This chapter provides an overview of Concentrations and Dilutions, Compound Formulas, and Alligations
I. Concentrations and Dilutions

A. Pharmaceutical concentrations come in different strengths to meet the various dosing needs of patients.

B. Terms to Remember

1. Concentrate- A highly condensed drug product that is diluted prior to administration
2. Dilution- The product obtained when an inactive ingredient, a diluent, is added to a concentrate
I. Concentrations and Dilutions

3. Diluent- An inactive substance that is added to a concentrate to make it less concentrated; can be a vehicle or a solvent
I. Concentrations and Dilutions

C. Antibiotics are often supplied to pharmacies in a concentrated form and must be customized to a patient's weight or medical condition. These drugs are designed to be diluted when added to a patient's IV bag (mini bag or large volume- 1L)
I. Concentrations and Dilutions

Safety Note: An injected dose generally has a volume greater than 0.1mL and less than 1mL.
I. Concentrations and Dilutions

D. Steps for Solving Typical Dilution Problems

1. Use ratio-proportion method to solve for the volume of the final product by using a ratio of diluted solution to desired concentration.
I. Concentrations and Dilutions

2. Determine the amount of diluent by subtracting the concentrate from the total volume
   a. Sometimes this amount is actually determined by adding “up to” the desired total quantity.
   b. It is helpful to calculate the necessary amount beforehand so that an adequate supply is available
I. Concentrations and Dilutions

Safety Note: Typically, the ratio-proportion method is preferred over the dimensional analysis method to solve these problems because it is easier to identify the parts of the equation with the ratio-proportion method.
I. Concentrations and Dilutions

E. Example- Concentrations

You are instructed to make 240 mL of a 0.45% w/v solution. You have a 100% w/v concentrate in stock. How much of the concentrate will you use, and how much of the diluent will be needed?
I. Concentrations and Dilutions

Part I: Determine the number of grams desired in the final solution.

\[
\frac{x \text{ g}}{240 \text{ mL}} = \frac{0.45 \text{ g}}{100 \text{ mL}}
\]

\[x \text{ g} = \frac{(240 \text{ mL}) \times 0.45 \text{ g}}{100 \text{ mL}}\]

\[x \text{ g} = 1.08 \text{ g}\]

Next, determine how much of the concentrated solution will be required to provide the desired number of grams.

\[
\frac{x \text{ mL}}{1.08 \text{ g}} = \frac{100 \text{ mL}}{100 \text{ g}} = \frac{1 \text{ mL}}{1 \text{ g}}
\]

\[x \text{ mL} = 1.08 \text{ mL}\]
Part II: Determine how many milliliters of diluent will be needed.

240 mL total volume − 1.08 mL concentrate = 238.92 mL diluent
I. Concentrations and Dilutions

F. Problem Sets (pg. 207-208, problem 26-30)
II. Compound Formulas

A. Similar to making a cake from scratch by using ingredients such as butter, sugar, eggs, flour, and baking powder. A formula is a written document, like a recipe. Some pharmacies routinely prepare compounded products for physicians who prescribe these special preparations on a regular basis.
II. Compound Formulas

B. Terms to Remember

1. Compounding- The process of using raw ingredients and/or other prepared ingredients to prepare a drug product for a patient.

2. Formula- A written document listing the ingredients and instructions needed to prepare a compound.
II. Compound Formulas

3. Compounded Stock Solution- A solution that is prepared in a large amount and kept in stock in the pharmacy to be divided for individual prescriptions
C. Formulas can be enlarged or reduced, to make more or less than what the original recipe made.

Safety Note: When enlarging or reducing a formula for compounding, always retain the correct proportion of ingredients from the original formula.
II. Compound Formulas

D. The dispensed compound must match the concentration and the amount ordered. Careful calculations must be done to ensure this accuracy.

Safety Note: Always document calculations before compounding.
II. Compound Formulas

E. Example- Compounding

1. You need to prepare 100 mL of an iodine solution for a patient.

<table>
<thead>
<tr>
<th></th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodine</td>
<td>30 g</td>
</tr>
<tr>
<td>Sodium iodide</td>
<td>25 g</td>
</tr>
<tr>
<td>Purified water</td>
<td>QSAD, 1000 mL</td>
</tr>
</tbody>
</table>

The formula indicates the resulting volume is 1000 mL, and your patient needs 100 mL.
II. Compound Formulas

So, you need $\frac{1}{10}$, (100 mL desired/1000 mL formula) of each amount.

<table>
<thead>
<tr>
<th></th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IODINE</td>
<td>$30 \text{ g} \div 10 = 3 \text{ g}$</td>
</tr>
<tr>
<td>SODIUM IODIDE</td>
<td>$25 \text{ g} \div 10 = 2.5 \text{ g}$</td>
</tr>
<tr>
<td>PURIFIED WATER</td>
<td>$1000 \text{ mL} \div 10 = 100 \text{ mL}$</td>
</tr>
</tbody>
</table>
II. Compound Formulas

2. You need to prepare four syringes for the following order.

Phenol 5% w/v syringes sodium chloride 5 mL

Calculate the amount of phenol needed in each syringe.

\[
\frac{x \text{ g}}{5 \text{ mL}} = \frac{5 \text{ g}}{100 \text{ mL}}
\]

\[x \text{ g} = 0.25 \text{ g or 250 mg/syringe}\]
II. Compound Formulas

For four syringes, you will need:

\[ 4 \text{ syringes} \times 250 \text{ mg/syringe} = 1000 \text{ mg phenol} \]

and

\[ 4 \text{ syringes} \times 5 \text{ mL sodium chloride/syringe} = 20 \text{ mL sodium chloride} \]
III. Alligations

A. Physicians may prescribe a concentration of medication that is not commercially available. Such prescriptions must be made by compounding:

1. Using concentrated stock solution, or
2. By combining two different solutions with the same active ingredient in differing strengths.
III. Alligations

B. The result of combining two different solutions with the same active ingredient in differing strengths is called an alligation.

For example, combining 1% and 5% hydrocortisone ointments to get a 3% ointment
III. Alligations

C. Terms to Remember

1. Alligation- The concentration obtained when two or more solutions of different strengths are combined. The result amount of each solution is calculated by using the alligation alternate method.
III. Alligations

2. Alligation Alternate Method- The mathematical calculation used to determine the amounts of two or more dilutions of differing strengths that will be mixed to prepare a product of a desired strength and quantity
III. Alligations

This method requires that you:

a. Change the percentages to parts of a proportion
b. Use the proportion to obtain the amounts of the two ingredients
c. Check the answer with the formula: milliliters × percent = grams
III. Alligations

D. Example- Alligation

1. Prepare 250 mL of dextrose 7.5% w/v using dextrose 5% (D5W) w/v and dextrose 50% (D50W) w/v. How many milliliters of each will be needed?
III. Alligations

Step 1

a. Set up a box arrangement and at the upper left corner, write the percent of the highest concentration (50%) as a whole number

50
III. Alligations

Step 1

b. At the lower-left corner, write the percent of the lowest concentration (5%) as a whole number.

\[ \begin{array}{ccc} 
50 \\
5 \\
\end{array} \]

c. In the center, write the desired concentration

\[ \begin{array}{ccc} 
7.5 \\
\end{array} \]
III. Alligations

Step 2

a. Subtract the center number from the upper-left corner and put it at the lower-right corner.

\[
\begin{array}{c}
50 \\
5 \\
\end{array}
\]

42.5 mL parts D5W
b. Subtract the lower-left number from the center number and put it at the upper-right corner.

50  7.5  2.5 mL parts D50W
5   42.5 mL parts D5W
c. The number 2.5 mL represents the number of parts of the 50% solution that will be needed to make the 7.5% solution.

\[
\begin{array}{c}
50 & 2.5 \text{ mL parts D50W} \\
5 & 42.5 \text{ mL parts D5W}
\end{array}
\]
III. Alligations

d. The number 42.5 mL represents the number of parts of the 5% solution that will be needed.

\[
\begin{array}{c}
50 \\
5
\end{array}
\quad 7.5
\quad 2.5 \text{ mL parts D50W}
\quad 42.5 \text{ mL parts D5W}
\]
III. Alligations

e. The sum of these two numbers is the total number of parts of the 7.5% solution

\[
\begin{align*}
50 & \quad 7.5 \\
5 & \quad 2.5 \text{ mL parts D50W} \\
& + \\
42.5 & \quad 4.5 \text{ mL parts D5W} \\
\end{align*}
\]

45 mL total parts D7.5W
III. Alligations

f. In terms of ratios, the ratio of the 5% solution to the 7.5% solution is 42.5:45.

\[
\begin{align*}
2.5 \text{ mL parts D50W} & \quad + \\
42.5 \text{ mL parts D5W} & \\
45 \text{ mL total parts D7.5W}
\end{align*}
\]
III. Alligations

g. In terms of ratios, the ratio of the 50% solution to the 7.5% solution is 2.5:45. Much less of the 50% is needed to make the 7.5% solution.

\[
2.5 \text{ mL parts D50W} + 42.5 \text{ mL parts D5W} = 45 \text{ mL total parts D7.5W}
\]
III. Alligations

Step 3

a. Calculate the volume needed for each dextrose solution.

- 50% Dextrose
- 5% Dextrose

b. Calculate the volume needed for the 50% dextrose solution

\[
\frac{x \text{ mL of 50\%}}{250 \text{ mL}} = \frac{2.5 \text{ mL parts } D_{50\%} W}{45 \text{ mL total parts } D_{7.5\%} W}
\]

\[x \text{ mL of 50\%} = \frac{(250 \text{ mL}) \times 2.5 \text{ mL parts}}{45 \text{ mL total parts}} D_{7.5\%} W\]

\[x \text{ mL of 50\%} = 13.8888 \text{ mL } D_{50\%} W, \text{ rounded to 13.89 mL}\]
III. Alligations

c. Calculate the volume needed for the 5% dextrose solution.

\[
\frac{x \text{ mL of 5%}}{250 \text{ mL}} = \frac{42.5 \text{ mL parts } D_5 W}{45 \text{ mL total parts } D_{7.5} W}
\]

\[x \text{ mL of 5%} = \frac{(250 \text{ mL}) \times 42.5 \text{ mL parts}}{45 \text{ mL total parts } D_{7.5} W}
\]

\[x \text{ mL of 5%} = 236.11 \text{ mL } D_5 W\]
III. Alligations

Step 4:

a. Add the volumes of the two solutions together. The sum should equal the required volume of dextrose 7.5%.

\[
\begin{align*}
236.11 \text{ mL} \\
+ 13.89 \text{ mL} \\
250.00 \text{ mL}
\end{align*}
\]
Step 5:

a. Check the answer by calculating the amount of solute (dextrose) in all three solutions. The number of grams of solute should equal the sum of the grams of solutes from the 50% solution and the 5% solution, using the formula:

\[ \text{mL} \times \% = \text{g} \]
III. Alligations

b. Check the answer

c. \( \text{mL} \times \% \text{ (as a decimal)} = \text{g} \)

\[
\begin{align*}
250 \text{ mL} \times 0.075 &= 18.75 \text{ g} \\
13.89 \text{ mL} \ D_{50}W \times 0.5 &= 6.945 \text{ g} \\
236.11 \text{ mL} \ D_{5}W \times 0.05 &= 11.805 \text{ g}
\end{align*}
\]

\[
\begin{align*}
11.805 \text{ g} \\
+6.945 \text{ g} \\
\hline
18.750 \text{ g}
\end{align*}
\]
III. Alligations

d. The amounts measured to prepare this prescription:
13.89 mL D50W and 236.11 mL D5W will be rounded to the nearest milliliter:
14 mL D50W and 236 mL D5W
III. Alligations

E. Sometimes it is necessary to calculate the final concentration or percentage strength of a mixture that is composed of known quantities and percentage strengths of two or more ingredients.
III. Alligations

1. The calculation used is called the alligation medial method.

a. Alligation Medial Method- The mathematical calculation used to find the final concentration created when two or more known quantities of known concentrations are compounded
III. Alligations

2. The resulting percentage is the “middle” or “medial” strength, as it is between the strengths of the ingredients.
III. Alligations

F. Example- Allegation Medial Method

You have been asked to prepare a mixture with the following ingredients: 30 g of 1% hydrocortisone cream, 20 g of 0.5% hydrocortisone ointment, and 10 g of Eucerin cream base. What will be the percentage of hydrocortisone in the final mixture?
III. Alligations

Solution 1
Using the ratio-proportion method

Step 1: Determine the amount of active ingredients in 30 g of 1% hydrocortisone cream.

\[ \frac{x \text{ g}}{30 \text{ g}} = \frac{1 \text{ g}}{100 \text{ g}} \]

\[ x = 0.3 \text{ g hydrocortisone} \]
Step 2: Determine the amount of active ingredients in 20 g of 0.5% hydrocortisone ointment.

\[ \frac{x \text{ g}}{20 \text{ g}} = \frac{0.5 \text{ g}}{100 \text{ g}} \]

\[ x \text{ g} = 0.1 \text{ g hydrocortisone} \]
III. Alligations

Solution 2

Using the dimensional analysis method:

Step 1: Determine the amount of active ingredients in 30 g of 1% hydrocortisone cream.

\[ 30 \text{ g} \times \frac{1 \text{ g}}{100 \text{ g}} = 0.3 \text{ g hydrocortisone} \]
III. Alligations

Step 2: Determine the amount of active ingredients in 20 g of 0.5% hydrocortisone ointment.

\[ 20 \text{ g} \times 0.5 \text{ g/100 g} = 0.1 \text{ g hydrocortisone} \]
III. Alligations

After completing Step 2 with the ratio proportion method and/or dimensional analysis method

Step 3: Determine the amount of grams in the final mixture.

30 g 1% cream + 20 g 0.5% ointment + 10 g Eucerin = 60 g final mixture
III. Alligations

Step 4: Add the active ingredients and divide by the total quantity to determine the final concentration

\[
\frac{0.3 \text{ g} + 0.1 \text{ g}}{60 \text{ g}} \times 100 = 0.6666\%, \text{ rounded to } 0.7\%
\]

Note: that the final concentration of 0.7% is between the concentrations of the ingredients. It is less than 1% and more than 0.5%.
IV. Least Measurable Quantity and Aliquot Measurements

A. When weighing ingredients, it is important to know the smallest amount that can be accurately weighed on your balance.

\[
\frac{100 \times \text{balance sensitivity}}{\text{permissible } \% \text{ margin of error}} = \text{least weighable quantity}
\]

B. Example - Least Measurable Quantity

\[
\frac{100 \times \text{balance sensitivity}}{3} = 100 \times 6 \text{ mg} = 200 \text{ mg}
\]
IV. Least Measurable Quantity and Aliquot Measurements

C. If a very small amount needs to be weighed, and the scale cannot measure that dose, an aliquot may be used.

1. Aliquot- A measured portion, fraction, or part of an ingredient that is placed into solution or into a mixture of other ingredients to aid in measuring a very small amount.
IV. Least Measurable Quantity and Aliquot Measurements

D. Steps for Weight Aliquot Measuring
   Step 1: Calculate the least weighable quantity (LWQ) based on the sensitivity of the balance and the permissible margin of error.
IV. Least Measurable Quantity and Aliquot Measurements

Step 2: Determine the amount of the ordered drug that you will actually weigh out. This amount must be equal to or larger than the least weighable quantity. To calculate the amount of drug to weigh out, multiply the amount of drug ordered by a whole number such as 2, 5, 10, or 20, until you have a weighable amount—that is, an amount greater than the least weighable quantity. The whole number you choose is called a factor. The factor chosen is arbitrary, but it must result in an amount greater than the least weighable quantity.
IV. Least Measurable Quantity and Aliquot Measurements

Step 3: Determine the amount of diluent (inert ingredient) to add.

a. Determine the total amount of mixture (drug + diluent) that will be required.
   \[ \text{drug weighed out} \times \text{factor} = \text{total amount mixture} \]

b. Calculate the amount of diluent needed.
   \[ \text{total amount of mixture} - \text{drug weighed out} = \text{diluent} \]
IV. Least Measurable Quantity and Aliquot Measurements

Step 4: Combine the drug and diluent measured in Steps 2 and 3 and mix them well so that the drug is evenly distributed throughout the mixture.
IV. Least Measurable Quantity and Aliquot Measurements

Step 5: Determine the amount of mixture needed to provide the originally-ordered amount by using the ratio-proportion method.

\[
\frac{X \text{ mg mixture}}{\text{amount of drug ordered}} = \frac{\text{total amount of mixture}}{\text{amount of drug weighed}}
\]
IV. Least Measurable Quantity and Aliquot Measurements

E. Example- Weight Aliquot
You receive a prescription for 15 mg of antibiotic in 10 mL Cherry Syrup USP. A 3% margin of error is allowed, and you are to use a balance with a sensitivity of 4 mg. What amount of aliquot mixture will contain the ordered amount of drug?
IV. Least Measurable Quantity and Aliquot Measurements

Step 1: Determine the least weighable quantity.

\[
\frac{100 \times \text{balance sensitivity}}{\text{permissible } \% \text{ margin of error}} = \frac{100 \times 4 \text{ mg}}{3} = 133 \text{ mg}
\]

So, at least 133 mg of the active ingredient must be weighed. At least this amount must be weighed for the diluent used as well.
IV. Least Measurable Quantity and Aliquot Measurements

Step 2: Determine the amount to be weighed.

15 mg × 10 = 150 mg

Step 3: Determine the total amount of mixture that will be required and the amount of inert ingredient.

150 mg active ingredient × 10 = 1500 mg total mixture

1500 mg total – 150 mg active = 1350 mg inert

You will weigh 1350 mg of the inert ingredient.
Step 4: Determine the total weight of the drug and diluent.

150 mg drug + 1350 mg diluent = 1500 mg
IV. Least Measurable Quantity and Aliquot Measurements

Step 5: Determine the amount of mixture needed to provide the originally ordered amount.

\[ x \text{ mg mixture} = \frac{(15 \text{ mg drug ordered}) \times (1500 \text{ mg mixture})}{150 \text{ mg drug}} \]

So, a 150 mg aliquot will contain 15 mg of the drug, the ordered amount of the drug.
IV. Least Measurable Quantity and Aliquot Measurements

F. Least Measurable Quantity and Aliquot Measurements

1. Aliquot can also be used to prepare pharmaceutical preparations that include very small volumes of a liquid.

2. The minimum amount that can be precisely measured must be considered.
IV. Least Measurable Quantity and Aliquot Measurements

G. Steps for Volume Aliquot Measuring

Step 1: Determine the minimum volume that can be measured accurately.

Step 2: Determine the multiple of the active ingredient that will provide the smallest volume that can be accurately measured.
IV. Least Measurable Quantity and Aliquot Measurements

Step 3: Determine the total volume of the mixture by multiplying the volume of active ingredient by the same multiple (factor) used in Step 2.

Step 4: Determine the amount of diluent needed by subtracting the amount of active ingredient calculated from the mixture total.
IV. Least Measurable Quantity and Aliquot Measurements

Step 5: Determine the amount of mixture needed to provide the originally ordered amount by using the ratio-proportion method.
IV. Least Measurable Quantity and Aliquot Measurements

H. Example- Volume Aliquot

You receive a prescription for 0.25 mL of a drug. The minimum volume of that can be accurately measured in your pharmacy is 1.0 mL. What amount of aliquot mixture will contain the ordered volume of drug?
IV. Least Measurable Quantity and Aliquot Measurements

Step 1: The minimum volume that can be measured accurately is 1.0 mL. The trailing zero indicates a measurement accuracy to a tenth of a milliliter.

Safety Note: A trailing zero is appropriate if it is used to communicate the accuracy of a measurement.
IV. Least Measurable Quantity and Aliquot Measurements

Step 2: Determine the multiple of the active ingredient that will provide the smallest volume that can be accurately measured.

0.25 mL × 4 = 1.0 mL active ingredient

Step 3: Determine the total volume of the mixture.

1.0 mL × 4 = 4.0 mL total mixture
Step 4: Determine the amount of diluent needed.

4.0 mL total – 1.0 mL active ingredient = 3.0 mL diluent needed
IV. Least Measurable Quantity and Aliquot Measurements

Step 5: Determine the amount of mixture needed to provide the originally ordered amount

\[
\frac{x \text{ mL mixture}}{0.25 \text{ mL drug}} = \frac{4.0 \text{ mL mixture}}{1.0 \text{ mL drug}}
\]

\[x \text{ mL mixture} = 1.0 \text{ mL}\]

So, a 1.0 mL aliquot will contain the needed ingredient.