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Expression of concentrations in pharmaceutical preparations.

Lab.1

abstract

The idea of experimenting to determine the concentration of any pharmaceutical substance (for example, sodium hydroxide, NaOH)

This experiment aims to determine the concentration of sodium hydroxide solution by titrating it with a reagent solution of standard hydrochloric acid of known concentration (0.1N), where sodium hydroxide reacts with hydrochloric acid according to the following equation:

$NaOH + HCl \longrightarrow NaCl + H2O$

At the end point, the medium is neutral, and using the phenolphthalein index, its color at this point changes from pinkish-red in the basic medium to colorless**.**

Introduction

A major feature observable with migration from folklore medicine to modern medical practice is dose standardization which opens room for research and development of existing knowledge. Quantifying the amount of a particular medicinal agent that elicits a given pharmacological response and ensuring reproducibility of such effect, has resulted in the concept of doses and dosage regimen for medicines and expression of quantities in relation to concentration. Several terms implying different strengths have been used in describing the **concentration of pharmaceutical products**. Some of these are: equivalents/volume, molarity, molality, osmolarity, parts per million, international units and different percentages. An understanding of these terms is key to maneuvering available strengths of products, preparing of desired amount of given medicine in line with the clinical condition of patient and achieving desired therapeutic outcome.

Pharmaceutical preparations come in **specific concentration expressions** whether they are in terms of weight, volume, or parts.

Interestingly, the way concentrations of ingredients in pharmaceutical products are expressed is the same as those of biochemical substances in the body. **Concentrations of biochemical substances in the body** are expressed in terms such as weight per weight, weight per volume, mole per volume, equivalents per volume *et cetera*. All these expressions are obtainable with pharmaceutical products. Therefore, knowledge of expressions of concentration of medicines can be applied to clinical practice.

A comprehensive coverage of the topic of concentration is in a sphere of its own under physical chemistry and pharmacy, but this chapter looks at some commonly seen concentrations in clinical practice. The examples provided are not exhaustive, in themselves, but provide a sound background for appreciating how different concentration terms are used in dosage forms and in clinical practice. A clear understanding of concentration expressions can add to the confidence of the practicing pharmacists in giving sound, accurate, and life-saving drug information to healthcare practitioners and particularly to the patients.

Molarity

The molarity of a solution describes the number of moles of the solute in a litre of the solution. This is a commonly seen expression of concentrations in laboratory researches in the physical sciences, pharmaceutical as well as medicinal chemistry.

$$\textbf{Molarity} = \frac{\textbf{moles of solute}}{\textbf{Litre of solution}}$$

Alternatively

$$\textbf{Molarity could be expressed as } \frac{\textbf{mass of substance per Litre}}{\textbf{molar mass of substance}}$$

The unit is mol/L with M as symbol.

Note: *A solution is a one phase liquid preparation composed of solute (that which is dissolved) and the solvent (that which dissolves)*.

Example 1.1

'Substance P' is a new analgesic to be formulated as effervescent granules. If 5 g of a 'substance P' with molecular mass 150 g/mole is dissolved in water to form 120 mL solution, calculate the molarity of the solution?

Solution

No of moles = $\frac{\text{mass of substance}}{\text{molar mass of substance}}$

$= \frac{5}{150}$

= 0.033 moles

Volume of solution is 120 mL = 0.12 L

Thus the molarity of the solution is $\frac{0.033}{0.12}$

= 0.275 M

Example 1.2

The fasting blood sugar of a patient was found to be 160 mg/dL. Express this in terms of molarity (molecular weight of glucose is 180).

Solution

160 mg/dL = 1600 mg/L

Molarity = $\frac{\text{mass of substance per Litre}}{\text{molar mass of substance}}$

$= \frac{1600}{180}$

= 8.89 mmol/L

To convert mmol/L to mol/L (M) is to divide by 1000

The molarity = $\frac{8.89}{1000}$

= 8.89 x 10^{-3} M

Note: Solutions with more than one solute could have more than one expressions of concentration with respect to the particular solute

present. So, such could have different molarities depending on the moles of solute used .

Normality

This is the number of equivalents of a solute in 1 litre of solution.
Mathematically,

Normality = $\frac{\textbf{number of equivalents of solute}}{\textbf{Litre of solution}}$

Number of equivalents = $\frac{\textbf{reacting or given mass}}{\textbf{equivalent weight}}$

To determine the number of equivalents in a given mass of solute, the equivalent weight should be known. The equivalent weight of an ion or compound is the weight of the ion, atom or compound that will interact with one electron on dissociation.

For example, the equivalent weight of Hydrogen (H) is approximately 1.0 g (interaction involves one electron) when in reaction. Calcium has 40 g/mol as its molecular mass. In reaction, Ca interacts with 2 electrons to give Ca^{2+} hence equivalent weight is 20 g but for Al (3 electrons are involved), its equivalent weight will be 9 g (i.e. 27 g/mol ÷3).

As a formula,

Equivalent weight = $\frac{\textbf{molecular mass (or mass of atom)}}{\textbf{valency}}$

The valency of an element is a measure of its combining power. It is the number of hydrogen atom that can combine with or replace one atom of the element**.**

Example 1.3

A patient with hypokalaemia is to be treated with potassium chloride solution. If 60 g quantity of potassium chloride salt is dissolved in water to form a 750 mL solution, what is the normality of the solution?

<u>Solution</u>

KCl has a molecular weight of 74.5 g/mole. Only one electron is involved, hence monovalency describes the interaction for both cation and anion on dissociation (K^+ Cl^-).

Hence

Equivalent weight = $\frac{\text{molecular weight}}{\text{valency}}$

$$= \frac{74.5}{1}$$

= 74.5 g/Eq

The gram equivalents of the KCl is $\frac{\text{reacting mass}}{\text{equivalent weight}}$

$$= \frac{60}{74.5}$$

= 0.805 Eq

Recall this 0.805 Eq is in 750 mL

Therefore, 1000 mL (1L) will contain $\frac{1000 \times 0.805}{750}$

= 1.074 Eq/L

= 1.074 N

Note: **<u>Molecular weight</u>** is used interchangeably with **<u>molar mass</u>** in this text. Also as a memory aid, determining the number of equivalents is similar to that of number of moles except for substitution of the denominator in the formula for mole with equivalent weight.

Example 1.4

Magnesium sulphate is a major component of an antacid; 70 g of the salt was used to prepare a solution that was to be added to aluminum hydroxide to form the desired antacid. Assuming the Magnesium solution prepared was 2.6 L, determine the normality of the solution.

Solution

Magnesium sulphate with a valency of 2 (Mg^{2+} $(SO_4)^{2-}$) has a molecular mass of 120 g/mole

Its equivalent weight is = $\frac{\text{molecular weight}}{\text{valency}}$

$$= \frac{120}{2}$$

$$= 60 \text{ g/Eq}$$

The number of equivalents in the given weight is $\frac{\text{reacting mass}}{\text{equivalent weight}}$

$$= \frac{70}{60}$$

$$= 1.167 \text{ Eq}$$

Recall 1.167 Eq (that is 70 g) of the magnesium sulphate was dissolved in a 2.6 L solution

The amount in 1L solution = $\frac{1.167 \text{ Eq}}{2.6 \text{ L}}$

$$= 0.45 \text{ Eq/L or } 0.45 \text{ N}$$

Note also that the reference values of concentration of certain electrolytes (potassium, sodium, calcium, chloride etc) in the serum or plasma are expressed as mEq/dL. Thus, a good grasp of the concept of normality and equivalents will improve the pharmacist's proficiency in assisting other health professionals in achieving the reference values especially when there has been electrolyte depletion or imbalance in patients associated with some specific disease conditions.

Molality

Both molarity and normality use volume in expressing concentration. Any fluctuation in temperature of such solution will result in change in the volume of the solution and by extension a variation in the concentration. It is noteworthy too that the volume of the solvent is not known, only that of the solution. These deficiencies are catered for when using molality as a means of concentration expression. Molality expresses the number of moles of a solute present in 1 kg of solvent. Using an equation,

molality = $\frac{\textbf{moles of solute}}{\textbf{weight of solvent in Kg}}$

The concern here is the solvent and not the solution. One advantage of expressing concentration this way is that the variation in concentration due to temperature fluctuation is avoided.

Example 1.5

The chemical structure of a new drug 'anxietin' known to calm political tension was recently elucidated and the molecular weight found to be 302 g/mol. In its pure form, 5 g of it dissolved in 60 g of water for injection, elicited an effective blockade of the adrenergic receptors. State the molality of this potent solution**.**

Solution

No of moles of solute = $\frac{\textbf{reacting mass}}{\textbf{molecular weight}}$

$$= \frac{\mathbf{5g}}{\mathbf{302g/mol}}$$

= 0.017 moles

Thus the 0.017 moles of anxietin was dissolved in 60 g of water.
The amount that will be in 1 kg (1000 g) of water is

$$= \frac{\mathbf{0.017moles}}{\mathbf{0.06kg}}$$

= 0.283 *m*

Osmolarity *and* Osmolality

These are expressions of concentration based on the number of osmoles per litre of solution (osmolarity) or number of osmoles per kilogram of solvent (osmolality).
Expressed as equations,

osmolarity = $\frac{\textbf{osmoles of solute}}{\textbf{Litre of solution}}$

Whereas

osmolality = $\frac{\textbf{moles of solute}}{\textbf{weight of solvent in Kg}}$

Here, the term 'mole' is replaced with the term 'osmoles'. An mole gives the number of osmotically active particles present in a given solution.
For non-electrolytes, the number of moles = the number of osmoles since they do not dissociate into ionic species. But in electrolytes, dissociation occurs; hence the number of mole is not the same as the number of osmoles.
In very simple terms, number of osmoles in electrolytes = number of moles × number of ions formed on complete dissociation.

Example 1.6
Calcium chloride solution to be used for management of hypocalcaemic tetany was extemporaneously prepared by dissolving 0.72 mole quantity of $CaCl_2$ in water to form 250 mL solution having a density of 1.5 g/mL. Calculate the osmolarity and osmolality of the solution?
Solution
$CaCl_2$ undergoes complete dissociation to give Ca^{2+} + $2Cl^-$
Thus 1 mole of $CaCl_2$ gives 3 osmotically active species (1 mole of Ca^{2+} and 2 mole of Cl^-)
Then 0.72 moles $CaCl_2$ will give (3 × 0.72) moles = 2.16 moles of $CaCl_2$

osmolarity = $\frac{\textbf{osmoles of solute}}{\textbf{Litre of solution}}$
$= \frac{\textbf{2.16 osmoles}}{\textbf{0.25 L}}$
= 8.64 osmolar

For osmolality, the weight of the solvent must be determined.
Recall, mass of solution = volume of solution × its density
Mass of solution = 250 mL × 1.5 g/mL
= 375g

Mass of solute = number of mole × molar mass
= 0.72 mol × 111 g/mole

= 79.92g.

Since mass of solution= mass of solute + mass of solvent,
Mass of solvent = mass of solution – mass of solute
= 375 - 79.92
= 295.08g which is the same as 0.2951 kg

$$\text{osmolality} = \frac{\text{osmoles of solute}}{\text{weight of solvent in Kg}}$$
$$= \frac{2.16\ osmoles}{0.2951\ \text{Kg}}$$
= 7.32osmolal

Percentage Weight by Weight (% w/w)

This expression of concentration indicates the amount of an ingredient (g) in 100 g of a substance. It could be the g of a solute in 100 g of the solution or a weight in g of a part in 100 g of the whole. It is a common expression seen on topical preparations and solid dosage forms.

$$\%\ \frac{\text{w}}{\text{w}} = \frac{100 \times \text{weight of particular ingredient}}{\text{weight of composition (preparation)}} \quad \ldots\ldots (6.9)$$

Example 1.7

Mycoten® cream contains 0.2 g clotrimazole in 20 g tube of cream. State the concentration in % w/w.

Solution

$$\%\frac{\text{w}}{\text{w}} = \frac{100\times\text{weight of particular ingredient}}{\text{weight of composition}}$$
$$= \frac{100\times0.2}{20}$$
= 1% w/w

Example 1.8

In the quest to ascertain that the strength of gentamycin cream in circulation in pharmacy stores are in line with standards, the regulatory agency analyzed

2 g from one of the 20 g pack brand and found it to contain 6 mg gentamycin. What is the concentration of gentamycin in the cream?

Solution

$$\%\frac{\mathbf{w}}{\mathbf{w}} = \frac{\mathbf{100 \times weight\ of\ particular\ ingredient}}{\mathbf{weight\ of\ composition}}$$

6 mg = 0.006 g

For every 2 g of the cream, 6 mg is gentamycin i.e. for the 20 g tube the gentamycin in it will be 60 mg

$$\%\frac{\mathbf{w}}{\mathbf{w}} = \frac{\mathbf{100 \times 0.006}}{\mathbf{2}}$$

= 0.3% w/w

Percentage Weight by Volume (% w/v)

This shows the amount of a given ingredient (in g) present in 100 mL volume of the composition. It is readily used in mixtures, infusions and solutions to reflect the concentration of a particular solute in the solution.

$$\%\frac{\mathbf{w}}{\mathbf{v}} = \frac{\mathbf{100\ \times\ weight\ of\ a\ particular\ ingredient\ (g)}}{\mathbf{Volume\ of\ composition\ (mL)}}$$

Example 1.9

Syrup paracetamol is presented as 125 mg/5 mL. Express this as percent weight by volume.

Solution

$$\%\frac{\mathbf{w}}{\mathbf{v}} = \frac{\mathbf{100 \times weight\ of\ ingredient(g)}}{\mathbf{Volume\ of\ composition\ (mL)}}$$

$$\%\frac{\mathbf{w}}{\mathbf{v}} = \frac{\mathbf{100 \times 0.125}}{\mathbf{5}}$$ **(since 125 mg = 0.125 g)**

= 2.5% w/v

So the syrup contains 2.5% w/v paracetamol.

Example 1.10

An extemporaneous preparation came to you for Carbamazepine 0.5% w/v to be administered 5 mL twice daily for 6 days. Assuming the protocol for your hospital is to use marketed tablets and flavored syrups for such pediatric preparation, what quantity of Carbamazepine will be in 5 mL syrup?

Solution

$$\% \frac{\mathbf{w}}{\mathbf{v}} = \frac{\mathbf{100 \times weight\ of\ ingredient\ (g)}}{\mathbf{Volume\ of\ composition\ (mL)}}$$

$$\mathbf{0.5} = \frac{\mathbf{100 \times x}}{\mathbf{5mL(volume\ to\ be\ administered)}}$$

x which is the amount of carbamazepine in 5 mL syrup is made the subject of the formula

$$x = \frac{\mathbf{5\ mL \times 0.5\ g/mL}}{\mathbf{100}}$$

= 0.025 g

= 25 mg

25 mg carbamazepine will be in every 5 mL of syrup.

Example 1.11

Every 1 mL ampoule of an artemether injection contains 80 mg artemether. An intellectually curious pharmacist decided to determine the density of the injection by simple method of using a measuring cylinder with a weighing balance and found it to be 1.28 g/mL. Attempt to express the strength of the injection in terms of % w/w and % w/v. What is the molarity of the artemether injection (Artemether is 298.37 g/mol).

Solution

Weight (mass) of artemether in 1 mL inj. = 80 mg

= 0.08 g

Weight (mass) of 1 mL inj = 1.28 g (implication of density)

$$\% \frac{\mathbf{w}}{\mathbf{w}} = \frac{\mathbf{100 \times weight\ of\ ingredient(g)}}{\mathbf{weight\ of\ composition\ (g)}}$$

$$= \frac{\mathbf{100 \times 0.08}}{\mathbf{1.28}}$$

= 6.25% w/w

$$\%\frac{w}{v} = \frac{100 \times \text{weight of ingredient}(g)}{\text{volume of composition (mL)}}$$

$$= \frac{100 \times 0.08}{1.00}$$

= 8.00% w/v

To calculate the molarity,

Number of mole of artemether $= \frac{\text{mass}}{\text{molar mass}}$

$$= \frac{0.08}{298.37}$$

= 0.000268 moles

1 mL of injection contains 0.000268 moles

Recall, Molarity is $= \frac{\text{moles of solute}}{\text{Litre of solution}}$

$= \frac{0.000268}{0.001L}$ **0.268M**

OR

1000 mL will contain 1000 x 0.000268 moles= 0.268moles

Therefore, the molarity is 0.268 M

Percentage Volume by Volume (% v/v)

This shows the amount of a given ingredient (in mL) present in 100 mL volume of the composition.

$$\%\frac{v}{v} = \frac{100 \times \text{volume of a particular ingredient (mL)}}{\text{Volume of composition (mL)}}$$

Example 1.12

What volume of eucalyptus oil is required to prepare 10,000 mL solution of eucalyptus (0.5% v/v) for inhalation to manage nasal congestion?

Solution

$$\%\frac{v}{v} = \frac{100 \times \text{volume of ingredient}}{\text{Volume of composition}}$$

$$0.5 = \frac{100 \times v}{10,000}$$

$$v = \frac{0.5 \text{ x } 10,000}{100}$$

= 50 mL

50 mL eucalyptus is required for the preparation.

Parts Per Million(ppm)

This expression describes very dilute or low concentrations of solutions. The same way percent means an amount or parts of ingredient in a hundred parts of preparation, parts per million (ppm) means number of parts of ingredient in a million parts of the preparation. Since the term part is used, the unit will depend on the unit or state of the components of the system.

Some systems are weight by weight (w/w), others are volume by volume (v/v) and yet some others are weight by volume (w/v). The weight by volume (w/v) concentrations is always defined in terms of grams and millilitres. For example, if a solution of copper sulfate is stated to be 1 ppm, the deduction will mean 1 g of copper sulfate (since it is solid) in 1,000,000 mL (1,000 L) of solution. However, if it were 1 ppm of aqueous solution of ethanol, it will be 1 mL in 1,000,000 mL of the solution. Also, 1 ppm solid dispersion becomes 1 g of a given solid in1,000,000g (1,000 Kg) of the dispersion.

Example 1.13

A Youth Corp member serving where clean portable water is a challenge decides to follow the professional advice to add sodium hypochlorite solution as 0.5 ppm to his water source before drinking. What amount of sodium hypochlorite would be in 50 L of the water?

Solution

0.5 ppm means 0.5 g in 1,000,000 mL (1,000 L) solution

1,000 L requires 0.5 g sodium hypochlorite

50 L will require $\frac{0.5 \times 50}{1000}$

= 0.025 g

25 mg of Sodium hypochlorite is present

Steps for an experiment to determine the concentration of sodium hydroxide NaOH

(1) Rinse the burette with plain water, then with distilled water two or three times, and then with a solution of hydrochloric acid (HCl).

(2) Fill the burette using a funnel with 0.1N hydrochloric acid (HCl) to the zero mark.

(3) Wash a conical flask (250ml) with plain water and then with distilled water.

(4) Wash a 10ml pipette with distilled water and then with sodium hydroxide (NaOH) solution.

(5) Draw out (10ml) of the sodium hydroxide (NaOH) solution and put it completely into the Erlenmeyer flask.

(6) Add two or three drops of phenolphthalein (ph.ph) to the solution in the conical flask (NaOH solution) to get a red-pink color.

(7) Begin the titration by gradually adding the burette hydrochloric acid (HCl) to the NaOH solution in the conical flask while constantly shaking the conical flask during the titration.

and at the end point, which is the point at which all the sodium hydroxide in the conical flask reacts with the acid according to the following reaction

NaOH + HCl——→NaCl + H2O

The evidence will become colorless. When this change in color occurs, we stop the calibration immediately.

Calculate the concentration (NaOH) of the unknown

$$(N \times V)_{acid} = (N' \times v')_{base}$$

$$(N \times V)_{HCl} = (N' \times V')_{NaOH}$$

$$N'_{NaOH} = \frac{(N \times V)HCl}{V' NaOH}$$

$$N'_{NaOH} = \frac{(0.1 \times V)HCl}{10}$$

$$N'_{NaOH} = \frac{0.1 \times VHCl}{10}$$

$$N'_{NaOH} = \text{----------}$$

Conclusion

The need for being familiar and understanding the different expressions of concentration is necessary because they are used for indicating strengths of pharmaceutical products. More importantly, for pharmacists as healthcare professionals with expertise in the handling of different medicinal products, proficiency in this area is a necessity in providing invaluable drug information to other health professionals and in making available appropriate, required, and accurate doses and regimen to achieve effective therapeutic outcome. Since concentrations of ingredients in pharmaceutical products are expressed the same way as biochemical substances in the body, it is easy for pharmacists to apply knowledge of concentration expressions to clinical practice.