Pharmaceutical Analytical Chemistry I

الأستاذ الدكتور جمعه الزهوري (دكتوراه صيدلة-ألمانيا 1991)

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Acids And Bases

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Concept of Acid-Base

· **acid – base theories**

•**pKa**

•**pH**

•**Calculation of pH value in different solution.**

•**Buffers solution**

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اكتشاف الحموض :

إن العلماء العرب المسلمين هم أول من عرفو الحموض منذ القرنين الثاني والثالث للهجرة (فقد ورد في كتاب معجم مشاهير الكيميائيين في العالم Lexikon der bedeudender chemiker الصادر عن جامعة لايبزيغ الألمانية) أن :

1-أبو بكر محمد بن يحيى بن ذكريا **الرازي** (240 – 320 هجري) المولود في 865 م في الري بالقرب من طهران والذي سمي بجالينوس عصره والذي عاش 30 عام في بغداد هو أول من حضر **حمض الكبريت** وسماه زيت الزاج لأنه استخلصه من الزاج الأخضر (كبريتات النحاس اللامائية) ، وللرازي حوالي 200 كتاب في الكيمياء والطب ، أشهر كتبه بالطب هو الحاوي في علم الداوي الذي ترجم لمعظم لغات العالم ودرس حتى نهاية القرن الثامن عشر في جامعات أوربا حتى أنه عندما تهدمت جامعة باريس بالقرن الرابع عشر وأرادو أن يقوموا بترميمها فاحتاجو لبعض المال فلم يجدو من يسلفهما المال إلا بعد أن استودعوا لدية الحاوي للرازي وكان منه نسختان احداهما في بغداد والأخرى في جامعة باريس .

ألف الرازي كتاب في الكيمياء وحمله للخليفة المنصور الساماني والي خراسان فأعجب به المنصور وكافأه بألف دينار ، ولكنه سأله بأن يخرج هذا الذي ذكر في الكتاب إلى حيز الفعل (تحويل المعادن الخسيسة لذهب) وعندما لم يستطع أمر بضربه على رأسه بالكتاب حتى يتمزق مما سبب له العمى .

2-أبو موسى جابر **بن حيان** الكوفي : عاش بالقرن الثاني للهجرة و هو مكتشف ومستحضر **حمض الأزوت** بتقطير ملح البارود (نترات البوتاسيوم) وسماه الماء الشديد أو الماء القوي لشدة تأثيره على المعادن . أشهر كتبه مبادىء علم الكيمياء ووصية جابر المترجم للاتيني .
بكل الأحوال محاولة جابر والرازي بتحويل المعادن الخسيسة لذهب جعلتهم يكتشفو التقطير والتصعيد ، الأستخلاص ، التجميد ، ....) .
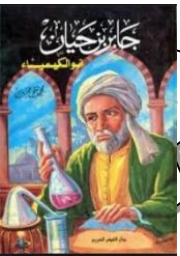
Acid

Anything that produces hydrogen ions in a water solution.

$$HCl + H_2O \longrightarrow H^+ + Cl^-$$

Base

Anything that produces hydroxide ions in a water solution

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

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Arrhenius Definition

- Acids produce hydrogen ions in aqueous solution. $HCl\ (a\ q) \longrightarrow H^+ + C\ l^-$

- Bases produce hydroxide ions when dissolved in water. $NaOH(aq) \longrightarrow Na^+ + OH^-$

- Limits to aqueous solutions.

- Only one kind of base.

- NH_3 ammonia could not be an Arrhenius base.

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Disadvantage of Arrhenius Theory

- *Unable to explain the reaction of acid and base in non aqueous media*

- *Unable to explain the mechanism of Amphotric substances*

  (Na_2HPO_4, $NaHCO_3$)

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Advantage of Arrhenius Theories

- **First Scientific Theory give definition for acid and base**

- **Helpful in aqueous media**

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Bronsted /Lowry Theory

Johannes Bronsted (1879-1947)

Thomas Lory (1874-1936)

1923 Theory

Acid = Substance that can donate proton H^+

Base = Substance that can accept proton H^+
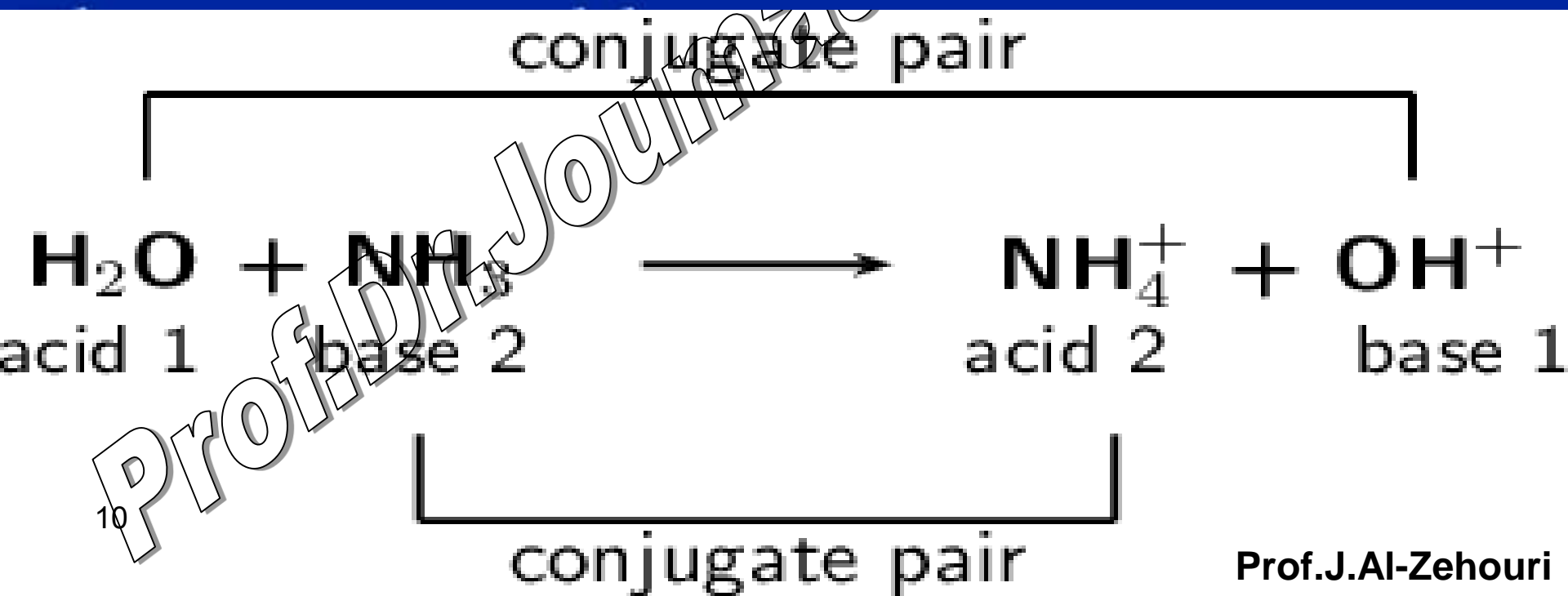
- Acid = proton donor
- Base = proton acceptor

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Pairs

General equation

$$HA(aq) + H_2O(l) \rightleftharpoons H_3O^+(aq) + A^-(aq)$$

Acid + Base $\rightleftharpoons$ Conjugate acid + Conjugate base

conjugate pair

$$H_2O + NH_3 \longrightarrow NH_4^+ + OH^+$$

acid 1   base 2   acid 2   base 1

conjugate pair

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Conjugate Pairs

$$HCl + H_2O \longrightarrow H_3O^+ + Cl^-$$

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

$$CH_3COOH + NH_3 \longrightarrow NH_4^+ + CH_3COO^-$$

$$NH_4+ + C_2H_5O^- \longrightarrow C_2H_5OH + NH_3$$

$$H_2O + NH_3 \longrightarrow NH_4^+ + OH^-$$

Conclusion

Conjugate acid–base pair

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

Weak acid Weak base Strong acid Strong base

Conjugate acid–base pair

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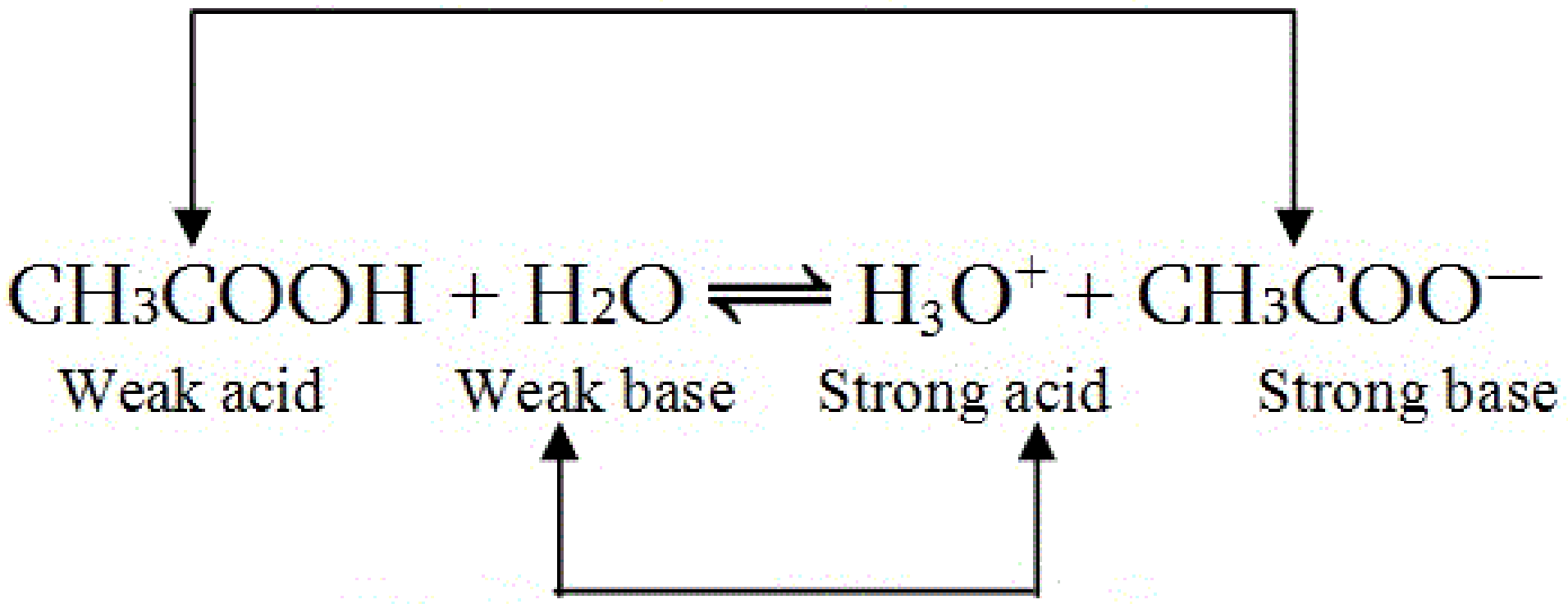
The strong of acid related to the ability of proton donor and the strong of base related to proton gainer

$$HCl + H_2O \longrightarrow H_3O^+ + Cl^-$$

$$HCl + CH_3COOH \rightleftharpoons CH_3COOH_2^+ + Cl^-$$

$$NH_3 + CH_3COOH \longrightarrow CH_3COO^- + NH_4^+$$

$$NH_3 + H_2O \rightleftharpoons OH^- + NH_4^+$$

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Water as solvent

1) Acid $NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-$

2) Base $HCl + H_2O \longrightarrow H_3O^+ + C\,l^-$

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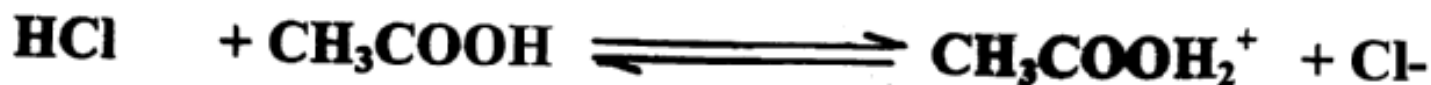
Salts behavior in aqueous media according to Bronsted –Lowry theory

$$CH_3COONa + H_2O \longrightarrow Na^+$$
$$\searrow CH_3COO^- + H_2O \longleftrightarrow CH_3COOH + OH^-$$

$$NH_4Cl + H_2O \longrightarrow Cl^-$$
$$\searrow NH_4^+ + H_2O \longleftrightarrow NH_3 + H_3O^+$$

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Acids	Bases
NH_4^+	NH_3
ACH	AC^-
HCO_3^-	CO_3^{--}
H_2SO4	$SO4^{--}$
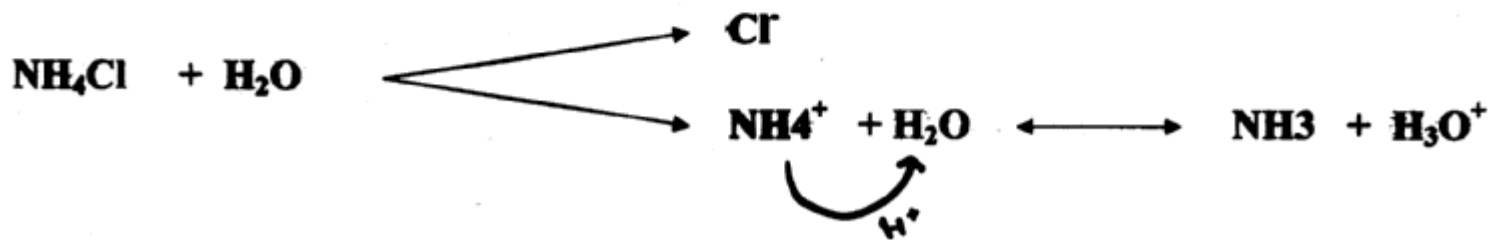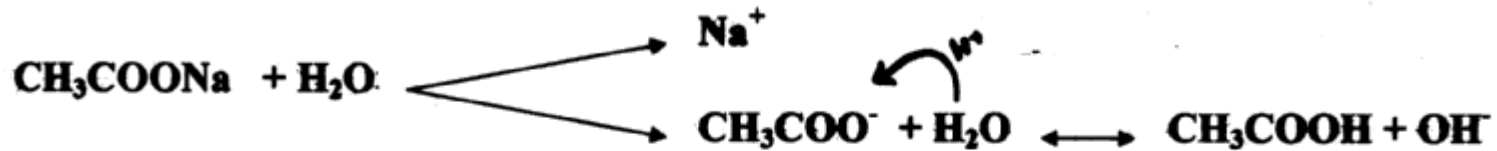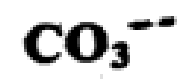
Base		Conjugate Acid
NH_3	→	NH_4^+
OH^-	→	HOH
H_2O	→	H_3O^+
CO_3^{2-}	→	HCO_3^-

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Advantage of Bronsted -Lowry Theory

- *Can explain the Behavior of Amphiprotic substance.*

- *Show the strong relation between acid and base regardless the type of solvent.*

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Classification of solvents according to Bronsted -Lowery theory

- *Amphiprotic (water)*
- *Protogenic   (Acetic acid)*
- *Protophillic   (Ammonia)*
- *Aprotic   (Benzene)*

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Disadvantage of the Bronsted – Lowry Theory

- *Unable to interpretation the acidic and basic Character for some substances which cant́ interpret with Arrhenius else.*

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Lewis Theory

Base = Substance that can donate a pair of electrons to another atom to form a new bond.

Acid = electron pair acceptor (electrophile)

Base = electron pair donor (nucleophile). It is related to compounds contain N , O,

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Lewis Acids and Bases

- Most general definition.
- Acids are electron pair acceptors.
- Bases are electron pair donors.
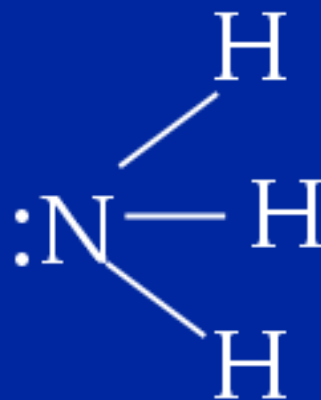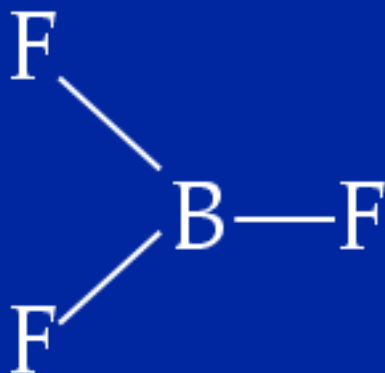
Lewis Acids and Bases

- Boron triflouride wants more electrons.
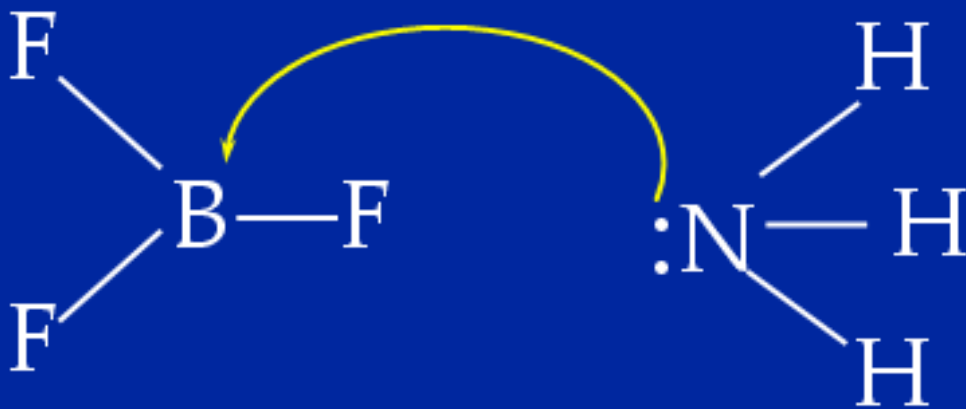
Lewis Acids and Bases
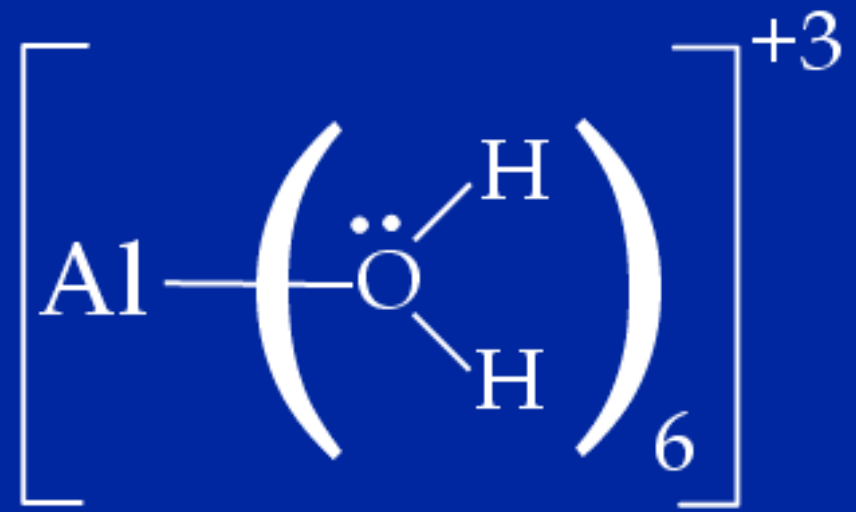
Advantage of Lewis theory

- **The ability to explain major of organic reaction.**

- **First time described the hydrogen free substance as acid. (BF_3)**

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Disadvantage of Lewis theory

- *Limited only with compound donor pair electron (must have O,N, or S).*

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Comparing between acid-base Theories

	Arrhenius	Bronsted	Lewis
Media	Aqueous	All	All
Acid	Liberate H^+	Give Proton	Receive pair electrons
Base	Liberate OH^-	Receive Proton	Donate pair electrons
Neutral reaction	Give Salt+Water	Transport the Proton from acid to the Base	Formation of Coordinate bond
Amphotric Substances	Don't mention	Give or receive proton	Don't mention

Which theories can explain the following?

$HI + H_2O \rightarrow H_3O^{+1} + I^{-1}$ Explained by all 3 theories

$HI + NH_3 \rightarrow NH_4^{+1} + I^{-1}$ Explained by BL & Lewis

$I_2 + NH_3 \rightarrow NH_3I^{+1} + I^{-1}$ Explained by Lewis

$I_2 + Cl \rightarrow ICl + I$ Cannot be explained by any of the theories

$X:^{-1} + Y^{+1} \rightarrow Y:X$ Explained by Lewis but not Arrenhius or BL

$H_2 + Cl_2 \rightarrow 2HCl$ Cannot be explained by any of the theories!

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For the following proton-transfer reaction predict whether the equilibrium lies predominately to the left or to the right:

$$HSO_4^-(aq) + CO_3^{2-}(aq) \rightleftharpoons SO_4^{2-}(aq) + HCO_3^-(aq)$$

$\longrightarrow$
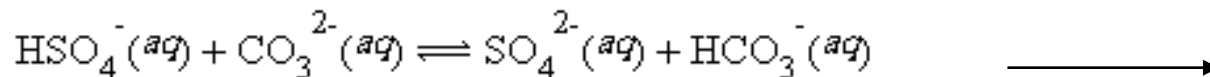
SOLUTION In this reaction the H^+ moves from HSO_4^- to CO_3^{2-}. Thus, we have

$$HSO_4^-(aq) + CO_3^{2-}(aq) \rightleftharpoons SO_4^{2-}(aq) + HCO_3^-(aq)$$

acid   base   conjugate base   conjugate acid

دائما التفاعل يفضل
تشكيل الحمض الضعيف
والأساس الضعيف
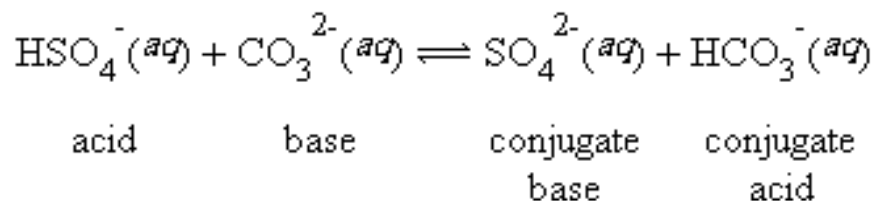
HSO_4^- is a stronger acid than HCO_3^-.

the equilibrium favors the direction in which the proton moves from the stronger acid and becomes bonded to the stronger base.

In other words, the

reaction favors formation of the weaker acid and the weaker base. Hence, the equilibrium position for this reaction lies to the right.

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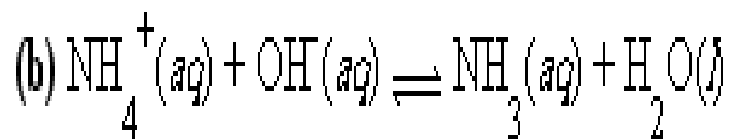## Practice Exercise

For each of the following reactions, predict whether the equilibrium lies predominately to the left or to the right:

(a) $PO_4^{3-}(aq) + H_2O(l) \rightleftharpoons HPO_4^{2-}(aq) + OH^-(aq)$ $\longleftarrow$

(b) $NH_4^+(aq) + OH^-(aq) \rightleftharpoons NH_3(aq) + H_2O(l)$ $\longrightarrow$

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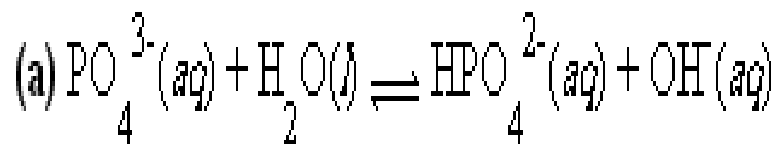
دائما التفاعل يفضل
تشكيل الحمض الضعيف
والأساس الضعيف

</div>

Answers: (a) left, (b) right

Acid dissociation constant K_a

- The equilibrium constant for the general equation.

- $HA(aq) + H_2O(l) \rightleftharpoons H_3O^+(aq) + A^-(aq)$

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

- H_3O^+ is often written H^+ ignoring the water in equation (it is implied).

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Concept of pKa

- Ka (Equilibrium constant) is very small value

  (e.g. Ka HCl = 10^{-5})

- pKa = log 1/Ka

- pKa = - log Ka

- pKa (small) $\longrightarrow$ Acid is strong

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The stronger the acid, the smaller is its pKa

- Very strong acid   pKa   < 1

  $HClO_4 \approx -10$, $HBr \approx -9$, $HCl \approx -7$, $H_2SO_4 \approx -3$, $HNO_3 \approx -1.4$

- Moderately strong acid   pKa 1-3

  $H_3PO_4 = 1.96$

- Weak acids   pKa 3 -5

  $CH_3COOH = 4.75$

- Very weak acid   pKa 5-15

  $NH_4^+ = 9.25$, $HCO_3^- \approx 10.4$, $H_2O_2 \approx 11.62$

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Acid and Base Strength

- Strong acids and Bases **completely** dissociate (ionize) in aqueous solution

$$[H^+] = [HA]$$
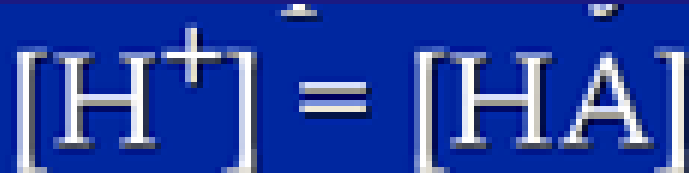
- Weak acids and Bases **incompletely** dissociate in aqueous solution

$$10^{-14} = [H^+][OH^-]$$

Some Weak Acids in Water at 25°C*

Acid	Molecular Formula	Structural Formula	Conjugate Base	K_a
Hydrofluoric	HF	H—F	F^-	6.8×10^{-4}
Nitrous	HNO_2	H—O—N=O	NO_2^-	4.5×10^{-4}
Benzoic	$HC_7H_5O_2$		$C_7H_5O_2^-$	6.5×10^{-5}
Acetic	$HC_2H_3O_2$		$C_2H_3O_2^-$	1.8×10^{-5}
Hypochlorous	HClO	H—O—Cl	ClO^-	3.0×10^{-8}
Hydrocyanic	HCN	H—C≡N	CN^-	4.9×10^{-10}
Phenol	HOC_6H_5		$C_6H_5O^-$	1.3×10^{-10}

* The proton that ionizes is shown in blue.

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Amphoteric

- Behave as both an acid and a base.
- Water autoionizes
- $2H_2O(l) \rightleftharpoons H_3O^+(aq) + OH^-(aq)$
- $K_W = [H_3O^+][OH^-] = [H^+][OH^-]$
- At 25°C $K_W = 1.0 \times 10^{-14}$
- In EVERY aqueous solution.
- Neutral solution $[H^+] = [OH^-] = 1.0 \times 10^{-7}$
- Acidic solution $[H^+] > [OH^-]$
- Basic solution $[H^+] < [OH^-]$

Back to Pairs

- Strong acids

- K_a is large

- $[H^+]$ is equal to $[HA]$

- A^- is a weaker base than water

- Weak acids

- K_a is small

- $[H^+] <<< [HA]$

- A^- is a stronger base than water

Strength of oxyacids

- The more oxygen hooked to the central atom, the more acidic the hydrogen.

- $HClO_4 > HClO_3 > HClO_2 > HClO$

- Remember that the H is attached to an oxygen atom.

- The oxygens are electronegative

- Pull electrons away from hydrogen

Scheme for Identification of Acids and Bases

Proton donor
or proton acceptor?

If proton donor,
then acid

If proton acceptor,
Then base

Inorganic

Organic

Inorganic

Organic

Strong except
HF, HCN, H_2S, H_3PO_4

Weak acid

If IA or IIA,
then strong

Weak base

Weak acid

If NH_4OH or not IA and IIA
Then weak
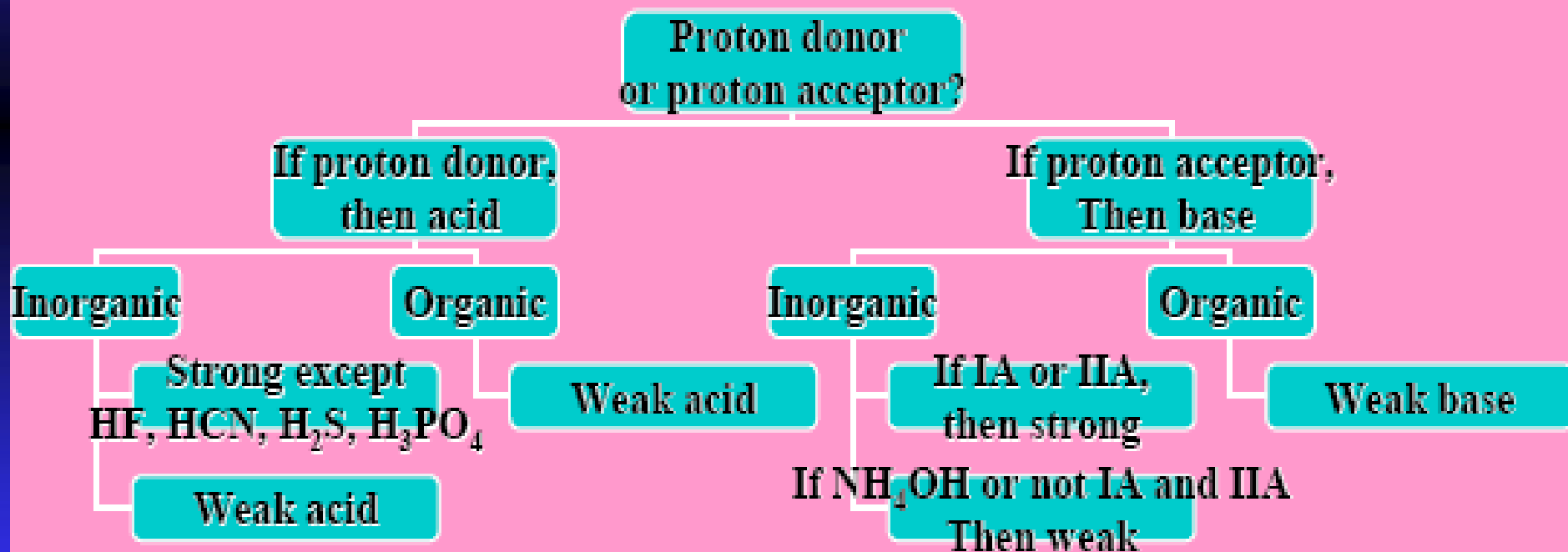
Periodic Table of the Elements

1A	2A	3B	4B	5B	6B	7B	8B	8B	8B	1B	2B	3A	4A	5A	6A	7A	8A
H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	Ac															

			Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
			Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Soren Peder Lauritz Sorensen (9 January 1868 – 12 February 1939) was a Danish chemist, famous for the introduction of the concept of pH, a scale for measuring acidity and alkalinity. He was born in Havrebjerg, Denmark.

$: (\text{Potentia Hydrogenii})\ pH$

Sorenson 1909 $pH = - \log [H^+]$

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

1) $HA \rightleftharpoons H^+ + A^-$

2) $H^+ + H_2O \rightleftharpoons H_3O^+ \Rightarrow K = \dfrac{[H_3O^+]}{[H^+][H_2O]} \Rightarrow$
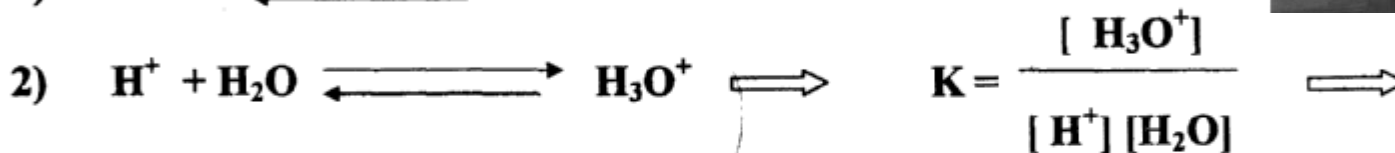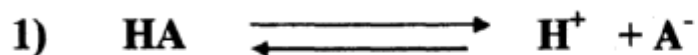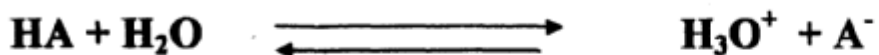
$$[H^+] = \frac{1}{K} \ \ X \ \ \frac{[H_3O^+]}{[H_2O]} \Rightarrow [H^+] = [H_3O^+]$$

$$\boxed{pH = - \log [H^+] = - \log [H_3O^+]}$$

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pH- Scale

- [H_3O+] $= 10^0 - 10^{-14}$

- $pH = - \log 10^{-14} = 14$

$1 = 10^0$

- $pH = - \log 10^0 = 0$

- pH scale 0 - 14

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$$[H^+]$$

$$10^0 \quad 10^{-1} \quad 10^{-3} \quad 10^{-5} \quad 10^{-7} \quad 10^{-9} \quad 10^{-11} \quad 10^{-13} \quad 10^{-14}$$

pH

| 0 | 1 | 3 | 5 | 7 | 9 | 11 | 13 | 14 |

Acidic   **Neutral**   **Basic**

| 14 | 13 | 11 | 9 | 7 | 5 | 3 | 1 | 0 |

pOH

$$10^{-14} \quad 10^{-13} \quad 10^{-11} \quad 10^{-9} \quad 10^{-7} \quad 10^{-5} \quad 10^{-3} \quad 10^{-1} \quad 10^0$$

$$[OH^-]$$

Relationships

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

$$pOH = -\log[OH^-] = \log\frac{1}{[OH^-]}$$

- $K_W = [H^+][OH^-]$
- $-\log K_W = -\log([H^+][OH^-])$
- $-\log K_W = -\log[H^+] + -\log[OH^-]$
- $pK_W = pH + pOH$
- $K_W = 1.0 \times 10^{-14}$
- $14.00 = pH + pOH$
- $[H^+], [OH^-], pH$ and pOH
  Given any one of these we can find the other three.

pH of pure water = 7

Calculating pH of Solutions

pH of strong acids solution

$$HCl \longrightarrow H^+ + C\,l^-$$

Ca   0   0   before dissociation

0   Ca   Ca   after dissociation
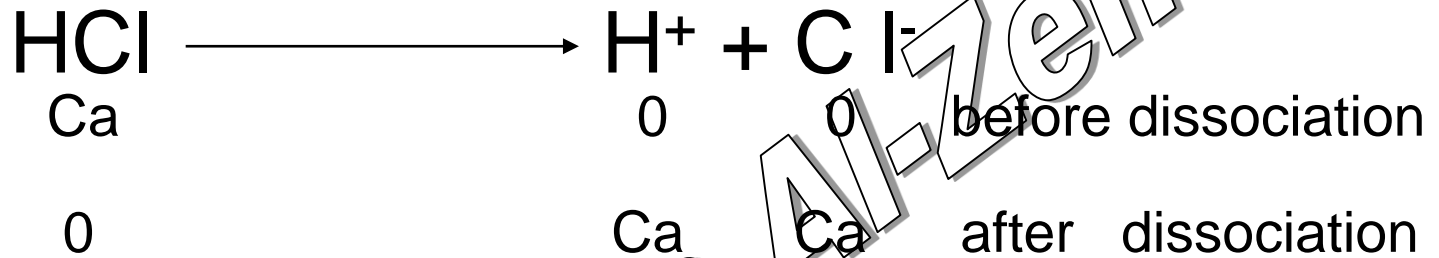
- $[C] = [H^+] = [H_3O^+]$
- $pH = -\log[H^+] = -\log C$

$$pH = -\log C$$

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pH of strong Bases solution

NaOH $\longrightarrow$ Na$^+$ + OH$^-$
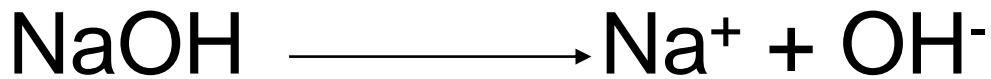
Cb   0   0   before dissociation

0   Cb   Cb   after dissociation

[C] = [OH$^-$]

pOH = -log [OH$^-$] = - log [C]

pH+pOH = 14

pH= 14-pOH   { pOH = -logOH}

pH= 14 + log OH

$$pH = 14 + \log C$$

pH of weak acids solution
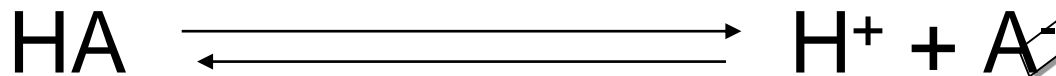
$$HA \rightleftharpoons H^+ + A^-$$

$$K_a = [H^+][A^-]/[HA] = [H^+][A^-]/C_a - [H^+]$$

$$[H^+] = [A^-]$$

$$Ka = [H^+]^2/C_a \longrightarrow [H+] = \sqrt{K_a \cdot C_a}$$

$$-\log[H^+] = -\tfrac{1}{2}\log Ka - \tfrac{1}{2}\log C$$

$$pH = \tfrac{1}{2} pKa - \tfrac{1}{2} \log c$$

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pH of weak bases solution

$B + H_2O \rightleftharpoons BH^+ + OH^-$
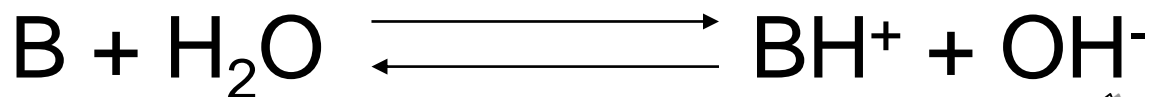
$Kb = [BH^+][OH^-]/[B]$

$\quad = [BH^+][OH^-]/C_b - [OH^-]$

$\quad = [OH^-]^2/C_b$

$[OH^-] = \sqrt{K_b \cdot C_b}$

$$pH = 7 + \tfrac{1}{2}\,pKa + \tfrac{1}{2}\,logC$$

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$$[OH^-] = \sqrt{Kb \cdot C}$$

Take the log and x(-1)

$$pOH = \frac{pKb - \log C}{2}$$

$$pH + pOH = pKw = 14$$

$$pH = 14 - \frac{pKb - \log C}{2}$$

$$pKa + pKb = 14$$

$$pH = pKa + pKb - \frac{pKb - \log C}{2}$$

$$pH = pKa + \underline{pKb - \tfrac{1}{2} pKb} + \tfrac{1}{2} \log C$$

$$pH = pKa + \tfrac{1}{2} pKb + \tfrac{1}{2} \log C$$

$$pH = \tfrac{1}{2} (2 pKa + pKb) + \tfrac{1}{2} \log C$$

$$pH = \tfrac{1}{2} (pka + 14) + \tfrac{1}{2} \log C$$

$$pH = \tfrac{1}{2} pKa + 14/2 + \tfrac{1}{2} \log C$$

$$pH = \tfrac{1}{2} pKa + \tfrac{1}{2} \log C + 7$$

$$\boxed{pH = 7 + \tfrac{1}{2} pKa + \tfrac{1}{2} \log C}$$

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pH of salt solution which formed from strong acid and strong base

$$NaCl \longrightarrow Na^+ + Cl^-$$

pH=7

pH of salt solution formed from strong acid with weak base

$$NH_4Cl \longrightarrow \begin{array}{l} NH_4^+ \longrightarrow NH_3 + H^+ \\ Cl^- \end{array}$$

$$pH = \frac{1}{2} pK_a - \frac{1}{2} \log C$$

pH of salt solution which formed from weak acid and strong base

- CH_3COONa

$$CH_3COONa \rightarrow Na^+$$
$$\searrow CH_3COO^- + H_2O \rightleftharpoons CH_3COOH + OH^-$$
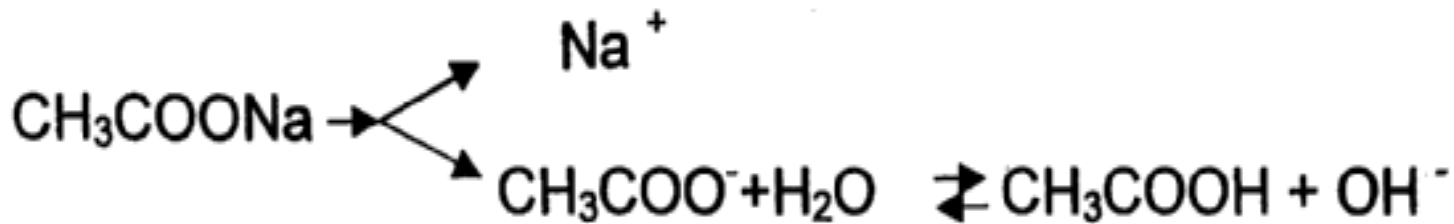
$$pH = 7 + \tfrac{1}{2}\,pKa + \tfrac{1}{2}\,\log C$$

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Buffer solution

Solution that tend to resist changes in pH as the result of dilution or the addition of small amounts of acids or bases.
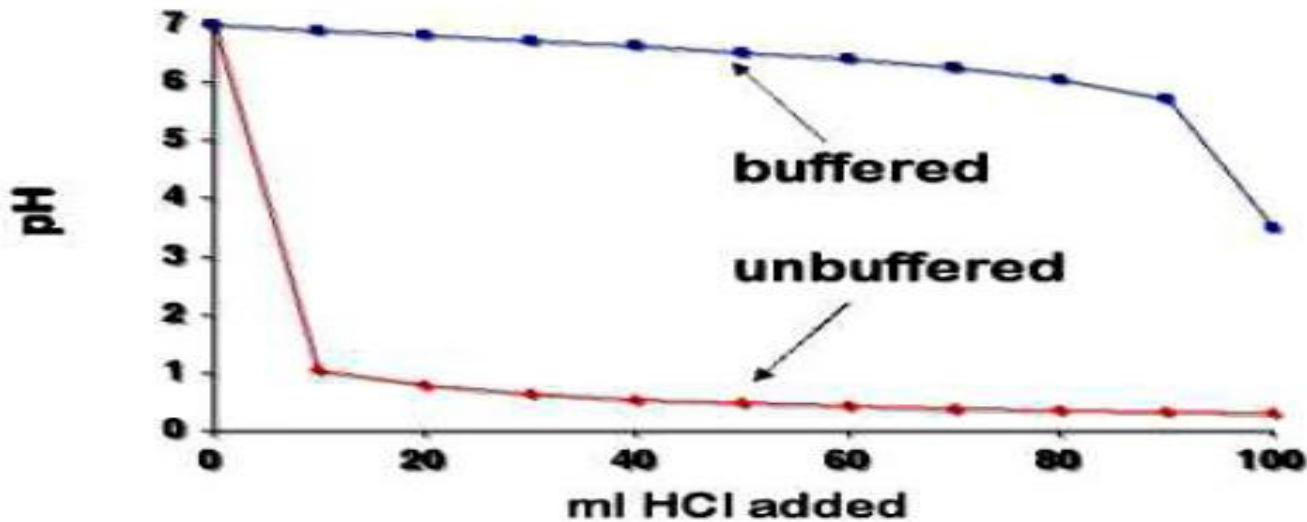
BUFFER SOLUTIONS

A buffer is a mixture of a weak acid and its conjugate base or a weak base and its conjugate acid that resists changes in pH of a solution.

(Buffer = weak acid + his salt (pH<7) or Weak base+ his salt (pH > 7)

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Calculation the pH of Buffer Solution

- CH$_3$COOH/CH$_3$COONa

$$CH_3COOH \rightleftharpoons CH_3COO^- + H^+$$

$$K_a = [CH_3COO^-] [H^+] \,'\, [CH_3COOH]$$

$$[H^+] = K_a \,.\, [CH_3COOH] / [CH_3COO^-]$$

$$\log[H^+] = \log K_a + \log [CH_3COOH] - \log [CH_3COO^-]$$

$$- \log [H^+] = - \log K_a - \log [CH_3COOH] + \log [CH_3COO^-]$$

$$pH = pK_a + \log [CH_3COO^-] / [CH_3COOH]$$

$$CH_3COONa \longrightarrow CH_3COO^- + Na^+$$

$$pH = pK_a + \log \; Cs/Ca$$

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Henderson- Hasselbalch equation

$$pH = pKa + \log \frac{\text{Concentration of Salt}}{\text{Concentration of acid}}$$

$pH = pka + \log A^-/HA$ (acid)

$pH = pKa + \log B/BH^+$ (base)

$$pH = pKa + \log \frac{[\text{nonprotonated species}]}{[\text{protonated species}]}$$
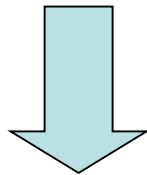
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Buffer Solution

When $C_a/C_s = 1$
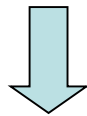
$$[H^+] = K_a$$

$$pH = pK_a$$
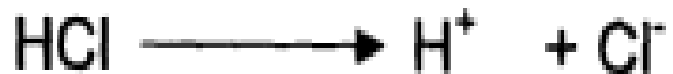
Buffer solution is more pH resistance

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Mechanism of action of the Buffers

I- (CH_3COOH/CH_3COONa)

- In case of acid addition :

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

$$H^+ + CH_3COO^- \longrightarrow CH_3COOH$$

- Strong acid changed to weak acid

- $C_a \uparrow \longrightarrow \log C_s/C_a$ (very little change)

Mechanism of action of the Buffers

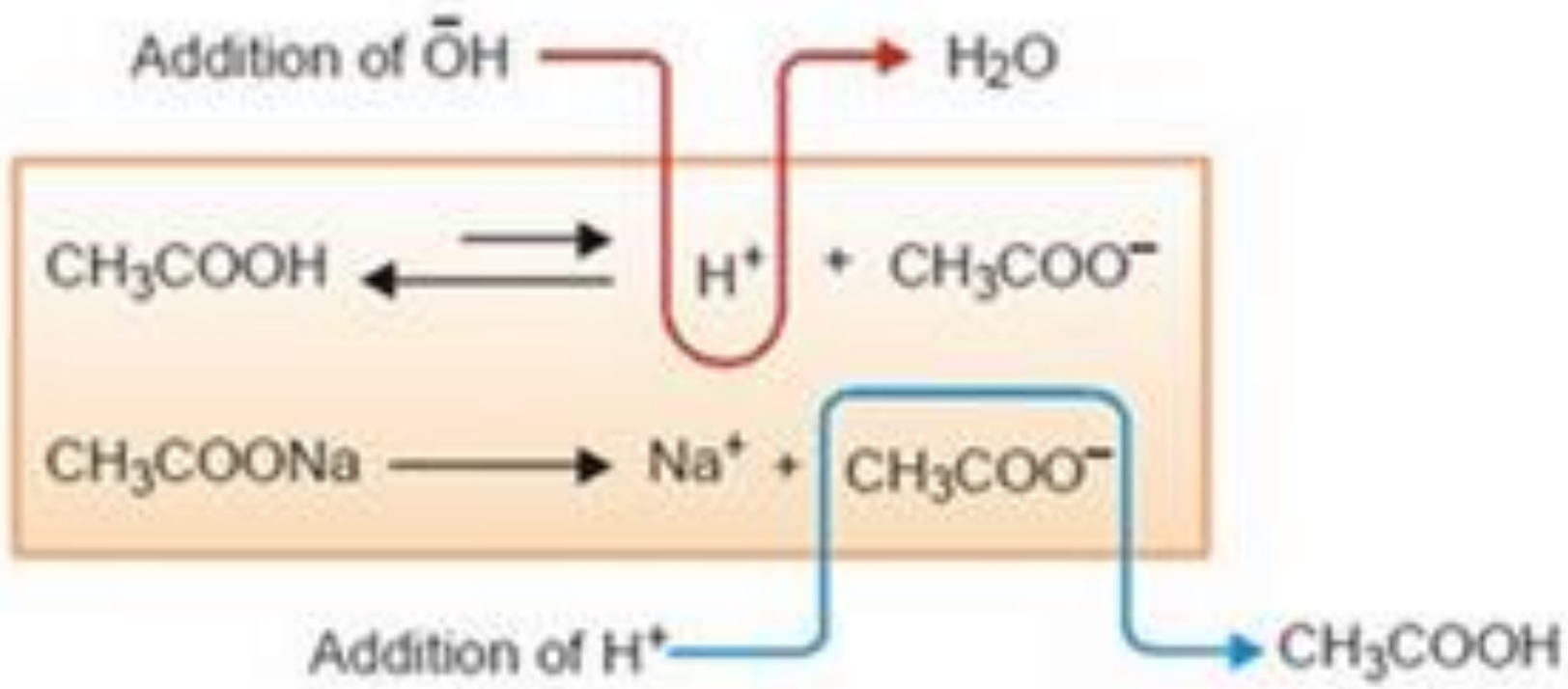## I- (CH_3COOH/CH_3COONa)

2- In case of Base addition :

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

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

- Strong Base Changed to weak base

- C_s $\log C_s/C_a$ (Very little Change)

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Mechanism of action of the Buffers

II- NH_4OH/NH_4Cl

- $NH_4OH \rightleftharpoons NH_4^+ + OH^-$

- $NH_4Cl \longrightarrow NH_4^+ + Cl^-$
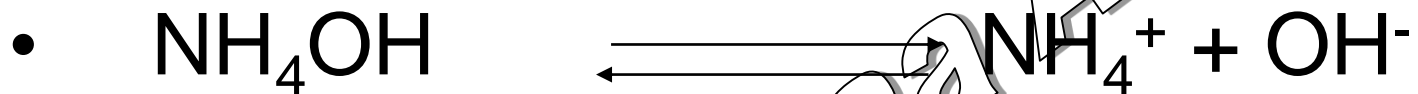
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Mechanism of action of the Buffers

II- NH_4OH/NH_4Cl

1- In case of acid addition :

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

$$H^+ + OH^- \longrightarrow H_2O$$
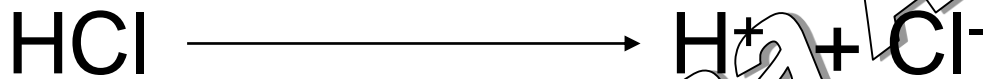
- Strong acid changed to neutral water.

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Mechanism of action of the Buffers

II- NH_4OH/NH_4Cl

2- In case of base addition :

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

$OH^- + NH_4 \longrightarrow NH_4OH \rightarrow NH_3 + H_2O$
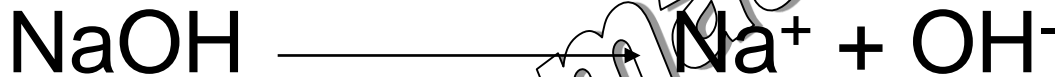
- Strong Base $\longrightarrow$ Weak base

$[NH_3] \uparrow \longrightarrow$ log NH_3/NH_4Cl (very little change)
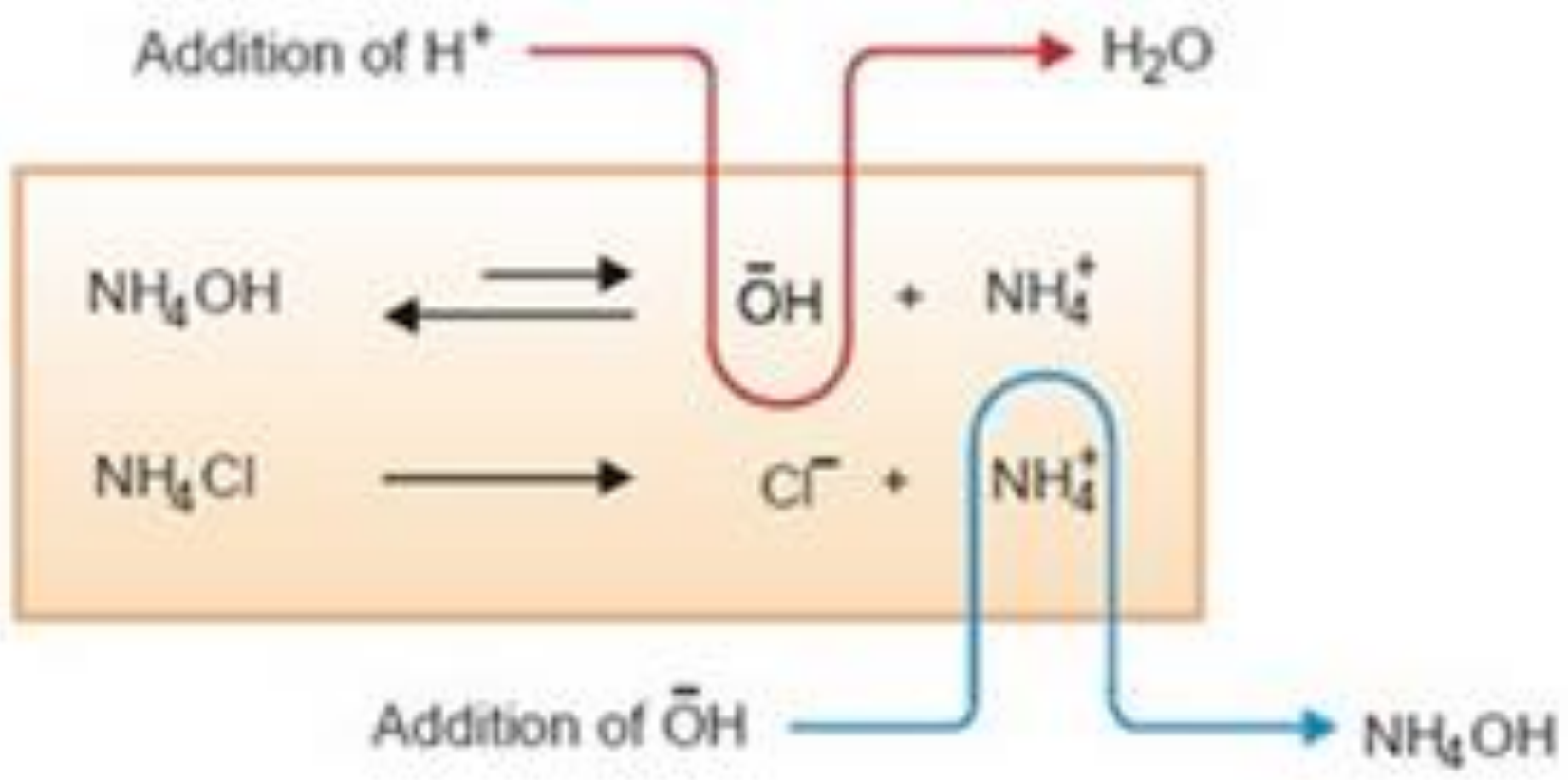
Calculate the change in pH after adding of 0.04 mol of sodium hydroxide to a liter of abuffer solution conatining 0.2 M concentrations of sodium acetate and acetic acid .The pKa value of acetic in 4.76.

$$pH = pKa + \log \frac{\text{Salt}}{\text{acid}}$$

$\Delta pH = ?$

$$= 4.76 + \log \frac{0.2}{0.2}$$

$$= 4.76 + \log 1$$

$$= 4.76 + 0 = 4.76$$

0.04 M NaOH sol.

Buffer solution 1 liter

$CH_3COOH + CH_3COONa$

0.2 M

The addition of 0.04 mol of sodium hydroxid 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 amount according to the following equation :
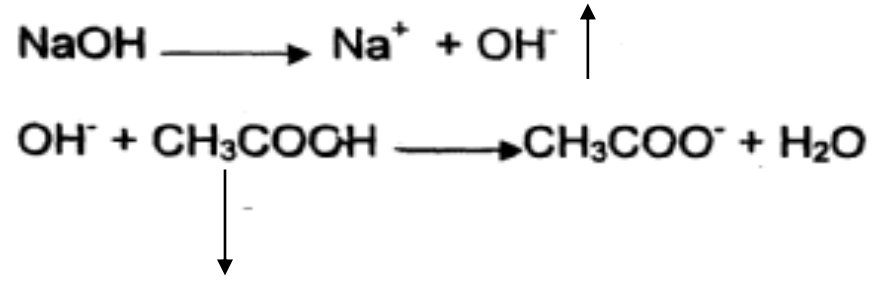
حساب pH بعد الأضافة

$$pH = pKa + \log \frac{Salt + Base}{Acid - Base}$$

$$= pKa + \log \frac{0.2 + 0.04}{0.2 - 0.04}$$

$$= pKa + \log \frac{0.24}{0.16}$$

$$pKa + \log \frac{0.24}{0.16} = 4.76 + 0.1761 = 4.94$$

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

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

Because the pH buffer before the addition of Sodium hydroxide was 4.76 ,The change in **pH= 4.94-4.76= 0.18** unit (answer)
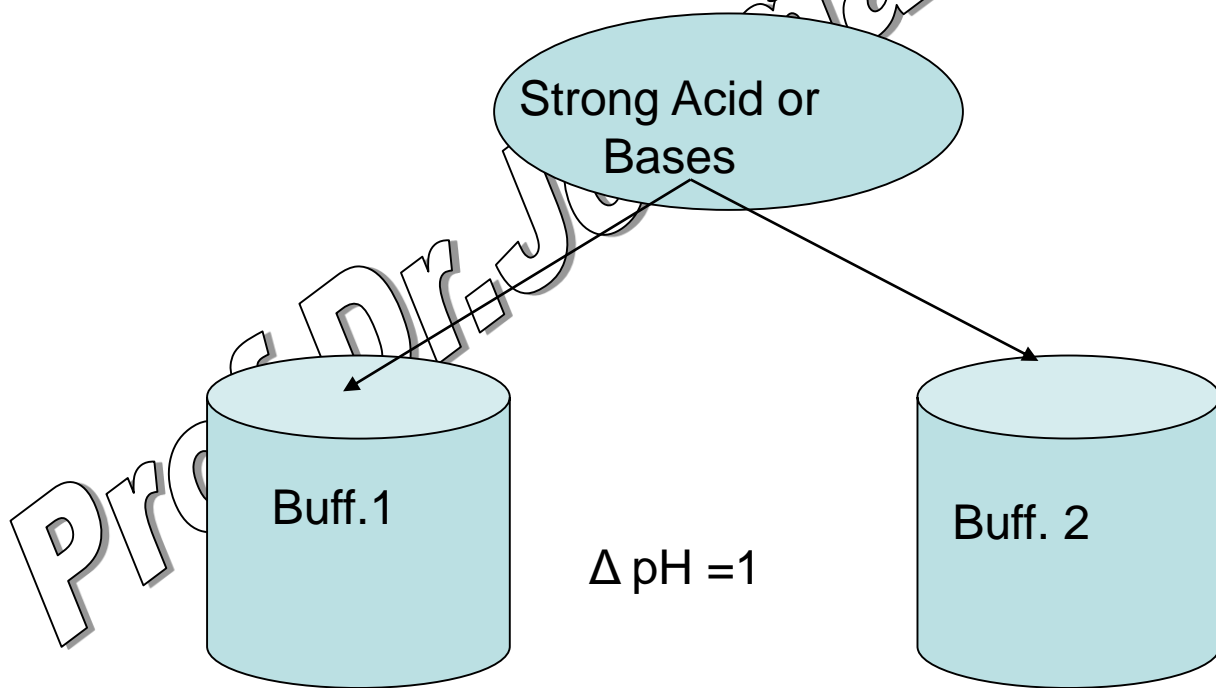
Conclusion

- Buffers do not maintain pH at an absolutely constant value, but changes in pH are relatively small when small amounts of acid or base are added.

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What is the Buffer Capacity?

- The buffer capacity of a buffer is the number of moles of strong acid or(strong base) needed to alter the pH of 1.00 L of a buffer solution by 1.00 unit.
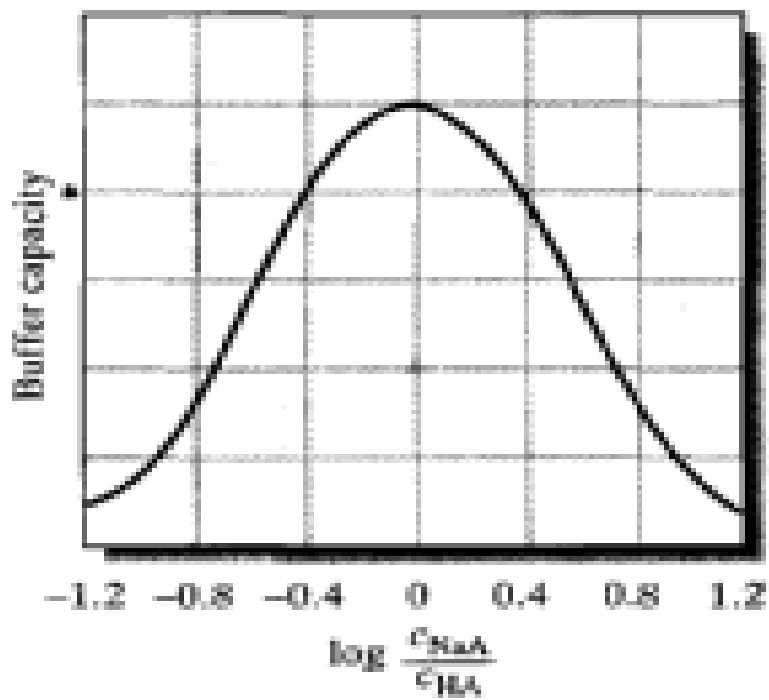
Strong Acid or Bases

الذي يستهلك عدد مولات اكثر لتغير pH درجة واحدة يكون أكثر سعة وقائية

Buff.1

Buff. 2

Δ pH =1

Buffer Capacity as a function of the ratio C_s/C_a

Ratio Cs/Ca =1   heist B.Capacity

pH table for different solutions :

Solution	pH
Strong acid	$-\log C$
Strong Base	$14 + \log C$
Weak acid	$\frac{1}{2} pKa - \frac{1}{2} \log C$
Weak base	$7 + \frac{1}{2} pKa + \frac{1}{2} \log C$
Salt from strong base and strong acid	7
Salt from strong acid and weak base	$\frac{1}{2} pKa - \frac{1}{2} \log C$
Salt from weak acid and strong base	$7 + \frac{1}{2} pKa + \frac{1}{2} \log C$
Salt from weak acid and weak base	$\frac{1}{2} pKa + \frac{1}{2} pKa$
Amphotric solution	$\frac{1}{2} pKa_1 + \frac{1}{2} pKa_2$
Buffer (weak acid + his salt)	$pK_a + \log C_s / C_a$
Buffer (weak base + his salt)	$pOH = pKb + C_s / C_b$

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Physiological Buffers

- Healthy Blood pH = (7.35-7.45) average =7.4
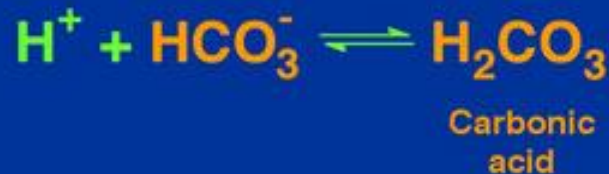
- HCO_3^- /H_2CO_3

- pH = 6.10 + log [HCO_3^-] / [H_2CO_3]
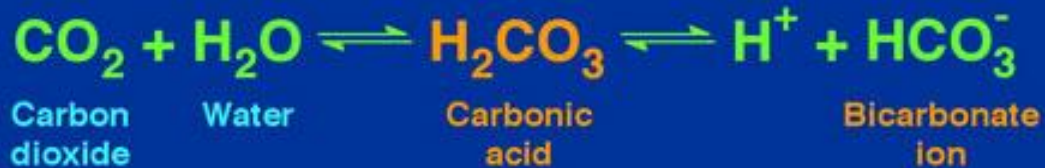
The pH of blood: The HCO_3^-/H_2CO_3 buffer system is present in blood. The pKa of plasma is 6.1 and concentration of HCO_3^- and H_2CO_3 are 0.025M and 0.00125M respectfully. Thus,

$$pH \text{ of blood} = pK_a + \log\frac{[Salt]}{[Acid]}$$

$$= 6.1 + \log\frac{0.025}{0.00125}$$

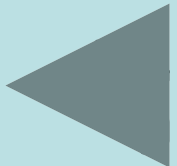$$= 7.4$$

BUFFERS MINIMIZE pH CHANGE

A buffer resists change in pH when an acid or base is added. Common buffering system, one that is in human blood, is carbonic acid and the bicarbonate ion.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

Carbon dioxide   Water   Carbonic acid   Bicarbonate ion

$$H^+ + HCO_3^- \rightleftharpoons H_2CO_3$$

Carbonic acid

$$OH^- + H_2CO_3 \longrightarrow HCO_3^- + H_2O$$

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pH- meter

Benefit of Henderson- Hasselbalch equation in pharmaceutical sciences

$$pH = pKa + \log \frac{\text{Concentration of Salt}}{\text{Concentration of acid}}$$

$pH = pka + \log A^-/HA$ (acid)

$pH = pKa + \log B/BH^+$ (base)

$$pH = pKa + \log \frac{[\text{nonprotonated species}]}{[\text{protonated species}]}$$

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I- Preparing Buffers

In principle , a buffer solution of any desired pH can be prepared by combining calculated quantities of a suitable conjugate acid/base pair.
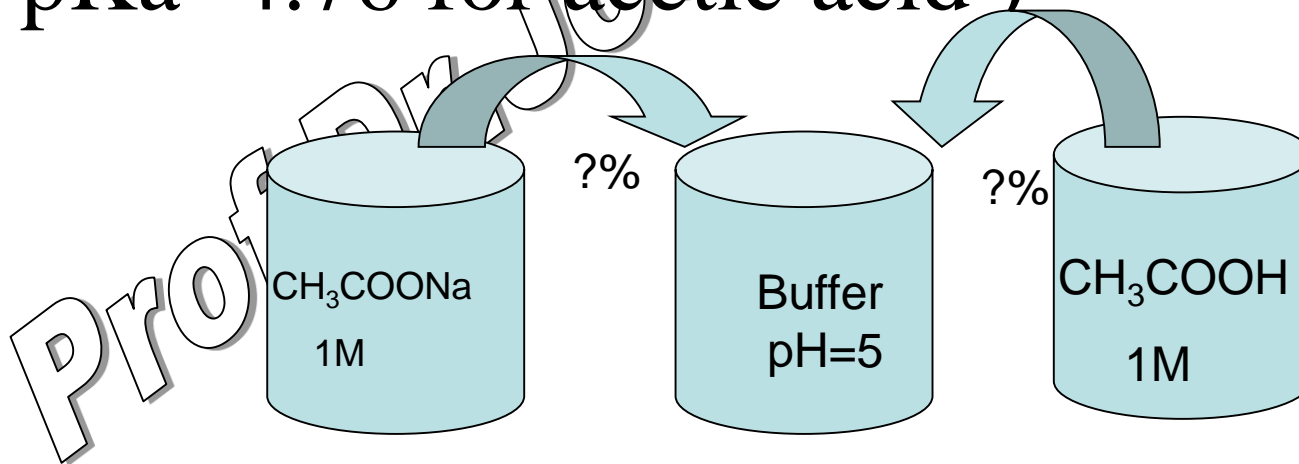
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Prepare of acetate buffer

Example :

What is The percentage of each acetic acid and sodium acetate (1M sol.) which needed to prepare Buffer solution with pH = 5

(pKa=4.76 for acetic acid)
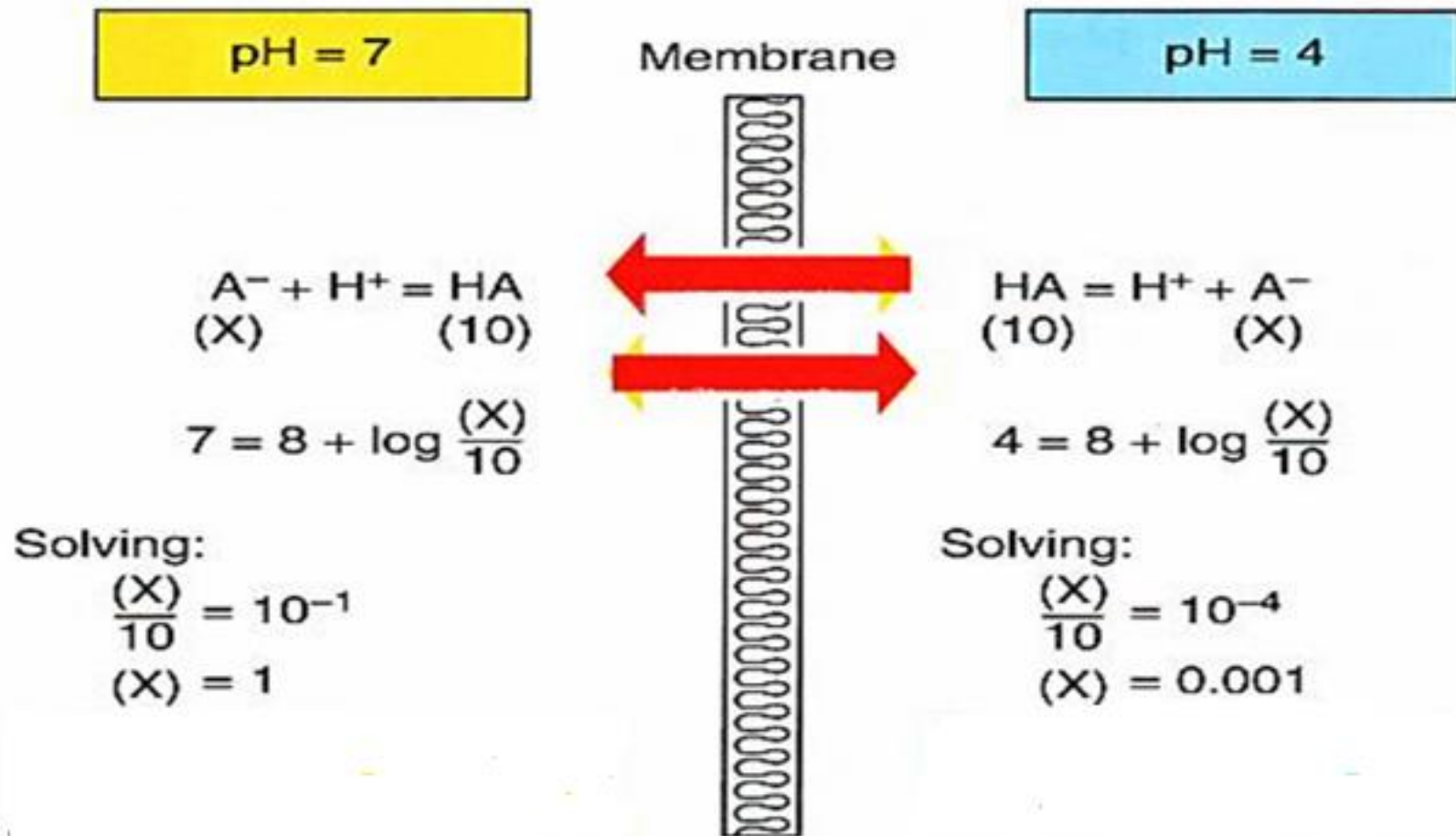
?%

?%

CH$_3$COONa
1M

Buffer
pH=5

CH$_3$COOH
1M

II- Evaluation of drug effect

- An acidic drug with pKa =2 is placed in a solution that has a pH of 3 .

  What is the ratio of ionized to unionized drug?

  Answer 10

| pH = 7 | Membrane | pH = 4 |

$A^- + H^+ = HA$
$(X) \quad\quad (10)$

$HA = H^+ + A^-$
$(10) \quad\quad (X)$

$7 = 8 + \log \frac{(X)}{10}$

$4 = 8 + \log \frac{(X)}{10}$

Solving:

$\frac{(X)}{10} = 10^{-1}$

$(X) = 1$

Solving:

$\frac{(X)}{10} = 10^{-4}$

$(X) = 0.001$

Equilibrium distribution of drug when pH is 4 on one side and 7 on the other side of membrane for an acid drug with a pK_a of 8.0. Nonionized form, HA, of the drug can readily cross the membrane. Thus, HA has the same concentration on both sides of the membrane. The concentration of nonionized drug is arbitrarily set at $10\,\mu g/ml$, and the expressions are solved to determine the concentration of ionized species at equilibrium.

Pilocarpine Hydrochloride
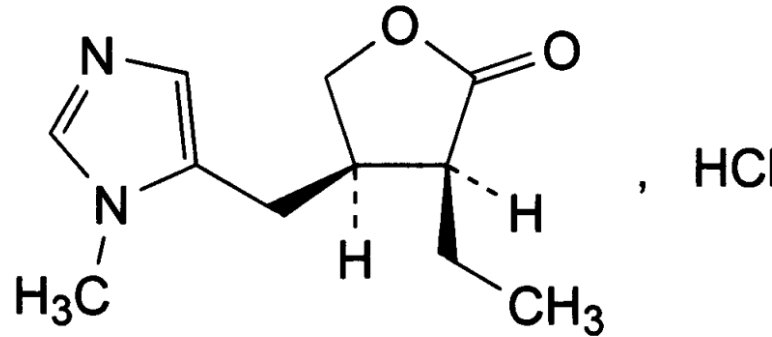
$C_{11}H_{16}N_2O_2$,HCl   244.7

Action and use
Cholinergic.   كولينيرجي= نظير ودي
Preparation
Pilocarpine Hydrochloride Eye Drops
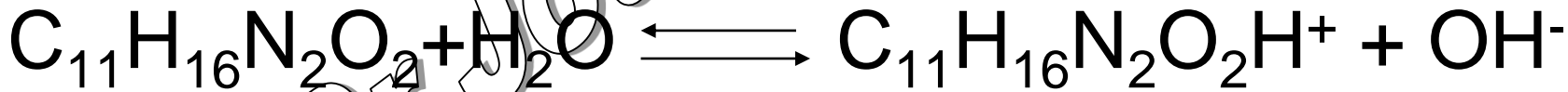
منبه نظير ودي يستخدم بحالة ارتفاع ضغط العين (الغلوكوما)

Pharmaceutical Application

The pK_b for Pilocarpin in ophthalmic drops solution = 7.15.

What is the percentage of free base at pH=7.4 (pH of eye liquid) ?

$$C_{11}H_{16}N_2O_2 + H_2O \rightleftharpoons C_{11}H_{16}N_2O_2H^+ + OH^-$$

pH = pKa + log B/BH+ (base)

III- EXTRACTION

- A compound will exist primarily in its acidic form if the pH of the solution is less than the compound s̊ pKa.

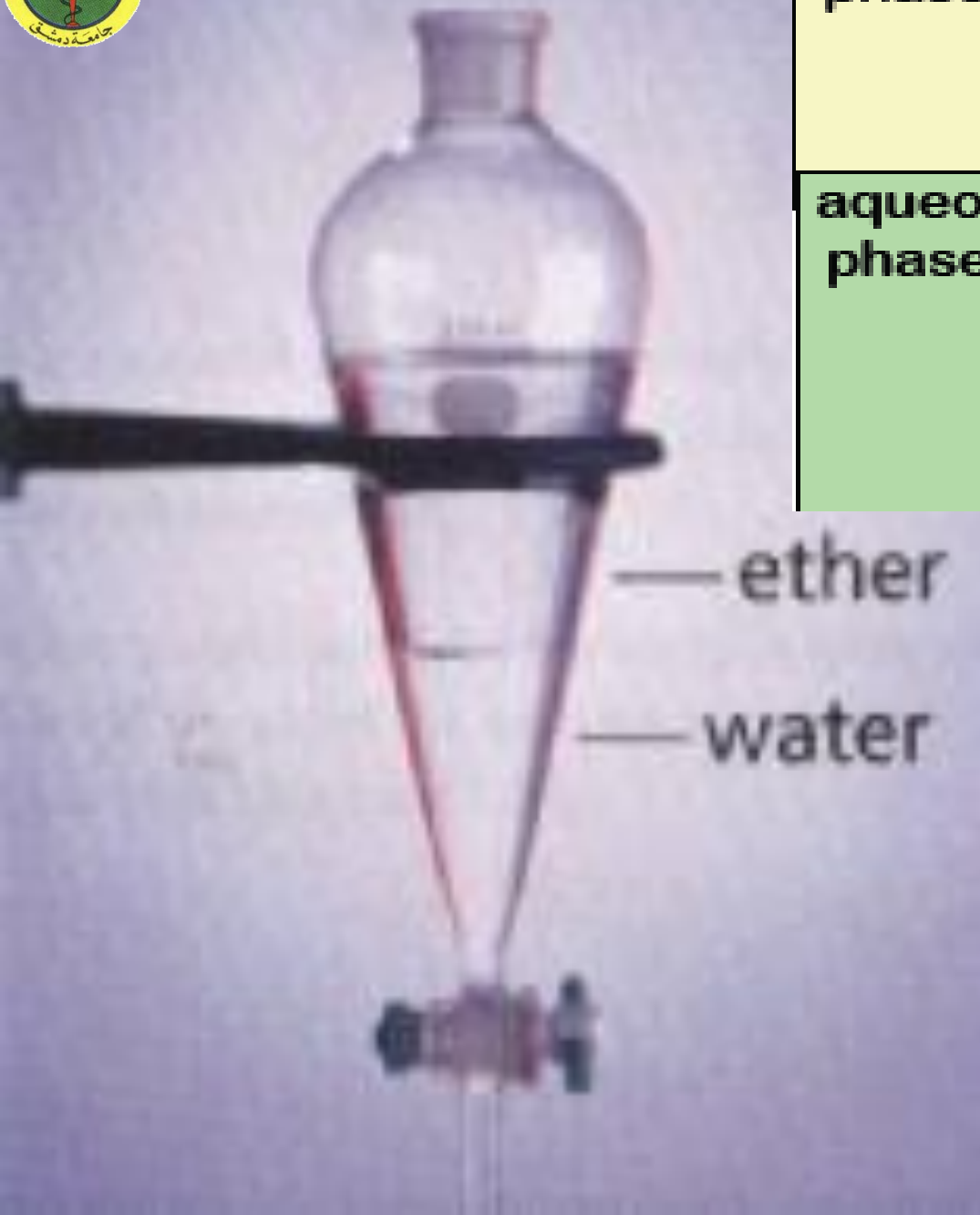- A compound will exist primarily in its basic form if the pH of the solution is greater than the compound s̊ pKa.

Henderson-Hasselbalch equation

Henderson-Hasselbalch equation can be very useful in the laboratory for separating the compounds in a mixture. Water and diethyl ether are not miscible liquids and , therefore, will form two layers when combined, the ether layer will lie above the more dense water layer.

Charged compounds are more soluble in water, whereas neural compounds are more soluble in ether. Two compounds, such as a carboxylic acid (RCOOH) with pKa of 5.0 and a protonated amine (RNH_3^+) with a pKa of 10.0 , dissolved in a mixture of water and ether, can be separated by adjusting the pH of the water layer . For example , if the pH of the water layer is 2, the carboxylic acid and the amine will both be in their acidic forms because the pH of the water is less than the pKa values of both compounds. The acidic form of a carboxylic acid will be more soluble in the ether layer, and the protonated amine will be more soluble in the water layer.

organic
phase 1

$$HA \qquad \downarrow$$

$$\uparrow\downarrow$$

aqueous
phase 2

$$HA$$

$$\uparrow\downarrow$$

$$H^+ + A^- \qquad \uparrow$$

—ether
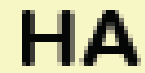
—water

For the most effective separation, the pH of the water layer should be at least two units away from the pKa values of the compounds being separated. Then the relative amounts of the compounds in their acidic and basic forms will be at least 100:1

$$Log\ A/HA = 2$$

$$A = 100\ HA$$

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- At what pH will the concentration of a compound with pKa of 8.4 be 100 time greater in its basic form than in its acidic form ?
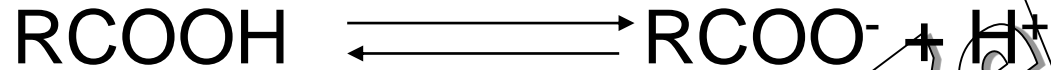
  Answer 10.4

- Solution :

      acidic form   basic form

      $RCOOH \rightleftharpoons RCOO^- + H^+$

If the concentration in the basic form is 100 times greater than concentration in the acidic from the Henderson- Haselbalch equation becomes :

$$pH = pKa + \log \frac{A^- \ (RCOO^-)}{HA \ (RCOOH)}$$

$pH = 8.4 + \log 100/1 = 8.4 + \log 10^2$

$pH = 10.4$

Thank you

Prof. J. Al-Zehouri

Q&A