VOLUME 5 NUMBER 2

Secundum Artem

Current & Practical Compounding Information for the Pharmacist.

Pharmaceutical Compounding Calculations

INTRODUCTION

Prescription compounding is a rapidly growing component of pharmacy practice. This can be attributed to a number of factors, including individualized patient therapy, lack of commercially available products, home healthcare, intravenous admixture programs, total parenteral nutrition programs and "problem solving" for the physician and patient in enhancing compliance with a specific therapeutic regimen. Pharmacists are creative and should have the ability to formulate patient-specific preparations for providing pharmaceutical care. Most compounded prescriptions require a number of calculations as part of preparation, packaging and dispensing.

Potential for Error:

One of the greatest potentials for error in prescription compounding is in the area of pharmacy math, or pharmacy calculations. Even though most of the processes are relatively simple, a misplaced decimal or "estimated" value for a medication can have serious consequences, including death. There is no excuse for ignorance in this area, and an individual unprepared to do the necessary calculations should not be involved in pharmaceutical compounding. It is of utmost importance that pharmacists be extremely well-grounded in the practice of pharmaceutical calculations as there is "zero tolerance" allowed in these vital operations.

This issue of *Secundum Artem* is provided as a review and reference source for commonly performed compounding calculations.

Solubility Expressions:

Solubility expressions in the literature and in the United States Pharmacopeia (USP) are "x:y" and "x in y", such as 1:4 and 1 in 4. This is stated as one part of solute plus 4 parts of solvent. This results in a 1:5 solution, or 1 part of solute in 5 parts of solution. A solubility expression is different from a ratio expression as just described. Let's look at it again. A solubility of 1:3 is 1 g solute + 3 mL solvent. This results in a 1:4 solution (1 part of solute in 4 parts of solution), a 1:3 solution is 1 g in 3 mL solution (sufficient solvent to make).

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Problem

One gram of boric acid is soluble in 18 mL water and makes a saturated solution. What is the percentage w/w and w/v of a saturated solution of boric acid? The total weight of the solution is 19 g. The strength of the solution w/w is 5.26%. The volume of the solution is between 18 and 19 mL and the w/v concentration is greater than 5.26%, possibly around 5.5%.

Problem

How much mannitol will be required to prepare 120 mL of a 1:10 solution?

$$\frac{1}{10} = \frac{x}{120} \qquad x = 12\text{ g}$$

12 grams of mannitol is placed in a graduated cylinder and solvent added to 120 mL.

Parts per "x" expressions

1 g/mL	100%	1 ppL (1 part per L)
1 mg/mL	0.1%	1 ppt (1 part per 1,000)
1 µg/mL	.0001%	1 ppm (1 part per 1,000,000) (also 1 g in 1,000,000 mL solution)
1 ng/mL	.0000001%	1 ppb (1 part per 1,000,000,000)

Problem

A pharmacist receives a prescription for 8 oz. of an oral rinse to contain 10 ppm Fluoride ion in

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Orange Flower Water. How much NaF would be required to prepare this Rx?

8 x 29.57 mL = 237 mL

$$\frac{10\ g}{1{,}000{,}000\ mL} = \frac{x\ g}{237\ mL}$$

x = .0024 g (2.4 mg) Fluoride Ion

Since 1 mg F = 2.2 mg NaF

$$\frac{1\ mg\ F}{2.2\ mg\ NaF} = \frac{2.4\ mg\ F}{x\ mg\ NaF}$$

x = 5.3 mg NaF

Calculation of the Number of Dosage Forms/ Volume to Dispense:

A pharmacist receives a prescription for Wormaway 1 mg/mL for a family to be given today and then repeated in seven days. What is the total quantity of Wormaway 1 mg/mL required for the family if the dose is 0.3 mg/Kg body weight?

Adult 1	175#/2.2	=	79.55 kg x 0.3	=	23.87 mg
Adult 2	125#/2.2	=	56.82 kg x 0.3	=	17.05 mg
Child 1	95#/2.2	=	43.18 kg x 0.3	=	12.95 mg
Child 2	75#/2.2	=	34.09 kg x 0.3	=	10.23 mg
Child 3	60#/2.2	=	27.27 kg x 0.3	=	8.18 mg
					72.28 mg/dose

72.28 mg/dose x 2 doses = 144.56 mg

$$\frac{144.56\ mg}{1\ mg/mL} = 144.56\ mL$$

Least Measurable Quantities (Volume/Weight):

1. A pharmacy has a torsion balance with a 5 mg sensitivity. What is the smallest quantity that can be weighed accurately with a maximum of 5% error?

   $$\frac{5\ mg \times 100}{5\%\ error} = 100\ mg$$

2. An electronic balance has a sensitivity reading of 0.1 mg. What is the smallest quantity that reasonably can be weighed?

A digital balance does not change its readout until the largest unit of material is placed on the balance pan. If the readability of a balance is 0.1 mg, the change in the digit on the right does not occur until 0.1 mg is added. In other words, 0.04 mg will not result in a digit change. If one tries to weigh 0.1 mg, one might actually place 0.14 mg of drug on the pan but the readout will only be 0.1. Therefore, use the same general principal as with torsion balances and weigh not less than 20 times the readability of the balance (2 mg).

Calibration of Droppers:

An anticholinergic liquid has been presented for a toddler at a dose of 0.25 mL. The dropper dispensed with the medication delivers 56 drops of the liquid per 2 mL. How many drops shall the parents be instructed to give the toddler?

56/2 = 28 drops/mL

$$\frac{0.25}{1} = \frac{x}{28} \qquad x = 7\ drops$$

WEIGHING/MEASURING/DRUG WEIGHTS

Reducing/Enlarging Formulas:

A formula for 100 mL of an ibuprofen gel requires 2 g of ibuprofen powder. What quantity of the gel would be required for 240 mL of the product?

$\underline{2} = \underline{X} \qquad X = 4.8\ g$

100 240

Partial dosage units:

Rx	Indomethacin	5 mg/5 mL
	Ora Plus	60 mL
	Ora Sweet qs	120 mL

How would you obtain the quantity of indomethacin required for this Rx using indomethacin 25 mg capsules?

5 mg/5 mL = 1 mg/mL
1 mg/mL x 120 mL = 120 mg needed
120 mg/25 mg/capsule = 4.8 capsules required.

1. Empty the contents of five capsules onto a tared weighing paper and weigh (Ex: 1.6 g).
2. The contents weigh 1.6 g. You need to remove

   $\frac{4.8}{5}$ = 0.96 x 1.6 g = 1.536 g

   of the mixture for the prescription.

Stock Solutions:

A pharmacist is preparing an ophthalmic decongestant solution in batch form. Each of three bottles will contain 15 mL. The preservative to be incorporated is 0.01% benzalkonium chloride (BAK). The pharmacist has a stock solution containing 17% BAK. How much of this stock solution would be required for the three bottles?

15 x 3 = 45 mL

45 x .0001 = .0045 g

$\frac{.0045}{x} = \frac{17}{100}$

x = 0.026 mL

Dilution Aliquots:

A pharmacist needs to obtain .015 mL of a flavoring oil for an oral liquid. Using alcohol as a solvent, and a pipet accurate to 0.01 mL, how can this appropriately be done?

1. Measure 0.1 mL of flavoring oil
2. Add 0.56 mL of alcohol and mix well

   $\frac{0.1}{(0.1 + 0.56)} = \frac{0.015}{x}$

   x = 0.099 or 0.1 mL

3. Remove 0.1 mL of the solution for the Rx

Specific Gravity in Weighing/ Measuring:

A pharmacist receives a prescription for 120 mL of a 3% w/v Hydrochloric Acid solution. The density of concentrated hydrochloric acid (37%) is 1.18 g/mL. How many milliliters of the concentrated acid would be required for the Rx?

3% = .03

.03 x 120 mL = 3.6 g required

Volume = $\frac{3.6\ g}{1.18\ g/mL}$ = 3.05 mL

37% = 0.37

$\frac{3.05\ mL}{0.37}$ = 8.24 mL

Hydrated and Anhydrous Crystals:

How much $MgSO_4 \cdot 7H_2O$ must be weighed to obtain 5 g of $MgSO_4$?

Mg = 24
S = 32
O = 16
H = 1

1. The weight of $MgSO_4$

Mg	1 x 24 = 24
S	1 x 32 = 32
O	4 x 16 = 64
	120

2. The weight of $MgSO_4 \cdot 7H_2O$

$MgSO_4$	1 x 120 = 120
H	14 x 1 = 14
O	7 x 16 = 112
	246

3. The quantity of $MgSO_4 \cdot 7H_2O$ required is

   $\frac{120}{246} = \frac{5}{x}$

   x = 10.25 g

4. 10.25 g of $MgSO_4 \cdot 7H_2O$ contains 5 g of $MgSO_4$

Potency of Salt Forms:

Polymyxin B sulfate has a potency of 6,000 units per mg. You need to prepare an ophthalmic solution (10 mL) containing 10,000 units per mL. How much polymyxin B sulfate, in mg, is required for the prescription?

10,000 U/mL x 10 mL = 100,000 U needed

$\frac{6{,}000\ U}{1\ mg} = \frac{100{,}000\ U}{x}$

x = 16.67 mg required

Mixing Products of Different Strengths:

1. A pharmacist receives an order for 120 g of a 0.1% corticosteroid ointment. On hand are 1 oz of 0.1%, ½oz. of 0.15% and 2½ oz of 0.005%, all in the same ointment base. If these three ointments are mixed together, how much additional corticosteroid powder should be added to prepare the prescription? (Assume the quantity of corticosteroid added will be negligible compared to the 120 g total weight.)

   120 x .001 = 120 mg needed

   30 x 0.001 = 30 mg

   15 x .0015 = 22.5 mg

   75 x .00005 = 3.8 mg

   Total 56.3 mg

   120 mg - 56.3 mg = 63.7 mg

2. In what quantities could 50% dextrose in water be mixed with 5% dextrose in water to obtain 900 mL of 15% dextrose in water?

50		10 ÷ 5 = 2
	15	
5		35 ÷ 5 = 7
		Total 9 parts

   $\frac{2}{9}$ x 900 = 200 mL of $D_{50}W$

   $\frac{7}{9}$ x 900 = 700 mL of D_5W

   900 mL Total Volume

Powders for Reconstitution:

The directions to constitute an amoxicillin suspension 250 mg/5 mL, 150 mL, state that 111 mL of Purified Water are required. The physician has requested the product be constituted at a concentration of 500 mg/mL. How much Purified Water would be required?

1. 150 mL - 111 mL = 39 mL occupied by powder
2. 250 mg/5 mL = 50 mg/mL
3. 50 mg/mL x 150 mL = 7.5 g of powder
4. 7.5/0.5 - 15 doses
5. 15 doses x 5 mL = 75 mL volume
6. 75 mL - 39 mL = 36 mL required

INGREDIENT-PRODUCT SPECIFIC CALCULATIONS

MilliEquivalents:

1. A prescription calls for 25 milliequivalents of sodium chloride. What quantity, in mg, would be required? 1 equivalent NaC1 = 58.5 gm, 1 milliequivalent = 58.5 mg;

   25 mEq x 58.5 mg/mEq = 1.463 g

2. A pharmacist receives an order for 10 mEq of Ca^+. How much of a standard 10% $CaC1_2$ solution should be used for this order?

   Ca = 40/2 = 20 mg/mEq

   $\frac{1\ mEq}{10\ mEq} = \frac{20\ mg}{x}$ x = 200 mg Ca required

   $CaC1_2$ = 40 + 71 = 111

   $\frac{40}{111} = \frac{200\ mg}{x}$

   x = 555 mg $CaC1_2$ required

   $\frac{10\ g}{100\ mL} = \frac{0.555\ g}{x}$ x = 5.55 mL of the 10% $CaC1_2$ solution

3. An Rx calls for 15 mEq of K+ (as KC1) and 10 mEq of Na+ (as NaC1) per tablespoonful with 240 mL to be prepared in a suitable vehicle (containing no K+ or Na+). How much KC1 and NaC1 would be required? (K=39, C1=35.5, Na=23, KC1=74.5, NaC1= 58.5).

   1 mEq KC1 weighs 74.5 mg

   $\frac{1\ mEq}{74.5\ mg} = \frac{15\ mEq}{x}$ x = 1.118 g

$\frac{15\ mL}{240} = \frac{1.118}{x}$ x = 17.89 g KC1 required

1 mEq NaC1 weighs 58.5 mg

$\frac{1\ mEq}{58.5\ mg} = \frac{10\ mEq}{x\ mg}$ x = 0.585 g

$\frac{15\ mL}{240\ mL} = \frac{0.585}{x}$ x = 2.106 g NaC1 required

Millimoles:

How many millimoles of NaC1 are contained in 1 liter of 0.9% Sodium Chloride Solution? (Formula weights: Na=23, C1=35.5, NaC1=58.5).

0.009 x 1000 mL = 9 g NaC1

1 mole NaC1 weighs 58.5 g

$\frac{1}{58.5g} = \frac{x}{9\ g}$ x = 0.154 mole = 154 millimoles

Osmolality:

1. What is the osmolality (number of milliosmoles) of 1 liter of 0.9% sodium chloride solution? (Assume complete dissociation)

   Na=23, C1=35.5, NaC1=58.5, NaC1 --> Na^+ + $C1^-$

   # millimoles NaC1 present per liter = 154 from previous problem

   154 millimoles NaC1 x 2 species (Na + C1) = 308 mOsmol/liter

2. What is the osmolality of 10% $CaC1_2$ solution? (Assume complete dissociation) (Formula weights: Ca=40, C1=35.5, $CaC1_2$=111g/L)

   10% $CaC1_2$ = 100 g/1000 mL

   $\frac{100\ g}{111\ g} = \frac{x}{1\ mole}$ x = 0.9 moles/liter = 900 millimoles

   $CaC1_2$ ----> Ca^{++} + 2 $C1^-$ = 3 species

   900 millimoles $CaC1_2$/L x 3 species = 2700 mOsmol/Liter

Units to Weight Conversions:

An Rx order calls for 150,000 units of nystatin per gram of ointment with 60 grams to be dispensed. How much nystatin would be weighed? (4400 USP Nystatin units/mg)

150,000 u/g x 60 g = 9,000,000 units needed

9,000,000/4400 u/mg = 2.045 g required

Shelf Life Estimates:

Shelf life estimates can be made using the equation:

$$t_{90}\ New = \frac{t_{90}\ Orig}{3^{\Delta T/10}}$$

Where ΔT = change in temperature

3 is a reasonable estimate for the "Q" value, based on energies of activation from the Arrhenius equation.

1. An antibiotic solution has a shelf life of 96 hours when in a refrigerator. If it is necessary that a patient use it in an ambulatory pump at approximate body temperature (30°C) over six hours, would it still retain at least 90% of its original potency during the entire period of administration?

   $t_{90} = \frac{96}{3^{25/10}}$ = 6.16 hours Ans. = yes

2. A prescription is received for an ophthalmic solution with a shelf life of four hours at room temperature. The preparation is to be administered in a physician's office at 12:00 noon the next day. Can it be prepared the evening before at about 8:00 p.m. and still retain at least 90% of its shelf life if stored in a refrigerator?

   $t_{90} = \frac{4}{3^{-20/10}} = \frac{4}{3^{-2}}$ = 36 hours Ans. = yes

3. A reconstituted antibiotic has a shelf life at room temperature of three days. How long would the preparation be good if stored in a refrigerator? (A reasonable estimate based on t_{90}.)

   $t_{90} = \frac{3d}{3^{-2}}$ = 3 X 9 = 27 days

Effervescent Calculations:

A prescription calls for an effervescent mixture of citric acid/tartaric acid (1:2) molar ratio with sodium bicarbonate to mask the taste of a drug. How much active drug, citric acid ($C_6H_8O_9 \cdot H_2O$), tartaric acid ($C_4H_6O_6$) and sodium bicarbonate ($NaHCO_3$) will be required for the prescription? (KC1=74.5, $NaHCO_3$=84, $C_6H_8O_7 \cdot H_2O$=210, $C_4H_6O_6$=150)

Rx	KC1	1 mEq/5 g tsp
	Tartaric Acid	
	Citric Acid	
	Sodium Bicarbonate	
	Lime Flavor Crystals	Q.S.

Dispense 100 grams

Assume the powder in final form will weigh 5 grams per teaspoonful. How much of the acids and the $NaHCO_3$ are required for this Rx? Assume the lime flavor crystals contribute negligible weight.

$\frac{100\ g}{5\ g/dose} = 20$ doses

20 doses x 74.5 mg / dose = 1.49 g KC1 required

100 g - 1.49 g = 98.51 g Effervescent Mix

To calculate the quantities of Citric Acid and Tartaric Acid that will be used in the ratio of 1 part citric acid + 2 parts tartaric acid to make 98.51 g of the effervescent mix when combined with the sodium bicarbonate:

Citric Acid

$3\ NaHCO_3 + C_6H_8O_7 \cdot H_2O \text{---}> 4H_2O + 3CO_2 + Na_3\ C_6H_5O_7$

[3 x 84] [210]

$\frac{1}{210} = \frac{x}{3 \times 84}$

x = 1.2 g

Therefore, 1 gram of citric acid reacts with 1.2 g sodium bicarbonate.

Tartaric Acid

$2\ NaHCO_3 + C_4H_6O_6 \text{---}> 2\ H_2O + 2\ CO_2 + Na_2\ C_4H_4O_6$

[2 x 84] [150]

$\frac{2}{150} = \frac{x}{2 \times 84}$

x = 2.24 g

Therefore, 2 grams of tartaric acid reacts with 2.24 g of sodium bicarbonate.

Adding together the values for sodium bicarbonate (1.2 g + 2.24 g), it will take 3.44 g of sodium bicarbonate for 1 gram of citric acid and 2 grams of tartaric acid.

The prescription requires 98.51 g of effervescent mix. The quantity of each ingredient can be calculated as follows:

1 part citric acid + 2 parts tartaric acid + 3.4 parts sodium bicarbonate = 6.4 parts total

$\frac{1}{6.4} \times 98.51 = 15.39$ g citric acid

$\frac{2}{6.4} \times 98.51 = \underline{30.78}$ tartaric acid

$\frac{3.4}{6.4} \times 98.51 = \underline{52.34}$ sodium bicarbonate

6.4 98.51 g total mix

To prepare the prescription, the following quantities of ingredient should be weighed accurately:

Potassium Chloride	1.49 g
Citric Acid	15.39 g
Tartaric Acid	30.78 g
Sodium Bicarbonate	52.34 g
Total	100 g

Surfactant Blending:

A prescription calls for 120 g of a cream using 3% Tween 80 and 1% Span 40. What is the HLB value of this mixture? (HLB of Tween 80 = 15.0, HLB of Span 40 = 6.7)

120 x .03 = 3.6 g	3.6 x HLB of 15 = 54
120 x .01 = 1.2 g	1.2 x HLB of 6.7 = 8
	4.8 62
	62 / 4.8 = 12.9 HLB

DOSAGE FORM SPECIFIC CALCULATIONS

Ophthalmic and Nasal Solutions – Sodium Chloride Equivalents:

How much sodium chloride is required to render the following Rx isotonic?

Rx	Lidocaine HC1	1%	(NaC1 equiv. = 0.22)
	Cocaine HC1	1%	(NaC1 equiv. = 0.16)
	Epinephrine Bitartrate	0.1%	(NaC1 equiv. = 0.18)
	Sterile Water qs	50 mL	
	Sodium Chloride	qs	
	50 x .01 = 0.5 x .22 =	0.110	
	50 x .01 = 0.5 x .16 =	0.080	
	50 x .001 = .05 x .18 =	.009	
		.199 g	

The ingredients represent the equivalent of 0.199 g of NaC1.

50 x .009 = 0.45 g	NaC1 to make 50 mL water isotonic
0.45 - 0.199 = 0.251 g	NaC1 needed to add to this Rx to make it isotonic

Ophthalmic and Nasal Solutions – Buffer Solutions & pH:

Rx	Optimycin	1%
	NaC1	qs
	Phosphate Buffer pH 6.5 qs	100 mL

Sorensen Modified Phosphate Buffer

Paddock Laboratories, Inc.
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Acid Stock Solution (1/15M)		Alkaline Stock Solution (1/15 M)	
Sodium Biphosphate, Anhy.	8.006 g	Sodium Phosphate Anhy.	9.473 g
Purified Water qs	1000	Purified Water qs	1000 mL

pH	mL of 1/15 M Sodium Biphosphate Solution	mL of 1/15 M Sodium Phosphate Solution
5.9	90	10
6.2	80	20
6.5	70	30
6.6	60	40
6.8	50	50
7.0	40	60
7.2	30	70
7.4	20	80
7.7	10	90
8.0	5	95

To prepare 100 mL of pH 6.5 phosphate buffer solution, use 70 mL of 1/15 Molar Sodium Biphosphate Solution and 30 mL of 1/15 Molar Sodium Phosphate Solution.

Nasal Solutions – Calibrating a Dropper/Sprayer:

A nasally administered product has a dose of 25 µg. A 0.5% solution is prepared and placed in a nasal spray bottle. Ten "squeezes" into a plastic bag by the patient weighed 500 mg. How many squeezes are required to administer the 25 µg dose? (assume weight of solution is 1 gram per mL, *i.e.*, 500 mg = 0.5 mL).

0.5% = 0.5 g/100 mL

$$\frac{0.5\text{ g}}{100\text{ mL}} = \frac{x\text{ g}}{0.5\text{ mL}}$$

x = .0025 g/0.5 mL or 2.5 mg/0.5 mL (2,500 µg/0.5 mL)

Since 10 squeezes expels 2,500 µg, there would be 250 µg in 1 squeeze

Capsule Filling – Powder Displacement:

A pharmacist receives a prescription for 15 mg piroxicam capsules, qty. 48. A #1 capsule filled with piroxicam weighs 245 mg; a capsule filled with lactose weighs 180 mg. How much piroxicam and lactose are required for the prescription? Prepare sufficient powder for 50 capsules (2 extra).

50 x 15 = 750 mg piroxicam

$$\frac{15}{245} = \frac{x}{180} \qquad x = 11\text{ mg}$$

15 mg piroxicam occupies a similar volume as does 11 mg lactose

180 mg - 11 mg = 169 mg lactose/capsule

169 x 50 = 8.45 g lactose required

Suppositories/Troches/Lozenges – Displacement Factors:

Rx Zinc Oxide 300 mg
Cocoa Butter qs

If the density factor for cocoa butter is 0.9 and for zinc oxide is 4.0, and the suppository mold holds 2.0 g of cocoa butter, how much cocoa butter would be required to prepare 12 of the suppositories for this prescription?

Solution

–Total weight if just cocoa butter was used:

12 x 2.0 g = 24 g

–The density ratio is:

4/0.9 = 4.44

–The weight of zinc oxide required is 3.6 g

–The amount of suppository base displaced by the active drug is:

3.6 g/4.44 = 0.81 g

–The weight of the suppository base for the prescription is:

24 g - 0.81 g = 23.19 g

Emulsions – Nucleus:

Rx Mineral Oil 30%
Acacia
Flavor, QS
Purified Water, QS 120 mL

Using a 4:2:1, Continental Method, how much Acacia is required for this Rx?

30% x 120 mL = 36 mL

Oil:Water:Acacia = 4:2:1

$$\frac{36}{4} = \frac{x}{1}$$

x = 9 grams of Acacia required.

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