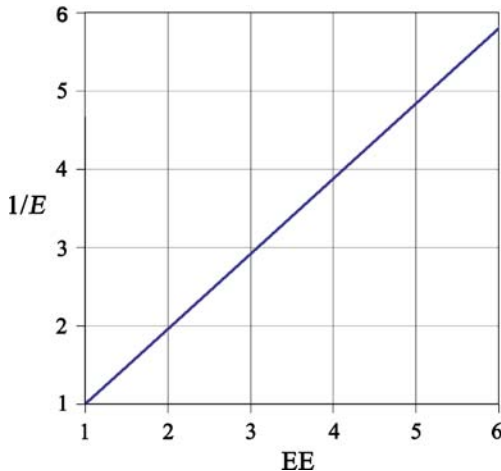


Fig. 4. Comparison of $1/E$ to EE

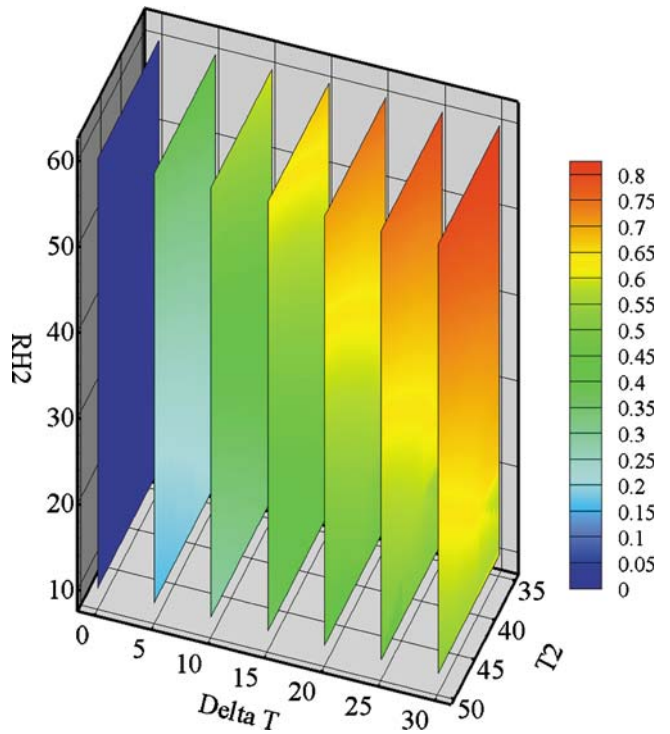


Fig. 5. E as a function of T_2 , ΔT , and RH_2 , sliced along ΔT axis

RESULTS AND DISCUSSION

Comparison to Original EE Calculation

The inverse of E as a function of EE is plotted in Fig. 4. A temperature and absolute humidity was chosen for Point 2, thereby fixing T_{wb} , and a solution spray rate was varied to produce a range over which T_1 could vary. Equation 17 together with the heat and mass balance equations were used to determine EE , while E was determined from Eq. 24. For this calculation, the moist air density in Eq. 17 was estimated at $T_{film} = (T_1 + T_2)/2$ in accordance with Ebey's analysis. The latent heat of vaporization was also estimated at T_{film} for the sake of thermodynamic consistency. Over the range of $EE=1-6$, the two calculations compare favorably with less than a maximum 4% discrepancy. It has been suggested in the literature (10) that the EE factor is ideally kept in a range from 3 to 6, corresponding to keeping E in the approximate range of 0.17–0.33.

E as a Function of Measured Inlet and Exhaust Temperature and Humidity

To illustrate how E varies with respect to both the temperature axis and humidity axis on a psychrometric chart, E is plotted as a function of T_2 , ΔT , and RH_2 in Figs. 5 and 6 for a subset of possible conditions. It is observed that E is relatively insensitive to changes in the temperature at Point 2, keeping ΔT and RH_2 constant. This conclusion can also be drawn from an examination of the psychrometric chart (Fig. 2), allowing Point 2 to vary over a constant RH contour while keeping ΔT constant. Similarly, it can also be seen that E would likewise be insensitive to changes in the Point 1 temperature, again keeping ΔT and RH_2 constant. Some variation in E is observed with respect to changes in the

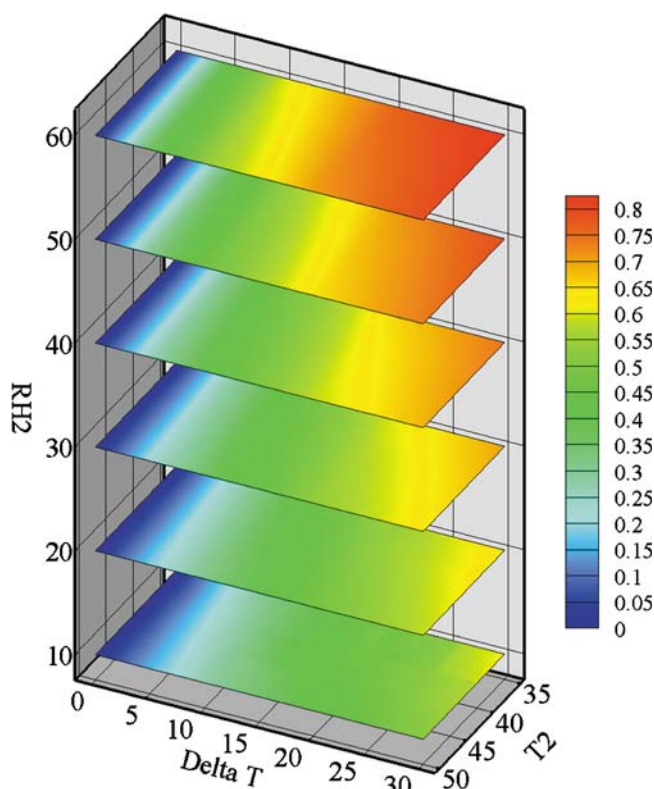


Fig. 6. E as a function of T_2 , ΔT , and RH_2 , sliced along RH_2 axis

temperature of either Point 1 or Point 2 because lines of constant RH tend to converge or diverge with dry bulb temperature. In contrast, E is a strong function of humidity at Point 2 (and likewise humidity at Point 1, since one is a function of the other via Eq. 4).

Practical Application of E to Aqueous Coating Design Space

The concept of design space is a key component of quality risk management in the drug product development process (16), otherwise known as Quality by Design. As has been shown, to specify the entire adiabatic coating operating line requires a minimum of three parameters. Temperature and humidity alone may be used, or alternately combinations of coating parameters such as spray rate, inlet humidity, and process air flow rate may be specified as long as the two points defining the adiabatic operating line can be explicitly determined from these parameters.

Generally speaking, the Design of Experiments approach is usually the most effective starting point for developing a design space for a unit operation where a first-principles understanding is lacking or insufficient to adequately describe the relationships between the relevant parameters. For a three-parameter design space for a tablet film coating, a traditional DoE screening design approach might employ a three-factor two-level factorial design consisting of nine to twelve experiments to roughly define the design space, while optimization of the design space may involve composite designs with more experimental points. A reduction in dimensionality of the design space from three parameters to one, by expressing the thermodynamic condi-

tion of the aqueous coating using E , would therefore represent a significant decrease in the experimental effort needed to develop a science-based tablet coating process. Additional benefits of using E as a single design space dimension would be (1) increased process flexibility, since coating parameters are allowed to vary only under the constraint that E alone fall within a certain range, and (2) clarity of process description and understanding, since E can be easily illustrated and understood via a psychrometric chart.

Practically speaking, however, a comprehensive coating design space may not only have a thermodynamic component but a coating polymer component as well, with the final coating design space consisting of the common overlap of the two. In particular, for proper film coalescence of an aqueous polymer coating film the bed temperature should exceed the minimum film forming temperature of the polymer dispersion, while the glass transition temperature of the polymeric coating may place an upper limit on the tablet bed temperature. In addition, inlet temperature may play a role in the coalescence of the tablet coating since the tablet bed is not truly uniform and isothermal, and heat-labile drug products may impose an additional upper constraint on the bed temperature. Finally, other process variables, e.g., gun distance, do not impact the overall heat or mass balance but can affect the quality of the spray. These parameters fall outside the thermodynamic model as described in this work, and the process scientist may still find that multiple design parameters are required to adequately define the coating process design space. However, the benefit of using the E parameter approach is that the coating polymer requirements are decoupled from the thermodynamic requirements of the coating process so that they can be considered independently, eliminating these interaction terms from the DoE analysis.

CONCLUSIONS

A first-principles approach was taken to the task of describing the thermodynamic conditions inside an aqueous tablet coater pertinent to tablet film quality. It was shown that a single parameter can describe the rate of drying of the wetted tablet bed and can be readily obtained by direct temperature measurements and psychrometric charting. This parameter as a design space variable can potentially reduce the dimensionality of the coating design space, hence the number of experiments needed to develop the coating process, streamlining both the process development and the process description in filing submissions. The psychrometric model described herein enhances a scientific understanding of the coating process, providing for a Quality by Design approach to minimizing the risk associated with aqueous tablet coating.

REFERENCES

1. S. Page, K-H. Baumann, and P. Kleinebudde. Mathematical Modeling of an Aqueous Film Coating Process in a Bohle Lab-Coater, Part 1: Development of the Model. *AAPS PharmSci-Tech.* 72:E1-E8 (2006).
2. K. Walter. Introduction to Real Time Process Determination. *Pharm. Eng.* 272:1-9 (2007).
3. K. Dewettinck, A. De Visscher, L. Deroo, and A. Huyghebaert. Modeling the steady-state thermodynamic operation point of top-spray fluidized bed processing. *J. Food Eng.* 39:131-143 (1999).

4. C.C. Larsen, J.M. Sonnergaard, P. Bertelsen, and P. Holm. A new process control strategy for aqueous film coating of pellets in fluidized bed. *Eur. J. Pharma. Sci.* **20**:273–283 (2003).
5. M.T. Ende, and A. Berchielli. A Thermodynamic Model for Organic and Aqueous Tablet Film Coating. *Pharm. Dev. Technol.* **101**:47–58 (2005).
6. G.C. Ebey. A Thermodynamic Model for Aqueous Film-Coating. *Pharm. Technol.* **114**:40–50 (1987).
7. Thomas Engineering, <http://www.thomaseng.com>.
8. P. Pandey, R. Turton, N. Joshi, E. Hammerman, and J. Ergun. Scale-up of a Pan-Coating Process. *AAPS PharmSciTech.* **74**:E1–E8 (2006).
9. R. Mueller, and P. Kleinebudde. Comparison of a Laboratory and a Production Coating Spray Gun With Respect to Scale-up. *AAPS PharmSciTech.* **81**:E1–E11 (2007).
10. E.S. Novit. Understanding the effects of process-air humidity on tablet coating. Tablet & Capsules. *Coating Desktop Reference* 11–15 (2008).
11. S.C. Porter. Scale-Up of Film Coating. In M. Levin (ed.), *Pharmaceutical Process Scale-up*, Marcel Dekker, New York, 2002, p. 262.
12. Psychrometrics. In ASHRAE Handbook—Fundamentals, American Society of Heating, Refrigeration, and Air-Conditioning Engineers, Atlanta, 1989, pp. 6.1–6.21.
13. F. Kreith. *Principles of Heat Transfer*, 3rd ed., Harper and Row, New York, 1973.
14. W.P. Jones. *Air Conditioning Engineering*, 5th ed., Butterworth-Heinemann, Oxford, 2001.
15. T.L. Reiland, J.A. Yeager, and R.A. Brusenback. Aqueous film-coating vaporization efficiency. *Drug Dev. Ind. Pharm.* **9**:945–958 (1983).
16. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Q8: Pharmaceutical Development, Annex to Q8. <http://www.ich.org/LOB/media/MEDIA4349.pdf> (accessed 09/29/08), part of Official Website for ICH. <http://www.ich.org> (accessed 09/29/08).