

Chapter 15

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

Part 1

Lecture 5

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Objectives

Upon successful completion of this chapter, the student will be able to:



Perform calculations for altering product strength through dilution or fortification.

Perform calculations for the preparation and use of stock solutions.

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.

❑ **Strengthened or concentrating of preparation by:**

1. **Addition of active ingredient.**
2. **Admixture with a like preparation of greater strength.**
3. **Evaporation of vehicle, if liquid.**

❑ **Diluting or decreasing strength of a preparation by:**

1. **Addition of diluent.**
2. **Admixture with a like preparation of lesser strength.**

Special considerations of altering product strength in pharmaceutical compounding

- ❖ **Reduction in strength of pharmaceutical product maybe desired to:**
 1. **Treat particular patient, based on patient age (e.g., pediatric or elderly).**
 2. **Medical status.**
 3. **Assist patient's initial response to a new medication.**
- ❖ **Strengthening of the product maybe desired to:**
(meet the specific medication needs of an individual patient).

Relationship between strength and total quantity

❑ The strength of a pharmaceutical preparation is based on its content of active ingredient relative to the whole.

Guidance: If the amount of active ingredient remains constant, a change in the total quantity (volume or weight) of the preparation will alter the strength inversely; (**strength decreases as the total quantity increases**), and visa versa.

❑ For example, 1 g in 10 mL = 10% w/v, whereas 1 g in 20 mL = 5% w/v. Thus, by doubling the volume, the strength is halved.

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 $Q_1 \times C_1 = Q_2 \times C_2$.

3. Traditional calculations, by determining the quantity of active ingredient present and relating that amount to the quantity of the total preparation.

Dilution of liquids

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

A. Solving by inverse proportion:

$$\begin{array}{rcl} 1500 \text{ ml} & 15\% & \\ 500 \text{ ml} & x\% & \end{array} \quad X = 5\%$$

B. Solving by equation:

$$Q_1 \text{ (quantity)} \times C_1 \text{ (concentration)} = Q_2 \text{ (quantity)} \times C_2 \text{ (concentration)}$$

$$500 \text{ (mL)} \times 15 \text{ (\%)} = 1500 \text{ (mL)} \times x \text{ (\%)} \quad X = 5\%$$

C. Solving by traditional calculations:

$$500 \times 0.15 = 75 \text{ ml of solute}$$

$$\begin{array}{rcl} 1500 \text{ ml} & 100\% & \\ 75 \text{ ml} & x\% & \end{array} \quad X = 5\%$$

2. 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 of the preservative?

a) Solving by inverse proportion

$$1:5000 = 1/5000 \times 100 = 0.02\% \text{ w/v}$$

$$\frac{0.02\%}{0.2\%} = \frac{125 \text{ ml}}{x \text{ ml}} \quad x = 1250 \text{ mL}$$

b) Solving by equation

$$125 \text{ (mL)} \times 0.2 \text{ (\%)} = x \text{ (mL)} \times 0.02 \text{ (\%)} \quad x = 1250 \text{ mL}$$

c) Solving by traditional calculations:

$$125 \text{ ml} \times 0.2 \text{ \% (g/mL)} = 0.25 \text{ g lauralkonium chloride}$$

$$\begin{array}{ccc} 0.02 \text{ g} & 100 \text{ mL} & \\ 0.25 \text{ g} & x & \end{array} \quad x = 1250 \text{ mL}$$

- 3. 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?**

Solving by equation:

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

$$80 \text{ (mL)} \times 20 \text{ (\%)} = x \text{ (mL)} \times 3 \text{ (\%)}$$

$$X = 533.3 \text{ mL} - 80 \text{ mL} = 435.3 \text{ mL of water added}$$

Or Solving by traditional calculations:

$$80 \text{ mL} \times 20\% \text{ (or } 0.2) \text{ g/ mL} = 16 \text{ g solute}$$

3 g	100 mL	X = 533.3 mL (quantity of 3% w/v solution that 16 g of solute will appear
16 g	x mL	

$$X = 533.3 \text{ mL} - 80 \text{ mL} = 435.3 \text{ mL of water added}$$

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

A) Convert mg to g

$$50 \text{ mg} / 1000 = 0.05 \text{ g} / 10 \text{ mL}$$

B) convert 0.05 g/ 10 ml to percentage

$$\begin{array}{ccc} 0.05 \text{ g} & 10 \text{ ml} & \\ x & 100 \text{ ml} & X = 0.5\% \end{array}$$

C) Solving by equation

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

$$10 \text{ (mL)} \times 0.5 \text{ (\%)} = 1000 \text{ (mL)} \times X \text{ (\%)}$$

$$X = 0.005\%$$

5. 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.

A) Convert mg to g

$$40 / 1000 = 0.04 \text{ g}$$

B) Calculate the amount of dopamine in each vial

$$\begin{array}{l} 0.04 \text{ g} \quad 1 \text{ mL} \\ X \quad 5 \text{ mL} \end{array} \quad X = 0.2 \text{ g}$$

C) Calculate the percentage of dopamine in each vial

$$\begin{array}{l} 0.2 \text{ g} \quad 5 \text{ mL} \\ X \quad 100 \text{ mL} \end{array} \quad X = 4\%$$

D) Calculate total infusion volume after addition of dopamine vial

$$5 \text{ mL (dopamine HCl injection)} + 250 \text{ mL (5\% dextrose injection)} = 255 \text{ mL}$$

E) Solving by equation:

$$Q1 \times C1 = Q2 \times C2 \quad (5 \text{ ml} \times 4 \% = 255 \text{ ml} \times X\%) \quad X = 0.078\% \text{ (w/v)}$$

6. 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.

A) Calculate the amount of cefazolin taken from injection

$$\begin{array}{l} 1\text{g} \quad 3\text{ mL} \\ X \quad 1.6\text{ mL} \quad X = 0.53\text{ g} \end{array}$$

B) Calculate the percentage of cefazoline used

$$\begin{array}{l} 0.53\text{ g} \quad 1.6\text{ mL} \\ X \quad 100\text{ mL} \quad X = 33.13\% \end{array}$$

C) The total volume of sodium chloride injection used to prepare 200 mL of I.V. infusion:

$$200 - 1.6 = 198.4\text{ mL}$$

E) Solving by equation:

$$Q_1 \times C_1 = Q_2 \times C_2 = (1.6 \times 33.13\% = 198.4 \times X\%) = 0.27\%$$

F) Calculate the concentration of cefazolin in infusion in mg/ml

$$0.27 / 1000 = 270\text{ mg}/100\text{ mL then in } 1\text{ mL} = 2.7\text{ mg} / \text{mL}$$

STRENGTHENING OF PHARMACEUTICAL PRODUCT

Strengthening of an existing pharmaceutical product could be accomplished by:

1

Addition of active ingredient

2

Admixture with a calculated quantity of a like product of greater concentration (known as alligation alternate).

Example: If a cough syrup contains in each teaspoonful, 1 mg of chlorpheniramine maleate and if a pharmacist desired to double the strength, how many milligrams of that ingredient would need to be added to a 60-mL container of the syrup. Assume no increase in volume?

$$\begin{array}{rcl} 1 \text{ mg} & 5 \text{ mL} & \\ X & 60 \text{ mL} & = 12 \text{ mg chlorpheniramine} \\ & & \text{maleate in original syrup.} \end{array}$$

To double the strength, 12 mg of additional chlorpheniramine maleate would be required.

Stock solutions

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

Example 1: How many milliliters of a 10% w/v stock solution should be used in preparing 1 gallon of a 0.05% w/v solution?

1 gallon = 3785 mL

Solving by equation:

$$Q_1 \times C_1 = Q_2 \times C_2$$

$$3785 \text{ mL} \times 0.05 \% = Q_2 \times 10 \%$$

$$Q_2 = 18.9 \text{ mL}$$

Example 2: How many milliliters of a 1% w/v 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?

To convert ratio (1: 20,000) to percent as follows:

$$\begin{array}{r} 1 \\ X \end{array} \quad \begin{array}{r} 20000 \\ 100 \end{array} \quad X = 0.005\%$$

Solving by equation:

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

$$4000 \text{ mL} \times 0.005 \% \text{ w/v} = Q2 \times 1 \% \text{ w/v}$$

$$Q2 = 20 \text{ mL}$$

Note: In pharmacy practice two portions must be defined:

- 1. Strength of a diluted portion of a solution**
- 2. Strength of the concentrated stock solution used to prepare it must be also be determined.**

Example: A pharmacist 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.

Uses: (e.g., for irrigation or soaking).

Benefits:

- a) Permits the dispensing of a relatively small volume of liquid.**
- b) Enabling a patient to prepare large volumes as needed, rather than carrying home gallons of a diluted solution from a pharmacy.**

Example 3: How much drug should be used in preparing 50 mL of a stock solution such that 5 mL diluted to 500 mL will yield a 1:1000 solution?

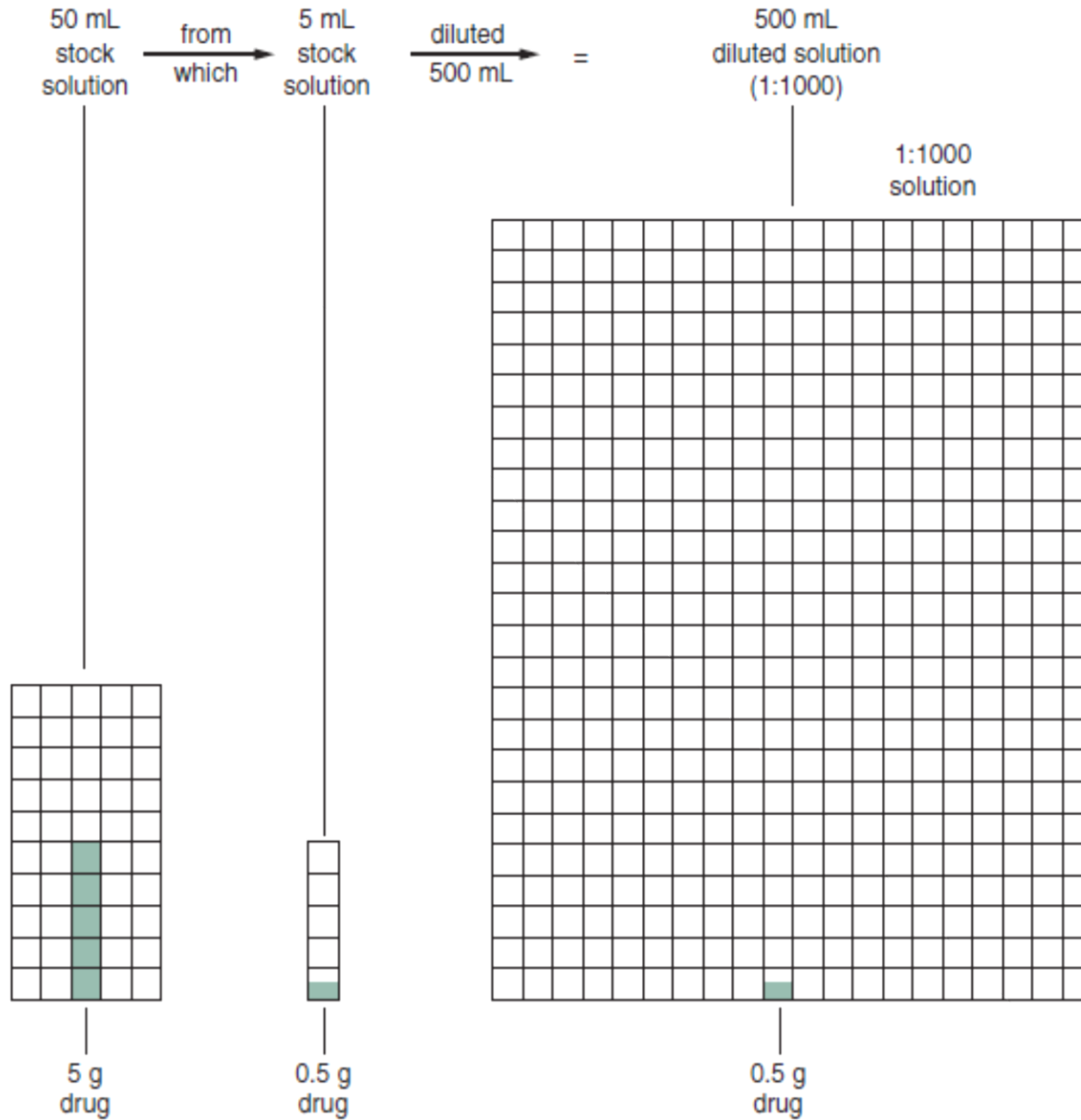
1 g 1000 mL
X 500 mL

$X = 0.5$ 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

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



Example 4: 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 0.3% w/v solution for irrigation?

0.3 g	100 mL	X = 3 g
X	1000 mL	

50 mL	3 g	X = 30 g
500 mL	x	

Example 5: 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?

$$\begin{array}{r} 0.13 \text{ g} \quad 100 \text{ mL} \\ X \quad 60 \text{ mL} \end{array}$$

X = 0.078 g of benzalkonium chloride in 60 mL of diluted solution, which is also the amount in 5 mL of the stronger (stock) solution to be prepared.

$$\begin{array}{r} 0.078 \text{ g} \quad 5 \text{ mL} \\ X \quad 100 \text{ mL} \end{array}$$

X = 1.56 g of benzalkonium chloride needed.

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

$$\begin{array}{r} 17 \text{ g} \quad 100 \text{ mL} \\ 1.56 \text{ g} \quad x \end{array}$$

X = 9.18 mL



**THANK
YOU**