

Reduced Acid-Neutralizing
Velocity of Spray-Dried Agglomerated
Magnesium Carbonate

Keyphrases □ Magnesium carbonate, agglomerated—spray dried, acid-neutralizing velocity □ Spray drying—agglomerated magnesium carbonate, acid-neutralizing velocity □ Acid-neutralizing velocity—spray-dried agglomerated magnesium carbonate

To the Editor:

In a recent article by Kawashima and Takenaka (1), certain conclusions were made based on the Hixson-Crowell law (2). This law is based on the following assumptions: (a) the film theory of Nernst-Brunner (3, 4) holds; (b) sink conditions apply; (c) the particles are spherical; (d) the substance dissolves isotropically, *i.e.*, has a constant shape factor; (e) there is no (measurable) particle-size *versus* solubility dependence; and (f) the powder is monodispersed.

Kawashima and Takenaka (1) used a rearranged form of the Hixson-Crowell law to get the relationships between diffusion layer thickness and parameters such as the initial particle size of the sample, temperature, and rate of agitation. They observed that the diffusion layer thickness increases linearly with increasing particle size and decreases curvilinearly with increasing temperature or agitation rate. The rearranged equation used had the following form:

$$\frac{d}{dt} [C_L/C_e] = (DS_w C_e/X) [1 - (C_L/C_e)]^{5/3} \quad (\text{Eq. 1})$$

where:

- C_L = concentration of solute (milligrams per milliliter)
- C_e = equilibrium solubility (milligrams per milliliter)
- S_w = specific surface area given by $6/(d_0\rho)$ (square centimeters per gram)
- d_0 = mean particle diameter (centimeters)
- D = diffusion coefficient (square centimeters per second)
- ρ = true particle density (grams per milliliter)
- X = diffusion layer thickness (centimeters)

The authors did not state the assumptions made in deriving Eq. 1 from the Hixson-Crowell law. These assumptions (except for sink condition) are the same as those that applied in deriving the Hixson-Crowell law itself, and the initial amount of the sample required (W_0) is given by the expression:

$$W_0 = VC_e = W_e \quad (\text{Eq. 2})$$

where V is the volume of the dissolution medium (milliliters), and W_e is the amount of solid required just to saturate the dissolution medium (grams).

For the dissolution studies, the authors (1) used salicylic acid and an initial weight of 0.5 g; they employed 450 ml of distilled water as the dissolution medium. They carried out their experiments at three different temperatures (27, 37, and 47°). The drawback in their experimental design is that the initial 0.5-g amount does not satisfy the condition of Eq. 2, *i.e.*, W_0 is different from W_e .

The United States Pharmacopeia lists the solubility of salicylic acid in distilled water at 25° as 0.0022 g/ml (5); therefore, the initial amount required for dissolution would be $W_0 = C_e V = 450 \times 0.0022 = 0.99$ g. Even at 25°, the amount used (0.5 g) falls short of this figure. Deviations would, of course, be much larger with increasing temperatures (*i.e.*, at 37 and 47°). It is obvious also that the amount used must change with temperature in the same ratio as the solubility changes.

Since the dissolution experiments carried out by Kawashima and Takenaka (1) were under conditions where $W_0 < W_e$, the proper nonsink equations for this condition would be the equations reported by Short *et al.* (6) and Patel and Carstensen (7). The Short-Sharkey-Rhodes equation in the form shown in Ref. 7 is:

$$\psi(W) = -\frac{DS_w W_0^{1/3}}{XV} t + \psi(W_0) \quad (\text{Eq. 3})$$

where:

$$\psi(W) = 0.5F^{-2} [\ln \{(U+F)^2/(F^2 - UF + U^2)\}] + \sqrt{3}F^{-2} \arctan[(2U-F)/(F\sqrt{3})] \quad (\text{Eq. 4})$$

where:

$$F^3 = W_e - W_0 \quad (\text{Eq. 5})$$

and:

$$W = U^3 = \text{amount (grams) of powder remaining} \quad (\text{Eq. 6})$$

According to the experimental conditions of Kawashima and Takenaka (1), Eq. 3 should have been used to describe the dissolution of salicylic acid and to calculate the diffusion layer thickness (X) from the slope of the dissolution profile. If Ref. 1 had contained tabulated values of C_L *versus* t , then Eq. 3 could have been used directly and, by knowing all values except X , X could have been calculated from the slope of ψ *versus* t plots.

Equation 3 has been used in this communication to reconstruct the dissolution profile for the conditions taken from Ref. 1. For one set of experiments carried out at 37° and 620 rpm, the values were as follows: $t = 37^\circ$, $W_0 = 0.5$ g, $W_e = 1.44$ g (Table I), $D = 4.85 \times$

Table I—Calculated Initial Amount Required According to Eq. 1

Temperature	Solubility, g/ml	Initial Amount Required According to Eq. 1, $W_0 = C_e V$, g	Initial Amount Used, g
27°	0.00231	1.04	0.5
37°	0.00320 ^a	1.44	0.5
47°	0.00465 ^b	2.09	0.5

^aDetermined in this laboratory. ^b Reference 8.

10^{-6} cm²/sec, $V = 450$ ml, $d_0 = 0.003$ cm, $\rho = 1.4$ g/ml, and $X = 34 \times 10^{-4}$ cm. Then:

$$\psi(W) = \psi(W_0) - \frac{DS_w W_0^{1/3}}{XV} t = 1.326 - 0.0036t \quad (\text{Eq. 7})$$

Equation 7 is obtained by substituting the given values in Eq. 3. It is important to note that the value of the diffusion layer (X) chosen here is taken from Ref. 1 but really it is an arbitrary value. The amount dissolved *versus* time is calculated under these conditions using Eq. 7 and is shown in Table II.

The data in Table II are treated according to Kawashima and Takenaka (1); the best-fit regression equation obtained was:

$$\log [d(C_L/C_e)/dt] = 2.16 \log \{1 - (C_L/C_e)\} - 2.613 \quad (\text{Eq. 8})$$

with a correlation coefficient of 0.989. The theoretical slope of this plot is 1.66, which is in conflict with Eq. 8. The diffusion layer thickness value calculated from Eq. 8 is 90 μ m, which also does not agree with the value used in Eq. 7 ($X = 34 \mu$ m).

Therefore, it is demonstrated here that Eq. 1 is not an appropriate model to fit the experimental results of Ref. 1. The slope of 1.66 reported in Ref. 1 is also questionable.

The best method for calculating the diffusion layer thickness (X) for the experiments carried out in Ref. 1 would be to use data points where the total amount dissolved is less than 20% of W_e and to treat the data according to the Hixson-Crowell cube root law (2). This method was used for the first five data points in Table II and gave a diffusion layer thickness (X) of 39 μ m, which is quite close to the chosen value of 34 μ m.

Table II—Amount Dissolved *versus* Time Calculated Using Experimental Conditions from Ref. 1 and Eq. 7

W_L^a , g Dissolved	W , g Un-dissolved	$\psi(W)$, g ^{-2/3}	Time, t , sec	$W_0^{1/3} - W^{1/3}$, g ^{1/3}
0	0.5	1.326	0	0
0.05	0.45	1.268	16	0.027
0.1	0.40	1.203	34	0.057
0.15	0.35	1.130	54	0.089
0.20	0.30	1.046	78	0.124
0.25	0.25	0.945	101	0.164
0.30	0.20	0.833	137	
0.35	0.15	0.689	177	
0.40	0.10	0.499	230	
0.45	0.05	0.216	308	

^aThe W_L (grams) values were assumed, and $\psi(W)$ was calculated. By using this value of $\psi(W)$ and Eq. 7, the corresponding time value was calculated.

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To the Editor:

It is appreciated that the estimates of the encapsulation ratio of spray-dried products depend on the method used for the calculation of diffusion layer thickness, and the validity of Patel's (1) general comments is accepted. However, his statement regarding the use of an initial weight of 0.5 g of salicylic acid in our studies requires modification.

In our investigations, samples of salicylic acid of 1.18, 1.55, and 2.24 g were placed in 450 ml of water at 27, 37, and 47°, respectively. This point is not immediately evident from our publication (2), since only the equilibrium concentration of solute was reported. Since flotation of part of the salicylic acid was observed at the initial stage of the dissolution study, a small excess of salicylic acid was added to the solvent. Therefore, our experimental conditions, where $W_0 \approx W_e$, can meet the requirement for applying the rearranged equation (2) of the Hixson-Crowell cube root law (3). The slope of plots of data based on this equation was 1.66 over 80–90% of the total amount dissolved.

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