

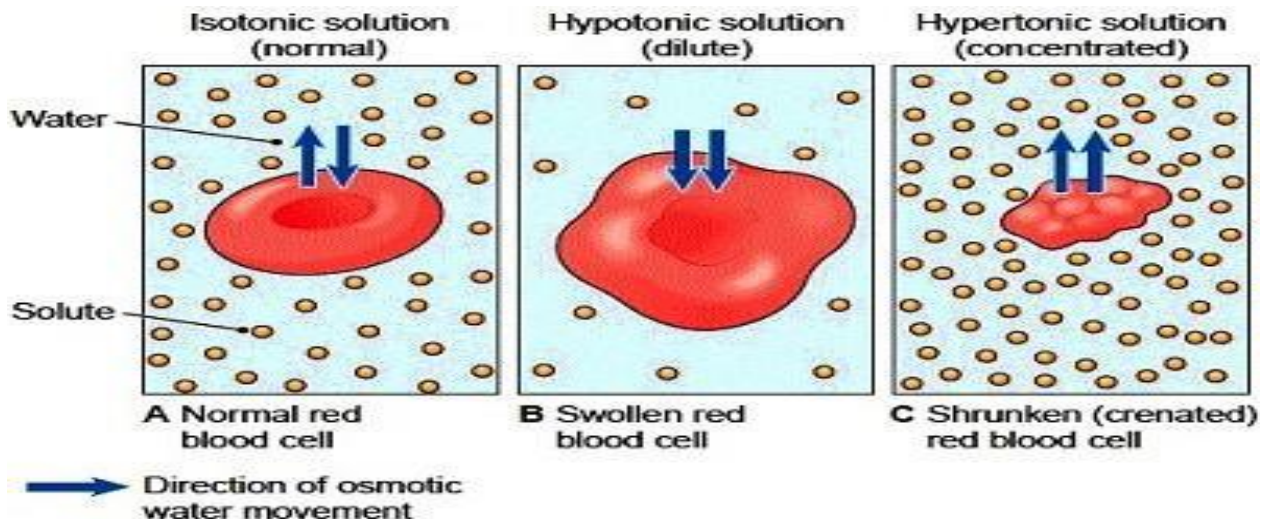
Isotonic and Buffer Solutions

It is generally accepted that for ophthalmic and parenteral administration, isotonic solutions are better tolerated by the patient than those at the extremes of hypo- and hypertonicity. Most ophthalmic preparations are formulated to be isotonic. Injections that are not isotonic should be administered slowly and in small quantities to minimize tissue irritation, pain, and cell fluid imbalance.

Definitions:

Osmosis is a phenomenon of passing of a solvent through a semipermeable membrane from a dilute solution into a more concentrated one, which makes the concentrations equalized.

- **Osmotic pressure:** The pressure responsible for passing of a solvent through a semipermeable membrane and is depend on the number of particles of solute(s) in a solution; the total number of particles of a solute in a solution is the sum of the undissociated molecules and the number of ions into which the molecules dissociated.
- **isosmotic** is a term use to describe two solutions that have the same osmotic pressure.
- **Isotonic solution:** A solution having the same osmotic pressure as a specific body fluid (meaning of equal tone with that specific body fluid).
- **Hypotonic Solution:** is a solution of lower osmotic pressure than that of a body fluid.
- **Hypertonic solutions:** the solutions having a higher osmotic pressure than that of a body fluid.

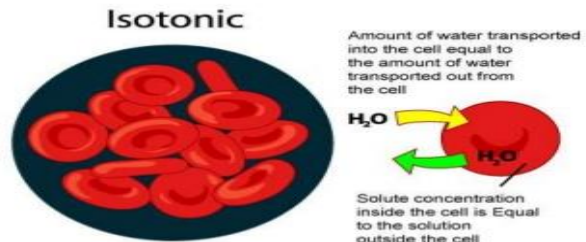


Isotonic solution

- A solution that has the same salt concentration as the normal cells of the body and the blood.

▪ Ex:

- 1- 0.9% NaCl .
- 2- Ringer Lactate .
- 3- Blood Component .
- 4- D5W.



(c) *Shrinking* is caused by water movement out of a cell in a *hypertonic* solution. Large volumes of hypertonic infusions containing dextrose, for example, can result in hyperglycemia, osmotic diuresis, and excessive loss of electrolytes.

(b) *Hemolysis* is caused by water movement into a cell in a *hypotonic* solution. Excess infusions of hypotonic fluids can result in the osmotic hemolysis of red blood cells and surpass the upper limits of the body's capacity to safely absorb excessive fluids.

• **Using of freezing points to determining tonicity of solutions:**

Like osmotic pressure, the other properties of solutions (*vapor pressure, boiling point, and freezing point*) depend on the number of particles in solution. Therefore, these properties are interrelated and a change in any one of them will result in a corresponding change in the others. Theoretically, any one of these properties may be used as a basis for determining tonicity. Practically and most conveniently, a comparison of freezing points is used for this purpose.

For nonelectrolyte:

1-The freezing point of both blood , serum and lacrimal fluid is about -0.52°C .

2- The scientist found When one gram molecular weight of any nonelectrolyte, is dissolved in 1000 g of water, the freezing point of the solution is about ($- 1.86^{\circ}\text{C}$).for example boric acid, has a molecular weight of 61.8; so one gram molecular weight is 61.8 g. thus (in theory),dissolved 61.8 g in 1000 g of water should produce a freezing point of -1.86°C .

3- Therefore: by make comparison between 1(freezing point of body fluid) and 2 (freezing point of boric acid, will find

$$\frac{-1.86^{\circ}\text{C}}{-0.52^{\circ}\text{C}} = \frac{61.8\text{ g}}{X} \quad X = 17.3\text{ g}$$

According to theory when dissolved 17.3 g of boric acid in 1000 g of water the result solution, will has the same tonicity of body fluid (blood serum and lacrimal fluid), this solution is isotonic solution.

For electrolyte:

Because the electrolyte particles dissociated into more number of particles, the osmotic pressure depend on degree of dissociation which represent by dissociated factor (*i*) If the number of ions is known, we may use the following values as dissociated factor, lacking better information :

Nonelectrolytes and substances of slight dissociation : 1.0

Substances that dissociate into 2 ions: 1.8

Substances that dissociate into 3 ions: 2.6

Substances that dissociate into 4 ions: 3.4

Substances that dissociate into 5 ions: 4.2

To calculate the weight of electrolyte required to prepare isotonic solution use following equation:

$$\frac{0.52 \times \text{molecular weight}}{1.86 \times \text{dissociation } (i)} = \text{g of solute per 1000 g of water}$$

Example: how many gram of NaCl required to prepare one liter of NaCl isotonic solution (m.w. 58.5 and *i*=1.8)?

$$\frac{-0.52^{\circ}\text{C} \times 58.5 \text{ g}}{-1.86^{\circ}\text{C} \times 1.8} = 9.09 \text{ g}$$

• **Example Calculations of the *i* Factor**

Zinc sulfate is a 2-ion electrolyte, dissociating 40% in a certain concentration. Calculate its dissociation (*i*) factor.

On the basis of 40% dissociation, 100 particles of zinc sulfate will yield:

40 zinc ions

40 sulfate ions

60 undissociated particles

=140 particles

Because 140 particles represent 1.4 times as many particles as were present before dissociation, the dissociation (*i*) factor is 1.4, answer.

- **Example Calculations of the Sodium Chloride Equivalent :**

The sodium chloride equivalent of a substance may be calculated as follows:

$$\frac{\text{Molecular weight of sodium chloride}}{i \text{ Factor of sodium chloride}} \times \frac{i \text{ factor of the substance}}{\text{Molecular weight of the substance}} = \text{Sodium chloride equivalent}$$

Papaverine hydrochloride (m.w. 376) is a 2-ion electrolyte, dissociating 80% in a given concentration. Calculate its sodium chloride equivalent.

Because papaverine hydrochloride is a 2-ion electrolyte, dissociating 80%, its *i* factor is 1.8.

$$\frac{58.5}{1.8} \times \frac{1.8}{376} = 0.156, \text{ or } 0.16, \text{ answer.}$$

- **Calculations of Tonic Agent Required**

The procedure for the *calculation of isotonic solutions with sodium chloride equivalents* may be outlined as follows:

Step 1. Multiply the amount (in grams) of each substance by its sodium chloride equivalent. The result is amount of sodium chloride represented by the ingredients in the prescription.

Step 2. Calculate the amount (in grams) of sodium chloride, alone, that would be contained in an isotonic solution of the volume specified in the prescription, namely, *the amount of sodium chloride in a 0.9% solution of the specified volume.* (Such a solution would contain 0.009 g/mL.)

Step 3. Subtract the amount of sodium chloride represented by the ingredients in the prescription (Step 1) from the amount of sodium chloride, alone, that would be represented in the specific volume of an isotonic solution (Step 2). The answer represents the amount (in grams) of sodium chloride to be added to make the solution isotonic.

Step 4. If an agent other than sodium chloride, such as boric acid, dextrose, or potassium nitrate, is to be used to make a solution isotonic, divide the amount of sodium chloride (Step 3) by the sodium chloride equivalent of the other substance.

• **Example Calculations of Tonicic Agent Required**

How many grams of sodium chloride should be used in compounding the following prescription?

Rx

Pilocarpine Nitrate		0.3 g
Sodium Chloride		q.s.
Purified Water	ad	30 mL
Make isoton. sol.		
Sig. For the eye.		

Step 1. $0.23 * 0.3 \text{ g} = 0.069 \text{ g}$ of sodium chloride represented by the pilocarpine nitrate

Step 2. $30 * 0.009 = 0.270 \text{ g}$ of sodium chloride in 30 mL of an isotonic sodium chloride solution

Step 3. 0.270 g (from Step 2)
 $- 0.069 \text{ g}$ (from Step 1)
 0.201 g of sodium chloride to be used, *answer.*

How many grams of boric acid should be used in compounding the following prescription?

Rx

Phenacaine Hydrochloride		1%
Chlorobutanol		1/2%
Boric Acid		q.s.
Purified Water	ad	60
Make isoton. sol.		
Sig. One drop in each eye.		

The prescription calls for 0.6 g of phenacaine hydrochloride and 0.3 g of chlorobutanol.

Step 1. $0.20 * 0.6 \text{ g} = 0.120 \text{ g}$ of sodium chloride represented by phenacaine hydrochloride

$0.24 * 0.3 \text{ g} = 0.072 \text{ g}$ of sodium chloride represented by chlorobutanol

Total: 0.192 g of sodium chloride represented *by both ingredients

Step 2. $60 * 0.009 = 0.540 \text{ g}$ of sodium chloride in 60 mL of an isotonic sodium chloride solution

Step 3. 0.540 g (from Step 2)
 $- 0.192 \text{ g}$ (from Step 1)
 0.348 g of sodium chloride required to make the solution isotonic

But because the prescription calls for boric acid:

Step 4. $0.348 \text{ g} / 0.52$ (sodium chloride equivalent of boric acid) = 0.669 g of boric acid to be used, *answer*

How many grams of potassium nitrate could be used to make the following prescription isotonic?

℞ Sol. Silver Nitrate 60
1:500 w/v
Make isoton. sol.
Sig. For eye use.

How many grams of sodium chloride should be used in compounding the following prescription?

℞ Ingredient X 0.5
Sodium Chloride q.s.
Purified Water ad 50
Make isoton. sol.
Sig. Eye drops.

Let us assume that ingredient X is a new substance for which no sodium chloride equivalent is to be found in Table 11.1, and that its molecular weight is 295 and its *i* factor is 2.4. The sodium chloride equivalent of ingredient X may be calculated as follows:

$$\frac{58.5}{1.8} \times \frac{2.4}{295} = 0.26, \text{ the sodium chloride equivalent for ingredient X}$$

Then,

Step 1. $0.26 \times 0.5 \text{ g} = 0.13 \text{ g}$ of sodium chloride represented by ingredient X

Step 2. $50 \times 0.009 = 0.45 \text{ g}$ of sodium chloride in 50 mL of an isotonic sodium chloride solution

Step 3. 0.45 g (from Step 2)

– 0.13 g (from Step 1)

0.32 g of sodium chloride to be used, *answer*.

CASE IN POINT 11.1³: A local ophthalmologist is treating one of his patients for a post-LASIK eye infection that is not responding to topical ciprofloxacin. These infections, although rare, can occur after laser in situ keratomileusis (LASIK) surgery for vision correction.

Topical amikacin sulfate has been shown to be effective for the treatment of eye infections due to ciprofloxacin-resistant *Pseudomonas*,⁴⁻⁵ *Burkholderia ambifaria*,⁶ *Mycobacterium chelonae*, and *Mycobacterium fortuitum*.⁷⁻⁹

The ophthalmologist prescribes 60 mL of a 2.5% amikacin sulfate isotonic solution, 2 drops in the affected eye every 2 hours.

Amikacin sulfate USP ($C_{22}H_{43}N_5O_{13} \cdot 2H_2SO_4$), m.w., 781.76, is an aminoglycoside-type antibiotic containing 3 ions.

- Determine the weight in grams of amikacin sulfate needed to prepare the solution.
- Calculate the sodium chloride equivalent (*E* value) for amikacin sulfate.
- Calculate the amount of sodium chloride needed to make the prepared solution isotonic.
- How many milliliters of 23.5 % sodium chloride injection should be used to obtain the needed sodium chloride?

- **Using an Isotonic Sodium Chloride Solution to Prepare Other Isotonic Solutions**

A 0.9% w/v sodium chloride solution may be used to compound isotonic solutions of other drug substances as follows:

Step 1. Calculate the quantity of the drug substance needed to fill the prescription or medication order.

Step 2. Use the following equation to calculate the volume of water needed to render a solution of the drug substance isotonic:

$$\frac{\text{g of drug} \times \text{drug's } E \text{ value}}{0.009} = \text{mL of water needed to make an isotonic solution of the drug}$$

(the volume of the drug substance is considered negligible)

Step 3. Add 0.9% w/v sodium chloride solution to complete the required volume of the prescription or medication order.

Ex : Using this method, determine the volume of purified water and 0.9% w/v sodium chloride solution needed to prepare 20 mL of a 1% w/v solution of hydromorphone hydrochloride (E = 0.22).

Step 1. $20 \text{ mL} \times 1\% \text{ w/v} = 0.2 \text{ g}$ hydromorphone needed

Step 2. $\frac{0.2 \text{ g} \times 0.22}{0.009} = 4.89 \text{ mL}$ purified water required to make an isotonic solution of hydromorphone hydrochloride, *answer*.

Step 3. $20 \text{ mL} - 4.89 \text{ mL} = 15.11 \text{ mL}$ 0.9% w/v sodium chloride solution required, *answer*.

Proof: $20 \text{ mL} \times 0.9\% = 0.18 \text{ g}$ sodium chloride or equivalent required

$0.2 \times 0.22 = 0.044 \text{ g}$ (sodium chloride represented by 0.2 g hydromorphone hydrochloride)

$15.11 \text{ mL} \times 0.9\% = 0.136 \text{ g}$ sodium chloride present

$0.044 \text{ g} + 0.136 \text{ g} = 0.18 \text{ g}$ sodium chloride required for isotonicity

Use of Freezing Point Data in Isotonicity Calculations

Freezing point data (ΔT_f) can be used in isotonicity calculations when the agent has a tonic effect and does not penetrate the biologic membranes in question (e.g., red blood cells). As stated previously, the freezing point of both blood and lacrimal fluid is -0.52°C . Thus, a pharmaceutical solution that has a freezing point of -0.52°C is considered isotonic.

TABLE 11.2 FREEZING POINT DATA FOR SELECT AGENTS

AGENT	FREEZING POINT DEPRESSION, 1% SOLUTIONS ($\Delta T_f^{1\%}$)
Atropine sulfate	0.07
Boric acid	0.29
Butacaine sulfate	0.12
Chloramphenicol	0.06
Chlorobutanol	0.14
Dextrose	0.09
Dibucaine hydrochloride	0.08
Ephedrine sulfate	0.13
Epinephrine bitartrate	0.10
Ethylmorphine hydrochloride	0.09
Glycerin	0.20
Homatropine hydrobromide	0.11
Lidocaine hydrochloride	0.063
Lincomycin	0.09
Morphine sulfate	0.08
Naphazoline hydrochloride	0.16
Physostigmine salicylate	0.09
Pilocarpine nitrate	0.14
Sodium bisulfite	0.36
Sodium chloride	0.58
Sulfacetamide sodium	0.14
Zinc sulfate	0.09

Freezing point depression data may be used in isotonicity calculations as shown by the following.

Example Calculations Using Freezing Point Data

How many milligrams each of sodium chloride and dibucaine hydrochloride are required to prepare 30 mL of a 1% solution of dibucaine hydrochloride isotonic with tear?

To make this solution isotonic, the freezing point must be lowered to -0.52° . From Table 11.2, it is determined that a 1% solution of dibucaine hydrochloride has a freezing point lowering of 0.08° .

Thus, sufficient sodium chloride must be added to lower the freezing point an additional 0.44° ($0.52 - 0.08$).

Also from Table 11.2, it is determined that a 1% solution of sodium chloride lowers the freezing point by 0.58° .

By proportion:

$$\frac{1\% (\text{NaCl})}{x\% (\text{NaCl})} = \frac{0.58^{\circ}}{0.44^{\circ}}$$

$$x = 0.76\% \text{ (the concentration of sodium chloride needed to lower the freezing point by } 0.44^{\circ}, \text{ required to make the solution isotonic)}$$

Thus, to make 30 mL of solution,

$$30 \text{ mL} \times 1\% = 0.3 \text{ g} = 300 \text{ mg dibucaine hydrochloride, and}$$

$$30 \text{ mL} \times 0.76\% = 0.228 \text{ g} = 228 \text{ mg sodium chloride, answers.}$$



CALCULATIONS CAPSULE

Isotonicity

To calculate the "equivalent tonic effect" to sodium chloride represented by an ingredient in a preparation, multiply its weight by its *E* value:

$$g \times E \text{ value} = g, \text{ equivalent tonic effect to sodium chloride}$$

To make a solution isotonic, calculate and ensure the quantity of sodium chloride and/or the equivalent tonic effect of all other ingredients to total 0.9% w/v in the preparation:

$$\frac{g (\text{NaCl}) + g (\text{NaCl tonic equivalents})}{\text{mL (preparation)}} \times 100 = 0.9\% \text{ w/v}$$

To make an isotonic solution from a drug substance, add sufficient water by the equation:

$$\frac{g (\text{drug substance}) \times E \text{ value (drug substance)}}{0.009} = \text{mL water}$$

This solution may then be made to any volume with isotonic sodium chloride solution to maintain its isotonicity.

The *E* value can be derived from the same equation, given the grams of drug substance and the milliliters of water required to make an isotonic solution.

Buffers and Buffer Solutions

Buffer solution: is a system, usually an aqueous solution, that possesses the property of resisting changes in pH with the addition of small amounts of a strong acid or base.

Their ability to resist changes in pH is referred to as *buffer action*; their efficiency is measured by the function known as *buffer capacity*.

Buffers are used to establish and maintain an ion activity within rather narrow limits.

In pharmacy, the most common buffer systems are used in:

- 1- the preparation of such dosage forms as injections and ophthalmic solutions, which are placed directly into pH-sensitive body fluids.
- 2- the manufacture of formulations in which the pH must be maintained at a relatively constant level to ensure maximum product stability.
- 3- pharmaceutical tests and assays requiring adjustment or maintenance of a specific pH for analytic purposes.

A buffer solution is usually composed of a weak acid and a salt of the acid, such as acetic acid and sodium acetate, or a weak base and a salt of the base, such as ammonium hydroxide and ammonium chloride. Typical buffer systems that may be used in pharmaceutical formulations include the following pairs:

"acetic acid and sodium acetate", "boric acid and sodium borate", and "disodium phosphate and sodium acid phosphate".

Derivation of The Buffer equation from dissociation constant, or K_a value equation.

K_a equation of a weak acid:

$$K_a = \frac{(H^+) (A^-)}{(HA)} \quad \text{where } \begin{array}{l} A^- = \text{salt} \\ HA = \text{acid} \end{array}$$

K_b for weak base

$$K_b = \frac{(B^+) (OH^-)}{(BOH)} \quad \text{in which } \begin{array}{l} B^+ = \text{salt} \\ \text{and } BOH = \text{base} \end{array}$$

$$pK_a = -\log K_a$$

When equation $K_a = \frac{(H^+) (A^-)}{(HA)}$ is expressed in logarithmic form, it is written:

$$pK_a = -\log (H^+) - \log \frac{\text{salt}}{\text{acid}}$$

and because $pH = -\log (H^+)$:

then
$$pK_a = pH - \log \frac{\text{salt}}{\text{acid}}$$

and
$$pH = pK_a + \log \frac{\text{salt}}{\text{acid}}$$

Buffer equation of weak acid

and the buffer equation for weak bases, which is derived from this relationship, may be expressed as:

$$pH = pK_w - pK_b + \log \frac{\text{base}}{\text{salt}}$$

pK_a Value of a Weak Acid with Known Dissociation Constant

Calculating the pK_a value of a weak acid, given its dissociation constant, K_a:

The dissociation constant of acetic acid is 1.75×10^{-5} at 25°C. Calculate its pK_a value.

and
$$\begin{aligned} K_a &= 1.75 \times 10^{-5} \\ \log K_a &= \log 1.75 + \log 10^{-5} \\ &= 0.2430 - 5 = -4.757 \text{ or } -4.76 \end{aligned}$$

Because
$$\begin{aligned} pK_a &= -\log K_a \\ pK_a &= -(-4.76) = 4.76, \text{ answer.} \end{aligned}$$

pH Value of a Salt/Acid Buffer System

Calculating the pH value:

What is the pH of a buffer solution prepared with 0.05 M sodium borate and 0.005 M boric acid? The pK_a value of boric acid is 9.24 at 25°C.

Note that the ratio of the components of the buffer solution is given in molar concentrations. Using the buffer equation for weak acids:

$$\begin{aligned} \text{pH} &= \text{pK}_a + \log \frac{\text{salt}}{\text{acid}} \\ &= 9.24 + \log \frac{0.05}{0.005} \\ &= 9.24 + \log 10 \\ &= 9.24 + 1 \\ &= 10.24, \text{ answer.} \end{aligned}$$

pH Value of a Base/Salt Buffer System

Calculating the pH value:

What is the pH of a buffer solution prepared with 0.05 M ammonia and 0.05 M ammonium chloride? The K_b value of ammonia is 1.80×10^{-5} at 25°C.

Using the buffer equation for weak bases:

$$\text{pH} = \text{pK}_w - \text{pK}_b + \log \frac{\text{base}}{\text{salt}}$$

Because the K_w value for water is 10^{-14} at 25°C, pK_w = 14.

$$\begin{aligned} \text{and} \quad K_b &= 1.80 \times 10^{-5} \\ \log K_b &= \log 1.8 + \log 10^{-5} \\ &= 0.2553 - 5 = -4.7447 \text{ or } -4.74 \\ \text{pK}_b &= -\log K_b \\ &= -(-4.74) = 4.74 \end{aligned}$$

$$\begin{aligned} \text{and} \quad \text{pH} &= 14 - 4.74 + \log \frac{0.05}{0.05} \\ &= 9.26 + \log 1 \\ &= 9.26, \text{ answer.} \end{aligned}$$

Molar Ratio of Salt/Acid for a Buffer System of Desired pH

Calculating the molar ratio of salt/acid required to prepare a buffer system with a desired pH value:

What molar ratio of salt/acid is required to prepare a sodium acetate-acetic acid buffer solution with a pH of 5.76? The pK_a value of acetic acid is 4.76 at 25°C. Using the buffer equation:

$$\begin{aligned} \text{pH} &= \text{pK}_a + \log \frac{\text{salt}}{\text{acid}} \\ \log \frac{\text{salt}}{\text{acid}} &= \text{pH} - \text{pK}_a \\ &= 5.76 - 4.76 = 1 \\ \text{antilog of } 1 &= 10 \\ \text{ratio} &= 10/1 \text{ or } 10:1, \text{ answer.} \end{aligned}$$

Quantity of Components in a Buffer Solution to Yield a Specific Volume

Calculating the amounts of the components of a buffer solution required to prepare a desired volume, given the molar ratio of the components and the total buffer concentration:

The molar ratio of sodium acetate to acetic acid in a buffer solution with a pH of 5.76 is 10:1. Assuming the total buffer concentration is 2.2×10^{-2} mol/L, how many grams of sodium acetate (m.w. 82) and how many grams of acetic acid (m.w. 60) should be used in preparing a liter of the solution?

Because the molar ratio of sodium acetate to acetic acid is 10:1,

$$\begin{aligned} \text{the mole fraction of sodium acetate} &= \frac{10}{1 + 10} \text{ or } \frac{10}{11} \\ \text{and the mole fraction of acetic acid} &= \frac{1}{1 + 10} \text{ or } \frac{1}{11} \end{aligned}$$

If the total buffer concentration = 2.2×10^{-2} mol/L,

$$\begin{aligned} \text{the concentration of sodium acetate} &= \frac{10}{11} \times (2.2 \times 10^{-2}) \\ &= 2.0 \times 10^{-2} \text{ mol/L} \\ \text{and the concentration of acetic acid} &= \frac{1}{11} \times (2.2 \times 10^{-2}) \\ &= 0.2 \times 10^{-2} \text{ mol/L} \end{aligned}$$

then 2.0×10^{-2} or $0.02 \times 82 = 1.64$ g of sodium acetate per liter of solution, and 0.2×10^{-2} or $0.002 \times 60 = 0.120$ g of acetic acid per liter of solution, answers.

The efficiency of buffer solutions—that is, their specific ability to resist changes in pH—is measured in terms of buffer capacity; the smaller the pH change with the addition of a given amount of acid or base, the greater the buffer capacity of the system.

Among other factors, the buffer capacity of a system depends on

1. the relative concentration of the buffer components
2. the ratio of the components. For example, a 0.5 M-acetate buffer at a pH of 4.76 would have a higher buffer capacity than a 0.05 M-buffer.

If a strong base such as sodium hydroxide is added to a buffer system consisting of equimolar concentrations of sodium acetate and acetic acid, the base is neutralized by the acetic acid forming more sodium acetate, and the resulting increase in pH is slight.

Actually, the addition of the base increases the concentration of sodium acetate and decreases by an equal amount the concentration of acetic acid. In a similar manner, the addition of a strong acid to a buffer system consisting of a weak base and its salt would produce only a small decrease in pH.

Change in pH with Addition of an Acid or Base

Calculating the change in pH of a buffer solution with the addition of a given amount of acid or base:

Calculate the change in pH after adding 0.04 mol of sodium hydroxide to a liter of a buffer solution containing 0.2 M concentrations of sodium acetate and acetic acid. The pK_a value of acetic acid is 4.76 at 25°C.

The pH of the buffer solution is calculated by using the buffer equation as follows:

$$\begin{aligned} \text{pH} &= \text{pK}_a + \log \frac{\text{salt}}{\text{acid}} \\ &= 4.76 + \log \frac{0.2}{0.2} \\ &= 4.76 + \log 1 \\ &= 4.76 \end{aligned}$$

The addition of 0.04 mol of sodium hydroxide converts 0.04 mol of acetic acid to 0.04 mol of sodium acetate. Consequently, the concentration of acetic acid is decreased and the concentration of sodium acetate is increased by equal amounts, according to the following equation:

$$\begin{aligned} \text{pH} &= \text{pK}_a + \log \frac{\text{salt} + \text{base}}{\text{acid} - \text{base}} \\ \text{and} \quad \text{pH} &= \text{pK}_a + \log \frac{0.2 + 0.04}{0.2 - 0.04} \\ &= \text{pK}_a + \log \frac{0.24}{0.16} \\ &= 4.76 + 0.1761 = 4.9361 \text{ or } 4.94 \end{aligned}$$

Because the pH before the addition of the sodium hydroxide was 4.76, the change in pH = 4.94 - 4.76 = 0.18 unit, answer.