Pharmaceutical calculation

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Text Book

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Chapter 15

Altering Product Strength, Use of Stock Solutions, and Problem Solving by Alligation

Objective

At the end of this chapter the student will be able to :

1. Perform calculations for altering product strength through dilution or fortification.
2. Perform calculations for the preparation and use of stock solutions.
3. Apply alligation medial and alligation alternate in problem solving.

Introduction

The strength of a pharmaceutical preparation may be ***increased*** or ***decreased*** **by** changing the proportion of active ingredient to the whole.

A preparation may be ***strengthened*** or ***made more concentrated*** **by:**

1. the addition of active ingredient,
2. by admixture with a like preparation of greater strength,
3. or through the evaporation of its vehicle, if liquid.

The strength of a preparation may be ***decreased*** or ***diluted*** **by:**

1. the addition of diluent or
2. by admixture with a like preparation of lesser strength.

Alternative methods of calculation for the alteration of the strength of pharmaceutical preparations are presented in this chapter

Special Considerations of Altering Product Strength in Pharmaceutical Compounding

In the course of pharmacy practice, there are occasions in which the alteration of the strength of a pharmaceutical preparation is either desirable or required.

The dilution of a liquid dosage form, as a solution or suspension, may be desired to provide a product strength more suitable for use by a particular patient (e.g., pediatric, elderly, those in disease states).

The diluent is selected ***based on*** its compatibility with the vehicle of the original product; that is, aqueous, alcoholic, hydroalcoholic, or other.

The dilution of a solid dosage form (as a powder or the contents of a capsule) or a semisolid dosage form (as an ointment or cream) also ***may be performed*** to alter the dose or strength of a product.

Again, the diluent is selected based on its compatibility with the original formulation.

Pharmacists also may find occasion to dilute concentrated acids, alcohol preparations, or very potent therapeutic agents, to meet special compounding requirements.

The **concentration of a liquid preparation**, as through the evaporation of a portion of its solvent or vehicle, rarely is performed nowadays.

However, the **fortification of a liquid, solid, or semisolid dosage form**, by the addition of a calculated quantity of additional therapeutic agent, remains a viable practice in pharmacy compounding.

Note: To simplify the calculation ,these rules may be applied:

1. When the ratio strengths are given , convert them to percentage strengths before setting up proportion. For example 1/10 =10%
2. Whenever proportional parts enter into a calculation , reduce them to lowest term. For example 75 parts :25 parts = 3 parts: 1 part.

Relationship Between Strength and Total Quantity

If a mixture of a given percentage or ratio strength is ***diluted*** to twice its original quantity, its active ingredient will be contained in twice as many parts of the whole, and its strength therefore will be ***reduced*** by one half.

By contrast, if a mixture is ***concentrated*** by evaporation to one-half its original quantity, the active ingredient (assuming that none was lost by evaporation) will be contained in one half as many parts of the whole, and the ***strength will be doubled.***

So, if **50 mL** of a solution containing **10 g** of active ingredient with a strength of **20%** or **1:5 w/v** are diluted to **100 mL**, the original volume is doubled, but the original strength is now reduced by one half to **10%** or **1:10 w/v**.

If, by evaporation of the solvent, the volume of the solution is reduced to **25 mL** or one half the original quantity, the **10 g** of the active ingredient will indicate a strength of **40%** or **1:2.5 w/v.**

If, then, the amount of active ingredient remains constant, any change in the quantity of a solution or mixture of solids is inversely proportional to the percentage or ratio strength; that is, ***the percentage or ratio strength decreases as the quantity increases***, and conversely.

This relationship is generally true for all mixtures ***except*** solutions containing components that contract when mixed together.

Problems in this section generally may be solved ***by any*** of the following methods:

1. Inverse proportion.
2. The equation:

(1st quantity) X (1st concentration) = (2nd quantity) X (2nd concentration)

or

$$Q1 \times C1 = Q2 \times C2.$$

3. By determining the quantity of active ingredient (solute) present or required and relating that quantity to the known or desired quantity of the preparation.

Dilution and Concentration of Liquids

Example Calculations of the Dilution and Concentration of Liquids

If 500 mL of a 15% v/v solution are diluted to 1500 mL, what will be the percentage strength (v/v)?

$$\frac{1500\ (\text{mL})}{500\ (\text{mL})} = \frac{15\ (\%)}{x\ (\%)}$$

$x = 5\%$, *answer.*

Or,

Q1 (quantity) X C1 (concentration) = Q2 (quantity) X C2 (concentration) 500 (mL) X 15 (%) = 1500 (mL) X x (%)

$x = 5\%$, *answer.*

Or,

500 mL of 15% v/v solution contains 75 mL of solute

$$\frac{1500\ (\text{mL})}{75\ (\text{mL})} = \frac{100\ (\%)}{x\ (\%)}$$

$x = 5\%$, *answer.*

How many milliliters of a 1:5000 w/v solution of the preservative lauralkonium chloride can be made from 125 mL of a 0.2% solution?

$$1{:}5000 = 0.02\% \text{ w/v}$$

$$\frac{0.02\ (\%)}{0.2\ (\%)} = \frac{125\ (\text{mL})}{x\ (\text{mL})}$$

$$x = \mathbf{1250\ mL}$$

$$\text{Q1 (quantity)} \times \text{C1 (concentration)} = \text{Q2 (quantity)} \times \text{C2 (concentration)}$$

$$125\ (\text{mL}) \times 0.2\ (\%) = x\ (\text{mL}) \times 0.02\ (\%)$$

$$x = \mathbf{1250\ mL}$$

$$125 \text{ mL} \times 0.2\% \text{ w/v} = 0.25 \text{ g lauralkonium chloride}$$

$$\frac{0.25 \text{ g} \times 100 \text{ mL}}{0.02 \text{ g}} = \mathbf{1250\ mL}$$

How many milliliters of water should be added to a 80 mL of a 20% w/v aqueous solution to prepare 3% w/v solution?

Q1 (quantity) x C1 (concentration) = Q2 (quantity) x C2 (concentration)
80 (mL) x 20 (%) = x (mL) x 3 (%)
X = 533.3 mL – 80 mL = 453.3 mL of water added

Or,
80 mL x 20% (or 0.2) g/ mL = 16 g solute
3 g 100 mL
16 g x mL

X = 533.3 mL (quantity of 3% w/v solution that 16 g of solute will appear

X = 533.3 mL – 80 mL = 453.3 mL of water added

If an injection containing a medication, 50 mg/10 mL, is diluted to 1L, calculate percent strength of the resulting solution?

Convert mg to g

50 mg/ 1000 = 0.05 g / 10 mL

convert 0.05 g/ 10 ml to percentage

0.05 g	10 ml	
x	100 ml	x= 0.5%

Q1 x C1 = Q2 x C2

10 (mL) x 0.5 (%) = 1000 (mL) x X (%)

X= 0.005%

Dopamine HCl injection is available in 5-mL vials each containing 40 mg of dopamine HCl per milliliter. The injection must be diluted before administration by intravenous infusion. If a pharmacist dilutes the injection by adding the contents of one vial to 250 mL of 5% dextrose injection, calculate the percent concentration of dopamine HCl in the infusion.

Convert mg to g

40/ 1000 = 0.04 g

Calculate the amount of dopamine in each vial

0.04 g   1 mL

X   5 mL   x=0.2 g

Calculate the percentage of dopamine in each vial

0.2 g   5 mL

X   100 mL   x= 4%

Calculate total infusion volume after addition of dopamine vial

5 mL (dopamine HCl injection) + 250 mL (5% dectrose injection) = 255 mL

Solving by equation:

Q1 x C1 = Q2 x C2 (5 ml x 4 % = 255 ml x X %)

X=0.078 %

If a pharmacist reconstitutes a vial to contain 1 g of cefazolin in 3 mL of injection, and then dilutes 1.6 mL of the injection with sodium chloride injection to prepare 200 mL of intravenous infusion, calculate the concentration of cefazolin in the infusion in percent and in mg/mL.

Q1 (quantity) × C1 (concentration) = Q2 (quantity) × C2 (concentration)

1.6 mL × 33.3% (1 g/3 mL) = 200 mL × x

x = **0.27% w/v cefazolin**

0.27% w/v = 0.27 g/100 mL = 270 mg/100 mL = **2.7 mg/mL cefazolin**

If 50 mL of a 1 : 20 w/v solution are diluted to 1000 mL, what is the ratio strength (w/v)?

Note: A student may find it simpler in solving certain problems to convert a given ratio strength to its equivalent percentage strength.

1:20 = 5%

$$\frac{1000\ (mL)}{50\ (mL)} = \frac{5\ \%}{x\ \%}$$

X= 0.25 % = 1: 400

Or,

Q1 (quantity) X C1 (concentration) = Q2 (quantity) X C2 (concentration)

50 (mL) X 5 (%) = 1000 (mL) X (%)

x = 0.25% = 1 : 400, *answer.*

Or,

50 mL of a 1 : 20 solution contains 2.5 g of solute

$$\frac{2.5\ (g)}{1\ (g)} = \frac{1000\ (mL)}{x\ (mL)}$$

x = 400 mL

Ratio strength = 1 : 400, *answer.*

If a syrup containing 65% w/v of sucrose is evaporated to 85% of its volume, what percentage (w/v) of sucrose will it contain?

Any convenient amount of the syrup, for example, 100 mL, may be used in the calculation. If we evaporate 100 mL of the syrup to 85% of its volume, we will have 85 mL.

$$\frac{85\ (\text{mL})}{100\ (\text{mL})} = \frac{65\ (\%)}{x\ (\%)}$$

x = 76.47% or 76%, *answer*.

If 1 gallon of a 30% w/v solution is to be evaporated so that the solution will have a strength of 50% w/v, what will be its volume in milliliters?

1 gallon = 3785 mL

$$\frac{50\ (\%)}{30\ (\%)} \qquad \frac{3785\ (\text{mL})}{x\ (\text{mL})}$$

x = 2271 mL, *answer*.

Stock solutions

Stock solutions are concentrated solutions of active (e.g., drug) or inactive (e.g., colorant) sub-stances and are used by pharmacists as a convenience to prepare solutions of lesser concentration.

How many milliliters of a 1:400 w/v stock solution should be used to make 4 liters of a 1:2000 w/v solution?

4 liters = 4000 mL

1:400 = 0.25%

1:2000 = 0.05%

$$\frac{0.25\ (\%)}{0.05\ (\%)} = \frac{4000\ (\text{mL})}{x\ (\text{mL})}$$

x = 800 mL, *answer.*

Or,

$$Q1 \times C1 = Q2 \times C2$$

$$4000\ (\text{mL}) \times 0.25\ (\%) = x \times 0.05\ (\%)$$

x = 800 mL, *answer.*

How many milliliters of a 1% stock solution of a certified red dye should be used in preparing 4000 mL of a mouthwash that is to contain 1:20,000 w/v of the certified red dye as a coloring agent?

1:20,000 = 0.005%

$$C1 \times Q1 = C2 \times Q2$$
$$0.005\% \times 4000 \text{ mL} = 1\% \times X \text{ mL}$$
$$X = 20 \text{ mL}$$

$$\frac{1\ (\%)}{0.005\ (\%)} = \frac{4000\ (\text{mL})}{x\ (\text{mL})}$$

x = 20 mL, *answer.*

Or,

4000 mL of a 1:20,000 w/v solution requires 0.2 g of certified red dye; thus:

$$\frac{1\ (\text{g})}{0.2\ (\text{g})} = \frac{100\ (\text{mL})}{x\ (\text{mL})}$$

x = 20 mL, *answer.*

How many milliliters of a 1:400 w/v stock solution should be used in preparing 1 gallon of a 1:2000 w/v solution?

1 gallon = 3785 mL
1:400 = 0.25%
1:2000 = 0.05%

$$C1 \times Q1 = C2 \times Q2$$
$$0.05\% \times 3785 \text{ mL} = 0.25\% \times X \text{ mL}$$
$$X = 757 \text{ mL}$$

$$\frac{0.25\ (\%)}{0.05\ (\%)} = \frac{3785\ (\text{mL})}{x\ (\text{mL})}$$

x = 757 mL, *answer.*

Or,

1 gallon of a 1:2000 w/v solution requires 1.89 g of active constituent; thus:

$$\frac{1.89\ (\text{g})}{1\ (\text{g})} = \frac{x\ (\text{mL})}{400\ (\text{mL})}$$

x = 756 mL, *answer.*

Some calculations are used in pharmacy practice in which :

1. the strength of a diluted portion of a solution is defined,
2. the strength of the concentrated stock solution used to prepare it must be determined.

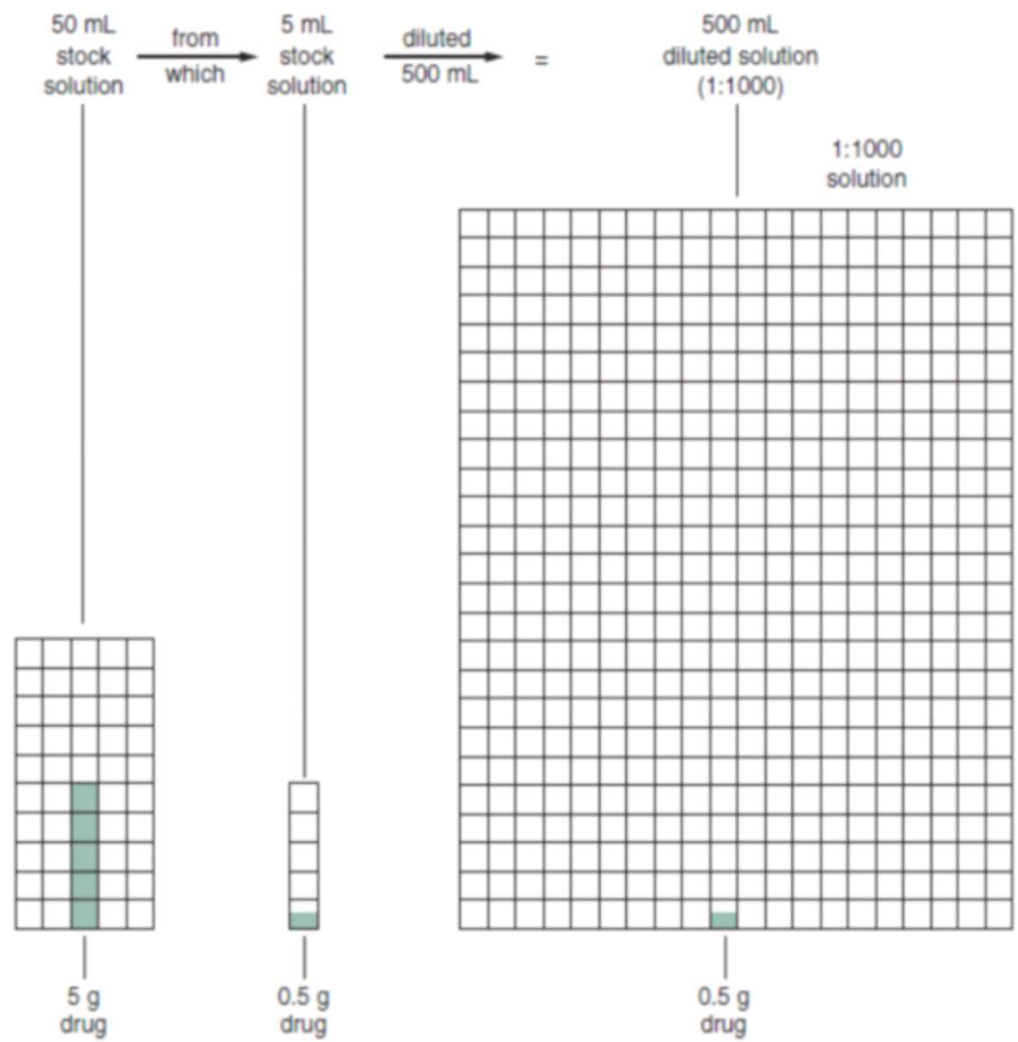
For example, by the need of a pharmacist to prepare and dispense a concentrated solution of a drug and direct the patient to use a specific household measure of a solution (e.g., 1 teaspoonful) in a specified volume of water (e.g., a pint) to make of solution of the desired concentration (e.g., for irrigation or soaking).

This permits:

1. the dispensing of a relatively small volume of liquid,
2. enabling a patient to prepare relatively large volumes as needed, rather than carrying home gallons of a diluted solution from a pharmacy.

How much drug should be used in preparing 50 mL of a solution such that 5 mL diluted to 500 mL will yield a 1:1000 solution?

The accompanying diagrammatic sketch should prove helpful in solving the problem.



1 g 1000 mL
X 500 mL

X = 0.5 g (the source of this amount is the 5 mL of the stock solution)

0.5 g 5mL
X 50mL

X = 5 g of drug needed to prepare 50 mL of solution

How many grams of sodium chloride should be used in preparing 500 mL of a stock solution such that 50 mL diluted to 1000 mL will yield a "1⁄3 normal saline"(0.3% w/v) for irrigation?

1000 (mL) X 0.003 = 3 g of sodium chloride in 1000 mL of "1⁄3 normal saline"(0.3% w/v), which is *also* the amount in 50 mL of the *stronger* (stock) solution to be prepared.

$$\frac{50\ (\text{mL})}{500\ (\text{mL})} = \frac{3\ (\text{g})}{x\ (\text{g})}$$

x = 30 g, *answer.*

How many milliliters of a 17% w/v concentrate of benzalkonium chloride should be used in preparing 100 mL of a stock solution such that 5 mL diluted to 60 mL will yield a 0.13% solution of benzalkonium chloride?

60 mL × 0.13% w/v = 0.078 g of benzalkonium chloride in 60 mL, which is also the amount in 5 mL of the stock solution.

Thus, the amount of benzalkonium chloride in 100 mL of the stock solution is:

$$0.078\text{ g} \times \frac{100\text{ mL}}{5\text{ mL}} = 1.56\text{ g}$$

And the amount o the 17% w/v concentrate to use is:

$$1.56\text{ g} \times \frac{100\text{ mL}}{17\text{ g}} = \mathbf{9.18\ mL}$$

Dilution and Fortification of Solids and Semisolids

The dilution of solids in pharmacy ***occurs when*** there is need to achieve a lower concentration of an active component in a more concentrated preparation (e.g., a powdered vegetable drug).

If 30 g of a 1% hydrocortisone ointment were diluted with 12 g of Vaseline, what would be the concentration of hydrocortisone in the mixture?

$$30\text{ g} + 12\text{ g} = 42\text{ g, weight of mixture}$$

$30\ (\text{g}) \times 1\ (\%) = 42\ (\text{g}) \times x\ (\%)$

$x = 0.71\%\ (\text{w/w})$

How many grams of zinc oxide should be added to 3200 g of 5% zinc oxide ointment to prepare an ointment containing 20% of zinc oxide?

3200 g X 0.05 = 160 g of zinc oxide in 3200 g of 5% ointment

3200 g − 160 g = 3040 g of base (diluent) in 3200 g of 5% ointment

In the 20% ointment, the diluent will represent 80% of the total weight

$$\frac{80\ (\%)}{20\ (\%)} = \frac{3040\ (g)}{X\ (g)}$$

x = 760 g of zinc oxide in the 20% ointment Because the 5% ointment already contains 160 g of zinc oxide,

760 g − 160 g = 600 g, *answer.*

H.W

How many grams of 20% benzocaine ointment and how many grams of ointment base (diluent) should be used in preparing 5 lb. of 2.5% benzocaine ointment?

Alligation

Alligation is an arithmetical method of solving problems that involves the mixing of solutions or mixtures of solids possessing different percentage strengths.

Alligation medial is a method by which the "***weighted average***" percentage strength of a ***mixture*** of two or more substances of ***known quantity*** and ***concentration*** may be easily calculated.

Example Calculations Using Alligation Medial

What is the percentage strength (v/v) of alcohol in a mixture of 3000 mL of 40% v/v alcohol, 1000 mL of 60% v/v alcohol, and 1000 mL of 70% v/v alcohol? Assume no contraction of volume after mixing.

0.40 X 3000 mL = 1200 mL
0.60 X 1000 mL = 600 mL
0.70 X 1000 mL = 700 mL

Totals: 5000 mL 2500 mL

2500 (mL) 5000 (mL) = 0.50 X 100 = 50%, *answer.*

- In some problems, the addition of a solvent or vehicle must be considered. It is generally best to consider the diluent as of zero percentage strength, as in the following problem.

What is the percentage strength of alcohol in a mixture of 500 mL of a solution containing 40% v/v alcohol, 400 mL of a second solution containing 21% v/v alcohol, and a sufficient quantity of a nonalcoholic third solution to make a total of 1000 mL?

$$0.40 \times 500\text{ mL} = 200\text{ mL}$$

$$0.21 \times 400\text{ mL} = 84\text{ mL}$$

$$0 \times \underline{100}\text{ mL} = \underline{0}\text{ mL}$$

$$\text{Totals: } 1000\text{ mL} \quad 284\text{ mL}$$

$$284\text{ (mL)} \div 1000\text{ (mL)} = 0.284 \times 100 = \mathbf{28.4\%\ v/v}$$

A pharmacist–herbalist wishes to consolidate the following assayed batches of Gingko biloba leaves: 200 g containing 22% w/w glycosides, 150 g containing 26% w/w glycosides, and 80 g containing 27% w/w glycosides. Calculate the percent of glycosides in the combined mixture.

$$0.22 \times 200\ g = 44\ g$$

$$0.26 \times 150\ g = 39\ g$$

$$0.27 \times \underline{80}\ g = \underline{21.6}\ g$$

$$\text{Totals:}\ 430\ g \quad 104.6\ g$$

$$104.6\ (g) \div 430\ (g) = 0.243 \times 100 = \mathbf{24.3\%\ w/w}$$

Alligation Alternate: This is a method used to determine the quantities of ingredients of differing strengths needed to make a mixture of a desired strength.

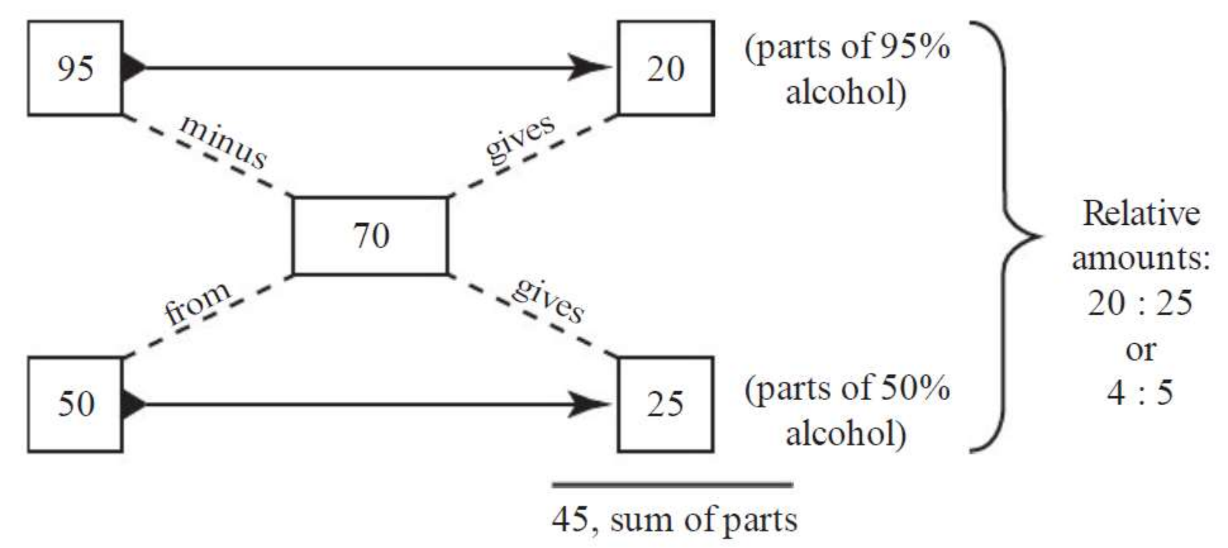
It involves matching pairs of ingredients, one higher in strength and one lower in strength than the desired strength, which lies somewhere in between.

As shown in the example below, the **desired strength is placed in the center of the working diagram**.

Example Calculations Using Alligation Alternate

In what proportion should alcohols of 95% and 50% strengths be mixed to make 70% alcohol?

Note that the difference between the *strength of the stronger component* (95%) and the *desired strength* (70%) indicates the *number of parts of the weaker* to be used (25 parts), and the difference between the *desired strength* (70%) and the *strength of the weaker component* (50%) indicates the *number of parts of the stronger* to be used (20 parts).



The mathematical validity of this relationship can be demonstrated.

Percent given	Percent desired	Proportional parts required
a		x
	c	
b		y

Given these data, the ratio of x to y may be derived algebraically as follows:

$$ax + by = c\,(x\ y)$$

$$ax + by = cx + cy$$

$$ax - cx = cy - by$$

$$x\,(a - c) = y\,(c - b)$$

$$\frac{x}{y} = \frac{c - b}{a - c}$$

Given a = 95%, b = 50%, and c = 70%, we may therefore solve the problems as follows:

$$0.95x + 0.50y = 0.70(x + y)$$

$$95x + 50y = 70x + 70y$$

$$95x - 70x = 70y + 50y$$

$$x(95 - 70) = y(70 - 50)$$

$$\frac{x}{y} = \frac{70 - 50}{95 - 70} = \frac{20}{25} = \frac{\mathbf{4\ (parts)}}{\mathbf{5\ (parts)}}$$

The result can be shown to be correct by *alligation medial*:

$$95 \times 4 = 380$$

$$\begin{array}{rr} 50 \times 5 & 250 \\ \hline \text{Total: } 9 & 630 \end{array}$$

$$630 \div 9 = 70\%$$

The customary layout of *alligation alternate*, used in the subsequent examples, is a convenient simplification of the preceding diagram.

In what proportion should 20% benzocaine ointment be mixed with an ointment base to produce a 2.5% benzocaine ointment?

Note that an “ointment base” has no drug content and thus is represented by a zero in the scheme.

20%	2.5%	2.5 parts of 20% ointment
0%		17.5 parts of ointment base

A hospital pharmacist wants to use three lots of zinc oxide ointment containing, respectively, 50%, 20%, and 5% of zinc oxide. In what proportion should they be mixed to prepare a 10% zinc oxide ointment?

Note that *pairs* must be used in each determination, one lower and one greater in strength than the desired strength.

50%		5 parts of 50% ointment
20%	10%	5 parts of 20% ointment
5%		10 + 40 = 50 parts of 5% ointment

In what proportions may a manufacturing pharmacist mix 20%, 15%, 5%, and 3% zinc oxide ointments to produce a 10% ointment?

Each of the weaker lots is paired with one of the stronger to give the desired strength, and because we may pair them in two ways, we may get two sets of correct answers.

20%		7 parts of 20% ointment
15%	10%	5 parts of 15% ointment
5%		5 parts of 5% ointment
3%		10 parts of 3% ointment

How many milliliters each of a 50% w/v dextrose solution and a 5% w/v dextrose solution is required to prepare 4500 mL of a 10% w/v solution?

50%	10%	5 parts of 50% solution
5%		40 parts of 5% solution

There is a *total* of 45 parts to prepare the 4500 mL mixture, or 100 mL per part (4500 mL/45 parts). And the amount of each component may be calculated by:

5 (parts) × 100 mL = **500 mL of the 50% w/v dextrose solution**

40 (parts) × 100 mL = **4000 mL of 5% w/v dextrose solution**

How many grams o 2.5% w/w hydrocortisone cream should be mixed with 360 g of 0.25% w/w cream to make a 1% w/w hydrocortisone cream?

2.5%	1%	0.75 parts of 2.5% cream
0.25%		1.5 parts of 0.25% cream

1.5 part	360 g	
1 part	X	X= 240 g

1 part	240 g	
0.75 part	X g	X= 180 g

The 0.25% w/w hydrocortisone cream is 1.5 parts o the whole with a given weight of 360 g. This means that each part is equivalent to 240 g [360 g/1.5 (parts)].
Thus, the quantity o the 2.5% w/w hydrocortisone cream required would be **180 g** [(240 g/0.75 part)].

How many grams o zinc oxide powder should be added to 3200 g o a 5% w/w zinc oxide ointment to prepare a 20% w/w zinc oxide ointment?

NOTE: In the allegation alternate diagram, the zinc oxide powder is 100% zinc oxide.

100%	20%	15 parts of the zinc oxide powder
5%		80 parts of the 5% zinc oxide ointment

Since each o the 80 parts (of the 5% zinc oxide ointment) is equal to 40 g [3200 g/80 (parts)],

80 part	3200 g	
1 part	x g	x= 40 g/part of the 5% zinc oxide ointment)

40 g × 15 (parts) = 600 g of the zinc oxide powder

Thank you