Pharmaceutical Analytical Chemistry I

الأستاذ الدكتور جمعه الزهوري (دكتوراه صيدلة-ألمانيا 1991)

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Acid-Base Titrations

Neutralization Reaction

Proton-Exchange Reaction

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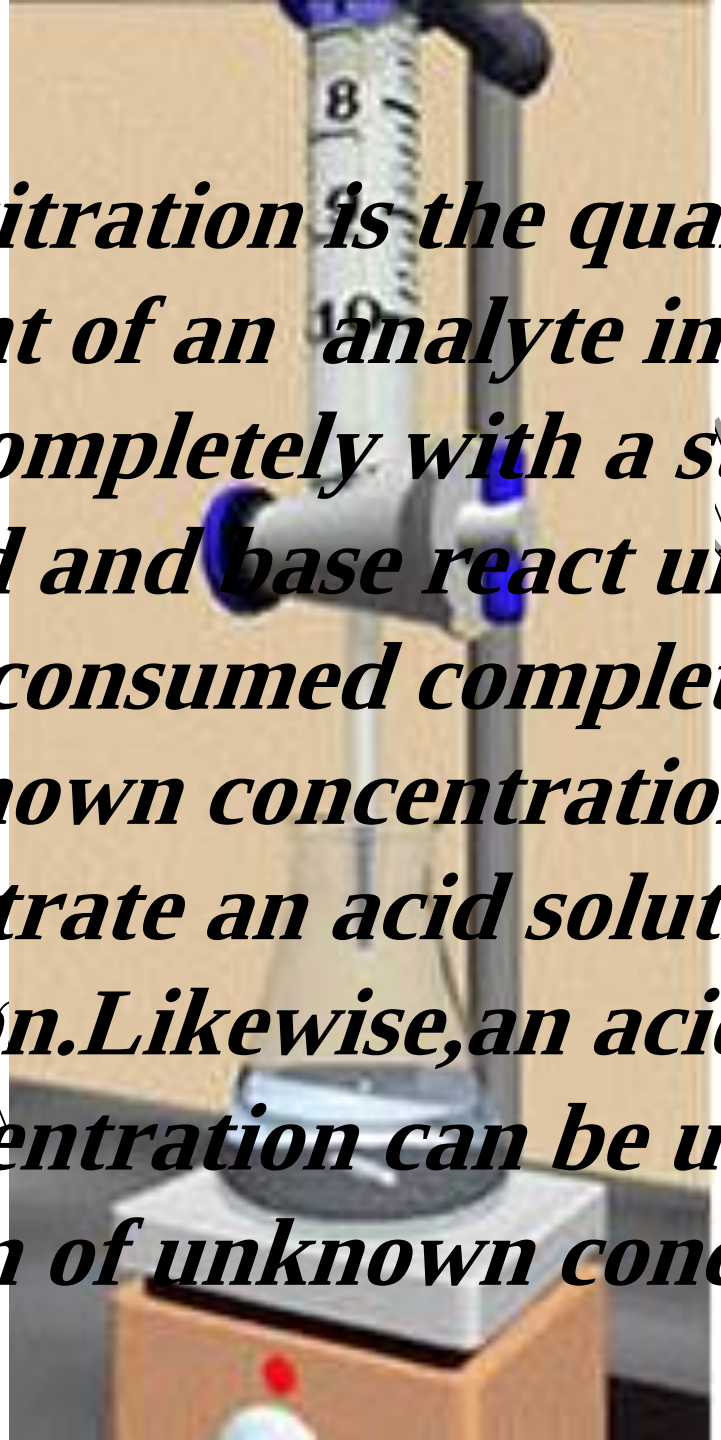


Recall that titration is the quantitative measurement of an analyte in solution by reacting it completely with a standardized reagent.Acid and base react until one of the reactants is consumed completely. A solution of base of known concentration can therfore be used to titrate an acid solution of unknown concentration.Likewise,an acid solution of known concentration can be used to titrate a base solution of unknown concentration.

Neutralization reaction

Acid + Base ⟶ Salt + Water + Temperature

$HCl + NaOH \longrightarrow NaCl + H_2O + \Delta H$

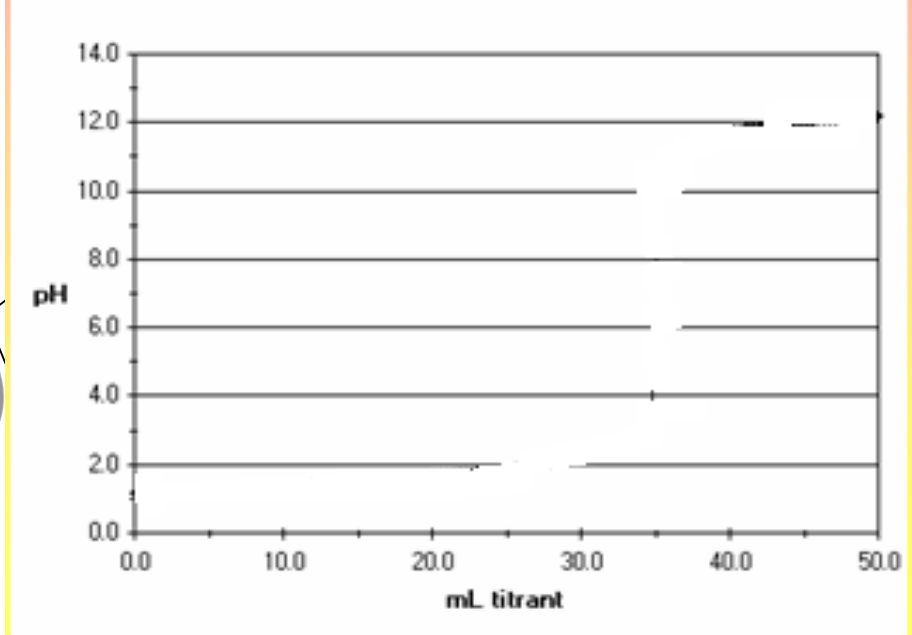
The Neutralization reaction is described by the equation

$$H_3O^+ + OH^- \longrightarrow 2H_2O$$

$\Delta H = -57.3 Kjmol^{-1}$ (=constant for all N.reactions)

Acid-Base Titration Curves

Acid-base titrations curves consist of a plot of reagent volume on the horizontal axis and the pH value on the vertical axis.



TITRATION CURVES

V=6

Why Titration Curves?

- Understand the detection of end points.
- Understand the sources of Titration errors.
- Choosing the feasibility indicator.
- Understand the mechanism of titration.

How can we Constructed(Drawing) titration curve ?

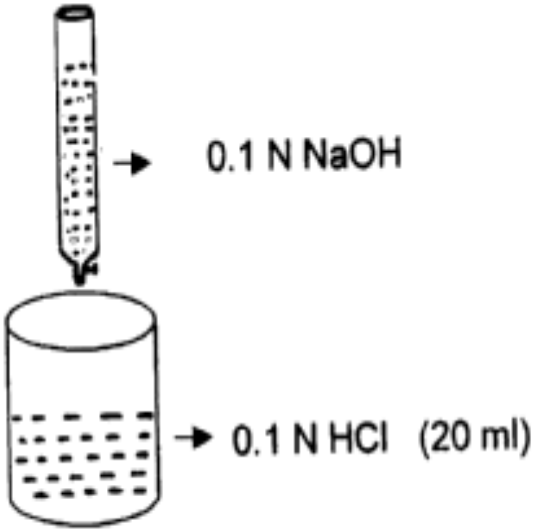
- Start point pH value
- Equivalence point pH value
- Preequivalence points pH values

Titration Curves

- Strong acid vs. strong base
- Weak acid vs. strong base
- Strong acid vs. weak base
- Weak acid vs weak base

I- Strong acid titrated with strong base

- Example : Titrate of 20 ml HCl 0.1 N with 0.1 N of NaOH.



1- Determine the Start pH value

- Start pH = the pH of HCl solution before the begin of titration.
- pH = - log C = - log 0.1 =1
- So the x and y values for the Start Point=

pH = 1 , V = 0 ml

2- Determine The Equivalent Point

- HCl + NaOH → $NaCl + H_2O$
- After the Consume of 20 ml of NaOH
- NaCl = Neutral
- pH = 7
- So the x and y values for Equivalent Point=

pH = 7 , V = 20 ml

Determine the Preequivalence Points

- Prior to equivalence point (HCl+NaCl)
- We will determine only the points due to the correct pH value.
- **At pH=2**
- pH=2 =-log [HCl] = -log 0.01N = - log 10^{-2}
- The Concentration of acid decreased 9 time(0.1-0.01 = 0.09) 0.1 decrease to 0,01
- 100 decease to x = 100 x 0.01 /0.1=90
- 90 % consumed (18 ml) , remained 10%(2ml)
- The x and y values for the 1. preequivalence point =

pH = 2 , V = 18 ml

At pH = 3

- pH = 3
- 3 = - log [HCl] = - log 0.001 = - log 10^{-3}
- The HCl concentration decrease 9 times (0.01 – 0.001= 0.009)
- (2 /10 x 9 = 1.8 ml) 18+1.8= 19.8 ml (99%)
- Remain 2x0.1 = 0.2 ml
- The x and y values for 2. Preequivalence point:

pH = 3 , V = 19.8 ml

At pH = 4

- 0.2 ml
- pH= 4 = - log[HCl] =- log0.000 = - log 10^{-4}
- HCl concentration decrease 9 times (0.001-.0001 = 0.009)
- 0.2/10 x 9 = 0.18 + 19.8 = 19.98 ml (99.9%)
- HCl remain = 0.2-0.18 = 0.02ml.
- The x and y values for 4. Preequivalence point =

pH = 4 , V = 19,98 ml

- **0.02 ml HCl + 0.02 NaOH = pH = 7 = E.Point**
- **Practical the volume of 1 drops = 0.04 ml**
- **0.02 ml will change the pH from 4 t0 7**
- **0.04 ml will change the pH from 4 to 10**
- **The last drop will change the pH 6 degree from 4 to 10**
- **When we continuo with addition of NaOH we will get an analogous curve [NaOH] = [OH^-]**

Titration table of strong acid with strong base

Curve Points	pH	$[H^+]$	[HCl] N	Residue of HCl ml	Neutralization %	Volume of added NaOH ml
Initial point	1	10^{-1}	0.1	20	0	0
Intermediate points	2	10^{-2}	0.01	20-18 = 2	90	18
	3	10^{-3}	0.001	20 - 19.8 = 0.2	99	19.8
	4	10^{-4}	0.0001	20 - 19.98 = 0.02	99.9	19.98
Equivalent point	7	10^{-7}	0	0	100	20
End Point	10	10^{-10}	-	-	-	Excess 0.02 ml

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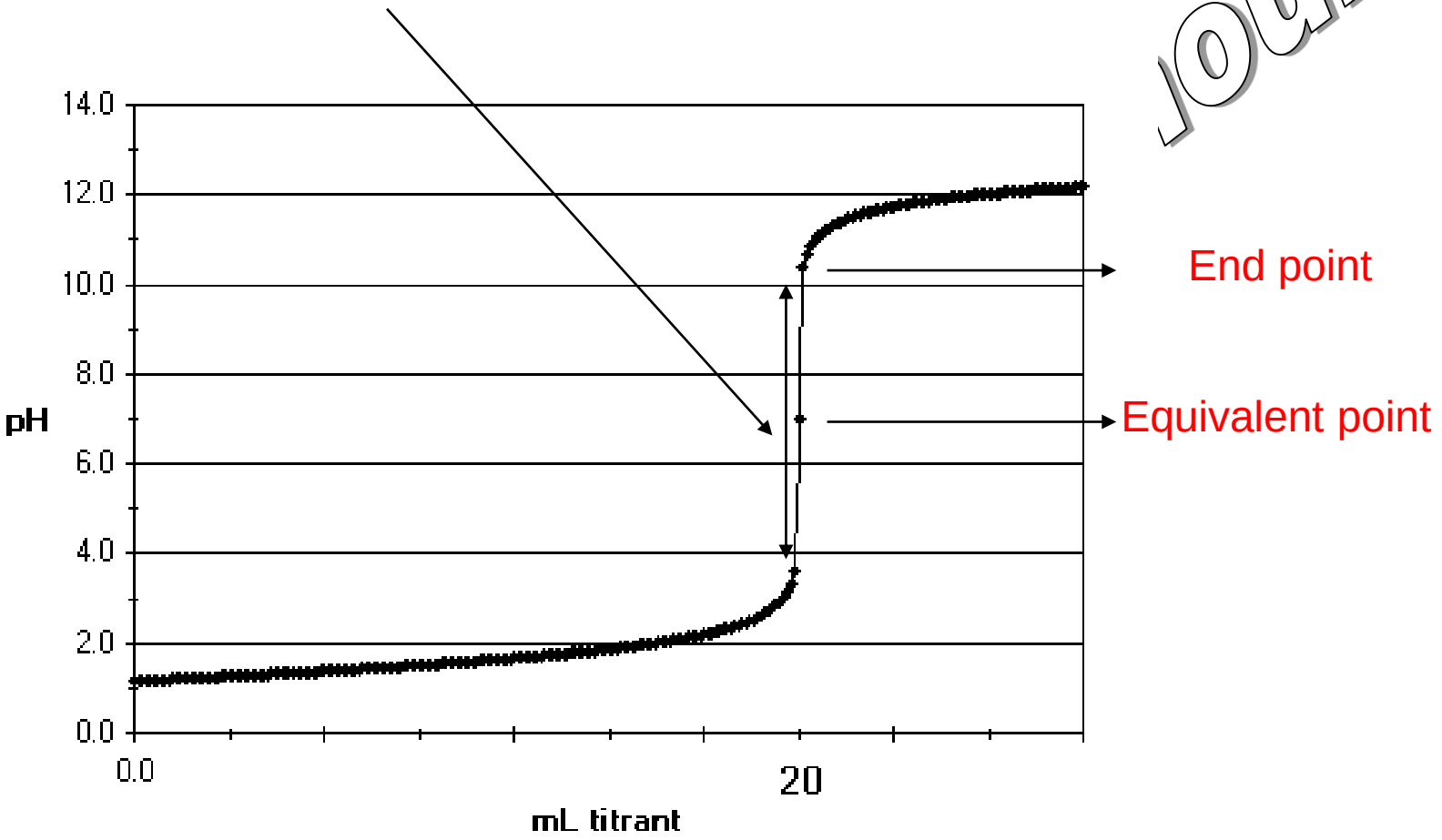
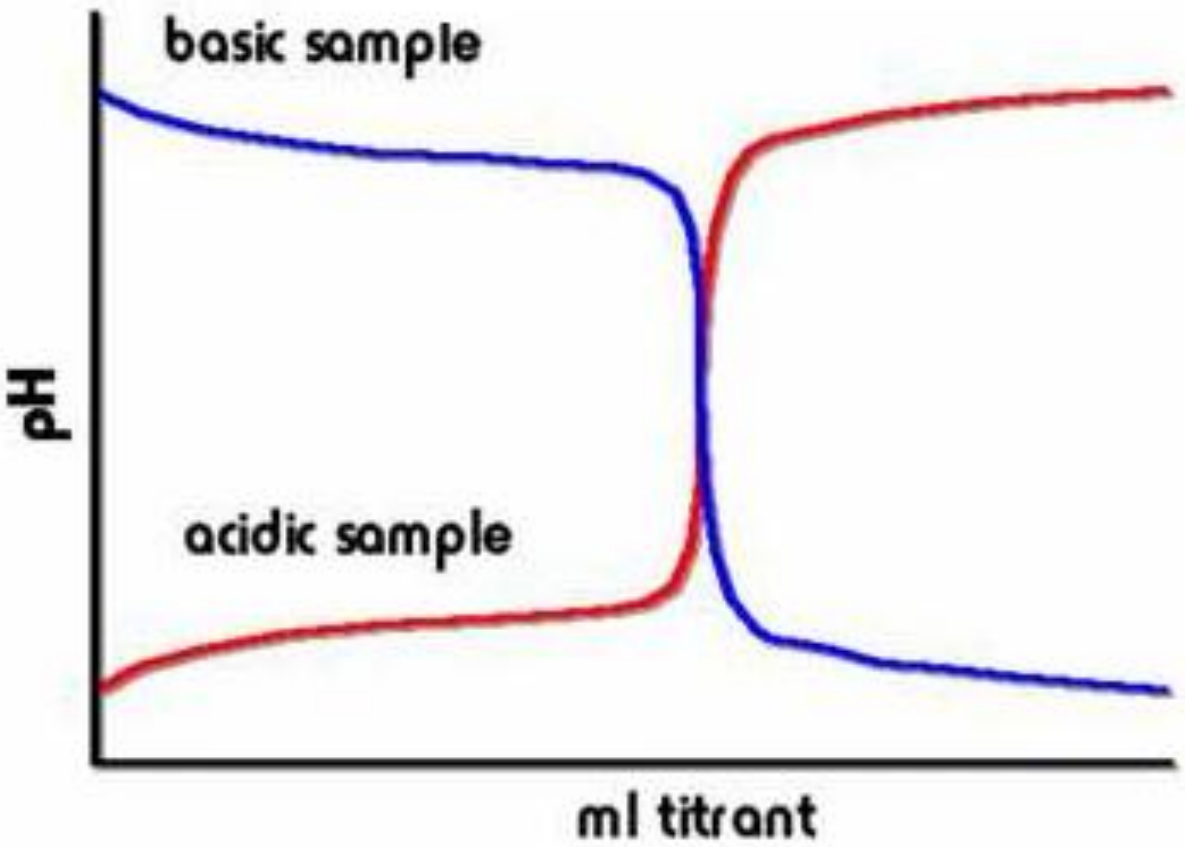


Titration curves for strong acid (20 ml HCl 0.1N with strong base (NaOH 0.1 N)

Titration curves

Strong acid with strong base



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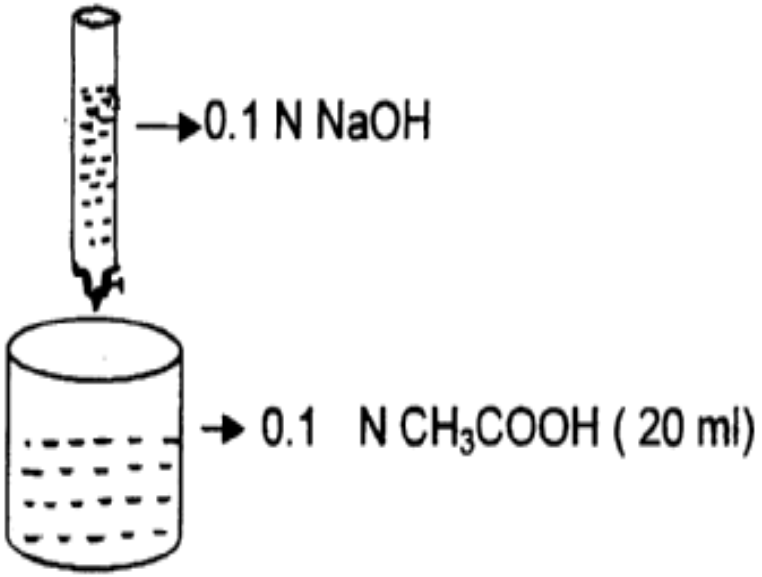
II- Weak acid titrated with strong base

- Example : titrate 20 ml 0.1 N acetic acid with 0.1 NaOH (pKa ACH = 4.74)



1- Determine the Initial pH value

- pH of start point = pH of weak acid solution.
- pH= ½ pKa- ½ logC = ½(4.74)- ½ log 10^{-1}= 2.87≈3
- So the x and y values for start point :

pH = 3 , V = 0 ml

2-Determine the pH of the Equivalence point

$CH_3COOH + NaOH \rightarrow CH_3COONa + H_2O$

pH = pH of weak base solution

$pH = 7 + 1/2\ pKa + 1/2\ \log C$

$pH = 7 + ½\ (4.74) + ½ \log 10^{-1} = 8.87 \approx 9$

- The x and y value for equivalence point :

pH=9 , V = 20 ml

3- Determine the Intermediate Points

- Weak acid with his salt (Buffer solution)
- $pH = pK_a + \log C_s/C_a$
- pH after addition of 5 ml of NaOH 0.1 N.
- Stock solution x 0.1 = 25 x Ca
- Ca= 0.1x15 /25 = 0.06 N
- Cs = 0.1x5 /25 = 0.02 N
- pH = 4.74 + log 0.02/0.06 = 4.26
- So x and y =

pH = 4.26 , V= 5 ml

Titration table of weak acid with strong base

Curve Points	pH	Cs (N)	Ca(N)	Total solution volume ml	Volume Of acid Residue ml	Neutrali-zation %	Volume of added NaOH ml
Initial point (start point)	2.87=3	0	0.1	20	20	0	0
Intermediate points	4.26	0.02	0.06	25	15	25	5
	4.74	0.03	0.03	30	10	50	10
	5.19	0.04	0.014	35	5	75	15
	5.34	0.044	0.11	36	4	80	16
	5.50	0.046	0.008	37	3	85	17
	5.71	0.047	0.005	38	2	90	18
	6.03	0.049	0.002	39	1	95	19
	7.44	0.05	0.0001	39.96	0.02	99.9	19.98
Equivalent point	8.87 =9	0.05	0	40	0	100	20
End Point	10	-	-	40.0 2			Excess 0.02 ml

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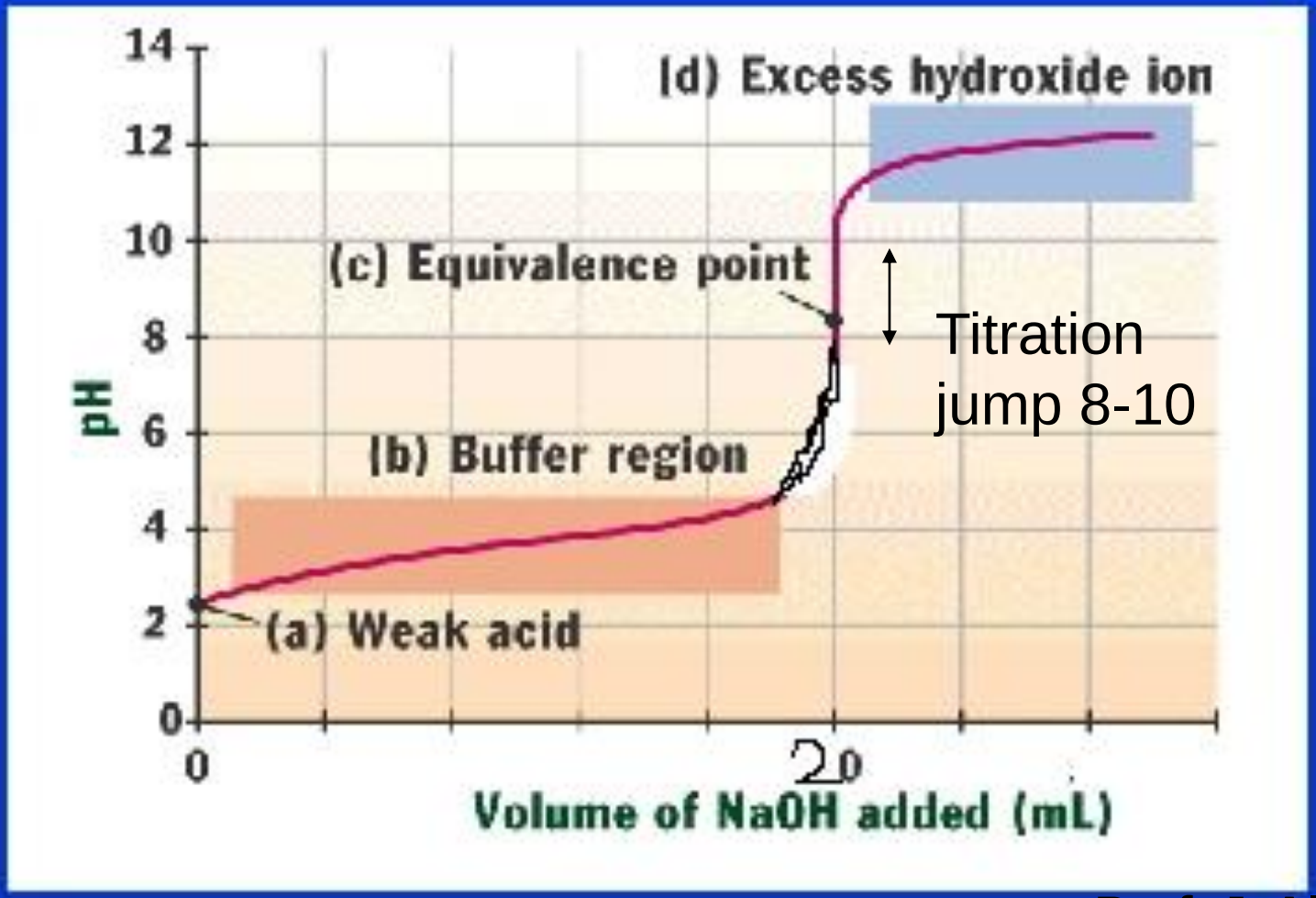
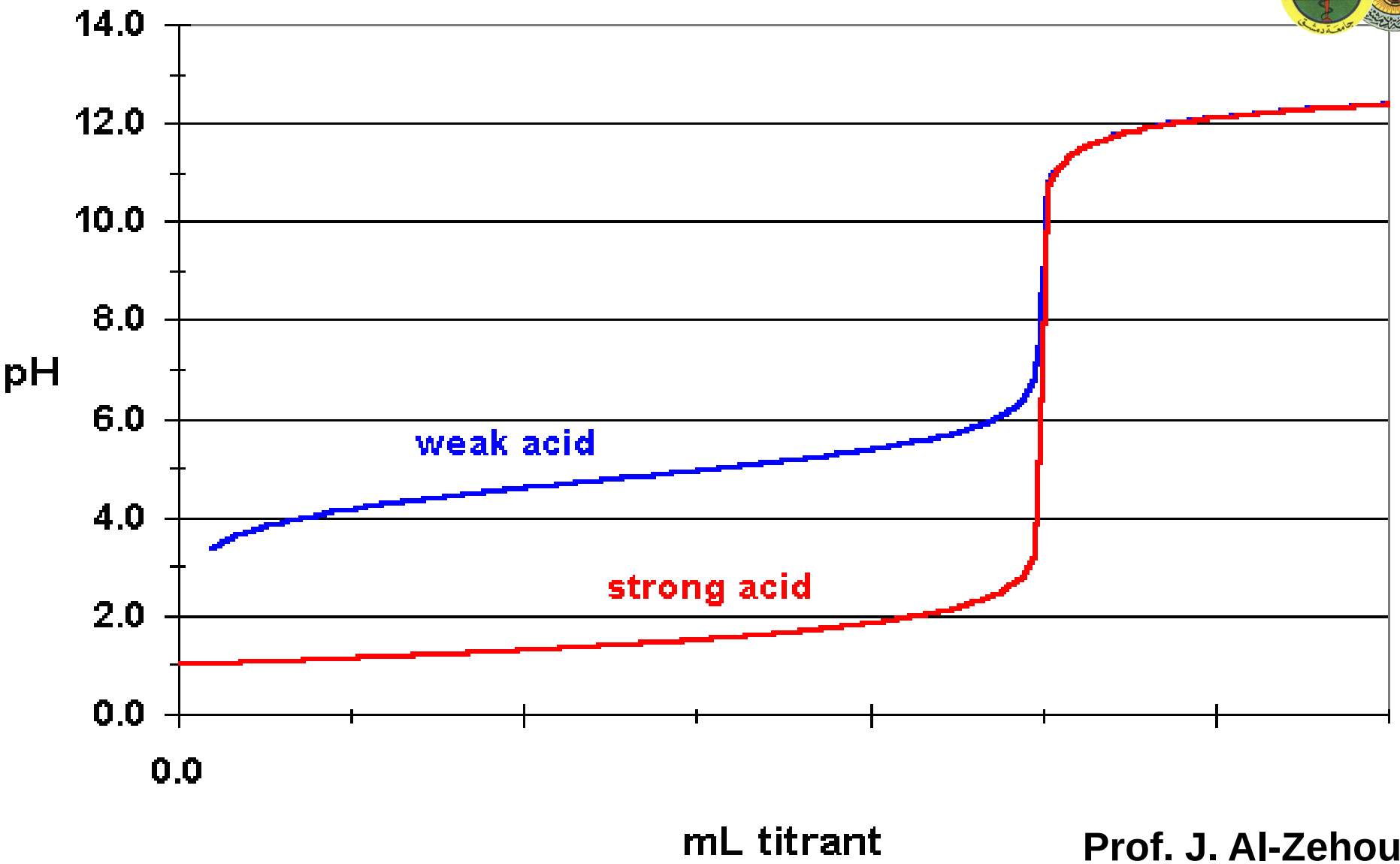
Titration of Weak Acids With Strong Bases



Compare between strong acid and weak acid



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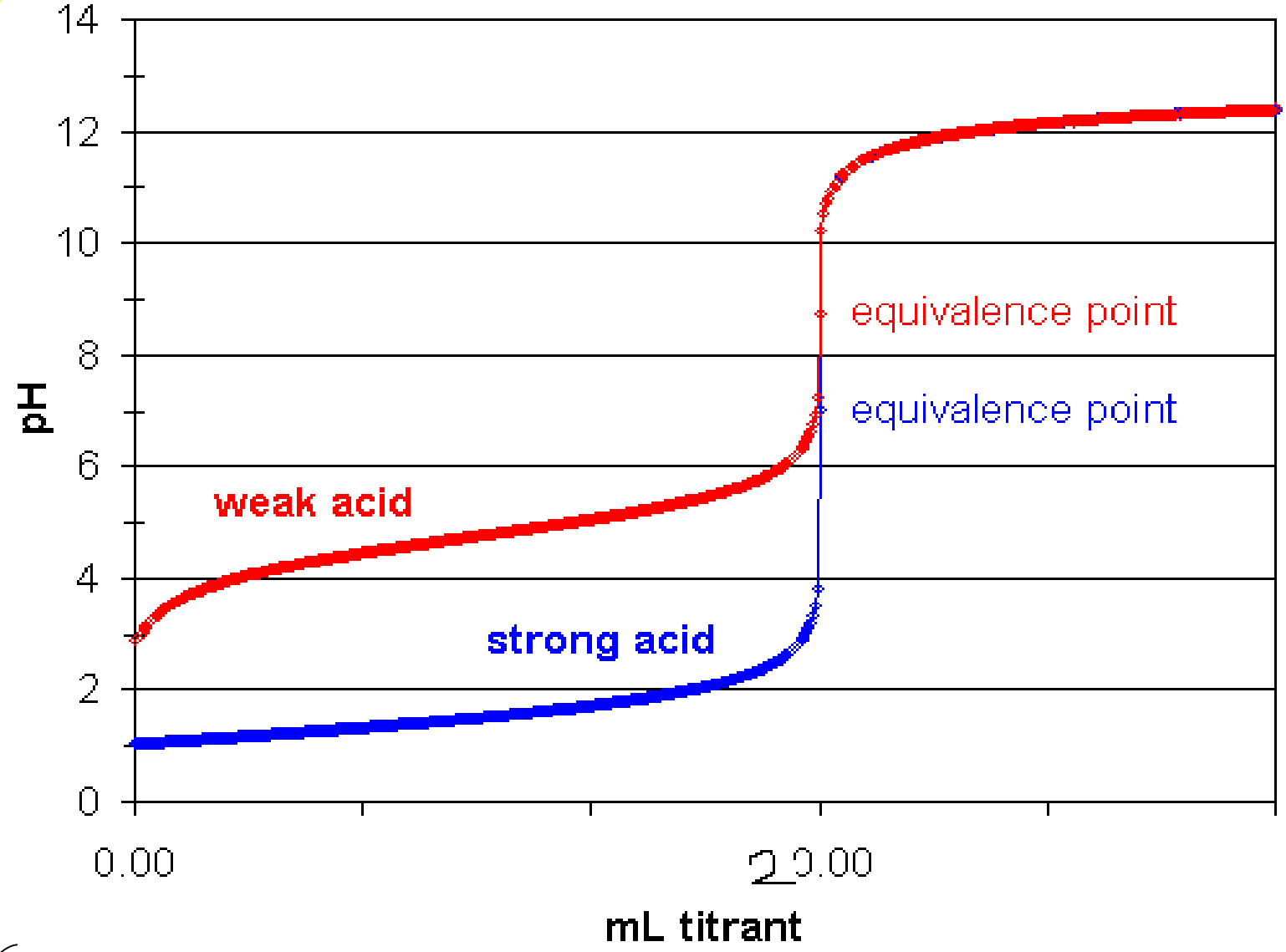
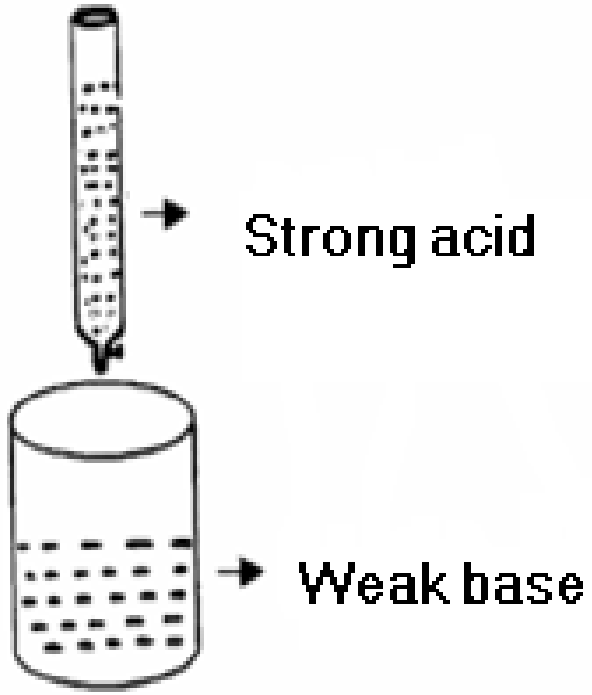
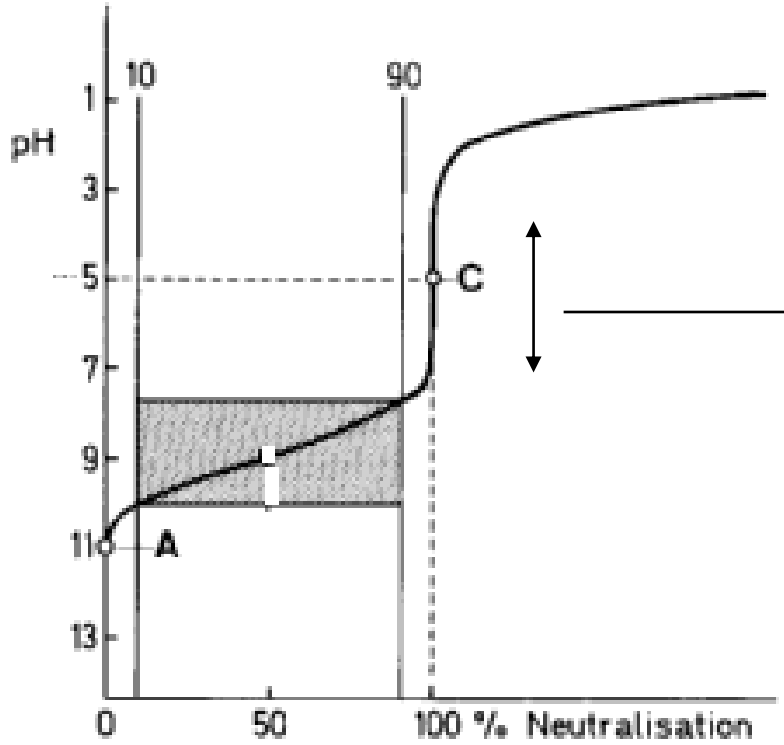

14
12
10
8
6
4
2
0
pH
0.00
20.00
mL titrant
equivalence point
equivalence point
weak acid
strong acid

III- Titration curve for weak base with strong acid





A ▪ Start point

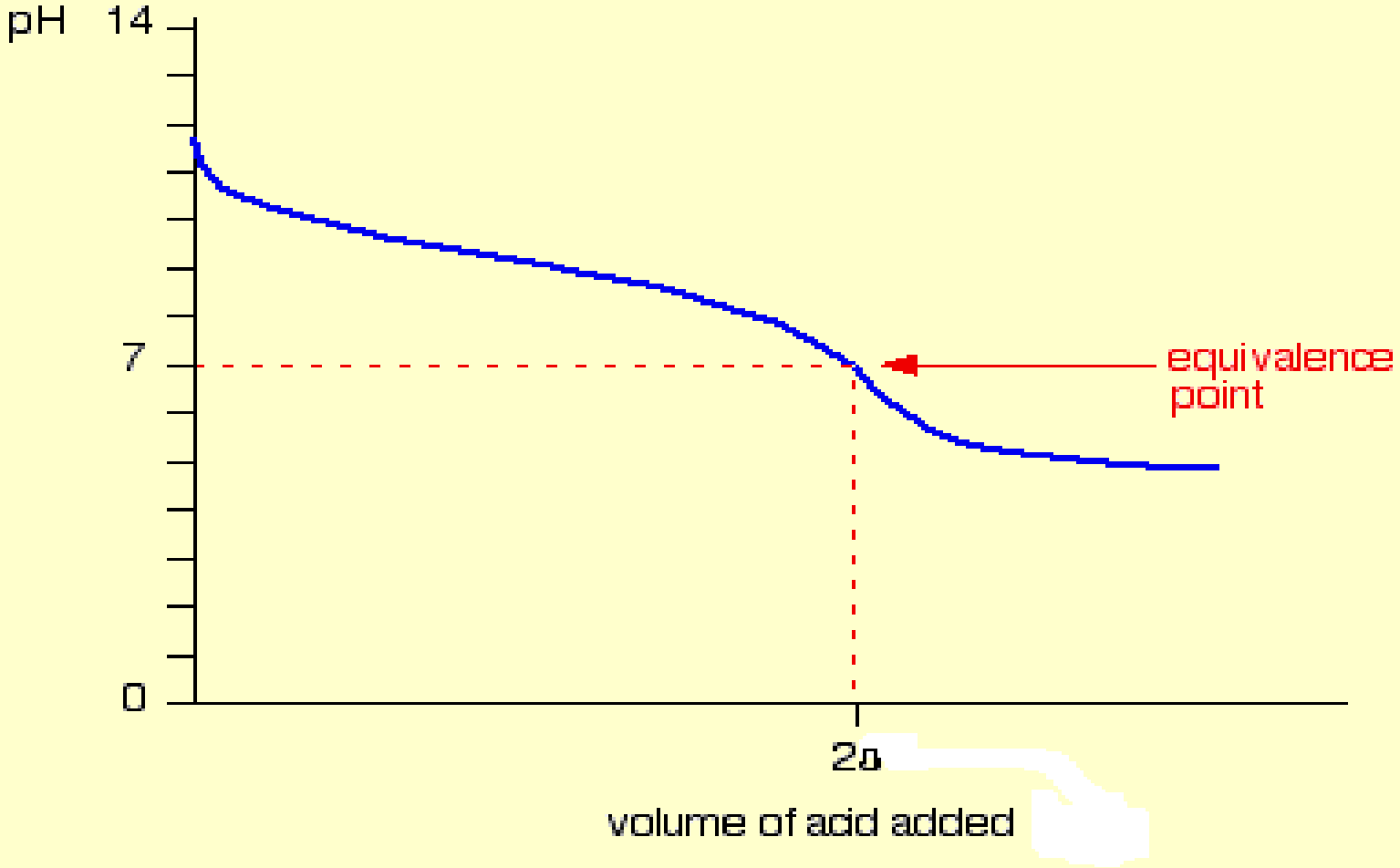
Titration jump 4-6

C ▪ Equivalent P

▪ Buffer region

Weak base v Strong acid

IV- titration of weak base with weak acid



Notice that there isn't any steep bit on this graph. Instead, there is just what is known as a "point of inflexion". That lack of a steep bit means that it is difficult to do a titration of a weak acid against a weak base.

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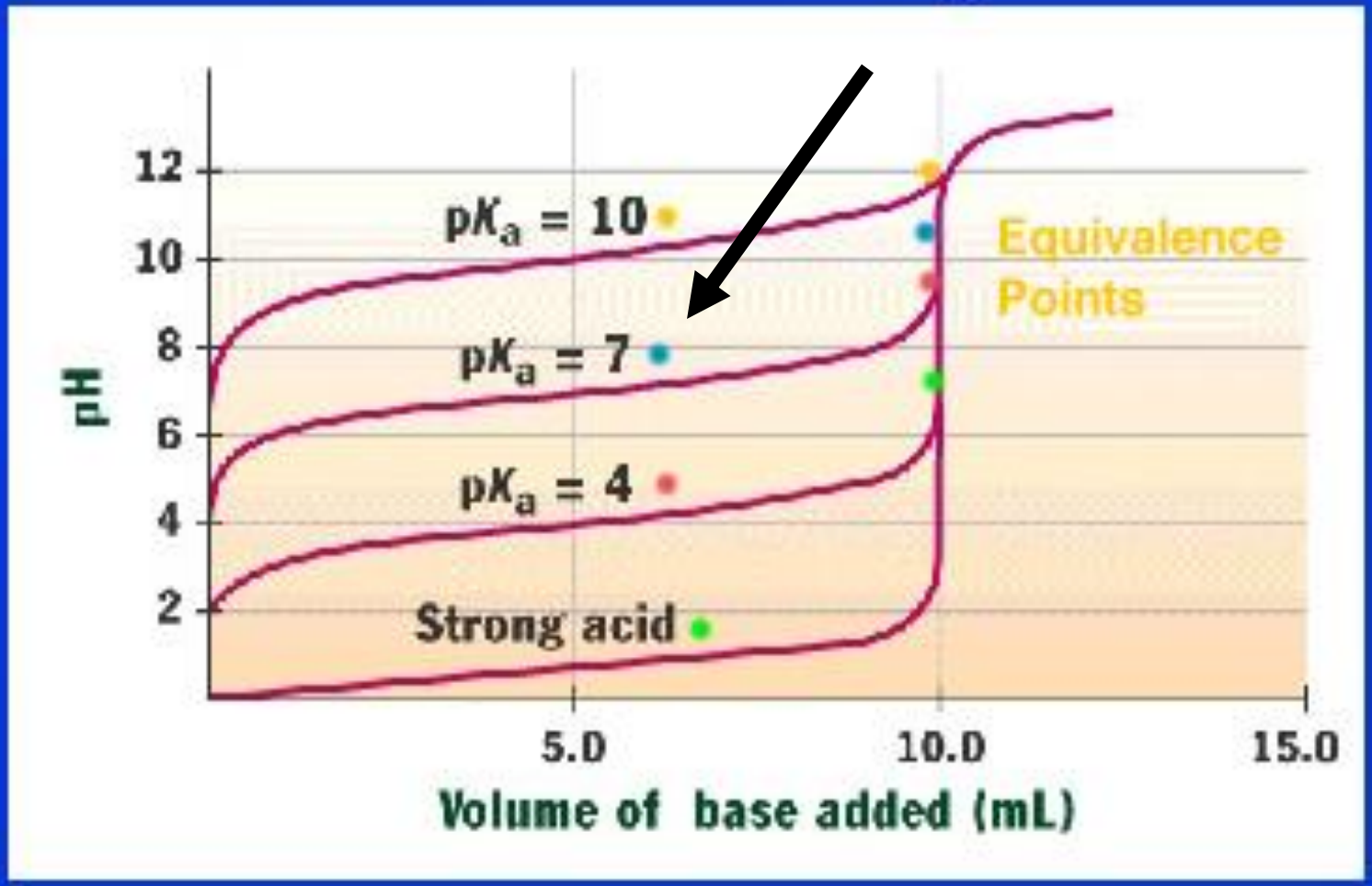
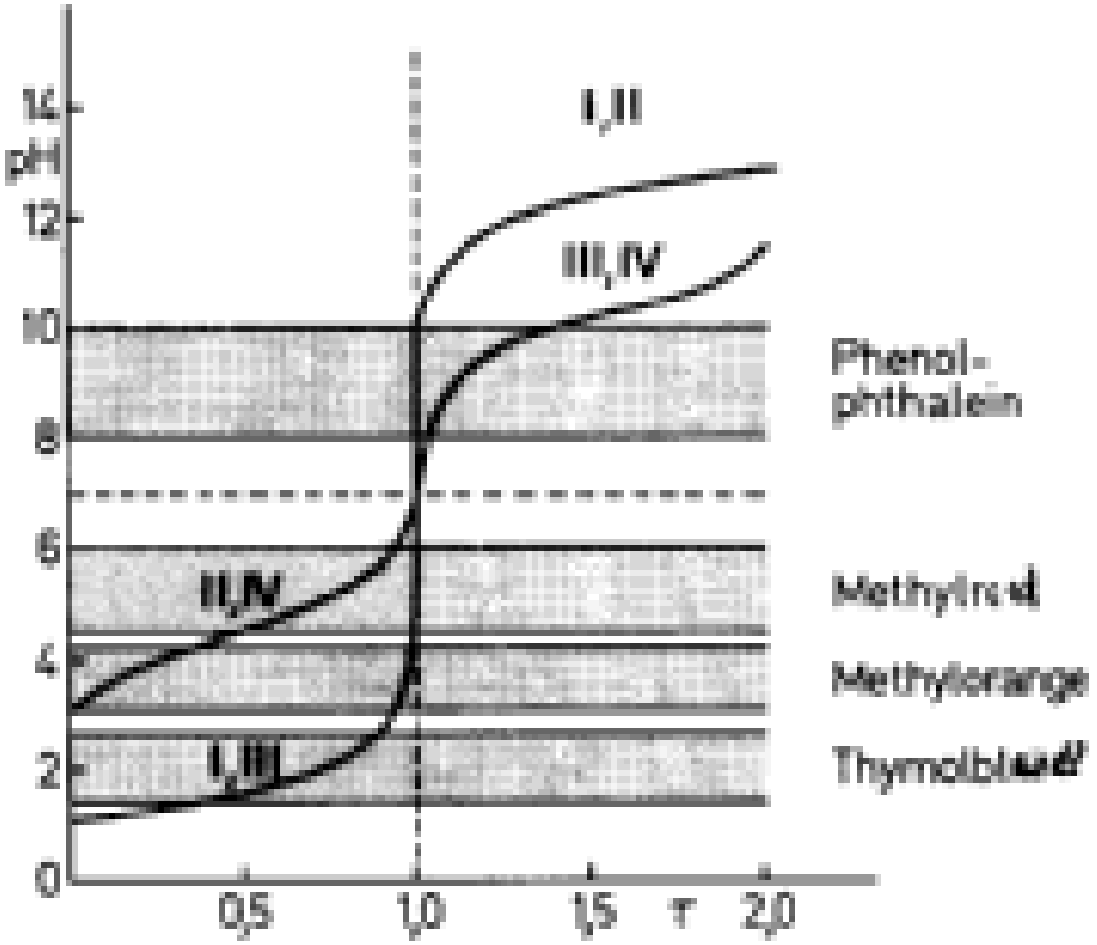
Titration Curves for Acids of Different Strengths



Acid-base titration Curves



Detection of the end point

- Electrochemical method (Potentiometer)
- Visual method (Colors Indicators)

Colors Indicators

Acid-base indicators are highly colored weak acids or bases.

$$HIndic \rightleftharpoons Indic + H^+$$

color 1 ⇌ color 2

Indicators

The pH for conversion of approximately 1/10 of our indicator if starting from acidic conditions is:

$$pH = pK_A + \log \frac{1}{10} = pK_A - 1$$

From the basic direction, it is:

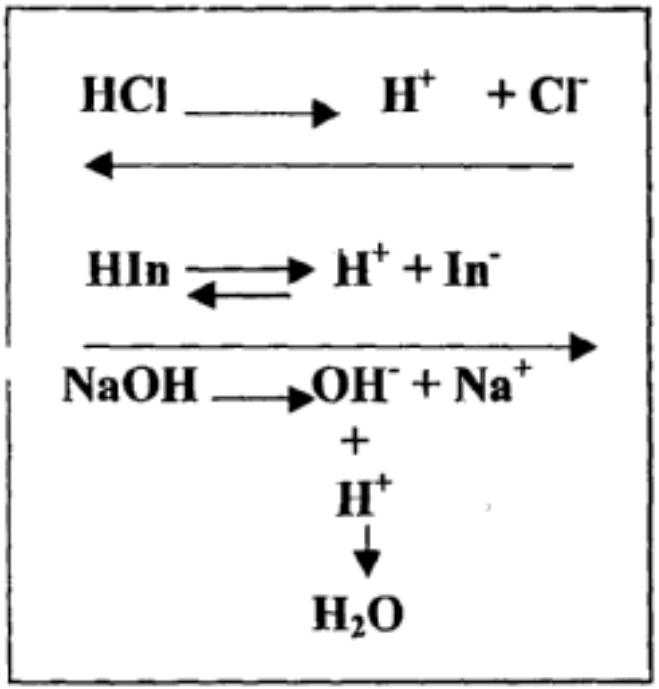
$$pH = pK_A + \log \frac{10}{1} = pK_A + 1$$

$$\Delta pH = (pKa + 1) - (pKa - 1) = 2$$

Mechanism of indicators effect

Acid media

Base media

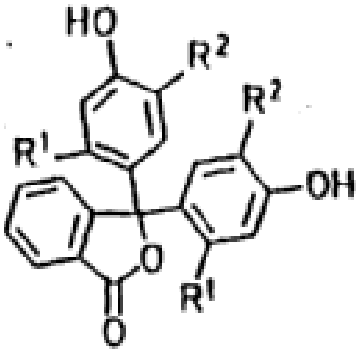


HIn Color

In- color

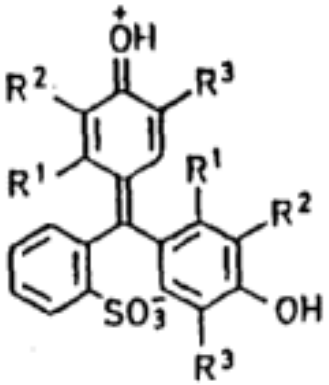
Chemical Classification of indicators

1. **Phthleine Group**



	R^1	R^2
Phenolphthalein	H	H
Thymolphthalein	$-CH_3$	$-CH(CH_3)_2$

2- Sulfophthaleine Group



Sulfophthaleine	R^1	R^2	R^3
Bromcresolgreen	$-CH_3$	Br	Br
Bromcresolpurpur	H	$-CH_3$	Br
Bromphenolblue	H	Br	Br
Bromthymolblue	$-CH_3$	Br	$-CH(CH_3)_2$
Cresolred	H	$-CH_3$	H
Phenolred	H	H	H
Thymolblue	$-CH_3$	H	$-CH(CH_3)_2$

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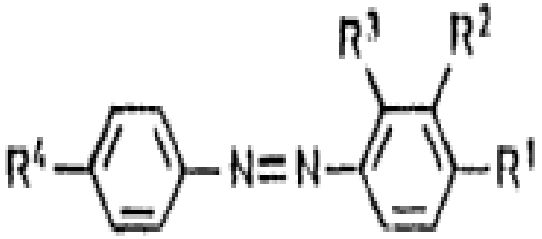
3- Azo-colors Group

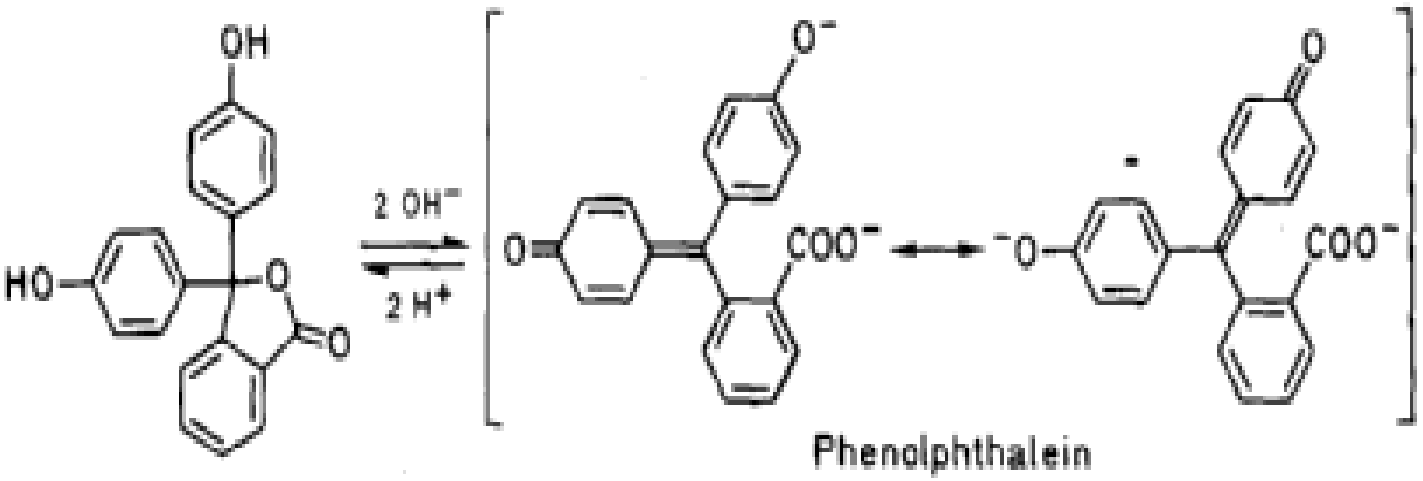


	R^1	R^2	R^3	R^4
Metanilyellow	H	$-SO_3Na$	H	$-NH-C_6H_5$
Methylorange	$-SO_3Na$	H	H	$-N(CH_3)_2$
Methylred	H	H	$-COOH$	$-N(CH_3)_2$
Tropaolin OO	$-SO_3Na$	H	H	$-NH-C_6H_5$

One Color Indicators

- In Acidic media Colorless
- Phenolphtalein $H_2IND \rightleftharpoons 2H^+ + Ind^{-2}$

Colorless 8-10 red

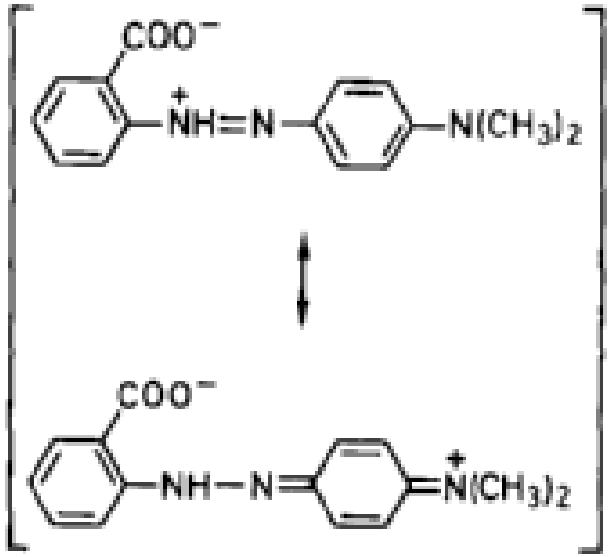


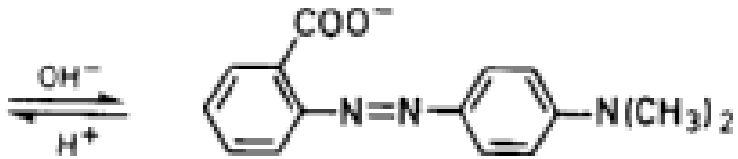
Phenolphthalein

Tow color Indicators

- Methyl red (red in acidic media , yellow in basic media) .Hind $\rightleftharpoons$ $H^+ + ind^-$

red 4.2 – 6.2 yellow





Methyl red

Indicators

During an acid-base titration, the indicator acts as an additional weak acid or base.

It must be weaker than the species being determined - titrated after analyte.

It must be present at relatively low concentrations so as not to interfere with the normal titration curve and equivalence point.

It must give a sharp and distinct color change.

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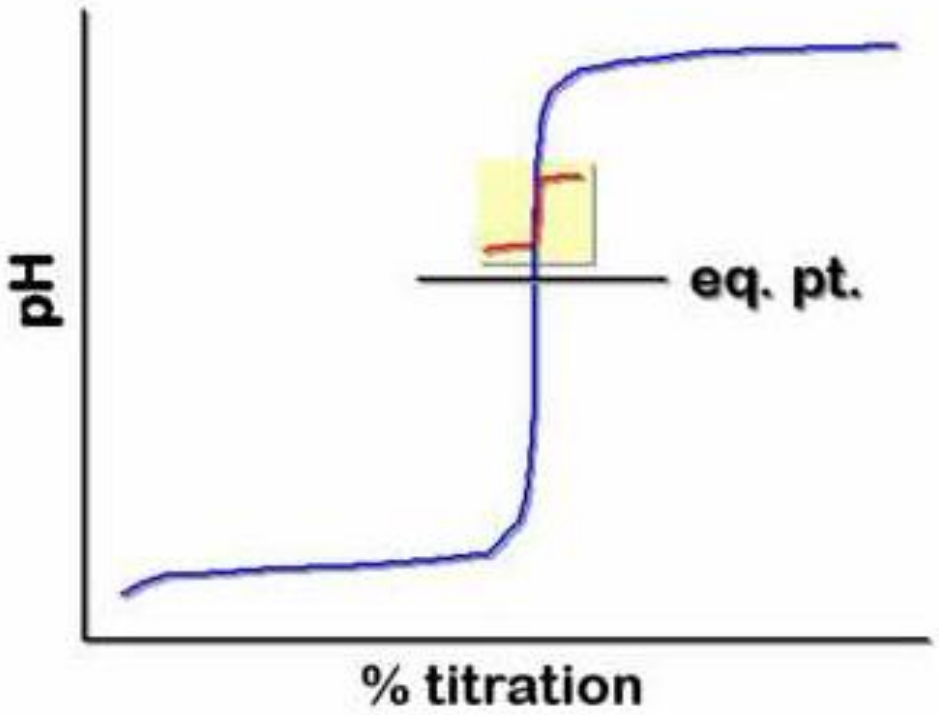
Indicators



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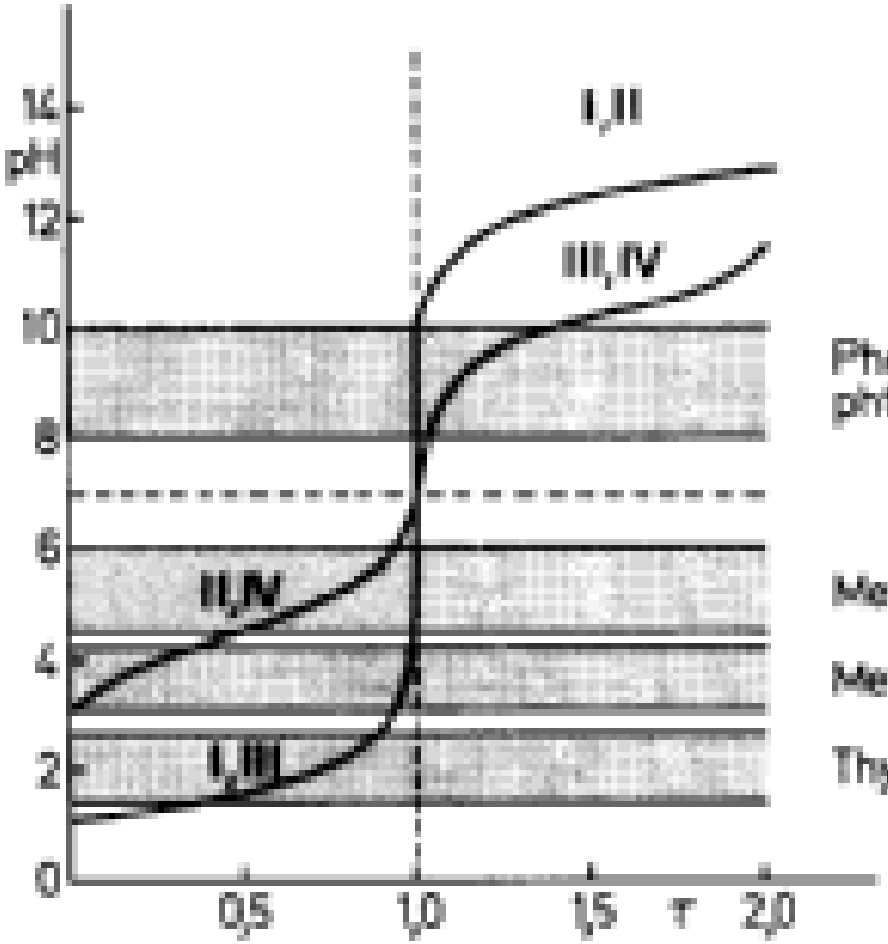
Indicator	Color			pH Range
	acidic	endpoint	basic	
bromocresol green	yellow	green	blue	4.0-5.6
methyl red	red	yellow	yellow	4.4-6.2
bromothymol blue	yellow	green	blue	6.2-7.6
phenolpthalein	colorless	light pink	red	8.0-10

Thymol blue	**red**	**yellow**	**1.2 – 2.8**
Phenol red	**yellow**	**reddish violet**	**6.8 - 8.4**

Choosing an Indicators, The feasibility of Titration



Phenol-phthalein → 8-10

Methyl red → 4.4 – 6.2

Methylorange → 3.1 - 4.4

Thymolblue → 1.2 - 2.8

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Pharmaceutical Applications

I. Raw material

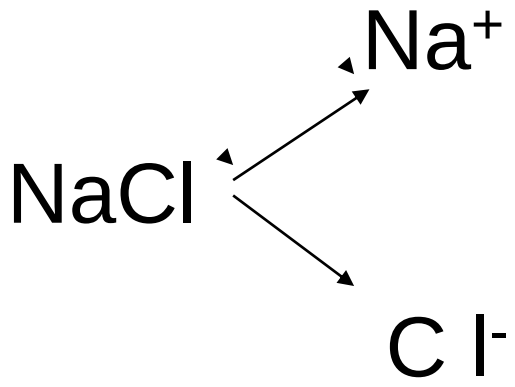
You ought to assay the following Pharmaceutical substances .Explain the analytical method that you will chose ,Why?

- NaCl
- $Na_2 CO_3$
- NH_4Cl
- Benzoic acid
- Salicylic acid
- Anhydrous Citric Acid

Sodium Chloride

NaCl

NaCl



(pH = 7, Can not be assay by acid-base titration)

- We can used Mohr's Method:

- $AgNO_3 + NaCl \rightarrow AgCl\downarrow + NaNO_3$

ppt

Sodium Chloride

58.44 *7647-14-5*

Action and use

Used in treatment of electrolyte deficiency.

Preparations

Oral Rehydration Salts

Potassium Chloride and Sodium Chloride Intravenous Infusion

Potassium Chloride, Sodium Chloride and Glucose Intravenous Infusion

Sodium Chloride Eye Drops

Sodium Chloride Eye Lotion

Sodium Chloride Intravenous Infusion

Sodium Chloride and Glucose Intravenous Infusion

Sodium Chloride Irrigation Solution

Compound Sodium Chloride Mouthwash

Sodium Chloride Solution

Sodium Chloride Tablets

Sodium Chloride

ASSAY

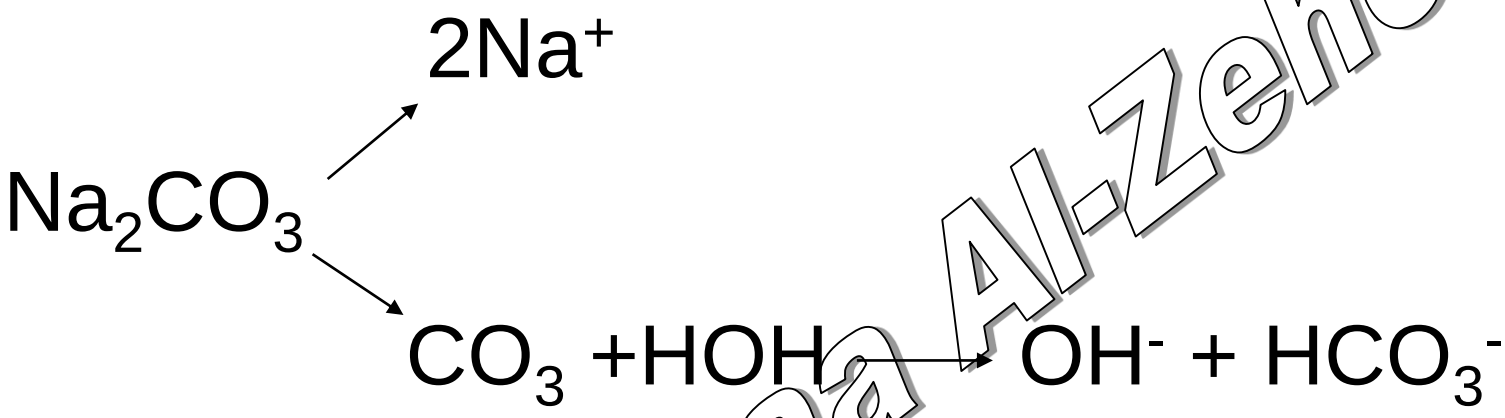
Dissolve 50.0 mg in *water R* and dilute to 50 ml with the same solvent. Titrate with *0.1 M silver nitrate* determining the end-point potentiometrically *(2.2.20)*.

1 ml of *0.1 M silver nitrate* is equivalent to 5.844 mg of NaCl.

Anhydrous Sodium Carbonate

Na_2CO_3

Na_2CO_3



- Weak base
- Can be titrate with HCl
- Titration range (Jump) 4-6
- Methyl red

Anhydrous Sodium Carbonate

(Ph Eur monograph 0773)

Na_2CO_3 106.0 *497-19-8*

DEFINITION

Anhydrous sodium carbonate contains not less than 99.5 per cent and not more than the equivalent of 100.5 per cent of Na_2CO_3, calculated with reference to the dried substance.

ASSAY

Dissolve 1.000 g in 25 ml of *water R*. Add 0.2 ml of *methyl orange solution R* as indicator. Titrate with *1 M hydrochloric acid* until the colour changes from yellow to red.

1 ml of *1 M hydrochloric acid* is equivalent to 52.99 mg of Na_2CO_3.

√

Ammonium Chloride

NH_4Cl

NH_4Cl

1) $NH_4Cl \rightarrow Cl^-$ and $NH_4^+ + H_2O \longrightarrow NH_3 + H_3O^+$

2) $4\ NH_4CL + 6\ HCHO \longrightarrow (CH2)_6N_4 + 4\ HCl + 6\ H_2O$

$HCl + NaOH \longrightarrow NaCl + H_2O$

$NH_4Cl = HCl = NaOH$

3) **Volhards method**

$NH_4Cl + AgNO_3 \longrightarrow AgCl + NH_4NO_3$

(excess)

$AgNO_3 + NH_4SCN \longrightarrow AgSCN + NH_4NO_3$

(excess)

Ammonium Chloride

General Notices

(Ph Eur monograph 0007) NH4Cl 53.49 *12125-02-9*

Action and use

Used for the acidification of urine and to correct metabolic alkalosis.

Preparation

Ammonium Chloride Mixture

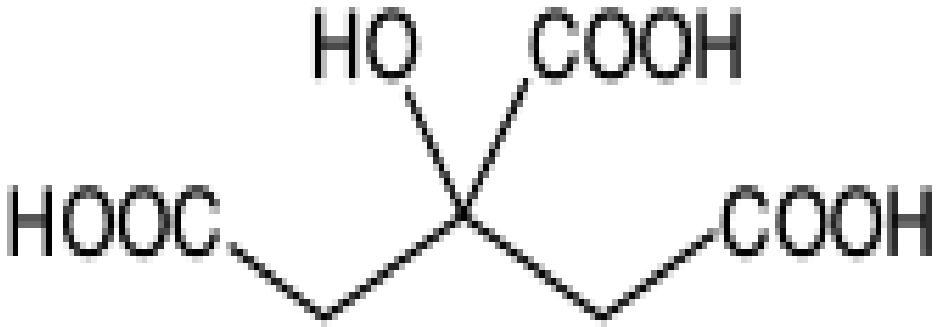
ASSAY

Dissolve 1.000 g in 20 ml of *water R* and add a mixture of 5 ml of *formaldehyde solution R*, previously neutralised to *phenolphthalein solution R*, and 20 ml of *water R*. After 1 min to 2 min, titrate slowly with *1 M sodium hydroxide*, using a further 0.2 ml of the same indicator.

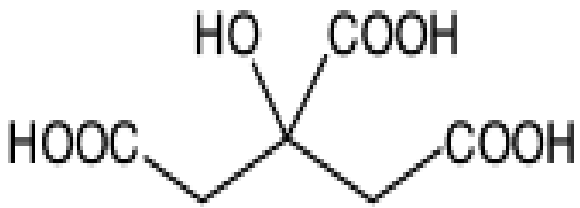
1 ml of *1 M sodium hydroxide* is equivalent to 53.49 mg of NH4Cl.

يجب أن تكون عينة المواد الأولية ممثلة لطبيعة المادة وجوهرها بحبث تؤخذ من أماكن مختلفة ومن عبوات متعددة ثم تمزج وتجانس

Anhydrous Citric Acid



Anhydrous Citric Acid



$C_6H_8O_7$ 192.1

ASSAY

Acidifying agent

Antioxidant

Buffering agent

chelating agent

Flavor enhancer

Anticoagulant citrate

For effervescent tablet اللامائيand Granules
للمضغوطات والمائي للحثيرات

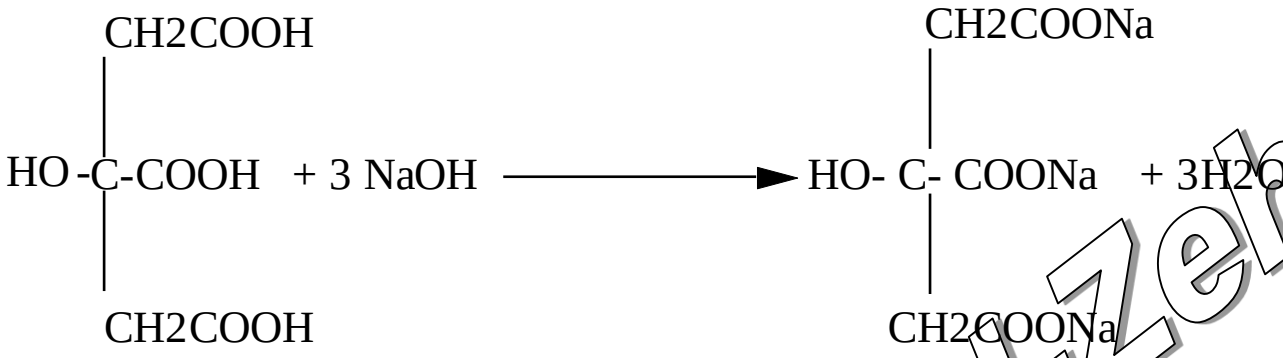
To dissolve renal calculi

Dissolve 0.550 g in 50 ml of *water R*. Titrate with *1*M *sodium hydroxide*, using 0.5 ml of *phenolphthalein solution R* as indicator.

1 ml of *1*M *sodium hydroxide* is equivalent to 64.03 mg of C6H8O7.

Anhydrous Citric Acid

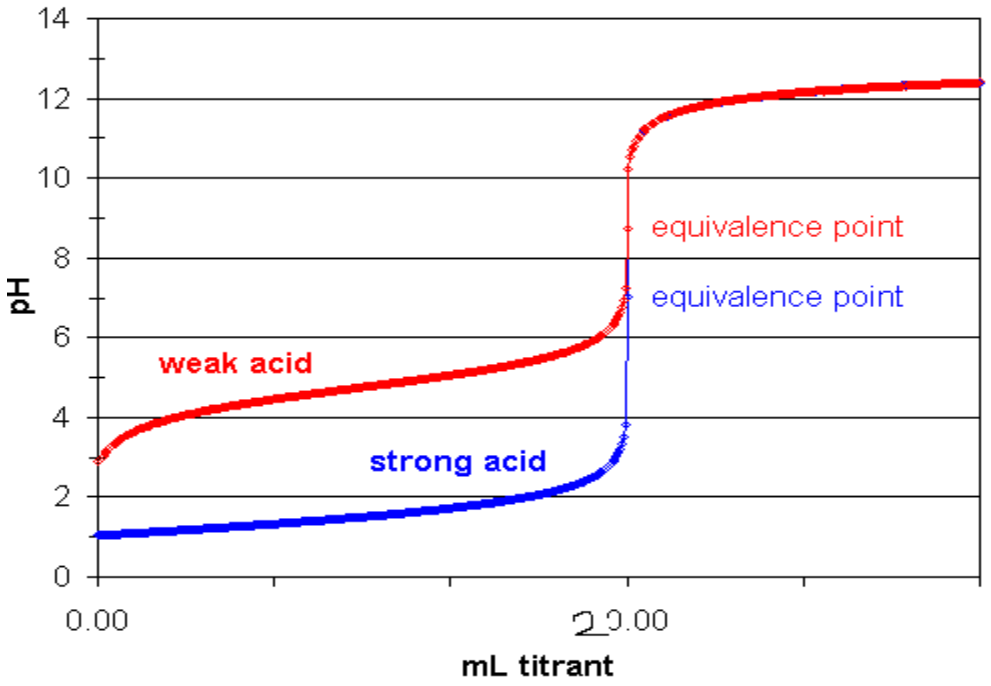
- Can we use another indicator ? Why ?
- Explain how we have got the Nr. 64.03 ?
- If we consumed to the end point 8.4 ml of sodium hydroxide . What is the % purity of citric acid ?(F=1.01)



192.1 g — 3000 ml 1M NNaOH

0.06403 — 1 ml

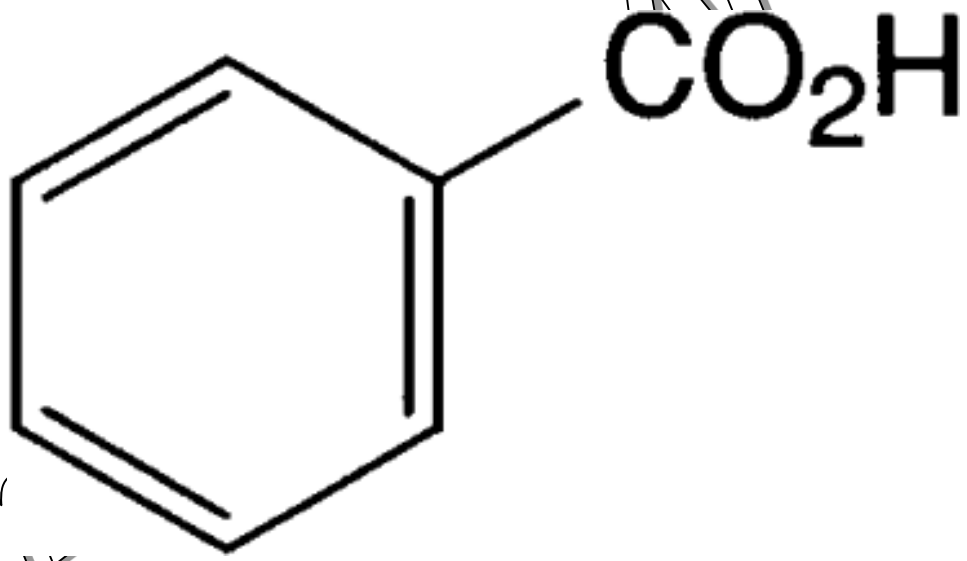
- Best indicator is Ph.Ph (Titration jump 8-10)



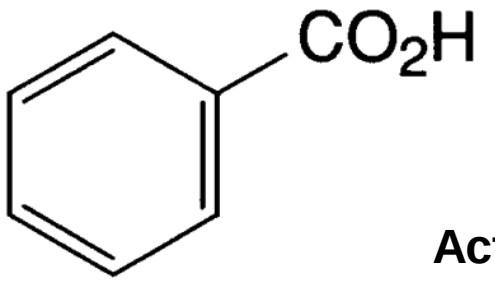
- Best indicator is Ph.Ph (Titration jump 8-10)

- $$C\ \% = \frac{8.4 \times 1.01 \times 64.03 \times 100}{550} = 98.7\ \%$$

Benzoic Acid



Benzoic Acid



$C_7H_6O_2$ *122.1*

Action and use

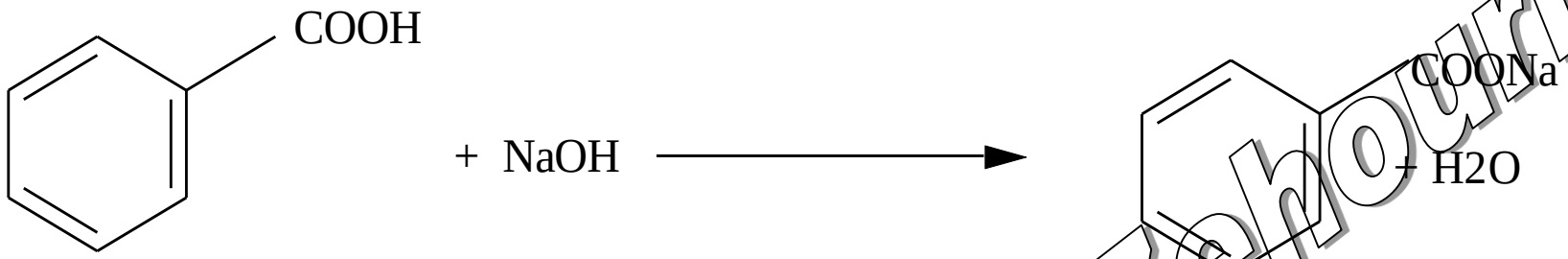
Antimicrobial preservative.

ASSAY

Dissolve 0.200 g in 20 ml of *alcohol R* and titrate with *0.1 M sodium hydroxide*, using 0.1 ml of *phenol red solution R* as indicator, until the colour changes from yellow to violet-red.

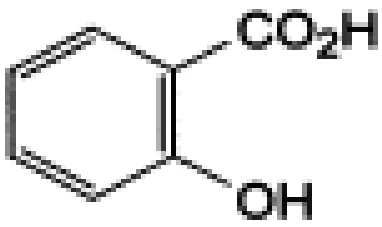
1 ml of *0.1 M sodium hydroxide* is equivalent to 12.21 mg of C7H6O2.

Ph Eur



122.1 **10000 ml 0.1 M**

12.21 mg **1ml 0.1 M NaOH**



$C_7H_6O_3$ 138.1

Action and use

Keratolytic.

Preparations

Salicylic Acid Collodion

Salicylic Acid Ointment

Coal Tar and Salicylic Acid Ointment

Zinc and Salicylic Acid Paste

Pharmaceutical Applications

II- Dosage forms

Dosage forms

- Lithium Carbonate tab.

- Sodium Bicarbonate Intravenous Infusion

- Salicylic Acid Ointment 2%

- Aspirin tab.

- Diphenhydramine Hydrochloride Oral Solution

Lithium Carbonate Tablets

300 mg

يؤخذ إما الجذر التربيعي للعدد الكلي للطبخة مضروب ب 0.4 أو 20 مصغوطة تسحق ويؤخذ من البودرة ما يكافىء وزن المادة الفعالة المطلوب

نعليمات

Dosage instruction

Storage condition

Name of product

Expiry date

Batch number

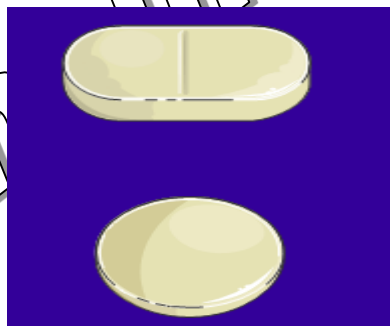
Name and quantity of active ingredient

HK registration number

Name of manufacturer

Address of manufacturer

Lithium Carbonate Tablets (300 mg)



Li_2CO_3 73.9 (use : Antimanic)

Assay

Weigh and powder 20 tablets. Add a quantity of the powder containing 1 g of Lithium Carbonate to 100 ml of *water*, add 50 ml of 1M *hydrochloric acid VS* and boil for 1 minute to remove the carbon dioxide. Cool and titrate the excess of acid with 1M *sodium hydroxide VS* using *methyl orange solution* as indicator. Each ml of 1M *hydrochloric acid VS* is equivalent to 36.95 mg of Li_2CO_3.

Lithium Carbonate Tablets

- Is this titration (direct, back or replacement)?
- If the average tablet weight is 600 mg ,What is the weight sample taken ?
- If we consumed 22.5 ml to the end point , What is the % of lithium carbonate in the tablet?

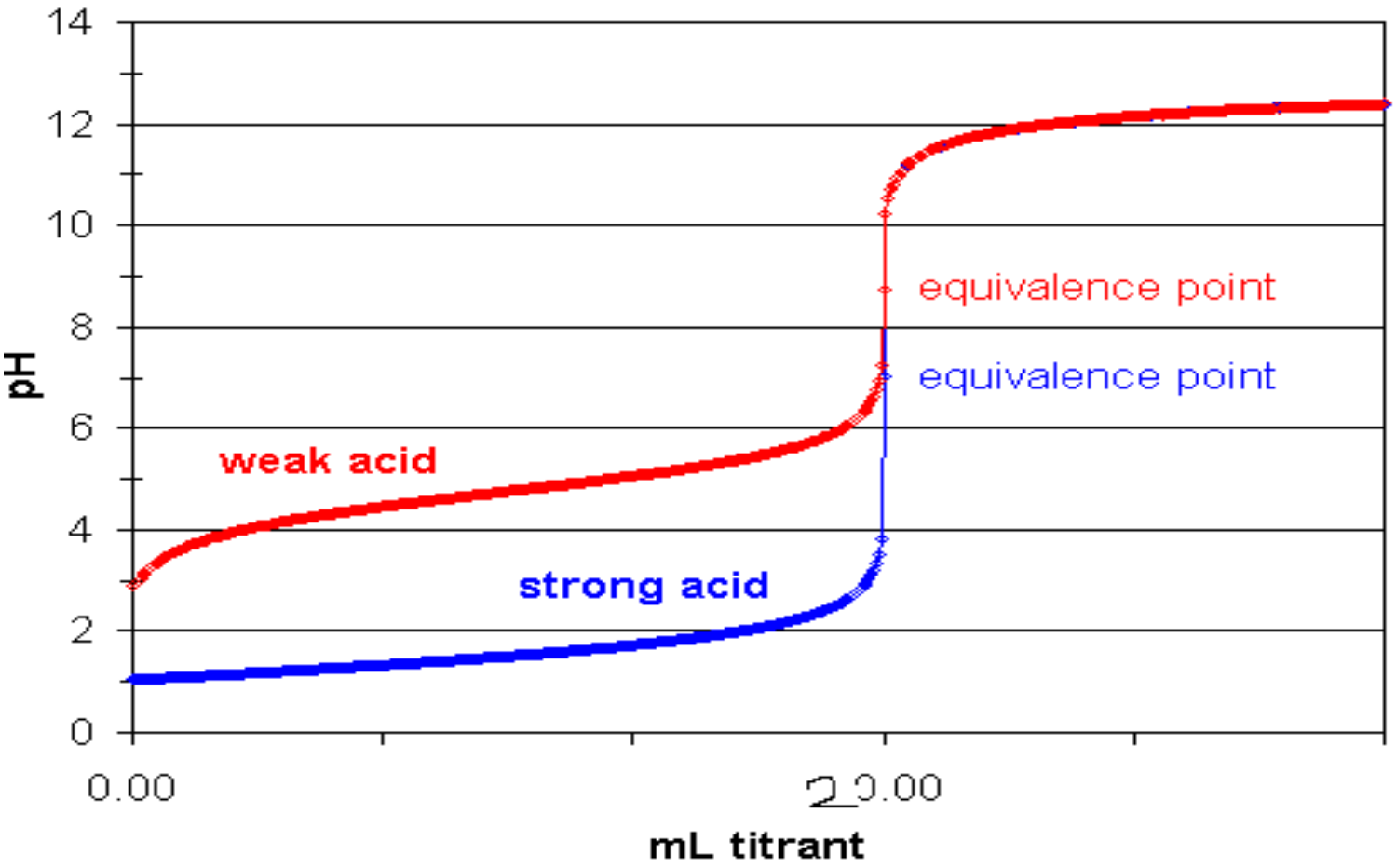
  (F=1)
- If Methyl orange is not available can we used another indicator ?

Answers

- Back
- 2000 mg
- C % = $\frac{(50 - 22.5) \times 1 \times 36.95 \times 100}{1000}$ = 101.6
- $Li_2CO_3 + 2HCl \longrightarrow 2LiCl + CO_2 + H_2O$

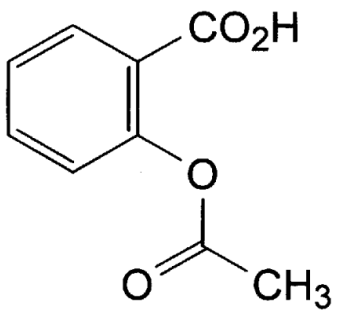
  1 g 50 ml (excess)
- $HCl + NaOH \longrightarrow NaCl + H_2O$

  Buret



Yes we can use another indicator like Ph.Ph , Methyl red , Bromcresol green , ……

Aspirin Tablets

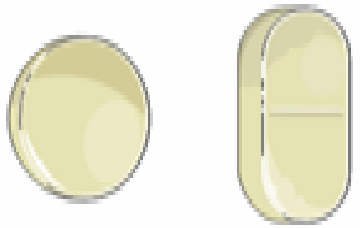


(Acetylsalicylic Acid,

$C_9H_8O_4$ 180.2

Action and use

Analgesic; antipyretic.



Preparations

Aspirin Tablets

Dispersible Aspirin Tablets

Effervescent Soluble Aspirin Tablets

Gastro-resistant Aspirin Tablets

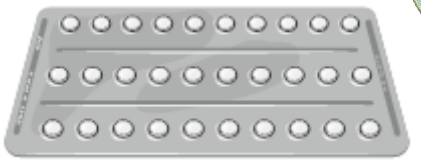
Aspirin and Caffeine Tablets

Co-codaprin Tablets

Dispersible Co-codaprin Tablets

content of aspirin, $C_9H_8O_4$

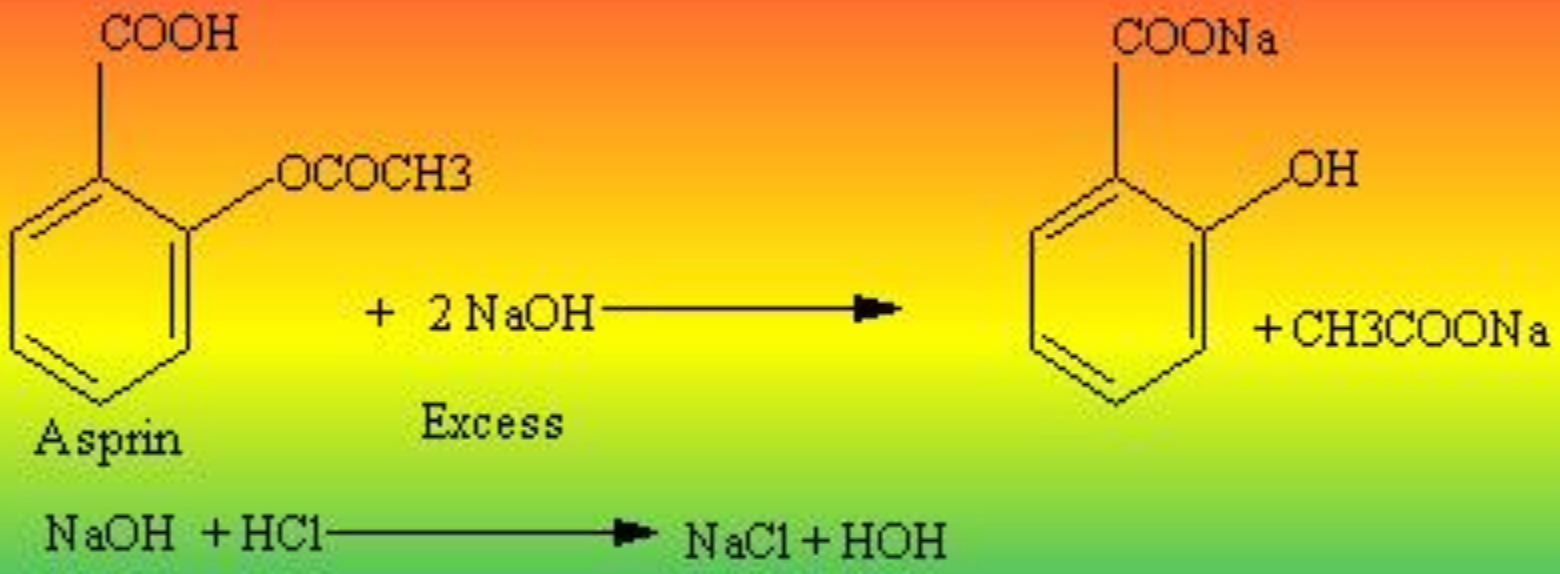
95.0 to 105.0% of the stated amount.



ASSAY

Weigh and powder 20 tablets. To a quantity of the powder containing 0.5 g of Aspirin add 30 ml of 0.5M *sodium hydroxide VS*, boil gently for 10 minutes and titrate the excess of alkali with 0.5M *hydrochloric acid VS* using *phenol red solution* as indicator. Repeat the operation without the substance being examined. The difference between the titrations represents the amount of sodium hydroxide required. Each ml of 0.5M *sodium hydroxide VS* is equivalent to 45.04 mg of $C_9H_8O_4$.

Back-titration



Phenol red (6.8 Yellow - 8.4 Reddish violet)

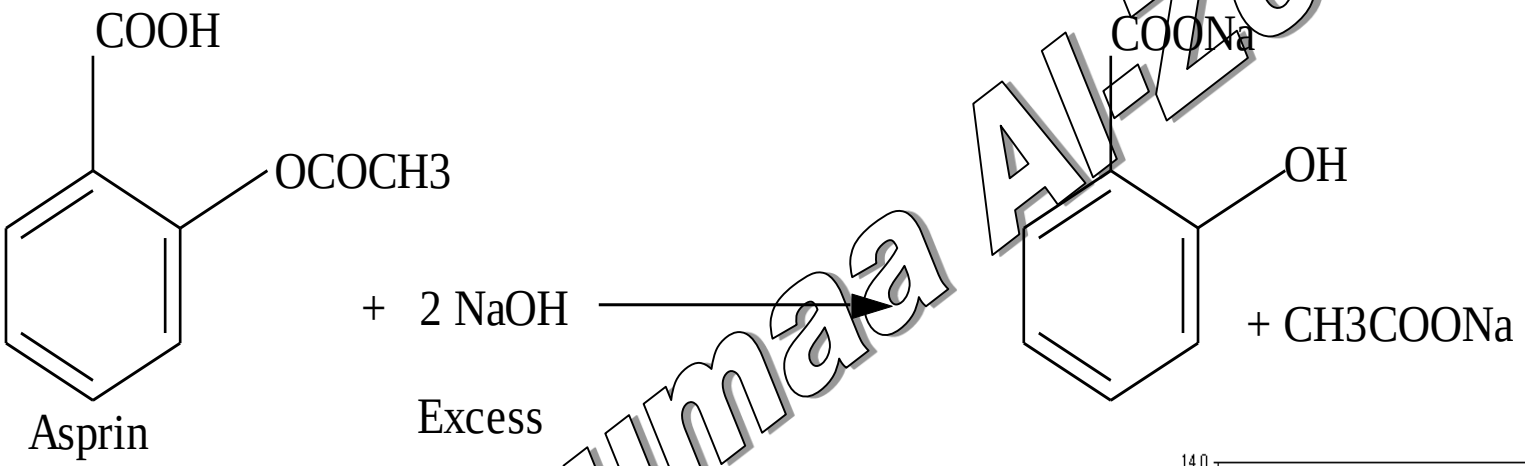
Aspirin

- What is the Type of this Titration ?
- Can we use another indicator ? Why ?
- Explain how we have got the Nr. 45.04 ?
- If we required to the end point 18.9 ml

  , What is the % purity of Aspirin ?

  (F=1)

Back-titration

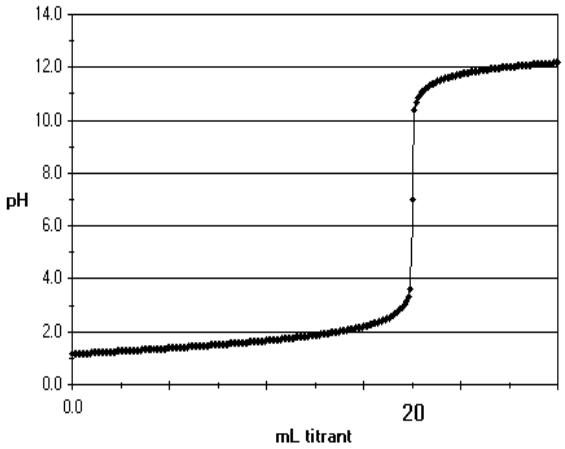


$$NaOH + HCl \rightarrow NaCl + HOH$$

1 M ASPIRIN ≡ 2 M NaoH

180.2 g 2000 ml NaOH 1M

180.2 g 4000 ml NaOH 0.5 Mol



Phenol red (6.8 Yellow - 8.4 Reddish violet)

$$\frac{(30 - 18.9) \times 1 \times 45.04 \times 100}{500} = 99.98\ \%$$

Sodium Bicarbonate Intravenous Infusi

Sodium Hydrogen Carbonate

$NaHCO_3$ 84.0

Action and use

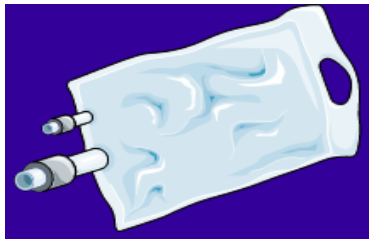
Antacid; used in treatment of electrolyte deficiency.

Preparations

Sodium Bicarbonate Ear Drops

Sodium Bicarbonate Eye Lotion

Sodium Bicarbonate Intravenous Infusion



Compound Sodium Bicarbonate Tablets

Content of sodium bicarbonate, $NaHCO_3$

94.0 to 106.0% of the stated amount.

هنا تؤخذ العينة بالحجم حيث يحدد حجمها بناء على التركيز المدون على العبوة

ASSAY

Titrate a volume containing 1 g of Sodium Bicarbonate with 0.5M *hydrochloric acid VS* using *methyl orange solution* as indicator. Each ml of 0.5M *hydrochloric acid VS* is equivalent to 42.00 mg of NaHCO3.

-تحمضن استقلابي pH اقل من 7.35 metabolic acidosis

$NaHCO_3 + H\,Cl \longrightarrow Na\,Cl + H_2O + CO_2$

1M ≡ 1 M

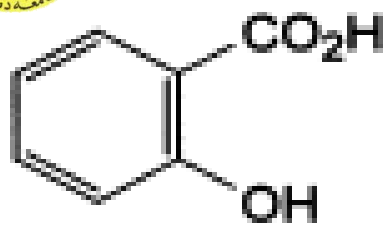
84 g ≡ 1000 ml HCl 1M

84 g ≡ 2000 ml HCl 0.5 M

0.042 ≡ 1 ml HCl 0.5 M

$$C\% = \frac{V \times F \times mEq \times 100}{\text{weight of sample taken}}$$

Salicylic Acid √



هنا لايوجد وزن وسطي
ولكن شرط أساسي
لأمكانية أخذ العينة هو
معرفة النسبة المئوية
للمادة الفعالة

$C_7H_6O_3$ 138.1

Action and use

Keratolytic.

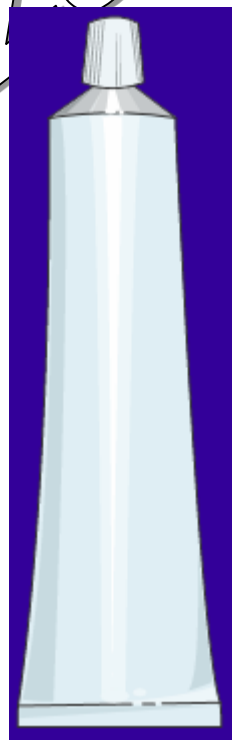
Preparations

Salicylic Acid Collodion

Salicylic Acid Ointment

Coal Tar and Salicylic Acid Ointment

Zinc and Salicylic Acid Paste



Prof. J. Al-Zehouri

Salicylic Acid Ointment

DEFINITION

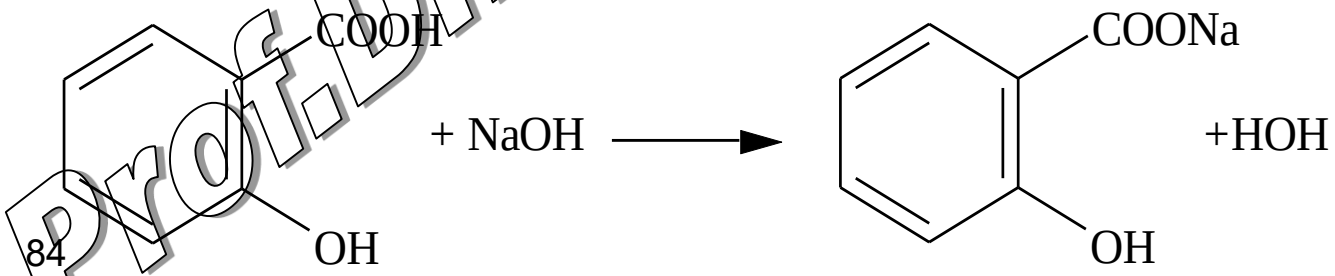
Salicylic Acid Ointment contains 2% w/w of Salicylic Acid in a suitable water-emulsifying basis.

Content of salicylic acid, C7H6O3

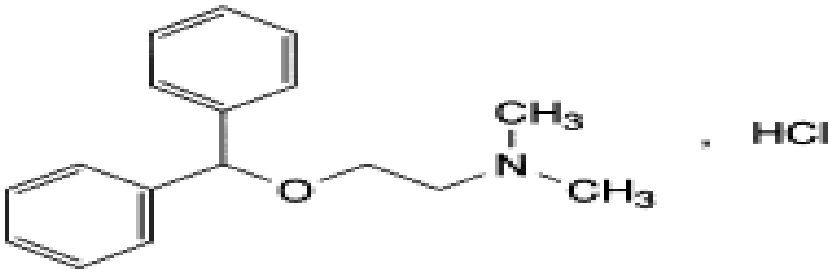
1.9 to 2.1% w/w.

ASSAY

Dissolve 10 g in a mixture of 20 ml of *ethanol* (*96%*), previously neutralised to *phenol red solution*, and 20 ml of *ether* and titrate with 0.1M *sodium hydroxide VS* using *phenol red solution* as indicator. Each ml of 0.1M *sodium hydroxide VS* is equivalent to 13.81 mg of C7H6O3.



Diphenhydramine Hydrochloride



العينة هنا قد تكون حجمية أو وزنية
(بحال كان بودرة قابلة للحل) ولكن
يفضل التعامل معها بعد الحل

$C_{17}H_{21}NO,HCl$ 291.8

Action and use

Histamine H_1-receptor antagonist.

Preparation

Diphenhydramine Oral Solution

H1 للحساسية

H2 للقرحة

Diphenhydramine Oral Solution

Content of diphenhydramine hydrochloride, $C_{17}H_{21}NO,HCl$

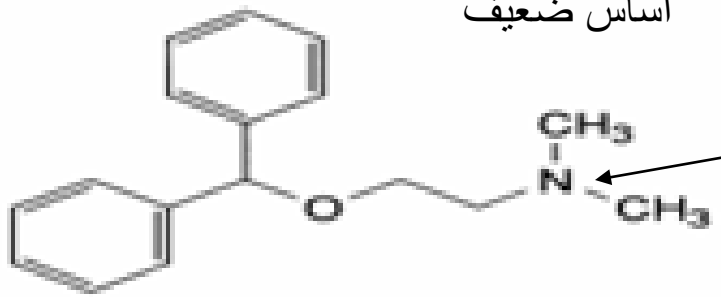
90.0 to 110.0% of the stated amount.

ASSAY

Acidify a quantity containing 0.1 g of diphenhydramine hydrochloride with 2M *hydrochloric acid*, shake with three 20 ml quantities of *ether* , discard the ether, make the aqueous solution alkaline with 5M *sodium hydroxide* and extract with successive 15 ml quantities of *ether* until extraction is complete. Wash the combined ether extracts with two 5 ml quantities of *water* , extract the combined washings with 15 ml of *ether* and evaporate the combined ether extracts to dryness. Dissolve the residue in 15 ml of 0.05M *sulphuric acid VS* and titrate the excess of acid with 0.1M *sodium hydroxide VS* using *methyl red solution* as indicator. Each ml of 0.05M *sulphuric acid VS* is equivalent to 29.18 mg of C17H21NO.HCl.

1 M ≡ ½ M H_2SO_4

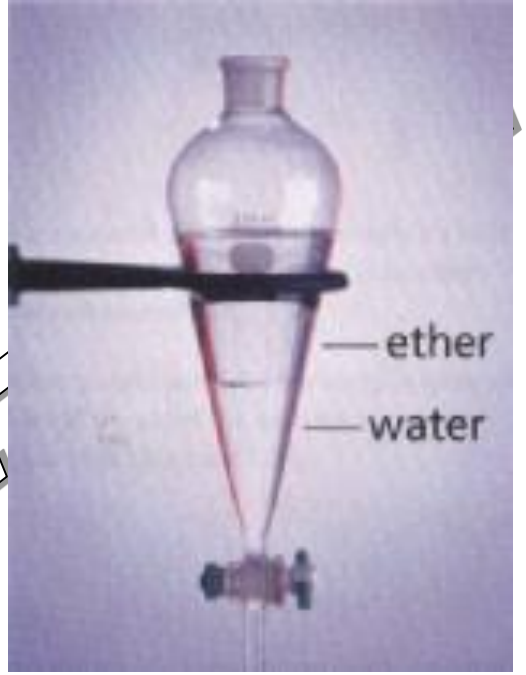
أساس ضعيف



حمض قويH2SO4

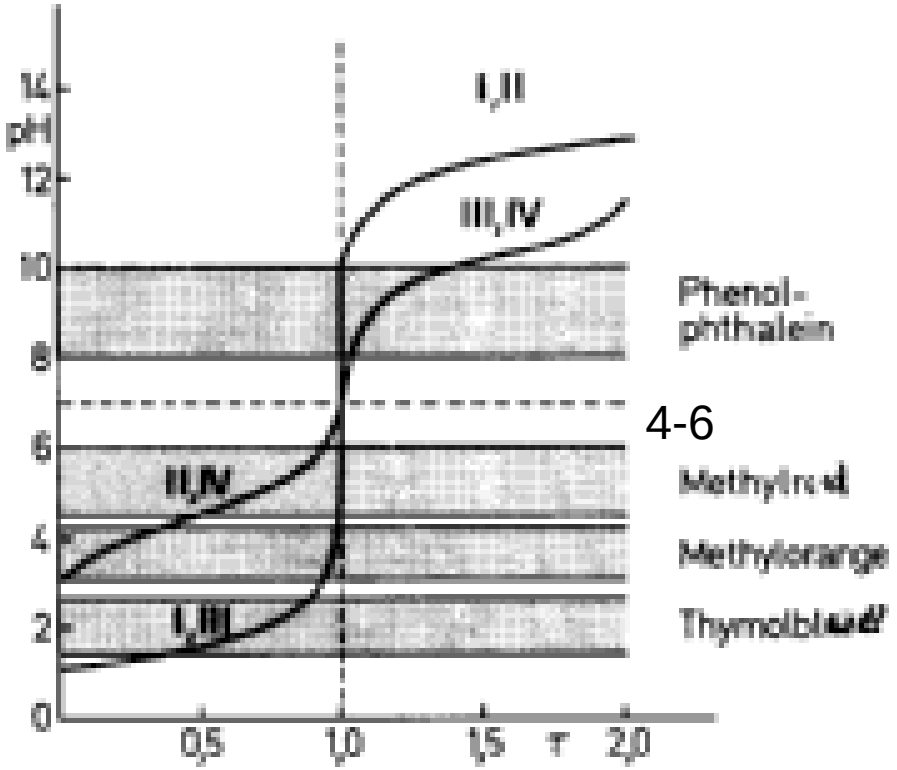
اخترنا حمض الكبريت لأنه أقوى من HCl

291.18 ≡ 10000 ml H_2SO_4 0.05 M



الأستخلاص 1 أعطينا بروتون للأبقاء على المادة بشكلها الملحي بالماء

الأستخلاص 2 سحبنا البروتونات لأبقاء المادة الأساس بالأيتر



4-6

- In case required 11.6 ml NaOH 0.1M

$$\frac{(15 - 11.6) \times 1 \times 29.18 \times 100}{100} = 102.3\ \%$$

Some dosage form which assayed in acid- base titration in aqueous media

Aminophylline injection	0.05 H_2SO_4	Bromcresolgreen	0.003003
Aspirin Tablets	0.5 M NaOH	Phenol red	0.04504
Compound sodiumbicarbonate tablets	0.5 M HCl	methylred	0.04200
Clofibrate Capsules	0.2 M HCl	Phenolphthalein	0.04854
Dexamphetamine Tablets	0.05M HCl	Methylred	0.009212
Diethylcarbamazine Tablets	0.05 M H_2SO_4	Bromcresolgreen	0.03914
Dimenhydrinate Tablets	0.01 M HCl	Methylred	0.004700

Some dosage form which assayed in acid- base titration in aqueous media

Dimenhydrinate injection	0.1 M HCl	Methylred	0.04700
Diphenhydramine Capsules	0.1 M HCl	Methylred	0.02918
Diphenhydramine Elixir	0.05 M H_2SO_4	Methylred	0.02918
Etamiphylline injection	0.05MH_2SO_4	Bromcresolgreen	0.05116
Etamiphyline Suppositories	0.05 M H_2SO_4	Bromcresolgreen	0.05116
Ethandamineoleate injection	0.05 M H_2SO_4	Methylorange	0.006108
Glycerol suppositors	0.1M NaOH	Bromcresolpurple	0.009210
Magnesiumhydroxide Cream	0.5 M H_2SO_4	Methylorange	0.02916
Medazepam Capsules	0.1 M NaOH	Phenolred	0.02413
Nicotinic acid Tab.	0.1 NaOH	Phenol red	0.01231
Paediartic chalk mixture	0.5 M NaOH	Methylred	0.02502

Some dosage form which assayed in acid- base titration in aqueous media

Paediartic Ipeceanna emetic	0.01M H_2SO_4	Methylred	0.004806
Phosphates Enema	0.5 M HCl	Bromcresolgreen	0.1790
Salicylic acid lotion	0.1 M NaOH	Phenolred	0.1381
Salicylic acid ointiment	0.1 M NaOH	Phenolred	0.181
Salsalate Capsules	0.1 M NaOH	Bromthymolblue	0.02582
Sodiumbicarbonate Ear drops	0.1 M HCl	Methylorange	0.008401
Sodiumbicarbonate injection	0.5 M HCl	Methylorange	0.04200
Sodiumcitrate Tablets	0.5 M HCl	Methylorange	0.04902
Sodium lactate injection	0.05 M H_2SO_4	Methylorange	0.01121
Sodium Valproate oral solution	0.1 M NaOH	Phenolphthalein	0.01662
Soda Oral Suspension	0.1 M HCl	Methyl orange	0.008401
Tolazamid Tablets	0.1 M NaOH	Phenolphthalein	0.02704
Tolbutamid Tablets	0.1 M NaOH	Phenolphthalein	0.02704

Prof. J. Al-Zehouri

Q&A