University of Tikrit

College of Pharmacy

Dilution and Concentration of Pharmaceutical Preparations

By

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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). There also is a type of diluted pharmaceutical preparation, termed a **trituration** that represents a useful means of preparing and administering very potent therapeutic substances.

Dilution and Fortification of Solids and Semisolids

Reducing or enhancing the strengths of creams and ointments is a usual part of a compounding pharmacist's practice to meet the special needs of patients. The dilution of semisolids is a usual part of a compounding pharmacist's practice in reducing the strengths of creams and ointments to meet the special needs of patients.

Dilution and Fortification of Solids and Semisolids

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?

$$30\ \text{g} \times 1\% = 0.3\ \text{g hydrocortisone}$$
$$30\ \text{g} + 12\ \text{g} = 42\ \text{g, weight of mixture}$$
$$\frac{0.3\ \text{g}}{42\ \text{g}} \times 100 = 0.71\%\ \text{(w/w), } \textit{answer.}$$

Or,

$$30\ (\text{g}) \times 1\ (\%) = 42\ (\text{g}) \times \text{x}\ (\%)$$
$$\text{x} = 0.71\%\ \text{(w/w), } \textit{answer.}$$

Dilution and Fortification of Solids and Semisolids

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?

$$5 \text{ lb.} = 454 \text{ g} \times 5 = 2270 \text{ g}$$

Or, Q1 * C1 = Q2 * C2

$$\frac{20\ (\%)}{2.5\ (\%)} = \frac{2270\ (\text{g})}{\text{x}\ (\text{g})}$$

$$\text{x} = 283.75 \text{ or } 284 \text{ g of } 20\% \text{ ointment, } \textit{and}$$

$$2270 \text{ g} - 284 \text{ g} = 1986 \text{ g of ointment base, } \textit{answers.}$$

Dilution and Fortification of Solids and Semisolids

Or,

$$5 \text{ lb.} = 454 \text{ g} \times 5 = 2270 \text{ g}$$

$$2270 \text{ g} \times 2.5\% = 56.75 \text{ g of benzocaine needed}$$

$$\frac{20 \text{ (g)}}{56.75 \text{ (g)}} = \frac{100 \text{ (g)}}{x \text{ (g)}}$$

$$x = 283.75 \text{ or } 284 \text{ g of 20\% ointment, } \textit{and}$$

$$2270 \text{ g} - 284 \text{ g} = 1986 \text{ g of ointment base, } \textit{answers.}$$

Triturations

Triturations

Triturations are dilutions of potent medicinal substances. They were at one time official and were prepared by diluting one part by weight of the drug with nine parts of finely powdered lactose. They are, therefore, 10% or 1:10 w/w mixtures. These dilutions offer a means of obtaining conveniently and accurately small quantities of potent drugs for compounding purposes. Although no longer official as such, triturations exemplify a method for the calculation and use of dilutions of solid medicinal substances in compounding and manufacturing procedures.

Triturations

A modern-day example of a trituration is the product Trituration of **MUSTARGEN** (mechlorethamine hydrochloride for injection), in which 10 mg of the highly toxic drug is triturated with 90 mg of sodium chloride. The trituration is dissolved in sterile water for injection or in sodium chloride injection prior to administration.

Triturations

Note: The term trituration as used in this context should not be confused with the like term trituration, which is the pharmaceutical process of reducing substances to fine particles through grinding in a mortar and pestle.

Triturations

How many grams of a 1:10 trituration are required to obtain 25 mg of drug?

10 g of trituration contain 1 g of drug

$$25 \text{ mg} = 0.025 \text{ g}$$

$$\frac{1 \text{ (g)}}{0.025 \text{ (g)}} = \frac{10 \text{ (g)}}{x \text{ (g)}}$$

$$x = 0.25 \text{ g, } \textit{answer.}$$

Triturations

How many milliliters of an injection prepared by dissolving 100 mg of a 1:10 trituration of mechlorethamine hydrochloride in sufficient water for injection to prepare 10 mL of injection is required to obtain 5 mg of drug?

$$100 \text{ mg of trituration} = 10 \text{ mg of drug}$$

$$10 \text{ mg of drug in } 10 \text{ mL of injection}$$

$$\frac{10 \text{ (mg)}}{5 \text{ (mg)}} = \frac{10 \text{ (mL)}}{x \text{ (mL)}}$$

$$x = 5 \text{ mL, } \textit{answer.}$$

Triturations

How many milligrams of a 1 : 10 dilution of colchicine should be used by a manufacturing pharmacist in preparing 100 capsules for a clinical drug study if each capsule is to contain 0.5 mg of colchicine?

$$0.5 \text{ mg} \times 100 = 50 \text{ mg of colchicine needed}$$

$$10 \text{ mg of dilution contain } 1 \text{ mg of colchicine}$$

$$\frac{1 \text{ (mg)}}{50 \text{ (mg)}} = \frac{10 \text{ (mg)}}{x \text{ (mg)}}$$

$$x = 500 \text{ mg, } \textit{answer.}$$

Alligation

- **Alligation** is an arithmetical method of solving problems that involve 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. By this method, the percentage strength of each component, expressed as a decimal fraction, is multiplied by its corresponding quantity; then the sum of the products is divided by the total quantity of the mixture; and the resultant decimal fraction is multiplied by 100 to give the percentage strength of the mixture. Of course, the quantities must be expressed in a common denomination, whether of weight or volume.

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.

$$
\begin{aligned}
0.40 \times 3000\ \text{mL} &= 1200\ \text{mL} \\
0.60 \times 1000\ \text{mL} &= 600\ \text{mL} \\
0.70 \times 1000\ \text{mL} &= 700\ \text{mL} \\
\text{Totals:}\quad 5000\ \text{mL} &\quad 2500\ \text{mL} \\
2500\ (\text{mL}) \div 5000\ (\text{mL}) &= 0.50 \times 100 = 50\%, \textit{ answer.}
\end{aligned}
$$

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?

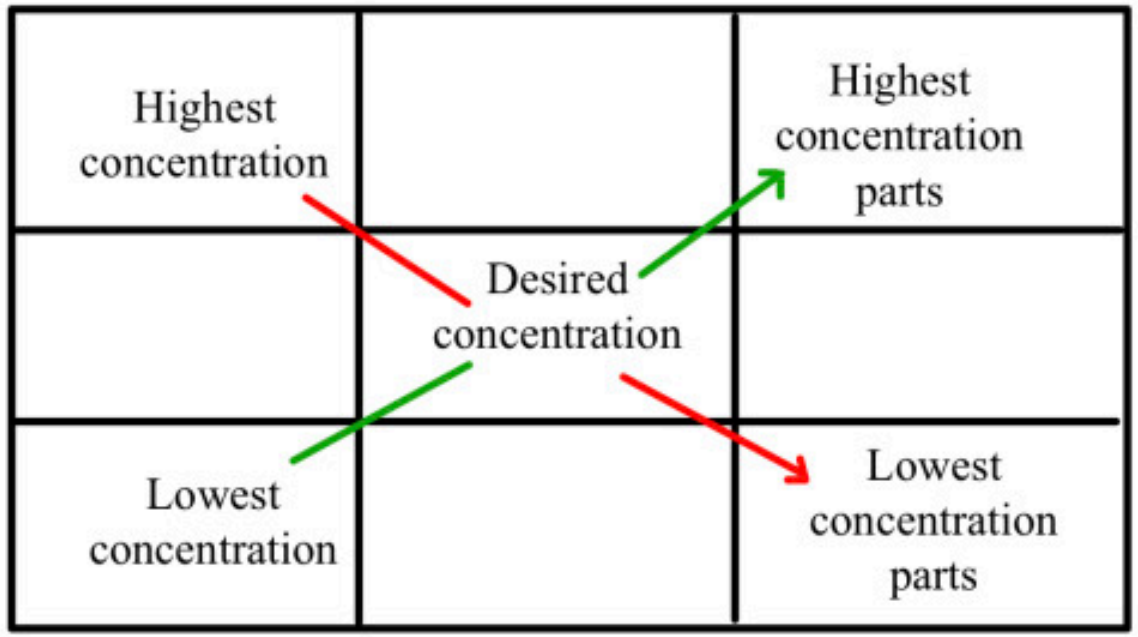
$$
\begin{aligned}
0.40 \times 500\ \text{mL} &= 200\ \text{mL} \\
0.21 \times 400\ \text{mL} &= 84\ \text{mL} \\
0 \times 100\ \text{mL} &= 0\ \text{mL} \\
\text{Totals:}\quad 1000\ \text{mL} &\quad 284\ \text{mL} \\
284\ (\text{mL}) \div 1000\ (\text{mL}) &= 0.284 \times 100 = 28.4\%, \textit{ answer.}
\end{aligned}
$$

Alligation

- **Alligation alternate:** is a method by which we may calculate the number of parts of two or more components of a given strength when they are to be mixed to prepare a mixture of desired strength.

- A final proportion permits us to translate relative parts to any specific denomination. The strength of a mixture must lie somewhere between the strengths of its components; that is, the mixture must be somewhat stronger than its weakest component and somewhat weaker than its strongest.

- As indicated previously, the strength of the mixture is always a ‘‘weighted’’ average; that is, it lies nearer to that of its weaker or stronger components depending on the relative amounts involved. This ‘‘weighted’’ average can be found by means of an extremely simple scheme, as illustrated in the subsequent diagram.



Highest concentration parts

(Desired - Lowest)

+

Lowest concentration parts

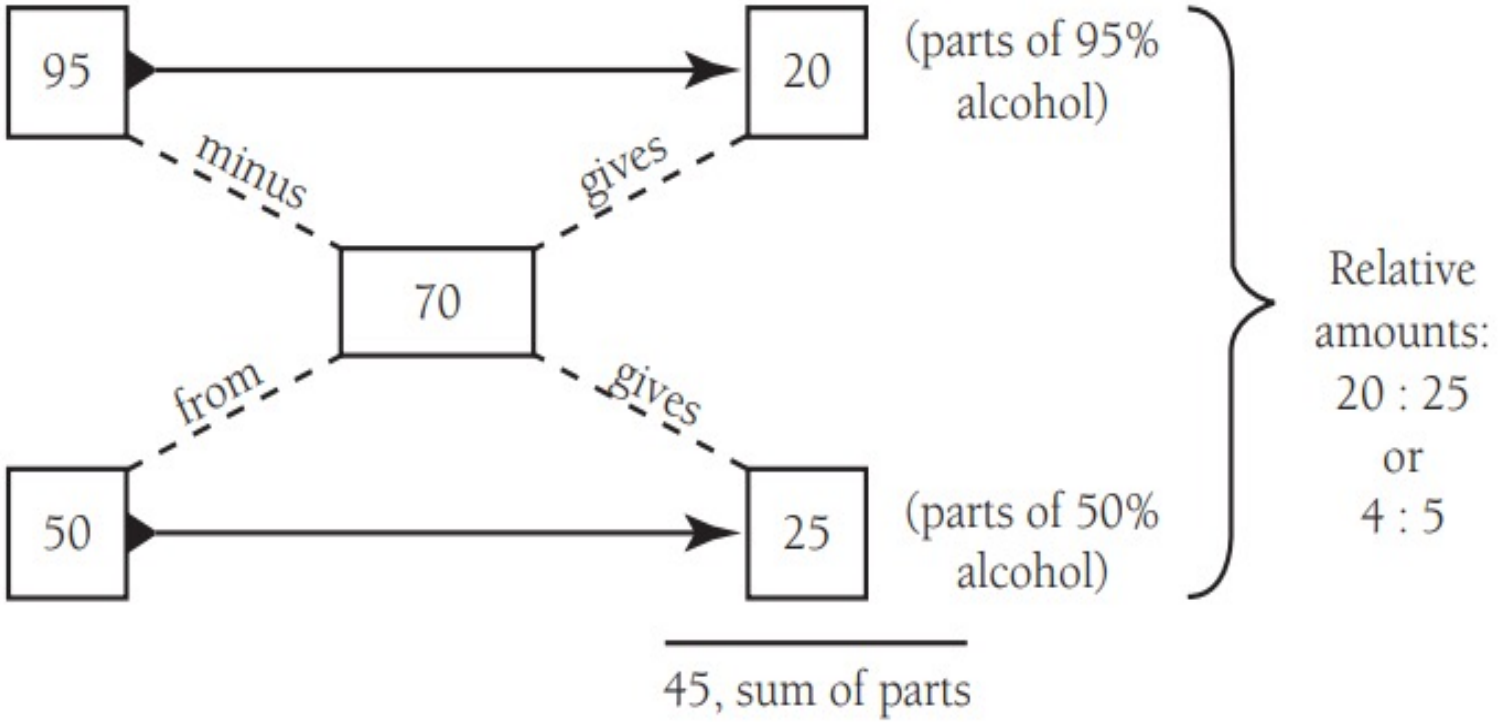
(Higher - Desired)

Total parts desired concentration

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 result can be shown to be correct by alligation medial:

0.95 * 4 = 3.8
0.50 * 5 = 2.5
Totals: 9 6.3

6.3 ÷ 9 = 7*100 = 70%

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

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

Relative amounts: 2.5:17.5, or 1:7, *answer.*

Check: $20 \times 1 = 20$

$0 \times 7 = 0$

Totals: 8 20

$20 \div 8 = 2.5\%$

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?

The two lots containing *more* (50% and 20%) than the desired percentage may be separately linked to the lot containing *less* (5%) than the desired percentage:

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

Relative amounts: 5:5:50, or 1:1:10, *answer*.

Check:
$$\begin{aligned} 50 \times 1 &= 50 \\ 20 \times 1 &= 20 \\ 5 \times 10 &= 50 \\ \text{Totals: } 12 &\quad 120 \end{aligned}$$

$$120 \div 12 = 10\%$$

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

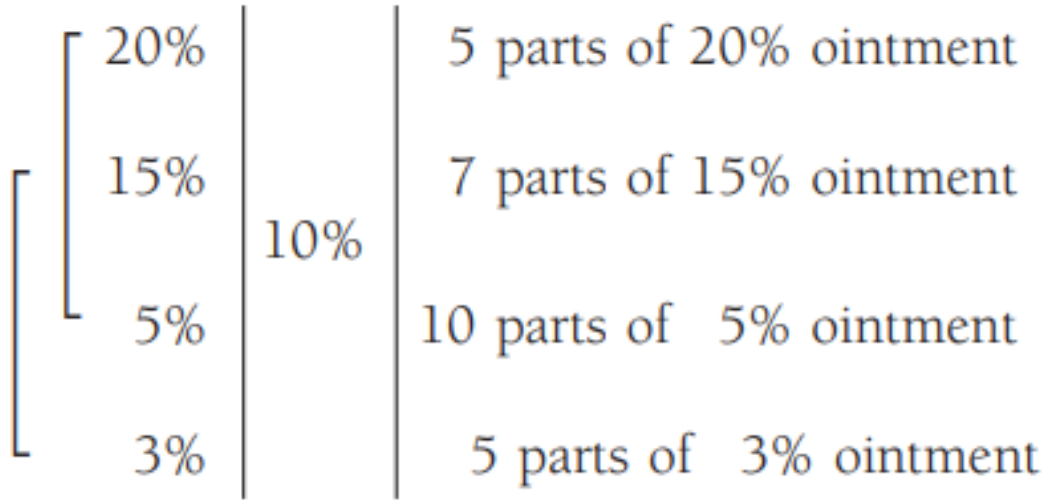
Relative amounts: 7:5:5:10, *answer.*

Check:

$$
\begin{aligned}
20 \times 7 &= 140 \\
15 \times 5 &= 75 \\
5 \times 5 &= 25 \\
3 \times 10 &= 30 \\
\text{Totals: } 27 & \quad 270
\end{aligned}
$$

$$270 \div 27 = 10\%$$

Or,



Relative amounts: 5:7:10:5, *answer.*

Check: $20 \times 5 = 100$
$15 \times 7 = 105$
$5 \times 10 = 50$
$3 \times 5 = 15$
Totals: 27 270

$270 \div 27 = 10\%$

How many milliliters each of a 2% w/v solution and a 7% w/v solution should be used in preparing 1 gallon of a 3.5% w/v solution?

1 gallon = 3785 mL

2%	3.5%	3.5 parts of 2% solution
7%		1.5 parts of 7% solution

Relative amounts: 3.5:1.5, or 7:3, with a total of 10 parts

$$\frac{10\ (\text{parts})}{7\ (\text{parts})} = \frac{3785\ (\text{mL})}{x\ (\text{mL})}$$

$$x = 2650\ \text{mL of 2\% solution, } \textit{and}$$

$$\frac{10\ (\text{parts})}{3\ (\text{parts})} = \frac{3785\ (\text{mL})}{y\ (\text{mL})}$$

$$y = 1135\ \text{mL of 7\% solution, } \textit{answers.}$$

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?

Zinc oxide (active ingredient) = 100%

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

Relative amounts: 15:80, or 3:16

$$\frac{16\ (\text{parts})}{3\ (\text{parts})} = \frac{3200\ (\text{g})}{x\ (\text{g})}$$

$$x = 600\ \text{g},\ \textit{answer.}$$

Check:

$$\begin{aligned} 100 \times 600 &= 60{,}000 \\ 5 \times 3200 &= 16{,}000 \\ \text{Totals:}\quad 3800 &\quad 76{,}000 \\ 76{,}000 \div 3800 &= 20\% \end{aligned}$$

THANK YOU

Dilution and Concentration