Anal.—Calc. for $C_{13}H_{14}N_2O_7 \cdot H_2O$: C, 48.90; H, 4.74; N, 8.78. Found: C, 48.80; H, 4.65; N, 8.61.

***N*-(4-Iodophenylcarbamoylmethyl)iminodiacetic Acid (VII)**—Compound VII was obtained from nitrilotriacetic acid (4.47 g, 0.023 mole), acetic anhydride (3.58 g, 0.035 mole), and 4-iodoaniline (5.12 g, 0.023 mole) (Method B). Recrystallization from 80% aqueous ethanol yielded white crystals, 5.62 g (62%), mp 194° dec.; IR (mineral oil): 3300 (NH) and 1710 and 1675 (C=O) cm^{-1}; PMR (dimethyl sulfoxide-d_6): δ 3.51 (s, 2H, NCH_2CON), 3.55 (s, 4H, NCH_2CO_2), 7.48 (d, 2H, Ar-H), and 7.60 (d, 2H, Ar-H) ppm.

Anal.—Calc. for $C_{12}H_{13}IN_2O_5$: C, 36.75; H, 3.34; N, 7.14. Found: C, 36.73; H, 3.51; N, 7.25.

Preparation of ^{99m}Tc-Complexes—A solution of 10 mg of compound in 0.5 ml of 0.1 *N* NaOH was prepared, and the pH was adjusted to 5–5.5 with 0.05 *N* HCl. After addition of 0.3 ml of generator eluate (obtained by saline elution of a 500-mCi ^{99}Mo–^{99m}Tc generator[3] at a specific concentration of 10–20 mCi/ml), the solution was purged with nitrogen for 5 min, and 0.1 ml of freshly prepared stannous chloride dihydrate solution (250 μg/ml in 0.001 *N* HCl) was then added. The solution was kept at room temperature for 20 min prior to use.

Electrophoresis and Chromatography[4]—Electrophoresis was performed on paper[5] at constant voltage (600 v, 30 min) with a 0.01 *M* sodium bicarbonate buffer (pH 7). Under these conditions, $^{99m}TcO_4^-$ migrated approximately 13 cm. A pertechnetate standard was utilized with all samples. The distance each complex migrated was determined by scanning the dried paper with a chromatogram scanner equipped with a 2.54-cm sodium iodide detector and a collimator, which consisted of 0.635 cm of lead with a 2.54-cm × 30-mm slit. The results obtained on any given electrophoragram were expressed as the following ratio:

$$R_s = \frac{\text{distance migrated by complex}}{\text{distance migrated by } ^{99m}TcO_4^-} \quad \text{(Eq. 1)}$$

These R_s values were essentially independent of the distance migrated by the pertechnetate ion over a range of at least 11–15 cm.

[3] E. R. Squibb & Sons, Princeton, N.J.

[4] Chromatography was performed on Eastman 13181 silica gel eluted with acetone.

[5] Whatman 3MM.

REFERENCES

(1) G. V. Taplin, O. M. Meridith, and H. Kade, *J. Lab. Clin. Med.*, **45**, 665 (1955).

(2) A. K. Tonkin and F. H. Deland, *J. Nucl. Med.*, **15**, 539 (1974).

(3) T. H. Lin, A. Khentigan, and H. S. Winchell, *ibid.*, **15**, 613 (1974).

(4) G. T. Krishnamurthy, M. Tubis, and J. S. Endow, *ibid.*, **13**, 447 (1972).

(5) M. K. Dewanjee, C. Fliegel, and S. Treeves, *ibid.*, **15**, 176 (1974).

(6) R. J. Baker, J. C. Bellen, and P. M. Ronai, *ibid.*, **16**, 720 (1975).

(7) P. M. Ronai, R. J. Baker, and J. C. Bellery, *ibid.*, **16**, 728 (1975).

(8) E. Harvey, M. Loberg, and M. Cooper, *ibid.*, **16**, 533 (1975).

(9) P. S. Callery, W. F. Faith, and M. D. Loberg, *J. Med. Chem.*, **19**, 962 (1976).

(10) H. D. Burns, L. G. Marzilli, D. Sowa, D. Baum, and H. N. Wagner, Jr., *J. Nucl. Med.*, **18**, 624 (1977).

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Dissolution Profiles of Drugs from Tablets

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Received January 3, 1977, from the *Pharmaceutical Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd., Yodogawa-ku, Osaka, 532, Japan.* Accepted for publication February 15, 1978.

Abstract □ A theoretical equation to describe the drug dissolution from a tablet was derived by combining an equation for the disintegration rate of a tablet with an equation for the dissolution of particles. The theory is based on the assumptions that: (*a*) dissolution occurs only from the particles released in a medium by tablet disintegration, (*b*) the number of particles released into a medium obeys the equation $N = N_0(T/T_d)^m$, and (*c*) the dissolution of particles, which are spherical in shape, is represented by the equation previously given by Brooke. Tablet dissolution *versus* time plots, obtained by calculating the equation with a computer, gave an S-shaped curve between the dissolution curve for particles starting at time zero and the curve for particles starting at the tablet disintegration time. The joint influences of disintegration and particle dissolution on the overall tablet dissolution profile also were examined. When dissolution of powders was rapid, disintegration of a tablet directly influenced its dissolution. When powders intrinsically dissolved slowly, the effect of disintegration on the tablet dissolution profile was slight.

Keyphrases □ Dissolution, tablet—theoretical equation derived, effects of tablet disintegration and particle dissolution □ Disintegration, tablet—effects on dissolution, theoretical equation derived □ Tablet dissolution—theoretical equation derived, effects of tablet disintegration and particle dissolution

The dissolution rate of a drug from its solid dosage forms is important relative to bioavailability since dissolution is usually the rate-limiting process in the absorption of poorly soluble drugs.

The overall dissolution profiles for solid dosage forms can be obtained from dissolution tests (1–3). The dissolution data obtained may involve factors related to the drug dissolution rate, the drug particle size (distribution), and the disintegration rate of the dosage forms. The effect of these factors on the dissolution profiles is so complex that no satisfactory quantitative evaluation of the dissolution properties of solid dosage forms is obtained from a measured dissolution profile.

Attempts to describe dissolution profiles include empirical functions that enable representation of the actual results with a minimum number of parameters (4–8). However, the values of the parameters of the distribution function employed give no useful information about the improvement of tablet dissolution.

Theoretical considerations of powder dissolution in relation to particle-size distribution were first attempted by Higuchi and coworkers (9, 10). A more exact equation then was developed that permits calculation of the dissolution profiles of log-normal powders with or without a computer (11–13). Later, a simple relationship was found between the tablet disintegration rate and time (14).

To evaluate tablet dissolution quantitatively, an equation was derived in the present study by combining an equation for tablet disintegration with an equation for

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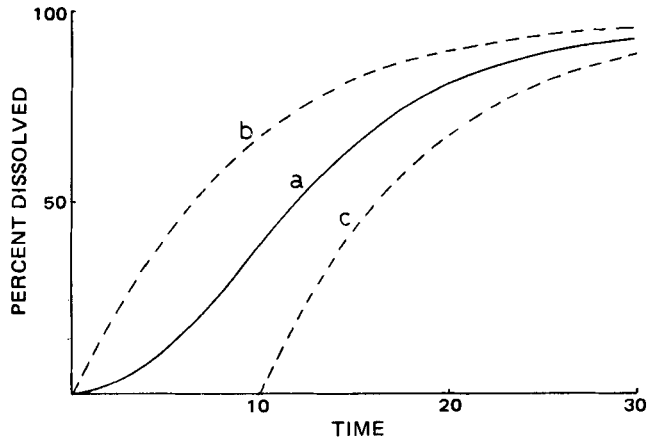

Figure 1—*Typical dissolution profile of a tablet.*

particle dissolution. The joint effect of disintegration and particle dissolution on the overall tablet dissolution profile was examined by calculating the equation with a computer.

THEORETICAL

Consider a tablet containing spherical drug particles whose diameters, a_0, follow a log-normal distribution. The probability function, f, of ln a_0 is given by:

$$f = \frac{1}{\sigma\sqrt{2\pi}} \exp[-(\ln M - \ln a_0)^2/2\sigma^2] \qquad \text{(Eq. 1)}$$

where M is the geometrical mean of a_0, and σ is the standard deviation.

Assume that the dissolution of a tablet occurs only from drug particles released from the tablet *via* disintegration or deaggregation. Assume that the release rate of particles into a medium is expressed, on the numbers basis, by the simple equation derived by Kitamori and Shimamoto (14):

$$N = N_0(T/T_d)^m \qquad \text{(Eq. 2)}$$

where N is the number of primary drug particles released from the tablet or granules *via* disintegration, N_0 is the total number of drug particles within the tablet, T is time ($0 \le T \le T_d$), T_d is disintegration time, and m is a constant concerned with the tablet disintegration rate.

A small number, dN, of particles released within a very narrow interval of time, dT, centered at T is given by:

$$dN = N_0(m/T_d{}^m)T^{m-1}\,dT \qquad \text{(Eq. 3)}$$

As the particles in the tablet distribute log-normally, the particles of very small number, dN, also follow the same log-normal distribution. If these particles dissolve isotropically under sink conditions, their weight undissolved at time t is given by the dissolution equation of log-normal powders derived by Brooke (11, 12), with time $t - T$ in place of time t because the particles start dissolving at time T, and is expressed by:

$$dW_t = \int_{\ln[(2k_i/p)(t-T)]}^{\infty} pV_{(t-T)}f\,dN\,d(\ln a_0) \qquad \text{(Eq. 4)}$$

where $V_{(t-T)}$ is the volume of undissolved particles initially having a_0 diameter at time t and is expressed by:

$$V_{(t-T)} = \frac{\pi}{6}[a_0 - (2k_i/p)(t-T)]^3 \qquad \text{(Eq. 5)}$$

Substituting $N_0(m/T_d{}^m)T^{m-1}\,dT$ into dN in Eq. 4 yields:

$$dW_t = \int_{\ln[(2k_i/p)(t-T)]}^{\infty} pV_{(t-T)}N_0f(m/T_d{}^m)T^{m-1}\,d(\ln a_0)\,dT \qquad \text{(Eq. 6)}$$

When $t < T_d$, the total weight of undissolved solid after time t is given by an integration of Eq. 6 with respect to T between time zero and t:

$$W_t = \int_0^t \int_{\ln[(2k_i/p)(t-T)]}^{\infty} pV_{(t-T)}N_0f(m/T_d{}^m)T^{m-1}\,d(\ln a_0)\,dT \qquad \text{(Eq. 7)}$$

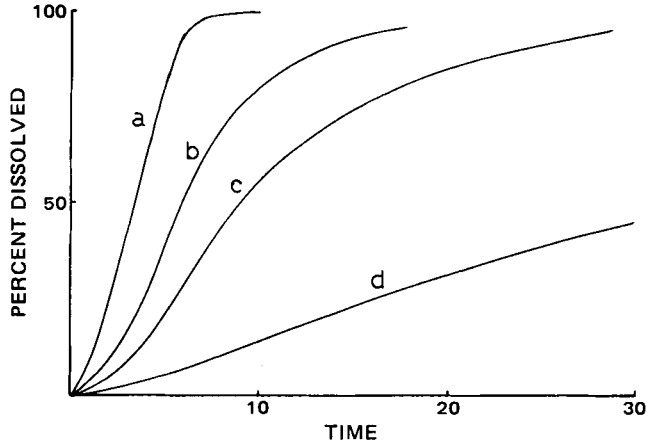

Figure 2—*Effect of the intrinsic dissolution rate of the particles before inclusion in tablets on the dissolution profiles of tablets. Key: a,* $k_i/pM = 0.333$; *b,* $k_i/pM = 0.0667$; *c,* $k_i/pM = 0.0333$; *and d,* $k_i/pM = 0.00667$. *Other variables are the same;* $\sigma = 0.5$, $T_d = 5.0$, *and* $m = 1.0$.

The total weight of the particles released from the tablet *via* tablet disintegration after time t is given by:

$$W_t{}^0 = N_0(t/T_d)^m \int_{-\infty}^{\infty} pV_0f\,d(\ln a_0) \qquad \text{(Eq. 8)}$$

Then the equation for the weight fraction dissolved before disintegration time is:

$$S_t = (W_t{}^0 - W_t)/W_0 \qquad \text{(Eq. 9a)}$$

$$S_t = (t/T_d)^m - \frac{\int_0^t \int_{\ln[(2k_i/p)(t-T)]}^{\infty} pV_{(t-T)}N_0(m/T_d{}^m)T^{m-1}f\,d(\ln a_0)\,dT}{\int_{-\infty}^{\infty} pN_0V_0f\,d(\ln a_0)} \qquad \text{(Eq. 9b)}$$

where W_0 is the initial weight of the particles in a tablet and is expressed by:

$$W_0 = \int_{-\infty}^{\infty} pV_0N_0f\,d(\ln a_0) \qquad \text{(Eq. 10)}$$

When $t > T_d$, the equation for the weight fraction dissolved is:

$$S_t = (W_0 - W_t)/W_0 \qquad \text{(Eq. 11a)}$$

$$S_t = 1 - \frac{\int_0^{T_d} \int_{\ln[(2k_i/p)(t-T)]}^{\infty} pV_{(t-T)}N_0(m/T_d{}^m)T^{m-1}f\,d(\ln a_0)\,dT}{\int_{-\infty}^{\infty} pV_0N_0f\,d(\ln a_0)} \qquad \text{(Eq. 11b)}$$

In double integrations in Eqs. 9*b* and 11*b*, the integral with respect to ln a_0 can be evaluated numerically by introducing a standard normal distribution, $F(x) = \int \exp(-x^2/2)/\sqrt{x}\,dx$, but the integral with respect to T cannot be solved directly. In this paper, these double integrations were approximated by the trapezoidal rule and numerically evaluated with a digital computer (see *Appendix* for details).

RESULTS AND DISCUSSION

When a tablet is placed in a medium according to the USP–NF dissolution test, dissolution occurs from its surface; granules are produced after its disintegration, and drug primary particles ultimately are released (5). In the disintegration–dissolution model described in this paper, it was assumed that the dissolution from drug primary particles produced after disintegration is the major route of tablet dissolution since the surface areas available for dissolution of poorly soluble drugs in a tablet or in granules are smaller than those in drug primary particles and can be neglected.

The calculation of the dissolution of a tablet with k_i/pM[1] = 0.133, σ

[1] It can be seen from Eq. A2 in the *Appendix* that k_i/pM is a variable for the tablet dissolution equation.

Table I—Dissolution Patterns for Tablets with T_d = 5.0, m = 1.0, σ = 0.5, and different k_i/pM Values

	Percent Dissolved at Time				
k_i/pM	5.0	10.0	15.0	20.0	30.0
0.0333	22.88	56.11	75.28	85.99	95.27
0.0667	39.47	80.63	93.60	97.72	99.63
0.1333	60.02	95.66	99.38	99.88	99.97
0.3333	82.04	99.87	99.99	99.99	99.99

Table II—Dissolution Patterns for Tablets with T_d = 5.0 and m = 1.0 Containing the Constituent Drug Particles with k_i = 0.1, p = 1.5, M = 1.0, and Different Standard Deviations

	Percent Dissolved at Time				
σ	5.0	10.0	15.0	20.0	30.0
0[a]	62.86	99.53	99.99	—	—
0.05	62.60	99.46	99.99	—	—
0.1	61.81	99.24	99.99	—	—
0.3	53.68	95.12	99.70	99.98	99.99
0.5	39.47	80.63	93.60	97.72	99.63
0.7	23.82	55.64	72.75	82.47	91.94

[a] Since Eq. 9*b* or 11*b* does not hold for σ = 0, the dissolution pattern for the tablet containing monosized drug was calculated at σ = 0.0001.

= 0.5, T_d = 10.0, and m = 1.0 gave an S-shaped curve (a) as shown in Fig. 1. The curve located between the dissolution profile (b) for the log-normal drug powder before inclusion in a tablet (k_i/pM = 0.133 and σ = 0.5) started at time zero, and the profile (c) for the same powder started at the disintegration time of the tablet. Since the particles start dissolving when they are released from the tablet according to the disintegration–dissolution model, the dissolution of a tablet is slower than the dissolution of the powder before inclusion in the tablet and faster than the dissolution of the same powder started at the disintegration time of the tablet.

The intrinsic dissolution rate (or solubility), the particle size (distribution), and the disintegration rate primarily determine the tablet dissolution profile. Their effect on the overall tablet dissolution profile can be examined by the computer calculation of the proposed equation.

First, the dissolution of the drug powder before inclusion in a tablet is essential for the dissolution of the tablet. Since S_t is a function of k_i/pM ($\propto \tau/M$) and not of k_i or M separately (see *Appendix*), an increase in k_i/pM can result from an increase in k_i or a decrease in the particle size of drug particles. The variation in the dissolution profile of a tablet with the value of k_i/pM is demonstrated in Fig. 2, where the tablets have the same disintegration time, 5.0, and the same coefficient of disintegration pattern, m = 1.0. A decrease in k_i/pM corresponds with the slower slope of the dotted curves so that the S-shaped curve located between both of them lies stretched. The relationship between amount dissolved and time is much less complicated for a powder than for a tablet, which must first disintegrate. Some typical results of dissolution of the tablet with T_d = 5.0, m = 1.0, and σ = 0.5 and different k_i/pM values are listed in Table I.

The standard deviations of the size distribution of particles before inclusion in a tablet should also affect the dissolution profile of the tablet. The calculated results for different drug powder distributions are shown in Table II. The calculated dissolution is not so sensitive to the distribution for smaller σ. For rather large standard deviations, however, the slower the calculated dissolution, the more broadly the drug particles

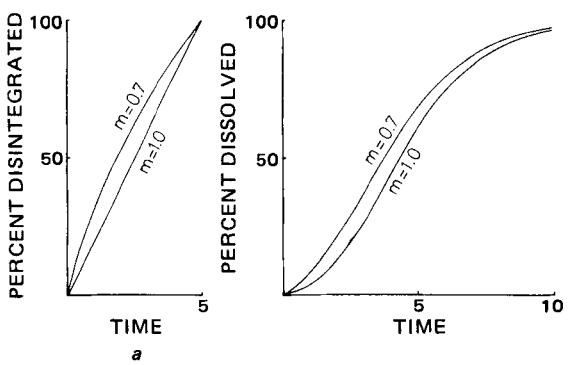

Figure 3—*Effect of the coefficient of disintegration,* m, *on the tablet dissolution profile. Variables are* k_i/pM = *0.133,* σ = *0.5, and* T_d = *5.0.*

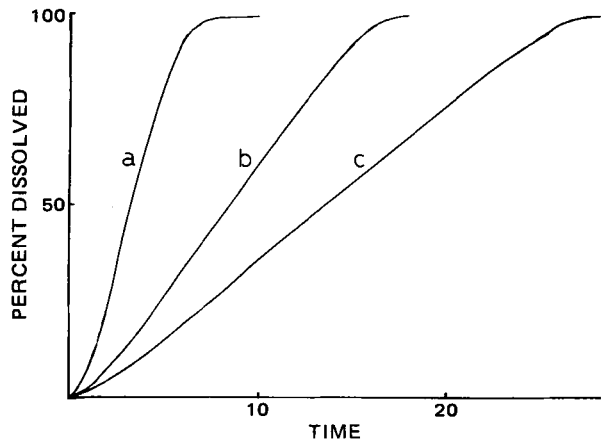

Figure 4—*Effect of disintegration time on the dissolution profiles of tablets. Key: a,* T_d = *5.0; b,* T_d = *15.0; and c,* T_d = *25.0. Other variables are the same;* k_i/pM = *0.333,* σ = *0.5, and* m = *1.0.*

distribute. This behavior is similar to the powder dissolution reported by Brooke (11).

The release profile of drug particles from a tablet varies with the value of the constant m in Eq. 2 as shown in Fig. 3*a*. In accordance with the change in the disintegration pattern, the dissolution profile of the tablet varies as shown in Fig. 3*b*. The shape of the dissolution curves for tablets is reflected by the value of the constant m. The value of m lies between 0.7 and 1.0; but, experimentally (14), the constant m ordinarily is almost unity so that the evaluation of tablet dissolution can be performed with m = 1.0.

The disintegration equation can be applied to the disintegration not only into particles but also into granules. In dissolution, however, a tablet must disintegrate into primary particles because of the assumption. Although a tablet disintegrates rapidly into granules, the surface area available for drug dissolution is so small that the dissolution would not be so fast unless primary particles are produced from the granules. From this point of view, the tablet that should have the fast dissolution rate must disintegrate in a medium into constituent particles.

With the assumption of Eq. 2, the disintegration time of a tablet also affects the tablet dissolution profile. The effect of the disintegration time of tablets on their dissolution profiles is shown in Fig. 4. An increase in disintegration time means an increase in the distance between both dissolution curves for particles before inclusion in a tablet starting at time zero and starting at its disintegration time, so an S-shaped dissolution curve of a tablet between them lies stretched and becomes straightened.

It is of interest to examine the joint influence of disintegration rate and particle dissolution rate on the overall tablet dissolution profile. Dissolution profiles with different T_d and k_i/pM values are shown in Fig. 5. Two pairs of curves, a and a′ and b and b′, are the dissolution profiles with different T_d values (T_d = 15.0 for a and b and 5.0 for a′ and b′) and equal k_i/pM values (k_i/pM = 0.333 for a and a′ and 0.0667 for b and b′). For

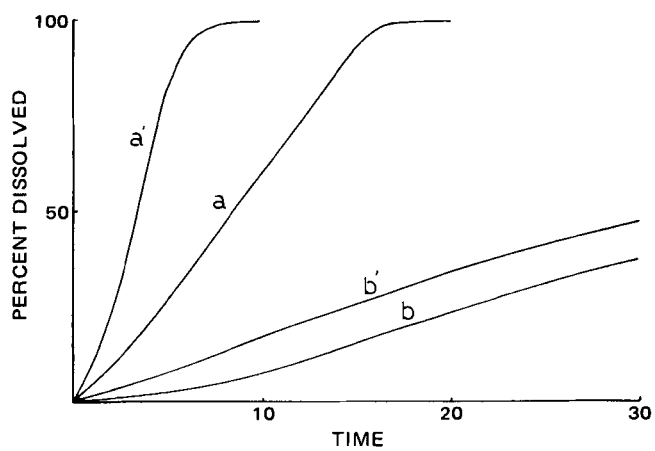

Figure 5—*Joint influence of the disintegration rate of a tablet and the dissolution rate of the constituent particles on the tablet dissolution profile.*

drugs that intrinsically dissolve slowly ($k_i/pM = 0.0667$), a decrease in disintegration time cannot greatly improve the tablet dissolution (curve b → b'), whereas the effect is great for fast dissolving drugs ($k_i/pM = 0.333$, curve a → a'). The T_d and k_i/pM values influence an overall dissolution profile in different ways, so that the evaluation of the dissolution properties of solid dosage forms merely from an overall dissolution profile might lead to an erroneous conclusion. Therefore, to evaluate the dissolution properties of solid dosage forms, disintegration measurements and dissolution tests of the powder before or after inclusion in a tablet should be carried out separately.

The developed equation is based on the simple disintegration–dissolution model. Actually, more complex factors may affect tablet dissolution. For instance, disintegration is not always the deaggregation into primary particles and particle-size distribution is not always log-normal. The equation also would not be applied to the case where drug particle-size distribution changes after compression. In spite of such restrictions, the proposed equation might still be useful to predict or examine tablet dissolution.

APPENDIX

Let the integration with respect to $\ln a_0$ in Eqs. 9*b* and 11*b* be $I(T)$:

$$I(T) = \frac{\int_{\ln[(2k_i/p)(t-T)]}^{\infty} pV_{(t-T)}N_0 f(m/T_d{}^m)T^{m-1}\, d(\ln a_0)}{\int_{-\infty}^{\infty} pN_0 v_0 f\, d(\ln a_0)} \quad \text{(Eq. A1)}$$

By letting $(m/T_d{}^m)T^{m-1} = r(T)$ and $(2k_i/p)(t - T) = \tau(T)$ for simplification and employing the method similar to that used by Brooke (11), Eq. A1 becomes:

$$I(T) = r(T)\left\{\left[1 - F\left(\frac{\ln[\tau(T)/M] - 3\sigma^2}{\sigma}\right)\right]\right.$$
$$-3[\tau(T)/M]\exp(-5\sigma^2/2)\left[1 - F\left(\frac{\ln[\tau(T)/M] - 2\sigma^2}{\sigma}\right)\right]$$
$$+3[\tau(T)/M]^2\exp(-4\sigma^2)\left[1 - F\left(\frac{\ln[\tau(T)/M] - \sigma^2}{\sigma}\right)\right]$$
$$\left.-[\tau(T)/M]^3\exp(-9\sigma^2/2)\left[1 - F\left(\frac{\ln[\tau(T)/M]}{\sigma}\right)\right]\right\} \quad \text{(Eq. A2)}$$

For numerical computation of $I(T)$, the following approximation (15) was used for $F(x)$:

$$F(x) = 1 - \frac{1}{\sqrt{2\pi}}\exp(-x^2/2)(ay + by^2 + cy^3 + dy^4 + ey^5) \quad \text{(Eq. A3)}$$

where $y = 1/(1 + 0.2316419x)$, $a = 0.319381530$, $b = -0.356563782$, $c = 1.781477937$, $d = -1.821255978$, and $e = 1.330274429$. Finally, Eqs. 9*b* and 11*b* can be given by:

$$\int_0^t I(T)\, dT \qquad (t < T_d)$$
$$\int_0^{T_d} I(T)\, dT \qquad (t \geq T_d)$$

For numerical computation, it can be approximated by the trapezoidal rule based on dividing T_d by a large number of n; for $t < T_d$:

$$\int_0^t I(T)\, dT \fallingdotseq \frac{h}{2}[(I_0 + I_{n'}) + 2(I_1 + I_2 + \ldots + I_{n'-1})] \quad \text{(Eq. A4)}$$

for $t \geq T_d$:

$$\int_0^{T_d} I(T)\, dT \fallingdotseq \frac{h}{2}[(I_0 + I_n) + 2(I_1 + I_2 + \ldots + I_{n-1})] \quad \text{(Eq. A5)}$$

where $I_i = I(T_i)$ $(i = 0, 1, 2, \ldots.)$, $h = T_d/n$, $n' = (nt)/T_d$, and $T_n = T_d$.

The double integration is evaluated practically by dividing disintegration time into about 500 intervals.

REFERENCES

(1) J. B. Johnson, P. G. Kennedy, and S. H. Rubin, *J. Pharm. Sci.*, **63**, 1931 (1974).
(2) A. C. Shah, C. Peot, and J. F. Ochs, *ibid.*, **62**, 671 (1973).
(3) A. C. Shah and J. F. Ochs, *ibid.*, **63**, 110 (1974).
(4) M. Gibaldi and S. Feldman, *ibid.*, **56**, 1238 (1967).
(5) J. G. Wagner, *ibid.*, **58**, 1253 (1969).
(6) F. Langenbucher, *J. Pharm. Pharmacol.*, **24**, 979 (1972).
(7) M. Behr, J. Dietrich, P. J. Mehta, D. Reher, and H. Sucker, *Pharm. Ind.*, **35**, 210 (1973).
(8) F. Langenbucher, *ibid.*, **38**, 472 (1976).
(9) W. I. Higuchi and E. N. Hiestand, *J. Pharm. Sci.*, **52**, 67 (1963).
(10) W. I. Higuchi, E. L. Rowe, and E. N. Hiestand, *ibid.*, **52**, 162 (1963).
(11) D. Brooke, *ibid.*, **62**, 795 (1973).
(12) *Ibid.*, **63**, 344 (1974).
(13) P. Veng Pedersen and K. F. Brown, *J. Pharm. Sci.*, **64**, 1192 (1975).
(14) N. Kitamori and T. Shimamoto, *Chem. Pharm. Bull.*, **24**, 1789 (1976).
(15) "Handbook of Mathematical Functions with Formulas, Graphs, and Mathematical Tables," M. Abramowitz and I. A. Stegun, Eds., National Bureau of Standards, Washington, D.C., 1965.

Conductivity of Drugs Used for Iontophoresis

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Abstract □ The electrical conductivities of drugs were measured *in vitro* using a conductivity MHO-meter. These experiments indicate that local anesthetics, vasoconstrictors, some corticosteroids, several anticancer drugs, and several antiviral agents are suitable for iontophoresis. The contribution to conductivity of buffers and nonspecific ions in the same solution with the drug also was defined.

Keyphrases □ Conductivity, electrical—various drugs measured *in vitro*, suitability for iontophoresis □ Iontophoresis suitability—various drugs, electrical conductivity measured *in vitro*

Iontophoresis is a simple, well-documented method of drug application for medication of tissues (1). It assures the penetration of electrically charged drugs into surface tissues. It is possible to medicate electrically any surface tissue with drugs having a positive or negative charge (1). The technique involves transporting selected ions electrically into a tissue by passing a direct electrical current through a medicating solution and the patient, using selected electrode polarity.

BACKGROUND

Iontophoresis has many advantages as a drug administration method. Systemic toxicity is virtually eliminated since only a minute amount of

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