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Dilution and Concentration of Pharmaceutical Preparations

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What you need to know?

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

1. A preparation may be *strengthened* or made more *concentrated* by the addition of active ingredient, by admixture with a like preparation of greater strength, or through the evaporation of its vehicle, if liquid.

2. The strength of preparation may be decreased or *diluted* by the addition of diluent or by admixture with a like preparation of lesser strength.

Introduction

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. 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.

Introduction

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.

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**.

Relationship Between Strength and Total Quantity

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.

Relationship Between Strength and Total Quantity

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.**

Relationship Between Strength and Total Quantity

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

1. Inverse proportion.
2. **The equation:**

   (1st quantity) * (1st concentration) = (2nd quantity) * (2nd concentration),

   or Q1 * C1 = Q2 * C2.

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)?

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

$$x = 5\%, \textit{ answer.}$$

Or,

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

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

$$x = 5\%, \textit{ answer.}$$

Dilution and Concentration of Liquids

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.

$$1:20 = 5\%$$

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

$$x = 0.25\% = 1:400, \textit{ answer.}$$

Or,

$$\frac{1000\ (\text{mL})}{50\ (\text{mL})} = \frac{1/20}{x}$$

$$x = \frac{1}{400} = 1:400, \textit{ answer.}$$

Or,

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

$$50\ (\text{mL}) \times 5\ (\%) = 1000\ (\text{mL}) \times (\%)$$

$$x = 0.25\% = 1:400, \textit{ answer.}$$

Dilution and Concentration of Liquids

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.

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

$$x = 76.47\% \text{ or } 76\%, \textit{answer.}$$

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

100 (mL) **x** 65 (%) = 85 (mL) **x** C2(%)

C2 = 76.47% or 76%, *answer*

Dilution and Concentration of Liquids

How many grams of 10% w/w ammonia solution can be made from 1800 g of 28% w/w strong ammonia solution?

$$\frac{10\ (\%)}{28\ (\%)} = \frac{1800\ (g)}{x\ (g)}$$

$$x = 5040\ g,\ \textit{answer.}$$

Or,

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

$$1800\ (g) \times 28\ (\%) = x\ (g) \times 10\%$$

$$x = 5040\ g,\ \textit{answer.}$$

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?

$$1 \text{ gallon} = 3785 \text{ mL}$$

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

$$x = 2271 \text{ mL, } \textit{answer.}$$

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

3785 (mL) **x** 30 (%) **=** Q2 (mL) **x** 50(%)

Q2 **=** 2271 mL, answer.

If 4 fl oz of a 1:2000 (w/v) solution of cetylpyridinium chloride are diluted to 1 pint. What will be the ratio strength (w/v) of the dilution?

1 pint = 16 fl oz

1:2000 = 0.05 %

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

4 (fl oz) * 0.05 (%) = 16 (fl oz) * C2(%)

C2 = 0.0125 %, 1:8000 answer.

Strengthening of a Pharmaceutical Product

This accomplished by the **addition of active ingredient** or by the **admixture with a calculated quantity of a like-product of greater concentration.**

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.

$$\frac{1 \text{ mg}}{5 \text{ mL}} \times 60 \text{ mL} = 12 \text{ mg chlorpheniramine maleate in original syrup}$$

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

Strengthening of a Pharmaceutical Product

CASE IN POINT 15.1: A pharmacist received a prescription for 100 mL of a cefuroxime axetil suspension to contain 300 mg of drug in each 5 mL. The pharmacist has 100 mL of a suspension containing 250 mg/5 mL and also has 250-mg scored tablets of the drug. How many tablets should be pulverized and added to the suspension to achieve the desired strength? Assume no increase in the volume of the suspension.

Strengthening of a Pharmaceutical Product

Cefuroxime axetil present in original suspension:

$$100 \text{ mL} \times \frac{250 \text{ mg}}{5 \text{ mL}} = 5000 \text{ mg}$$

Cefuroxime axetil required in strengthened suspension:

$$100 \text{ mL} \times \frac{300 \text{ mg}}{5 \text{ mL}} = 6000 \text{ mg}$$

Cefuroxime axetil to add:

$$6000 \text{ mg} - 5000 \text{ mg} = 1000 \text{ mg}$$

Tablets required:

$$1000 \text{ mg} \times \frac{1 \text{ tablet}}{250 \text{ mg}} = 4 \text{ tablets, } \textit{answer}.$$

Strengthening of a Pharmaceutical Product

A Second Look

The pharmacist observed that after adding the pulverized tablets, the suspension measured 102 mL in volume. Calculations revealed that rather than the prescribed drug strength of 300 mg/5 mL, there were 294.1 mg/5 mL. What should the pharmacist do to bring the suspension to the desired strength?

Strengthening of a Pharmaceutical Product

There are a number of ways in which this problem could be addressed. One way would be to add another 250-mg pulverized tablet, calculate the volume of suspension that could be prepared at a concentration of 300 mg/5 mL, dispense 100 mL of that and discard the remaining volume.

Cefuroxime axetil in strengthened suspension plus another tablet:

6000 mg + 250 mg = 6250 mg cefuroxime axetil

Volume of suspension that could be prepared at a concentration of 300 mg/5 mL:

$$\frac{5 \text{ mL}}{300 \text{ mg}} \times 6250 \text{ mg} = 104.17 \text{ mL}$$

Volume to dispense:

100 mL, and

Volume to discard:

4.17 mL, *answers*.

Proof: "If there are 6250 mg of cefuroxime axetil in 104.17 mL, how many milligrams would be present in each 5 mL?"

$$6250 \text{ mg} \times \frac{5 \text{ mL}}{104.17 \text{ mL}} = 299.99 \text{ or } 300$$

mg, *answer*.

THANK YOU

Dilution and Concentration