Assistant Prof. Dr. Duaa Jaafar Al-Tamimi

Objectives:

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

- ✓ Describe instruments for volumetric measurement and characterize their differences in application and accuracy.
- ✓ Describe the correct procedure when using a pharmaceutical balance.
- ✓ Define *sensitivity requirement* and apply it in calculations.
- ✓ Perform calculations by the aliquot method.
- ✓ Demonstrate an understanding of *percentage of error* in pharmaceutical measurement.

Why we need to learn about pharmaceutical measurements?

The role of the pharmacist in providing pharmaceutical care includes the ability and responsibility to ***compound***—that is, to accurately weigh, measure volume, and combine individual therapeutic and pharmaceutical components in the formulation and preparation of prescriptions and medication orders

Measurement of volume

The selection of measuring instrument should be <u>based on the level of precision required</u>

Select the graduate with a capacity equal to or just exceeding the volume to be measured

- ➢ The narrower the bore or chamber, the lesser the error in reading the meniscus and the more accurate the measurement

Measurements of weight

Sensitivity requirement: The load that will cause a change of one division on the index plate of the balance.

- Class A prescription balance has a ***sensitivity requirement (SR)*** of 6 milligrams or less with no load and with a load of 10 grams in each pan.
- *To avoid errors of greater than 5% when using this balance, the pharmacist should not weigh less than 120 milligrams of material (i.e., a 5% error in a weighing of 120 milligrams is 6 milligrams)*.

sensitivity requirement may be determined by the following procedure:

١. Level the balance.

٢. Determine the rest point of the balance.

٣. Determine the smallest weight that causes the rest point to shift one division on the index plate.

✓ Most commercially available Class A balances have a maximum capacity of 120 grams

Electronic analytical balance

✓ Capable of weighing accurately 0.1 milligram

✓ Self-calibrating

✓ Equipped with convenient digital readout features.

✓ The usual maximum capacities for balances of this precision range from about 60 grams to 210 grams depending upon the model

Aliquot method of weight and measurement

Why use this method؟

When a degree of precision in measurement required is beyond the capacity of the available instrument.

Aliquot is a fraction, portion, or part that is contained an exact number of times in another.

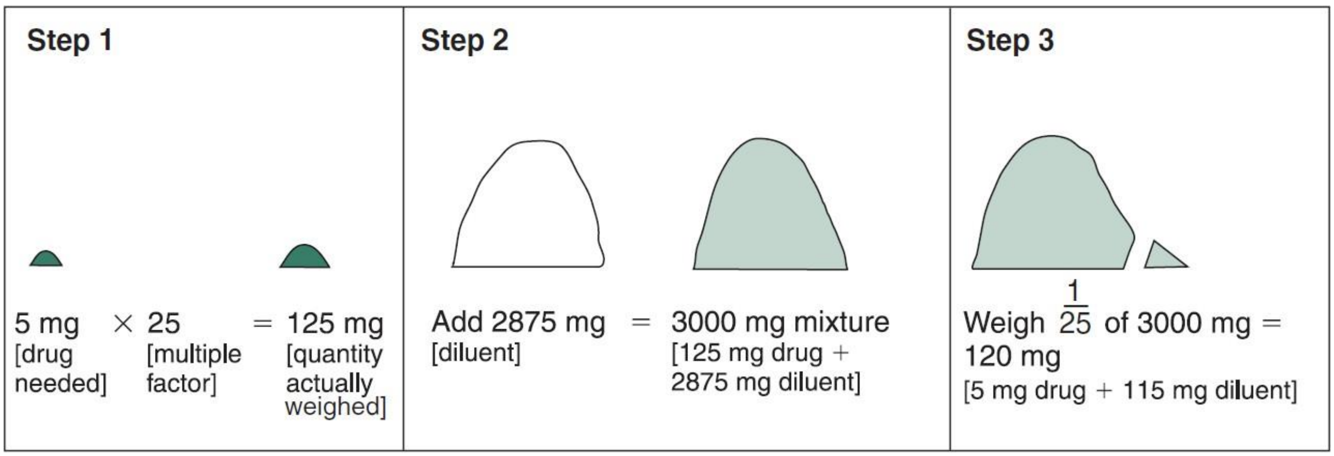

FIGURE 3.6 Depiction of the aliquot method of weighing using the example described on the next page.

Step 1: Calculate the smallest quantity of a substance that can be weighed on a balance with the desired precision

The equation used:

$$\frac{100\% \times \text{Sensitivity Requirement (mg)}}{\text{Acceptable Error (\%)}} = \text{Smallest Quantity (mg)}$$

Example:

On a balance with an SR of 6 mg, and with an acceptable error of no greater than 5%, a quantity of not less than 120 mg must be weighed.

$$\frac{100\% \times 6\text{ mg}}{5\%} = 120\text{ mg}$$

Step 2: Weigh an amount of the drug equal to or greater than the least weighable amount and calculate the enlargement factor: weighed amount/desired amount

Step 3: choose aliquot weight equal to or larger than the smallest weighable amount

Step 4: determine mixture weight = aliquot X factor

Step 5: calculate weight of diluent needed = mixture – drug

$$\frac{100\% \times \text{Sensitivity Requirement (mg)}}{\text{Acceptable Error (\%)}} = \text{Smallest Quantity (mg)}$$

$$\frac{100\% \times 6}{error\ \%} = 125\ \text{mg, error}\ \% = 4.8\%$$

↑amount to be weighed → ↓error

Amount drug actually weighed to prepare the mixture

125 mg

Total amount of the mixture (drug + diluent)

3000 mg

5 mg

Amount drug needed for the prescription

?

$$? = \frac{3000\text{mg} \times 5\cancel{\text{mg}}}{125\cancel{\text{mg}}} = 120\ \text{mg}$$

Amount of the mixture to be weighed to get the desired amount of the drug

Step 2: weigh 125 mg, factor = 125/5 = 25

Step 3: choose aliquot weight equal to or larger than the smallest weighable amount, choose 120 mg

Step 4: determine mixture weight = aliquot X factor = 120 X 25 = 3000

Step 5: calculate weight of diluent needed = mixture – drug = 3000 – 125 = 2875 mg

A torsion prescription balance has a sensitivity requirement of 6.5 milligrams. Explain how you would weigh 15 milligrams of atropine sulfate with an accuracy of ± 5%, using lactose as the diluent.

Sensitivity requirement = 6.5 mg

$$smallest\ quantity = \frac{100\% \times SR}{error\ \%} = 130 \text{ mg}$$

١. Smallest amount = 130 mg

٢. Weight 150 mg atropine sulfate (130/15 = 8.6 so we choose 150 to get an easy-to-use factor) factor =150/15 = 10

٣. Choose aliquot weight 130 mg

٤. Mixture weight = aliquot X factor = 130 X 10 = 1300

٥. Calculate weight of diluent needed = mixture – drug = 1300 mg – 150 = 1150 mg

٦. Check to make sure 130 mg contains 15 mg drug:

150 mg drug	1300 mg mixture	
?	130 mg mixture	? = 150 X 130 /1300 = 15 mg

Important note: You can choose to weigh

5. A prescription balance has a sensitivity requirement of 6.5 milligrams. Explain how you would weigh 20 milligrams of a substance with an error not greater than 2%.

SR = 6.5

Error 2%

Amount drug needed = 20 mg

١. Least weighable amount = 100 X 6.5 / 2 = 385 mg

٢. Weight 400 mg atropine sulfate (400/20 = 20)

٣. Choose aliquot weight 385 mg (you can choose 400 mg)
٤. Mixture weight = aliquot X factor = 385 X 20 = 7700
٥. Calculate weight of diluent needed = mixture – drug = 7700 mg – 400 = 7300 mg

٦. Check to make sure 385 mg contains 20 mg drug:

400 mg 3700 mg

20 mg ? , aliquot = 7300 X 20 /400 = 385 mg of the mixture to contain 20 mg substance

Or: if you choose to use 400 mg as the aliquot weight

(20 X 400) – 400 = 8000 – 400 = 7600 mg diluent,
400g 8000 mg
20 mg ? aliquot = 8000 X 20 /400 = 400 mg

Measuring volume by the aliquot method

A formula calls for 0.5 milliliter of hydrochloric acid. Using a 10-milliliter graduate calibrated from 2 to 10 milliliters in 1-milliliter divisions, explain how you would obtain the desired quantity of hydrochloric acid by the aliquot method.

Step 1. Select a multiple of the desired quantity that can be measured with the required precision.

Step 2. Dilute the multiple quantity with a compatible diluent (usually a solvent for the liquid to be measured) to an amount evenly divisible by the multiple selected.

Step 3. Measure the aliquot of the dilution that contains the quantity originally desired

If 4 is chosen as the multiple, and if 2 milliliters is set as the volume of the aliquot, then:

1. Measure 4 × 0.5 mL, or 2 mL of the acid
2. Dilute with 6 mL of water
   to make 8 mL of dilution
3. Measure ¼ of dilution, or 2 mL of dilution, which will contain 0.5 mL of hydrochloric acid, *answer*.

6. ℞ Sodium Citrate 5 g
Tartar Emetic 0.015 g
Cherry Syrup ad 120 mL

Using a balance with a sensitivity of 4 mg, an acceptable weighing error of 5% and cherry syrup as the solvent for tartar emetic, how could you obtain the correct quantity of tartar emetic to fill the prescription?

Amount drug to be weighed > 80 mg, weigh 90 mg

Dissolve in 12 ml

12 ml 90 mg

? 15 mg ? = 12 ml X 15 mg / 90 mg = 2 ml

- Weigh 90 mg drug
- Dissolve on 12 ml cherry syrup
- Use 2 ml to fill the prescription

Percentage of error

measurements in the community pharmacy are never *absolutely* accurate

- Need to recognize the limitations of the instruments used and the magnitude of the errors that may be incurred.
- Need to know

١. the *apparent* weight or volume measured

٢. the possible excess or deficiency in the actual quantity obtained.

Percentage of error the maximum potential error multiplied by 100 and divided by the quantity desired.

$$Percentage\ of\ error = \frac{Error\ \times 100\%}{Quantity\ desired}$$

Using a graduated cylinder, a pharmacist measured 30 milliliters of a liquid. On subsequent examination, using a narrow-gauge burette, it was determined that the pharmacist had actually measured 32 milliliters. What was the percentage of error in the original measurement?

Answer:

32 ml - 30 ml = 2 ml, the volume of error

(2 mL X 100%)/30 mL = 6.7%

A prescription calls for 800 milligrams of a substance. After weighing this amount on a balance, the pharmacist decides to check by weighing it again on a more sensitive balance, which registers only 750 milligrams. Because the first weighing was 50 milligrams short of the desired amount, what was

the percentage of error?

Answer:

50 mg the weight of error

(50 mg X 100%)/800 mg = 6.25%

3. A torsion prescription balance has a sensitivity requirement of 4 milligrams. Explain how you would weigh 5 milligrams of hydromorphone hydrochloride with an error not greater than 5%. Use lactose as the diluent.

The smallest quantity that should be weighed on the balance:

$$\frac{100\% \quad \times 4\ mg}{5\%} = 80\ mg$$

Quantity desired: 5 mg

Multiple factor selected: 20, weigh 100 mg of the drug (20X5 = 100)

Aliquot portion selected: 90 mg

Hydromorphone hydrochloride (20 X 5)	=	100 mg
Lactose	=	1700 mg
Aliquot mixture	=	1800 mg

Proof: 1/20 of the drug 100 mg/20 = 5 mg

1/20 of the diluent 1700 mg /20 = 85 mg

90 mg aliquot

7. A formula calls for 0.6 milliliter of a coloring solution. Using a 10-milliliter graduate calibrated from 2 to 10 milliliters in 1-milliliter units, how could you obtain the desired quantity of the coloring solution by the aliquot method? Use water as the diluent.

Multiple factor selected: 5

Aliquot volume selected: 2 ml

Measure 3 ml of the coloring solution (0.6 ml X 5 = 3 ml)

Dilute to 10 ml

Measure 2 ml

Proof:

10 ml dilution	3 ml coloring agent
?	0.6 ml coloring agent

? = 10 ml X 0.6 ml/ 3 ml = 2 ml

HW: A pharmacist needed to weigh 20 mg of a drug using a balance with a sensitivity requirement of 6.5 mg and error not greater than 2%. This was his plan: weigh 340 mg drug, dilute with 5440 mg diluent to make 5780 mg, weigh 325 mg. Is his work correct?

11. In compounding a prescription, a pharmacist weighed 0.050 gram of a substance on a balance insensitive to quantities smaller than 0.004 gram. What was the maximum potential error in terms of percentage?

14. A graduate weighs 35.825 grams. When 10 milliliters of water are measured in it, the weight of the graduate and water is 45.835 grams. Calculate the weight of the water and express any deviation from 10 grams as percentage of error.

15. In preparing a certain ointment, a pharmacist used 28.35 grams of zinc oxide instead of the 31.1 grams called for. Calculate the percentage of error on the basis of the desired quantity.

Error = quantity measured – desired quantity

= 28.35 g – 31.1 g = - 2.75 g = 2.75 g (negative sign means we are measuring less than needed)

Percentage of error = (error X 100%) / desired quantity

= (2.75 g X 100%) / 31.1 g = 8.84 %

CASE IN POINT 3.1: A pharmacist is asked to compound the following formula for the preparation of 100 capsules:[3]

Estriol	**200 mg**
Estrone	**25 mg**
Estradiol	**25 mg**
Methocel E4M	**10 g**
Lactose	**23.75 g**

Using a balance that has an SR of 6 mg, the aliquot method of weighing, lactose as the diluent, and an error in weighing of 4%, show, by calculations, how the correct quantity of estrone can be obtained to accurately compound the formula.

CASE IN POINT 3.2: A physician prescribed 25 4-mg capsules of a drug for a special needs patient, knowing that the dose prescribed was considered "subtherapeutic." The lowest strength commercially available tablets contain 25 mg.

The pharmacist decided to select the minimum required number of 25-mg tablets (4 tablets); reduce them to a powder with a mortar and pestle; weigh the powder (280 mg); and continue the process using the aliquot method. She called upon her pharmacy student intern to calculate (a) the minimum quantity of lactose (diluent) to use in preparing the crushed tablet-diluent mixture and (b) the quantity of the mixture to use to fill each capsule.

The prescription balance had a SR of 6 mg and a weighing error of 5% was acceptable.

Show your calculations for (a) and (b), and (c) prove that your answer to (b) is correct by demonstrating that each capsule would indeed contain 4 mg of drug.

PRACTICE PROBLEMS

Calculations of Aliquot Parts by Weighing

1. A prescription calls for 50 milligrams of chlorpheniramine maleate. Using a prescription balance with a sensitivity requirement of 6 milligrams, explain how you would obtain the required amount of chlorpheniramine maleate with an error not greater than 5%.

2. A prescription balance has a sensitivity requirement of 0.006 gram. Explain how you would weigh 0.012 gram of atropine sulfate with an error not greater than 5%, using lactose as the diluent.

3. A torsion prescription balance has a sensitivity requirement of 4 milligrams. Explain how you would weigh 5 milligrams of hydromorphone hydrochloride with an error not greater than 5%. Use lactose as the diluent.

4. A torsion prescription balance has a sensitivity requirement of 0.004 gram. Explain how you would weigh 0.008 gram of a substance with an error not greater than 5%.

5. A prescription balance has a sensitivity requirement of 6.5 milligrams. Explain how you would weigh 20 milligrams of a substance with an error not greater than 2%.

Calculations of Aliquot Parts by Measuring Volume

6. ℞ Sodium Citrate 5 g
   Tartar Emetic 0.015 g
   Cherry Syrup ad 120 mL

   Using a balance with a sensitivity of 4 mg, an acceptable weighing error of 5% and cherry syrup as the solvent for tartar emetic, how could you obtain the correct quantity of tartar emetic to fill the prescription?

7. A formula calls for 0.6 milliliter of a coloring solution. Using a 10-milliliter graduate calibrated from 2 to 10 milliliters in 1-milliliter units, how could you obtain the desired quantity of the coloring solution by the aliquot method? Use water as the diluent.

8. Using a 10-milliliter graduate calibrated in 1-milliliter units, explain how you would measure 1.25 milliliters of a dye solution by the aliquot method. Use water as the diluent.

9. The formula for 100 milliliters of pentobarbital sodium elixir calls for 0.75 milliliter of orange oil. Using alcohol as a diluent and a 10-milliliter graduate calibrated in 1-milliliter units, how could you obtain the desired quantity of orange oil?

Calculations of Percentage of Error

10. A pharmacist attempts to weigh 120 milligrams of codeine sulfate on a balance with a sensitivity requirement of 6 milligrams. Calculate the maximum potential error in terms of percentage.

11. In compounding a prescription, a pharmacist weighed 0.050 gram of a substance on a balance insensitive to quantities smaller than 0.004 gram. What was the maximum potential error in terms of percentage?

12. A pharmacist weighed 475 milligrams of a substance on a balance of dubious accuracy. When checked on a balance of high accuracy, the weight was found to be 445 milligrams. Calculate the percentage of error in the first weighing.

13. A 10-milliliter graduate weighs 42.745 grams. When 5 milliliters of distilled water are measured in it, the combined weight of graduate and water is 47.675 grams. By definition, 5 milliliters of water should weigh 5 grams. Calculate the weight of the measured water and express any deviation from 5 grams as percentage of error.

14. A graduate weighs 35.825 grams. When 10 milliliters of water are measured in it, the weight of the graduate and water is 45.835 grams. Calculate the weight of the water and express any deviation from 10 grams as percentage of error.

15. In preparing a certain ointment, a pharmacist used 28.35 grams of zinc oxide instead of the 31.1 grams called for. Calculate the percentage of error on the basis of the desired quantity.

16. A pharmacist attempts to weigh 0.375 gram of morphine sulfate on a balance of dubious accuracy. When checked on a highly accurate balance, the weight is found to be 0.400 gram. Calculate the percentage of error in the first weighing.

ANSWERS TO "CASE IN POINT" AND PRACTICE PROBLEMS

Case in Point 3.1

The smallest quantity that should be weighed on the balance:

$$\frac{100\% \times 6\text{ mg}}{4\%} = 150\text{ mg}$$

Quantity desired (estrone): 25 mg
Multiple factor selected: 6
Aliquot portion selected: 150 mg

Estrone (25 × 6)	150 mg
Lactose	750 mg
Aliquot mixture	900 mg
Aliquot portion (900 mg ÷ 6)	150 mg of mixture will provide 25 mg estrone, *answer*

Case in Point 3.2

The smallest quantity that should be weighed on the balance:

$$\frac{100\% \times 6\text{ mg}}{5\%} = 120\text{ mg}$$

(a) Quantity of mixture required to prepare 25 capsules each containing the weighable quantity of 120 mg:

120 mg × 25 (capsules) = 3000 mg

Quantity of lactose required equals the quantity of mixture required less the weight of the crushed tablets:

3000 mg − 280 mg = 2720 mg or 2.72 g of lactose required, *answer*.

(b) Quantity of mixture to fill each capsule:

3000 mg ÷ 25 (capsules) = 120 mg, *answer*.

(c) Proof of 4 mg of drug per capsule:
Amount of drug in mixture:

4 mg (per tablet) × 25 (tablets) = 100 mg

Amount of drug per capsule:

100 mg ÷ 25 (capsules) = 4 mg, *answer*.

or,

$$\frac{100 \text{ mg } (drug)}{3000 \text{ mg } (mixture)} = \frac{x}{120 \text{ mg } (mixture)}$$
= 4 mg, *answer*.

Practice Problems

Aliquot Parts by Weighing

1. Weigh 150 mg chlorpheniramine maleate
   Dilute with 450 mg
   to make 600 mg
   Weigh 200 mg
2. Weigh 120 mg atropine sulfate
   Dilute with 1380 mg
   to make 1500 mg
   Weigh 150 mg
3. Weigh 80 mg hydromorphone hydrochloride
   Dilute with 1520 mg
   to make 1600 mg
   Weigh 100 mg
4. Weigh 160 mg
   Dilute with 3840 mg
   to make 4000 mg
   Weigh 200 mg
5. Weigh 400 mg
   Dilute with 7600 mg
   to make 8000 mg
   Weigh 400 mg

Aliquot Parts by Measuring Volume

6. Weigh 90 mg
   Dilute to 12 mL
   Measure 2 mL
7. Measure 3 mL
   Dilute to 10 mL
   Measure 2 mL
8. Measure 5 mL
   Dilute to 8 mL
   Measure 2 mL
9. Measure 3 mL orange oil
   Dilute to 8 mL
   Measure 2 mL

Percentage of Error

10. 5%
11. 8%
12. 6.32%
13. 1.4%
14. 0.1%
15. 8.84%
16. 6.67%