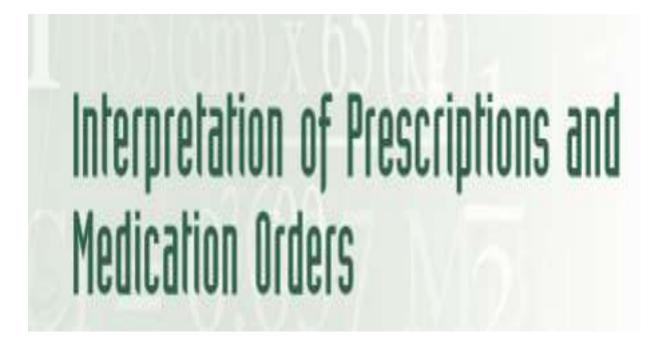
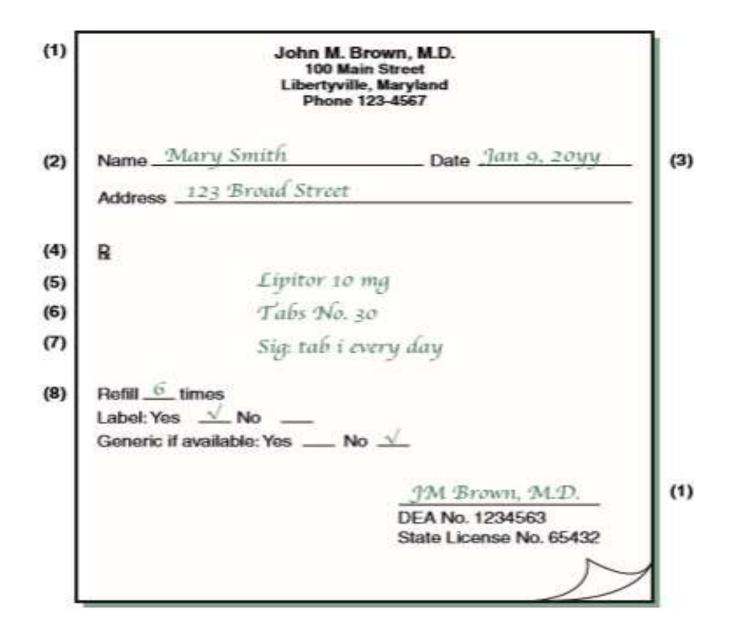
Pharmaceutical Calculations

13th Edition

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 Prescriber information and signature (2) Patient information (3) Date prescription was written (4) B symbol (the Superscription), meaning "take thou." "you take," or "recipe" (5) Medication prescribed (the Inscription) (6) Dispensing instructions to the pharmacist (the Subscription) (7) Directions to the patient (the Signa) (8) Special instructions. It is important to note that for any Medicaid or Medicare prescription and according to individual state laws, a handwritten language by the prescriber, such as "Brand necessary," may be required to disallow generic substitution.

Use of Roman Numerals on Prescriptions

Roman numerals commonly are used in prescription writing to designate quantities, as the: (1) quantity of medication to be dispensed and/or (2) quantity of medication to be taken by the patient per dose.

The student may recall the eight letters of fixed values used in the Roman system:

| 55 | = | 3/2 | Lorl | = | 50 |
|------------|-----|-----|--------|---|------|
| l, i, or j | = | 1 | Corc | = | 100 |
| Vorv | н | 5 | D or d | = | 500 |
| Xorx | :=: | 10 | M or m | = | 1000 |

TABLE 4.2 SELECTED ABBREVIATIONS, ACRONYMS, AND SYMBOLS USED IN PRESCRIPTIONS AND MEDICATION ORDERS^{a,b}

| ABBREVIATION | | ABBREVIATION | |
|--|--|--|--|
| (LATIN ORIGIN') | MEANING | (LATIN ORIGIN ^c) | MEANING |
| Prescription Filling Directions | | pt. | pint |
| aa. or (ana) ad (ad) disp. (dispensatur) div. (dividatur) | of each up to; to make dispense divide | qt. ss or ss (semissem tbsp. tsp. | quart one half tablespoonful teaspoonful |
| d.t.d. (dentur tales doses) | give of such doses | Signa/Patient Instructions | |
| ft (fiat) M. (mice) No. (numero) non rep. or NR (non | make mix number do not repeat | a.c. (ante cibos) ad lib. (<i>ad libitum</i>) admin A.M. (<i>ante</i> <i>meridiem</i>) | before meals at pleasure, freely administer morning |
| repatatur) q.s. (quantum sufficit) | a sufficient quantity | aq. (aqua) ATC b.i.d. (bir in dia) | water around the clock |
| q.s. ad (quantum sufficiat ad) Sig. (Signa) | a sufficient quantity to make write (directions on label) | b.i.d. (bis in die) c or č (cum) d (die) dil. (dilutus) et | twice a day with day dilute and |

h. or hr. (hora) h.s. (hora somni) i.c. (inter cibos) min. (minutum) m&n N8V noct. (nocie) NPO (non per os) p.c. (post cibos) P.M. (post meridiem) p.o. (per os) p.r.n. (pro re nata) g (quaque) GAM g4h, g8h, etc. g.i.d. (quarter in die) rep. (repetatur) s (sine) s.i.d. (semel in die) s.o.s. (si opus sit)

, stat. (statim) t.i.d. (ter in die) ut dict. (ut dictum) wk. hour at bedtime between meals minute morning and night nausea and vomiting night nothing by mouth after meals afternoon; evening

by mouth (orally) as needed every every morning every ____ hours four times a day

repeat without once a day if there is need; as needed *immediately* three times a day as directed week Examples of prescription directions to the pharmacist:

(a) M. ft. ung.

Mix and make an ointment.

(b) Ft. sup. no xii

Make 12 suppositories.

(c) M. Jt. cap. d.t.d. no. xxiv

Mix and make capsules. Give 24 such doses.

Examples of prescription directions to the patient:

(a) Caps. i. q.i.d. p.c. et h.s.

Take one (1) capsule four (4) times a day after each meal and at bedtime.

(b) gtt. ii rt.eye every a.m.

Instill two (2) drops in the right eye every morning.

(c) tab. ii stat tab. 1 q. 6 h. × 7 d.

Take two (2) tablets immediately, then take one (1) tablet every 6 hours for 7 days.

Examples:

B Hydrochlorothiazide 50 mg No. XC Sig. i q AM for HBP

If the prescription was filled initially on April 15, on about what date should the patient return to have the prescription refilled?

Answer: 90 tablets, taken 1 per day, should last 90 days, or approximately 3 months, and the patient should return to the pharmacy on or shortly before July 15 of the same year.

Penicillin V Potassium Oral Solution Disp.____mL Sig. 5 mL q 6h ATC × 10 d

How many milliliters of medicine should be dispensed? Answer: 5 mL times 4 (doses per day) equals 20 mL times 10 (days) equals 200 mL.

125 mg/5 mL

% Compliance rate =
$$\frac{\text{Number of days supply of medication}}{\text{Number of days since last Rx refill}} \times 100$$

Example:

What is the percent compliance rate if a patient received a 30-day supply of medicine and returned in 45 days for a refill?

% Compliance rate =
$$\frac{30 \text{ days}}{45 \text{ days}} \times 100 = 66.6\%$$
, answer.















FIGURE 3.1 Examples of conical and cylindric graduates, a pipet, and a pipet-filling bulb for volumetric measurement.



FIGURE 3.3 Torbal torsion balance and Ohaus electronic balance. (Courtesy of Total Pharmacy Supply, Inc.)

Weighing by the Aliquot Method

The *aliquot method of weighing* is a method by which small quantities of a substance may be obtained within the desired degree of accuracy by weighing a larger-than-needed portion of the substance, diluting it with an inert material, and then weighing a portion (aliquot) of the mixture calculated to contain the desired amount of the needed substance. A stepwise description of the procedure is depicted in Figure 3.6 and is described as follows:

Aliquot Method of Weighing and Measuring

Preliminary Step. Calculate the smallest quantity of a substance that can be weighed on the balance with the desired precision.

The equation used:

 $\frac{100\% \times \text{Sensitivity Requirement (mg)}}{\text{Acceptable Error (\%)}} = \text{Smallest Quantity (mg)}$

Example:

On a balance with an SR of 6 mg, and with an acceptable error of no greater than 5%, a quantity of not less than 120 mg must be weighed.

$$\frac{100\% \times 6 \text{ mg}}{5\%} = 120 \text{ mg}$$

Step 1. Select a multiple of the desired quantity that can be weighed with the required precision.

- If the quantity of a required substance is *less than* the minimum weighable amount, select a "multiple" of the required quantity that will yield an amount equal to or greater than the minimum weighable amount. (A larger-than-necessary multiple may be used to exceed the minimum accuracy desired.)
- Example:

If the balance in the example in the preliminary step is used, and if 5 mg of a drug substance is required on a prescription, then a quantity at least **25 times** (the multiple) the desired amount, or 125 mg (5 mg \times 25), must be weighed for the desired accuracy. (If a larger multiple is used, say 30, and 150 mg of the substance is weighed [5 mg \times 30], then a weighing error of only 4% would result.)

Step 2. Dilute the multiple quantity with an inert substance.

- The amount of inert diluent to use is determined by the fact that the aliquot portion of the drug-diluent mixture weighed in Step 3 must be equal to or greater than the minimum weighable quantity previously determined.
- By multiplying the amount of the aliquot portion to weigh in *Step 3* by the multiple selected in *Step 1*, the total quantity of the mixture to prepare is determined.
- Example:

According to the preliminary step, 120 milligrams or more must be weighed for the desired accuracy. If we decide on 120 mg for the aliquot portion in Step 3, and multiply it by the multiple selected in Step 1 (i.e., 25), we arrive at 3000 mg for the total quantity of the drug-diluent mixture to prepare. Subtracting the 125 mg of drug weighed in Step 1, we must add 2875 mg of diluent to prepare the 3000 mg of drug-diluent mixture.

Step 3. Weigh the aliquot portion of the dilution that contains the desired quantity.

- Since 25 times the needed amount of drug substance was weighed (Step 1), an aliquot part equal to ¹/₂₅ of the 3000-mg drug-diluent mixture, or 120 mg, will contain the required quantity of drug substance.
- Proof: $\frac{1}{25} \times 125 \text{ mg} (\text{drug substance weighed in Step 1}) = 5 \text{ mg}$ $\frac{1}{25} \times 2875 \text{ mg} (\text{diluent weighed in Step 2}) = \frac{115 \text{ mg}}{120 \text{ mg aliquot part}}$

Measuring Volume by the Aliquot Method

Examples:

A formula calls for 0.5 milliliter of hydrochloric acid. Using a 10-milliliter graduate calibrated from 2 to 10 milliliters in 1-milliliter divisions, explain how you would obtain the desired quantity of hydrochloric acid by the aliquot method.

If 4 is chosen as the multiple, and if 2 milliliters is set as the volume of the aliquot, then:

- 1. Measure 4 \times 0.5 mL, or 2 mL of the acid
- 2. Dilute with <u>6 mL</u> of water to make 8 mL of dilution
- Measure ¹/₄ of dilution, or 2 mL of dilution, which will contain 0.5 mL of hydrochloric acid, answer.

Percentage of Error

Because measurements in the community pharmacy are never *absolutely* accurate, it is important for the pharmacist to recognize the limitations of the instruments used and the magnitude of the errors that may be incurred. When a pharmacist measures a volume of liquid or weighs a material, two quantities become important; (1) the *apparent* weight or volume measured, and (2) the possible excess or deficiency in the actual quantity obtained.

Percentage of error may be defined as the maximum potential error multiplied by 100 and divided by the quantity desired. The calculation may be formulated as follows:

 $\frac{\text{Error} \times 100\%}{\text{Quantity desired}} = \text{Percentage of error}$

Example:

Using a graduated cylinder, a pharmacist measured 30 milliliters of a liquid. On subsequent examination, using a narrow-gauge burette, it was determined that the pharmacist had actually measured 32 milliliters. What was the percentage of error in the original measurement?

32 milliliters - 30 milliliters = 2 milliliters, the volume of error

$$\frac{2 \text{ mL} \times 100\%}{30 \text{ mL}} = 6.7\%, \text{ answer.}$$

Examples:

When the maximum potential error is \pm 4 milligrams in a total of 100 milligrams, what is the percentage of error?

 $\frac{4 \text{ mg} \times 100\%}{100 \text{ mg}} = 4\%, \text{ answer.}$

A prescription calls for 800 milligrams of a substance. After weighing this amount on a balance, the pharmacist decides to check by weighing it again on a more sensitive balance, which registers only 750 milligrams. Because the first weighing was 50 milligrams short of the desired amount, what was the percentage of error?

 $\frac{50 \text{ mg} \times 100\%}{800 \text{ mg}} = 6.25\%$, answer.

Measure of Weight

The primary unit of weight in the SI is the gram, which is the weight of 1 cm³ of water at 4°C, its temperature of greatest density.

The table of metric weight:

| 1 kilogram (kg) | = 1000.000 grams |
|-------------------------------|------------------|
| 1 hectogram (hg) | = 100.000 grams |
| 1 dekagram (dag) | = 10.000 grams |
| 1 gram (g) | = 1.000 gram |
| 1 decigram (dg) | = 0.1000 gram |
| 1 centigram (cg) | = 0.010 gram |
| 1 milligram (mg) | = 0.001 gram |
| 1 microgram (μ g or mcg) | = 0.000,001 gram |
| | |

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| 1 centigram (cg) | = 0.010 gram |
| 1 milligram (mg) | = 0.001 gram |
| 1 microgram (µg or mcg) | = 0.000,001 gram |

TABLE 2.3 SOME USEFUL EQUIVALENTS

| Equivalents of Length | | | |
|----------------------------|------------|----------|------|
| 1 inch | = | 2.54 cm | |
| 1 meter (m) | = 39.37 in | | 7 in |
| Equivalents of Volume | | | |
| 1 fluidounce (fl. oz.) | = | 29.57 mL | |
| 1 pint (16 fl. oz.) | = | 473 | mL |
| 1 quart (32 fl. oz.) | = | 946 | mL |
| 1 gallon, US (128 fl. oz.) | = | 3785 | mL |
| 1 gallon, UK | - | 4545 | mL |
| Equivalents of Weight | | | |
| 1 pound (lb, Avoirdupois) | = | 454 | q |
| 1 kilogram (kg) | = | 2.2 | Īb |

- 4. (a) If a 10-mL vial of insulin contains 100 units of insulin per milliliter, and a patient is to administer 20 units daily, how many days will the product last the patient? (b) If the patient returned to the pharmacy in exactly 7 weeks for another vial of insulin, was the patient compliant as indicated by the percent compliance rate?
- 5. A prescription is to be taken as follows: 1 tablet q.i.d. the first day; 1 tablet t.i.d. the second day; 1 tablet b.i.d. × 5 d; and 1 tablet q.d. thereafter. How many tablets should be dispensed to equal a 30-day supply?

Percentage and Ratio

Chapter 6

Percent weight-in-volume (w/v) expresses the number of grams of a constituent in 100 mL of solution or liquid preparation and is used regardless of whether water or another liquid is the solvent or vehicle. Expressed as: % w/v. **Percent volume-in-volume** (v/v) expresses the number of milliliters of a constituent in 100 mL of solution or liquid preparation. Expressed as: % v/v. **Percent weight-in-weight** (w/w) expresses the number of grams of a constituent in 100 g of solution or preparation. Expressed as: % w/w.

TABLE 6.1 EXAMPLES OF PHARMACEUTICAL DOSAGE FORMS IN WHICH THE ACTIVE INGREDIENT IS OFTEN CALCULATED AND EXPRESSED ON A PERCENTAGE BASIS PERCENTAGE BASIS EXAMPLES OF APPLICABLE DOSAGE FORMS

Weight-in-volume Solutions (e.g., ophthalmic, nasal, otic,topical, large-volume parenterals), and lotions.

Volume-in-volume Aromatic waters, topical solutions, and Emulsions.

Weight-in-weight Ointments, creams, and gels

For the purposes of computation, percents are usually changed to equivalent decimal fractions.

This change is made by dropping the percent sign (%) and dividing the expressed numerator

by 100.

Thus, 12.5% 12.5/100, or 0.125; and

0.05% , 0.05/100, or 0.0005.

We must not forget that in the reverse process (changing a decimal to a percent), the decimal is multiplied by 100 and the percent sign (%) is affixed.

Percentage is an essential part of pharmaceutical calculations. The pharmacist encounters it frequently and uses it as a convenient means of expressing the concentration of an active or inactive material in a pharmaceutical preparation. Multiply the required number of millilitres by the percentage strength, expressed as a decimal,

to obtain the number of grams of solute or constituent in the solution or liquid preparation. The volume, in millilitres, represents the weight in grams of the solution or liquid preparation as if it

were pure water.

Volume (mL, representing grams) % (expressed as a decimal) grams (g) of solute or constituent

Examples of Weight-in-Volume Calculations

How many grams of dextrose are required to prepare 4000 mL of a 5% solution?

4000 mL represents 4000 g of solution

5% = 0.05

 $4000 \text{ g} \times 0.05 = 200 \text{ g}$, answer.

Or, solving by dimensional analysis:

$$\frac{5 \text{ g}}{100 \text{ mL}} \times 4000 \text{ mL} = 200 \text{ g, answer.}$$

How many grams of potassium permanganate should be used in compounding the following prescription?

RPotassium Permanganate0.02%Purified Water ad250 mLSig. as directed.250 mL represents 250 g of solution0.02% = 0.0002250 g × 0.0002 = 0.05 g, answer.

How many grams of aminobenzoic acid should be used in preparing 8 fluidounces of a 5% solution in 70% alcohol?

8 fl. oz. = 8 × 29.57 mL = 236.56 mL 236.56 mL represents 236.56 g of solution 5% = 0.05 236.56 g × 0.05 = 11.83 g, answer. To calculate the percentage weight-in-volume of a solution or liquid preparation, given the weight of the solute or constituent and the volume of the solution or liquid preparation, it should be remembered that the volume, in milliliters, of the solution represents the weight, in grams, of the solution or liquid preparation as if it were pure water.

What is the percentage strength (w/v) of a solution of urea, if 80 mL contains 12 g?

80 mL of water weighs 80 g

$$\frac{80 \text{ (g)}}{12 \text{ (g)}} = \frac{100 \text{ (\%)}}{\text{x (\%)}}$$
$$x = 15\%, \text{ answer.}$$

Calculating the volume of a solution or liquid preparation, given its percentage strength weight-in-volume and the weight of the solute or constituent, involves the following:

How many milliliters of a 3% solution can be made from 27 g of ephedrine sulfate?

$$\frac{3 (\%)}{100 (\%)} = \frac{27 (g)}{x (g)}$$

x = 900 g, weight of the solution if it were water
Volume (in mL) = 900 mL, answer.

Percentage Volume-in-Volume

Liquids are usually measured by volume, and the percentage strength indicates the number of parts by volume of an ingredient contained in the total volume of the solution or liquid preparation considered as 100 parts by volume. If there is any possibility of misinterpretation, this kind of percentage should be specified: e.g., 10% v/v.

Examples of Volume-in-Volume Calculations

How many milliliters of liquefied phenol should be used in compounding the following prescription?

| Ŗ | Liquefied Phenol | 2.5% |
|---|------------------------|--------|
| | Calamine Lotion ad | 240 mL |
| | Sig. For external use. | |

Volume (mL) × % (expressed as a decimal) = milliliters of active ingredient

 $240 \text{ mL} \times 0.025 = 6 \text{ mL}$, answer.

Or, solving by dimensional analysis:

$$\frac{2.5 \text{ mL}}{100 \text{ mL}} \times 240 \text{ mL} = 6 \text{ mL}, answer.$$

In preparing 250 mL of a certain lotion, a pharmacist used 4 mL of liquefied phenol. What was the percentage (v/v) of liquefied phenol in the lotion?

$$\frac{250 \text{ (mL)}}{4 \text{ (mL)}} = \frac{100 \text{ (\%)}}{\text{x (\%)}}$$
$$\text{x} = 1.6\%, \text{ answer.}$$

What is the percentage strength v/v of a solution of 800 g of a liquid with a specific gravity of 0.800 in enough water to make 4000 mL?

800 g of water measures 800 mL 800 mL ÷ 0.800 = 1000 mL of active ingredient

 $\frac{4000 \text{ (mL)}}{1000 \text{ (mL)}} = \frac{100 \text{ (\%)}}{\text{x (\%)}}$ x = 25%, answer.

The volume of a solution or liquid preparation, given the volume of the active ingredient and its percentage strength (v/v), may require first determining the volume of the active ingredient from its weight and specific gravity.

Peppermint spirit contains 10% v/v of peppermint oil. What volume of the spirit will contain 75 mL of peppermint oil?

 $\frac{10 (\%)}{100 (\%)} = \frac{75 (mL)}{x (mL)}$

If a veterinary liniment contains 30% v/v of dimethyl sulfoxide, how many milliliters of the liniment can be prepared from 1 lb of dimethyl sulfoxide (sp gr 1.10)?

1 lb = 454 g454 g of water measures 454 mL 454 mL ÷ 1.10 = 412.7 mL of dimethyl sulfoxide

$$\frac{30 (\%)}{100 (\%)} = \frac{412.7 (mL)}{x (mL)}$$

x = 1375.7 or 1376 mL, answer.

Percentage Weight-in-Weight

Percentage weight-in-weight (*true percentage* or *percentage by weight*) indicates the number of parts by weight of active ingredient contained in the total weight of the solution or mixture considered as 100 parts by weight.

Examples of Weight-in-Weight Calculations

How many grams of phenol should be used to prepare 240 g of a 5% (w/w) solution in water? Weight of solution (g) \times % (expressed as a decimal) = g of solute 240 g \times 0.05 = 12 g, answer. How many grams of a drug substance are required to make 120 mL of a 20% (w/w) solution having a specific gravity of 1.15?

120 mL of water weighs 120 g 120 g \times 1.15 = 138 g, weight of 120 mL of solution 138 g \times 0.20 = 27.6 g plus enough water to make 120 mL, *answer*. Sometimes in a weight-in-weight calculation, the weight of one component is known but *not* the total weight of the intended preparation. This type of calculation is performed as demonstrated by the following example.

How many grams of a drug substance should be added to 240 mL of water to make a 4% (w/w) solution?

100% - 4% = 96% (by weight) of water 240 mL of water weighs 240 g

 $\frac{96 (\%)}{4 (\%)} = \frac{240 (g)}{x (g)}$ x = 10 g, answer. It is usually impossible to prepare a specified *volume* of a solution or liquid preparation of given weight-in-weight percentage strength because the volume displaced by the active ingredient cannot be known in advance. If an excess is acceptable, we may make a volume somewhat more than that specified by taking the given volume to refer to the solvent or vehicle and from this quantity calculating the weight of the solvent or vehicle (the specific gravity of the solvent or vehicle must be known). Using this weight, we may follow the method just described to calculate the corresponding weight of the active ingredient needed.

CALCULATIONS CAPSULE

Specific Gravity

The specific gravity (sp gr) of a substance or a pharmaceutical preparation may be determined by the following equation:

Specific gravity = $\frac{\text{Weight of substance (g)}}{\text{Weight of equal volume of water (g)}}$

The following equation may be used to convert the volume of a substance or pharmaceutical preparation to its weight:*

Weight of substance = Volume of substance × Specific gravity

Or simply,

$g = mL \times sp gr$

The following equation may be used to convert the weight of a substance or pharmaceutical preparation to its volume:*

 $Volume of substance = \frac{Weight of substance}{Specific gravity}$

Or simply,

$$mL = \frac{g}{sp gr}$$

* The full explanation on why these equations work may be found in the section "Use of Specific Gravity in Calculations of Weight and Volume," on page 73. How should you prepare 100 mL of a 2% (w/w) solution of a drug substance in a solvent having a specific gravity of 1.25?

100 mL of water weighs 100 g 100 g \times 1.25 = 125 g, weight of 100 mL of solvent 100% - 2% = 98% (by weight) of solvent

$$\frac{98 (\%)}{2 (\%)} = \frac{125 (g)}{x (g)}$$
$$x = 2.55 g$$

Therefore, dissolve 2.55 g of drug substance in 125 g (or 100 mL) of solvent, answer.

If the weight of the finished solution or liquid preparation is not given when calculating its percentage strength, other data must be supplied from which it may be calculated: the weights of both ingredients, for instance, or the volume and specific gravity of the solution or liquid preparation.

If 1500 g of a solution contains 75 g of a drug substance, what is the percentage strength (w/w) of the solution?

$$\frac{1500 \text{ (g)}}{75 \text{ (g)}} = \frac{100 \text{ (\%)}}{\text{x (\%)}}$$
$$x = 5\%, \text{ answer}$$

Or, solving by dimensional analysis:

$$\frac{75 \text{ g}}{1500 \text{ g}} \times 100\% = 5\%$$
, answer.

If 5 g of boric acid is added to 100 mL of water, what is the percentage strength (w/w) of the solution?

100 mL of water weighs 100 g 100 g + 5 g = 105 g, weight of solution

$$\frac{105 \text{ (g)}}{5 \text{ (g)}} = \frac{100 \text{ (\%)}}{x \text{ (\%)}}$$
$$x = 4.76\%, \text{ answer.}$$

If 1000 mL of syrup with a specific gravity of 1.313 contains 850 g of sucrose, what is its percentage strength (w/w)?

1000 mL of water weighs 1000 g 1000 g \times 1.313 = 1313 g, weight of 1000 mL of syrup

$$\frac{1313 \text{ (g)}}{850 \text{ (g)}} = \frac{100 \text{ (\%)}}{\text{x (\%)}}$$
$$x = 64.7\%, \text{ answer.}$$

Weight-in-Weight Calculations in Compounding

Weight-in-weight calculations are used in the following types of manufacturing and compounding problems.

What weight of a 5% (w/w) solution can be prepared from 2 g of active ingredient?

$$\frac{5 (\%)}{100 (\%)} = \frac{2 (g)}{x (g)}$$

x = 40 g, answer.

How many milligrams of hydrocortisone should be used in compounding the following prescription?

| Ŗ | Hydrocortisone | 1/8% |
|---------|--------------------------------------|---------------|
| - 34.55 | Hydrophilic Ointment ad | 10 g |
| | Sig. Apply. | |
| | $\frac{1}{8}\% = 0.125\%$ | |
| 10 ; | $g \times 0.00125 = 0.0125$ g or 12. | 5 mg, answer. |

How many grams of benzocaine should be used in compounding the following prescription?

2% 2

Benzocaine Polyethylene Glycol Base ad Make 24 such suppositories Sig. Insert one as directed.

2 g \times 24 = 48 g, total weight of mixture 48 g \times 0.02 = 0.96 g, answer. **CASE IN POINT 6.2³:** A pharmacist receives the following prescription but does not have hydrocortisone powder on hand. However, the pharmacist does have an injection containing 100 mg of hydrocortisone per milliliter of injection. A search of the literature indicates that the injection has a specific gravity of 1.5.

- B Hydrocortisone 1.5% Cold Cream qs 30 g
 - (a) How many grams of hydrocortisone are needed to fill the prescription?
 - (b) How many milliliters of the hydrocortisone injection would provide the correct amount of hydrocortisone?
 - (c) How many grams of cold cream are required?
- (a) 30 g × 0.015 (1.5% w/w) = 0.45 g hydrocortisone needed, answer.
- (b) $\frac{0.1 \text{ g}}{1 \text{ mL}} = \frac{0.45 \text{ g}}{\text{x mL}}$; x = 4.5 mL hydrocortisone injection, answer.
- (c) 4.5 mL × 1.5 (specific gravity) = 6.75 g (weight of hydrocortisone injection); 30 g - 6.75 g = 23.25 g cold cream needed, answer.

Ratio Strength

The concentrations of weak solutions are frequently expressed in terms of ratio strength. Because all percentages are a ratio of parts per hundred, ratio strength is merely another way of expressing the percentage strength of solutions or liquid preparations (and, less frequently, of mixtures of solids). For example, 5% means 5 parts per 100 or 5:100. Although 5 parts per 100 designates a ratio strength, it is customary to translate this designation into a ratio, the first figure of which is 1; thus, 5:100 = 1:20.

When a ratio strength, for example, 1:1000, is used to designate a concentration, it is to be interpreted as follows:

- For solids in liquids = 1 g of solute or constituent in 1000 mL of solution or liquid preparation.
- For liquids in liquids = 1 mL of constituent in 1000 mL of solution or liquid preparation.
- For solids in solids = 1 g of constituent in 1000 g of mixture.

The ratio and percentage strengths of any solution or mixture of solids are proportional, and either is easily converted to the other by the use of proportion.

Example Calculations Using Ratio Strength

Express 0.02% as a ratio strength.

 $\frac{0.02 (\%)}{100 (\%)} = \frac{1 (\text{part})}{\text{x (parts)}}$ x = 5000Ratio strength = 1:5000, answer.

Express 1:4000 as a percentage strength.

$$\frac{4000 \text{ (parts)}}{1 \text{ (part)}} = \frac{100 \text{ (\%)}}{x \text{ (\%)}}$$
$$x = 0.025\%, \text{ answer.}$$

A certain injectable contains 2 mg of a drug per milliliter of solution. What is the ratio strength (w/v) of the solution?

$$2 \text{ mg} = 0.002 \text{ g}$$
$$\frac{0.002 \text{ (g)}}{1 \text{ (g)}} = \frac{1 \text{ (mL)}}{x \text{ (mL)}}$$
$$x = 500 \text{ mL}$$
Ratio strength = 1:500, answer.

What is the ratio strength (w/v) of a solution made by dissolving five tablets, each containing 2.25 g of sodium chloride, in enough water to make 1800 mL?

 $2.25 \text{ g} \times 5 = 11.25 \text{ g of sodium chloride}$ $\frac{11.25 \text{ (g)}}{1 \text{ (g)}} = \frac{1800 \text{ (mL)}}{\text{x (mL)}}$ x = 160 mLRatio strength = 1:160, answer.

How many grams of potassium permanganate should be used in preparing 500 mL of a 1:2500 solution?

 $\begin{array}{rcl} 1:2500 &= 0.04\% \\ 500 \ (g) \ \times \ 0.0004 &= 0.2 \ g, \ answer. \end{array}$

Or,

1:2500 means 1 g in 2500 mL of solution

$$\frac{2500 \text{ (mL)}}{500 \text{ (mL)}} = \frac{1 \text{ (g)}}{x \text{ (g)}}$$

x = 0.2 g, answer

How many milligrams of gentian violet should be used in preparing the following solution?

 B:
 Gentian Violet Solution
 500 mL

 1:10,000
 Sig. Instill as directed.
 1:10,000 = 0.01%

 $500 \text{ (g)} \times 0.0001 = 0.050 \text{ g or } 50 \text{ mg}, answer.$

Or, 1:10,000 means 1 g of 10,000 mL of solution

$$\frac{10,000 \text{ (mL)}}{500 \text{ (mL)}} = \frac{1 \text{ (g)}}{x \text{ (g)}}$$

x = 0.050 g or 50 mg, answer.

How many milligrams of hexachlorophene should be used in compounding the following prescription?

B Hexachlorophene 1:400
 Hydrophilic Ointment ad 10 g
 Sig. Apply.

1:400 = 0.25%10 (g) × 0.0025 = 0.025 g or 25 mg, answer. Or,

1:400 means 1 g in 400 g of ointment

$$\frac{400 \text{ (g)}}{10 \text{ (g)}} = \frac{1 \text{ (g)}}{x \text{ (g)}}$$

x = 0.025 g or 25 mg, answer.

Example Calculations of the Size of a Dose

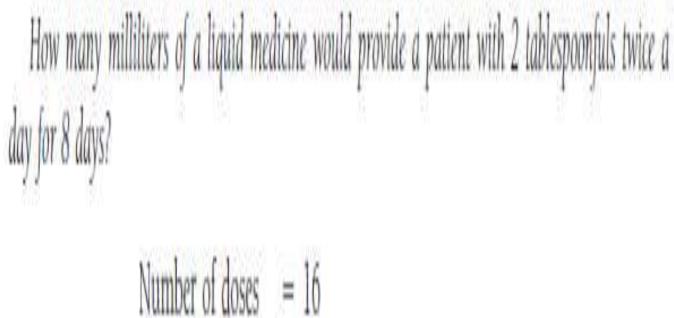
How many teaspoonfuls would be prescribed in each dose of an elixir if 180 mL contained 18 doses? Size of dose = $\frac{180 \text{ mL}}{18}$ = 10 mL = 2 teaspoonfuls, answer.

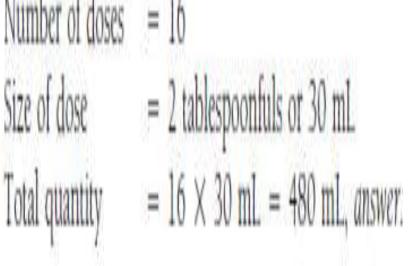
How many drops would be prescribed in each dose of a liquid medicine if 15 mL contained 60 doses? The dispensing dropper calibrates 32 drops/mL.

$$15 \text{ mL} = 15 \times 32 \text{ drops} = 480 \text{ drops}$$

Size of dose $= \frac{480 \text{ (drops)}}{60} = 8 \text{ drops}, answer.$

Example Calculations of the Total Quantity of Product





Additional Examples of Calculations of Dose

If 0.050 g of a substance is used in preparing 125 tablets, how many micrograms are represented in each tablet?

$$\frac{0.050 \text{ g} = 50 \text{ mg} = 50,000 \ \mu\text{g}}{\frac{50,000 \ (\mu\text{g})}{125}} = 400 \ \mu\text{g}, \text{ answer}.$$

How many milliliters of a mixture would provide a patient with a teaspoonful dose to be taken three times a day for 16 days?

```
Number of tsp doses = 16 \times 3 = 48 tsp
Total quantity = 48 \times 5 mL = 240 mL, answer.
```

How many grams of a drug will be needed to prepare 72 dosage forms if each is to contain 30 mg?

Number of doses= 72Size of dose= 30 mgTotal quantity= 72
$$\times$$
 30 mg = 2160 mg = 2.16 g, answer.

A cough mixture contains 48 mg of hydromorphone hydrochloride in 8 fl. oz. How many milligrams of hydromorphone hydrochloride are in each 2-teaspoonful dose?

1 fl. oz. = 6 tsp.
8 fl. oz. = 48 tsp.
48 tsp
$$\div$$
 2 = 24 doses
48 mg \div 24 = 2 mg, answer.

Or,

$$\frac{48 \text{ (tsp.)}}{2 \text{ (tsp.)}} = \frac{48 \text{ (mg)}}{x \text{ (mg)}}$$
$$x = 2 \text{ mg, answer.}$$

It takes approximately 4 g of ointment to cover an adult patient's leg. If a physician prescribes an ointment for a patient with total leg eczema to be applied twice a day for 1 week, which of the following product sizes should be dispensed: 15 g, 30 g, or 60 g?

Number of doses = 2 per day
$$\times$$
 7 days = 14
Size of dose = 4 g
Total quantity = 14 \times 4 g = 56 g; thus, 60 g product size, answer.

How many milligrams each of hydrocodone bitartrate and guaifenesin will be contained in each dose of the following prescription?

| | 0.12 g | |
|---|--|--|
| sin | 2.4 g | |
| rup ad | 120 mL | |
| Sig. Teaspoonful for cough. | | |
| 1 teaspoonful = 5 mL | | |
| | | |
| $0.12 \text{ g} \div 24 = 0.005 \text{ g} = 5 \text{ mg}$ hydrocodone bitartrate, a | | |
| $2.4 \text{ g} \div 24 = 0.1 \text{ g} = 100 \text{ mg guaifenesin, answers.}$ | | |
| | onful = 5 mL = 24 doses 24 = 0.005 | |

How many grams of a drug substance are required to make 120 mL of a solution each teaspoonful of which contains 3 mg of the drug substance?

$$1 \text{ teaspoonful} = 5 \text{ mL}$$

$$\frac{5 \text{ (mL)}}{120 \text{ (mL)}} = \frac{3 \text{ (mg)}}{x \text{ (mg)}}$$

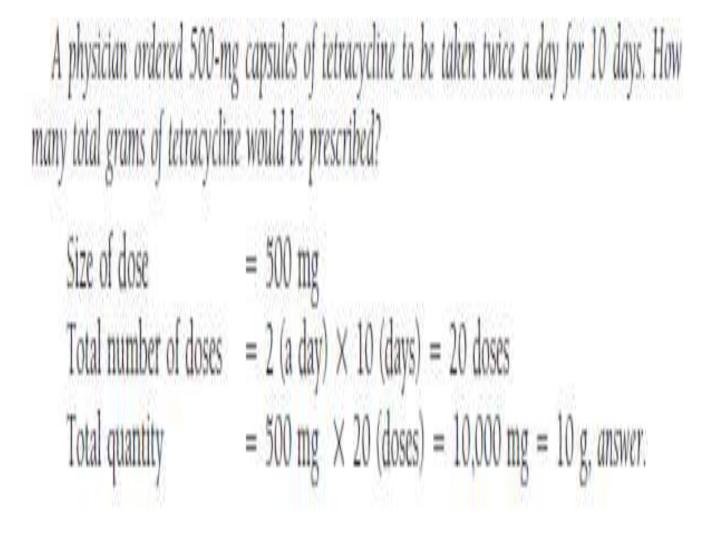
$$x = 72 \text{ mg or } 0.072 \text{ g, answer.}$$

If a preparation contains 5 g of a drug in 500 mL, how many grams are contained in each tablespoonful dose?

1 tablespoonful = 15 mL

$$\frac{500 \text{ (mL)}}{15 \text{ (mL)}} = \frac{5 \text{ (g)}}{x}$$

$$x = 0.15 \text{ g, answer.}$$





Example Calculations of Dose Based on Age

An over-the-counter cough remedy contains 120 mg of dextromethorphan in a 60-mL bottle of product. The label states the dose as $1\frac{1}{2}$ teaspoonfuls for a child 6 years of age. How many milligrams of dextromethorphan are contained in the child's dose?

$$\frac{1\frac{1}{2} \text{ teaspoonfuls}}{\frac{60 \text{ mL}}{120 \text{ mg}} = \frac{7.5 \text{ mL}}{x \text{ mg}}}$$
$$x = 15 \text{ mg dextromethorphan, answer.}$$

TABLE 8.1 CALCULATION OF PEDIATRIC DOSAGES OF DIGOXIN BASED ON AGE AND WEIGHT

| AGE | DIGOXIN DOSE (µg/kg) | | |
|----------------|----------------------|--|--|
| Premature | 15 to 25 | | |
| Full term | 20 to 30 | | |
| 1 to 24 months | 30 to 50 | | |
| 2 to 5 years | 25 to 35 | | |
| 5 to 10 years | 15 to 30 | | |
| Over 10 years | 8 to 12 | | |

From the data in Table 8.1, calculate the dosage range for digoxin for a 20-month-old infant weighing 6.8 kg.

$$\frac{30 \ \mu g}{x \ \mu g} = \frac{1 \ \text{kg}}{6.8 \ \text{kg}} \quad \frac{50 \ \mu g}{x \ \mu g} = \frac{1 \ \text{kg}}{6.8 \ \text{kg}}$$
$$\frac{x \ \mu g}{x \ \mu g} = \frac{1 \ \text{kg}}{6.8 \ \text{kg}}$$
$$\frac{x \ \mu g}{x \ \mu g} = \frac{1 \ \text{kg}}{6.8 \ \text{kg}}$$
$$\frac{x \ \mu g}{x \ \mu g} = \frac{1 \ \text{kg}}{6.8 \ \text{kg}}$$

CALCULATIONS CAPSULE

Dose Based on Body Weight

A useful equation for the calculation of dose based on body weight is:

Patient's dose (mg) = Patient's weight (kg)
$$\times \frac{Drug \text{ dose (mg)}}{1 \text{ (kg)}}$$

This equation is based on a drug dose in mg/kg and the patient's weight in kilograms. When different units are given or desired, other units may be substituted in the equation as long as the terms used are consistently applied.

The usual initial dose of chlorambucil is 150 mcg/kg of body weight. How many milligrams should be administered to a person weighing 154 lb.?

Solving by the equation: 150 mcg = 0.15 mg Patient's dose (mg) = 154 lb. $\times \frac{0.15 \text{ mg}}{2.2 \text{ lb.}} = 10.5 \text{ mg}$ chlorambucil, answer. Or, solving by ratio and proportion: 150 mcg = 0.15 mg 1 kg = 2.2 lb. $\frac{2.2 \text{ lb}}{154 \text{ lb}} = \frac{0.15 \text{ mg}}{x \text{ mg}}$; x = 10.5 mg chlorambucil, answer. The usual dose of sulfisoxazole for infants over 2 months of age and children is 60 to 75 mg/kg of body weight. What would be the usual range for a child weighing 44 lb.?

| 1 kg | = 2.2 lb |
|--|-------------|
| 20 kg | = 44 lb |
| 60 mg/kg × 20 kg | = 1200 mg |
| 75 mg/kg × 20 kg | = 1500 mg |
| Thus, the dosage range would be 1200 to 1500 | mg, answer. |

| BODY WEIGHT | | TOTAL mg/DAY | | | |
|-------------|--------|--------------|---------|---------|--|
| KILOGRAMS | POUNDS | 0.5 mg/kg | 1 mg/kg | 2 mg/kg | |
| 40 | 88 | 20 | 40 | 80 | |
| 50 | 110 | 25 | 50 | 100 | |
| 60 | 132 | 30 | 60 | 120 | |
| 70 | 154 | 35 | 70 | 140 | |
| 80 | 176 | 40 | 80 | 160 | |
| 90 | 198 | 45 | 90 | 180 | |
| 100 | 220 | 50 | 100 | 200 | |

Dosing Tables

For some drugs dosed according to body weight or body surface area, dosing tables appear in product literature to assist the physician and pharmacist. An example is presented in Table 8.2.

Using Table 8.2 and a daily dose of 0.5 mg/kg, how many 20-mg capsules of the drug product should be dispensed to a patient weighing 176 lb. if the dosage regimen calls for 15 weeks of therapy?

2 capsules/day \times 7 days/week \times 15 weeks = 210 capsules, answer.

Example Calculations of Dose Based on Body Surface Area

A useful equation for the calculation of dose based on BSA is:

Patient's dose =
$$\frac{\text{Patient's BSA (m^2)}}{1.73 \text{ m}^2} \times \text{Drug dose (mg)}$$

If the adult dose of a drug is 100 mg, calculate the approximate dose for a child with a BSA of 0.83 m^2 , using (a) the equation and (b) Table 8.3.

(a) Child's dose =
$$\frac{0.83 \text{ m}^2}{1.73 \text{ m}^2} \times 100 \text{ mg} = 47.97 \text{ or } 48 \text{ mg}$$
, answer.
(b) According to Table 8.3, a BSA of 0.83 m² represents 48% of the average adult BSA of 1.73 m²; thus, the child dose would be 48% of the usual adult dose:

 $100 \text{ mg} \times 0.48 = 48 \text{-mg}$ dose for child, answer.

TABLE 8.3 APPROXIMATE RELATION OF SURFACE AREA AND WEIGHTS OF INDIVIDUALS OF AVERAGE BODY DIMENSION

| | | SURFACE AREA | PERCENTAGE | |
|-----------|--------|--------------|-------------------|--|
| | | IN SQUARE | OF ADULT DOSE* | |
| KILOGRAMS | POUNDS | METERS | | |
| 2 | 4.4 | 0.15 | 9 | |
| 3 | 6.6 | 0.20 | 11.5 | |
| 4 | 8.8 | 0.25 | 14 | |
| 5 | 11.0 | 0.29 | 16.5 | |
| 6 | 13.2 | 0.33 | 19 | |
| 7 | 15.4 | 0.37 | 21 | |
| 8 | 17.6 | 0.40 | 23 | |
| 9 | 19.8 | 0.43 | 25 | |
| 10 | 22.0 | 0.46 | 27 | |
| 15 | 33.0 | 0.63 | 36 | |
| 20 | 44.0 | 0.83 | 48 | |
| 25 | 55.0 | 0.95 | 55 | |
| 30 | 66.0 | 1.08 | 62 | |
| 35 | 77.0 | 1.20 | 69 | |
| 40 | 88.0 | 1.30 | 75 | |
| 45 | 99.0 | 1.40 | 81 | |
| 50 | 110.0 | 1.51 | 87 | |
| 55 | 121.0 | 1.58 | 91 | |

* Based on average adult surface area of 1.73 square meters.

Adapted from Martin EW et al., Techniques of Medication, J. B. Lippincott, 1969:31, who adapted it from Modell's Drugs of Choice (Mosby).

Using Table 8.4, find the dose of the hypothetical drug at a dose level of 300 mg/m² for a child determined to have a BSA of 1.25 m². Calculate to verify.

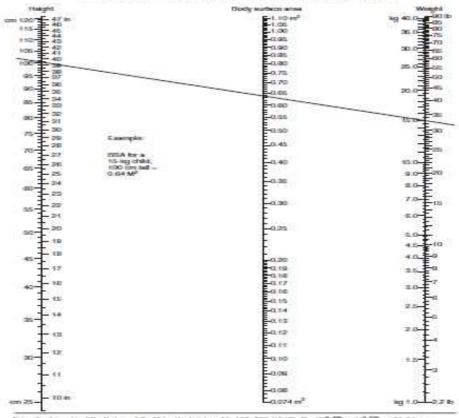
From Table 8.4, the dose = 375 mg, answer. From calculations: $300 \text{ mg/m}^2 \times 1.25 \text{ m}^2 = 375 \text{ mg dose}$, answer.

TABLE 8.4 PEDIATRIC DOSING GUIDELINE FOR A HYPOTHETICAL DRUG BASED ON BSA

| | | DOSE LEVEL | | | |
|-----------------------|-------------------------------|-------------------|-------------------|-------------------------------|--|
| PATIENT'S BSA (m²) | 250 mg/m ² DOSE | 300 mg/m² DOSE | 350 mg/m² DOSE | 400 mg/m ² DOSE | |
| 0.25 | 62.5 mg | 75 mg | 87.5 mg | 100 mg | |
| 0.50 | 125 mg | 150 mg | 175 mg | 200 mg | |
| 1.00 | 250 mg | 300 mg | 350 mg | 400 mg | |
| 1.25 | 312.5 mg | 375 mg | 437.5 mg | 500 mg | |
| 1.50 | 375 mg | 450 mg | 525 mg | 600 mg | |

Nomograms

Most BSA calculations use a standard *nomogram*, which includes both weight and height. Nomograms for children and adults are shown in Figures 8.1 and 8.2. The BSA of an individual is determined by drawing a straight line connecting the person's height and weight. The point at which the line intersects the center column indicates the person's BSA in square meters. In the



Nomogram for Determination of Body Surface Area from Height and Weight

From the bornule of Ou Bobs and Ou Bobs, Arch Intert Med 17, 043 (1918): $S = W^{0.426} \times H^{0.726} \times 71.54$, or log $S = \log W \times 0.425 + \log H \times 0.725 + 1.8564$ (S = body surface to cm², W = weight in leg, H = height in cm².

FIGURE 8.1 Body surface area of children, (Rom Dam K, Lenner C, Gelgy JR Scientific Tables, 7th Lit Base, Sectoreland JE Googy TOTOSTE)

CALCULATIONS CAPSULE

Dose Based on Body Surface Area

A useful equation for the calculation of dose based on body surface area is:

Patient's dose =
$$\frac{Patient's BSA (m^2)}{1.73 m^2} \times Drug dose (mg)$$

If there is need to determine a patient's BSA, a nomogram, or the following equation may be used:

Patient's BSA (m²) =
$$\sqrt{\frac{Patient's height (cm) \times Patient's weight (kg)}{3600}}$$

If the adult dose of a drug is 75 mg, what would be the dose for a child weighing 40 lb. and measuring 32 in. in height using the BSA nomogram?

From the nomogram, the BSA = 0.60 m^2

$$\frac{0.60 \text{ m}^2}{1.73 \text{ m}^2} \times 75 \text{ mg} = 26 \text{ mg}, answer.$$

If the dose of a drug is 5 mg/m², what would be the dose for a patient with a BSA of 1.9 m²? 5 mg \times 1.9 = 9.5 mg, answer.

$$BSA, m^{2} = \sqrt{\frac{Ht (cm) \times Wt (kg)}{3600}}$$

alculate the BSA for a patient measuring 165 cm in height and weighing 65 kg.
$$BSA, m^{2} = \sqrt{\frac{165 (cm) \times 65 (kg)}{3600}}$$

$$BSA = 1.73 m^{2}, answer.$$

By using Table 8.5, calculate the IV drug dose for a 3-pound 3-ounce neonate. $3 \text{ pounds} = 3 \times 454 \text{ g} = 1362 \text{ g}$ $3 \text{ ounces} = 3 \times 28.35 \text{ g} = 85 \text{ g}$ Weight of neonate = 1362 g + 85 g = 1447 g1447 g/1000 = 1.447 kg $30 \text{ mg/kg} \times 1.447 \text{ kg} = 43.4 \text{ mg}$ every 12 hours, answer.

TABLE 8.5 PARENTERAL DOSAGE SCHEDULE FOR A HYPOTHETICAL DRUG BASED ON PATIENT AGE AND CONDITION BEING TREATED

| 6 | DOSE | ROUTE | FREQUENCY |
|--|------------------------------|----------|-----------|
| Adults | | | 100 |
| Urinary tract infection | 250 mg | IV or IM | q12h |
| Bone and joint infections | 2 g | IV | q12h |
| Pneumonia | 500 mg-1 g | IV or IM | q8h |
| Mild skin infections | 500 mg-1 g | IV or IM | q8h |
| Life-threatening infections | 2 g | IV | q8h |
| Lung infections (normal kidney function) | 30–50 mg/kg (NMT 6 g/day) | IV | q8h |
| Neonates (up to 1 month) | 30 mg/kg | IV | q12h |
| Infants and Children (1 month to 12 years) | 30–50 mg/kg (NMT 6g/day) | IV | q8h |

Example Calculations of Chemotherapy Dosage Regimens

```
Regimen: VC<sup>13</sup>
Cycle: 28 d; repeat for 2–8 cycles
Vinorelbine, 25 mg/m<sup>2</sup>, IV, D 1,8,15,22
Cisplatin, 100 mg/m<sup>2</sup>, IV, D 1.
```

For each of vinorelbine and cisplatin, calculate the total intravenous dose per cycle for a patient measuring 5 ft. 11 in. in height and weighing 175 lb.

From the nomogram for determining BSA (a) find the patient's BSA and (b) calculate the quantity of each drug in the regimen.

```
(a) BSA = 2.00 \text{ m}^2, answer.
```

(b) Vinorelbine: 25 mg \times 2.00 (BSA) \times 4 (days of treatment) = 200 mg, (icplatin: 100 mg \times 2.00 (BSA) \times 1 = 200 mg answers

Cisplatin: 100 mg \times 2.00 (BSA) \times 1 = 200 mg, answers.

```
Regimen: CMF<sup>10</sup>
Cycle: 28 d
Cyclophosphamide, 100 mg/m<sup>2</sup>/d po, D 1–14.
Methotrexate, 40 mg/m<sup>2</sup>, IV, D 2,8.
Fluorouracil, 600 mg/m<sup>2</sup>, IV, D 1,8.
```

Calculate the total cycle dose for cyclophosphamide, methotrexate, and fluorouracil for a patient having a BSA of 1.5 m².

Cyclophosphamide:100 mg \times 1.5 (BSA) \times 14 (days) = 2100 mg = 2.1 g,Methotrexate:40 mg \times 1.5 \times 2Fluorouracil:600 mg \times 1.5 \times 2=1800 mg = 1.8 g, answers.

 The drugs may be administered concomitantly or alternately on the same or different days during a prescribed treatment cycle (e.g., 28 days). The days of treatment generally follow a prescribed format of written instructions, with D for "day," followed by the day(s) of treatment during a cycle, with a dash (-) meaning "to" and a comma (,) meaning "and." Thus, D 1-4 means "days 1 to 4," and D1,4 means "days 1 and 4."10

Isotonic solution

 When a solvent passes through a semipermeable membrane from a dilute solution into a more concentrated one, the concentrations become equalized and the phenomenon is known as *osmosis*.

 The pressure responsible for this phenomenon is termed *osmotic pressure* and varies with the nature of the solute.

- If the solute is a nonelectrolyte, its solution contains only molecules and the osmotic pressure varies with the concentration of the solute.
- If the solute is an electrolyte, its solution contains ions and the osmotic pressure varies with both the concentration of the solute and its degree of dissociation.
- Thus, solutes that dissociate present a greater number of particles in solution and exert a greater osmotic pressure than *un*dissociated molecules.

 Like osmotic pressure, the other colligative properties of solutions, vapor pressure, boiling point, and freezing point, depend on the number of particles in solution.

 Therefore, these properties are interrelated and a change in any one of them will result in a corresponding change in the others.

- Two solutions that have the same osmotic pressure are termed *isosmotic*.
- Many solutions intended to be mixed with body fluids are designed to have the same osmotic pressure for greater patient comfort, efficacy, and safety. A solution having the same osmotic pressure as a *specific* body fluid is termed *isotonic* (meaning of equal tone) with *that* specific body fluid.
- Solutions of *lower* osmotic pressure than that of a body fluid are termed *hypotonic*, whereas those having a *higher* osmotic pressure are termed *hypertonic*.
- Pharmaceutical dosage forms intended to be added directly to the blood or mixed with biological fluids of the eye, nose, and bowel are of principal concern to the pharmacist in their preparation and clinical application.

Most ophthalmic preparations are formulated to be isotonic

Injections that are not isotonic should be administered slowly and in small quantities tominimize tissue irritation, pain, and cell fluid imbalance ➤ Large volumes of hypertonic infusions containing dextrose, for example, can result in hyperglycemia, osmotic diuresis, and excessive loss of electrolytes.

Excess infusions of hypotonic fluids can result in the osmotic hemolysis of red blood cells and surpass the upper limits of the body's capacity to safely absorb excessive fluids. Physical/Chemical Considerations in the Preparation of Isotonic Solutions

The calculations involved in preparing isotonic solutions may be made in terms of data relatingThe calculations involved in preparing isotonic solutions may be made in terms of data relating to the <u>colligative properties</u> of solutions.

Theoretically, any one of these properties may be used as a basis for determining <u>tonicity</u>. Practically ,a comparison of <u>freezing points</u> is used for this purpose.

It is generally accepted that **-0.52°C** is the freezing point of both blood serum and lacrimal fluid.

Boric acid, for example, has a molecular weight of 61.8; thus (in theory), 61.8 g in 1000 g of water should produce a freezing point of -1.86° C. Therefore:

$$\frac{1.86 (^{\circ}C)}{0.52 (^{\circ}C)} = \frac{61.8 (g)}{x (g)}$$
$$x = 17.3 g$$

In short, 17.3 g of boric acid in 1000 g of water, having a weight-in-volume strength of approximately 1.73%, should make a solution isotonic with lacrimal fluid.

$$\frac{1.86 (^{\circ}C) \times 1.8}{0.52 (^{\circ}C)} = \frac{58.5 (g)}{x (g)}$$
$$x = 9.09 g$$

Hence, 9.09 g of sodium chloride in 1000 g of water should make a solution isotonic with blood or lacrimal fluid. In practice, a 0.90% w/v sodium chloride solution is considered isotonic with body fluids.

Simple isotonic solutions may then be calculated by using this formula:

 $\frac{0.52 \times \text{molecular weight}}{1.86 \times \text{dissociation (i)}} = \text{g of solute per 1000 g of water}$

0.52x molecular weight/1.86 = g of solute per 1000 ml of water forms isotonic solution of non electrolyte e.g.Dextrose.

0.52x molecular weight/1.86x dissociation factor(i) = g of solute per 1000 ml of water forms isotonic solution of an electrolyte e.g.Nacl.

- Nonelectrolytes and substances of slight dissociation1.0
- Substances that dissociate into 2 ions: 1.8
- Substances that dissociate into 3 ions: 2.6
- Substances that dissociate into 4 ions: 3.4
- Substances that dissociate into 5 ions: 4.2

Example Calculations of the / Factor

Zinc sulfate is a 2-ion electrolyte, dissociating 40% in a certain concentration. Calculate its dissociation (i) factor.

On the basis of 40% dissociation, 100 particles of zinc sulfate will yield:

40 zinc ions 40 sulfate ions 60 undissociated particles or 140 particles

Because 140 particles represent 1.4 times as many particles as were present before dissociation, the dissociation (i) factor is 1.4, answer.

Zinc chloride is a 3-ion electrolyte, dissociating 80% in a certain concentration. Calculate its dissociation (i) factor.

On the basis of 80% dissociation, 100 particles of zinc chloride will yield:

80 zinc ions 80 chloride ions 80 chloride ions 20 undissociated particles or 260 particles

Because 260 particles represents 2.6 times as many particles as were present before dissociation, the dissociation (i) factor is 2.6, *answer*.

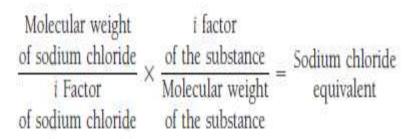
| | MOLECULAR | | | SODUM CHLORDE EQUIVALEN | |
|---|-----------|--------------|-----|-------------------------------|--|
| SUBSTANCE | WEIGHT | KO MS | 1 | (E VALUE) | |
| Antazoline phosphata | 363 | 2 | 1.8 | 0.16 | |
| Antipyrine | 188 | | 3.0 | 0.17 | |
| Atropine suitate H ₂ O | 695 | 30 | 2.6 | 0.12 | |
| Benoxinate hydrochionide | 345 | 2 | 1.8 | 0.17 | |
| Benzalkonium chloride | 360 | 2 | 1.8 | 0.16 | |
| Beturyi alcohol | 108 | 1 | 1.0 | 0.30 | |
| Boric add | 61.8 | | 1.0 | 0.52 | |
| Chioramphenicol | 323 | ÷ | 1.0 | 0.10 | |
| Chiorobutatiol | 177 | ÷. | 1.0 | 0.24 | |
| Chiortetracycline hydrochloride | 515 | 2 | 1.8 | 0.11 | |
| Cocaine hydrochioride | 340 | 2 | 1.8 | 0.16 | |
| | 512 | 2 | 1.8 | 0.11 | |
| Cromolyn sodium | 328 | 2 | 1.8 | 0.18 | |
| Cyclopentolate hydrochloride Democarium bromide | 717 | 3 | 2.6 | 0.12 | |
| | 180 | 1 | 1.0 | 0.18 | |
| Destrose (anhydrous) | 198 | - 2 0 | 1.0 | 0.16 | |
| Destrose H ₂ D | | | 1.8 | | |
| Diplivefrim hydrochionide | 388 | 2 | | 0.15 | |
| Ephedrine hydrochloride | 202 | 2 | 1.8 | 0.29 | |
| Ephedrine sulfate | 429 | 3 | 2.6 | 0.23 | |
| Epinophnino bitartrate | 333 | 2 | 1.8 | 0.18 | |
| Epinaphryl borate | 209 | 3 | 1.0 | 0.16 | |
| Eucatropina hydrochioride | 325 | 2 | 1.5 | 0.18 | |
| Fluorescein sodium | 376 | 3 | 2.6 | 0.31 | |
| Glycarin | 92 | 3 | 1.0 | 0.34 | |
| Homatropine hydrobromide | 356 | 2 | 1.8 | 0.17 | |
| Hydroxyamphetamine hydrobromide | 232 | 2 | 1.8 | 0.25 | |
| tdoxuridine | 354 | τ. | 1.0 | 0.09 | |
| Lidocaitia trydrochiorida | 289 | 2 | 1.8 | 0.22 | |
| Mannibol | 182 | | 1.0 | 0.18 | |
| Morphine suffate SH ₂ O | 759 | 3 | 2.6 | 0.11 | |
| Naphazo-line hydrochloride | 247 | 2 | 1.8 | 0.27 | |
| Cisymetazoline hydrochiorida | 297 | 2 | 1.8 | 0.20 | |
| Citytetracycline hydrochioride | 497 | 2 | 1.8 | 0.12 | |
| Phenacalne hydrochloride | 353 | 2 | 1.8 | 0.20 | |
| Phenobarbital sodium | 254 | 2 | 1.8 | 0.24 | |
| Phenylephrine hydrochloride | 204 | 2 | 1.8 | 0.32 | |
| Physostigmine sailcylate | 413 | 2 | 1.8 | 0.16 | |
| Physostigmine suifate | 640 | 3 | 2.6 | 0.13 | |
| Pliocarpina hydrochloride | 245 | 2 | 1.8 | 0.24 | |
| Pilocarpine nitrate | 271 | 2 | 1.5 | 0.23 | |
| Potassium biphosphate | 135 | 2 | 1.8 | 0.43 | |
| Potassium chioride | 74.5 | 2 | 1.8 | 0.76 | |
| Potassium lodide | 166 | 2 | 1.8 | 0.34 | |
| Potassium nitrate | 101 | 2 | 1.8 | 0.58 | |
| Potassium peniciliin G | 372 | 2 | 1.8 | 0.18 | |
| Procaine hydrochioride | 273 | 2 | 1.8 | 0.21 | |
| Properaceline hydrochionide | 331 | 2 | 1.8 | 0.18 | |
| Scopolamine hydrobromide 3H ₂ O | 438 | 2 | 1.8 | 0.12 | |
| Silver nitrate | 179 | 2 | 1.8 | 0.33 | |
| Sodium bicarbonate | 84 | 2 | 1.8 | 0.65 | |
| The second se | 381 | 5 | 4.2 | 0.42 | |
| Sodium borate 10H ₂ O | 301 | | | - 10. And | |

TABLE 11.1 SODIUM CHLORIDE EQUIVALENTS (E VALUES)

(contributed)

Example Calculations of the Sodium Chloride Equivalent

The sodium chloride equivalent of a substance may be calculated as follows:



Papaverine hydrochloride (m.w. 376) is a 2-ion electrolyte, dissociating 80% in a given concentration. Calculate its sodium chloride equivalent.

Because papaverine hydrochloride is a 2-ion electrolyte, dissociating 80%, its i factor is 1.8.

$$\frac{58.5}{1.8} \times \frac{1.8}{376} = 0.156$$
, or 0.16, answer.

Table 11.1 gives the *sodium chloride equivalents* (*E* values) of each of the substances listed. These values were calculated according to the rule stated previously. *If the number of grams of a substance included in a prescription is multiplied by its sodium chloride equivalent, the amount of sodium chloride represented by that substance is determined*.

The procedure for the *calculation of isotonic solutions with sodium chloride equivalents* may be outlined as follows:

Step 1. Calculate the amount (in grams) of sodium chloride represented by the ingredients in the prescription. Multiply the amount (in grams) of each substance by its sodium chloride equivalent.

Step 2. Calculate the amount (in grams) of sodium chloride, alone, that would be contained in an isotonic solution of the volume specified in the prescription, namely, *the amount of sodium chloride in a 0.9% solution of the specified volume*. (Such a solution would contain 0.009 g/mL.) *Step 3.* Subtract the amount of sodium chloride represented by the ingredients in the prescription (Step 1) from the amount of sodium chloride, alone, that would be represented in the specific volume of an isotonic solution (Step 2). The answer represents the amount (in grams) of sodium chloride to be added to make the solution isotonic.

Step 4. If an agent other than sodium chloride, such as boric acid, dextrose, or potassium nitrate, is to be used to make a solution isotonic, divide the amount of sodium chloride (Step 3) by the sodium chloride equivalent of the other substance.

Example Calculations of Tonicic Agent Required

How many grams of sodium chloride should be used in compounding the following prescription?

- Pilocarpine Nitrate
 Sodium Chloride
 Purified Water ad
 Make isoton. sol.
 Sig. For the eye.
- Step 1. 0.23×0.3 g = 0.069 g of sodium chloride represented by the pilocarpine nitrate Step 2. $30 \times 0.009 = 0.270$ g of sodium chloride in 30 mL of an isotonic sodium chloride solution
- Step 3. 0.270 g (from Step 2)
 - 0.069 g (from Step 1)
 - 0.201 g of sodium chloride to be used, answer.

How many grams of boric acid should be used in compounding the following prescription?

flPhenacaine Hydrochloride1%Chlorobutanol1/2%Boric Acidq.s.Purified Water ad60Make isoton. sol.5ig. One drop in each eye.

The prescription calls for 0.6 g of phenacaine hydrochloride and 0.3 g of chlorobutanol.

Step 1. $0.20 \times 0.6 \text{ g} = 0.120 \text{ g}$ of sodium chloride represented by phenacaine hydrochloride $0.24 \times 0.3 \text{ g} = 0.072 \text{ g}$ of sodium chloride represented by chlorobutanol

Total: 0.192 g of sodium chloride represented by both ingredients

- Step 2. 60 \times 0.009 = 0.540 g of sodium chloride in 60 mL of an isotonic sodium chloride solution
- *Step 3*. 0.540 g (from Step 2)

-<u>0.192</u> g (from Step 1)

0.348 g of sodium chloride required to make the solution isotonic

But because the prescription calls for boric acid:

Step 4. 0.348 g \div 0.52 (sodium chloride equivalent of boric acid) = 0.669 g of boric acid to be used, *answer*.

How many grams of potassium nitrate could be used to make the following prescription isotonic?

Rx Sol. Silver Nitrate601:500 w/vMake isoton. sol.Sig. For eye use.

The prescription contains 0.12 g of silver nitrate.

Step 1. 0.33 X 0.12 g = 0.04 g of sodium chloride represented by silver nitrate

Step 2. 60 X 0.009= 0.54 g of sodium chloride in 60 mL of an isotonic sodium chloride solution

Step 3. 0.54 g (from step 2)

- 0.04 g (from step 1)

0.50 g of sodium chloride required to make solution isotonic Because, in this solution, sodium chloride is incompatible with silver nitrate, the tonic agent of choice is potassium nitrate. Therefore,

Step 4. 0.50 g ÷ 0.58 (sodium chloride equivalent of potassium nitrate) = 0.86 g of potassium

nitrate to be used, answer.

How many grams of sodium chloride should be used in compounding the following prescription?

| Ingredient X | 0.5 |
|-------------------|------|
| Sodium Chloride | q.s. |
| Purified Water ad | 50 |
| Make isoton. sol. | |
| Sig. Eye drops. | |

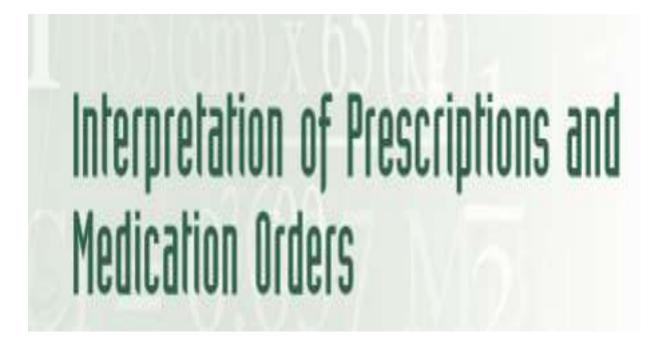
Let us assume that ingredient X is a new substance for which no sodium chloride equivalent is to be found in Table 11.1, and that its molecular weight is 295 and its *i* factor is 2.4. The Step kolfient entries to be used, answer $\frac{58.5}{1.8} \times \frac{2.4}{295} = 0.26$

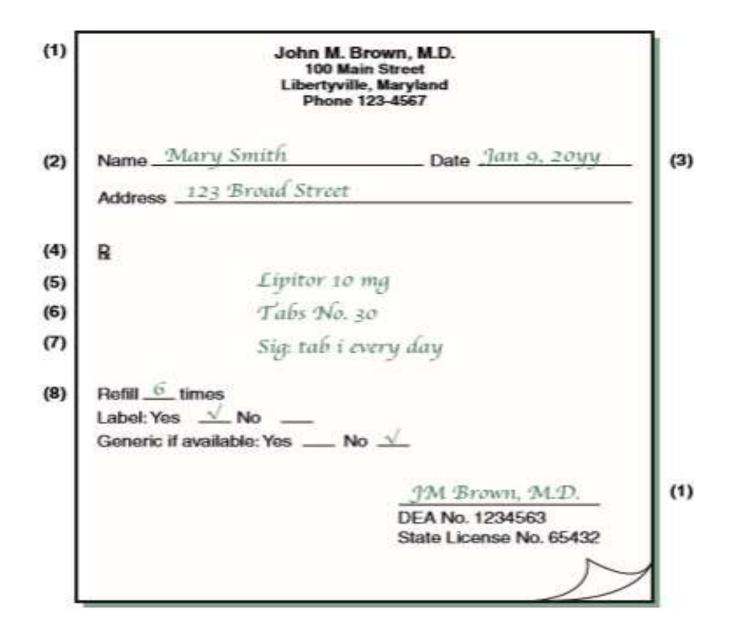
Pharmaceutical Calculations

13th Edition

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 Prescriber information and signature (2) Patient information (3) Date prescription was written (4) B symbol (the Superscription), meaning "take thou." "you take," or "recipe" (5) Medication prescribed (the Inscription) (6) Dispensing instructions to the pharmacist (the Subscription) (7) Directions to the patient (the Signa) (8) Special instructions. It is important to note that for any Medicaid or Medicare prescription and according to individual state laws, a handwritten language by the prescriber, such as "Brand necessary," may be required to disallow generic substitution.

Use of Roman Numerals on Prescriptions

Roman numerals commonly are used in prescription writing to designate quantities, as the: (1) quantity of medication to be dispensed and/or (2) quantity of medication to be taken by the patient per dose.

The student may recall the eight letters of fixed values used in the Roman system:

| 55 | = | 3/2 | Lorl | = | 50 |
|------------|-----|-----|--------|---|------|
| l, i, or j | = | 1 | Corc | = | 100 |
| Vorv | Ξ | 5 | D or d | = | 500 |
| Xorx | :=: | 10 | M or m | = | 1000 |

TABLE 4.2 SELECTED ABBREVIATIONS, ACRONYMS, AND SYMBOLS USED IN PRESCRIPTIONS AND MEDICATION ORDERS^{a,b}

| ABBREVIATION | | ABBREVIATION | |
|--|--|--|--|
| (LATIN ORIGIN') | MEANING | (LATIN ORIGIN ^c) | MEANING |
| Prescription Filling Di | rections | pt. | pint |
| aa. or (ana) ad (ad) disp. (dispensatur) div. (dividatur) | of each up to; to make dispense divide | qt. ss or ss (semissem tbsp. tsp. | quart one half tablespoonful teaspoonful |
| d.t.d. (dentur tales doses) | give of such doses | Signa/Patient Instructions | |
| ft (fiat) M. (mice) No. (numero) non rep. or NR (non | make mix number do not repeat | a.c. (ante cibos) ad lib. (<i>ad libitum</i>) admin A.M. (ante meridiem) | before meals at pleasure, freely administer morning |
| repatatur) q.s. (quantum sufficit) | a sufficient quantity | aq. (aqua) ATC b.i.d. (bir in dio) | water around the clock |
| q.s. ad (quantum sufficiat ad) Sig. (Signa) | a sufficient quantity to make write (directions on label) | b.i.d. (bis in die) c or č (cum) d (die) dil. (dilutus) et | twice a day with day dilute and |

h. or hr. (hora) h.s. (hora somni) i.c. (inter cibos) min. (minutum) m&n N8V noct. (nocie) NPO (non per os) p.c. (post cibos) P.M. (post meridiem) p.o. (per os) p.r.n. (pro re nata) g (quaque) GAM g4h, g8h, etc. g.i.d. (quarter in die) rep. (repetatur) s (sine) s.i.d. (semel in die) s.o.s. (si opus sit)

, stat. (statim) t.i.d. (ter in die) ut dict. (ut dictum) wk. hour at bedtime between meals minute morning and night nausea and vomiting night nothing by mouth after meals afternoon; evening

by mouth (orally) as needed every every morning every ____ hours four times a day

repeat without once a day if there is need; as needed *immediately* three times a day as directed week Examples of prescription directions to the pharmacist:

(a) M. ft. ung.

Mix and make an ointment.

(b) Ft. sup. no xii

Make 12 suppositories.

(c) M. Jt. cap. d.t.d. no. xxiv

Mix and make capsules. Give 24 such doses.

Examples of prescription directions to the patient:

(a) Caps. i. q.i.d. p.c. et h.s.

Take one (1) capsule four (4) times a day after each meal and at bedtime.

(b) gtt. ii rt.eye every a.m.

Instill two (2) drops in the right eye every morning.

(c) tab. ii stat tab. 1 q. 6 h. × 7 d.

Take two (2) tablets immediately, then take one (1) tablet every 6 hours for 7 days.

Examples:

B Hydrochlorothiazide 50 mg No. XC Sig. i q AM for HBP

If the prescription was filled initially on April 15, on about what date should the patient return to have the prescription refilled?

Answer: 90 tablets, taken 1 per day, should last 90 days, or approximately 3 months, and the patient should return to the pharmacy on or shortly before July 15 of the same year.

Penicillin V Potassium Oral Solution Disp.____mL Sig. 5 mL q 6h ATC × 10 d

How many milliliters of medicine should be dispensed? Answer: 5 mL times 4 (doses per day) equals 20 mL times 10 (days) equals 200 mL.

125 mg/5 mL

% Compliance rate =
$$\frac{\text{Number of days supply of medication}}{\text{Number of days since last Rx refill}} \times 100$$

Example:

What is the percent compliance rate if a patient received a 30-day supply of medicine and returned in 45 days for a refill?

% Compliance rate =
$$\frac{30 \text{ days}}{45 \text{ days}} \times 100 = 66.6\%$$
, answer.















FIGURE 3.1 Examples of conical and cylindric graduates, a pipet, and a pipet-filling bulb for volumetric measurement.



FIGURE 3.3 Torbal torsion balance and Ohaus electronic balance. (Courtesy of Total Pharmacy Supply, Inc.)

Weighing by the Aliquot Method

The *aliquot method of weighing* is a method by which small quantities of a substance may be obtained within the desired degree of accuracy by weighing a larger-than-needed portion of the substance, diluting it with an inert material, and then weighing a portion (aliquot) of the mixture calculated to contain the desired amount of the needed substance. A stepwise description of the procedure is depicted in Figure 3.6 and is described as follows:

Aliquot Method of Weighing and Measuring

Preliminary Step. Calculate the smallest quantity of a substance that can be weighed on the balance with the desired precision.

The equation used:

 $\frac{100\% \times \text{Sensitivity Requirement (mg)}}{\text{Acceptable Error (\%)}} = \text{Smallest Quantity (mg)}$

Example:

On a balance with an SR of 6 mg, and with an acceptable error of no greater than 5%, a quantity of not less than 120 mg must be weighed.

$$\frac{100\% \times 6 \text{ mg}}{5\%} = 120 \text{ mg}$$

Step 1. Select a multiple of the desired quantity that can be weighed with the required precision.

- If the quantity of a required substance is *less than* the minimum weighable amount, select a
 "multiple" of the required quantity that will yield an amount equal to or greater than the
 minimum weighable amount. (A larger-than-necessary multiple may be used to exceed the
 minimum accuracy desired.)
- Example:

If the balance in the example in the preliminary step is used, and if 5 mg of a drug substance is required on a prescription, then a quantity at least **25 times** (the multiple) the desired amount, or 125 mg (5 mg \times 25), must be weighed for the desired accuracy. (If a larger multiple is used, say 30, and 150 mg of the substance is weighed [5 mg \times 30], then a weighing error of only 4% would result.)

Step 2. Dilute the multiple quantity with an inert substance.

- The amount of inert diluent to use is determined by the fact that the aliquot portion of the drug-diluent mixture weighed in Step 3 must be equal to or greater than the minimum weighable quantity previously determined.
- By multiplying the amount of the aliquot portion to weigh in *Step 3* by the multiple selected in *Step 1*, the total quantity of the mixture to prepare is determined.
- Example:

According to the preliminary step, 120 milligrams or more must be weighed for the desired accuracy. If we decide on 120 mg for the aliquot portion in Step 3, and multiply it by the multiple selected in Step 1 (i.e., 25), we arrive at 3000 mg for the total quantity of the drug-diluent mixture to prepare. Subtracting the 125 mg of drug weighed in Step 1, we must add 2875 mg of diluent to prepare the 3000 mg of drug-diluent mixture.

Step 3. Weigh the aliquot portion of the dilution that contains the desired quantity.

- Since 25 times the needed amount of drug substance was weighed (Step 1), an aliquot part equal to ¹/₂₅ of the 3000-mg drug-diluent mixture, or 120 mg, will contain the required quantity of drug substance.
- Proof: $\frac{1}{25} \times 125 \text{ mg} (\text{drug substance weighed in Step 1}) = 5 \text{ mg}$ $\frac{1}{25} \times 2875 \text{ mg} (\text{diluent weighed in Step 2}) = \frac{115 \text{ mg}}{120 \text{ mg aliquot part}}$

Measuring Volume by the Aliquot Method

Examples:

A formula calls for 0.5 milliliter of hydrochloric acid. Using a 10-milliliter graduate calibrated from 2 to 10 milliliters in 1-milliliter divisions, explain how you would obtain the desired quantity of hydrochloric acid by the aliquot method.

If 4 is chosen as the multiple, and if 2 milliliters is set as the volume of the aliquot, then:

- 1. Measure 4 \times 0.5 mL, or 2 mL of the acid
- 2. Dilute with <u>6 mL</u> of water to make 8 mL of dilution
- Measure ¹/₄ of dilution, or 2 mL of dilution, which will contain 0.5 mL of hydrochloric acid, answer.

Percentage of Error

Because measurements in the community pharmacy are never *absolutely* accurate, it is important for the pharmacist to recognize the limitations of the instruments used and the magnitude of the errors that may be incurred. When a pharmacist measures a volume of liquid or weighs a material, two quantities become important; (1) the *apparent* weight or volume measured, and (2) the possible excess or deficiency in the actual quantity obtained.

Percentage of error may be defined as the maximum potential error multiplied by 100 and divided by the quantity desired. The calculation may be formulated as follows:

 $\frac{\text{Error} \times 100\%}{\text{Quantity desired}} = \text{Percentage of error}$

Example:

Using a graduated cylinder, a pharmacist measured 30 milliliters of a liquid. On subsequent examination, using a narrow-gauge burette, it was determined that the pharmacist had actually measured 32 milliliters. What was the percentage of error in the original measurement?

32 milliliters - 30 milliliters = 2 milliliters, the volume of error

$$\frac{2 \text{ mL} \times 100\%}{30 \text{ mL}} = 6.7\%, \text{ answer.}$$

Examples:

When the maximum potential error is \pm 4 milligrams in a total of 100 milligrams, what is the percentage of error?

 $\frac{4 \text{ mg} \times 100\%}{100 \text{ mg}} = 4\%, \text{ answer.}$

A prescription calls for 800 milligrams of a substance. After weighing this amount on a balance, the pharmacist decides to check by weighing it again on a more sensitive balance, which registers only 750 milligrams. Because the first weighing was 50 milligrams short of the desired amount, what was the percentage of error?

 $\frac{50 \text{ mg} \times 100\%}{800 \text{ mg}} = 6.25\%$, answer.

Measure of Weight

The primary unit of weight in the SI is the gram, which is the weight of 1 cm³ of water at 4°C, its temperature of greatest density.

The table of metric weight:

| 1 kilogram (kg) | = 1000.000 grams |
|-------------------------|------------------|
| 1 hectogram (hg) | = 100.000 grams |
| 1 dekagram (dag) | = 10.000 grams |
| 1 gram (g) | = 1.000 gram |
| 1 decigram (dg) | = 0.1000 gram |
| 1 centigram (cg) | = 0.010 gram |
| 1 milligram (mg) | = 0.001 gram |
| 1 microgram (µg or mcg) | = 0.000,001 gram |
| | |

Measure of Weight

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| 1 gram (g) | = 1.000 gram |
| 1 decigram (dg) | = 0.1000 gram |
| 1 centigram (cg) | = 0.010 gram |
| 1 milligram (mg) | = 0.001 gram |
| 1 microgram (µg or mcg) | = 0.000,001 gram |

TABLE 2.3 SOME USEFUL EQUIVALENTS

| Equivalents of Length | | | |
|----------------------------|---|----------|----|
| 1 inch | = | 2.54 cm | |
| 1 meter (m) | = | 39.37 in | |
| Equivalents of Volume | | | |
| 1 fluidounce (fl. oz.) | = | 29.57 mL | |
| 1 pint (16 fl. oz.) | = | 473 | mL |
| 1 quart (32 fl. oz.) | = | 946 | mL |
| 1 gallon, US (128 fl. oz.) | = | 3785 | mL |
| 1 gallon, UK | - | 4545 | mL |
| Equivalents of Weight | | | |
| 1 pound (lb, Avoirdupois) | = | 454 | q |
| 1 kilogram (kg) | = | 2.2 | Īb |

- 4. (a) If a 10-mL vial of insulin contains 100 units of insulin per milliliter, and a patient is to administer 20 units daily, how many days will the product last the patient? (b) If the patient returned to the pharmacy in exactly 7 weeks for another vial of insulin, was the patient compliant as indicated by the percent compliance rate?
- 5. A prescription is to be taken as follows: 1 tablet q.i.d. the first day; 1 tablet t.i.d. the second day; 1 tablet b.i.d. × 5 d; and 1 tablet q.d. thereafter. How many tablets should be dispensed to equal a 30-day supply?