4

BIOCHEMISTRY

Faculty of medicine – JU2018

◉ Sheet ○ Slides

Done By

Aboud Aldabobi+Khaled

Contributed in the Scientific Correction

Aboud Aldabobi

Contributed in the Grammatical Correction

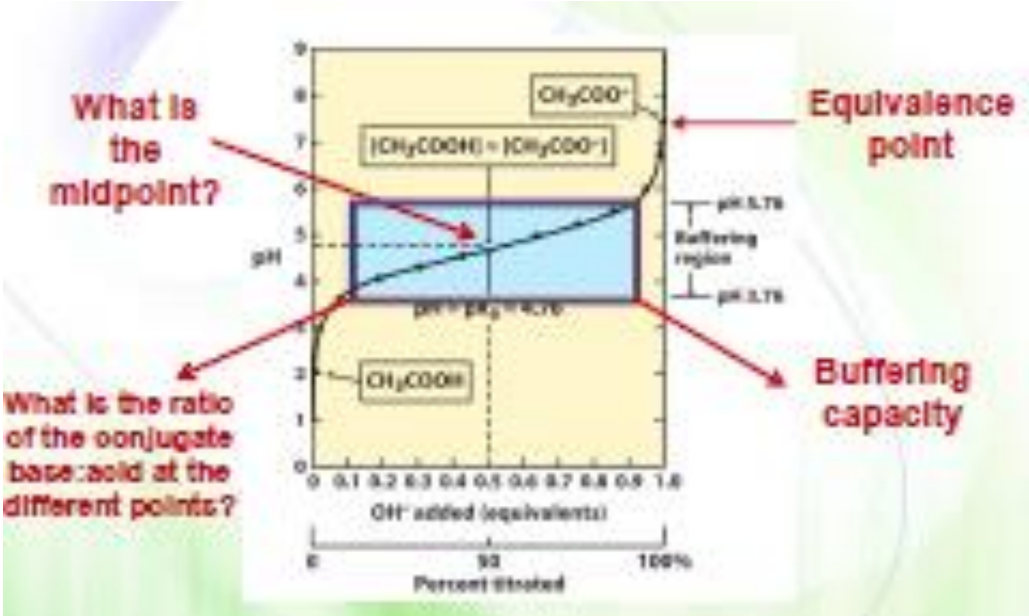
Aboud Aldabobi

Doctor

Dr. Mamoun+Dr.Diala

Revision

The value of the (Pka) equals the value of the (pH) when the concentration of conjugate base equals the concentration of the acid



- Notice that the midpoint of the acetic acid titration curve is the point when the

  [Acetic acid] = [Acetate]

- At this point, the amount of the added base equals 0.5Eq (Half of the amount needed to reach the Equivalence point)
- At the Equivalence point, the acid has been neutralized (The acid is completely neutralized means that all the acid have been used up and doesn't mean the PH equals 7, the PH at the Equivalence pint depends on the Pka of the acid)

- Remember (The Buffer capacity indicates the solution's ability to maintain a certain constant PH)

- The amounts of the acid and the conjugate base at both ends of the buffering region are not enough to buffer and maintain the PH

- As we know that 1Eq of any base could neutralize 1Eq of any acid, if you were given the volume of the added base to reach the equivalence point you could easily calculate the amount of the acid was titrated

Choosing a suitable buffer depends on

1-The value of the PH must be maintained

-(H_2PO_4/HPO_4^-) suitable as a buffer near PH=7.2
-(CH_3COOH/CH_3COO^-) suitable as a buffer near PH=4.76

2- The concentration of the buffer

-Higher concentration of a buffer means higher resistance of PH changing

(Dr. Mamoun said that the B.C is not changed by increasing the concentration, where as Dr. diala said that it could be changed 🙆, and by googling it I found that it could be changed 🤷‍♂)

→But the main idea is that when you have a higher concentration of the buffer you can add more acid or base before the PH is changed (your buffer is more effective) but in the end you cannot change the buffering region (Pka ±1)

Multi-protic buffer

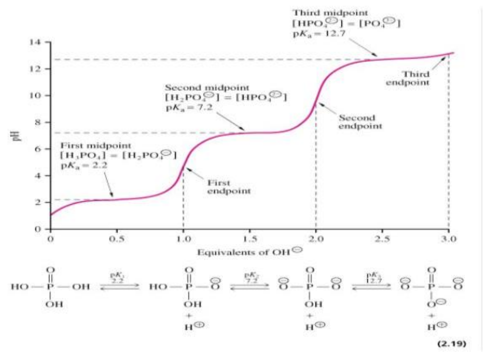
- ❖ It is a buffer that can resist the change of the PH at different capacities

- ❖ The number of these capacities depend on the number of OH- or H+ can be donated from the base or the acid respectively

- ❖ The titration Curve of such buffers consists of multiple curves connected to each other, Why?!

  - ➢ This is because that at each level of deprotonation, there is a huge change in the Pka of the acid (Every time you lose a proton it will be harder to lose another one next time)

Fig. 2.18 Titration curve for phosphoric acid (H_3PO_4)



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- ➢ To reach the equivalence point of the phosphoric acid, we need the 3Eq of base instead of one

- The amino acids also are titrated at two steps 😱
- Each amino acid has a carboxylic group which acts as an acid, also it has an amino group which acts as a base
- When the carboxylic group loses its proton, the amino group accepts it and become (NH4+) which also acts as an acid
- The acidic amino acids (Their R-Group acts as an acid) are titrated at 3 steps instead of 2 and this is due to their R-Group which can donate a proton
- Note: All the exercises mentioned in the slides can be found in the end of this sheet with some solutions

Buffers in our body were already mentioned in the previous sheet so no need to rewrite them ✨and we are going to focus on the bicarbonate buffer

Now bicarbonate buffer

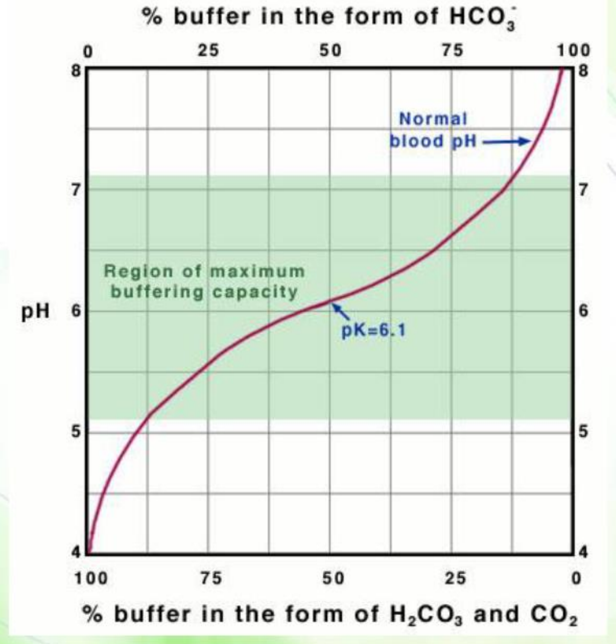
$$CO_2\,(d) + H_2O \underset{}{\overset{K_h}{\rightleftharpoons}} H_2CO_3$$

$$H_2CO_3 \overset{K_a}{\rightleftharpoons} H^+ + HCO_3^-$$

- This buffer system acts as a first line of defense in our body in case of the PH was changed and it is followed by the activity of 2 major organs (Lungs and Kidneys) which represent the second and the third lines of defense respectively
- The Respiratory system controls the concentration of CO2 and O2 by increasing or decreasing the rate of breathing
- Whereas the Renal system controls the concentration of HCO3- by increasing or decreasing the rate of absorption

NOTICE (in the picture):

The Pka of the bicarbonate buffer is 6.1 so the capacity ranges between (5.1-7.1), but the blood pH is 7.4!!! which is outside the buffering capacity!!!



- Remember that the biological buffers slightly differ than the chemical buffers and the best explanation of the previous issue is

1- It is in an open system (continually interacts and exchanges with the environment), your body can control rate of breathing to maintain pH (unconsciously).

2- Bicarbonate is present in a relatively high concentration in the ECF (24mmol/L) (can be controlled easily) (20 to 1 ratio with carbonic acid due to Henderson-Hasselbalch Equation).

3- The components of the buffer system are effectively under physiological control: the CO2 by the lungs, and the bicarbonate by the kidneys.

Any change in the normal blood PH is considered a pathological condition which can be life-threating situation

Acidosis and alkalosis

This pathological condition occurs when the PH of the blood is out of the normal range (7.35-7.45)

Acidosis

-When the PH of the blood is lower than 7.35

**When we have a high concentration of CO2 in our blood the reaction of producing the carbonic acid shifts to the right, producing a higher concentration of carbonic acid, thus increasing the concentration of the produced HCO3- and H+ (High concentration of protons causes Acidosis)

$2\ H_2O + CO_2 \rightleftharpoons H_2CO_3 + H_2O \rightleftharpoons H_3O^+ + HCO_3^-$

Two types of acidosis

- Respiratory Acidosis
  - When your lungs cannot get rid of enough CO2 such in
    - Chronic air way conditions (Asthma)
    - Emphysema (lung condition that causes shortness of breath and the air sacs of the lungs are damaged) [Extra]
  - In this case we have a Renal compensation which means that the kidneys will absorb more HCO3-, higher concentration of this conjugate base is able now to neutralize the excess of protons and the normal PH is restored
- Metabolic acidosis
  - Occurs when the kidneys cannot eliminate enough acids or when they get rid of a lot of bases, and we have 4 types of metabolic acidosis but we gonna mention 2 of them

1- Diabetic acidosis.
   *common in people with diabetes
   - When your body lack enough insulin the liver starts to produce the ketone bodies especially the (Ketoacidosis)

   - The ketone bodies are also produced from the liver during the low food intake (fasting or even starvation)

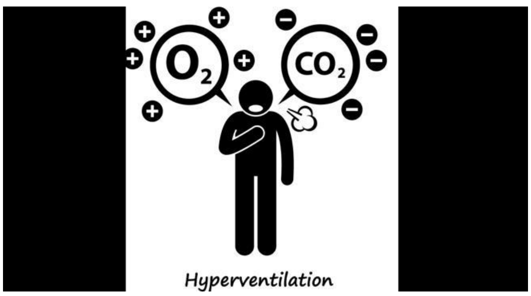
2- Lactic Acidosis
   - Due to the accumulation of lactic acid in the blood (the lactic acid is the byproduct of anaerobic respiration when the glucose breaks down without oxygen)

Alkalosis

-The PH of the blood is higher than 7.45

➢ Respiratory Alkalosis

   ▪ In Hyperventilation when the lungs get rid of high amounts of CO2



- Metabolic Alkalosis
  - Administration of Salts

  - Large loss of potassium in a short time

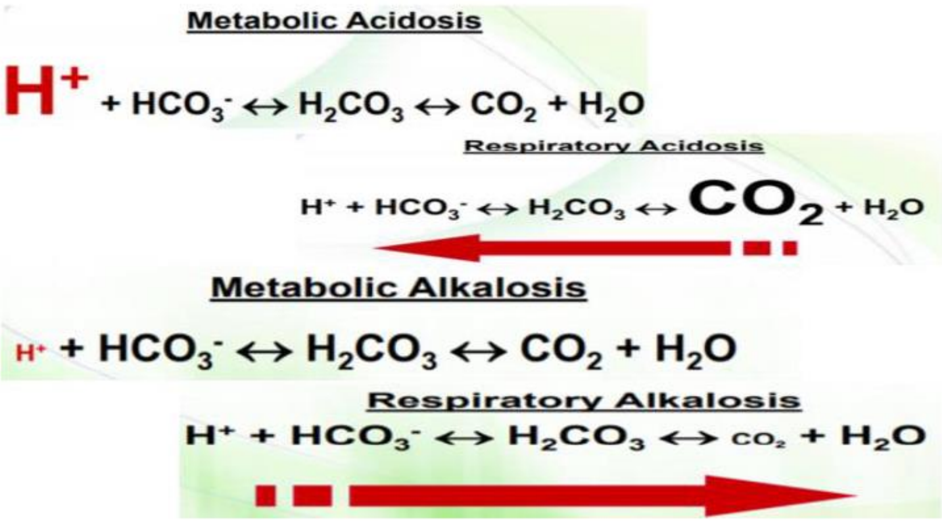
  - Why does Potassium deficiency cause metabolic alkalosis?

    -This due to the cotransport system of potassium with protons inside the blood (K+ out, H+ in) so low concentration of K+ causes a low concentration of protons which increases the PH of the blood

    - Low potassium levels lead to high aldosterone levels which increases the absorption of Na+ and maybe (HCO3-), higher concentration of (HCO3-) shifts the reaction to the left, decreases the concentration of the protons and increasing the PH

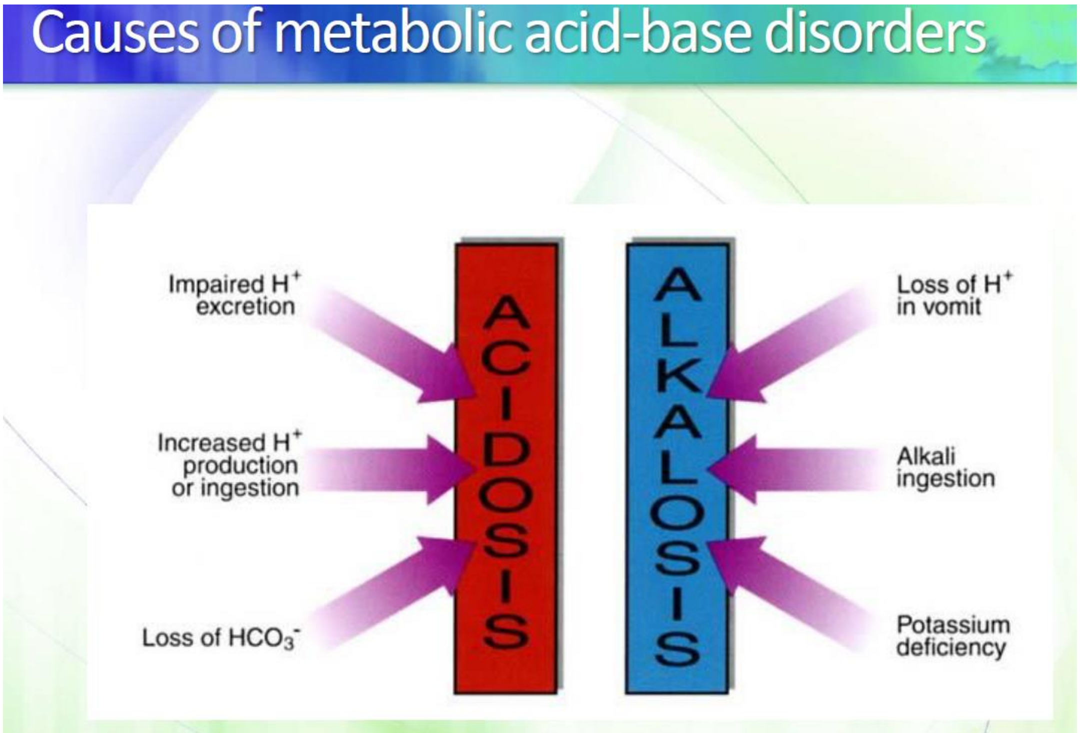
  - In this case we have a (Respiratory compensation), in which the breathing rate is decreased, increasing the concentration of CO2 in the blood and restoring the normal PH ✌

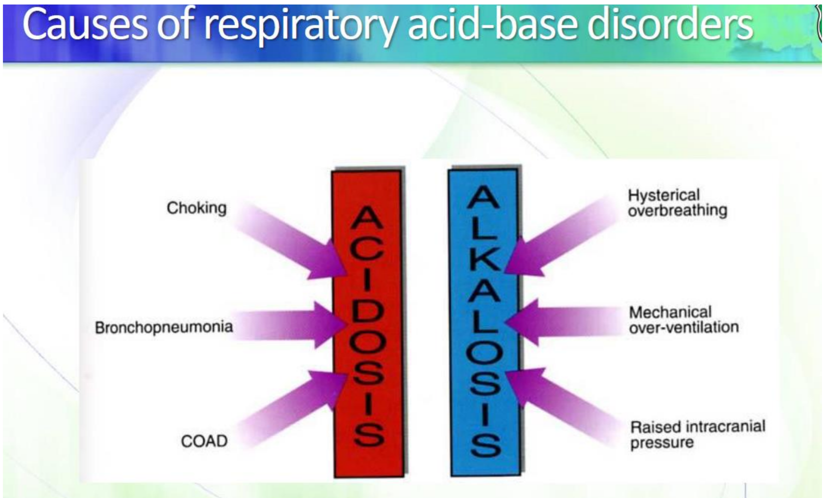
Processes from slides:



	1- Acidosis (pH<7.35)		2- Alkalosis (pH>7.45)	
TYPES	Metabolic (defective kidneys)	Respiratory (defective lungs)	Metabolic	Respiratory
CAUSES	1-Production of ketone bodies (starvation): Diabetic people or in Ramadan the body is full of ketone bodies **which are acidic**, organs use them as a source of energy, they are produced from fatty acids). 2- low secretion of bicarbonate 3- when you take a lot of aspirin	Pulmonary (asthma;emphysema) Happens when CO_2 is accumulated in the body=> more H_2CO_3=> more H^+ => less pH	1-Administration of salts or bases. 2-High secretion of bicarbonate from kidneys	**Hyperventilation (anxiety)** The Panic Attack (afraid of something) causes Vertigo because you can't control your breathing, the body automatically controls the rate of breathing (coma), the best solution is to breath is a bag to increase the CO_2 %.
Processes	Low HCO_3^- => more acid dissociates=> more H^+=> less pH	Difficulties in breathing =>CO_2 accumulates in the body=> more H_2CO_3=> more H^+ => less pH	High HCO_3^-=> more CO_2=> less H^+ => high pH	hyperventilating (low CO2)=> decrease in H+=> high pH

For illustration





- Causes of acidosis and alkalosis in the last 2 pictures are not to be memorized

Compensation

- It means when an organ is defective, the other takes the lead to fix the PH
- The change in the pCO3 or the HCO3- due to primary event
- If underlying problem is metabolic, hyperventilation or hypoventilation can help, and this is a **respiratory compensation**.
- If problem is respiratory, renal mechanisms can bring about metabolic compensation (By increasing or even decreasing the absorption of (HCO3-)
- The compensation could be complete or partial
    - Complete if the normal PH is restored
    - Partial if you notice an abnormal concentration of CO2 and HCO3- but the normal PH is not restored yet (so you know that the body had already begun the process to restore the normal PH)

Acid-Base Disorder Change	Primary Change	Compensatory
Respiratory acidosis	pCO_2 up	HCO_3^- up
Respiratory alkalosis	pCO_2 down	HCO_3^- down
Metabolic acidosis	HCO_3^- down	PCO_2 down
Metabolic alkalosis	HCO_3^- up	PCO_2 up

- When we have respiratory acidosis the [CO2] increases so the reaction shifts to the left, the protons increase, and the pH decreases so the primary change is the increasing of [CO2], as a result of that the kidney increase the absorption of bicarbonate so the reaction shifts to the right again
- In respiratory alkalosis [CO2] decreases, the reaction shifts to the left, and the pH goes up. The Renal compensation decreases absorption of bicarbonate so the reaction shifts to the right and the PH will be normal again

$$H^+ (aq) + HCO_3^- (aq) \rightleftharpoons H_2CO_3 (aq) \rightleftharpoons H_2O\ (l) + CO_2\ (g)$$

	pH	pCO_2	HCO_3^-
Resp. acidosis	Normal But<7.40	↑	↑
Resp. alkalosis	Normal but>7.40	↓	↓
Met. Acidosis	Normal but<7.40	↓	↓
Met. alkalosis	Normal but>7.40	↑	↑

	pH	pCO_2	HCO_3^-
Res.Acidosis	↓	↑	↑
Res.Alkalosis	↑	↓	↓
Met. Acidosis	↓	↓	↓
Met.Alkalosis	↑	↑	↑

- In this partial compensation you can notice the abnormal concentrations of both CO2 and HCO3-, but the normal PH is not restored yet

Now I will but some quistions from the slides and their solutions

We have to thank our classmate (Reema alattar) for providing us with these answers

Q1- Predict then calculate the pH of a buffer containing
A- 0.1M HF and 0.12M NaF? (Ka = 3.5 x 10-4)

1 A

0.1 M = conc of HF (acid)

0.12 M = conc of NaF (salt or conjugate base)

$Ka = 3.5 \times 10^{-4}$

(1)

$\Rightarrow Ka = \frac{[H_3O^+][F^-]}{[HF]}$

$[H_3O^+] = \frac{3.5\times10^{-4} \times 0.1}{0.12}$

$[H_3O^+] = 2.9 \times 10^{-4}$ M

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

$PH = \boxed{3.53}$

(2)

$PH = Pka + \log \frac{[F^-]}{[HF]}$

$PH = 3.45 + 0.079$

$PH = \boxed{3.53}$

$\boxed{* \; Pka = -\log Ka \quad Pka = -X - 3.45}$

B-0.1M HF and 0.1M NaF, when 0.02M HCl is added to the solution?

2) 0.1 M = [HF] , 0.02 M of HCl is added
0.1 M = [NaF] to the soln.

HCl is strong acid, completely dissociated ⇒

$HCl \rightarrow H_3O^+ + Cl^-$

the conc of HCl as acid equal to the conc of H_3O^+

$$K_a = \frac{[H_3O^+] \times [F^-]}{[HF]}$$

$$3.5 \times 10^{-4} = [H_3O^+] \times \frac{0.02 - 0.1}{0.02 + 0.1} \quad \frac{0.08}{0.12}$$

$[H_3O^+] = \rightarrow 5.25 \times 10^{-4}$

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

$\boxed{pH =}\ 3.27$

Q2- What is the pH of a lactate buffer that contain 75% lactic acid and 25% lactate? (pKa = 3.86)

B) lactic acid [HA] = 75% ⇒ 0.75

lactate $[A^-]$ = 0.25

pKa = 3.86

Based on Henderson

$$pH = pKa + \log \frac{[A^-]}{[HA]}$$

$pH = 3.86 + -0.47$

$\boxed{pH = 3.38}$

Q3- What is the concentration of 5 ml of acetic acid knowing that 44.5 ml of 0.1 N of NaOH are needed to reach the end of the titration of acetic acid? Also, calculate the normality of acetic acid.

$\boxed{C}$

$eq = eq$

nVM

(acid) $nMV =$ (base)

$1 \times M \times 5 = 1 \times 44.5 \times 0.1$

M of acid $= 0.89$ molar

the idea here depends on titration

Q4- What is the pKa of a dihydrogen phosphate buffer when pH of 7.2 is obtained when 100 ml of 0.1 M NaH2PO4is mixed with 100 ml of 0.1 M Na2HPO4?

~~Exer~~

Exercises slide $\boxed{17}$ PH & buffers

$\boxed{A}$

$PH = Pka = 7.2$

Since we have the conc of the acid equal to the conc of the conjugate base
=> this is the mid point

Q5- A solution was prepared by dissolving 0.02 moles of acetic acid (HOAc; pKa = 4.8) in water to give 1 liter of solution. What is the pH?

# of moles = 0.02

Volume = 1 L

$Pka = 4.8 \Rightarrow Ka = 1.6 \times 10^{-5}$

because $Pka = -\log Ka$

the conc of the acid $= \frac{0.02}{1} = 0.02$ molar

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

$\sqrt{1.6 \times 10^{-5} \times 0.02} = \sqrt{X^2}$

$X = [H_3O^+] = [A^-] = 5.6 \times 10^{-4}$

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

$= -\log (5.6 \times 10^{-4})$

$\boxed{PH = 3.24}$

Q6- To this solution was then added 0.008 moles of concentrated sodium hydroxide (NaOH). What is the new pH? (In this problem, you may ignore changes in volume due to the addition of NaOH).

0.008 moles of NaOH are added

→ ignore the changes in volume → 1 liter

$M_{\text{of NaOH}} = \frac{0.008}{1} = 0.008$ molar

→ we add strong base which is NaOH → it will react with protons ~~forming~~ decreasing the conc of the acid, increasing the $\boxed{PH}$ a little.

→ the previous conc of Ac = 0.02 M

the remaining conc after the addition of 0.008 ⟹ 0.02 − 0.008 = 0.012 M

$$PH = PKa + \log \frac{[A^-]}{[HA]}$$

$$PH = 4.8 + \log \frac{0.008}{0.012}$$

$$= 4.63$$

"As Doctors we must never forget that we have the opportunity to do more good in one day than most people have in a month 🙌🩺👨‍⚕️$👩‍⚕️$"
By (Suneel Dhand)