# 1

# Mathematical Concepts

## 1.1 Introduction

Pharmacy as a profession is art, business, and science. The science of pharmacy, also known as *pharmaceutical science*, requires knowledge of mathematics. Experimentation in pharmaceutical science produces quantitative measures with specific values. Handling these measures mathematically depends on how to apply rules to define them. In turn, these definitions of measures lead to a description of experimental entities. For example, to define a solution's pH, a pH meter is normally used in the measurement. Knowledge of the pH value can define the concentration of hydronium ions present in the solution. The relationship that allows transformation of the pH value to a concentration term is a mathematical expression known as *Sörensen's equation*:

$$\mathrm{pH} = -\log[\mathrm{H_3O^+}] \tag{1.1}$$

If the pH meter reads pH 10.8 for the solution, Eq. (1.1) may be used for the determination of $[\mathrm{H_3O^+}]$:

$$10.800 = -\log[\mathrm{H_3O^+}]$$
$$[\mathrm{H_3O^+}] = 1.58 \times 10^{-11}\,\mathrm{M}$$

Thus, the concentration of hydronium ions in solution was computed from Eq. (1.1) by mathematical manipulation employing the rules of logarithms. The mathematical operator "p" represents the function (−log) in the equation. Thus, (−log $[\mathrm{H^+}]$) becomes pH.

Mathematical rules can also aid a pharmaceutical scientist in describing the blood profile following administration of a drug in patients. Following intravenous administration of a drug, the drug is placed in circulation and achieves its highest concentration immediately following injection. The concentration of the drug decreases thereafter through distribution to tissues and via metabolic pathways. The drug disappearance from the circulation over time may be described by an exponential function following the general expression

$$C_{\mathrm{blood}} = C_{\mathrm{initial}}\, e^{-kt} \tag{1.2}$$

where $C_{\mathrm{blood}}$ is the drug concentration at time $t$, $C_{\mathrm{initial}}$ is the initial concentration of the drug in the blood immediately following administration, and $k$ is the elimination rate constant. Equation (1.2) can be made linear by converting it to its logarithmic form:

$$\ln C_{\mathrm{blood}} = \ln C_{\mathrm{initial}} - kt \tag{1.3}$$

The transformation of Eq. (1.2) to Eq. (1.3) requires knowledge of the rules of logarithms. *Pharmacokinetics*, which is the study of drug absorption, distribution, and elimination, uses these mathematical manipulations of data to improve patients' therapeutic outcomes. Equation (1.3) describes a linear relationship between the natural logarithm of drug blood concentration and time. This linear relationship is not only important in pharmacokinetics, but its applications are well utilized in physical pharmacy applications.

In this chapter, we cover the major important mathematical concepts that pharmaceutical scientists utilize in their studies. With the advancement of computer technology, many of these mathematical applications are handled by a computer software program or even by a basic scientific calculator.

## 1.2 Significant Figures and Rounding off Numbers

The United States Pharmacopeia (USP) emphasizes on the use of significant figures in reporting numerical results. To that end, the reader is encouraged to consult the USP or other resources concerning this topic for more details. The following rules apply to reporting values obtained from mathematical manipulations of data:

1) Intermediate numerical values may be retained to their original decimal figures and the final results are then reported to the significant figures desired.

*Integrated Pharmaceutics: Applied Preformulation, Product Design, and Regulatory Science*, Second Edition.
Antoine Al-Achi, Mali Ram Gupta, and William Craig Stagner.

Companion website: www.wiley.com/go/Al-Achi/IntegratedPharmaceutics

2) Zero value may or may not be significant depending on the way it is being reported. A significant zero is emphasized in the number being reported, such as in 109.0 mg. The zero in this number is significant, and thus there are four significant figures in 109.0 mg. However, the zero value appearing immediately after the decimal point in 0.0109 mg is not significant, thus this number has only three significant figures. And the number 0.0009 mg has only one significant figure.
3) In the value such as 1090 mg, the last zero may or may not be considered an approximate digit, depending on the method of analysis being used.
4) When performing mathematical operations, the final number is reported with the least number of significant figures used to generate that number. For example, multiplying 3.40 (three significant figures) by 208.0 (four significant figures) results in the value of 707.2, which should be reported as 707 (the 2 in the final number is not significant). However, if one of the numbers is an absolute value, such as the case with the number of tablets in a bottle, then the final result is reported to the next possible significant figures in the operation. For example, 34 tablets (exact number) of a multivitamin product were reported to have in each tablet 50.00 mg (four significant figures) of vitamin C. Then, $34 \times 50.00 = 1700$ mg (four significant figures).
5) Rounding off the final number to the desired significant figures: If the final number is reported to three significant figures, and the final number was 89.87, then this value would be rounded off to 89.9; likewise if the number is 89.83, it is rounded off to 89.8. Notice that we added (+1) in first case when the last digit was greater than 5 (the same rule applies if the last digit was exactly 5), and we dropped the digit from the answer when the number was less than 5.
6) For logarithms, the number of significant figures in the antilogarithm equals the number of digits in the mantissa. For example, if $\log x = 10.800$ (three significant figures in the mantissa/the part of the number that follows the decimal point), the antilogarithm value would be reported as $6.31 \times 10^{10}$ (notice that the value 6.31 has three significant figures).

## 1.3 The Simple Linear Relationship

When two variables $x$ and $y$ vary with each other linearly, their function may be written as

$$y = a + bx \tag{1.4}$$

where $y$ is the dependent variable and $x$ is the independent variable. The slope of the line is $b$, and the $y$-intercept is $a$. The coefficient $b$ can be positive or negative in value. When $b$ is positive, an increase in $x$ results in an increase in $y$. Conversely, if $b$ is negative, an increase in $x$ produces a decrease in $y$. Although Eq. (1.4) can be found manually, the usual method is to input the $y$ and $x$ values into a computer program to generate a linear equation. For example, the following data were obtained from a spectrophotometric experiment measuring the concentration of aspirin in solution:

| Concentration (mg/mL) | Absorbance |
|---|---|
| 0.0325 | 0.003 |
| 0.0650 | 0.006 |
| 0.1250 | 0.011 |
| 0.2500 | 0.023 |
| 0.5000 | 0.049 |

To obtain the linear relationship between concentration and absorbance, a simple scientific calculator may be used. The following equation is obtained:

$$\text{Absorbance} = -0.0008 + [0.1 \times \text{concentration (mg/mL)}] \tag{1.5}$$

Comparing Eq. (1.4) with Eq. (1.5), the absorbance value is the dependent variable and the concentration is the independent variable. The $y$-intercept is negative in this case, and statistically speaking, is not different from zero. The coefficient $b$ is positive, which is expected from relationships that represent Beer's law (Figure 1.1). It is important always to check whether or not the mathematical relationship adheres to the scientific norms. Using Eq. (1.5), the concentration of aspirin in an unknown solution may be estimated. For example, if the absorbance of an unknown solution of aspirin is 0.015, the estimated concentration of aspirin in solution is

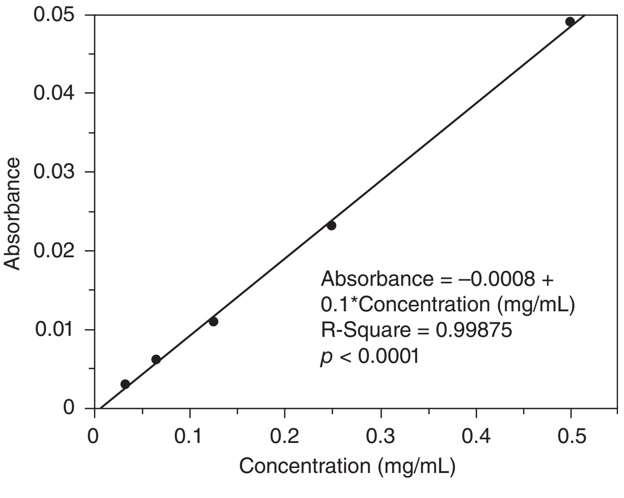

**Figure 1.1** Positive linear relationship between the concentration of aspirin in solution and absorbance readings. Data points are experimental values, and the solid line is the best-fit line for the data.

$$0.015 = -0.0008 + 0.1 \times \text{concentration (mg/mL)}$$
$$\text{concentration (mg/mL)} = 0.2$$

Note that the $y$-intercept of −0.0008 was used in estimating the concentration.

Based on Beer's law, the absorbance value is the logarithm of the ratio $I_0/I$, where $I_0$ and $I$ are the intensities of the incident and emitted light, respectively. The absorbance value is logarithmic; however, the spectrophotometer readily calculates its value and the operator does not need to handle logarithmic calculations. Equation (1.5) follows the general format of *Beer's law:*

$$\text{Absorbance} = \text{absorptivity} \times \text{pathlength of light} \times \text{concentration} \tag{1.6}$$

Comparing Eq. (1.4) with Eq. (1.6), the theoretical $y$-intercept value must be zero, and the coefficient $b$ is absorptivity × pathlength of light. The pathlength of light is predetermined by the instrument's tube holder (normally, 2 cm in length), and thus the slope of line $b$ allows calculation of the absorptivity value, which is an important physical characteristic of a drug. (The absorptivity value varies with the solvent, the temperature, and the wavelength being used in the experiment.) Under the conditions of this experiment, the absorptivity may be calculated as follows,assuming that the pathlength was 2 cm:

$$b = \text{absorptivity} \times \text{pathlength of light}$$
$$0.10 = \text{absorptivity} \times 2$$
$$\text{absorptivity} = 0.050\ \text{mL}/(\text{mg} \cdot \text{cm})$$

For some linear relationships, the slope of the line is negative. For example, Eq. (1.3) has a negative slope. The negative slope of Eq. (1.3) indicates that concentration of the drug in blood decreases with time. It should be emphasized, however, that the linear relationship is between the logarithm of the drug concentration versus time and not the concentration of the drug versus time. Thus, when presented with data such as drug concentration versus time (Figure 1.2), convert the drug concentration to logarithmic terms (natural or base-10) and then plot [ln (Drug Blood Concentration)] versus time. The resulting graph is a straight line (Figure 1.3).

| Time (h) | Concentration (μg/mL) | ln (concentration) |
|---|---|---|
| 0.25 | $1.0 \times 10^{1}$ | 2.30258509 |
| 4 | $1.0 \times 10^{0}$ | 0 |
| 6 | $2.0 \times 10^{-1}$ | −1.6094379 |
| 8 | $1.0 \times 10^{-1}$ | −2.3025851 |
| 10 | $8.0 \times 10^{-2}$ | −2.5257286 |
| 12 | $5.0 \times 10^{-2}$ | −2.9957323 |

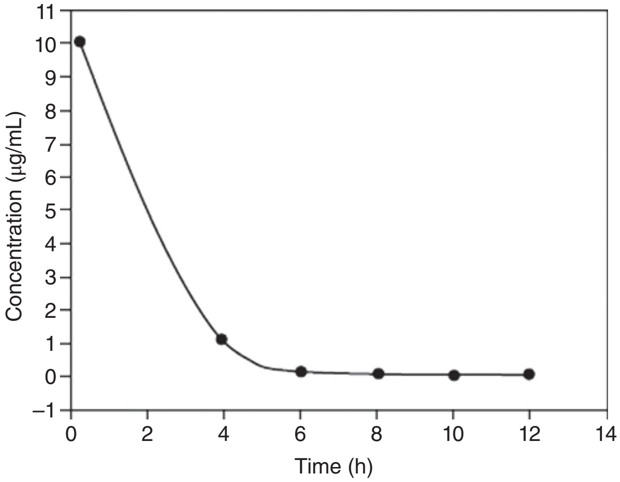

**Figure 1.2** Exponential decrease in drug blood concentration vs. time.

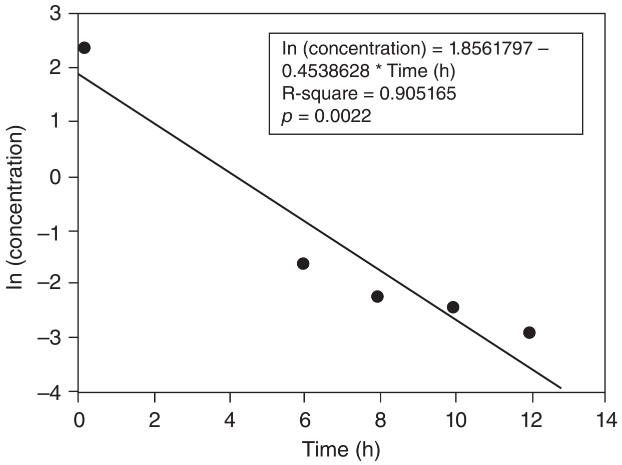

**Figure 1.3** Linear relationship of the natural logarithm of drug blood concentration vs. time.

The equation that relates the drug blood concentration vs. time is presented as

$$\ln(\text{concentration}) = 1.8561797 - 0.4538628 \times \text{time (h)} \tag{1.7}$$

From this equation, the first-order rate constant for elimination may be calculated from the slope:

$$\text{Slope} = -0.4538628 = -k_{\text{el}}$$

Therefore,

$$k_{\text{el}} = 0.45\ \text{h}^{-1}$$

The value of $k_{\text{el}}$ indicates that 45% of the drug concentration remaining is eliminated each hour.

## 1.4 Exponential Rules

In physical pharmacy expressions, many of the calculations require handling terms with exponents. The rules for handling exponents are (Stein 1977; Anton 1980):

1) Any number raised to the power of zero results in a value of 1: $x^0 = 1$
2) Any number raised to the power of 1 will equal its value: $x^1 = x$
3) $x^n \times x^m = x^{n+m}$
4) $x^n/x^m = x^{n-m}$
5) $1/x^n = x^{-n}$
6) $(x^n)^2 = x^{2n}$

In preparing buffer solutions, the ability of the resulting solution to resist a change in its pH is known as the *buffer capacity*. In calculating the buffer capacity value, the hydronium ion concentration, the acid dissociation constant, and the total buffer concentration must be known. Assuming that the total buffer concentration was 1 M, $[H_3O^+] = 1.0 \times 10^{-4}$M, and $K_a = 1.47 \times 10^{-4}$, the buffer capacity can be estimated from these values. The equation for calculating the buffer capacity is (Martin et al. 1983)

$$\text{Buffer capacity} = 2.303\,C\,\frac{K_a[\mathrm{H_3O^+}]}{\{K_a + [\mathrm{H_3O^+}]\}^2}$$

$$\text{Buffer Capacity} = (2.303)(1)\frac{(1.47 \times 10^{-4})(1.0 \times 10^{-4})}{\{(1.47 \times 10^{-4}) + (1.0 \times 10^{-4})\}^2}$$

$$\text{Buffer Capacity} = 0.56$$

The higher the value of the buffer capacity, the higher the resistance of the buffer is to a change in pH.

## 1.5 Logarithmic Rules

For most pharmaceutical applications, the *logarithmic function* serves to convert a nonlinear relationship to a linear one. Linearity allows easier calculations for coefficients from a mathematical model. Logarithmic functions are thought of as exponential equations; thus, $y = x^z$ translates into $z = \log_x y$ ($\log_x$ = logarithm of base $x$). There are two important logarithm symbols: log and ln; log is the logarithm to the base 10, whereas *ln* denotes a natural logarithmic function to the base $e$ ($e$ = 2.71828 ...). When handling logarithmic terms in an equation, the following mathematical rules apply (Stein 1977; Anton 1980):

1) $\ln x = 2.303 \log x$
2) $\log(x \times z) = \log x + \log z$ and $\ln(x \times z) = \ln x + \ln z$
3) $\log(x/z) = \log x - \log z$ and $\ln(x/z) = \ln x - \ln z$
4) $\log x = z$ or $x = 10^z$ and $\ln x = z$ or $x = e^z$
5) $\log x^z = z \log x$ and $\ln x^z = z \ln x$
6) $\ln e = 1$
7) $\log 10 = 1$

For example, consider Eq. (1.7) and convert the equation to its log form of base 10:

$$\begin{aligned}
&\ln(\text{concentration}) = 1.8561797 - 0.4538628 \times \text{time (h)}\\
&2.303 \log(\text{concentration}) = 1.8561797 - 0.4538628\\
&\times \text{time (h)}\\
&\log(\text{concentration}) = 0.8059833 - 0.1970746\\
&\times \text{time (h)}
\end{aligned} \tag{1.8}$$

Equations (1.7) and (1.8) are mathematically identical, and they produce the same value for the elimination rate constant. In applying Eq. (1.8) for calculating $k$, the slope of the equation is used:

$$\text{Slope} = -0.1970746 = \frac{-k}{2.303}$$

Therefore, $k = (2.303) \times (0.1970746) = 0.45\ \mathrm{h^{-1}}$, which is the same value (rounded to two significant figures) as that obtained using Eq. (1.7).

In Chapter 8, concepts related to the shelf-life determination of drug products are introduced. One area of concerns is the effect of a change in storage temperature on the stability of a drug. One equation uses the logarithm of the ratio of degradation rate constants at two different temperatures: $\log(k_2/k_1)$. The following calculations illustrate the use of logarithmic rules in solving such equations:

$$\begin{aligned}
&k_1 = 0.034\ \mathrm{min^{-1}}\\
&k_2 = \text{unknown}\\
&\log\frac{k_2}{k_1} = 0.842
\end{aligned}$$

To find $k_2$ we use,

$$\begin{aligned}
&\log\frac{k_2}{0.034} = 0.842\\
&\log k_2 - \log(0.034) = 0.842\\
&\log k_2 = 0.842 + \log(0.034) = -0.6265\\
&k_2 = 10^{-0.6265} = 0.24\ \mathrm{min^{-1}}
\end{aligned}$$

(*Refer to logarithm rule 4 above*)

Since drug degradation occurs with faster rates at higher temperatures than at lower ones, $k_2$ must occur at a temperature much higher than that observed with $k_1$.

Methods for the sterilization of pharmaceutical units may be divided into thermal and nonthermal. Thermal methods utilize heat as a means of achieving the destruction of microorganisms. The rate at which microbes get killed may be described by

$$M = M_0 e^{-kt} \tag{1.9}$$

where $M_0$ and $M$ are the initial microbial population and that at time $t$, respectively. The rate constant for the process of microorganism killing is $k$. Equation (1.9) can be rearranged to read

$$\frac{M}{M_0} = e^{-kt}$$

Taking the natural logarithm of both sides of the equation results in

$$\ln \frac{M}{M_0} = \ln\left(e^{-kt}\right) = -kt \tag{1.10}$$

(*Recall logarithm rules 5 and 6 where* $\ln x^z = z \ln x$ *and* $\ln e = 1$)

Equation (1.10) allows calculations of the rate constant if $M_0$ and $M$ are known. For example, the initial population of spores was $1.00 \times 10^4\ \text{mL}^{-1}$; following 60 seconds of exposure to a temperature of 120 °C, the population was reduced to $10\ \text{mL}^{-1}$. Calculate the rate constant:

$$\ln \frac{10}{10^4} = -k(60\ \text{s})$$

$$k = 0.115\ \text{s}^{-1}$$

This means that 11.5% of the remaining population of microorganisms is destroyed every second at 120 °C.

As was mentioned earlier, the pH is an important concept in pharmaceutical sciences. The following steps illustrate how pH is inversely proportional to hydrogen ion molar concentration using the logarithmic rules:

$$\text{pH} = -\log[\text{H}^+] = (-1)\log[\text{H}^+]$$

$$\text{pH} = \log[\text{H}^+]^{-1}\ [\text{based on logarithmic rule 5}]$$

$$\text{pH} = \log\left(\frac{1}{[\text{H}^+]}\right) [\text{according to exponent property 5}]$$

Thus, an increase in the hydrogen ion molar concentration of a solution results in a decrease in the pH value, and reverse.

Let us consider the following relationship (the ideal solubility equation) as an example for applying the above mathematical concepts:

$$x_2 = e^{-\Delta H_f \frac{T_m - T}{R(T_m T)}}$$

where $x_2$ is the solubility of the solute at temperature $T$ (Kelvin) expressed in mole fraction, $T_m$ is the melting point of the solid solute, $R$ is gas constant, and $\Delta H_f$ is the molar heat of fusion.

Taking the natural logarithm of both sides of the equation:

Based on logarithmic rules:

$$\ln x_2 = \left[-\Delta H_f \frac{T_m - T}{R(T_m T)}\right] \ln e$$

$$\ln x_2 = \left[\frac{-\Delta H_f\, T_m + \Delta H_f T}{R(T_m T)}\right]$$

$$\ln x_2 = \left[-\Delta H_f\, T_m)/R(T_m T)\right] + \left[\Delta H_f\, T)/R(T_m T)\right]$$

$$\ln x_2 = \left(-\frac{\Delta H_f}{RT}\right) + \left(\frac{\Delta H_f}{RT_m}\right)$$

The term $(\Delta H_f/RT_m)$ contains all constant values for a given solute.

The equation is a linear function of the format: $y = a + bx$ (refer to Eq. 1.4). Given $y = \ln x_2$, $x = (1/T)$, and $(\Delta H_f/RT_m) = a$ (the constant). If we set aside the constant term $(\Delta H_f/RT_m)$, then:

$$-\ln x_2 = \frac{\Delta H_f}{RT}$$

$$\ln x_2{}^{-1} = \frac{\Delta H_f}{RT}$$

$$\ln\left(\frac{1}{x_2}\right) = \frac{\Delta H_f}{RT}$$

Therefore, for an ideal solution, the molar solubility of the solute ($x_2$) is directly proportional to the solution's temperature; however, it is inversely proportional to the molar enthalpy of fusion.

It should be noted that logarithmic, exponential, and trigonometric functions are considered to be transcendental functions that cannot be expressed as algebraic operations (i.e. addition or multiplication). In other words, they transcend algebraic functions. This distinction becomes important when handling dimensional analysis, since transcendental operations are dimensionless.

## 1.6 Differential Equations

Differential equations may be employed to solve rate-related problems such as when studying drug degradation at a given rate and order of reaction. *Integration* is viewed as summation and is the opposite of differentiation. In pharmaceutical sciences, the notion of *differentiation* is commonly applied to topics that involve rates, such as drug degradation over time, drug diffusion through a membrane over time, and the rate by which a drug disappears from circulation following administration. The general format for the rate using a differential format is *dA/dt*, where *d* indicates a small quantity. Thus, *dA/dt* indicates that a small change in $A$ occurs for every small change in $t$. When applied to a differential equation, integration (symbol = $\int$) "sums up" all these small changes, thus, integration is considered to be a summation process.

The solutions for some important differential equations in physical pharmacy can be summarized as follows (Stein 1977; Anton 1980):

1) ***Zero order*:**

$$
\begin{aligned}
&\frac{dA}{dt} = -k_0A^0\\
&dA = -k_0dt\\
&\int_0^A dA = -k_0\int_0^t dt\\
&A - A_0 = -k_0(t - t_0)\\
&\text{given } t_0 = 0, A = A_0 - k_0t
\end{aligned}
\tag{1.11}
$$

2) ***First order*:**

$$
\begin{aligned}
&\frac{dA}{dt} = -k_1A^1\\
&\frac{dA}{A} = -k_1dt\\
&\int_0^A \frac{dA}{A} = -k_1\int_0^t dt\\
&\ln A - \ln A_0 = -k_1(t - t_0)\\
&\text{given } t_0 = 0, \quad \ln A = \ln A_0 - k_1t
\end{aligned}
\tag{1.12}
$$

3) ***Second order*:**

$$
\begin{aligned}
&\frac{dA}{dt} = -k_2A^2\\
&\frac{dA}{A^2} = -k_2dt\\
&\int_0^A \frac{dA}{A^2} = -k_2\int_0^t dt\\
&-\frac{1}{A} - \frac{-1}{A_0} = -k_2(t - t_0)\\
&\text{given } t_0 = 0,\\
&\frac{1}{A} = \frac{1}{A_0} + k_2t
\end{aligned}
\tag{1.13}
$$

4) ***Partial derivatives*** (Adamson 1969): When a variable such as $y$ is a function of two or more other variables ($q, x, w, \ldots$), the notion of partial derivatives ($\partial$) is applicable. Thus, we express $y$ with respect to $q, x$, as follows (the subscripts indicate that these variables are held constant during the differentiation calculation):

$$
\begin{aligned}
&\left(\frac{\partial y}{\partial q}\right)_{x,w}\\
&\left(\frac{\partial y}{\partial x}\right)_{q,w}\\
&\left(\frac{\partial y}{\partial w}\right)_{q,x}
\end{aligned}
$$

For example, the diffusion coefficient ($D$) is a function of temperature ($T$), viscosity of solution ($\eta$), and radius of particles ($r$). $A$ is Avogadro's number and $R$ is the gas constant:

$$
D = \frac{RT}{\pi\eta rA} \tag{1.14}
$$

Thus, to write $D$ as a function of $T$, $\eta$, and $r$, the following expressions may be used:

$$
\begin{aligned}
&\left(\frac{\partial D}{\partial T}\right)_{\eta,r}\\
&\left(\frac{\partial D}{\partial \eta}\right)_{T,r}\\
&\left(\frac{\partial D}{\partial r}\right)_{T,\eta}
\end{aligned}
$$

When all variables change simultaneously,

$$
dD = \left(\frac{\partial D}{\partial T}\right)_{\eta,r} dT + \left(\frac{\partial D}{\partial \eta}\right)_{T,r} d\eta + \left(\frac{\partial D}{\partial r}\right)_{T,\eta} dr
$$

Assuming that the temperature is held constant, $D$ is a function of viscosity and the radius of particles, $D = f(\eta, r)$. From Eq. (1.14),

$$
\begin{aligned}
&D = \frac{RT}{\pi A}\eta^{-1}r^{-1}\\
&D = (\text{constant})\ \eta^{-1}r^{-1}\\
&D_\eta = -(\text{constant})\ \eta^{-2}r^{-1}\\
&D_r = -(\text{constant})\ \eta^{-1}r^{-2}
\end{aligned}
\tag{1.15}
$$

where $D_\eta$ is the partial derivative of $D$ with respect to the viscosity of the solution, and $D_r$ is the partial derivative of $D$ with respect to the radius of the particles.

5) *Second-order partial derivatives*: With the temperature held constant, Eq. (1.15) can be written as a function of the viscosity of solution and the particle radius:

$$
\begin{aligned}
&D = f(\eta, r)\\
&\frac{\partial(\partial f/\partial\eta)}{\partial r} = \frac{\partial^2 f}{\partial\eta\partial r}
\end{aligned}
\tag{1.16}
$$

Equation (1.16) is the form of a second-order partial derivative.

For example, given $D$ at 25 °C, we have

$$
D = 31.31 \times 10^{-23}\ \eta^{-1}r^{-1}
$$

To find $\partial^2D/(\partial\eta\partial r)$, we write

$$
\begin{aligned}
\frac{\partial^2 D}{\partial\eta\partial r} &= \frac{\partial(\partial D\partial r)}{\partial\eta} = \frac{\partial(-(\text{constant})\eta^{-1}r^{-2})}{\partial\eta}\\
&= (\text{constant})\eta^{-2}r^{-2} = 31.31 \times 10^{-23}\ \eta^{-2}r^{-2}
\end{aligned}
$$

In thermodynamics (see Chapter 2), a change of volume of an ideal gas at a constant temperature does not result in a change in the internal energy of the system. Thus,

$$\left(\frac{\partial E}{\partial V}\right)_T = 0 \tag{1.17}$$

In addition, from the *gas law expression*, $PV = nRT$, and at a given constant pressure, the following partial differential equation may be written for the change of volume with a change in temperature:

$$\left(\frac{\partial V}{\partial T}\right)_P \tag{1.18}$$

Equation (1.18) and the gas law expression lead to

$$\left(\frac{\partial V}{\partial T}\right)_P = \frac{nR}{P} \tag{1.19}$$

And for 1 mol of an ideal gas ($n = 1$), $(\partial V/\partial T)_P = R/P =$ constant (Adamson 1969).

## 1.7 Expanding and Reducing Formulas

Pharmacists and pharmaceutical scientists are often asked to prepare volumes or quantities different from those given in a prescription or formula. When faced with either expanding or reducing formulas, a simple proportion method is sufficient to solve the problem. For example, a technician was asked to prepare 200 mL of the following buffer solution:

| | |
|---|---|
| $K_2HPO_4$ | 0.50 g |
| $KH_2PO_4$ | 0.35 g |
| Purified water, enough to make | 500 mL |

Using 200/500 as a proportion, each value in the formula is multiplied by this ratio:

$$(0.50\ \text{g})(200/500) = 0.20\ \text{g}$$
$$(0.35\ \text{g})(200/500) = 0.14\ \text{g}$$
$$(500\ \text{mL})(200/500) = 200\ \text{mL}$$

In preparing the buffer solution, the technician mixes 0.20 g of $K_2HPO_4$ and 0.14 g of $KH_2PO_4$ and dissolves them in enough purified water to make 200 mL of solution. If the volume of the solution to be prepared were 1 L instead of 200 mL, the calculations above would be repeated using the ratio 1000/500 in the calculations.

Another possible use of formula expansion or reduction is to be asked to calculate the amount of solute needed for a given volume of solution. Assume that a pharmacist was asked to prepare 500 mL of the following solution:

$Na^+$ 8 mEq
Purified water, enough to make 100 mL

Following the method described above, multiply the quantities in the formula by the ratio 500/100:

$Na^+$ $(8)(500/100) = 40$ mEq
Purified water, enough to make $(100)(500/100) = 500$ mL

If the pharmacist was to use NaCl (molecular mass = 58.44 g/mol) as the salt to provide sodium ions in solution, 40 mEq of NaCl equals (40 mEq) × (0.05844 g/mEq) or 2.34 g. Thus, the pharmacist dissolves 2.34 g of NaCl in enough purified water to make 500 mL of solution.

## 1.8 Weights and Measures

In formulating a dosage form, pharmaceutical scientists use the weight of ingredients to reflect their relative quantities in the product. The reason weights are used and not volumes because they are more accurate to measure than volumes, and they are not influenced by temperature change as volumes do. Even liquid ingredients are expressed in their weight. If in the original formulation from its source the ingredient is expressed in volume units, these may be converted to weight units using the density or the specific gravity of the liquid. For example, the specific gravity of polyethylene glycol 400 (PEG 400) is 1.140. Thus, 1 mL of PEG 400 weighs 1.140 g. If a product requires 60 mL of PEG 400, then the formulator would use 68.40 g of the liquid PEG. Care must be exercised in transferring viscous liquids from one container to another. While pouring the liquid, the viscous liquid should remain as far away from the walls of the receiving container as possible, and the operator should allow enough time for complete drainage from the delivering device. Graduate cylinders are often used for such a transfer. Volatile oils (essential oils) should never be stored or dispensed in plastic containers as they tend to diffuse through the plastic material and damage it. Glass is a safe choice to use in handling the essential oils. However, glass is not a good container to consider when it comes to solutions containing fluoride ions. The presence of calcium in the glass makes it easy for fluoride ions to combine with it, and over time, the solution loses its content of fluoride. There are four types of glass used in pharmaceutical manufacturing. These are Type I, Type II, Type III, and Type NP. Type I glass is made of borosilicate (boric oxide and silicon dioxide), while the other three types are composed of soda-lime material (sodium oxide and calcium oxide). Type NP is for general use, non-parenteral products. The other three types may be used to house parenteral preparations.

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## Glossary

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| **Beer's law** | States that the absorbance value of a drug solution is directly and linearly proportional to the concentration of the drug in solution. The Beer's law equation is given as $\text{Abs} = \text{As} \times l \times C$, where Abs is the absorbance, As the absorptivity, $l$ the path-length, and $C$ the concentration of the drug in solution. |
| **Buffer capacity** | An indicator of the degree of resistance that a buffer has toward a change in its pH upon challenging it with acids or bases. The higher the value of the buffer capacity, the higher the resistance of the buffer is to a change in pH. |
| **Differential equations** | May be employed to solve rate-related problems, such as when studying drug degradation at a given rate and order of reaction. The general format for the rate using a differential format is $dA/dt$, where $d$ indicates a small quantity. Thus, $dA/dt$ indicates that a small change in $A$ occurs for every small change in $t$. |
| **Gas law equation for an ideal gas** | $PV = nRT$, where $P$ is the pressure, $V$ is the volume, $n$ the number of moles, $R$ the gas constant, and $T$ the temperature in kelvin. |
| **Integration** | Viewed as summation; the opposite of differentiation. When applied in a differential equation, integration ($\int$) "sums up" all these small changes. |
| **Logarithmic functions** | Thought of as exponential equations; thus, $y = x^z$ translates into $z = \log_x y$ ($\log_x$ = logarithm of base $x$). |
| **Microbial population estimation for sterilization processes** | The rate at which microbes get killed may be described by the equation $M = M_0 e^{-kt}$, where $M_0$ and $M$ are the initial microbial population and that at time $t$, respectively. The rate constant for the process of microorganism killing is $k$. |
| **Partial derivatives** | When a variable such as $y$ is a function of two or more other variables ($q$, $x$, $w$ ...), the notion of partial derivatives ($\partial$) is applicable. |
| **pH** | The pH scale is used to measure the concentration of hydronium ions $[H_3O^+]$ in solution. |