Physical pharmacy lecture

Second stage

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Physical pharmacy – lecture 1

Concentration expression

October - 2021

Why We Study Physical Pharmacy?

Physical pharmacy is a fundamental course that leads to proper understanding of subsequent courses in Pharmaceutics and pharmaceutical technology.

Physical pharmacy integrates knowledge of mathematics, physics and chemistry and applies them to the pharmaceutical dosage form development.

It focus on the theories behind the phenomena needed for dosage form design

Enable the pharmacist to make rational decisions on scientific basis concerning the art and technology of solutions, suspensions, emulsions, etc.

Physical pharmacy provides the basis for understanding the chemical and physical phenomena that govern the in vivo and in vitro actions of pharmaceutical products.

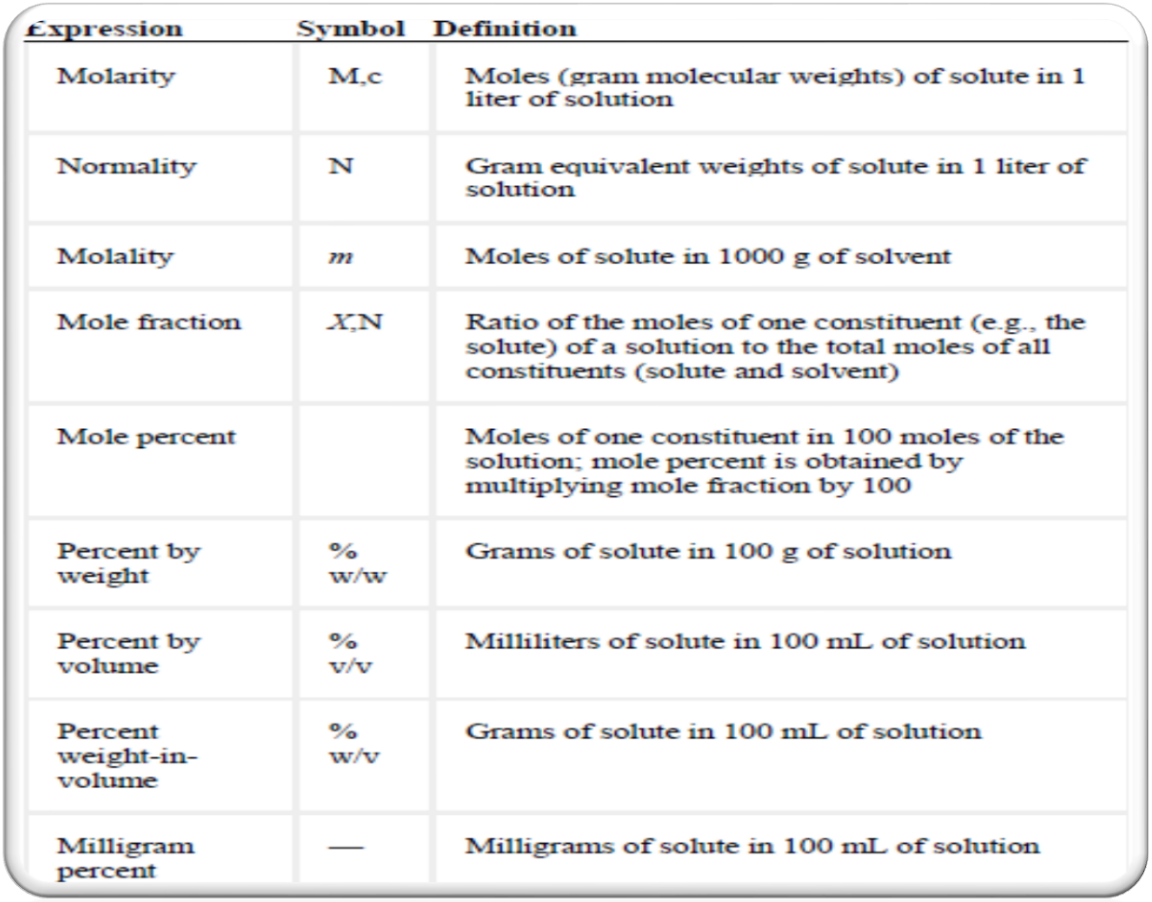
Review and definitions:

Concentration: is a quantity of solute in a definite volume of solution, or quantity of solute in a definite mass of solvent or solution.

- Molarity: M,
- Normality: N,
- Molality: m,
- Mole fraction: x,
- Mole percent x%,
- Percentage w/w%; w/v%; v/v%,

II. Concentration expressions

- Concentration of solution can be expressed in terms of the quantity of solute in a definite volume or mass of solution or the quantity of solute in a definite mass of solvent. As shown below:



Expression	Symbol	Definition
Molarity	M,c	Moles (gram molecular weights) of solute in 1 liter of solution
Normality	N	Gram equivalent weights of solute in 1 liter of solution
Molality	*m*	Moles of solute in 1000 g of solvent
Mole fraction	*X*,N	Ratio of the moles of one constituent (e.g., the solute) of a solution to the total moles of all constituents (solute and solvent)
Mole percent		Moles of one constituent in 100 moles of the solution; mole percent is obtained by multiplying mole fraction by 100
Percent by weight	% w/w	Grams of solute in 100 g of solution
Percent by volume	% v/v	Milliliters of solute in 100 mL of solution
Percent weight-in-volume	% w/v	Grams of solute in 100 mL of solution
Milligram percent	—	Milligrams of solute in 100 mL of solution

Solubility is quantitatively expressed in terms of molality, molarity, and percentage.

Disadvantages of molarity & normality:-

1. They have the disadvantages of changing value with temperature because of the expansion or contraction of liquids and should not be used when one wishes to study the properties of solution at various temperatures.

2. It is difficult to study properties of solvents such as vapour pressure & osmotic pressures which are related to the concentration of the solvent. The volume of solvent is not usually known, and it varies for different solution of the same concentration (depends on solute and solvent).

While, the Molality has not had the above disadvantages since it is prepared it terms of weight unit, hence; it is used more likely in theoretical studies. Additionally, mole fraction (X) has simple & distinct way to express the relationship between solute & solvent molecules.

Note: density or specific gravity = weight or mass / volume.

1-Molarity: **number of moles of solute in 1 liter of solution.**

$$\text{No. of moles} = \frac{\text{wt. of solute}}{\text{m. wt. of solute}}$$

$$M = \frac{\text{no. of moles/ liter}}{\text{volume of solution}}$$

$$M = \frac{\text{wt}}{\text{m. wt.}} * \frac{1000}{\text{Vml}} \qquad \text{.........(1).}$$

2-Normality: **number of equivalents of solute in 1 liter of solution.**

$$\text{No. of equivalents} = \frac{\text{wt. of solute}}{\text{eq.. wt. of solute}}$$

$$N = \frac{\text{no. of eq. / liter}}{\text{volume of solution}}$$

$$N = \frac{\text{wt.}}{\text{eq . wt.}} * \frac{1000}{\text{Vml}} \qquad \text{.........(2).}$$

Hint/ eq. wt. = $\frac{\Sigma \text{ atomic weights}}{n}$

$$N = n * M$$

3-Molality: number of moles in 1000g of solvent.

$$m = \frac{\text{no. of moles}}{\text{1000g of solvent}} \qquad \text{.......... (3)}$$

4-Mole fraction: the ratio of moles of solute to the moles of solution (summation of solute and solvent).

$$X1 = \frac{n1}{n1 + n2} \qquad \text{.... (4) Mole fraction of solute}$$

$$X2 = \frac{n2}{n1 + n2} \qquad \text{....(5) Mole fraction of solvent}$$

n1 & n2 are moles of solute and solvent respectively.

5-Mole fraction percent:

$$X1\% = \frac{n1}{n1 + n2} * 100 \qquad \text{.... (6) Mole fraction percent of solute}$$

6-Percentage:

a: w/v%: weight of solute in 100ml of solution.

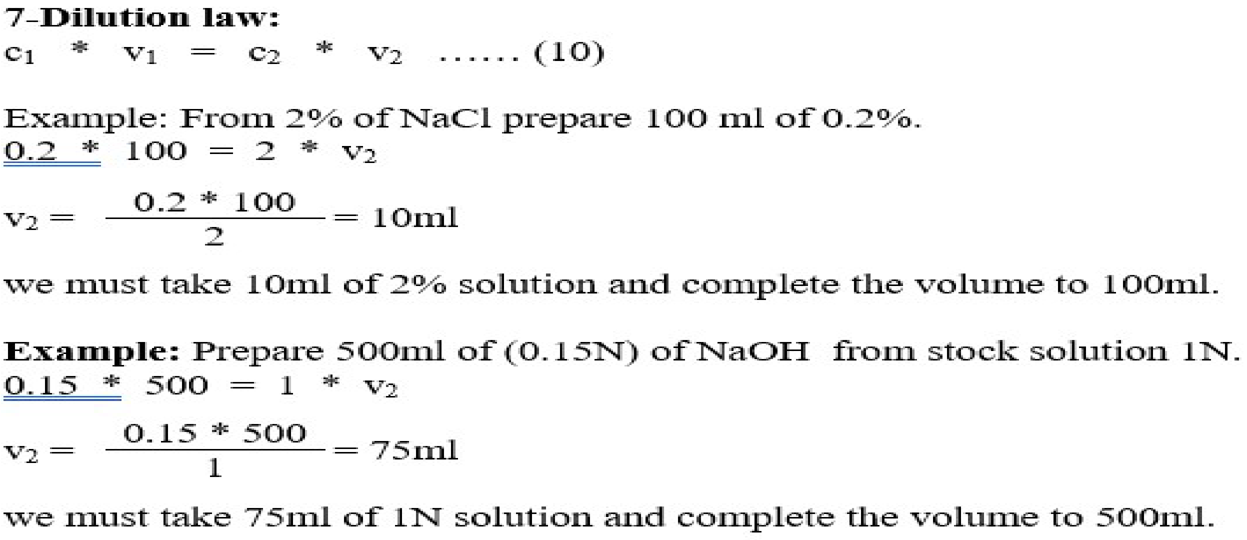
b: v/v%: volume of solvent in 100ml of solution.

c: w/w%: weight of solute in 100g of mixture.

$$w/v\% = \frac{\text{wt.}}{\text{Volume of solvent}} * 100 \qquad \text{............(7)}$$

$$w/v\% = \frac{V\,olume}{\text{Total Volume}} * 100 \qquad ....(8\ )$$

$$w/v\% = \frac{wt.}{\text{Total weight}} * 100 \qquad ....(9)$$



7-Dilution law:

$$c_1 * v_1 = c_2 * v_2 \quad ......\ (10)$$

Example: From 2% of NaCl prepare 100 ml of 0.2%.

$0.2 * 100 = 2 * v_2$

$$v_2 = \frac{0.2 * 100}{2} = 10ml$$

we must take 10ml of 2% solution and complete the volume to 100ml.

Example: Prepare 500ml of (0.15N) of NaOH from stock solution 1N.

$0.15 * 500 = 1 * v_2$

$$v_2 = \frac{0.15 * 500}{1} = 75ml$$

we must take 75ml of 1N solution and complete the volume to 500ml.

Percentage :

The term percent and its corresponding sign (%)

- mean "by the hundred" or "in a hundred,"
- May also be expressed as a ratio, represented as a common or decimal fraction.
- For example, 50% means 50 parts in 100 of the same kind, and may be expressed as 50/100 or 0.50.

For the purposes of computation, percent's are usually changed to equivalent decimal fractions.

- is made by dropping the percent sign (%) and dividing the expressed numerator by 100.
- 12.5% =12.5/100 or 0.125;
- 0.05 %= 0.05/100, or 0.0005.

Changing a decimal to a percent:

- The decimal is multiplied by 100 and the percent sign (%) is affixed.
- As a convenient means of expressing the concentration of an active or inactive material in a pharmaceutical preparation.

Percentage preparations :

- The percentage concentrations of active and inactive constituents in various types of pharmaceutical preparations are defined as follows by the United States Pharmacopeia :

Percent weight-in-volume (w/v) :

- expresses the number of grams of a constituent in 100 mL of solution or liquid preparation,
- is used regardless of whether water or another liquid is the solvent or vehicle. l Expressed as: ____% w/v

Percentage preparations:

Percent volume-in-volume (v/v)

- Expresses the number of milliliters of a constituent in 100 mL of solution or liquid preparation Expressed as: ____% v/v.
- Percent weight-in-weight (w/w)
- Expresses the number of grams of a constituent in 100 g of solution or preparation.
- Expressed as: ___% w/w.

The term percent, or symbol, %, when used without qualification means:

- for solutions or suspensions of solids in liquids, percent weight-in-volume;
- for solutions of liquids in liquids, percent volume-in volume;
- For mixtures of solids or semisolids, percent weight in-weight ;
- for solutions of gases in liquids, percent weight-in volume.

Special Considerations in Percentage Calculations

- In general, the nature of the ingredients in a pharmaceutical preparation determines the basis of the calculation.
- A powdered substance dissolved or suspended in a liquid vehicle would generally be calculated on a weight-in-volume basis;
- A powdered substance mixed with a solid or semisolid, such as an ointment base, would generally be calculated on a weight In weight basis.
- A liquid component in a liquid preparation would be calculated on a volume-in-volume basis.

Specific gravity is a factor in a number of calculations involving percentage concentration.

- Many formulations are presented on the basis of weight, even though some of the ingredients are liquids.
- It may be necessary to convert weight to liquid or, in some instances, vice versa.
- Thus, the student should recall the equations from the previous chapter, namely:

$$g = mL \times sp\ gr$$

$$mL = \frac{g}{sp\ gr}$$

In a **true expression of percentage** (i.e., parts per one hundred parts),

- the percentage of a liquid preparation (e.g., **solution**, **suspension, lotion**, etc.) would represent the grams of solute or constituent in 100 g of the liquid preparation.

- a different definition of percentage for solutions and for other liquid preparations:
- Represent grams of a solute or constituent in **100 mL** of solution or liquid preparation.
- the "correct" strength of a **1% (w/v)** solution or other liquid preparation is defined as containing 1 g of constituent in 100 mL of product

Percentage weight-in-volume :

- This variance to the definition of true percentage is based on an assumption that the solution/liquid preparation has a specific gravity of 1, as if it were water.
- each 100 mL of solution/liquid preparation is presumed to weigh 100 g and thus is used as the basis

for calculating percentage weight-in-volume (e.g., 1%
w/v = 1% of [100 mL taken to be] 100 g = 1 g in 100 mL).

Weight of Active Ingredient in a Specific Volume, Given its Percentage Weight-in- Volume

- Taking **water** to represent any solvent or vehicle, we may prepare weight-in- volume percentage solutions or liquid preparations by the metric system if we use the following rule.
- Multiply the required number of milliliters by the percentage strength, expressed as a decimal, to obtain the number of grams of solute or constituent in the solution or liquid preparation.

Volume (mL) X % (expressed as a decimal) = g of solute or constituent

Example 1: How many grams of dextrose are required to prepare 4000 mL of a 5% solution?

Solution:
4000 mL represent 4000 g of solution 5% = 0.05

4000 g X 0.05 = 200 g, answer.

Or, solving by dimensional analysis:

5 g/100 mL X 4000 mL = 200 g, answer.

Example 2: How many grams of potassium permanganate should be used in compounding the following prescription?

Solution:

Potassium Permanganate 0.02%
Purified Water ad 250.0 mL
Sig. As directed.

250 mL represent 250 g of solution
0.02% = 0.0002
250 g X 0.0002 = 0.05 g, answer.

Example 3: How many grams of aminobenzoic acid should be used in preparing 8 fluidounces of a 5% solution in 70% alcohol?

Solution:

8 fl. oz. = 8 X 29.57 mL = 236.56 mL
236.56 mL represents 236.56 g of solution
5 %= 0.05
236.56 g X 0.05 = 11.83 g, answer.

Percentage Weight-in-Volume of Solution, Given Weight of Solute or Constituent and Volume of Solution or Liquid Preparation

Example 4: What is the percentage strength (w/v) of a solution of urea, if 80 mL contain 12 g?

Solution :

80 mL of water weigh 80 g

$$x = \frac{12(g)}{80(g)} \times 100\%$$

$$x = 15\%, answer.$$

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Volume of Solution or Liquid Preparation, Given Percentage Strength Weight-in-Volume and Weight of Solute

Example 5: How many milliliters of a 3% solution can be made from 27 g of ephedrine sulfate?

Solution:

$$\frac{x(g)}{27(g)} = 3\%$$

x = 900 g, weight of the solution if it were water Volume (in mL) = 900 mL, answer.

Percentage volume-in-volume

- Liquids are usually measured by volume,
- The percentage strength indicates the number of parts by volume of the active ingredient contained in the total volume of the solution or liquid preparation considered as 100 parts by volume.
- If there is any possibility of misinterpretation, this kind of percentage should be specified: e.g., 10 %(v/v).

Volume of Active Ingredient in a Specific Volume, Given Percentage Strength Volume-in-Volume.

Example 6: How many milliliters of liquefied phenol should be used in compounding the following prescription? Liquefied Phenol 2.5% Calamine Lotion ad 240.0 mL Sig. For external use.

Solution :

Volume (mL) X % (expressed as a decimal) = milliliters of active ingredient

240 mL X 0.025= 6 mL, answer.

Or, solving by dimensional analysis

(2.5 mL/ 100 mL)X 240 mL = 6 mL, answer.

Percentage Volume-in-Volume of Solution or Liquid Preparation, Given Volume of Active Ingredient and Volume of Solution

- the required volumes may have to be calculated from given weights and specific gravities.

Example 7: In preparing 250 mL of a certain lotion, a pharmacist used 4 mL of liquefied phenol. What was the percentage (v/v) of liquefied phenol in the lotion?

Solution:

$$x = \frac{4(mL)}{250(mL)} \times 100\%$$

$$x = 1.6\%, answer.$$

PERCENTAGE WEIGHT-IN-WEIGHT :

- true percentage or percentage by weight
- indicates the number of parts by weight of active ingredient contained in the total weight of the solution or mixture considered as **100 parts** by weight.
- Liquids are not customarily measured by weight. Therefore, a weight-in-weight solution or liquid preparation of a solid or a liquid in a liquid should be so designated: e.g., 70% (w/w).

Weight of Active Ingredient in a Specific Weight of Solution or Liquid Preparation, Given its Weight in Weight Percentage Strength.

Example 8: How many grams of phenol should be used to prepare 240 g of a 0.5% (w/w) solution in water?

Solution: Weight of solution (g) X % (expressed as a decimal) = g of solute
240 g X 0.05 = 12 g, answer.

Weight of Active Ingredient in a Specific Weight of Solution or Liquid Preparation, Given its Weight in- Weight Percentage Strength.

Example 9: How many grams of a drug substance are required to make 120 mL of a 20% (w/w) solution having a specific gravity of 1.15?

Solution:
120 mL of water weigh 120 g
120 g X 1.15 = 138 g, weight of 120 mL of solution
138 g X 0.20 = 27.6 g plus enough water to make 120 mL, answer.
Or,
solving by dimensional analysis:

$$120\,mL \times \frac{1.15\,g}{1\,mL} \times \frac{20\%}{100\%} = 27.6\,g, \textit{answer.}$$

Weight of Either Active Ingredient or Diluent, Given Weight of the Other and Percentage Strength (w/w) of Solution.

- The weights of active ingredient and diluent are Proportional to their percentages.

Example 10: How many grams of a drug substance should be added to 240 mL of water to make a 4 % (w/w) solution?

Solution: 100%- 4% = 96% (by weight) of water 240 mL of water weigh 240 g

$$\frac{96(\%)}{4(\%)}=\frac{240(g)}{x(g)},\ x=10\ g, answer.$$

Example 11: How should you prepare 100 mL of a 2 % (w/w) solution of a drug substance in a solvent having a specific gravity of 1.25?

Solution :

100 mL of water weigh 100 g
100 g X 1.25 = 125 g, weight of 100 mL of solvent
100% - 2% = 98% (by weight) of solvent

$$\frac{98(\%)}{2(\%)}=\frac{125(g)}{x(g)},\ x=2.55\ g.$$

Therefore, dissolve 2.55 g of drug substance in 125 g (or 100 mL) of solvent, answer.

Calculating Percentage Strength Weight-in- Weight

- If the weight of the finished solution or liquid preparation is not given when calculating its percentage strength, other data must be supplied from which it may be calculated:
- the weights of both ingredients,
- the volume and specific gravity of the solution or liquid preparation.

Examples 12: If 1,500 g of a solution contain 75 g of a drug substance, what is the percentage strength (w/w) of the solution?

$$\frac{1500(g)}{75(g)}=\frac{100(\%)}{x(\%)},\quad x=5\%, answer.$$

Weight-in-Weight Calculating in Compounding:

Example 13: What weight of a 5% (w/w) solution can be prepared from 2 g of active ingredient?

Solution:

$$\frac{2(g)}{x(g)} = 5\%, \quad x = 40\ g, \ answer.$$

Weight-in-Weight Mixtures of Solids and Semisolids:

- Solids and semisolids are usually measured by weight,
- The percentage strength of a mixture of solids indicates the number of parts by weight of the active ingredient contained in the total weight of the mixture considered as 100 parts by weight.

Amount of Active Ingredient in a Specified Weight of a Solid/Semisolid Mixture, Given its Percentage Strength (w/w).

Example14: How many milligrams of hydrocortisone should be used in compounding the following prescription?

Solution:

Hydrocortisone	1/8%
Hydrophilic Ointment ad	10 g

Sig. Apply.
1/8% = 0.125%
10 g X 0.00125 = 0.0125 g or 12.5 mg, answer.

Ratio strength

- The concentration of weak solutions or liquid preparations is frequently expressed in terms of ratio strength.
- Ratio strength is merely another way of expressing the percentage strength of solutions or liquid preparations (and, less frequently, of mixtures of solids).

- For example, 5% means 5 parts per 100 or 5:100.
- Although 5 parts per 100 designates a ratio strength, it is customary to translate this designation into a ratio, the first figure of which is 1; thus, 5:100 = 1: 20.

1/1000, used to designate a concentration, is to be interpreted as follows:

- For solids in liquids = 1 g of solute or constituent in 1000 mL of solution or liquid preparation.
- For liquids in liquids = 1 mL of constituent in 1000 mL of solution or liquid preparation.
- For solids in solids = 1 g of constituent in 1000 g of mixture.
- The ratio and percentage strengths of any solution or mixture of solids are proportional, and either is easily converted to the other by the use of proportion

Ratio Strength Given Percentage Strength.

Example 15: Express 0.02% as ratio strength.

$$\frac{0.02(\%)}{100(\%)} = \frac{1(part)}{x(parts)}, \quad x = 5000$$

$$Ratio\ strength = 1:5000, answer.$$

Percentage Strength Given Ratio Strength.

Example16: Express 1: 4000 as percentage strength.

$$\frac{100(\%)}{x(\%)} = \frac{4000(parts)}{1(part)}, \quad x = 0.025\%, answer.$$

Ratio Strength of Solution or Liquid Preparation, Given Weight of Solute in a Specified Volume.

Example17: A certain injectable contains 2 mg of a drug per milliliter of solution. What is the ratio strength (w/v) of the solution?

Solution:

2 mg = 0.002 g

$$\frac{0.002(g)}{1(g)} = \frac{1(mL)}{x(mL)}, \quad x = 500\,mL$$

Ratio strength=1:500, answer.

Example18 : What is the ratio strength (w/v) of a solution made by dissolving five tablets, each containing 2.25 g of sodium chloride, in enough water to make 1800 mL?

Solution:

2.25 g X 5 = 11.25 g of sodium chloride

$$\frac{11.25(g)}{1(g)} = \frac{1800(mL)}{x(mL)}, \quad x = 160\,mL$$

Ratio strength = 1 : 160, answer.

Problems Involving Ratio Strength.

- translate the problem into one based on percentage strength
- solve it according to the rules and methods discussed under percentage preparations.

Example19: How many grams of potassium permanganate should be used in preparing 500 mL of a 1:2500 solution?

Solution:

1:2500 = 0.04%
500 (g) X 0.0004 = 0.2 g, answer.
Or,
1:2500 means 1 g in 2500 mL of solution

$$\frac{2500(mL)}{500(mL)} = \frac{1(g)}{x(g)}, \quad x = 0.2\,g, answer.$$

Example20: How many milligrams of gentian violet should be used in preparing the following solution?

Solution:

Gentian Violet Solution 500 mL
1:10,000
Sig. Instill as directed.
1:10,000 = 0.01%
500 (g) X 0.0001 = 0.050 g or 50 mg, answer.

Or,

1:10,000 means 1 g of 10,000 mL of solution

$$\frac{10,000(mL)}{500(mL)} = \frac{1(g)}{x(g)}, \quad x = 0.050\,g, or\ 50\,mg, answer.$$

Simple conversions of concentration to "mg/ml"

- In patient care settings, need to convert rapidly product concentrations expressed as percentage strength, ratio strength, or as grams per liter (as in IV infusions) to milligrams per milliliter (mg/mL).

To convert product strengths expressed as grams per milliliter (g/mL) to mg/mL

- convert the numerator to milligrams
- divide by the number of milliliters in the denominator.

Example21: Convert a product concentration of 1 g per 250 mL to mg/mL .

1 g=1000 mg

1000 ÷ 250= 4 mg/mL, answer.

- Proof or alternate method:

1 g/250 mL = 1000 mg/250 mL

= 4 mg/mL

Milligrams percent (mg%)

- Expresses the number of milligrams of substance in 100 mL of liquid.
- is used frequently to denote the concentration of a drug or natural substance in a biologic fluid, as in the blood.
- The concentration of no protein nitrogen in the blood is 30 mg% means that each 100 mL of blood contains 30 mg of no protein nitrogen.
- As noted in the following section, "Expressing

Clinical Laboratory Test Values," quantities of substances present in biologic fluids also commonly are stated in terms of milligrams per deciliter (mg/dL) of fluid.

Parts per million (ppm) and parts per billion (ppb)

- The strengths of very dilute solutions are commonly expressed in terms of parts per million (ppm) or parts per billion (ppb),
- i.e., the number of parts of the agent per 1 million or 1 billion parts of the whole.
- Fluoridated drinking water, used to reduce dental caries, often contains 1 part of fluoride per million parts of drinking water (1:1,000,000).

Parts per million (ppm) and parts per billion (ppb)

- may be used to describe the quantities of trace impurities in chemical samples and trace elements in biologic samples.
- Depending on the physical forms of the trace substituent and the final product, a concentration expressed in ppm or ppb could, in theory, be calculated on a weight-in-volume, volume-in-volume, or weight-in weight basis.
- For all practical purposes, the unit-terms of the solute and solution are generally considered like units (i.e., the same type of "parts").

Equivalent Values of Percent Strength, Ratio Strength, and Parts per Million or Parts per Billion.

Example22: Express 5 ppm of iron in water in percent strength and ratio strength.

Solution:

5 ppm = 5 parts in 1,000,000 parts
= 1:200,000, ratio strength,
= 0.0005%, percent strength, answers.

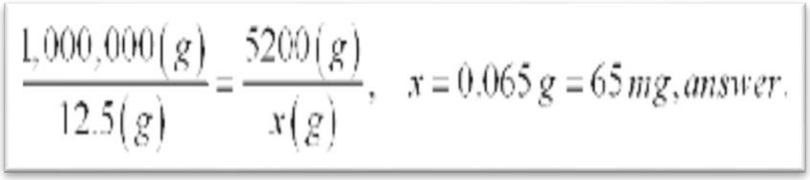
Using Parts per Million or Parts per Billion in Calculations.

Example23: The concentration of a drug additive in an animal feed is 12.5 ppm. How many milligrams of the drug should be used in preparing 5.2 kg of feed?

Solution:

12.5 ppm = 12.5 g (drug) in 1,000,000 g (feed)

Thus,



$$\frac{1{,}000{,}000(g)}{12.5(g)} = \frac{5200(g)}{x(g)}, \quad x = 0.065\,g = 65\,mg, answer.$$

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Percentage volume-in-volume

- Liquids are usually measured by volume,
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- If there is any possibility of misinterpretation, this kind of percentage should be specified: e.g., 10 %(v/v).

Volume of Active Ingredient in a Specific Volume, Given Percentage Strength Volume-in-Volume.

Example 5: How many milliliters of liquefied phenol should be used in compounding the following prescription? Liquefied Phenol 2.5%
Calamine Lotion ad 240.0 mL Sig. For external use.

Solution :

Volume (mL) X % (expressed as a decimal) = milliliters of active ingredient

240 mL X 0.025= 6 mL, answer.
Or, solving by dimensional analysis
(2.5 mL/ 100 mL)X 240 mL = 6 mL, answer.

Percentage Volume-in-Volume of Solution or Liquid Preparation, Given Volume of Active
Ingredient and Volume of Solution

- the required volumes may have to be calculated from given weights and specific gravities.

By ratio- proportion: 2.5% means 2.5 ml of active ingredient in 100 ml of solution. The solution of 240 ml must be in the same proportion .:

2.5 / 100 = X/240
X= 6 ml, answer.

Solve by Dimensional Analysis.

Example 6: In preparing 250 mL of a certain lotion, a pharmacist used 4 mL of liquefied phenol. What was the percentage (v/v) of liquefied phenol in the lotion?

Solution:

$$x = \frac{4(mL)}{250(mL)} \times 100\%$$

$$x = 1.6\%, answer.$$

PERCENTAGE WEIGHT-IN-WEIGHT :

- true percentage or percentage by weight
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- Liquids are not customarily measured by weight. Therefore, a weight-in-weight solution or liquid preparation of a solid or a liquid in a liquid should be so designated: e.g., 70% (w/w).

Example 7: How many grams of phenol should be used to prepare 240 g of a 0.5% (w/w) solution in water?

Solution: Weight of solution (g) X % (expressed as a decimal) = g of solute
240 g X 0.05 = 12 g, answer.

Weight of Active Ingredient in a Specific Weight of Solution or Liquid Preparation, Given its Weight in- Weight Percentage Strength.

Example 8: How many grams of a drug substance are required to make 120 mL of a 20% (w/w) solution having a specific gravity of 1.15?

Solution:

120 mL of water weigh 120
120 g X 1.15 = 138 g, weight of 120 mL of solution
138 g X 0.20 = 27.6 g plus enough water to make 120 mL, answer.

Or,

solving by dimensional analysis:

$$120\,mL \times \frac{1.15\,g}{1\,mL} \times \frac{20\%}{100\%} = 27.6\,g, answer.$$

Weight of Either Active Ingredient or Diluent, Given Weight of the Other and Percentage Strength (w/w) of Solution.

- The weights of active ingredient and diluent are Proportional to their percentages.

Example 9: How many grams of a drug substance should be added to 240 mL of water to make a 4 % (w/w) solution?

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$$\frac{96(\%)}{4(\%)} = \frac{240(g)}{x(g)}, x = 10\,g, answer.$$

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Solution :

100 mL of water weigh 100 g
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$$\frac{98(\%)}{2(\%)} = \frac{125(g)}{x(g)},\ x = 2.55\,g.$$

Therefore, dissolve 2.55 g of drug substance in 125 g (or 100 mL) of solvent, answer.
Calculating Percentage Strength Weight-in- Weight

- If the weight of the finished solution or liquid preparation is not given when calculating its percentage strength, other data must be supplied from which it may be calculated:
- the weights of both ingredients,
- the volume and specific gravity of the solution or liquid preparation.

Examples 11: If 1,500 g of a solution contain 75 g of a drug substance, what is the percentage strength (w/w) of the solution?

$$\frac{1500(g)}{75(g)} = \frac{100(\%)}{x(\%)},\quad x = 5\%,\ answer.$$

Weight-in-Weight Calculating in Compounding:

Example 12: What weight of a 5% (w/w) solution can be prepared from 2 g of active ingredient?

Solution:

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Percentage Strength Given Ratio Strength.

Example14: Express 1: 4000 as percentage strength.

$$\frac{100(\%)}{x(\%)}=\frac{4000(parts)}{1(part)},\quad x=0.025\%, answer.$$

Ratio Strength of Solution or Liquid Preparation, Given Weight of Solute in a Specified Volume.

7

Example15: A certain injectable contains 2 mg of a drug per milliliter of solution. What is the ratio strength (w/v) of the solution?

Solution:

2 mg = 0.002 g

$$\frac{0.002(g)}{1(g)}=\frac{1(mL)}{x(mL)},\quad x=500\ mL$$

Ratio strength=1:500, answer.

Example16 : What is the ratio strength (w/v) of a solution made by dissolving five tablets, each containing 2.25 g of sodium chloride, in enough water to make 1800 mL?

Solution:

2.25 g X 5 = 11.25 g of sodium chloride

$$\frac{11.25(g)}{1(g)} = \frac{1800(mL)}{x(mL)}, \quad x = 160\,mL$$

Ratio strength = 1 : 160, *answer.*

Problems Involving Ratio Strength.

- translate the problem into one based on percentage strength
- solve it according to the rules and methods discussed under percentage preparations.

Example17: How many grams of potassium permanganate should be used in preparing 500 mL of a 1:2500 solution?

Solution:
1:2500 = 0.04%
500 (g) X 0.0004 = 0.2 g, answer.
Or,
1:2500 means 1 g in 2500 mL of solution

$$\frac{2500(mL)}{500(mL)}=\frac{1(g)}{x(g)}, \quad x=0.2\,g, answer.$$

H .W:

Q1: Convert the following:

1- 72% =72 /100 =

2- 0.35 = 35% = /100 = 7/

3- 0.182 = %.

Q2: What is 5% expressed as a ratio strength, Transpose for X and Solve?

Q3: What is 1 part in 500 expressed as a percentage, Transpose for X and Solve?

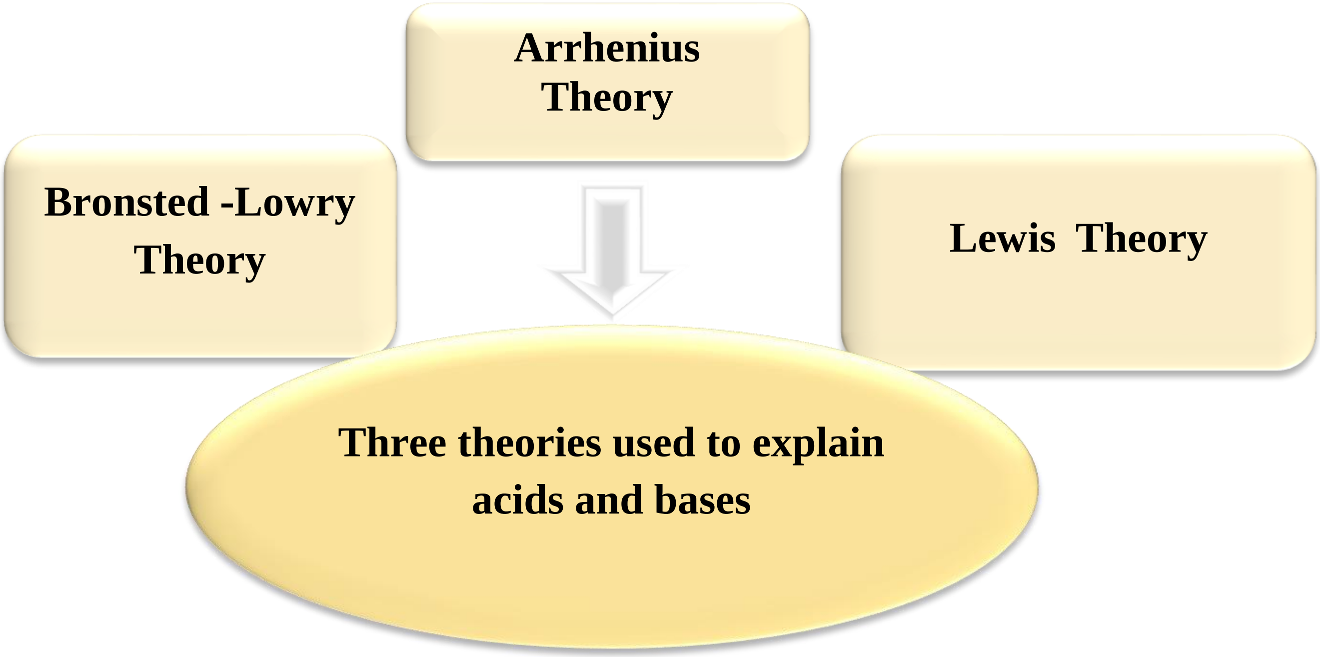
Q4: What is 1 mg / 5 ml expressed as a percentage, Transpose for X and solve?

Physical pharmacy – lecture 4

Concentration expression

October - 2021

Theory of Acids and bases :



Arrhenius Theory

Bronsted -Lowry Theory

Lewis Theory

Three theories used to explain acids and bases

ARRHENIUS THEORY for ACIDS and BASES

- Acid
- Dissociates in water to produce hydrogen ions (H+)

Arrhenius acid: is a substance that increases the concentration of the hydronium ion, H_3O^+ , when dissolved in water .

- $\mathbf{HCl \longrightarrow H_3O^+ + Cl^-}$

- **Base**
- Dissociates in water to produce hydroxide ions, (OH-)

<u>Arrhenius base :</u> is a substance that dissociates into hydroxide ions OH and cations in solution

- NaOH $\longrightarrow$ **Na^+ + OH^-**

Examples:

- **$HNO_3(aq) \longrightarrow H+ \ (aq) + NO_3^- \ (aq)$**
- **$NaOH\ (aq) \longrightarrow Na^+\ (aq) + OH^-\ (aq)$**

The limitations of Arrhenius theory

- Restricted to aqueous solution
- Does not account for the basicity of substances, especially ammonia

<u>Problems with Arrhenius Theory</u>

- **H_3O^+** Hydronium ion rather than **H^+**
- **$OH(H_2O)_3^-$** presents in solution, not **OH^-**
- Other substances also have acidic or basic properties

<u>BrØnsted –Lowry Theory</u>

- **Acid :** Is a proton donor (a substance that can transfer H+)

A Brønsted Lowry acid (or simply Brønsted acid): is specie that <u>Donates a protons</u>

$$HA \longrightarrow H^+ + A^-$$

- **Base :** Is a proton acceptor

So, an acid-base reaction is a proton-transfer reaction

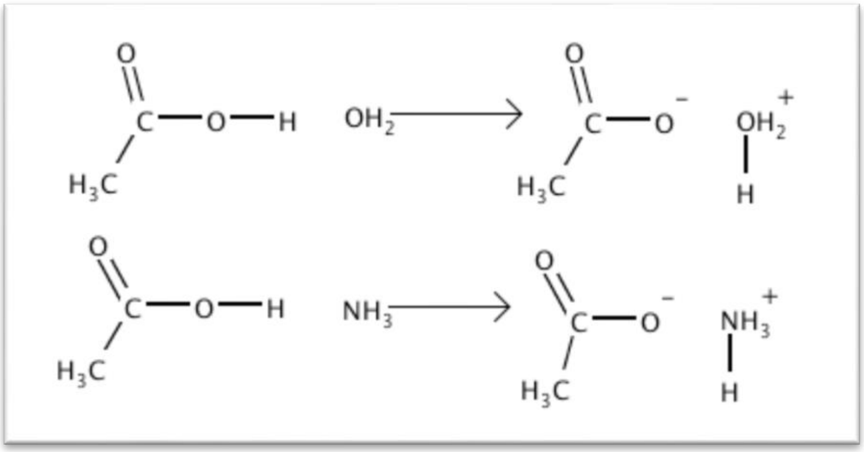
Brønsted Lowry base: is the substance that can accept a proton.

$$B + H^+ \longrightarrow BH^+$$

- The theory can explain the acidity and basicity of weak acid and base. This compound partially dissociates in water. Thus, the symbol ($\longleftrightarrow$) is used to show that the reaction is reversible. When a BrØnsted –Lowry acid is

Placed in water, it donates a proton to the solvent. Hence water act as Brønsted –Lowry base.

Brønsted Lowry acid - base theory has several advantages over Arrhenius Theory: ex acetic acids



- CH_3COOH acts as an Arrhenius acid because it acts as a source of H_3O when Dissolved in water, and it acts as a Brønsted acid by donating a proton to water.

- In the second example CH_3COOH undergoes the same transformation, in this case donating a proton to ammonia (NH_3), but cannot be described using the Arrhenius definition of an acid because the reaction does not produce hydronium

$$HA + H_2O \longleftrightarrow H_3O^+ + A^-$$

HA	H_2O	H_3O^+	A^-
H^+ donor Acid	H^+ acceptor BASE	H^+ donor Conjugate Base	H^+ acceptor Conjugate Acid

- In the reverse reaction, the **hydroxide ion** acts as a proton acceptor (base), and the NH_4^+ ion act as a proton donor (acid).

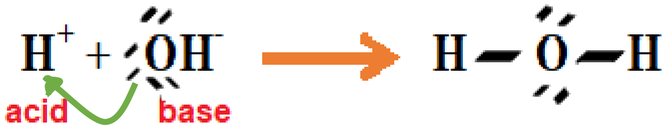
- Substances such as water, ions such as hydrogen sulphate ion are both Bronsted Lowry acids and bases. They are known as **ampholytes** and show **amphiprotic** behaviour

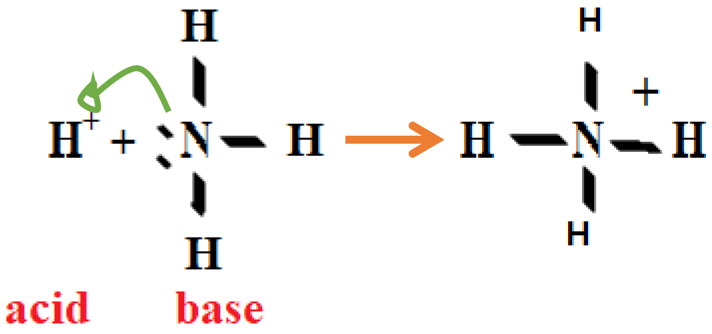
$$HSO_4^- + H_2O \longleftrightarrow H_3O^+ + SO_4^{-2}$$

$$HSO_4^- + H_2O \longleftrightarrow OH^- + H_2SO_4$$

Lewis Theory

- Lewis defined an acid as an electron pair acceptor and a base as an electron pair donor





Example: of reaction between ammonia, NH3and boron trifluoride, BF3

$$BF_3 + \ :NH_3 \longrightarrow F_3B:NH_3$$

Relative Strength of Bronsted–Lowry Acids and Bases

- **Degree of Dissociation**

A strong acid will have a higher tendency to dissociate to form the hydroxonium ion as compared to a weaker acid. Hence the higher the degree of dissociation of acids, the stronger the acid.

- **The acids in order of increasing strength is:**

$$CH_3COOH < HNO_2 < HSO_4^- < HCl$$

The strength of bases depends on their ability to form the OH-ions in aqueous solution. Strong bases will have a higher ‘degree of dissociation’ than weak bases

- **The bases in order of increasing strength is:**

$$NO_2^- < CH_3COO^- < NH_3$$

Physical pharmacy – lecture 5

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Weak Interactions in Aqueous Systems Hydrogen Bonding Gives Water Its Unusual Properties:

Water has a higher

- melting point (0°C)
- boiling point (100°C)
- Heat of vaporization (2,260 J/g) than most other common solvents.

Structure of the water shows dipolar nature.

- the two H atoms have localized partial positive charges (δ^+)
- The O atom has a partial negative charge (δ^-) **(Fig. 5-1a)**.

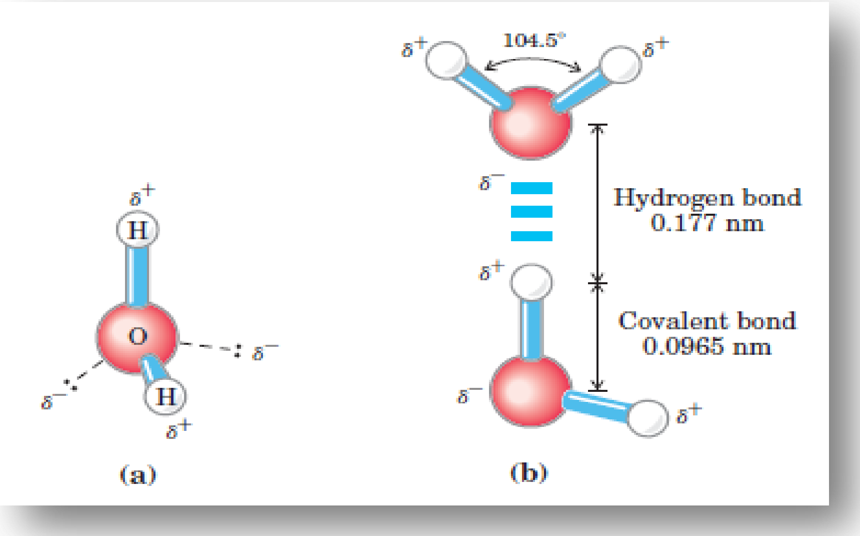


FIGURE 5-1 Structure of the water molecule.

- There is an electrostatic attraction between the O atom of one water molecule and the H of another, called a **hydrogen bond (Fig. 5-1b)**.
  - two H_2O molecules are joined by a hydrogen bond.
  - H bonds are longer and weaker than covalent O-H bonds.
- Hydrogen bonds between water molecules provide the cohesive forces that make water a liquid at room temperature and a crystalline solid (ice) with a highly ordered arrangement of molecules at cold temperatures.
- Hydrogen bonds are formed between an electronegative atom (the hydrogen acceptor, usually oxygen or nitrogen) and a hydrogen atom covalently bonded to another electronegative atom (the hydrogen donor) in the same or another molecule **(Fig. 5-2).**

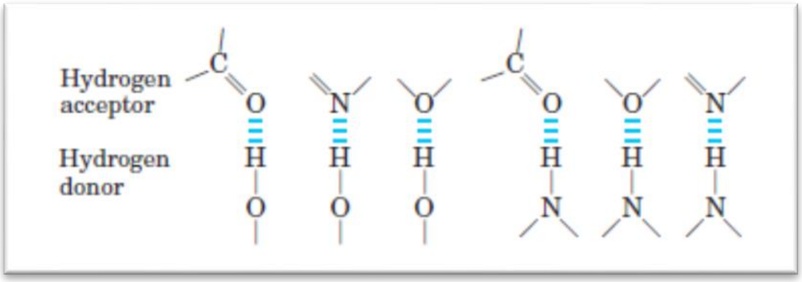


FIGURE 5-2 Common hydrogen bonds in biological systems.

- Polar biomolecules dissolve readily in water forming hydrogen bonds
  - because they can replace water-water interactions with more energetically favorable water-solute interactions.
- Some biologically important hydrogen bonds (**Fig. 5-3)**.

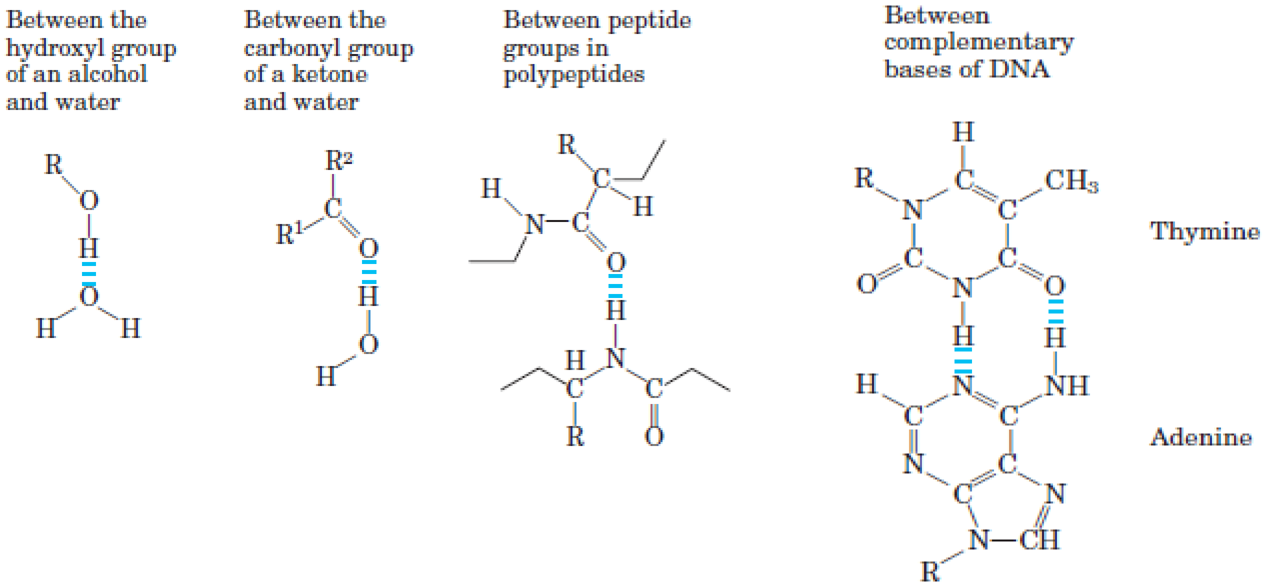


FIGURE 5-3 Some biologically important hydrogen bonds.

Amphoterism : is an ion or molecule can act as an acid or base depending upon the reaction conditions

- **Water in NH_3 serves as an acid**

$$\underset{\text{Acid}}{H_2O} + \underset{\text{Base}}{NH_3} \rightleftharpoons \underset{\text{Acid}}{NH_4^+} + \underset{\text{Base}}{OH^-}$$

- **Water in acetic acid serves as a base**

$$\underset{\text{Base}}{H_2O} + \underset{\text{Acid}}{CH_3CO_2H} \rightleftharpoons \underset{\text{Acid}}{H_3O^+} + \underset{\text{Base}}{CH_3CO_2^-}$$

Conjugate acid Of H_2O

Conjugate base of acetic acid

Acid/base properties of water

- A substance is said to be amphoteric , if it can behave as an acid or as a base. Water is the most common amphoteric substance.

- The equilibrium expression of water is given as:

$$\mathbf{K_w = [H^+][OH^-] = 1.0 \times 10^{-14} \text{ at } 25°C}$$

- Where K w is called the ion product constant (or the dissociation constant for water) which refers to the autoionization of water.
- (Don t forget that K w is temp. dependent)

At 0 ° C , $K_w = 0.114 \times 10^{-14}$
at 50 ° C, $K_w = 5.47 \times 10^{-14}$
At 100 ° C, $K_w = 49 \times 10^{-14}$

Example 1: Calculate the hydrogen and hydroxide ion concentrations of pure water at 25°C and 100 ° C?

Solution: Because OH^- and H^+ are formed only from the dissociation of water, their concentrations must be equal:
$[H^+]= [OH^-]$
From the K_w equation, we get $[OH^-] = [H^+]$
At 25 ° C,
$[OH^-]= [H^+] = (1.00 \times 10^{-14})^{1/2} = 1.00 \times 10^{-7}$ M
At 100 ° C,
$[OH^-]= [H^+] = (49 \times 10^{-14})^{1/2} = 7.0 \times 10^{-7}$ M

Auto ionization of water:

$$2H_2O(l) \rightleftharpoons H_3O^+(aq) + OH^-(aq)$$

.: Kw = [H 2 O] has no concentration

$$:.\ Kw = \frac{[H3O+][OH-]}{[H2O(l)]2} = [H_2O] \text{ has no concentration}$$

$$K_W = [H_3O^+][OH^-] = [H^+][OH^-] = 1.0 \times 10^{-14} \text{ (at 25 o C)}$$

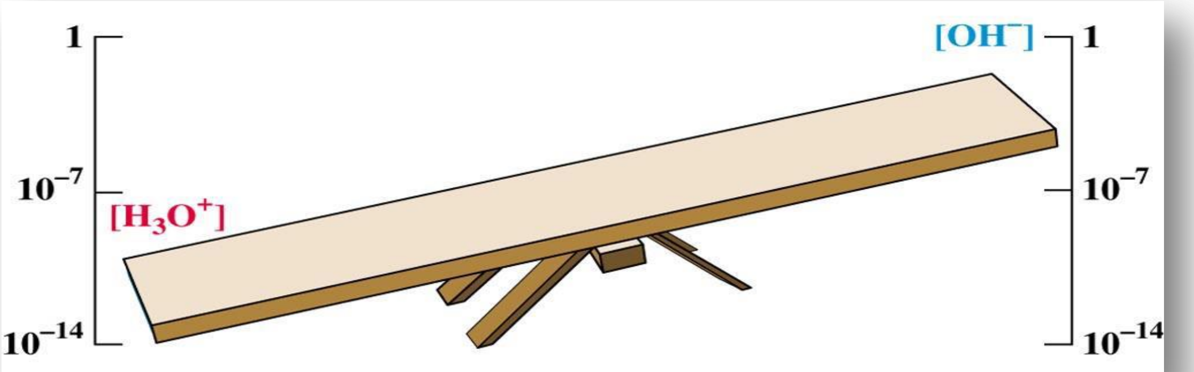
- In pure water $[H^{+}]$ $[OH^{-}]$

Notice that:

- A neutral solution, where $[H^{+}] = [OH^{-}]$

The change in $[H^{+}]$ or $[OH^{-}]$ results in change in the nature of solution

- An acidic solution, where $[H^{+}] > [OH^{-}]$
- A basic solution, where $[H^{+}] < [OH^{-}]$



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Acid/Base Dissociation Constant (Ka and Kb):

- Consider a weak monoprotic acid, HA, which dissociates partially in water:

$$HA + H_2O \longleftrightarrow H_3O^{+} + A^{-}$$

At equilibrium,

$$\frac{[H_3O^{+}][A^{-}]}{[HA]} = K_a$$

- The higher the value of K_a (that is the equilibrium position is more towards the right hand side) the stronger the acid
- Weak base, B, which dissociates partially in water:

$$B + H2O \longleftrightarrow HB^{+} + OH^{-}$$

At equilibrium,

$$\frac{[HB^{+}][OH^{-}] = Kb}{[B]}$$

- The higher the value of Kb, the stronger the base

PKa and pKb:

- Is another way of expressing the acid/base dissociation constant

$$PK_a = -\log K_a$$
$$PK_b = -\log K_b$$

- The larger the value of K_a or Kb, the smaller the value of pKaor pKb.

Exercise: Calculate the pK_b for the bases.

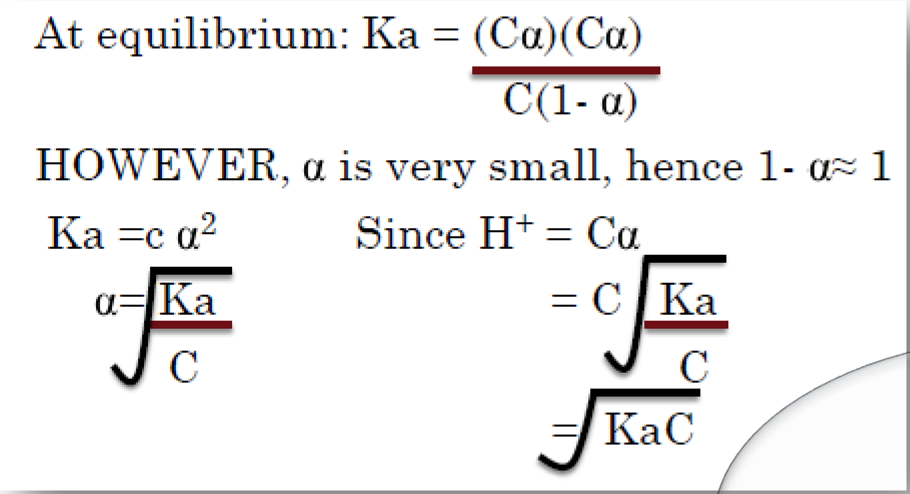
Acid	NH_3	CH3COO	NO_2^{-}
K_b/mol dm^{-3}	1.8×10^{-5}	5.6×10^{-10}	2.2×10^{-11}

- Arrange the bases in order of increasing strength

Ostwald Dilution Law and Dissociation Constant:

Consider a weak acid, HA, of concentration C mol dm-3and degree of dissociation of $\propto$

	HA	$\longleftrightarrow$	H^+	$+$	A^-
Initial	C		0		0
Equilibrium	$C\,(1-\alpha)$		$C\,\alpha$		$C\,\alpha$



At equilibrium: $Ka = \frac{(C\alpha)(C\alpha)}{C(1-\alpha)}$

HOWEVER, α is very small, hence $1-\alpha \approx 1$

$Ka = c\,\alpha^2$ Since $H^+ = C\alpha$

$\alpha = \sqrt{\frac{Ka}{C}}$ $= C\sqrt{\frac{Ka}{C}}$

$= \sqrt{KaC}$

For weak base

$B + H_2O \longleftrightarrow HB^+ + OH^-$

$[OH] = \sqrt{KbC}$

Ionic Product of Water:

- The ion product of water
  - Hydrogen ion (H^+)is key = It indicates the acidity @ basicity of the solution
  - **Equilibrium constant** for the autoionization of water

$$H_2O(l) \leftrightarrow H^+(aq) + OH^-(aq)$$

$$K_c = \frac{[H^+][OH^-]}{[H_2O]}$$

- Since, the degree of dissociation of water is extremely small, the concentration of water can be considered constant

$$K_c[H_2O] = \mathbf{K_w} = \mathbf{[H^+][OH^-]}$$

$$K_w = (1.0 \text{ x } 10^{-7} \text{ mol dm}^{-3})(1.0\text{x}10^{-7} \text{ mol dm}^{-3}) = 1.0\text{x}10^{-14} \text{ mol}^2 \text{ dm}^{-6}$$

- The ionic product of water can be expressed in terms of pKw, where
  - $\mathbf{pK_w = -log\ K_w}$

    $= -log(1.0\text{x}10^{-14}) = 14$
- From the expression:
  - $\mathbf{K_w = [H^+][OH^-]}$

- Another expression can be derived by taking the (-log) of the Kwexpression

  pKw= POH + pH
- Thus, if the pOH of the solution is known, its pH value can be calculated from the above relationship

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Physical pharmacy – lecture 6

Concentration expression

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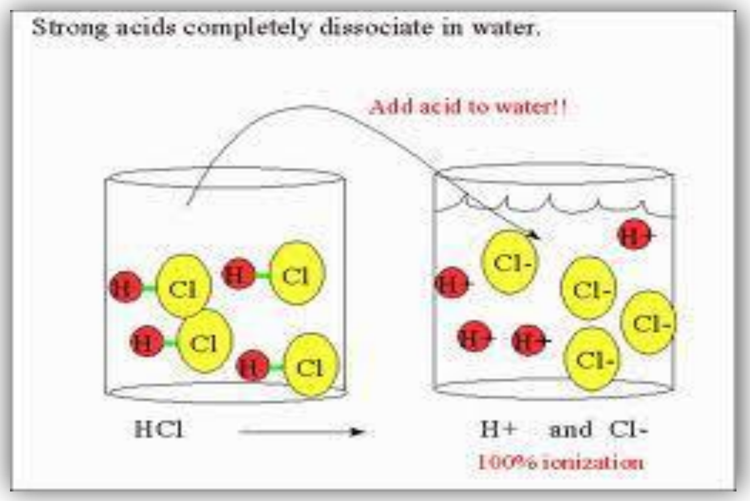
Acids and Bases and Their Reactions:

Acid Strength:

- The strength of an acid is defined by the equilibrium position of its dissociation reaction:

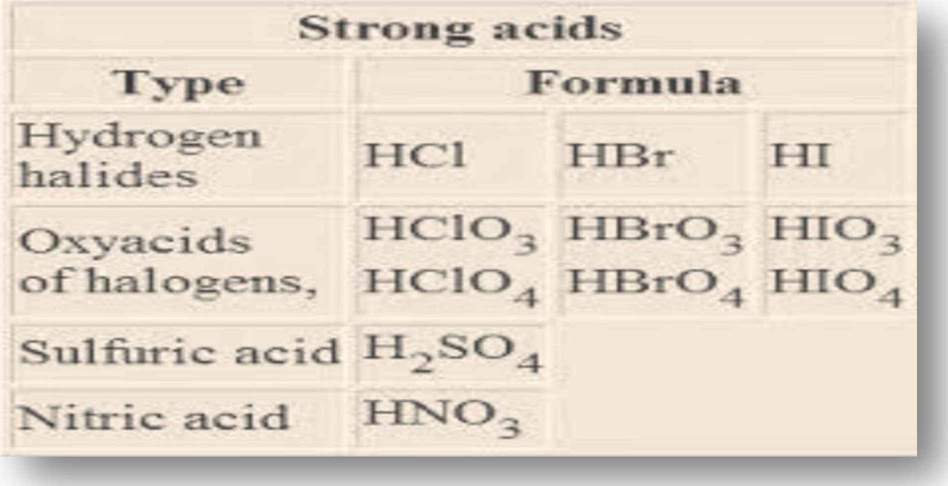
$$HA_{(aq)} + H_2O \rightarrow H_3O^{+}{}_{(aq)} + A^{-}{}_{(aq)}$$

- A strong acid: is one that dissociates completely in water to produce H aq
- Is one for which this equilibrium lies far to the right
- This means that almost all the original HA is dissociated (ionized).



$$\textbf{HCl (aq)} \longrightarrow \textbf{H}^{+}\textbf{ (aq) + Cl}^{-}\textbf{ (aq)}$$ **(reaction essentially complete)**

Strong Acids:

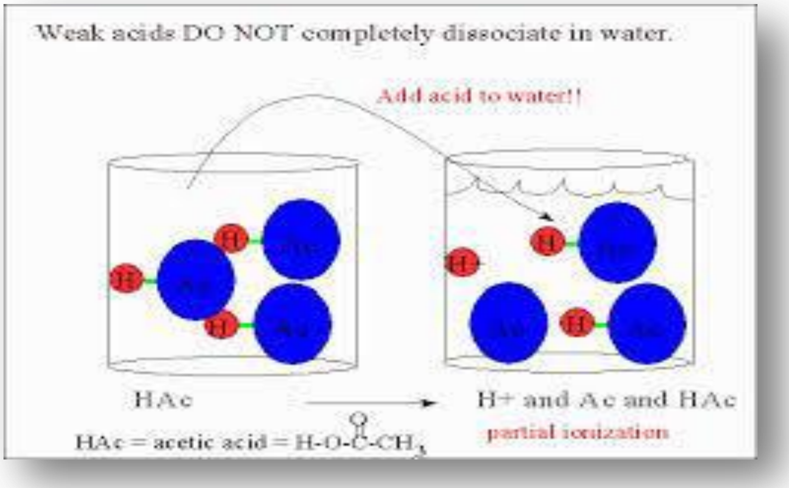


Strong acids

Type	Formula		
Hydrogen halides	HCl	HBr	HI
Oxyacids of halogens,	$HClO_3$ $HClO_4$	$HBrO_3$ $HBrO_4$	HIO_3 HIO_4
Sulfuric acid	H_2SO_4		
Nitric acid	HNO_3		

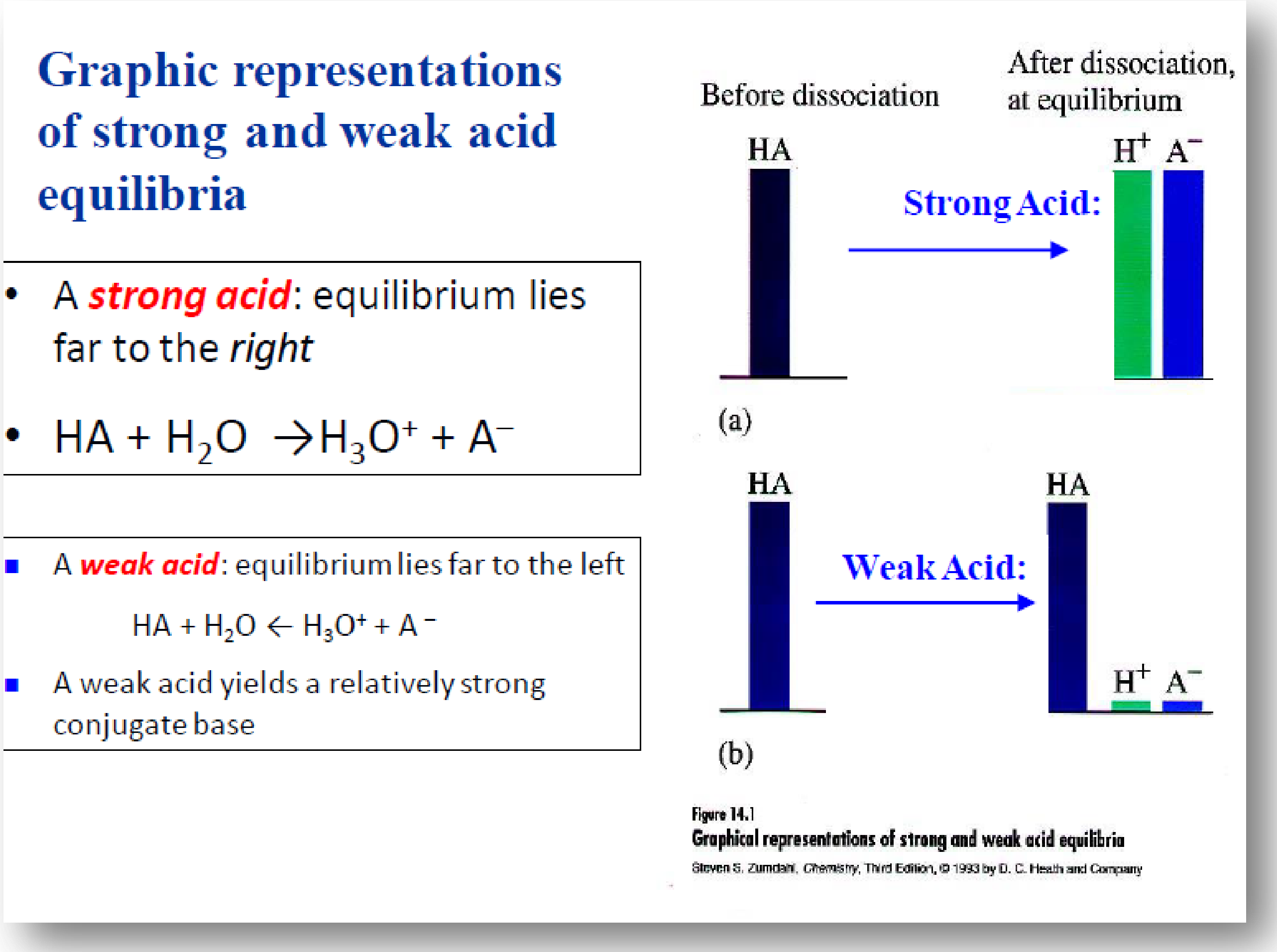
Weak acids

- A weak acid is one for which the equilibrium lies far to the left.
- A weak acid dissociates only to a very small extent.



Weak acids DO NOT completely dissociate in water.

- A weak acid has a strong conjugate base.



Graphic representations of strong and weak acid equilibria

- A ***strong acid***: equilibrium lies far to the *right*
- $HA + H_2O \rightarrow H_3O^+ + A^-$

- A ***weak acid***: equilibrium lies far to the left

  $HA + H_2O \leftarrow H_3O^+ + A^-$

- A weak acid yields a relatively strong conjugate base

Figure 14.1
Graphical representations of strong and weak acid equilibria
Steven S. Zumdahl, Chemistry, Third Edition, © 1993 by D. C. Heath and Company

The Calculation of pH for Strong Acids

$$Ph = -\log [H_3O^+] = -\log [H^+]$$

Calculate the pH of 0.10 M solution of HCl

$$HCl \longrightarrow H^+ + Cl^-$$

0.1M 0.1 0.1

$$Ph = -\log [0.1] = -\log [1 \times 10^{-1}] = -[-1] + \log 1 = 1$$

$$POH = pKw - pH = 14 - 1 = 13$$

Or

$$[OH^-] = K_w / [H^+] = 10^{-14} / 10^{-1} = 10^{-13}$$

Example 3: How we calculate pH value of 1.0×10^{-8} M HCL?

Solution: HCl is a strong acid and is completely ionized….
1.0×10^{-8} M HCl is very dilute acid, it produces less H ion concentration then water so in that case ionization of water is consider i.e. the concentration of H from water cannot be neglected

$$\mathbf{10^{-8}\ M\ HCl \longrightarrow H^{+}\ (10^{-8}\ M) + Cl^{-}\ (10^{-8}\ M)}$$

$$\begin{array}{cccccc} H_2O & \rightleftharpoons & H^{+} & + & OH^{-} \\ -X & & (10^{-8} + X) & & (X) \end{array}$$

$$K_w = 10^{-14} = (H^{+}) \times (OH^{-}) = (10^{-8} + X) \times (X)$$

$$\therefore \quad X = 10^{-14} \ / \ (10^{-8} + X) \quad \text{,, } 10^{-8} \text{ is very small value, so it can be neglected}$$

$$X \approx 10^{-7} \qquad \text{total } H^{+} = 10^{-7} + 10^{-8} = 1.1 \times 10^{-7}$$

$$pH = -\log(1.1 \times 10^{-7}) = -(-7) - \log 1.1 = 7 - 0.041 = 6.96$$

Example 4: What is the pH of 200 ml 0.5 , 1 and 5 M H_2SO_4 ?

$$\begin{array}{ccccc} H_2SO_4 & \longrightarrow & H^+ & + & HSO_4^- \\ x & & x & & x \end{array}$$

K_{a1}, is so large that we can consider this as going to completion.

then; $HSO_4^- \rightleftharpoons H + SO_4^{2-}$ $K_{a2} = 0.01$

Initially	H_2SO_4	$\longrightarrow$	H^+	+	HSO_4^-
	0.5		0.5		0.5
Cont	HSO_4^-	$\longleftrightarrow$	H	+	SO_4^{2-}
	0.5		x		x
End	0.5-x		0.5+x		x

At equilibrium $Ka_2 = \dfrac{(0.5+X) \times X}{(0.5 - X)} = 0.01$ $X^2 + 0.51 X - 0.005 = 0$

$X = \frac{1}{2a}(-b \pm \sqrt{(b^2 - (4ac))})$ X = 0.0096 mol/L $[H^+]$ = 0.5+0.0096=0.5096 mol/l

$pH = -\log[H^+] = -\log[0.5096] = 0.29$

What is the pH of 0.05 N H_2SO_4?
Normality = Equivalents × Molarity
Molarity =0.05 2 = 0.025 M

Calculate the pH of Strong Acid Base Solutions:

Example 5: Calculate the pH (at 25 o C) of an aqueous solution that has an OH^- (aq) concentration of 1.2 x 10 6 M (i.e., mol/liter).

Solution:

The concentration of H^+(aq) is

$[H^+][OH^-] = K_W$

$[H^+] = K_W /[OH^-] = 10^{-14}\ 1.2 \times 10^{-6} = 8.3 \times 10^{-9}$

Ph =-log [8.3 x 10^-9] = 8.1

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Concentration expression

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Calculating pH of weak acid solutions

- **Weak** acids dissociates **partially (<1%)** unlike **strong** acids that dissociates **completely**.
- For weak acid, as **they are not 100% ionized in water,** the previous steps to calculate the pH can't be valid but we should take in account the dissociation constant K_a which is much more complicated

#1: $HA \rightleftharpoons H^+ + A^-$

$$\boxed{K_a = \frac{[H^+][A^-]}{[HA]}}$$

Bases:

- All the hydroxides of group 1 A elements (LiOH, NaOH, KOH, RbOH and CsOH) are strong bases, but only NaOH and KOH are common laboratory Reagents as the others are very expensive.
- The alkaline earth (group 2 A) hydroxides are also strong bases.
- In General, all the previous concepts for acids can also be applied to bases. Bases

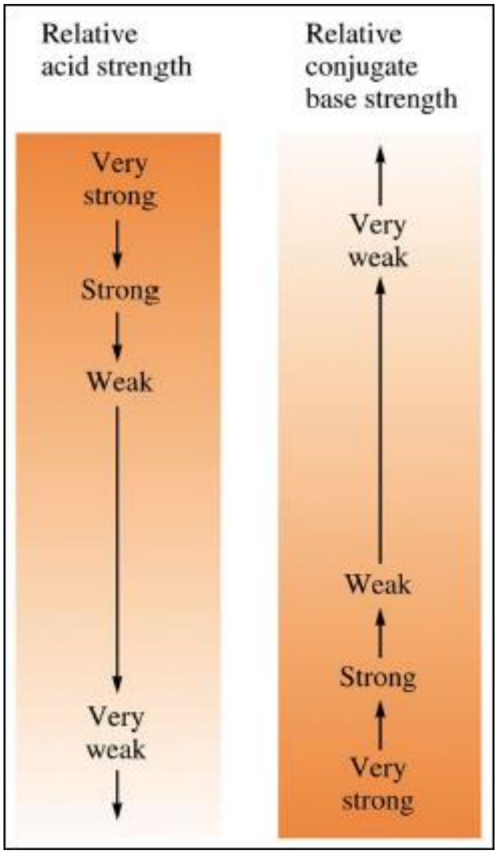
Base Strength

- strong acids have weak conjugate bases
- weak acids have strong conjugate bases

The strength of a base is inversely related to the strength of its conjugate acid; the weaker the acid, the stronger its conjugate base, and vice versa

$pKa + pK_b = pK_w$

This equation applies to an acid and its conjugate base.



Strong Bases

A strong base reacts completely with water to produce OH^- (aq) ions.

$$\begin{array}{ccc} NaOH\,(s) & \longrightarrow & Na^+\,(aq) + OH^-\,(aq) \\ 0.1M & & 0.1 \qquad\qquad 0.1 \end{array}$$

Dissolving 0.10 mol. of NaOH in enough water to make 1.0 L of solution gives a final concentration of 0.10 M for OH aq). From this you can calculate pH and pOH

$$\boxed{[H^+][OH^-] = K_w}$$

$$[H^+] = K_w/[OH^-] = 10^{-14}/10^{-1} = 10^{-13}$$

$$[OH^-] = 10^{-1} \qquad [H^+] = 10^{-13}$$

$$pOH = -\log(OH^-) = 1 \qquad pH = 13$$

Example 7: What is pH of 10 $^{-8}$ M solution of NaOH?

$$10^{-8}\text{ M NaOH} \rightarrow Na^+ \ (10^{-8}\text{ M}) + OH^- \ (10^{-8}\text{ M})$$

$$\underset{-X}{H_2O} \rightleftharpoons \underset{(X)}{H^+} + \underset{(10^{-8}+X)}{OH^-}$$

$$K_w = 10^{-14} = (H^+) \times (OH^-) = (X) \times (10^{-8} + X)$$

$\therefore \quad X = 10^{-14} / (10^{-8} + X)$,, 10^{-8} is very small value, so it can be neglec

$X \approx 10^{-7}$ total $OH^- = 10^{-7} + 10^{-8} = 1.1 \times 10^{-7}$

$$pOH = -\log(1.1 \times 10^{-7}) = -(-7) - \log 1.1 = 7 - 0.02 = 6.98$$

Weak Bases:

$B\ (aq) + H_2O\ (l) \rightleftharpoons BH^+\ (aq) + OH^-\ (aq)$ B = Base

K_b is the basicity constant $K_b = [BH^+][OH^-]/[B]$

$[OH^-] = K_b\,[B]/[BH^+]$ $pOH = pK_b - \log\ [B]/[BH^+]$

Calculations for solutions of weak bases are similar to those for weak acids. **Bases** (B) compete with **OH $^-$,** a very strong base, for H$^+$ ions.

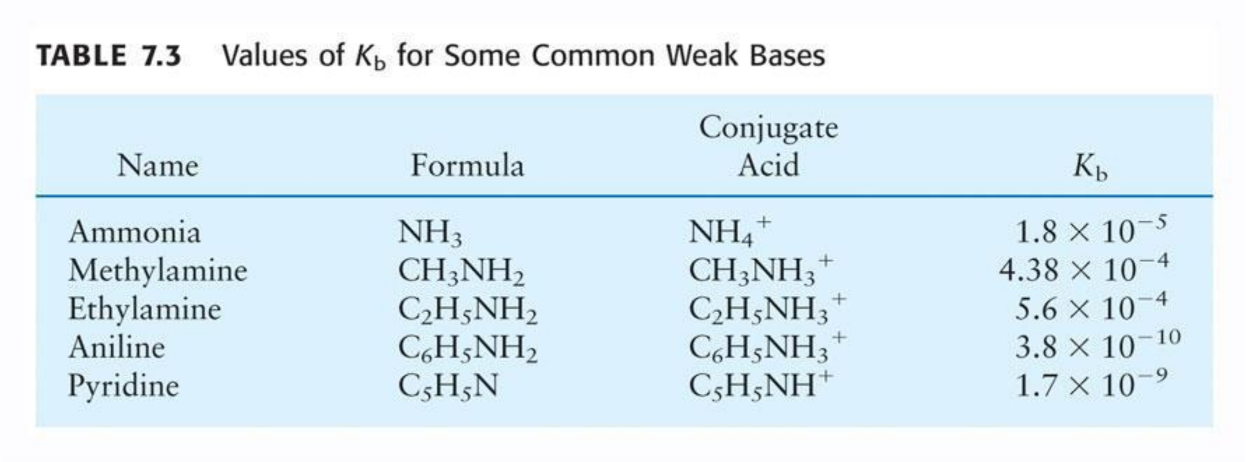


TABLE 7.3 Values of K_b for Some Common Weak Bases

Name	Formula	Conjugate Acid	K_b
Ammonia	NH_3	NH_4^+	1.8×10^{-5}
Methylamine	CH_3NH_2	$CH_3NH_3^+$	4.38×10^{-4}
Ethylamine	$C_2H_5NH_2$	$C_2H_5NH_3^+$	5.6×10^{-4}
Aniline	$C_6H_5NH_2$	$C_6H_5NH_3^+$	3.8×10^{-10}
Pyridine	C_5H_5N	$C_5H_5NH^+$	1.7×10^{-9}

Example 8: Calculate the pH for a 15.0 M NH_3 ($K_b = 1.8 \times 10^{-5}$)

$$\mathbf{NH_3\,(aq) + H_2O \rightleftharpoons NH_4^+ + OH^-}$$

Solution :

$$K_b = 1.8\text{x}10^{-5} = \frac{[NH_4^+][OH^-]}{[NH_3]} = \frac{(x)(x)}{(15.0)}$$

$$X = [OH^-] = [NH_4^+] = 1.6\text{x}10^{-2}\ M$$

$$[H^+] = K_w/[OH^-] = 1.0\text{x}10^{-14}/1.6\text{x}10^{-2} = 6.3\text{x}10^{-13}\ M$$

$$pH = -\log\ (6.3\text{x}10^{-13}) = 12.20$$

- Also we can calculate the pOH directly from $[OH^-]$ and then subtract it from 14

Physical pharmacy – lecture 8

Ionic Equilibrium

November – 2021

Relationship Between K_a and K_b

(A)A simple relationship exists between the dissociation constant of a weak acid HB and that of its conjugate base B^-, or between BH^+ and B, when the solvent is amphiprotic. This can be obtained by multiplying equation **(**7-12**)** by equation :

$$K_aK_b = \frac{[H_3O^+][B^-]}{[HB]} \cdot \frac{[OH^-][HB]}{[B^-]}$$
$$= [H_3O^+][OH^-] = K_w$$

And

$$K_b = \frac{K_w}{K_a}$$

Or

$$K_a = \frac{K_w}{K_b}$$

Ionization of Polypro tic Electrolytes

Acids that donate a single proton and bases that accept a single proton are called **monoprotic electrolytes.** A **polypro tic (polybasic) acid** is one that is capable of donating two or more protons, and a polypro tic base is capable of accepting two or more protons. A diprotic (dibasic) acid, such as carbonic acid, ionizes in two

Stages, and a triprotic (tribasic) acid, such as phosphoric acid, ionize in three stages. The equilibria involved in the protolysis or ionization of phosphoric acid, together with the equilibrium expressions, are

$$H_3PO_4 + H_2O = H_3O^+ + H_2PO_4^-$$

$$\frac{[H_3O^+][H_2PO_4^-]}{[H_3PO_4]} = K_1 = 7.5 \times 10^{-3}$$

$$H_2PO_4^- + H_2O = H_3O^+ + HPO_4^{2-}$$

$$\frac{[H_3O^+][HPO_4^{2-}]}{[H_2PO_4^-]} = K_2 = 6.2 \times 10^{-8}$$

$$HPO_4^{2-} + H_2O = H_3O^+ + PO_4^{3-}$$

$$\frac{[H_3O^+][PO_4^{3-}]}{[HPO_4^{2-}]} = K_3 = 2.1 \times 10^{-13}$$

In any polypro tic electrolyte, the primary proteolysis is greatest, and succeeding stages become less complete at any given acid concentration.

The negative charges on the ion HPO_4^{2-} make it difficult for water to remove the proton from the phosphate ion, as reflected in the small value of $K3$. Thus, phosphoric acid is weak in the third stage of ionization, and a solution of this acid contains practically no PO_4^{3-} ions.

Each of the species formed by the ionization of a polypro tic acid can also act as a base. Thus, for the phosphoric acid system,

$$PO_4^{3-} + H_2O \rightleftharpoons HPO_4^{2-} + OH^-$$

$$K_{b1} = \frac{[HPO_4^{2-}][OH^-]}{[PO_4^{3-}]} = 4.8 \times 10^{-2}$$

$$K_{b2} = \frac{[H_2PO_4^-][OH^-]}{[HPO_4^{2-}]} = 1.6 \times 10^{-7}$$

$$H_2PO_4^- + H_2O \rightleftharpoons H_3PO_4 + OH^-$$

$$K_{b3} = \frac{[H_3PO_4][OH^-]}{[H_2PO_4^-]} = 1.3 \times 10^{-12}$$

(B)

- **Consider an aqueous of ethanoic acid**:

$$CH_3COOH + H_2O \longleftrightarrow CH_3COO^- + H_3O^+$$

$$K_a = \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH]}$$

- **Consider an aqueous solution containing the ethanoate ion (which is the conjugate base of CH3COOH):**

$$CH_3COO^- + H_2O \longleftrightarrow CH_3COOH + OH^-$$

$$K_b = \frac{[CH_3COOH][OH^-]}{[CH_3COO^-]}$$

- **Multiplying K_a and K_b:**

$$K_a \times K_b = \frac{[\cancel{CH_3COO^-}][H_3O^+]}{[\cancel{CH_3COOH}]} \times \frac{[\cancel{CH_3COOH}][OH^-]}{[\cancel{CH_3COO^-}]}$$

$$K_a \times K_b = [H_3O^+][OH^-]$$

$$K_w = [H^+][OH^-]$$

- **Taking –log throughout:**

$$-\log K_a + -\log K_b = -\log K_w$$

- **Hence, for an acid/base conjugate pair:**

$$\boxed{pK_a + pK_b = pK_w}$$

Example: Calculate the pH of 0.10 mol. dm-3solution of sodium ethanoate. (K$_a$ for CH3COOH= 1.8x10-5moldm-3

Answer

$$CH3COO^- + H_2O \longleftrightarrow CH_3COOH \quad + OH^-$$

[OH-]= KbC

$$Kb \text{ for } CH_3COO^- = \frac{1.0x10^{-14}}{1.8x10^{-5}} = 5.55x10^{-10} \text{ mol dm}^{-3}$$

$$[OH^-]= 5.55x10^{-10} \ x\ 0.1 = 7.45x10^{-6}$$

$$pOH= -\log 97.45x10^{-6} = 5.13$$

$$pH = 14-5.13$$

$$= \mathbf{8.87}$$

Ampholytes

The species $H_2PO_4^-$ and HPO_4^{2-} can function either as an acid or a base. A species that can function either as an acid or as a base is called an **ampholyte** and is said to be **amphoteric** in nature. In general, for a polyprotic acid system,
Amino acids and proteins are ampholytes of particular interest in pharmacy. If glycine hydrochloride is dissolved in water, it ionizes as follows:

$$^+NH_3CH_2COOH + H_2O \rightleftharpoons {}^+NH_3CH_2COO^- + H_3O^+ \quad (7\text{–}50)$$

$$^+NH_3CH_2COO^- + H_2O \rightleftharpoons {}^+NH_2CH_2COO^- + H_3O^+ \quad (7\text{–}51)$$

The species $^+NH_3CH_2COO^-$ are amphoteric in that, in addition to reacting as an acid as shown in equation **(**7-51**)**, it can react as a base with water as follows:

$$^+NH_3CH_2COO^- + H_2O \rightleftharpoons {}^+NH_3CH_2COOH + OH^- \quad (7\text{–}52)$$

The amphoteric species $^+NH_3CH_2COO^-$ is called a zwitter ion and differs from the amphoteric species formed from phosphoric acid in that it carries both a positive and a negative charge, and the whole molecule is electrically neutral. The pH at which the zwitter ion concentration is a maximum is known as the **isoelectric point**. At the isoelectric point the net movement of the solute molecules in an electric field is negligible.

Sörensen's pH

$$pH = \log \frac{1}{[H_3O^+]}$$

$$pH = -\log[H_3O^+]$$

The pH of a solution can be considered in terms of a numeric scale having values from 0 to 14, which expresses in a quantitative way the degree of acidity (7 to 0) and alkalinity (7-14). The value 7 at which the hydrogen and hydroxyl ion concentrations are about equal at room temperature is referred to as the ***neutral point,*** or neutrality. The neutral pH at 0°C is 7.47, and at 100°C it is 6.15.

A better definition of pH involves the activity rather than the concentration of the ions:

$$pH = -\log a_{H^+}$$

$$pH = -\log(\gamma_{\pm} \times c)$$

pK and pOH

$$pH + pOH = pK_w$$

$$pH = -\log[H_3O^+]$$

The pH of a solution can be considered in terms of a numeric scale having values from 0 to 14, which expresses in a quantitative way the degree of acidity (7 to 0) and alkalinity (7-14). The value 7 at which the hydrogen and hydroxyl ion concentrations are about equal at room temperature is referred to as the **neutral point,** or neutrality. The neutral pH at 0°C is 7.47, and at 100°C it is 6.15.

Acid-Base Properties of Salts

- **Neutral Solutions:**

Salt formed from a strong acid and a strong base is dissolved in water.

Example: $NaOH + HCl \longrightarrow NaCl + H_2O$

Salts containing an alkali metal or alkaline earth metal ion (except Be^{2+}) **and** the conjugate base of a **strong** acid (e.g. , Br$^-$, and NO^{3-}).

$$NaCl\ (s) \xrightarrow{H_2O} Na^+\ (aq) + Cl^-\ (aq)$$

Na$^+$ and Cl$^-$ are not hydrolysed by water. There is no production of extra H$^+$ or OH-ions. Hence, the solution is **neutral**.

- **Basic Solutions:**

Salts derived from **a strong base and a weak acid**.

$$NaCH_3COOH\ (s) \xrightarrow{H_2O} Na^+\ (aq) + CH_3COO^-\ (aq)$$

$$CH_3COO^-\ (aq) + H_2O\ (l) \rightleftharpoons CH_3COOH\ (aq) + OH^-\ (aq)$$

Acid-Base Properties of Salts

An example is:

$$\underset{\text{Weak base}}{NH_3\,(aq)} + \underset{\text{Strong acid}}{HCl\,(aq)} \longrightarrow NH_4Cl\,(aq)$$

In water, ammonium chloride dissociates completely into ammonium ions and chloride ions:

$$NH_4Cl\,(s) \xrightarrow{H_2O} NH_4^+\,(aq) + Cl^-\,(aq)$$

The ammonium ion, NH_4^+, acts as a Bronsted-Lowry acid and donates a proton to water

$$NH_4^+ + H_2O(aq) \rightleftharpoons NH_3\,(aq) + H_3O^+\,(aq)$$

On the other hand, **the Cl^- ions do not react with water:**

$Cl^-\,(aq) + H_2O\,(l) \rightleftharpoons HCl\,(aq) + OH^-$ (this reaction does not take place)

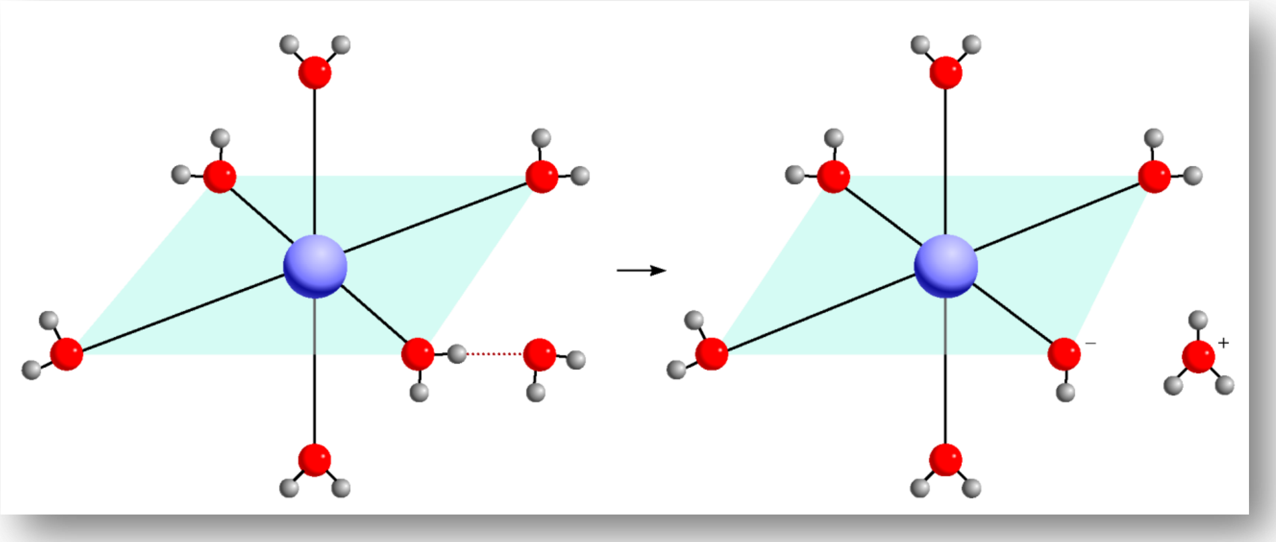
Because HCl (a strong acid) formed must dissociate completely to H^+ and Cl^- ions.

Salts with small, highly charged metal cations (*e.g.* Al^{3+}, Cr^{3+}, and Be^{2+}) and the conjugate base of a strong acid.

$$Al(H_2O)_6\,(aq)^{3+} \rightleftharpoons Al(OH)(H_2O)_5\,(aq)^{2+} + H^+\,(aq)$$

Acid Hydrolysis of $Al3^+$

$$Al(H_2O)_6^{3+} \quad + \quad H_2O \longrightarrow \quad Al(OH)(H_2O)_5^{2+} \quad + \quad H_3O^+$$



Acid-Base Properties of Salts

Solutions in which both the cation and the anion hydrolyze:

- Kb for the anion > K_a for the cation, solution will be basic
- Kb for the anion < K_a for the cation, solution will be acidic
- Kb for the anion $\approx K_a$ for the cation, solution will be neutral

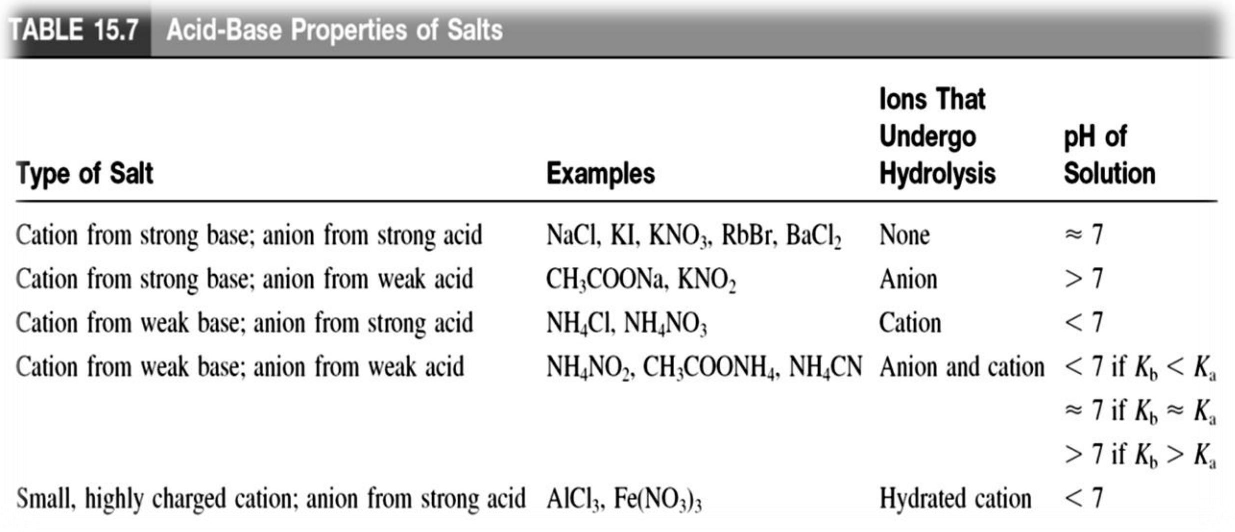


TABLE 15.7 Acid-Base Properties of Salts

Type of Salt	Examples	Ions That Undergo Hydrolysis	pH of Solution
Cation from strong base; anion from strong acid	NaCl, KI, KNO_3, RbBr, $BaCl_2$	None	≈ 7
Cation from strong base; anion from weak acid	CH_3COONa, KNO_2	Anion	> 7
Cation from weak base; anion from strong acid	NH_4Cl, NH_4NO_3	Cation	< 7
Cation from weak base; anion from weak acid	NH_4NO_2, CH_3COONH_4, NH_4CN	Anion and cation	< 7 if $K_b < K_a$ ≈ 7 if $K_b \approx K_a$ > 7 if $K_b > K_a$
Small, highly charged cation; anion from strong acid	$AlCl_3$, $Fe(NO_3)_3$	Hydrated cation	< 7

Hydrolysis

- Remembering the following equations must hold simultaneously

$$K_w = \left[H^+\right] \times \left[OH^-\right]$$

$$K_a = \frac{\left[H^+\right] \times \left[Ac^-\right]}{\left[HAc\right]} \text{ and } K_b = \frac{\left[NH_4^{\ +}\right] \times \left[OH^-\right]}{NH_4OH}$$

- Also, it can be shown that

$$K_h = K_w / K_a \times K_b$$

$$pK_h = pK_w - pK_a + pK_b$$

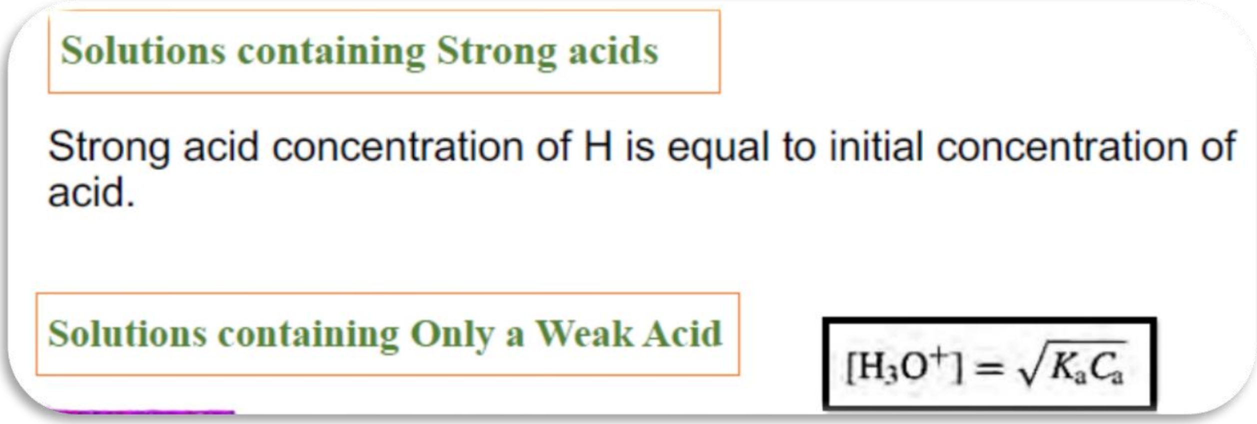
Physical pharmacy – lecture 9

Ionic Equilibrium

November – 2021

Isoelectric point (IEP)

- It is pH at which zwitterion concentration at maximum
- It has been used for determination of protein and amino acids.
- The molecules have ------------- solubility at IEP.
- The net charge of a molecule at its IEP is -----------.
- Charge of a molecule at pH above its IEP is ----------- and below is -----------

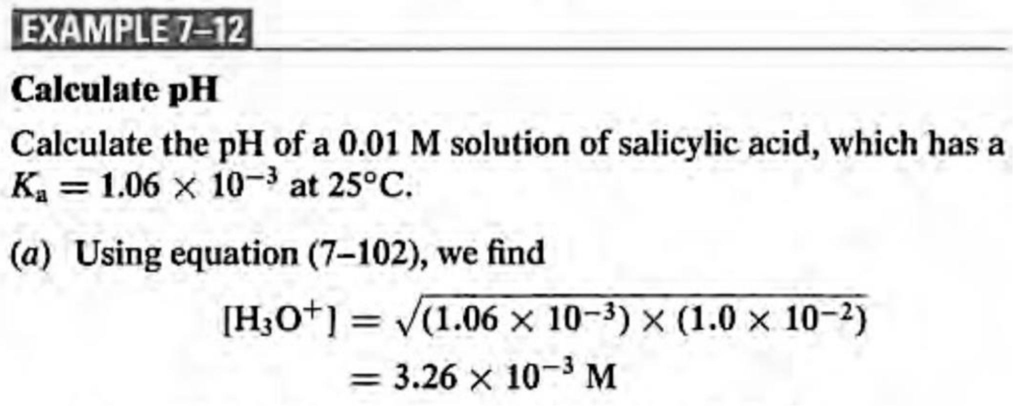


Solutions containing Strong acids

Strong acid concentration of H is equal to initial concentration of acid.

Solutions containing Only a Weak Acid

$$[H_3O^+] = \sqrt{K_a C_a}$$



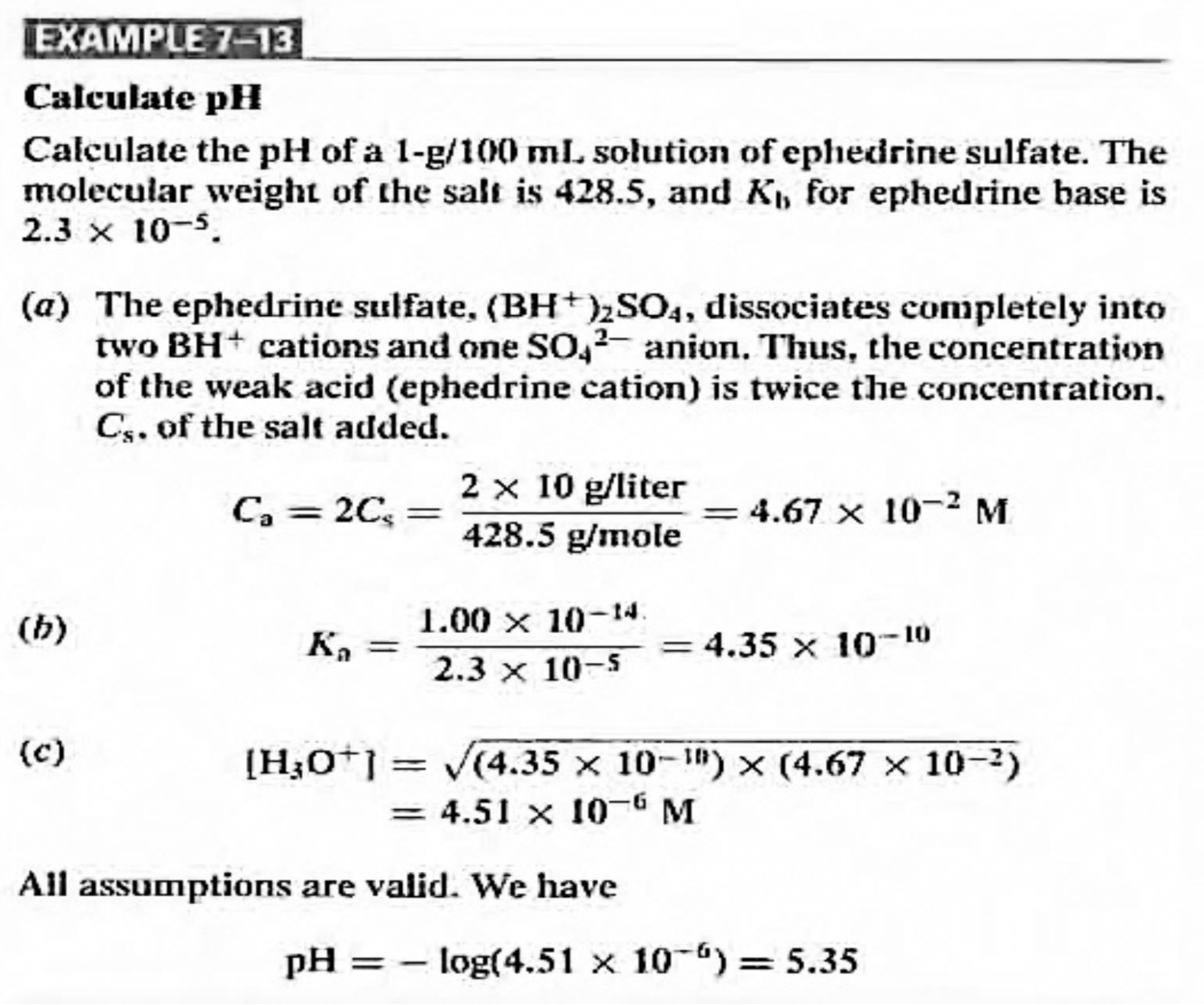
EXAMPLE 7–12

Calculate pH

Calculate the pH of a 0.01 M solution of salicylic acid, which has a $K_a = 1.06 \times 10^{-3}$ at 25°C.

(*a*) Using equation (7–102), we find

$$[H_3O^+] = \sqrt{(1.06 \times 10^{-3}) \times (1.0 \times 10^{-2})}$$
$$= 3.26 \times 10^{-3}\ M$$



EXAMPLE 7–13

Calculate pH

Calculate the pH of a 1-g/100 mL solution of ephedrine sulfate. The molecular weight of the salt is 428.5, and K_b for ephedrine base is 2.3×10^{-5}.

(*a*) The ephedrine sulfate, $(BH^+)_2SO_4$, dissociates completely into two BH^+ cations and one SO_4^{2-} anion. Thus, the concentration of the weak acid (ephedrine cation) is twice the concentration, C_s, of the salt added.

$$C_a = 2C_s = \frac{2 \times 10 \text{ g/liter}}{428.5 \text{ g/mole}} = 4.67 \times 10^{-2} \text{ M}$$

(*b*)

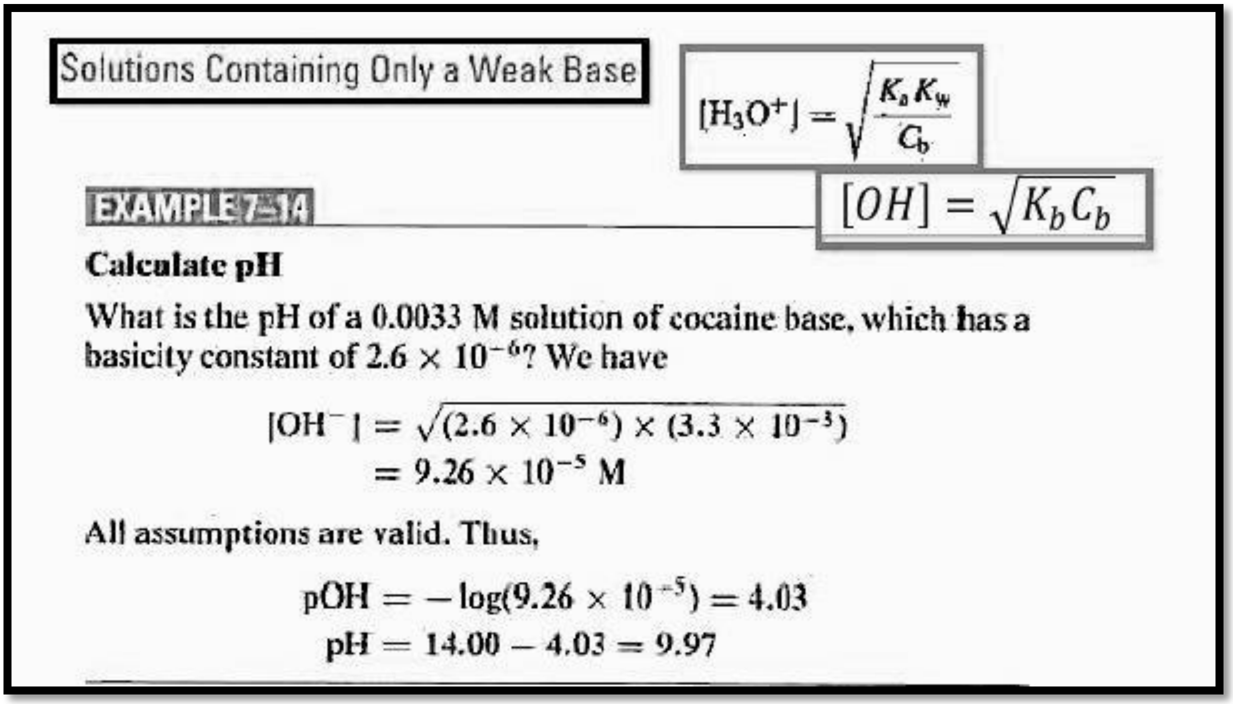
$$K_a = \frac{1.00 \times 10^{-14}}{2.3 \times 10^{-5}} = 4.35 \times 10^{-10}$$

(*c*)

$$[H_3O^+] = \sqrt{(4.35 \times 10^{-10}) \times (4.67 \times 10^{-2})}$$
$$= 4.51 \times 10^{-6} \text{ M}$$

All assumptions are valid. We have

$$\text{pH} = -\log(4.51 \times 10^{-6}) = 5.35$$



Solutions Containing Only a Weak Base

$$[H_3O^+] = \sqrt{\frac{K_a K_w}{C_b}}$$

$$[OH] = \sqrt{K_b C_b}$$

EXAMPLE 7-14

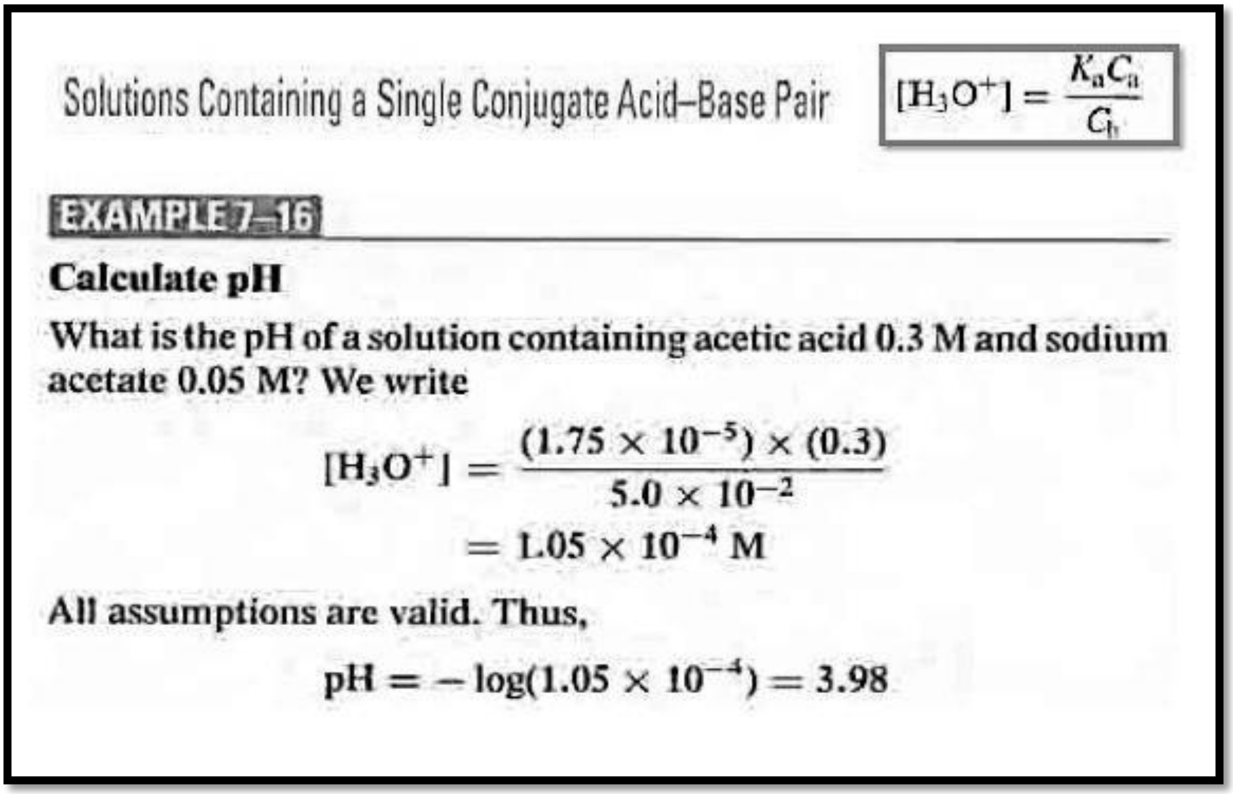
Calculate pH

What is the pH of a 0.0033 M solution of cocaine base, which has a basicity constant of 2.6×10^{-6}? We have

$$[OH^-] = \sqrt{(2.6 \times 10^{-6}) \times (3.3 \times 10^{-3})}$$
$$= 9.26 \times 10^{-5}\ M$$

All assumptions are valid. Thus,

$$pOH = -\log(9.26 \times 10^{-5}) = 4.03$$
$$pH = 14.00 - 4.03 = 9.97$$



Solutions Containing a Single Conjugate Acid–Base Pair

$$[H_3O^+] = \frac{K_a C_a}{C_b}$$

EXAMPLE 7-16

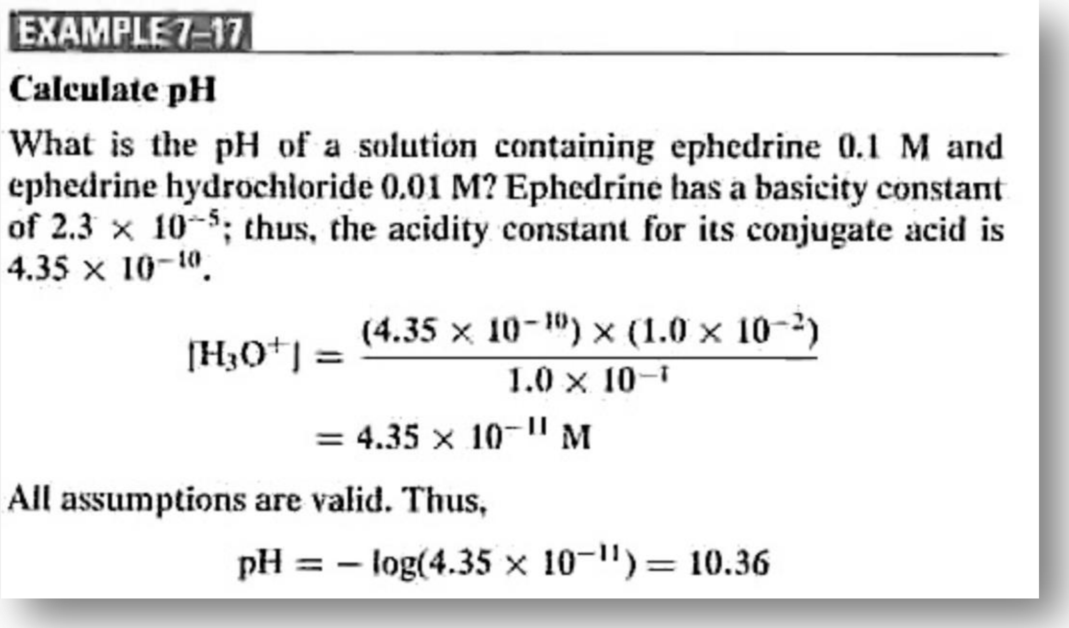
Calculate pH

What is the pH of a solution containing acetic acid 0.3 M and sodium acetate 0.05 M? We write

$$[H_3O^+] = \frac{(1.75 \times 10^{-5}) \times (0.3)}{5.0 \times 10^{-2}}$$
$$= 1.05 \times 10^{-4}\ M$$

All assumptions are valid. Thus,

$$pH = -\log(1.05 \times 10^{-4}) = 3.98$$



EXAMPLE 7–17

Calculate pH

What is the pH of a solution containing ephedrine 0.1 M and ephedrine hydrochloride 0.01 M? Ephedrine has a basicity constant of 2.3×10^{-5}; thus, the acidity constant for its conjugate acid is 4.35×10^{-10}.

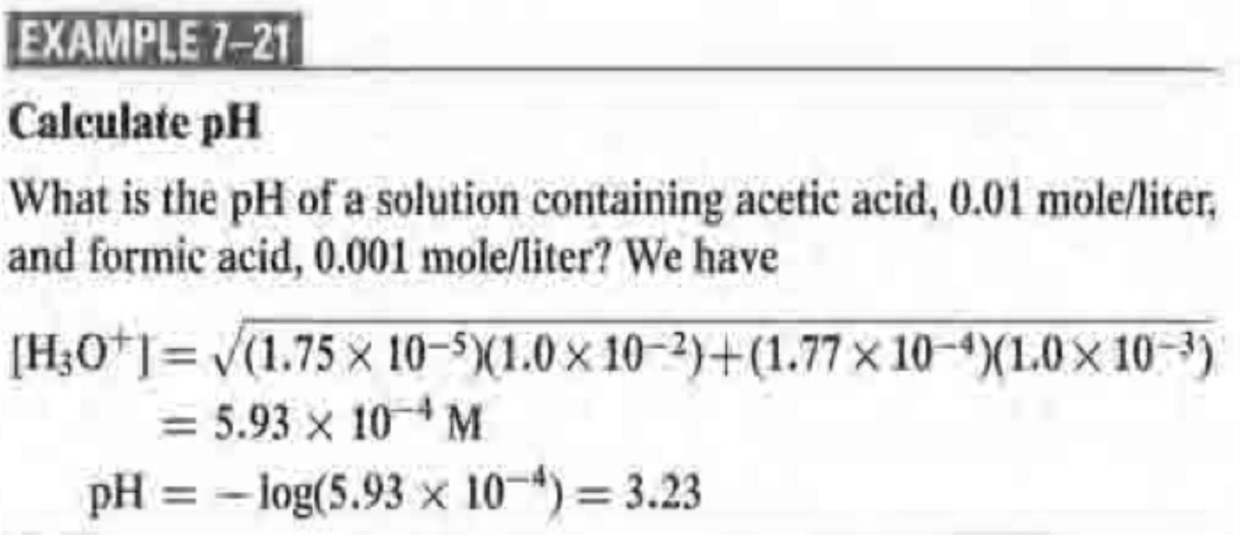
$$[H_3O^+] = \frac{(4.35 \times 10^{-10}) \times (1.0 \times 10^{-2})}{1.0 \times 10^{-1}}$$
$$= 4.35 \times 10^{-11}\ M$$

All assumptions are valid. Thus,

$$pH = -\log(4.35 \times 10^{-11}) = 10.36$$

Solutions Containing Two Weak Acids

$$[H_3O^+] = \sqrt{K_1C_{a1} + K_2C_{a2}}$$

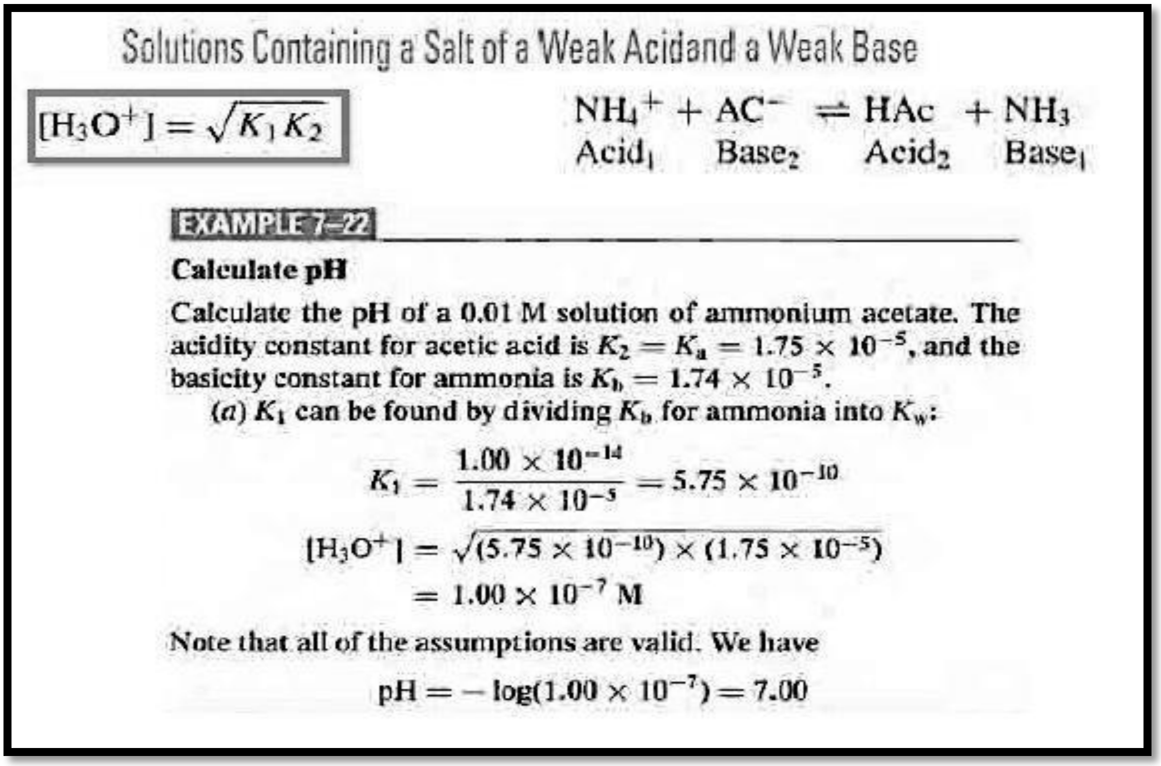


EXAMPLE 7–21

Calculate pH

What is the pH of a solution containing acetic acid, 0.01 mole/liter, and formic acid, 0.001 mole/liter? We have

$$[H_3O^+] = \sqrt{(1.75 \times 10^{-5})(1.0 \times 10^{-2}) + (1.77 \times 10^{-4})(1.0 \times 10^{-3})}$$
$$= 5.93 \times 10^{-4}\ M$$
$$pH = -\log(5.93 \times 10^{-4}) = 3.23$$



Solutions Containing a Salt of a Weak Acidand a Weak Base

$$\boxed{[H_3O^+] = \sqrt{K_1 K_2}}$$

$$\underset{\text{Acid}_1}{NH_4^+} + \underset{\text{Base}_2}{AC^-} \rightleftharpoons \underset{\text{Acid}_2}{HAc} + \underset{\text{Base}_1}{NH_3}$$

EXAMPLE 7–22

Calculate pH

Calculate the pH of a 0.01 M solution of ammonium acetate. The acidity constant for acetic acid is $K_2 = K_a = 1.75 \times 10^{-5}$, and the basicity constant for ammonia is $K_b = 1.74 \times 10^{-5}$.

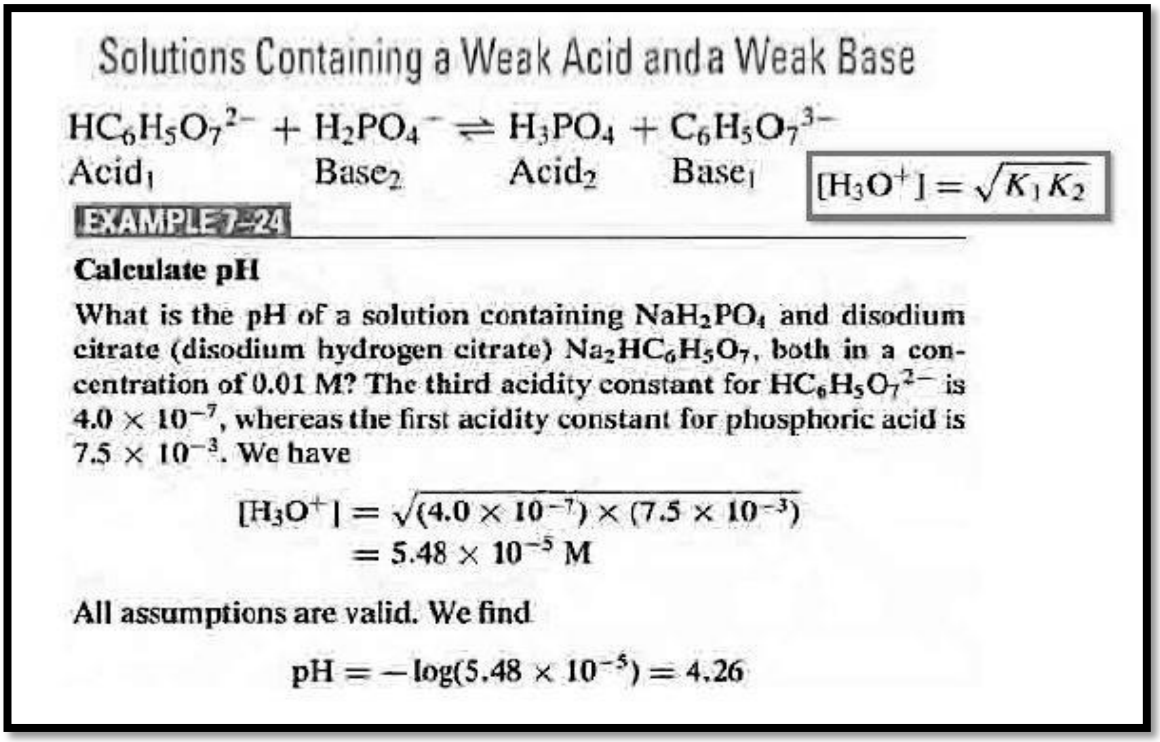
(*a*) K_1 can be found by dividing K_b for ammonia into K_w:

$$K_1 = \frac{1.00 \times 10^{-14}}{1.74 \times 10^{-5}} = 5.75 \times 10^{-10}$$

$$[H_3O^+] = \sqrt{(5.75 \times 10^{-10}) \times (1.75 \times 10^{-5})}$$
$$= 1.00 \times 10^{-7}\ M$$

Note that all of the assumptions are valid. We have

$$pH = -\log(1.00 \times 10^{-7}) = 7.00$$



Solutions Containing a Weak Acid anda Weak Base

$$\underset{\text{Acid}_1}{HC_6H_5O_7^{2-}} + \underset{\text{Base}_2}{H_2PO_4^-} \rightleftharpoons \underset{\text{Acid}_2}{H_3PO_4} + \underset{\text{Base}_1}{C_6H_5O_7^{3-}}$$

$$\boxed{[H_3O^+] = \sqrt{K_1 K_2}}$$

EXAMPLE 7–24

Calculate pH

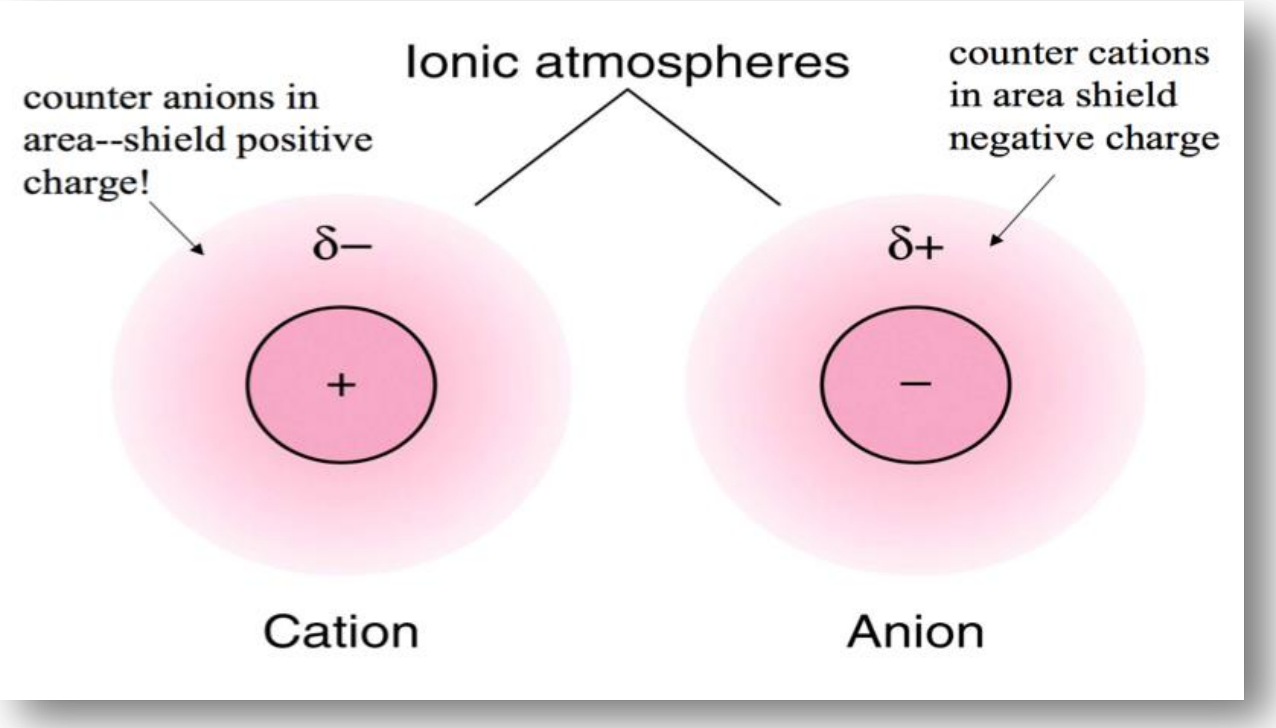
What is the pH of a solution containing NaH_2PO_4 and disodium citrate (disodium hydrogen citrate) $Na_2HC_6H_5O_7$, both in a concentration of 0.01 M? The third acidity constant for $HC_6H_5O_7^{2-}$ is 4.0×10^{-7}, whereas the first acidity constant for phosphoric acid is 7.5×10^{-3}. We have

$$[H_3O^+] = \sqrt{(4.0 \times 10^{-7}) \times (7.5 \times 10^{-3})}$$
$$= 5.48 \times 10^{-5}\ M$$

All assumptions are valid. We find

$$pH = -\log(5.48 \times 10^{-5}) = 4.26$$

Ionic strength



Ionic strength

ionic strength---I or μ ---a measure of the total ion concentration in solution----but ions with more charge are counted more due to stronger electrostatic interactions with other ions (I.e., can influence the increase “ionic atmosphere” greater than singly charged ions)

$$\mu = \frac{1}{2}\sum_i c_i z_i^2$$

where c_i is conc. of i^{th} species and z_i is the charge on i^{th} species

What is ionic strength of 0.01 M NaCl solution?

$\mu = 1/2\,([Na^+]z_{Na}^2 + [Cl^-]z_{Cl}^2) = 1/2\,(0.01\,(1)^2 + 0.01(-1)^2) = 0.01$ M

What is ionic strength of 0.01 M Na_2SO_4 solution?

$\mu = 1/2([Na^+]z_{Na}^2 + [SO_4^{-2}]z_{SO4}^2) = 1/2(0.02\,(1)^2 + 0.01\,(-2)^2) = 0.03$ M

Effect of Ionic Strength on Acidity Constants

$$HB + H_2O \rightleftharpoons H_3O^+ + B$$

$$K = \frac{\alpha_{H_3O} + \alpha_B}{\alpha_{HB}} = \frac{[H_3O^+][B]}{[HB]} \cdot \frac{\gamma H_3O^+ \gamma_B}{\gamma_{HB}}$$

For monotropic molecule

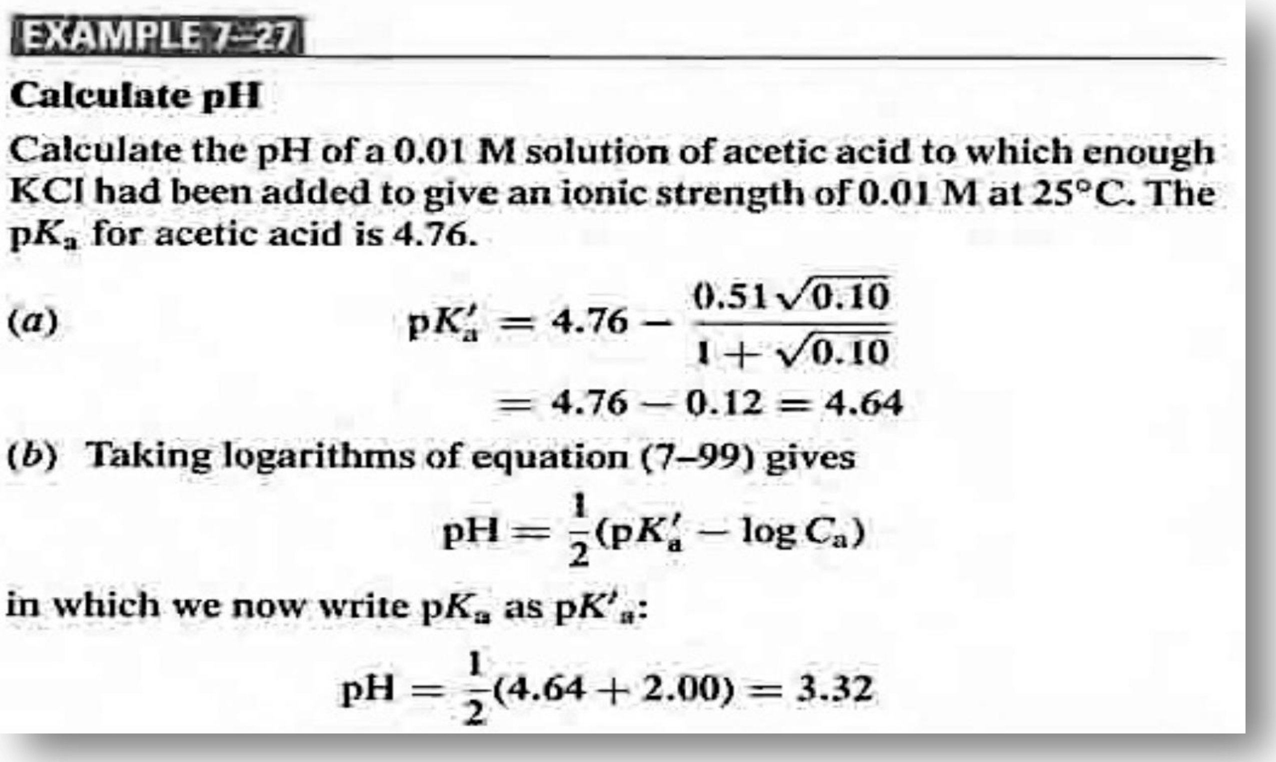
$$\boxed{pK' = pK + \frac{0.51(2Z - 1)\sqrt{\mu}}{1 + \sqrt{\mu}}}$$

For zwitterion molecule

$$\boxed{pK'_1 = pK_1 + \frac{0.51\sqrt{\mu}}{1 + \sqrt{\mu}} - K_r\mu}$$

$$\boxed{pK'_2 = pK_2 - \frac{0.51\sqrt{\mu}}{1 + \sqrt{\mu}} + K_r\mu}$$

K_r=Salting in constant=0.32 for amino acid in water



EXAMPLE 7–27

Calculate pH

Calculate the pH of a 0.01 M solution of acetic acid to which enough KCl had been added to give an ionic strength of 0.01 M at 25°C. The pK_a for acetic acid is 4.76.

(*a*)

$$pK'_a = 4.76 - \frac{0.51\sqrt{0.10}}{1 + \sqrt{0.10}}$$

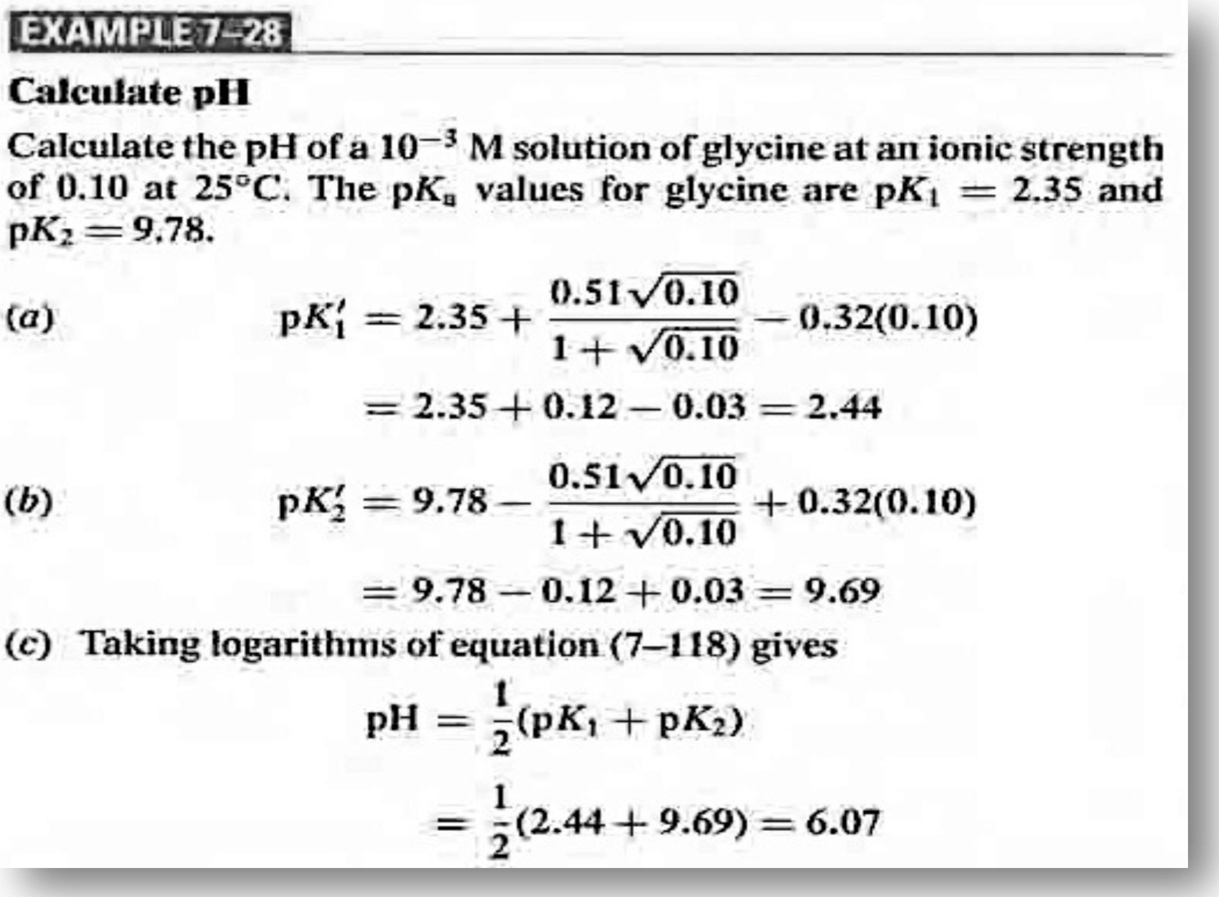
$$= 4.76 - 0.12 = 4.64$$

(*b*) Taking logarithms of equation (7–99) gives

$$pH = \frac{1}{2}(pK'_a - \log C_a)$$

in which we now write pK_a as pK'_a:

$$pH = \frac{1}{2}(4.64 + 2.00) = 3.32$$



EXAMPLE 7–28

Calculate pH

Calculate the pH of a 10^{-3} M solution of glycine at an ionic strength of 0.10 at 25°C. The pK_a values for glycine are pK_1 = 2.35 and pK_2 = 9.78.

(*a*)
$$pK_1' = 2.35 + \frac{0.51\sqrt{0.10}}{1+\sqrt{0.10}} - 0.32(0.10)$$
$$= 2.35 + 0.12 - 0.03 = 2.44$$

(*b*)
$$pK_2' = 9.78 - \frac{0.51\sqrt{0.10}}{1+\sqrt{0.10}} + 0.32(0.10)$$
$$= 9.78 - 0.12 + 0.03 = 9.69$$

(*c*) Taking logarithms of equation (7–118) gives

$$pH = \frac{1}{2}(pK_1 + pK_2)$$
$$= \frac{1}{2}(2.44 + 9.69) = 6.07$$

Physical pharmacy – lecture 10

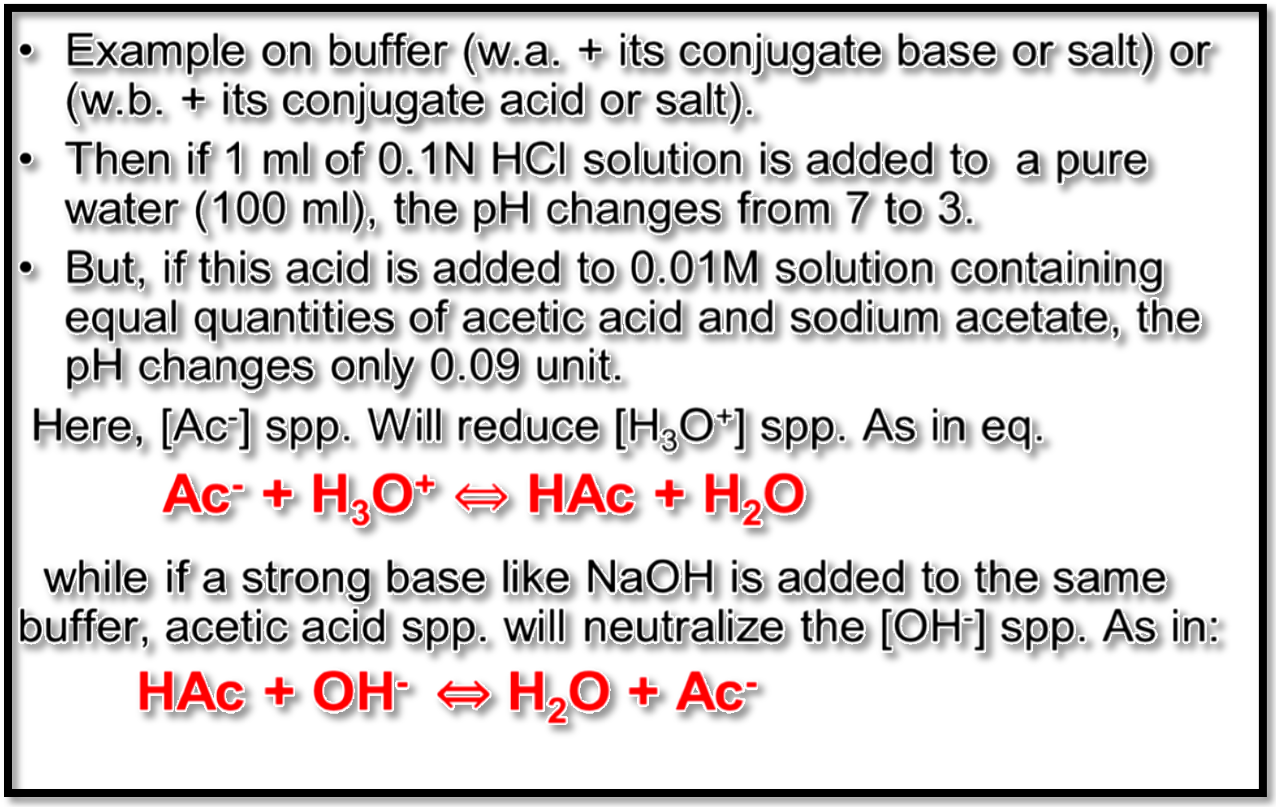
Buffer Solutions

November – 2021

Introduction

•Buffers are compounds or mixtures of compounds that, by their presence in solution, resist the changes in pH upon the addition of small quantities of acids or
Alkali.

- The resistance to a change in pH is known as **buffer action**.
- While if a small amount of a strong acid or base, is added to water or NaCl solution, the pH is altered considerably (there is no buffer action).



- Example on buffer (w.a. + its conjugate base or salt) or (w.b. + its conjugate acid or salt).
- Then if 1 ml of 0.1N HCl solution is added to a pure water (100 ml), the pH changes from 7 to 3.
- But, if this acid is added to 0.01M solution containing equal quantities of acetic acid and sodium acetate, the pH changes only 0.09 unit.

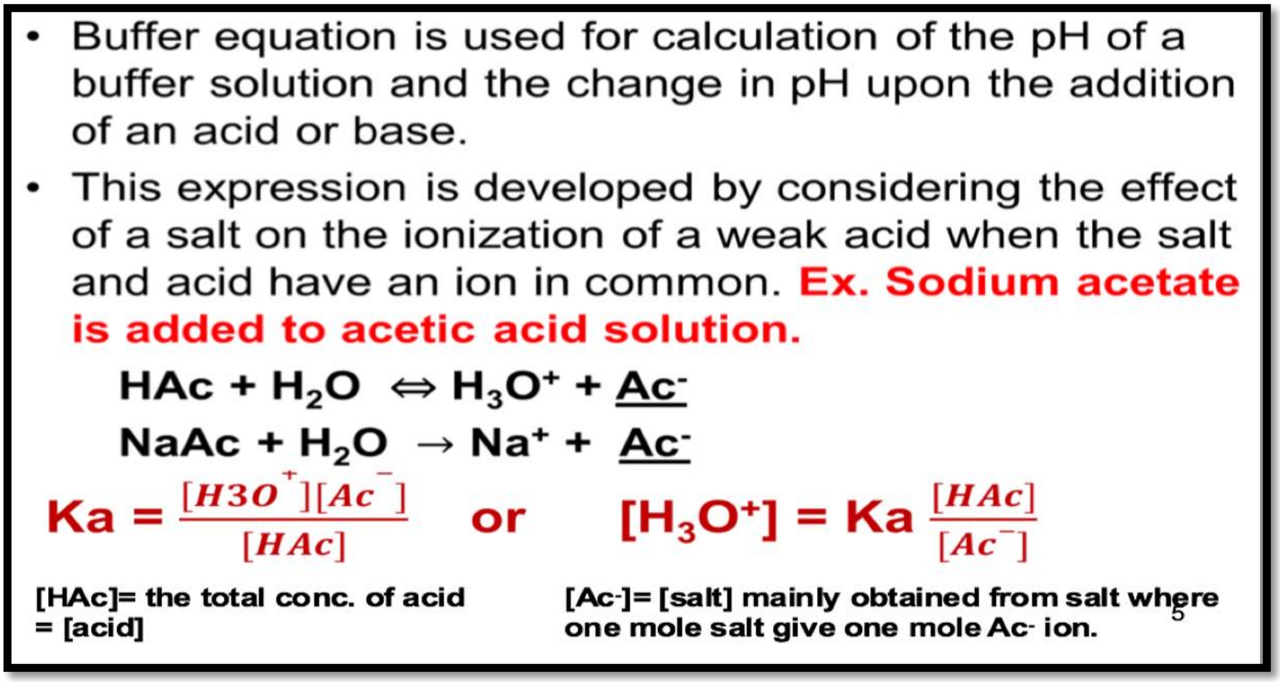
Here, $[Ac^-]$ spp. Will reduce $[H_3O^+]$ spp. As in eq.

$$Ac^- + H_3O^+ \Leftrightarrow HAc + H_2O$$

while if a strong base like NaOH is added to the same buffer, acetic acid spp. will neutralize the $[OH^-]$ spp. As in:

$$HAc + OH^- \Leftrightarrow H_2O + Ac^-$$

The buffer equation



- Buffer equation is used for calculation of the pH of a buffer solution and the change in pH upon the addition of an acid or base.
- This expression is developed by considering the effect of a salt on the ionization of a weak acid when the salt and acid have an ion in common. **Ex. Sodium acetate is added to acetic acid solution.**

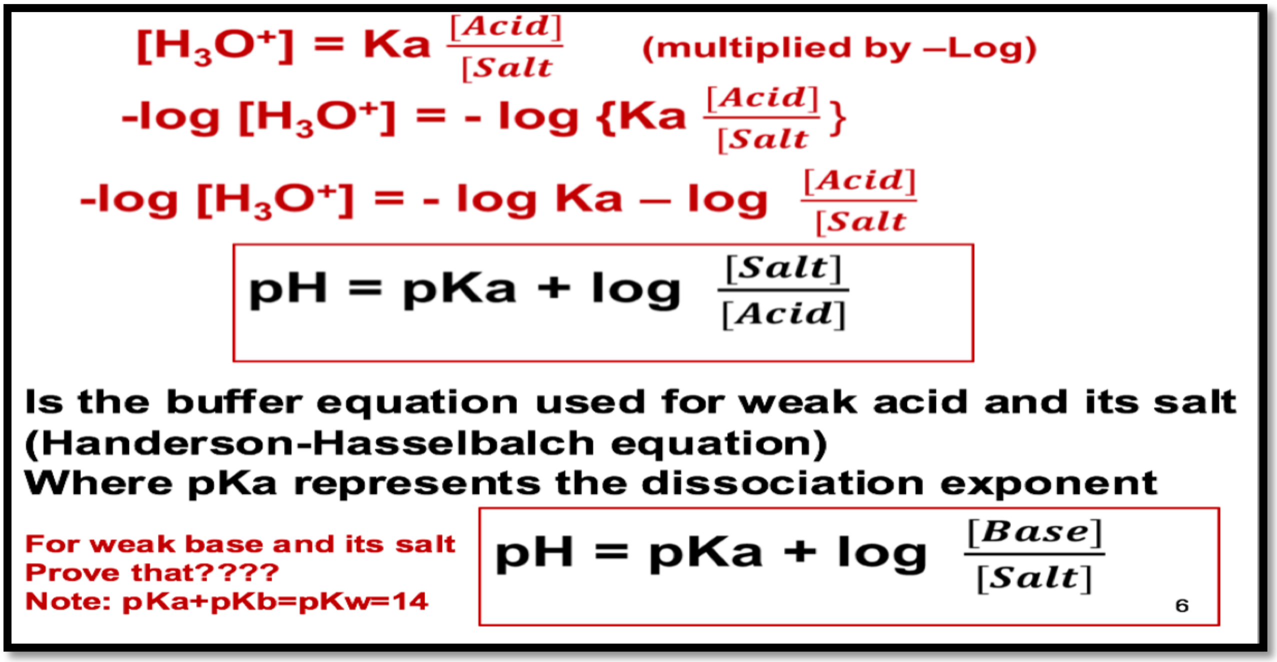
$$HAc + H_2O \Leftrightarrow H_3O^+ + \underline{Ac^-}$$

$$NaAc + H_2O \rightarrow Na^+ + \underline{Ac^-}$$

$$Ka = \frac{[H3O^+][Ac^-]}{[HAc]} \quad \text{or} \quad [H_3O^+] = Ka\,\frac{[HAc]}{[Ac^-]}$$

[HAc]= the total conc. of acid = [acid]

[Ac⁻]= [salt] mainly obtained from salt where one mole salt give one mole Ac⁻ ion.



$$[H_3O^+] = Ka\,\frac{[Acid]}{[Salt} \qquad \text{(multiplied by –Log)}$$

$$-\log [H_3O^+] = -\log \{Ka\,\frac{[Acid]}{[Salt}\}$$

$$-\log [H_3O^+] = -\log Ka - \log \frac{[Acid]}{[Salt}$$

$$\boxed{pH = pKa + \log \frac{[Salt]}{[Acid]}}$$

Is the buffer equation used for weak acid and its salt (Handerson-Hasselbalch equation)
Where pKa represents the dissociation exponent

For weak base and its salt
Prove that????
Note: pKa+pKb=pKw=14

$$\boxed{pH = pKa + \log \frac{[Base]}{[Salt]}}$$

Example: What is the molar ratio [Salt]/ [Acid] required to prepare an acetate buffer at pH= 5 (pK_a= 4.76)?

Solution:

$$5.0 = 4.76 + \log \frac{[\text{Salt}]}{[\text{Acid}]}$$

$$\log \frac{[\text{Salt}]}{[\text{Acid}]} = 5.0 - 4.76 = 0.24$$

$$\frac{[\text{Salt}]}{[\text{Acid}]} = \text{antilog}\, 0.24 = 1.74$$

Therefore, the mole ratio of salt to acid is 1.74/1. Mole percent is mole fraction multiplied by 100. The mole fraction of salt in the salt–acid mixture is 1.74/(1 + 1.74) = 0.635, and in mole percent, the result is 63.5%.

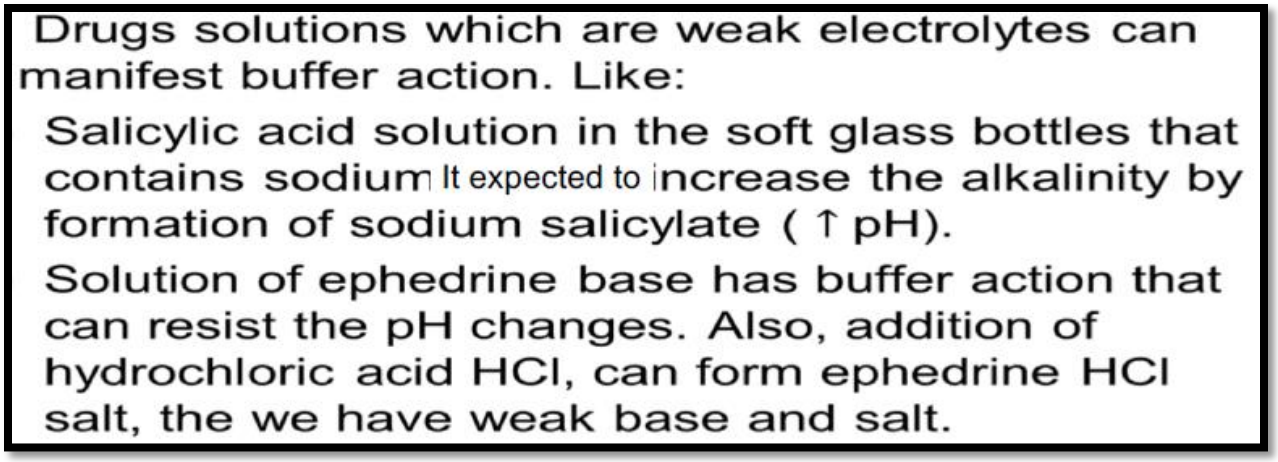
Factors affecting pH of buffer solutions

1) Addition of neutral salt, can change pH by altering the ionic strength.
2) Dilution (water addition), can change pH by altering the ionic strength (depending on the dilution value), so we have positive dilution (↑ pH) and negative dilution (↓ pH).
3) Temperature, can affect the basic buffers more than acidic one by affecting Kw value.

Acetate buffer pH increase with temp. while borate buffer pH decrease

Note: Dilution value*:* is the change in pH on diluting the buffer solution to one half of its original strength.

Drugs as Buffer

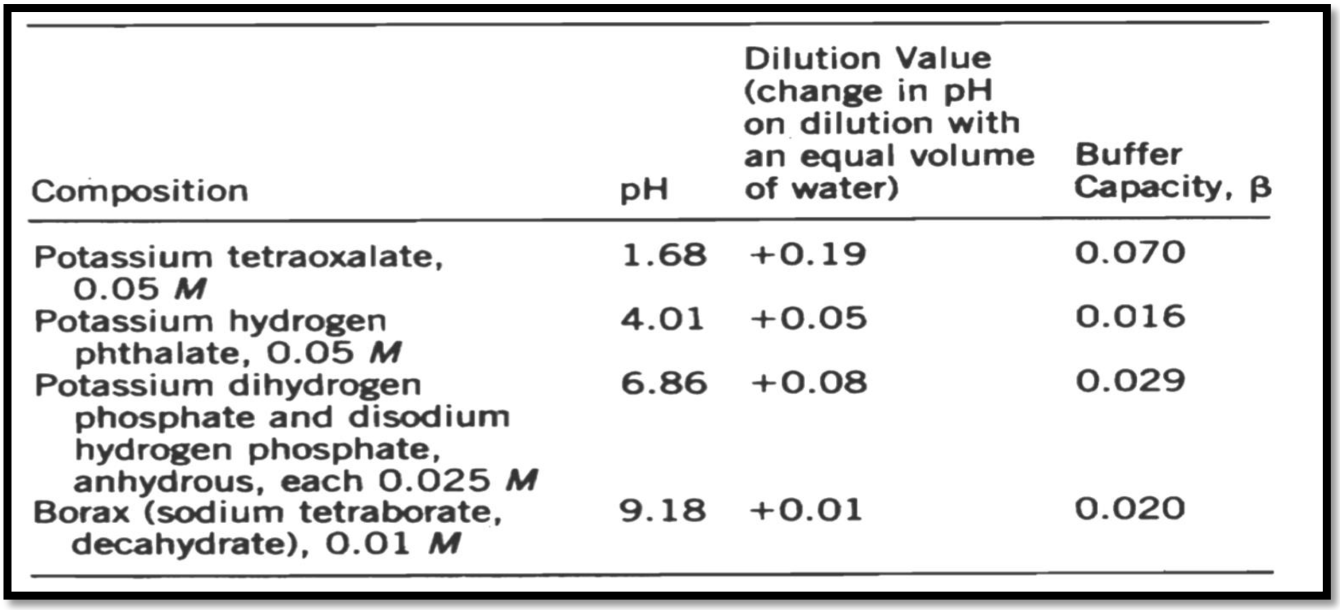


Drugs solutions which are weak electrolytes can manifest buffer action. Like:

Salicylic acid solution in the soft glass bottles that contains sodium It expected to increase the alkalinity by formation of sodium salicylate (↑ pH).

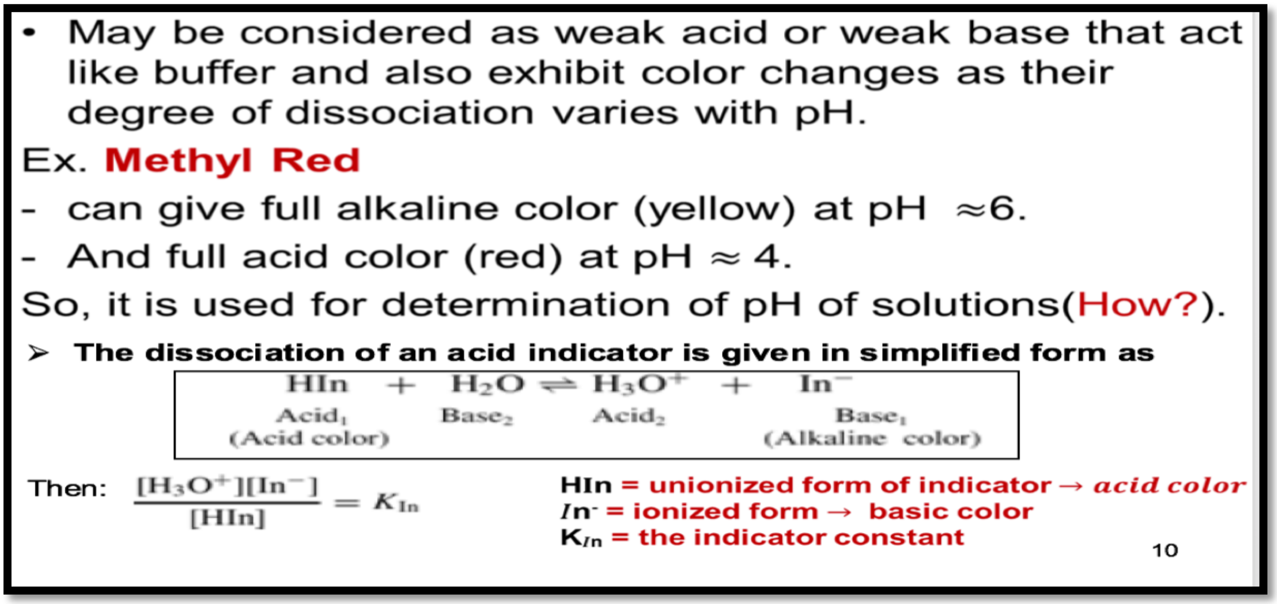
Solution of ephedrine base has buffer action that can resist the pH changes. Also, addition of hydrochloric acid HCl, can form ephedrine HCl salt, the we have weak base and salt.

Note: These actions are often weak (only one definite pH range) to counteract the pH changes brought about by CO_2 of the air and the bottle alkalinity, so the buffers must be added.



Composition	pH	Dilution Value (change in pH on dilution with an equal volume of water)	Buffer Capacity, β
Potassium tetraoxalate, 0.05 *M*	1.68	+0.19	0.070
Potassium hydrogen phthalate, 0.05 *M*	4.01	+0.05	0.016
Potassium dihydrogen phosphate and disodium hydrogen phosphate, anhydrous, each 0.025 *M*	6.86	+0.08	0.029
Borax (sodium tetraborate, decahydrate), 0.01 *M*	9.18	+0.01	0.020

pH Indicators



- May be considered as weak acid or weak base that act like buffer and also exhibit color changes as their degree of dissociation varies with pH.

Ex. **Methyl Red**

- can give full alkaline color (yellow) at pH ≈6.
- And full acid color (red) at pH ≈ 4.

So, it is used for determination of pH of solutions(How?).

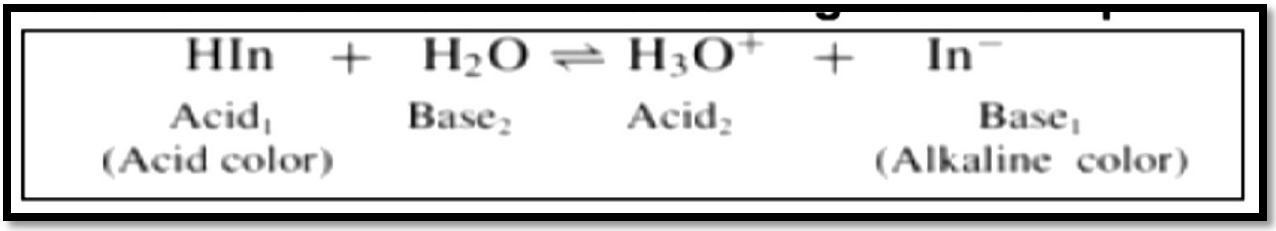
➢ **The dissociation of an acid indicator is given in simplified form as**

$$\underset{\substack{\text{Acid}_1\\\text{(Acid color)}}}{HIn} + \underset{\text{Base}_2}{H_2O} \rightleftharpoons \underset{\text{Acid}_2}{H_3O^+} + \underset{\substack{\text{Base}_1\\\text{(Alkaline color)}}}{In^-}$$

Then: $$\frac{[H_3O^+][In^-]}{[HIn]} = K_{In}$$

HIn = unionized form of indicator → *acid color*
In^- = ionized form → basic color
K_{In} = the indicator constant

10



$$\underset{\substack{\text{Acid}_1\\\text{(Acid color)}}}{HIn} + \underset{\text{Base}_2}{H_2O} \rightleftharpoons \underset{\text{Acid}_2}{H_3O^+} + \underset{\substack{\text{Base}_1\\\text{(Alkaline color)}}}{In^-}$$

The color of indicator is a function of pH of the solution, how?

- If acid is added to the solution of indicator, this causes increase in $[H_3O^+]$ shifting the reaction toward lift (common ion effect) forming more $[HIn]$= predominant → ***acid red color***.
- If base is added, causing decrease in $[H_3O^+]$ by reaction with acid, shifting the reaction toward right, forming more ionized form $[In^-]$

→ **Base yellow color** **Is predominant**

Colorimetric methods for pH calculation

- **Applications:**

1. Less expensive compare to other methods
2. Used for non-color aqueous solution
3. Used for non-aqueous solutions

- **Limitations:**

1. less accurate and less convenient.
2. They are acid or bases and if added to buffered solution causing significant change in pH.

Buffer capacity

Or **buffer efficiency**, **buffer index** or **value**, represents the magnitude of The resistance of a buffer to pH changes. Or the ratio of the increment of Strong base (or acid) to the small changes in pH brought about by this Addition

$$\beta = \frac{\Delta B}{\Delta pH}$$

Where, $\Delta\ is\ delta = a finite\ change$
$\Delta\ B = the\ small\ increment\ in\ gram\ equivalent\ per\ liter\ of\ strong\ base\ added\ to\ the\ buffer\ solution\ to\ produce\ a\ pH\ change\ of$ (ΔpH).

Then, according to this equation, addition of one gram equivalent of strong base (Or acid) to one liter of the buffer solution results in the change of one pH unit.

How can you make an approximate calculation for buffer capacity?

For example: Acetate buffer containing (**0.1mole** each of acetic acid and sodium acetate in one liter of solution) to which **0.01mole** of NaOH is added

Resulting in increase of salt conc. $[Na^+ \; Ac^-]$ by (0.01 mole/liter), and [HAc] conc. decreases proportionally because each increment of base converts 0.01mole of acetic acid into 0.01mole of sodium acetate according to the following equation:

$$\begin{array}{cccc} \text{HAc} & + \text{NaOH} \rightleftharpoons & \text{NaAc} & + H_2O \\ (0.1 - 0.01) & (0.01) & (0.1 + 0.01) & \end{array}$$

And

$$\text{pH} = \text{p}K_a + \log \frac{[\text{Salt}] + [\text{Base}]}{[\text{Acid}] - [\text{Base}]}$$

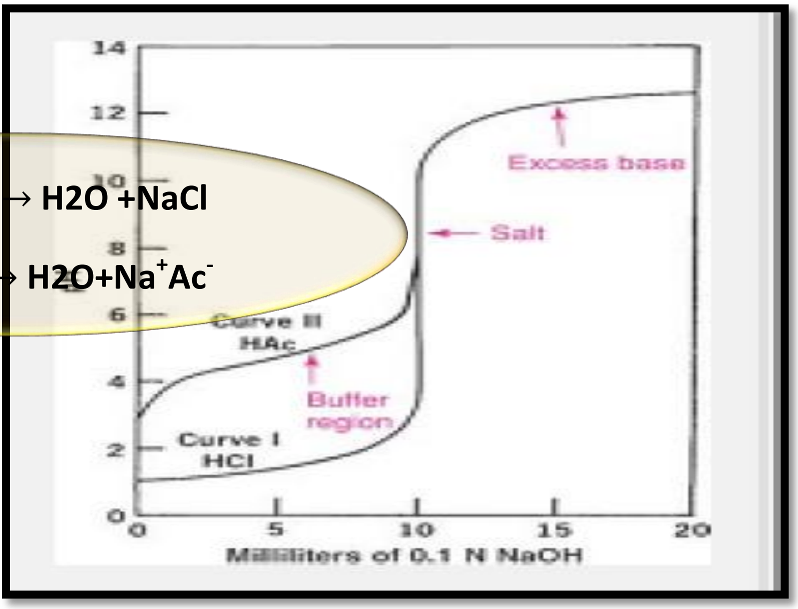
Buffer capacity

The buffer capacity depends on:

- the value of the ratio **[salt]/[acid]**, increasing as the ratio approaches unity
- The magnitude of the **individual concentrations** of the buffer components, the buffer becoming more efficient as the salt and acid concentrations are increased.

Neutralization curves and buffer capacity:

By considering the titration curves of strong and weak acids when they are mixed with increasing quantities of alkali, the reaction of an equivalent of an acid with an equivalent of the base called neutralization.



$HCl + NaOH \rightarrow H_2O + NaCl$

$HCl + NaOH \rightarrow H_2O + Na^+Ac^-$

Physical pharmacy – lecture 11

Buffer Solutions

November – 2021

Buffers in Pharma. & Biological systems

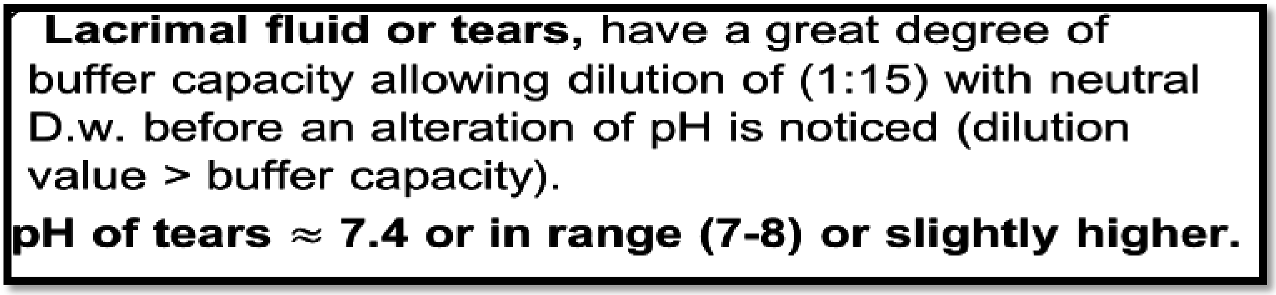
In vivo biologic buffer system:

- **Blood** maintained the pH at **7.4** by so-called primary buffers in **the plasma** and the secondary buffers in **the erythrocytes**.

Plasma contains (carbonic acid/bicarbonate, acid/alkali salts of Phosphoric acid and plasma proteins).

Erythrocytes contain two buffer systems (hemoglobin/ox hemoglobin and acid/alkali potassium salts of phosphoric acid).

- It is usually life threatening for the pH of the blood to go below 6.9 or above 7.8, as in diabetic coma (pH as low as 6.8). Then, it is important for maintaining pH in a range of (7-718.8)



Lacrimal fluid or tears, have a great degree of buffer capacity allowing dilution of (1:15) with neutral D.w. before an alteration of pH is noticed (dilution value > buffer capacity).

pH of tears ≈ 7.4 or in range (7-8) or slightly higher.

For urine, the 24-hr. urine collection of a normal adult have the pH averaging about 6 units, or it may be as low as 4.5 or as high as 7.8.

When the pH of urine is below normal value, hydrogen ions are excreted by kidney. Conversely when the pH is about 7.4, Hydrogen ions are retained by the kidney action.

Pharmaceutical buffers:

Are used for:

1. Formulation of ophthalmic solutions
2. Colorimetric determination of pH
3. Research studies in which pH must be held constant

There are different types with different pH ranges containing mixtures of solutions (found in pharmacopeia) with or without is tonicity enhancer (like NaCl).

1. Mixtures of boric acid and monohydrated sodium bicarbonate at various proportions with pH range 5-9.
2. Mixtures of the salts of sodium phosphate, pH range 6-8.
3. Boric acid and sodium borate range 7-9.
4. NaOH and KH_2PO_4 , range 5.8-8

Influence of buffer capacity and pH on tissue irritation:

• Tissue irritation, due to large pH differences between the solution being administered and the physiologic environment in which it is used, will be **minimal**:

(a) The **lower** the buffer capacity of the solution,

(b) The **smaller** the volume used, for a given concentration, and

(c) The **larger** the volume and buffer capacity of the physiologic fluid.

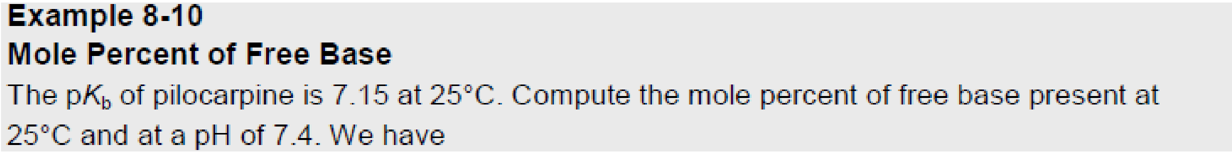
Buffer capacity and tissue irritation:

- Eye irritation may be resulted from the presence of free form of a drug at the physiologic pH; it is more often due to the acidity of the eye solution.
- Phosphate buffer can cause more irritation than boric acid buffer due to higher buffer capacity of pH. Buffer.
- Parenteral solution are usually not buffered or they are buffered to a low capacity so that, the buffer of the blood may readily bring them within the physiologic pH range.
- For oral administration, like aspirin is absorbed more rapidly in system buffered at low buffer capacity than in system containing no buffer or in highly buffered preparations. Gastric irritation is also affected by buffer capacity.

Stability versus optimum therapeutic response:

Dissociated form of weakly acidic or basic drugs often has a higher therapeutic activity than the dissociated salt form (less lipophilic).

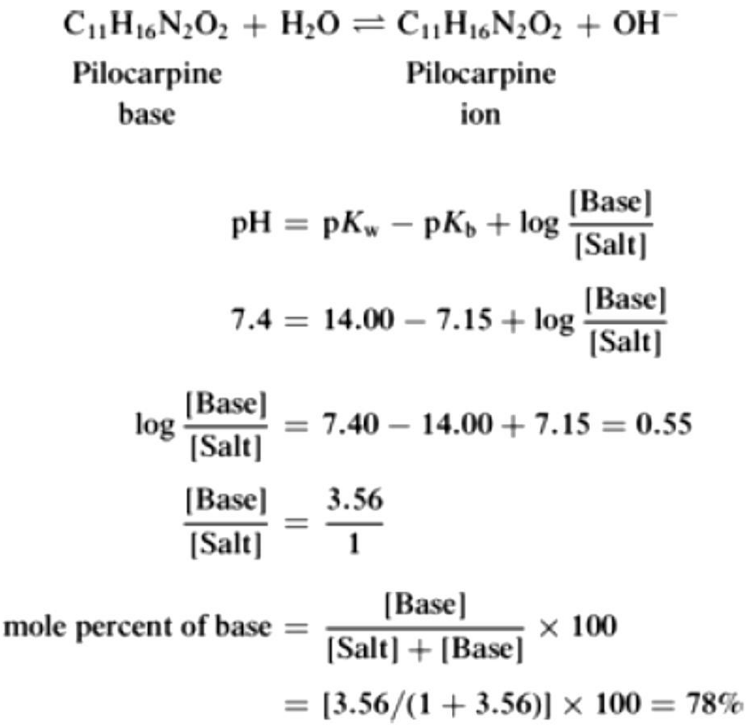
- For ophthalmic drugs (weakly basic alkaloid, pilocarpine, pk_b= 7.15), therapeutic response is increased as the pH of solution and hence the concentration of the dissociated base were increased.
- At low pH about 4, ionic form predominates, so low penetration or slow.
- Tears with pH about 7.4, the drug found mainly in free base form.



Example 8-10

Mole Percent of Free Base

The pK_b of pilocarpine is 7.15 at 25°C. Compute the mole percent of free base present at 25°C and at a pH of 7.4. We have



$$\underset{\text{Pilocarpine base}}{C_{11}H_{16}N_2O_2} + H_2O \rightleftharpoons \underset{\text{Pilocarpine ion}}{C_{11}H_{16}N_2O_2} + OH^-$$

$$pH = pK_w - pK_b + \log \frac{[\text{Base}]}{[\text{Salt}]}$$

$$7.4 = 14.00 - 7.15 + \log \frac{[\text{Base}]}{[\text{Salt}]}$$

$$\log \frac{[\text{Base}]}{[\text{Salt}]} = 7.40 - 14.00 + 7.15 = 0.55$$

$$\frac{[\text{Base}]}{[\text{Salt}]} = \frac{3.56}{1}$$

$$\text{mole percent of base} = \frac{[\text{Base}]}{[\text{Salt}] + [\text{Base}]} \times 100$$

$$= [3.56/(1 + 3.56)] \times 100 = 78\%$$

The solutions of drugs can be buffered al a low buffer capacity and at pH that is a compromise between that of optimum stability and the pH for maximum therapeutic action.

pH & Solubility

The influence of buffering on the solubility of an alkaloidal base:

- At a low pH, a base is predominantly in the ionic form, which is usually very soluble in aqueous media.
- As the pH is raised, more dissociated base is formed.
- When the amount of base exceeds the limited water solubility of this form, free base precipitates from solution.
- Therefore, the solution should be buffered at a sufficiently low pH so that the concentration of alkaloidal base in equilibrium with its salt is calculated to be **less** than the solubility of the free base at the storage temperature.
- Stabilization against precipitation can thus be maintained.

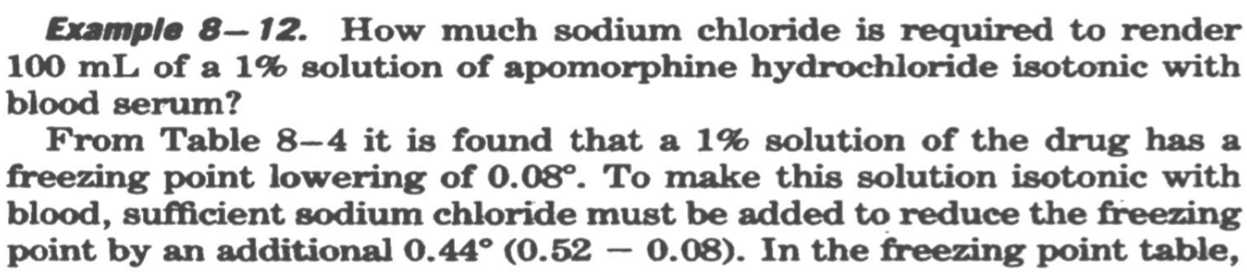
Buffered isotonic solutions

Isotonic solutions cause no swelling or contraction of the tissues with which they come in contact, and produce no discomfort when instilled in the eye, nasal tract, blood, or other body tissues.

Hypertonic solution: ….. Shrink RBCs
Hypotonic solution: ……. Haemolysis

Methods of Adjusting Tonicity & Ph

Cryoscopic Method: L iso



Example 8–12. How much sodium chloride is required to render 100 mL of a 1% solution of apomorphine hydrochloride isotonic with blood serum?

From Table 8–4 it is found that a 1% solution of the drug has a freezing point lowering of 0.08°. To make this solution isotonic with blood, sufficient sodium chloride must be added to reduce the freezing point by an additional 0.44° (0.52 − 0.08). In the freezing point table, it is also observed that a 1% solution of sodium chloride has a freezing point lowering of 0.58°. By the method of proportion,

$$\frac{1\%}{X} = \frac{0.58°}{0.44°}\,;\ X = 0.76\%$$

Thus, 0.76% sodium chloride will lower the freezing point the required 0.44° and will render the solution isotonic. The solution is prepared by dissolving 1.0 g of apomorphine hydrochloride and 0.76 g of sodium chloride in sufficient water to make 100 mL of solution.

Sodium Chloride Equivalent Method:

$$E \cong 17\,\frac{L_{iso}}{MW} \qquad (8\text{–}45)$$

Example 8–13. Calculate the approximate E value for a new amphetamine hydrochloride derivative (molecular weight 187).

Since this drug is a uni-univalent salt, it has an L_{iso} value of 3.4. Its E value is calculated from equation (8–45):

$$E = 17\,\frac{3.4}{187} = 0.31$$

Sodium Chloride Equivalent Method:

Example 8–14. A solution contains 1.0 g ephedrine sulfate in a volume of 100 mL. What quantity of sodium chloride must be added to make the solution isotonic? How much dextrose would be required for this purpose?

The quantity of the drug is multiplied by its sodium chloride equivalent E, giving the weight of sodium chloride to which the quantity of drug is equivalent in osmotic pressure

Ephedrine sulfate: 1.0 g × 0.23 = 0.23 g

The ephedrine sulfate has contributed a weight of material osmotically equivalent to 0.23 g of sodium chloride. Since a total of 0.9 g of sodium chloride is required for isotonicity, 0.67 g (0.90 − 0.23) of NaCl must be added.

If one desired to use dextrose instead of sodium chloride to adjust the tonicity, the quantity would be estimated by setting up the following proportion. Since the sodium chloride equivalent of dextrose is 0.16,

$$\frac{1\text{ g dextrose}}{0.16\text{ g NaCl}} = \frac{X}{0.67\text{ g NaCl}}$$

$$X = 4.2\text{ g of dextrose}$$