PHARMACEUTICAL CHEMISTRY-I

First Year Diploma in Pharmacy

M.R. RAMAMANOHAR

Strictly according to the latest syllabus of
Diploma in Pharmacy

PHARMACEUTICAL CHEMISTRY-I

M.R. RAMA MANOHAR

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PREFACE

It is an immense pleasure to bring out the **"First edition"** of this book which is designed and edited according to the syllabus prescribed as per education regulation 1991,by pharmacy council of India.

Sincere effort has been made to present the subject matter in the form of questions and answers which covers almost all the syllabus and is given very briefly so that the students find the material very useful and handy.

This book not only helps the diploma students but also serve the very purpose of those studying professional graduation course to go through some of the fundamentals.

The author is very thankful to his teachers and others those who have inspired and helped him in bringing out this book and in particular M\s Spectrum publications Bangalore for taking keen interest in the publication of this book. the excellent work carried by Mrs.Archana Rajeev for D.T.P work is very much appreciated.

Suggestions to improve the quality of this book are most welcome.

AUTHOR

PHARMACEUTICAL CHEMISTRY- I
SYLLABUS

1. General discussion on the following in organic compounds including important physical and chemical properties, medicinal and pharmaceutical uses, storage conditions and chemical incompatibility.

(a) Acids, bases and buffers- boric acid, hydrochloric acid,strong ammonium hydroxide, calcium hydroxide, sodium hydroxide and official buffers.

(b) Antioxidents : Hypophosphorous acid, Sulphur-di-oxide, Sodium bisulphite, Sodium meta-bisulphite, Sodium Thiosulphate, Nitrogen and Sodium Nitrite.

(c) Gastro-intestinal agents -

(i) Acidifying agents : Dilute Hydrochloric acid.

(ii) Antacids : Sodium bicarbonate, Aluminium hydroxide gel, Aluminium phosphate, Calcium Carbonate, Magnesium Carbonate, Magnesium trisilicate, Magnesium Oxide, Combinations of antacid preparations.

(d) Topical agents :

(i) Protectives - Talc, Zinc Oxide, Calamine, Zinc stearate, Titanium dioxide, Silicon Polymers.

(ii) Antimicrobials and Astringents : Hydrogen peroxide *, Chlorinated lime, potassium permanganate, Iodine, Solutions of Iodine, Povidone, - Iodine, Boric acid, Borax, Silver nitrate, mild silver protein, Mercury, yellow, mercuric oxide, Ammoniated mercury.

(iii) Sulphur and its compounds : Sublimated sulphurs, Precipitated sulphur, Selenium Sulphide.

(iv) Astringents : Alum and Zinc Sulphate.

(e) Dental products : Sodium Fluoride, Stannous Fluoride, Calcium Carbonate, Sodium metaphosphate, Dicalcium phosphate, Strontium Chloride, Zinc Chloride

(f) Inhalants : Oxygen, Carbon-dioxide, Nitrous Oxide.

(g) Respiratory Stimulants : Ammonium Carbonate

(h) Expectorants and Emetics : Ammonium Chloride *, potassium Iodide, Antimony potassium tartrate.

(i) Antidotes - Sodium Nitrite.

2. Major Intra and Extracellular electrolytes -

(a) Electrolytes used for replacement therapy - Sodium Chloride & its preparations. Potassium chloride and its preparations.

(b) Physiological acid base balance and electrolytes used : Sodium acetate, potassium acetate, Sodium bicarbonate injection, Sodium citrate, Potassium Citrate, Sodium lactate injection, Ammonium chloride and its injection.

(c) Combination of Oval electrolyte powders and solutions.

(3) Inorganic official compounds of Iron, Iodine and calcium : Ferrous sulphate and calcium Gluconate.

4. Radio Pharmaceuticals and contrast media : Radio activity - Alpha, Beta and Gamma Radiations, Biological Effects of radiations, Measurement of Radioactivity. G.M. Counter - Radio isotopes - their uses, storage and precautions with special references to the official preparations. Radio opaque Contrast Media - Barium sulphate.

(5) Quality Control of Drugs and Pharmaceuticals : Importance of Quality Control, Significant errors, methods used for quality control, Source of impurities in Pharmaceuticals, Limit tests for chlorides, sulphates, Arsenic, Iron and heavy metals.

(6) Identification tests for cations and anions as per Indian Pharmacopoeia.

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QUALITY CONTROL IN PHARMACY AND LIMIT TESTS

INTRODUCTION :

Chemical purity implies freedom from impurities.A state of absolute purity is virtually unobtainable,but may be obtained as closely desired, provided sufficient care is exercised during the process.In other words(to say) it is practically impossible to lay down standards for drugs and medicinal substances which provides complete absence of even any one impurity. But in practice it is often necessary to have pure for all pharmaceutical purposes.

The basis of maintaining the quality of a product could be seen through Good Manufacturing Practise(GMP). GMP is any practice which renders the drug or substances directly or indirectly, to be pure safe, effective (after administration) and reliable. To achieve good quality control one should consider **Total Quality Control (TQC)**, which include all those aspects starting from the procurement of raw material to the finished product available at the drug store and till it is consumed by the customer. Thus this TQC includes not only the parameters of GMP but also the storage handling and preserving the drug substance until its ultimate use.

The major areas of quality control include all the steps to determine, within how much reasonable limits that the drug is **a)** of a genuine quality and of nature **b)** physically and chemically pure **c)** contains the amount of the Medicament or Ingredient as stated on the label **d)** rendered in such a form to be effective after administration e)it retains quality in terms of its shelf life and stability.

In order to maintain quality of a substance quality control is effected. The job of quality Control is to test a drug for its **'Quality'** as well as its **'Quantity'**. In order to ascertain in both these parameters of qualitative identification and quantitative determination a number of various procedures and

standards are followed. In every country the standards for a drug quality and the procedures for its determination of the quantity of drug are set by state, or centre by an expert committee. These standards and procedures are set after consideration of recommendations of various expert bodies and then these are published in the form of books (compendiums) like **pharmacopoeias, Pharmacopoeial codex, formularly** etc, further these books are revised from time to time and supplements are issued betweenrevisions to keep the things up to date with respect to the matters pertaining to the quality of the drug solutions.

Q .1. : Discuss the source of impurities in pharmaceuticals.

Ans : 'Impurity' is an impurity to say, but is of any substance which renders the product directly or indirectly to be unsafe, ineffective after administration from which the purpose of the customer is not served, ultimately thus an impure product is thrown out wasted.

The sources of impurities, form which they enter into the product are discussed below.

1. Raw material employed in manufacture.

The raw materials from which the substance or chemicals are manufactured often contain impurities.The same impurities gets incorporated into the final product.

For ex. rock salt contains small amount of calcium sulphate and magnesium sulphate. If sodium chloride is prepared from this source, certainly it contains the small amounts of calcium sulphate and magnesium sulphate.

2 Method of manufacture.

The various methods employed for the manufacture also incorporate new impurities due to contamination by reagents and solvents as described below.

a) Reagent employed in the process.

For ex, in the process of preparing calcium carbonate by interaction of soluble calcium salt and a soluble carbonate 'Soluble alkali' arises from sodium carbonate used in the process which washing process failed to remove.

b) Reagents added to remove other impurities.

For ex, Potassium bromide is liable to contains traces of barium. It is added in the course of manufacturing process to remove excess of sulphate, in turn incorporate another new impurity.

c) Solvents used

For ex, In manufacturing of most of inorganic chemicals, water is used as solvent. The use of tap water containing the traces of Na, Ca^{2+}, Mg^{2+}, Cl, SO^{--}_4s, gives rise to the new impurities.

d) Reaction vessels

Reaction vessels usually made up of metals like copper, Iron or lead. Solvent action may cause the corrosion and the metal ions tend to pass into the solution and contaminate the product.

For ex glass vessels may give up traces of alkali.

3. Atmospheric Contaminents.

Atmospheric pollution causes considerable risk of contamination by dust, SO_2 and arsenic. The most common contaminents are Co_2 and water vapours.

4. Manufacturing hazards.

a) Particulate contamination

The presence of unwanted particulate matter can arise in a number of ways such as accidental inclusion of dirt or glass or porcelain pieces, metallic and plastic fragments from sieves, granulating, tableting and filling machines or even from product containers.

Ex usual ex is the metallic particles found in eye ointments packed in metal tubes.

b) Process errors

Processing errors such as incomplete solution of a solution in liquid preparation contributes reasonably and therefore special precautions such as filtration is needed in order to avoid the addition of undissolved solute particles into the product. Similarly uneven distribution of suspended matter is also another example.

c) Cross- contamination

Particularly the handling of powders, granules and tablets in large bulk, frequently creates a considerable amount of air-borne dust, which is not controlled. Therefore the operators are provided with head caps and face masks and other special extraction equipments are used in order to limit these impurities through cross contamination.

d) Microbial Contamination

Products such as liquid preparations and creams applied for broken skin are liable to bacterial mould or fungal contamination from the atmosphere, and rarely from the equipment.

The other examples includes the preparations intended for parental administration and Opthalmic products which are not properly sterilised.

e) Packing errors

Products of similar appearance same size, shape and colour (ex. tablets) can constitute a potential source of danger through mis-labeling. Therefore handling of such products in proximity should be avoided.

5. Inadequate Storage.

a) Filth - products stored may become contaminated with dust, the bodies of insects etc particularly with the bulk storage of raw materials, especially that of vegetable drugs.

b) Chemical instability - or Decomposition.

The nature of decomposition often catalysed by light, traces of acid or alkali, air (oxidation,) Water vapour, CO_2, and traces of metallic ions.

Therefore, light sensitive materials are stored in darkened vessels to prevent photochemical decomposition.

Eg:- Special precaution in the use of opaque capsule shells to protect chordiazepoxide to prevent decomposition from light.

Materials liable to oxidation or to attack moisture or CO_2 if specially sensitive may require displacement of air from the container by Nitrogen: for less sensitive product it is sufficient if they are stored in sealed containers.

Oxidation is prevented the addition of appropriate antioxidents like BHT (Butylated hydroxy toluene), Thymol etc.

(c) Reaction with Container materials

Reaction between the container material and contents constitutes a hazard which cannot be ignored.

Eg:- Salicylic acid Ointment must not be packed with metal tubes, unless they have processed internally to inhibit reaction.

Atropine sulphate injection, sterilized by autoclaving must be packed in glass ampules which comply with the test of hydrolytic resistance.

(a) Physical changes :-

Changes in the crystal size and form, agglomeration caking of suspended particles, which are not always preventable may lead to marked changes in the efficiency of the product.

For Ex, Multidose suspensions, which are inefficient particle distribution (rapid settling & claying) gives rise to under dosage at first and then to over dosage.

(e) Effect of temperature

If the products are not stored under suitable or specified temperatures there are liable for decomposition and therefore, for Ex, Pastes and ointments and all other products are stored so as to retain their consistancy at higher temperatures and appropriate standards are laid down for them.

Recommended Storage conditions.

Instruction / Specification	Interpretation
i. Store in a Refrigerator (U.N.S.F)	Temp. between 2 & 8°c
ii. Store in a cold place (U.N.S.F)	not more than 8°c
iii. Store in a cool place (B.P)	Between 10 & 15°c
iv. Store in a cool place (U.N.S.F)	Between 8 & 15° c
v. Protect from Heat	not more than 30° c
vi. Store in a dry place	Relative humidity < 5%

Q. 2. : What is quality control? Discuss it importance in Pharmaceutical industry.

Ans : The term **'Quality'** as applied to the drugs and its products include all such factors which directly or indirectly contributes to the safety, effectiveness and reliability of the product. i.e., To be a safe, effective and reliable product it should not contain any impurities or contamination from any end.

Quality control or Total Quality control is that aspect which includes all those aspects starting from the procurement of the raw material to the finished product until it is consumed by the customer. Thus, it will not only includes the parameters of Good manufacturing practice but also storage - handling and preserving the product till its use.

Every final product in pharmaceutical industry is formulated for particular cause and purpose. When administered into the body it should serve the cause and purpose desired. To serve the cause and purpose desired the product should be safe and effective (produce action) when it is administered or

used. Thus, the product should maintain its character until it is used. In order to sustain the character, it is very important to see that, no any substance in the final product interferes with the character of the product. In other words, the product should not contain any other impurities or contaminants which interferes with the final product or drug. In order to avoid the entry of such contamination of impurities **'Quality control'** is very much essential.

By adopting various procedures of Quantitative, Qualitative and Quality control methods one could check whether the product complies with the standard prescribed officially or not. If the product complies with the prescribed standard then only, you can say that the product will serve the desired purpose if not it is a mere waste.

Therefore, it is very important to adopt the **'Quality Control'** in pharmaceutical industry. No one pharmaceutical industry in the world and no one, formulation in the world has not got the system of **'Quality Control '**. Practically one should understand the importance of quality control in a better way, once he enters the pharmacy profession.

Q. 3. : What are the Quantitative methods used for ascertaining quality in pharmaceutical industry ?

Ans : Depending upon the nature and character of a drug and its formulation, various quantitative analytical methods are used. This include, Physiochemical methods which are based on some specific physical and chemical properties of a substance or drug being analysed. This includes determination of Specific gravity, density, viscosity, Surface tension, refractive index optical rotation etc. and other types of all Volumetric analysis. Utilising the physiochemical properties use of instrumental methods like PH - Potentiometry, Polarography, Calorimetry, Conductometry, Spectrophotometry, florimetry, flame-photometry etc are carried out.

The other separational techniques for quantitative determination includes the techniques like chromatography, precipitation, Gravimetry, complex formation (complexometry),

proximal assays and other special instruments which are newly introduced and very much accurate like HPLC (High pressure liquid chromatography) are also used.

Q. 4. : Differentiate between Accuracy and precision. Discuss the ways for determining accuracy. (Under analytical errors)

Ans : Accuracy refers to the agreement or acceptance of experimental result with the true value and it is usually expressed in terns of error.

Precision is defined as the degree of agreement between various results of same quality. In other words it is the reproducibility of a result. Good precision are not necessarily accurate.

An analytical chemist always attempt for the reproducible results (i.e., precision) to assure highest possible accuracy.

It is vital and customary to find out whether the results of expectations are true and accurate. This will be done by expressing in different ways.

The data of the experiment or analysis is subjected to some mathematical treatment as shown following.

Mean = $\bar{X}$ average of all readings.

Range = R Difference between the largest and smallest readings in a series of measurement.

Average deviation = 'D'

'D' is Determined by finding the differences between the individual results and mean, irrespective of sign, summation of differences and dividing by the number of determinations.

$$D = \Sigma \frac{[Xi - X]}{N}$$

where $\bar{X}$ = mean

Xi = individual reading

N = No. of measurements.

and here the 'Relative Average deviation ' is found by dividing the average deviation 'd' by the Mean X.

i.e., $\frac{d}{\bar{X}}$

Standard deviation = **S** is formed by the formula

$$S = \frac{\Sigma [X_i - \bar{X}]^2}{N}$$

This standard deviation is also called variance.

If the number of measurements or reading is less than 10, then the equation takes the form,

$$S = \frac{\Sigma [Xi - \bar{X}]^2}{(N-1)}$$

The co-efficient of variation which is also called **Relative Standard Deviation** is found by dividing the standard deviation by the mean and multiplying by 100

i.e Co-efficient Variation = $\frac{S}{\bar{X}} \times 100$

Standard error S.E calculated by dividing standard deviation by under root of

i.e **S. E** = $\frac{S}{\sqrt{N}}$

Q 6. Discuss the principle and procedure for the limit test for chlorides and sulphates.Give the reactions involved.

Ans : Principle

The chloride and sulphate test is based on the principle of the measurement of opalescence/turbidity produced by the known amount of substance i.e,standard and comparing the same with that of the opalescence/turbidity produced by the sample.

For comparison of turbidity for different substances with varying amount of impurity, the amount of substance to be used is varied and not the standard P.copoeias does not give any numerical values to the limits,as it is not practicable and its contents will be influenced to a great extent by the large quantities of the substances present.

a) Limit test for chloride based on the reaction between soluble chloride ions with silver nitrate reagent in the medium of nitric acid.The resultant insoluble silver nitrate reagent in the medium of nitric acid.The resultant insoluble silver chloride renders the solution turbid. The intensity of the turbidity depends on the amount of silver chloride formed which in turn depends on the amount of soluble chloride present in the substance under test.Thus formed turbidity is compared with the turbidity formed with the standard i.e,produced by addition of silver nitrate to known amount of chloride ion solution.

Reactions involved

$$2NaCl + AgNO_3 \longrightarrow AgCl + 2NaNO_3$$

Turbidity produced

b) In case of limit test for suphates, the solution of the subject under list or sample solution, mixed with Barium sulphate reagent in the medium of hydrochloric acid and the turbidity so produced is compared with standard turbidity which is produced in the similar manner with the known quantity of sulphate ion.

Reactions involved -

$$H_2SO_4 + BaCl_2 \longrightarrow BaSO_4 + HCl.$$

Note - In performing these limited tests it is essential to follow the directions indicated by pharmacopoeia.

Procedure for the limit list for chlorides

Sample

Prepare the sample solution dissolving specified quantity of the substance in suitable medium (usually water) as indicated in the monography + 10ml dilute HNO_3. Adjust the volume upto the mark of 50ml with Water + 1ml $AgNO_3$ solution. Stir well with glass rod and allow to stand for 5 minutes.

(b) Standard solutions

1ml 0.05945%, w/v Nac l solution or as indicated in the monography + 10 ml dilute HNO_3. Adjust the volume upto the mark of 50ml with water + 1ml $AgNO_3$ solutions stir well with glass rod & allow to stand for 5 minutes.

Observation

The Opalescence produced by the sample is compared with that of the standard viewing transversely over a black or dark background.

Procedure for the limit list for sulphates.

(a) Sample Turbidity

Prepare the sample solution as specified under the monograph + 2ml dilute. HCl & Adjust the volume to make 45ml with water + 5ml Barium sulphate reagent.

Immediately stirred well with glass rod & allow to stand for 5minutes.

(b) Standard turbidity : 1ml 0.1089% w/v K_2SO_4 solutions or as specified under the official monograph + 2ml dilute HCl. Adjust the volume to 45ml with water + 5ml Barium sulphate reagent.
Stirred immediately with glass rod & allowed to stand for 5 minutes.

Observation
The turbidity produced by the sample is compared with that of the standard turbidity to give the conclusion.

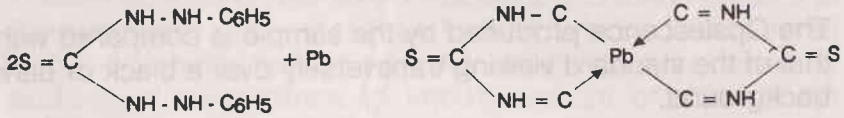
Q 7. Discuss the limit list for lead.

Principle -

Limit test is based on the reaction between the lead and Diphenyl thiocarbazone **(Dithiozone)**

Dithiozone in chloroform has a peculiar property of extracting lead from aqueous alkaline solutions as lead dithiazone complex which is red in chloroform solutions. Since dithiozone in chloroform gives green colour, the resulting colour is of violet shade.

In this method lead is present as impurity and is separated by extracting in the alkaline solution with Dithiazone extraction solution. The interference and influence of other metal ions etc is eliminated by adjusting the optimum pH of the solution by using ammonium Citrate, Potassium cyanide and hydroxyl amine hydrochloride reagent.



Dithiazone Lead Dithiazone -complex

Procedure

(a) Sample solutions-

Prepare the sample as directed by the monograph transfer to the separator + 6ml ammonic citrate solutions + 2ml hydroxylamine hydrochloride solutions + 2 drops phenyl red indicator. Make the solutions just alkaline until it gives red colour by strong ammonia solutions + 2ml Potassium cyanide. Immediately extract the solution several times each time using 5ml dithiozone (here extraction solutions consists of 3g dithiazone in 100ml chloroform & 5ml alcohol).

Drain each chloroform extract into another separating funnel till the solutions retains colour. Shake the combine dithiazone solutions for 30 seconds with 30ml 1% w/v HNO_3 and discard chloroform layer.

To the acidic solutions add exactly 5ml standard lead dithiozone solutions and 4ml Ammonium cyanide solutions shake for 30 seconds.

Standard solutions-

The similar procedure is carried out with know amount of lead dithiazone solutions.

The colour of the chloroform produced by the sample is compared with that of standard lead solution. Standard lead solutions contains that amount of lead i.e., permitted in the sample.

Q 8. : Discuss the limited test for Iron.

Ans : Principle -

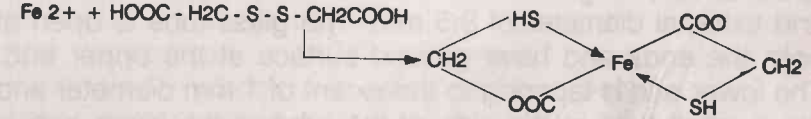
It is based is based on the reaction between Iron in ammonical solutions with thioglycollic acid in presence of citric acid. The colour ranges from pale pink to deep reddish purple due to the formation of ferrous thioglycollate.

Original state of Iron is un important as the thioglycollic acid reduces ferric form to ferrous form (Fe^{2+}). This test is very sensitive and the interference of other metal ions here is eliminated by making use of 20% w/v citric acid solutions which forms complex with others metal ions.

Reactions:-

$Fe^{+++} + 2H_2CSHCOOH$ $Fe^{++} + HOOCH_2C - S - S - CH_2COOH$

Ferric form Thioglycollic acid. Ferrous form Dimer of Thioglycollic acid



Procedure-

(a) For sample solutions.

Prepare sample solutions as directed by the monography + 2ml 20% citric acid + 2 drops thioglycollic acid solutions is mixed and make alkaline by ammonia, testing with Red lit-

mus, dilute upto the mark with water and allowed to stand for 5 meters.

b)For standard solution -

2 ml standard iron solution (prepared as per the specifications of monograph) + 2 ml 20% citric acid solution + 2 drops thioglycollic acid solution is mixed and make alkaline by ammonia solution, by testing with red litmus, diluted upto the mark with water. Stir well and allowed to stand for 5 minutes.

Observation:

The colour produced by the sample solution is compared with that of the standard solution and the test is concluded.

Q. 9. Discuss the limit test for Arsenic.

Ans. : Principle :

The test involves the conversion of Arsenic to Arsine by reduction reaction with Zinc and HCl. Reaction of the liberating gas with mercuric chloride paper produces a yellow stain, which can be compared with that produced from a known amount of Arsenic.

Specifications of the Apparatus used for the test.

The wide mouthed bottle used has the capacity of 120 ml and the dimensions of the glass tube used have the specification, length 200 mm, internal diameter of 6.5 mm and external diameter of 8.5 mm. The glass tube is open at both the ends and have ground surface at the upper end. The lower end is tapering to the extent of 1 mm diameter and the a small hole at the side of the tube at the lower end is necessary to prevent condensed liquid from being forced up the tube by pressure of the hydrogen developed in the bottle thus blocking the tube.

The tube is packed with cotton wool previously impregnated with lead acetate solution and dried. This is to remove the traces of hydrogen sulphide from the liberated gases which is otherwise interfere with the test. A small extension glass

tube of same specification as said above is similarly flanged at one end is used to fix the mercuric chloride paper in position in such a way that all the Arsine will pass through a circle of paper of 6.5 mm in diameter. The two glass tubes with the mercuric chloride paper in place are held together by a clip or elastic band [In practice for the convenience, two rubber bungs are used to keep the mercuric chloride paper in position held by a clip].

Reaction between Arsine and mercuric chloride paper is represented as

$$2\,AsH_3 + HgCl_2 \longrightarrow Hg\begin{matrix}AsH_2\\AsH_2\end{matrix} + 2\,HCl$$

The reaction result in the formation of yellow or brown stain on mercuric chloride paper.

The intensity or depth of the colour is proportional to the amount of Arsenic present.

Mercuric chloride paper becomes discoloured onn exposure to light and therefore stored in dark.

Procedure to carryout the limit test.

TEST SOLUTION	STANDARD SOLUTION
1. Dissolve specified amount of sample in specified quanity of water as soecified under the monograph + 10ml of Stannated Hydrochlioric acid and transfer to the bottle.	1. Prepare the standard solution as specified under the monograph + 10ml of Stanated hydrochloric acid. Add 50ml of H_2O

(i) Add 1g of Potassium iodide to each solution [This liberates hydriodic acid which helps in reduction of pentavalent arsine to the trivalent state from which arsine is formed by Reduction].

(ii) Add 10g of granulated zinc to each solution and immediately insert the bung with the tube which is already assembled with the mercuric chloride paper in position.

(iii) Allow both the solutions to continue the reaction for 40 minutes at room temperature.Evolution of hydrogen may be slow at first,if necessary,if permissible,raise the temperature to 40°C to ensure a steady reaction but too vigorous evolution of gas.Both solutions are treated in the same manner

(iv) After 40 minutes,compare the test and standard strain.

The substance is said to be comply with the test if the colour of the test stain is not darker than that of standard stain.

–X–

SOLUBILITY IN PHARMACEUTICAL INDUSTRY

INTRODUCTION :

The knowledge of **'solubility'** of various pharmaceutical substance is very important for a pharmacist not only in the analytical field but also in the manufacturing process. This is so because many medicines are the combination of various drugs of different chemical characters, in order to recognize the possibility of precipitation, complexation, chemical reactions and incompatibility.

The process of dissolution of solute in a solvent to affect the solution involves mutual separation of particles from their initial environment. In case of electrolytes ions and in case of non electrolytes molecules take part. In case of electrolytes strong bond existing between the ions need to be broken by solvent molecules, in the process of 'solubilisation'. Solute must be able to separate the neighbouring solvent molecules in order to provide space for itself in solvent structure. In the similar way solvent molecules must be able to separate solute particles by breaking their internal bonds. The important factor for consideration in this process is the field strength of particles involved in the process.

Solvent with high ionic (Polar) character tend to dissolve most substance of ionic (Polar) nature. On the other side, solvents with low polarity are less effective in solubilisation process.

The process of dissolution continues till the equilibrium stage is reached i.e., when the number of ions dissolving becomes equal to the number of ions coming to the solid slate, At that stage when no more solution dissolves in solvent, it is said that **saturation** occurred.

Thus, the term Solubility is defined as the concentration of dissolved solute at an equilibrium at saturation point. When the concentration of any solute exceeds solubility, It results either in precipitation or a stage of super saturation where more amount of solute is held in liquid phase with out thrown out.

SOLUBILITY BEHAVIOUR :

In the field of pharmacy, it is a very common practice to express solubility in terms like solubie very soluble, sparingly soluble, slightly soluble etc. It is very important to know exactly what that terminology means. In the official books, the solubilities are indicated, as the amount of solvent required for fixed amount of solute.

Here is a table which gives the meaning of the terminologies used and the ratio of Solute to solvent.

Terminology	**Apparent quantity of solvent by volume for 1 part of solute by weight.**
1. Very Soluble	Less than 1 part
2. Freely soluble	From 1-10 parts.
3. Soluble	From 10-30 parts.
4. Sparingly soluble	From 30-100 parts.
5. Slightly soluble	From 100-1000 parts.
6. Insoluble	More than 10,000 parts.

Q.1. : Explain the terms :
(a)Normal solution (b) Molar solution (c) Molal solution (d) Percent solution which suitable examples.

Ans : (a) Normal solution : When a solution contains 1g equivalent weight of a substance per litre, it is known as (IN) or 1 Normal solution.

Normality : It is defined as the number of gram equivalent weight of solute present in one litre of solution.

For Eg : If one gram equivalent weight of the solute present in 1 litre of solution it is said to be 1N or 1 normal solution.

To prepare Normal solution, it is important to know the equivalent weight. This differs from substance to substance. For example

(i) In case of Red -ox reactions the equivalent weight of an oxidant or reductant is the molecular weight divided by the number of electrons, which one mole of substance gains or losses in a reaction, thus equivalent weight of $KMnO_4$ is $\frac{1}{5}$ th of its molecular weight.

(ii) In case of acids it is that weight which contains 1g of replaceable hydrogen (C-008g) for monobasic acids the equivalent weight is identical to its molecular weight for dibasic acids the equivalent weight is $\frac{1}{2}$ of its molecular weight.

(iii) The equivalent weight of a base is that which contains one replaceable hydroxyl group (17.008 of hydroxyl ion)

(b) Molar solution : The solution containing one mole that is molecular weight in gms per litre of solution and indicated by 'M'

If the solutions contains very small amount of solutes, they are expressed in millimolar concentration (mM) and defined as the number of millimolar/ ml of solution.

$$1mM = 1 \times 10^{-3} M$$

(c) Molal solution : Solution containing are mole of solute per thousand gm of solvent (1Kg of solvent) is called Molal solution.

It is less common and much of use in the reactions or equations to express thermodynamic properties of solution.

(d) Percent solution :

The conversion of solution are expressed in terms of %

(i) In % w/w, the number of grams of sclute in 100 grams of solvent.

(ii) In % w/v, the number of grams of solute in 100 ml of solvent and vice versa.

(iii) In % v/v, the number of ml of solute in 100ml of solvent.

The Term solubility indicates a numerical value. It is important that the mode of reporting should be specified.

One should be borne in mind that the solubility is valid for saturated solution at specified temperature. Any change in temperature with pressure will change in solubility.

Q. 2. : Explain the importance of solubility product in pharmacy

Ans : Principle of Solubility product :

Solubility product is expressed in 'KSP' the value is useful in indicating whether there will be precipitation or not in addition of certain ions to the solution.

For insoluble salt, however, insoluble it may be, always have some solubility in water. An equilibrium is established between the suspended salt (X^aY^b) in excess of water at its saturation point.

The equilibrium can be represented as :

$X^aY^b \longrightarrow X^aY^b$ (assuming complete dissociation of salt)

solid $\longleftarrow$ solution

According to law of mass action,

$$\frac{[X]^a [Y]^b}{[X^a Y^b]} = K$$ where K is a constant.

Since solid phase is in excess, the conversion of dissolved phase is also considered constant.

$\therefore \quad K [X^aY^b] = [X]^a [Y]^b.$

The product $[X]^a [Y]^b = K_{SP}$ known as solubility product constant.

According to the principle of solubility product the conversion of $[X]^a$ and $[Y]^b$ ions in a saturated solution of X^aY^b remains constant at constant temperature.

If the conversion of $[X]^a$ ions increases the conversion of $[Y]^b$ ions decreases to maintain K_{SP} constant. Thus in a saturated solution of $[X^aY^b]$ addition of any one ion brings precipitation.

Addition of a foreign electrolyte which brings precipitation of a slightly soluble salt is known **'Salting effect'** Phenomenon is frequently used as a technique of separation in pharmaceutical analysis.

Q.3. : Enumerate colligative properties of solution and discuss the depression of freezing point for molecular weight determination.

Ans : The important colligative properties possessed by the solutions are,

(a) The lowering of vapour pressure
(b) Elevation in boiling point
(c) The depression in freezing point
(d) Osmotic pressure and
(e) Tonicity.

These colligative properties are different from the physical & chemical properties of their solutions. They are independent of the number of particles present in the solution. Greater the number of particles present in solution greater is the extent of the given colligative property.

Depression in freezing point : It is known that the freezing point of a solution is lower than that of pure solvent.

According to Charles Blagdin, the lowering of freezing point of a solvent is directly proportional to the amount of solute dissolved in it. Thus, the depression of freezing point of a solvent is directly proportional to the molecular concentration of solute present in it. Equimolecular solutions have same freezing point.

The depression of freezing point shown by electrolytes & non - electrolytes :–

Electrolytes depress the freezing point more than non-electrolytes due to greater ionization. In dilute solutions quantitative relations hold good. The lowering of freezing point is expressed in terms of 'Kf' known as molal freezing point depression constant Kf is given by,

$$Kf = \frac{RT_O M_1}{1000 \Delta HF}$$

Where R = Gas constant

T_o = Absolute freezing point of pure solvent

M_1 = Molecular weight of Pure solvent.

ΔHf = Heat of fusion of pure solvent.

The change in freezing point is given by

ΔTf = mkf where

m = molality of solution

kf = molal freezing point constant

Different solvents have fixed depressant values, For example freezing point at 0^oc for Benzene is 5.5, for ethanol is -112 and for water is 0.0.

From the constant for a particular solvent, the molecular weight of a substance can be calculated.

If M_2 is the molecular weight of solute, W_1 is weight of solvent, W_2 weight of solute, T is the observed lowering of

freezing point and kf is the freezing point constant for the solvent, M_2 is given by

$$M_2 = \frac{1000 \times Kf \times W_2}{\Delta T \times W_1}$$

This is one of the easiest method of molecular weight determination for non - electrolytes.

Q. 4. : What is Osmotic pressure? Give its importance in biological system ?

Ans : If two solutions of different concentartions are separated by a semi- permeable membrane, the solvent tends to flow through the membrane from the region of low concentartion to the region of higher concentartion until equilibrium is reached. This process of passage of solvent through membrane is known as Osmosis.

Osmotic pressure denoted by π is the pressure gradient (difference) which exists across the membrane due to concentartions changes.

Osmotic pressure π = mRT where m = difference of molal concentartions of 2 solutions

R = Gas constant.

T = Obsolute temperature.

In the given volume of solutions the Osmotic pressure is dependent on the number of particles (or ions or molecules).

Osmotic pressure is a very important in biological system for the regulation of the maintenance of isotonic conditions of body fluids.

In industrial practice solutions of various tonicity are used.

This tonicity is also important in maintaining and regulating of various cell functions.

The isotonic solutions have Osmotic pressure equal to the Osmotic pressure of the intra-cellular fluid. i.e., π solution = π cell. (For convience it is equal to 0.9% NaCl solution which is isotonic with the body fluid).

In hyper tonic solutions, π solution > π cell i.e., the solution exerts more osmatic pressure than the body fluid/Intra cellular fluid and in hypotonic solutions, π solution < π cell, in other words the solution exerts low osmotic pressure than that of the Intra Cellular fluid.

– X –

ANTI – OXIDENTS

We are familiar that many substances used in the pharmaceutical industry are sensitive to air and moisture. For the presence of which makes the material or substance undergo deterioration by the presence of Oxygen present in air/moisture. In fact even oil also undergo this process called rancidity. The agent which are used in order to prevent this oxidative process which renders the substance deteriorated are called Anti-oxidents. These even can act and function chemically as reducing agents. The compounds like BHT(Butylated hydroxy Toluene) BHA (Butylated hydroxy anisole), Ascorbyl palmitate, sod meta Bisulphatre, Hypophosphorous acid and many more constitute this class. In spite of adding anti/oxidents, many times it is necessary to add preservatives ALSO IN THE FORMULATION OF MANY PHARMACEUTICAL preparations. These preservatives prevent the growth of micro organism and there by soilage of preparation. They may act in the way of antioxidants act or they may act differently.

The antioxident usually prevents the oxidation of active substance by getting oxidised itself. The inorganic type of antioxidents acts as reducing agent and are used in the formulations or preparations containing easily oxidisable substance.

Q 1. : Discuss the mechanism of action of antioxidents.

Ans. : We know about the mechanism of Oxidation - Reduction reaction Oxidation is the loss of electrons and Reductio n is the gain of electrons basically the same mechanism of action holds good for the action of antioxidents. The reaction can be equated as,

$$OX + e \rightleftharpoons Red.$$

The anti-oxident being a reducing agent gets oxidised itself and there by prevents the oxidation of the substance.

The electrical potential developed in a cell can be measured by voltmeter and measurement of electrode potential is given by 'Nernst equation':

$$E_{cell} = E^{o}_{cell} - \frac{0.0591}{n} \log \frac{[OX]}{[RED]}$$

Where, E_{cell} - potential of cell in volts.

E^{o}_{cell} - standard potential

0.0591 - constant (called Numerical combination of gas constant, absolute temperature and Faraday constant)

n = number of electrons involved in

$\frac{[OX]}{[RED]}$ = Ratio of the concentration of oxident and reductant respectively.

By this electrode system the efficiency of chemical substance to under go oxidation - Reduction is determined. Here, E^{o}_{cell} is found by the table of standard electrode potential. This in turn is a tool to know about the nature and potentials strength of the anti-oxident. A strong antioxident will protect the material or substance for longer period when used in small quantities.

This is how majority of all inorganic anti/oxidents act.

The organic compounds selectively acts as antioxidents and preservatives. The organic compounds classified into,

a) Quinol gp. Example, Tocopherols, Hydroxy coumarines.

b) Amines - Example, cephalins, Leciithin

c) Pyrogallol group - Example, amyl gallate, n propyl gallate.

d) Benzoic acid derivatives.- Example, Benzoic acid, derivatives of propyl and methytl parabens.

The essential criteria of these compounds should be non-toxic, palatable, compatable, soluble in aqueous solvents, neutral in nature, should not impart any colour or odour to the product.

These organic type of compuonds acts as antibacterial, antiseptic, antifungal, bacteriostatic and are commonly used in foods and pharmaceutical formulations.

Q. 2.: What are all the criteria for the selection of inorganic antioxidents ?

Ans : The main criteria for the selection is the Nernst eqnation from which you know the nature and strength of the antioxident used. The other considerations for its selection should be,

i) its toxicity – should be non-toxic.

ii) its Compatibility – should be chemically and physiologically compatible

iii) its Inertness- should be chemically inert

iv) solubility- should not posses any solubility problem either in oxidised or reduced form.

Q. 3. : Give the method of preparations, properties uses and assay of Hypophosphorus acid.

Ans : Hypophosphorus acid

Formula- HPH_2O_2 (H_3PO_2)

Molecular wt. - 66.

Contains between 30-32% H_3PO_2 and is freely soluble in water.

Properties - Odourless, colourless or slightly yellowish tint liquid.

Syrupy in nature forms crystalline solid at 17.4°c.

It has two important chemical properties –

a) Reducing properties. b) acidic properties.

a) It reduces many substances to form phosphorus acid and then finally to phosphoric acid. For example with Iodine - forms iodide ions and it decolourises acidic solution of Potassium permanganate.

$$H_3PO_2 + 2\,I_2 + 2H_2O \longrightarrow 4HI + H_3PO_4$$

b) -as only one hydrogen is ionisabale here it acts as monobasic acid.

$H_3PO_2 + H_2O \longrightarrow H_3O^+ + PH_2O_2$ -

The acid can be neutralised by alkali hydroxides or carbonates.

$2HPH_2O_2 + Na_2CO_3 \longrightarrow 2NaPH_2O_2 + H_2O + CO_2$.

Preparations- obtained by decomposing boiling aqeous calcium hypophosphite solutions with oxalic acid.

The calcium oxalate insoluble precipitate is filtered and cocentrated in vacuum.
Alternatively it is also prepared by reacting calcium hypophosphite with slight excess of Sulphuric Acid.

Assay :–

Since it is a monobasic acid, it can be directly titrated with standard Sodium Hydroxide using methyl orange or methyl red as indicator.

Incompatibility –

Being a reducing agent, it gets readily oxidised itself by oxidising agents Mercury, Silver, lead salts are reduced partly to metallic state which exhibits darkening in colour of pharmaceutical preparations.

Uses:- 1) Used as reducing agent mainly, in syrups containing ferrous iodide to prevent the formation of ferric ions and to form free iodine.

Q. 4. : List the compounds of Sodium which acts as antioxidents. Give the method of preparation, uses, properties and assay of any two.

Ans. : The common compounds of Sodium used as antioxidents are,
a) Sodium thiosulphate b) Sodium metabisulphite
c) Sodium nitrate.

Sodium Thiosulphate :

Formula - $Na_2S_2O_3.5H_2O$

Moecular weight .- 248.2

Properties- colourless, transparent, crystalline powder- Bitter, cooling taste. Soluble in water and insoluble in alcohol. On boiling solution decomposes by reduction to sulphide and oxidation to sulphate.

$4Na_2S_2O_3 \longrightarrow 3Na_2SO_4 + Na_2S_5$

A good reducing agent reduces ferric salt to ferrous salt- both in neutral and acidic medium.

1. Neutral media

$2FeCl_3 + 2\ Na_2S_2O_3 \longrightarrow 2FeCl_2 + 2NaCl + Na_2S_4O_6$

2. Acid media.

$2FeCl_3 + Na_2S_2O_3 + H_2O \longrightarrow 2FeCl_2 + 2NaCl + H_2SO_4 + S.$

Preparation-

From Soda ash, Sulphur-di-oxide, and sulphur.

Soda ash dissolved in hot water -To this Sulphur-di-oxide is passed. Treat the resulting solution with further amount of soda ash and is then treated with sulphur. Solution is concentrated and allowed for crystallisation.

$Na_2CO_3 + H_2O + 2SO_2 \longrightarrow 2NaHSO_3 + CO_2$

$2NaHSO_3 + Na_2CO_3 \longrightarrow 2Na_2SO_3 + H_2O + CO_2$

$Na_2SO_3 + S \longrightarrow Na_2S_2O_3$

Assay –

Directly assayed by titrating accurately weighed quantity of sample in 25ml water with 0.1 N standard iodine solution using starch solution as indicator, added near the end point.

Uses –

1) Considered useful in parasytic skin diseases, ring worm infections, etc.

2) as an antidote in cyanide poisoning.

3) Causes catharetic action in large doses.

4) Extensively used in photographic industry.

Sodium Nitrite

Formula- $NaNO_2$

Molecular weight.-69

Properties -

Occurs as white crystals or granular powder and saline taste. When exposed to atmosphere oxidised to Sodium nitrate. Soluble in water but sparingly soluble in alcohol. Aqueous solution is alkaline because nitrous acid is a weak acid and its salts are readily hydrolysed in solutions.

Sodium nitrite easily decomposed by acidification wuth Sulphuric acid.

$$2\,NaNO_2 + H_2SO_4 \longrightarrow Na_2SO_4 + 2HNO_2$$

$$3HNO_2 \longrightarrow H_2O + 2NO + HNO_3$$

$$2NO + O_2 \longrightarrow 2NO_2$$

(From air)

It is a good reducing agent. Assayed against Potassium permanganate because of its reducing property.

It also acts as oxidised agent as we see in acidified potasium iodide solution.

$$2HNO_2 + 2KI + H_2SO_4 \longrightarrow I_2 + 2NO + 2H_2O + K_2SO_4$$

Preparations-

By the catalytic oxidisation of ammonia gives Nitric oxide gas (NO) By absorbing nitric oxide gas thus obtained and oxygen into Sodium carbonate solution -Sod. nitrate is obtained. Then the solution is concentrated to crystallise out the product.

$$2Na_2\,CO_3 + 4NO + O_2 \longrightarrow 4NaNO_2 + 2CO_2$$

Assay -

By oxidation - reduction reaction in which nitrate is oxidised to nitrate by potassium permnanganate solution.

A solution containing a weighed quantity of sample added slowly to O.1N acidified (with 5 ml Sulphuric acid) Pot. permanganate solution. Immediately, on contact with acid, nitrous acid is produced which is oxidised to nitric acid. Since nitrous acid is volatile, while adding the tip of the pipette is kept below the level of solution. The excess of standard O.1N oxalic acid is added, mixture is heated to 80^{o} C and excess of oxalic acid is back titrated with standard $KMnO_4$ solution.

The reason for titrating back the excess of oxalic acid with potassium permanganate instead of titrating excess potassium permanganate with oxalic acid is that it is easier to detect the appearance of colour than its disappearance of colour in a solution.

Uses :

1) Considered effective in Angina Pectoris
2) used in cyanide poisoning.
3) used as food preservative.

– X –

GASTRO - INTESTINAL AGENTS

The agents or drugs or chemical substances which are used to treat the gastro intestinal disorders are called Gastro-intestinal agents. Thus the gastro-intestinal agent includes Acidifying agents, Antacids, catharetics, Protective and Adsorbents, Appetizers etc.

Q .1 : What are Acidifying agents? Give example.

Ans: Acidifying agents. Drugs which are used to increase the acidity are termed Acidifying agents. They are used to increase the metabolic acidosis and some are used to increase the Gastric hydrochloric acid.

In some of patients, due to some reasons, there is no secretion of Hydrochloric acid. This condition is known as **'Achlorhydria'.** The symptoms includes mild diarrhoea, loss of appetite, abdominal pain etc. This lack of secretion of Hydrochloric acid (which is very important in the process of digestion of the food) causes gastro-intestinal disturbances.

In Some patients suffering form carcinoma of stomach, Gasterectomy, and Chronic gastritis there is total lack of secretion of Hydrochloric acid. In such patients administration of Hydrochloric acid directly or acidifying agents reported to be useful. Whereas some other individuals with Hyperthyroidism, Tuberculosis, Chronic alcoholism and elderly patients respond to stimulation by Histamine. They are treated with histanmine phosphate.

Hence inorder to treat Achlorhydria, one of the most commonly used is dilute Hydrochloric acid.

Dilute HCl:- 10% w/w of concentrated Hydrochloric acid prepared by diluting concentrated Hydrochloric acid employed in 5ml dose, depending on the severity of **'Achlorhydria'.** To protect the effect of Hydrochloric acid on teeth the solution is administered using straw.

Q.2. : What are antacids? Discuss briefly about Aluminium hydroxide gel as an antacid.

Ans : The drugs or the substances which are used to counteract the excess of gastric acid present in the body are termed Antacids. These relieves the abdominal pain due to Hyperchlorhydria. The efficiency of an antacid is measured by its neutralising capacity.

Aluminium Hydroxide Gel:- I.P. [Contains not less than 3 . 5% & not more than 4.4% w/w of Aluminium oxide.]

This is an aqueous suspension of Aluminium oxide with varying proportions of Basic Aiuminium carbonate and bicorbonate. The preparation may also contain Glycerine, Saccharine, sorbitol or sucrose as sweetning agents. Mentha oil or peppermint oil used as flavouring agent, Sodiurn. benzoate or any other suitable preservative is added.

This is one of the widely used class of antacid which are used in three forms and which are official in various

Assay:- Assayed for Aluminium oxide contents by complexometric titration using back titration technique.

Known weight of the sample is dissolved by warming in the mixture of Hydrochloric acid and water. Standard known amount of sod. EDTA is added. pH is adjusted using Sodium Hydroxide solution and excess of disodium EDTA is determined by adding Hexamine and titrating with standard lead nitrate solution using xylenol orange as indicator.

The acid consuming capacity is also determined as an important measure of its efficiency as described in the official books.

Uses :

1) Used mainly as slow acting antacid.

2) have mild astringent & adsorptive actions.

3) in the treatment of peptic ulcers and Hyperchlorhydria.

Mechanism Of Action- This reacts with Hydrochloric acid to form Aluminium chloride which has astringent effect and may cause constipation and occassionally vomitting.

Q. 3. : Discuss briefly about antacid therapy. How antacid property is evaluated ?

Ans : Under normal physiological conditions, Hydrochloric acid is secreted by epithelial cells of Gastric mucosa. Thus the pH of the stomach wil be around 1 if the stomach is empty the pH is around 6-7 if the food is injested. In case of the condition known **'Hyperchlorhydria'** the production/secretion of HCl in the stomach will be more than that of normal. This may be due to the inflamation of gastric mucosa as in Gastritis or any other reason. This leads to peptic ulcers. Depending on the area affected, they are termed Oesophagal, Gastric or deodenal ulcer. The treatment of this ulcer/peptic ulcers include the use of antacids.

By their virtue, antacids neutralises the acid in the stomach. Being alkaline base, they directly react with the acid and neutralises the acid. The action of the antacid should be gradual without evoking rebound acidity. Since the production of Hcl is a continuous process, the therapy of antacids is also of longer duration. Since it is of longer duration, the drugs used as antacids should not have any side effects.

Therefore an ideal antacid is the one which actively reacts with the acid and neutralises it, without producing any adverse side effects even after prolonged use.

For the evaluation of Antacid, Acid neutralising capacity test is employed.

Invitro-based on adding a known quantity of antacid to a given amount of HCl and the pH at different time intervals for determining the amount of acid consumed by the sample.

To be an effective and ideal antacid measuring, it should have following properties

1) have fine particle form and should be insoluble in water.

2) should not produce its effect gradually and over a prolonged period.

3) should not produce systemic alkalosis.

4) should not have any adverse side effects.

5) should be stable and readily available.

6) should not produce large quantity of gas on reacting with gastric acid.

Q .4.: List the compositions of calcium and Magnessium used as antacid. Give the method of preparation, uses and assay for calcium carbonate and Mg trisilicate.

Ans : Compounds of calcium used as antacid.

1.Calcium carbonate I.P., B.P.

Compounds of Magnesium used as antacid.

1. heavy and light Magnesium. carbonate.
2. Heavy and light Magnesium oxide.
3. Magnesium hydroxide
4. Milk of Magnesia.
5. Magnesium trisilicate etc.

Calcium carbonate –

Formula $CaCO_3$

Molecular weight. 100.09

Contains not less than 98.0% & not more than 100.5% of $CaCO_3$ calculated with reference to dried substance.

Properties : Odourless, fine, white, microcrystalline powder and is tasteless. Stable in air nearly insoluble in water and alcohol. Solubility is increased by the presence of Ammonium salts and CO_2.

Calcium Carbonate neutralises acids- a common property with all the carbonate

$$CaCO_3 + 2HCl \longrightarrow CaCl_2 + CO_2 + H_2O$$

Preparations-

By interaction of Sodium carbonate and calcium chloride. The precipitate is filtered and washed.

$$Na_2CO_3 + CaCl_2 \longrightarrow CaCO_3 + 2NaCl.$$

Assay- Complexometric titration. -using Sodium EDTA as titrent and calcon mixture as indicator.

Uses- 1) used as non-systemic antacid

Dose 1-5g daily according to the need.

Heavy and light Magnesium carbonate-

Composition approximately- $3MgCO_3$. $Mg(OH)_2$ $5H_2O$-

A Hydrated basic Mg Carbonate and contains equivalent of Mg. Oxide not less than 40% and not more than 45%. They only differ in unit bulk densities. As per Indian Pharmacopoeia Heavy Mg carbonate 15g occupies a volume of 30 ml whereas light, Mg carbonate same weight occupies a volume of 120ml.

Properties-

Heavy Mg carbonate - a granular powder; light Mg Corbonate available as very light powder. Both are tasteless, odourless and white in colour insoluble in H_2O and alcohol, soluble in mineral acid with effervosence when heated. They are converted to Mg oxide loosing CO_2 and water.

$$3MgCO_3\ Mg(OH)_2\ 5H_2O \longrightarrow 4MgO + 3CO_2 + 5H_2O$$

Preparation:

Heavy Mg carbonate- Double decomposition with Mg sulphate and sod. carbonate. These are separately dissolved in H_2O and the solution is mixed in the ratio of 1:1 and concentrated. Boil the residue with H_2O and filter the insoluble Mg Carbonate on cloth. Wash till freed from sulphate ion and dried.

$$MgSO_4 + Na_2CO_3 \longrightarrow MgCO_2 + Na_2SO_4.$$

In case of light Mg carbonate the process of preparation differs only in concentration of reagents used and the temperature of reaction.

Assay –

By complexometric titration using Sod. EDTA. after adjusting the PH by ammonia- amonium chloride buffer.

Q 5. : Give the mechanism of action of Magnesium antacids? Describe the method of preparation and Assay of Milk of Magnesia.

Ans : All Mg Containing antacids has very poor water solubility. They go into solution when acid consumes a small amount of anions present when pH of the stomach approaches neutrality, the dissolution of Mg salt decreases and when pH of stomach is neutral, the dissolution stops. Thus anion in the antacid gives its antacid effect. Because of the Mg cation, there also have loxative property. Therefore they are used in combination with aluminum or calcium antacids which are constipative.

Milk of Magnesia-

An aqueous suspension of Hydrated Mg hydroxide which contains not less than 7% & not more than 8.5% w/w of Mg hydroxide. It may also contain some suitable preservatives.

Preparation -

By interacting Sodium hydroxide with Magnesium sulphate.

Light Mg oxide mixed into a smooth paste with solution of NaOH, diluted with H_2O and the suspension poured in this stream into a solution of Mg. sulphate, stirring continuously. Allow the precipitate to settle and decant the upper clear liquid. Transfer the residue on a filter, washed with H_2O till free from sulphate ions. Precipitate is mixed with suffcient H_2O to produce the desired volume.

$$MgO + H_2O \longrightarrow Mg(OH)_2$$

$$MgSO_4 + 2NaOH \longrightarrow Mg(OH)_2 + Na_2SO_4$$

Assay –

Accurately weigh specied amount of sample into the flask. Add 25 ml 1N H_2SO_4, 50 ml H_2O. Excess of acid is back titrated with 1N Sod hydroxide using methyl red as indicator.

Storage- store in a tightly closed container in a cool dry place.

Uses –

1) used as antacid.

2) used as a laxative.

3) used as alkaline mouth wash.

Dose-

a) 5-10 ml as antacid

b) 10-30 ml as laxative.

Q. 6. : What combination of antacids are commercially available? Why is Simithicone added in antacid preparation?

Ans : The combination of antacids which are commercially available are;

1. Compound Magnessium trisilicate oral powder- contains Mg trisilicate, chalk powder, Sodium bicorbonate & Heavy Mg carbonate each 250 g.

2. Compound Magnesium trisilicate tablets- contains - Mg trtisilicate 250 mg, dried aluminium hydroxide gel 120 mg and peppermint as flavour in each tablet.

3. Compound Magnesium trisilicate mixture- suspension, containing Mg trisilicate, light Mg carbonate and sodium carbonate 5% w/w each in a suitable vehicle with peppermint flavour.

In many cases, antacids are combined with Simithicone type of compounds for their antiflatuent action as they are antifoaming agents and cause dispersion of gas.

Q. 7. : List the compounds of Bismith used as Protectives. Outline the method of preparation, action, uses of Bismuths subnitrite.

Ans : The compounds of Bismuth used as protectives are ;

1) Bismuth Subcarbonate.

2) Bismuth subnitrite.

3) Bismuth subgallate.

4) Bismuth milk- Syn., - Bismuth Magma or Bismuth cream.

Bismuth Subnitrite :–

App. formula- $[Bi(OH)_2 NO_3]_4 Bi(OH)$ is a basic bismuth nitrite.

On ignition at 105°C which gives not less than 79 % of Bi_2O_3.

Properties -

White, Hygroscopic powder. Practically insoluble in H_2O and alchohol but readily dissolves in excess of HCl or HNO_3.

Bismuth Subnitrate slowly hydrolysis in water and liberates nitric acid, incompatabilities with carbonates, salts of organic acids, reducing agents and iodines are observed.

Preparation-

By adding solution of NaOH to Bismuth nitrate solution at the temperature of 15 °C with stirring till the pH reaches 5. Precipitate of Bismuth subnitrate is collectecd by filtration, washed with cold H_2O and dried at about 50 °C.

Assay –

Accurately weighed amount of the sample is ignited to a constant weight in a tarred crucible and Bi_2O_3 is weighed.

Uses –

1) used as an Astringent, Adsorbent and protective commonly in the treatment of Diarrhoea and intestinal inflammation.

2) used in the preparation of milk of Bismuth as a main constituent.

Q. 8. : Discuss the mechanism of action of Purgatives (chatharetics) giving suitable examples.

Ans : Drugs which bring about defaceation are called **chatharetics.** Depending on the intensity of their action they are classified Purgatives and Laxatives. Purgatives generally mild in thier action whereas laxatives are still mild type Purgatives.

Constipation is the most commonly seen disturbance in many individuals. This may be due to illness, ignorance of the urge for defaction or due to Psychological status. Some other factors like weakness of intestine, intestinal spasm, injury or damage, use of certain drugs and some times diet also. In condition like constipation fecal meterial becomes dry and hard. For the releif in constipation or to treat this conditions laxatives and purgatives are used and brings out the elimination of bowl contents.

Purgatives or Chatharetics act mainly by four mechanisms.

1. Stimulant Purgatives-/Irritant Purgatives :

These act by irritating the intestinal tract there by brings the stimulation of pesistalsis movements which in turns promotes defecation. As they act directly on intestine and stimulate peristalsis, they are called stimulants.

Ex. segroda, castoroil, Podoplyllum, Bisacodyl, Aloe, Senna etc.

2. Bulk purgative :

Due to their virtue they are inbsoluble in H_2O and swells by absorbing water therby increase the bulk of intestinal contents, and brings out peristalsis movements of the intestine.

Example: Methyl cellulose, Sodium carboxyl methyl cellulose, Isapghol, Gum, Agar-Agar etc.

3. Lubricant Purgatives :

Act by the property of lubrication, since the contents of intestine becomes hard due to absorption of water resulting in difficulty in clearing the bowels. These substances act as

lubricants and brings smooth clearence of fecas. Example; Liquid paraffin, Mineral oils, Glycerine etc.

4. Saline Catharetics :

Act by increasing the Osmotic load on intestine by absorbing large quantity of H_2o and this stimulates peristalsis. Poorly absorbable cations like calcium, Magnisium and anions such as phosphate, sulphate, tartrate contributes this effect. They are mainly inorganic material and H_2O soluble, taken with plenty of H_2O This excess of water taken helps in reducing excessive loss of body fluids, nausea and vomitting.

Example : Mg salts, sulphate, and tartrate salts of sodium and potassium. These drugs are readily soluble but poorly absorbed and act mainly by their osmotic property in intestinal lumen.

Q.9. : Give the method of preparation, uses and assay of (a) Magnesium sulphate (b) Calomel.

Ans :

(a) Magnesium sulphate-

Formula SO_4 $7H_2O$.

MOLECULAR WEIGHT . 246.47

Synonym – Epsom salt.

Contains not less than 99 % and not more than 100 % $MgSO_4$ calculated with reference to ignited substance.

Properties –

Colourless crystals, cool, saline and has bitter taste. Freely soluble in water, sparingly in alcohol and dissolves slowly in Glycerine.

Preparation –

By the action of dil. H_2 SO_4 or Mg. carbonate or Magnesium oxide.

$$Mg\ CO_3 + H_2SO_4 \longrightarrow MgSO_4 + H_2O + CO_2 .$$

Solution is concentrated and crystals are filtered out.

Assay –

By complexometric titration, using sodium EDTA as titrant using Moderent black mixture as indicator.

Storage -

Store in a well closed container in a cool dry place.

Uses –

1) Used as a laxative.

2) Used as a antacid.

b) Calomel

Formula : HgCl

Molecular weight 236.1

Commonly known as Mercurous chloride. Contains not more than 99.6% HgCl.

Properties –

Odourless, tasteless, Heavy, white powder. Insoluble in water, alcohol and cold dil acids. Stable in air but when exposed to light turns slightly grey. Becomes yellowish white when tritrated with pressure.

Preparation –

By heating the mixture of mercunrous sulphate and Sodium chloride. Condense the vapours of mercurous chloride produced.

By heating mercury with H_2SO_4 Mercuric sulphate is obtained. Mercuric chloride is washed with H_2O to remove poisonous Mercuric chloride and then washed with dil HNO_3 to remove metallic mercury. Again washed with H_2O heat again and the sublimate is collected.

$$Hg + 2H_2SO_4 \longrightarrow Hg\ SO_4 + SO_2 + 2\ H_2O.$$

$$HgSO_4 + Hg \longrightarrow Hg_2SO_4$$

$$Hg_2SO_4 + 2\ NaCl \longrightarrow Hg_2\ Cl_2\ (2\ HgCl) + Na_2SO_4.$$

Assay –

Analysed by forming complex with Iodine.

Accurately weighed sample is transferred to iodine -flask. Excess iodine solution and potasium iodide solution are added, stoppered kept aside for few minutes with occasional shaking. Excess of Iodine s titrated with standard sodium thio sulphate solution using starch solution as indicator.

Storage –

Stored in a tightly closed container, protected from light.

Uses –

1) Used as a catharetic.

– X –

TOPICAL AGENTS

Q .1.: What are Topical agents? Classify them giving suitable examples.

Ans : As the name of the title indicates, there are the agents that are applied on the skin or mucous membrane and acts locally- at that particular area where they are applied. The action exerted by each of the agent depends on its nature and chemical properties. They may produce the astringent , demulsunt, adsorbent, emollient or protective effect. Some of the agents even exibits antimicrobial and astringent activity when applied topically.

Here the role and the usefulness of some important topical agents and their preparations having topical activity is discussed.

According to their mode of action, these topical agents are broadly classified as,
A) Protectives and Adsorbents. B) Antimicrobial agents.
C) Astringents D) Miscellaneous compounds.

PROTECTIVES AND ADSORBENTS :

Q. 2. : Describe the action of Protective astringents? Write brief account of silicone polymers as protectives.

Ans : The agents that cover the skin or mucous membrane, form possible irritants are called **'Protectives'.** These substance being insoluble and chemically inert act by forming a coat or film on the skin. In the same way, dusting powder forms adherent continuous film on intact skin and exibits protective action being in the state of fine sub-divisions.

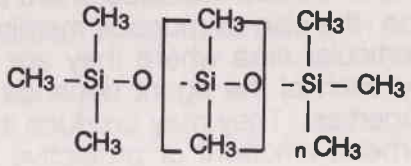
Some substances chemicaly inert adsorb dissolved or suspended particles gases, toxins etc are known as 'Adsorbents'. These are mainly intended to be used internally to prevent the unwanted and irritant action on mucous membrane.

Some of the substances may posses both Protective-Absorbent properties when applied topically.

Silicone Polymers :–

Generally known as Silicone oils.

GENERAL FORMULA,



As represented with the variation of 'n' the viscosity of silicone oils also vary.

Synthetically these are prepared by the process of polymerisation.

In general, silicon oils, due to their oily nature used as water repellant and protective to skin (from contact with irritants). It also acts as antiflatulent and used in antacid preparations.

Dimethicone-

Forms a protective layer on skin like plastic and acts as water protective agent. It is oily, stable and has low surface tension. Mainly used in ointments, sprays, lotions and creams.

Simithicone-

Prepared form dimethyl polysiloxane. Used as antiflatuent, antispasmodic, Sedative and digestant. Usual dose is 40-80 mg at bed time.

Q.3.: Give the method of preparation, properties and assay of Titanium dioxide and calamine.

Ans : Titanium dioxide -

Contains not less than 98 % calculated with reference to the dried substance.

Properties :

Odourless, tasteless, fluppy powder. Partially insoluble in water in dilute mineral acids. Dissolves slowly in hot Sulphuric acid.

Preparation :

The ore is heated with concentrated Sulphuric acid when sulphate of iron and titanium are dissolved in water the precipitate of titanium di oxide is obtained by hydrolysis.

Assay :

By complexometric Sodium editate back titration using ammonium sulphate, sample is dissolved in hot sulphuric acid and a definite volume is made. To a known volume of Hydrogen peroxide strong ammonium solution. Hexamine buffer and excess disodium Edetate is added and excess back titrated with Zinc chloride.

Uses :

1) Used as a good topical protective (due to opacity of compound)

2) Commonly employed in skin protective creams and pastes as it protects skin form harmful effects from Ultra Violet radiation.

3) Used in cosmetics and also in paints.

Calamine :

It is the mixture of ZnO with small amount of Ferric oxide. Contains not less than 98% & not more than 100.5 % of ZnO calculated after ignition.

B.P. says it as a basic Zinc carbonate suitably coloured with iron oxide.

Properties :

Almost odourless and tasteless and occoured as pink powder. The powder, passed through sieve number 100. Practically insoluble in water,soluble in mineral acids.

Preparation :

By heating native Zinc carbonate, the Zinc oxide required for calamine is manufactured. Then by mixing with ferric oxide upto 1% and passing the powder through sieve Number 100, calamine is collected.

Assay :

Ignite and cool the specified weight of sample and is weighed. Dissolve it in excess Sulphuric acid (1N) and filtered. Wash the residue with hot water till free form acidity. Filtrate and washings are combined. Add amonium chloride to prevent precipitation of ferric hydroxide during titration. The contents are titrated with 1N Sodium hydroxide using methyl orange as indicator.

Uses :

1) Used as mild astringent, antiseptic and protectant for skin.

2) used for soothing effect to treat skin itching and irritations.

The preparations of Calamine in common use includes,
a) calamine lotion. b) Aqueous calamine cream.
c) Calamine ointment.

Q .4. : Give the method of preparation, properties, Assay procedure and uses of Zinc oxide and Talc

Ans :

Zinc Oxide :

Contains 99–100.5 % of ZnO calculated with reference to the ignited substance to Constant weight.

Properties :

Odourless, tasteless, white amorphons fine powder. It absorbs CO_2 from air insoluble in water and alcohol, soluble in dilute mineral acids and Ammonia.

$ZnO + H_2SO_4 \longrightarrow ZnSO_4 + H_2O.$

$ZnO + 2\ NaOH \longrightarrow Na_2\ ZnO_2 + H_2O$

Preparation :

Obtained by heating mettalic Zinc in air current at high temparature. Metal turns into oxide which is collected as a fine white powder.

$2\ Zn + O_2 \longrightarrow 2\ ZnO$

Medicinal grade ZnO-Obtained by double decomposition of Zinc Sulphate. This Zinc Sulphate is added to the boiling solution of sodium carbonate. Pecipitated Zinc carbonate is collected, washed until free form sulphate, dried and ignited.

$ZnSO_4 + Na_2CO_3 \longrightarrow ZnCO_3 + Na_2SO_4$

$ZnCO_3 \longrightarrow ZnO + CO_2$

Assay :

By acidimetric back titration method. Since ZnO is a base insoluble in water it cannot be titrated directly with acid. Therefore dissolved in excess of standard acid and excess of acid is back titrated. Ammonium chloride used to prevent the pecipitation of Zinc hydroxide. The precipitate interferes in the detection of end point. Methyl orange is used as the indicator.

Storage :

Stored in a well closed container since it absorbs Carbon oxide.

Common preparations of ZnO includes,

a) ZnO – compound paste. b) Hydrous ZnO Ointment.

c) ZnO Ointment. d) Zinc Gelatin.

Talc : Synonym : purified taste; talcum powder.

Formula : $3\ MgO.\ 4SiO_2\ H_2O$

Properties :

Odourless, Tasteless, free form grittiness, very fine white powder. Practically insoluble in water and in dilute solutions of acids or alkalis. It adheres to skin.

Preparations :

By boiling fine powdered talc with dilute Hydro chloric acid and allowing the inslouble talc to settle. Supernatant liquid is decanted, washed thoroughly till free from acid. Acid treatment removes the impurities from talc.

Uses :

1) Used as lubricant, protective and dusting powder.

2) Used to protect the skin from irritation due to friction.

3) Used commonly in cosmetic preparations for external use.

4) Used as filtering aid.

ANTI – MICROBIAL AGENTS :

Q.5. : Discuss the various mechanism of action of inorganic antimicrobial agents.

Ans : Anti-microbial Agent is the broad terminology describing activity against microbes. Following specific terminology describes exact mechanism of action.

a) Antiseptics :

Substances that kill or prevent the growth of microorganisms. Specific for preperation intended to be applied on living tissues.

b) Disinfectants :

Prevents infection by destruction of pathogenic micro-organisms. Used generally with reference to the substance applied to inanimate objects.

c) Germicide :

Those which kills microorganisms. The more specific terminology like bactericide / fungicide/ virucide denotes denotes exact action.

d) Bacteriostatic :

The primary function of these agents is to inhibit the growth and development of bacteria. Thus drugs which do not kill the bacteria but arrests the growth of bacteria are called Bacteriostatic agents.

Desirable properties used as topical anti-infectives.

1) should have Antiseptic or Germicide activity
2) should have rapid onset of action and sustained activity.
3) should have good therapetic index and should indicate the usefulness in the concentration employed.
4) should not produce local cellular damage or interference body defenses.
5) should not produce systemic toxicity- on local application.

6) should have broad spectrum activity.

7) should posses favourable liquid water distribution co-efficient for its best efficiency.

Mechanism of action :

The mode of action of organic class of drugs/compounds including antibiotics is well documented. Here till date as some inorganic class of drugs are used as anticeptic disinfectant their mechanism of action need eloboration. Inorganic class of compounds generally exhibit antimicrobial action by

1) Oxidation. 2) Halogenation or
3) Protein binding or pecipitating mechanism.

1. Oxidation :

The compounds which liberates oxygen like peroxides, permangnate and certain oxo-halogen anions act by this Mechanism. They act on proteins containing sulphadyl gp and oxidises free sulphadyl to disulphide and inactive its function.

2. Halogenation :

Those which librates chlorine or hypochlorate or Iodine act by this mechanism. They act on peptide linkage and alters

its properties. This results in destruction of specific function of protein ends with death of organism.

3. Protein precipitation or binding -

This is observed with many metals. The nature of interaction with protein occurs through polar group of protein which acts as ligands and metal oin. as Lewis acid. The chelate complex formed leading to inactivation of protein. In general action is non-specific. Depending upon the concentration and the extent of reaction astringent, irritant, corrosive or even caustic action is observed on the host.

Silver, Copper, Mercury and Zinc are some of the metallic cations with germicidal action.

Q.5.: Give method of preparation and assay of :

a) Hydrogen peroxide. b) Potassium permanganate & c) Chlorinated lime.

Ans :

a) Hydrogen Peroxide –

Contains not less than 5% & not more than 7% w/v Hydrogen peroxide corresponding to about 20 times its volume of oxygen available with 0.025% w/v of suitable stabilizing agent.

Preparation :

a) Add the paste of Barium peroxide in ice-cold water to a calculated quantity of ice-cold dil sulphuric acid. Insoluble barium sulphate is filtered off.

$$BaO_2 + H_2SO_4 \longrightarrow BaSO_4 \downarrow + H_2O$$

b) Also manufactured by the electrolysis of ice-cold 50% Sulphuric acid followed by distillation under reduced pressure.

Assay :

By oxidation-reduction by permanganate method. The sample is suitable diluted and 5N sulphuric acid is added

and contents are titrated with potassium permanganate solution till faint pink colour is obtained.

$$2KMnO_4 + 3H_2SO_4 + 5H_2O_2 \longrightarrow K_2SO_4 + 2MnSO_4 + 8H_2O + 5O_2 \downarrow$$

Storage :

Stored in containers protected from light provided with a vent for the escape of oxygen and keep it in a cool place. The lable should inidcater whether it contains stabilising agent or not.

Uses :

1) Used primarily for its antiseptic action.

2) Since enzyme brings out the decomposition of Hydrogen peroxide into water and oxygen therefore Hydrogen peroxide when comes in contact it abrass(cut) the tissue.

$$2H_2O_2 \longrightarrow 2H_2O + O_2 \downarrow$$

b) Chlorinated lime –

Formula - $Ca(OCl)\,Cl.\,H_2O$

Commonly known as bleaching powder, contains about 30% w/w of chlorinated lime.

Preparation :

By the action of chlorine on calcium hydroxide. Slaked lime is thoroughly spread on shelves in a suitable container and chlorine gas is introduced at the top of the chamber and passed through the contents of shelves. Usually done at 25° c thus minimising the formation of calcium chloride. After the absorption of chlorine is completed, powdered lime is blown into the chamber to absorb the excess of chlorine.

$$Ca(OH)_2 + Cl_2 \longrightarrow Ca(OCl)\,Cl + H_2O.$$

The process is complex, the first products are basic chlorides and basic hypochlorates etc. By further action of chlorine lather charged into calcium hypochlorate. The available substance also contains small portions of calcium chloride.

Assay :

Based on oxidation – reduction reaction.

When added into water , chlorinated lime liberates chlorine slowly. (But on filtration and shaking with water, the chlorine is released readily). Aqueous suspension of sample is treated with Acetic acid in presence of potassium iodide in Iodine -flask. Acetic acid liberates chlorine from the sample which displays the equivalent amount of Iodine in potassium iodide. This liberated Iodine is titrated with standard (0.1N) Sodium thiosulphate solution using starch solution as indicator.

$$Ca(OCl)Cl + 2CH_3COOH \longrightarrow [CH_3(COO)]_2 Ca + HOCl + HCl.$$

$$HOCl + HCl \longrightarrow Cl_2 + H_2O$$

$$2KI + Cl_2 \longrightarrow 2KCl + I_2$$

$$I_2 + Na_2S_2O_3 \longrightarrow Na_2S_4O_6 + 2NaI$$

Storage :

Store in a well closed container in a cool place. It is affected by moisture and heat.

Uses :

1) Mainly used for its disinfecting and bleaching properties.
2) Commonly employed for chlorination of water & in the treatment of swimming tank.
Action is due to the liberated chlorine.

Q .6. List the official preparations of Iodine.

Ans : The official preparations of I_2 includes,

1) Aqueous Iodine solution
2) Weak Iodine solution
3) Strong Iodine solution
4) Povidone- Iodine solution

Q. 7 : Describe the action uses and assay of povidone - I_2 solution.

Ans : Povidone – Iodine solution.

Povidone is nothing but polyvinyl Pyrrolidine. The result or the complex formed by the interaction of povidone and

Iodine is Povidine -Iodine complex. This contains 10% w/v of available iodine. The complex is yellowish brown or has characteristic colour and is amorphous powder. Soluble in water and alcohol solution is transparent has reddish brown colour with faint smell of iodine. The aqueous solution has acidic PH.

Assay :

Assayed by the available iodine content.

For Povidone - Iodine complex, known weight of the sample dissolved in water using a stirrer for complete solution. It is titrated with standard sodium thiosulphate solution using starch as indicator. A blank is also performed.

For solution :

A known volume of sample is titrated against standard Sodium sulphate solution (0.02N)

Uses :

1) Povidine Iodine should be diluted before use for the reason that, 10% of the solution contains, only 0.001% of free iodine content. If it is diluted to 0.1% the iodine content increases and the solution becomes more powerful bactericidal.
2) Used in disinfection of skin, mouth or wounds.
3) Very effective in the management of burns and cuts.

The important advantages of this over other Iodine preparations is that is water soluble, non-irritant, has less toxicity and non-staining. It even can easily removed form skin and cloths by washing.

Storage :

Stored in a well closed container.
The available povidone- Iodine solution or preparations include
a) Aqueous solutions (0.1-1% of available Iodine)
b) Surgical scrub (0.75-1%)
c) Veginal gel (0.1%)
d) Aerosol (0.5%)

Q. 8. : Discuss briefly about the properties , preparations, Assay and Uses of Boric acid.

Ans :

Boric acid.

FORMULA-H_3BO_3

MOLECULAR WEIGHT 61.83

Contains not less than 99.5% & not more than 100.5% of H_3BO_3 calculated with reference to the substance dried over sulphuric acid for 5 hours.

In nature boric acid obtained in the form of Resonite-$Na_2B_4O_7$ $4H_2O$, Borax $Na_2B_4O_7.10.H_2O$, Borocalcite-$CaB_4O_7.4.H_2O$, Colemanite-Ca_2O_{11} $5H_2O$.

Properties :

Available in three forms -
a) colourless, odourless, pearly seales b) White odourless powder

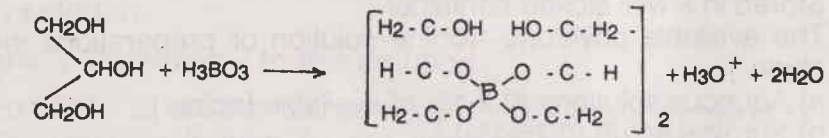
c) Six sided triclinic crystals, stable in air, sparingly soluble in water but more in boiling water and alcohol. Readily dissolves in glycerine. Boric acid is a weak acid and heating of orthoboric acid produces various dehydration products depending on the temperature to which it is heated.

For ex., at 100^{o} C $H_3BO_3 \longrightarrow HBO_2 + H_2O$ Metaboric acid.

at 160^{o} C $4HBO_2 \longrightarrow H_2B_4O_7 + H_2O$ Tetra boric acid.

further heating $H_2B_4O_7 \longrightarrow 2B_2O_3 + H_2O$ Borontrioxide.

When boric acid dissolved in glycerine it behaves as a strong acid. The glycero boric acid is a Monoprotic acid.



Preparation : On laboratory scale,

method 1) To the boiling solution of borax in water add dilute sulphuric acid Following reaction takes place resulting in the preparation of Boric acid.

$Na_2B_4O_7 + H_2SO_4 + 5\,H_2O \longrightarrow Na_2SO_4 + 4H_3BO_3$

2) For medicinal use high grade boric acid is prepared by treating Sodium Borate with HCl. Then it is dried.

3) On large scale (commercial manufacture)-

By the decomposition of naturally occurring borates like resonite, colemanite etc.,

Powdered colemanite mixed with boiling water. Suspension is heated with sulphur dioxide gas to liberate Boric acid.

$Ca_2\,B_6O_{11}.5H_2O + 2SO_2 + 4H_2O \longrightarrow 2CaSO_4 + 6\,H_3BO_3$

Assay :

Since it is a weak acid, it cannot be accurately titrated with standard alkali. As we know when it is dissolved in glycerine it acts like a strong monobasic acid, and can be titrated with standard alkali using phenolpthalin as indiçator.

Note : To increase the acidity of the weak acid, here other polyhydroxy compounds like mannitol can also be used.

Storage : Store in a well closed container.

The commonly used boric acid preparations include;

1) Boric acid solution (5%) 2) Boroglycerine glycerite 3%

3) Boric acid ointment 10%

Uses :

1) Used to maintain the acidic Ph in many topical solutions

2) Used in ointments for its emmolient and antisdeptic action as it is non-irritating and less toxic.

3) Boric acid in the form of solution mainly used as eye and mouth washes for local anti-infective action.

4) Used as an ingredient in dusting powders.

5) Used in the preparation of buffer solutions.

Q. 9. : Describe the principle involved in the assay of a) Borax b) Mild silver protein.

Ans :

a) Borax –

FORMULA- $Na_2B_4O_7.10H_2O$

MOLECULAR WEIGHT. 381.4.

Assay :

Borax can be directly titrated with Hydrochloric acid. This titration results in the formation of orthtoboric acid and Sodium chloride a slight excess of Hydrochloric acid is added at the end point which gives the colour change to the indicator methyl red, as orthoboric acid acts indifferent to the indicator methyl red.

$$Na_2B_4O_7 + 10\,H_2O + 2\,HCl \longrightarrow NaCl + 4\,H_3BO_3 + 5H_2O.$$

Accurately weighed sample about 3g dissolved in 75 ml water and titratedwith 0.5N HCl using Methyl red solution as indicator.

Each ml of 0.5N Hydrochloric acid = 0.09536 g of $Na_2B_4O_7.10.H_2O$.

b) Mild Silver Protein –

Silver is rendered colloidal by the presence of proteins or the combination with it and therefore the title.

Assay :

First accurately weighed sample is heated gently and thin ignited to remove carboneceous matter residue obtained dissolved in nitric acid, diluted with water and titrated with ammonium thiocyanate using ferric ammonium sulphate as indicator.

Q.10. : Give the method of preparation, properties, uses and assay of a) Ammoniated mercury b) Yellow mercuric Oxide.

Ans :

a) Ammoniated Mercury :

FORMULA – $NH_2(Hg)Cl$

MOLECULAR WEIGHT 252.07

Contains not less than 98% w/w NH_2 HgCl.

Properties :

Odourless, stable, white amorphous powder. Darkness when exposed to light. Practically insoluble in water alcohol and ether.

Preparation :

Prepared in the laboratory, by adding Mercuric chloride to a mixture of dil. ammonia solution with water by constant stirring. Precipitate is collected and washed with water and dried below the temperature 30°C.

$$HgCl_2 + NH_3 \longrightarrow Hg\begin{matrix}NH_2\\Cl\end{matrix} + NH_4Cl$$

Assay :

The substance is treated with potassium iodide solution with stirring. Mercuric iodide if any formed converted to potassium mercuric iodide by the addition of Potassium Iodide. The liberated Ammonia and Potassium hydroxide is treated with Hydrochloric acid using the indicator methyl orange.

$$NH_2HgCl + 2KI + H_2O \longrightarrow HgI_2 + NH_3 + KOH + KCl$$

$$HgI_2 + 2KI \longrightarrow K_2HgI_4$$

According to U.S.P. by using hot acetic acid solution the mercury from ammoniated mercury is separated as Zinc amalgam. Amalgam this separated dissolved in dilute Nitric

acid by heating. Thus, mercury is converted into mercuric nitrate. The solution is diluted and heated with dil potassium permanganate solution drop by drop to oxidise mercurous to mercuric form. Slight excess of potassium permanganate is reduced by the addition of oxalic acid carefully. Resulting solution is treated with ammonium thiocyanate using ferric ammonium sulphate as indicator.

Uses :

1) Because of slow release of mercuric ions used as mild antiseptic.

2)used in the treatment of various skin diseases caused by fungi, lice and other infestations.

3) Commonly employed in ointment in 5% strength and also as a dusting powder.

b) Yellow mercuric Oxide.

FORMULA – HgO

MOLECULAR WEIGHT 216.59

Contains not less than 99% of Hgo with reference to the substance dried at 105degree for one hour.

Properties :

Stable, odourless, orange, yellow, heavy amorphous powder. Gets discoloured when exposed to light. Readily soluble in dilute Hydrochloric acid and dilute Nitrc acid and practically insoluble in water and alcohol. A compound of medicinal use, mercuric olcate is formed with oleic acid. It decomposes into Oxygen and vapour of metallic mercury on heating, to red hot.

$$2HgO \longrightarrow O_2 + 2\,Hg$$

Preparation – Pour the concentrated solution of mercuric chloride to the dilute Sodium Hydroxide solution with cont. agitation. Allow to stand at room temperature for 1 hour supernent liquid is decanted and the precepitate is washed with water till the washings are free from alkali. The yellow

precepitate obtained is dried on absorbent paper at 30^{o} C. To get bright orange yellow product, all the above operations are carried out in dark.

$$HgCl_2 + 2NaOH \longrightarrow Hg(OH)_2 + 2NaCl.$$

$$Hg(OH)_2 \longrightarrow HgO + H_2O$$

Assay :

By titrimetric thiocyanate method.

Accurately weighed quantity of the substance dissolved in nitric acid and water. The solution is diluted and titrated with ammonium thiocyanate solution using ferric ammonium sulphate as indicator.

Storage :

Stored in a well closed container prevented from light.

Uses :

1) Used for its mild antiseptic action

2) Mainly used 1% preparation or strength for opthalmic use to treat the concerned inflammation and conjuvitis.

Q.11. : Explain briefly about :

1) Mercuric compounds 2) Silver and its properties.

Ans :

1) Mercury and its preparations. :

Mercury occurs as mercury, mercurous and Mercuric compounds-are strong oxidising agents and even mild reducing agents cause decomposition. Mercuric form readily forms complex with wide range of ligands.

These compounds find a number of applications medicinally and in pharmaceutical field. The mercury and its compounds or preparations are light sensitive, toxic, irritant, bacterio static and have non-specific protein precipitation action. Organo mercuric compounds comparatively less irritates, has germicidal, diuretic action , antifungal, disinfectant, antisyphyllic action etc.

Some of the most important and commonly used mercuric topical applications include;

1)Mercury

2) Yellow mercuric oxide.

3) Mercuric oxide eye ointment

4) Ammoniated mercury.

5) Ammoniated mercury ointment. etc.

2) Silver and its compounds and preparations-

From the many silver compounds and preparations, silver nitrate and its preparation are mainly of medicinal interest. Silver salts in general posses germicidal, astringent, irritant and corrosive action depending on the concentration used.

Silver ions precipitates proteins form the tissue fluids. The germicidal and astringent properties is due its action on proteins. Being photosensitive, it causes discolouration of skin. Silver and its compounds show various types of incompatabilities because of its sensitivity to light the silver compounds and preparation are stored in dark coloured bottles, (prevented from light).

The medicinally and pharmaceutically used silver and its compounds and preparations include;

1) Silver nitrate.

2) Mild silver protein.

3) Strong Silver protein.

ASTRINGENTS :

Q.12. : What are Astringents? Topically how they are useful? List the compounds of Aluminium used as astringents with their method of assay.

Ans : Generally, the agents or substances used possessing the properties of precipitating the proteins are called **'Astringents'**. They are applied topically cause precipitation of protein by coagulation. The action produced depends on

the extent of penetration and type of chemical action resulting with protein. Astringents also show

a) Stops the bleeding by coagulation of blood and constriction of small blood vessels.
b) anti-inflammatory action
c) anti perspiration action.
d) antimicrobial action by precipitating the body proteins.

The compounds of aluminium used as astringents are,

1) Alum (Potassium aluminium sulphate) - $KAI(SO_4)12H_2O$
2) Aluminium chloride- $AlCl_3\ 6H_2O$
3) Aluminium sulphate - $Al_2\ (SO_4)_3\ H_2O$
4) Aluminium subacetate solution- $Al\ (CH_3COO)_2\ OH$.

1. Assay of Alum –

Assayed by the gravimetric method. Accurately weigh about 2g of substance dissolved in 300 ml water. Add 20ml of aluminium chloride solution, 5 drops methyl red and sufficient quantity of ammonia solution to get a distinct yellow colour. Solution in heated to boiling, filtered and precipitate washed with ammonium nitrate solution (2.5%) till it is free from chloride. Precipitate of Al_2O_3 is dried to constant weight at 120 ^oC and weighed.

Each gram of residue ≡ 9.307 g of $KAl(SO_4)_2\ 12\ H_2O$

2. Assay of Aluminium sulphate –

On complexometric back titration method known weight of the substance dissolved in 1N Hydrochloric acid. Excess of disodium edetate is added. Solution is neutralised to methyl orange heated and treated with standard lead nitrate solution using xylenol orange as indicator.

Q .13. : Give the method of preparation, uses and assay of a) Zinc chloride b) Zinc sulphate c) Zinc stearate.

Ans : a) Zinc Chloride :

FORMULA – $ZnCl_2$

MOLECULAR WEIGHT. 136.29

Contains not less than 95% & not more than 100.5% $ZnCl_2$

Properties :

Deliquesent, Odourless, white Crystalline granules or powder soluble in water, freely soluble in alcohol and glycerine. Aqueous solution has the acidic PH (4.0) due to the hydrolysis to form Hydrochloric acid and basic Zinc chloride similar to aluminium salts.

$$ZnCl_2 + H_2O \longrightarrow Zn(OH)Cl + H^+ + Cl^-$$

Preparation :

Prepared by reacting granular or metallic Zinc with HCl. The solution is evaporated to dryness.

$$Zn + 2HCl \longrightarrow ZnCl_2 + H_2 \uparrow$$

It is also obtained by the action of Zinc oxide or carbonate with suitable amount of Hydrochloric acid.

Assay :

Complexometric titration method.

Dissolve accurately weighed compounds in water and a definite volume is made. To a known volume of solution ammonia-ammonium chloride buffer is added. Eriochrome black T used as indicator and the solution is titrated against standard sodium Edetate.

Storage :

Store in a well closed container as it is deliquesent and absorbs Carbon-di-oxide.

Uses :

1) Used as a powerful astringent and mild antiseptic.
2) Used in mouth wash and deodorant preparations.
3) Used in various dental preparations as 'desensitize' of dentin.
4) Also used in fire proofing wood.

b) Zinc Stearate :

FORMULA-$ZnSO_4$. $7H_2O$.

MOLECULAR WEIGHT 287.6

Contains 99.0-108% of $ZnSO_4\ 7H_2O$

Properties :

Odourless, colourless, transparent needles or crystals or powder. Has astringent taste. Very much soluble in water and glycerine, insoluble in alcohol. Aqueous solution has the acidic Ph 5.0. With ammonium and potassium forms a double salt $ZnSO_4$, K_2SO_4 $6H_2O$. It decomposes on strong heating.

Preparation :

In large scale, prepared by heating Zinc sulphide (Zinc blend) in presence of air under specified conditions. Heated mass is dissolved in hot water , filtered and concentrated for crystallization.

$$ZnS + 2O_2 \longrightarrow ZnSO_4$$

2) Digesting metallic Zinc granules in dilute sulphuric acid solution is filtered and treated with chlorine to oxidise any impurity of ferrous to ferric sulphate which is then precipitated by hydroxide and removed . Filtrate is concentrated for crystallisation.

$$Zn + H_2SO_4 \longrightarrow ZnSO_4 + H_2$$

Assay :

By gravimetric method as ZnO. Now this is assayed by complexometric titration method.

Accurately weight about 0.3g of sample, dissolved in 100ml water. Add 5ml ammonia- ammonium chloride buffer and make up the volume to 250ml. Take 25ml of solution + 100ml water and 1ml Eriochrome black T indicator and titrate against 0.05m disodium editate to get deep blue and point.

Each ml of 0.05M disodium editate $\equiv$ 0.01438g of $ZnSO_4$. $7H_2O$.

Uses :

1) Used as mild germicide and astringent.
2) Used in topical applications as protective.

3) Used internally as emetic.
4) As protectives used in bandages, adhesive tapes etc.

c) Zinc Stearate :

FORMULA- $CH_3[(CH_2)_{16}COO]_2Zn$.

A mixture of Zinc and solid organic acids obtained from fats. Contains not more than 12.5% and not less than 14.5% ZnO

Properties :

White, fine, amorphous powder free form grittiness insoluble in water and alcohol. Aqueous suspension is neutral.

Preparation :

Prepared from sodium stearate and Zinc sulphate. Gradually add the melted stearic acid to a hot solution of sodium hydroxide or carbonate in jacked hot pans. Sodium stearate is prepared. It is allowed to cool and Zinc sulphate is added. Precipitate of Zinc stearate is collected, washed till free form sulphate and dried.

$$C_{17}H_{35}COOH + NaOH \longrightarrow C_{17}H_{35}COONa + H_2O$$

$$2C_{17}H_{35}COONa + ZnSO_4 \longrightarrow (C_{17}H_{35}COO)_2Zn + Na_2SO_4.$$

Assay :

Weigh about 1g of sample boiled with 50ml of 0.1N H_2SO_4 - 10 times filtered and washed. combined filtrate and washings treated by following procedure as under

Each ml 0.05M disodium edetate ≡ 0.004068 g of ZnO.

Uses :

1) Used as mild astringent
2) Used in dermatology for its protective action.
3) Used in ointment and dusting powders.
4) Used as lubricant in tableting.

Q.14. : Describe the preparation, properties and uses of :

a) precipitated sulphur

b) Sublimed sulphur.

c) Selenium sulphide.

Ans :

a) Precipitated sulphur-

It is an allotropic form of sulphur.

Properties :

Odourless, tasteless, grayish, yellowish soft powder. Burns with blue flame when heated. It consists of amorphous particles without crystals as evident by microscopical appearance.

Preparation :

Heating together sublimed sulphur and milk of lime for 1hour, during which calcium pentasulphide and thiosulphate are formed.

$$2Ca(OH)_2 + 12S \longrightarrow 2CaS_5 + Ca\,S_2O_3 + 3H_2O$$

Mixture is filtered and dilute hydrochloric acid is added. Keep stirring till the solution is alkaline. The precipitated sulphur is filtered, washed till neutral to I and does not give test for calcium with ammonium oxalate solution. the substance is dried rapidly.

$$CaS_5 + 2HCl \longrightarrow CaCl_2 + H_2S + S$$

Uses :

1) Primarily used in ointments as Scabicide.

2) Used in treatment of sebhorrea, acne, pimples, and psoriasis.

3) Used as Keratolytic agent.

b) Sublimed sulphur :

Synonym : Flowers of sulphur.

Properties :

Fine rhombic yellow crystals or powder with faint odour. Practically insoluble in H_2O soluble in carbondisulphide. It is opaque rounded, amorphous particles or aggregates of

semicrystalline mass as evident by microscopical appearence.

Preparation :

By the process of sublimation whereby vapours of sulphur is produced by heating any form of sulphur and condensed. In refinery, molten sulphur is placed in iron retorts which communicate with stone chambers. the sulphur vapours enters the stone chamber they convert into SO_2 by ignition. These vapours are passed through relatively cold gas and condenses on the walls and floors of the chambers in fine crystalline form.

Uses :

1) Used as an ingredient in sulphur ointment.
2) Used as scabicide.

c) Selenium Sulphide :

FORMULA- SeS_2

MOLECULAR WEIGHT - 143.09

Contains b/w 52-55% of selenum.

Properties:- Bright orange powder with faint sulphide odour. Practically insoluble in water and org. solvents.

Preparations :

By passing gas of hydrogen sulphide into seleneous acid or by adding seleneous acid to a saturated solution of hydrogen sulphide. The precipitate is collected and dried.

$$H_2SeO_3 + 2H_2S \longrightarrow SeS_2 + 3H_2O.$$

Uses :

1) Used topically as antidandruff.
2) Used in shampoos as antisebhorric.

Note – As the compound is highly toxic, extra care should be exercises during its use not to introduce it into eyes or mouth.

– X –

DRUGS USED IN DENTAL PRACTICE

In order to keep the tooth healthy and strong, dental hygiene is recognised since very long time. The various chemical substances and dental products are used for the same purpose. It is evident that clean and healthy teeth keeps good health and clean tooth cannot decay.

Many organic and a wide variety of inorganic compounds like anticarics agents, cleaning agents, polishing agents etc. are used in dentistry or in dental practice.

Q.1. : What are Anticaries agents? Explain the role of fluoride as anticaries agent.

Ans : Tooth decay or dental caries defined as the disease of tooth caused by the acids released by the action of micro organism which is characterised by decalcification of tooth with foul odour in mouth. It is known that dental caries begins on the surface of teeth and the exact Mechanism of action and cause is not known. Acids produced by metabolism of carbohydrates fermenting carbohydrates act on teeth produce leisons on which bacteria gets localised and results in dental caries.

The agents that keeps the teeth healthy and clean are called **'Dentrifices'**, used in the prevention of dental caries. Example . Ammoniated tooth paste, Urea ammonia containing powders, antibiotics etc. The compounds are having their own limitations besides advantages.

Flouride plays very vital role in preventing dental caries. The compounds or salts or solution containing very little amount of fluoride (1PPm) are used. They are rapidly absorbed, transported and deposited on the developing teeth or in bone. Flouride prevents the action of acids or Enzymes

which produce leisons. When the excess of fluoride is administered (2-3 PPm) results in **'dental fluorosis'** where it produced mottled enamel.

Fluoridation of water is the most common and effective way of oral administration. water contains 0.5-1PPm of fluoride. It can be given orally with fruit juice or drinking water with such a concentration to have 1ppm/day. Sodium fluoride tablets or solution in the dose of 2 .2mg/day is employed. For topical application 2% solution is used on teeth.

Q. 2 : What are cleansing agents and Polishing agents ?

Ans : Cleansing agents generally has satisfactory abrasive property. They have coarse to fine particle size. These agents remove the stains and to achieve this abrassiveness is essential. Phosphates have well known anti-caries and cleaning property. Dibasic and tribasic Calcium phosphate, Sodium metaphospahate, are some examples for cleansing agents used in tooth pastes and powders. Pumic powder and calcium carbonate are the other examples.

This polishing effect is also achieved by abrassiveness. One of the requirement of a dentrifice is to have polishing effect. i.e., overall to give whiteness to teeth. Desensitising agents are those which reduce the sensitivity of teeth to heat and cold. This property is shown by astringent type of compounds for which they have incorporated into the preparation of dental products. these are (desensitising agent) probably acts like local anesthetic. Ex. Strontium chloride, Zinc chloride.

Q. 3. : Describe the method of preparation, uses and assay of a) Sodium fluoride b) Dibasic calcium phosphate.

Ans : a) Sodium fluoride.

FORMULA – NaF

MOLECULAR WEIGHT. 41.99.

Contains not less than 98% of NaF calculated with reference to dried substance.

Properties :

Odourless, colourless crystals or white powder soluble in water insoluble in alcohol. Aqueous solutions are corrosive to glass and hence made from distilled water and stored in dark, pyrex bottles.

This is a weak acid- Hydrofluoric acid is produced by acidification and is poisonous.

Aqueous solution of salt is alkaline.

Preparation :

1) By neutralising Hydrofluric acid with sodium carbonate

$$2HF + Na_2CO_3 \longrightarrow 2NaF + H_2O + CO_2$$

2) By decomposition of calcium fluoride with sodium carbonate

$$CaF_2 + Na_2CO_3 \longrightarrow 2\,NaF + Ca\,CO_3$$

The insoluble calcium carbonate is filtered off.

Assay :

Complexometric titration method.

Weighed quantity of sample dissolved in water, Add small quantity of Sodium chloride and alcohol. Contents are heated to boiling excess of lead nitrate is added drop wise by stirring. Cool the solution. Filter the coagulated precipitate residue, washed with dilute alcohol and combined filtrate and washings are titrated with disodium edetate using xylenol orange as indicator.

Storage :

Should be stored in well closed pyrex bottles in dark.

Uses :

1) Used to prevent the dental caries.

2) topically used as 2% solution on surface of teeth.

3) Enters the enamel and becomes part of enamel structure and becomes much effective in retardation and prevention of dental carries.

b) Dibasic calcium phosphate- $CaHPO_4$

The compounds is discussed in detail under the compounds of calcium.

Uses :

1) As a electrolyte replenisher in the ratio 1:1 of calcium and phosphorous.

2) Used as a supplement, required for the growth in children, pregnant women and lactating mothers.

3) Externally as dentrifices for cleaning action.

4) Moderate abrassive property makes it suitable for tooth-paste and powders.

Q .3 : Give the properties and uses of stannous fluoride, Pumice, sodium meta phosphate and Strontium chloride.

Ans :

a) Stannous fluoride :

Stannous fluoride solution (Tin fluoride solution) prepared by dissolving in water and freshly prepared solution is used in dentistry.

Properties :

White crystalline powder. Posses unpleasent astringent - salty taste, soluble in water. Insoluble in alcohol and organic solvents. Aqeuous solutions rapidly deteriorates rapidly on standing to stannic form resulting in turbidity due to oxidation.

Uses :

1) Used in fluoride treatment of teeth.

b) Pumice :

It consists of complex silicates of aluminium, potassium and Sodium in variable composition. Product of volcanic origin.

Properties :

Tasteless, odourless, hard grayish-white powder. Stable in air and insoluble in water. Gritty in nature- On seiving catagorised to superfine, fine and coarse pumice powder.

Uses :

1) Used as filtering and distributing agent used depending on particle size.

2) Used as abrassive in metal polishes.

3) Used in soaps and cleaning powder because of its grittiness.

4) As a dental abvassive in dental preparation.

c) Sodium metaphosphate-$NaPO_3$

Synonym - Graham's salt.

Colourless, glassy hygroscopic, tasteless, odourless powder. Gritty in nature soluble in water.

Uses :

1) Polymeric form of $NaPO_3$, acts as a very good cleaning agent.
2) One polymeric form, Calgon used in water softening
3) Used in prevention and removal of boiler seals.

d) Strontium chloride- $SrCl_2\ 6H_2O$.

Colourless crystals and white granules soluble in water and alcohol.

Preparation :

By the action of stronium carbonate with Hydrochloric acid until effervsence is ceased. Filter the solution concentrate and allowed for crystallisation.

Uses :

1) Used as desensitising agent in dental remedies.

– X –

INHALANTS

INTRODUCTION :

The drugs or chemical substances which are inhaled in the vapour form are called **'Inhalants'.** Inhalants as a anesthetic are administered by closed mask method. These inhalants exerts physiological action by bringing out the changes in physiological functions. The effect exerted depends on the nature of the gas, its concentration and the condition in which it is used as the action and effect of gas will be different under different conditions. The most commonly employed gases practically include O_2, CO_2, N_2O etc.

Q .1 : Discuss the role of CO_2 and O_2 in biological system.

Ans :

Role of CO_2 :

As we are aware that, CO_2 is the waste product produced in the body which is carried by blood in the cells and in the plasma. A large quantity of CO_2 is eliminated by lungs in the expired air. CO_2 exits in 3 forms

a) as carbonic acid- when combines with water.

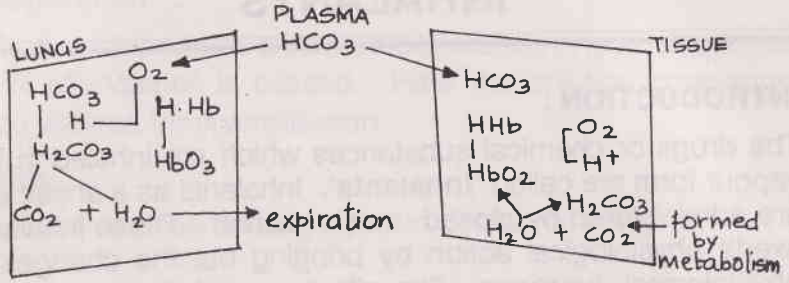
b) Carbamino bound form- when combined with proteins.

c) as bicarbonates- when combine with other cations.

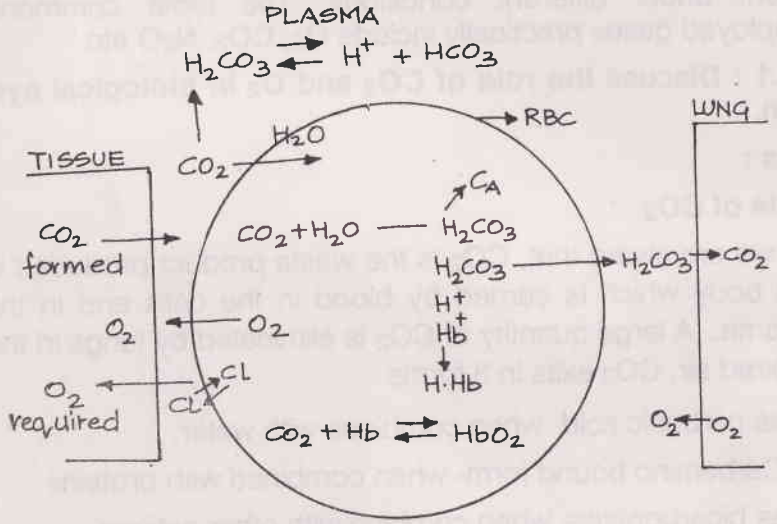
Under normal physiological conditions, CO_2 is utilised for maintaining the PH of blood by carbonic acid formation, and its conversion to bicarbonates etc. It is observed that increase in bicarbonate ion results in increase in Ph of body fluids during which increase in CO_2 levels through carbonic acid decreases it. Both effects are balanced by excretion process.

The interchange or exchange of gases occurs in lungs, tissues and blood as indicated by the diagram.

I.



II. Transport mechanism or Exchange of gases in lungs, tissues, blood.



Besides CO_2, ammonia produced in kidney by deamination of amino acid also plays an important role in maintaining acid base balance of body.

b) Role of O_2

O_2 is vital for living cells. Essential to carry out the normal activities of cell and for the production of energy. Energy is used by the cells for the synthesis of Adenosine Triphosphate (ATP) which in turn when hydrolysed, releases energy. Enzymes also plays an important role in the reaction.

O_2 is transported by Haemoglobin. The concentration of hemoglobin plays an important role in transport mechanism. O_2 combines with hemoglobin reversibly and forms Oxy hemoglobin as shown.

$$Hb + O_2 \longrightarrow HbO_2$$

This combination readily dissociates and releases O_2 in the cell. The factors affecting the formation and dissociation of O_2 included temperature, electrolytes, effect of CO_2, Carbon monoxide PH etc.

Similar to O_2, CO_2 also forms carboxy hemoglobin with hemoglobin which is a very fast process. This reduces the amount of hemoglobin available for transportation of O_2.

Haemoglobin also has remarkable buffering capacity which is due to the acceptance of H^+ ions by the reduced hemoglobin Haemoglobin in oxyform is a strong acid than reduced form.

By inhalation by respiration, Oxygenation of blood takes place in alveoli of lungs. The requirement of O_2 by the body varies in different conditions.

Q 2. Give the method of preparation , properties, uses and assay for Oxygen and Nitrons Oxide.

Ans :

a) Oxygen.

FORMULA O_2

MOLECULAR WEIGHT 32

An important constituent of air constituting 21% of the total volume of atmosphere is O_2.

According to I.P, it contains not less than 99% v/v of O_2 with traces of other gases available and supplied in metallic cylinders in compressed form.

Properties :

Colourless, odourless, tasteless, gas has density of 1.105

O_2 dissolves in 32 volume of H_2O, 36 volume of alcohol at 1 atms pr. Primarily O_2 functions or acts as oxidizing agent.

It forms oxides when combined with non-metals.

Example :

1) $S + O_2 \longrightarrow SO_2$

2) $C + O_2 \longrightarrow CO_2$;

3) $2P + 5O_2 \longrightarrow 2P_2O_5$

It forms corresponding oxides when combine with metals.

Example

1) $4\ Fe + 3O_2 \longrightarrow 2Fe_2O_3$;

2) $2Mg + O_2 \longrightarrow 2MgO$

It doesn't combine directly with halogems and gas.

Preparation

1) By fractionation of liquid air. 2) By electrolisis of water.

1. Air is purified (Moisture, CO_2 dust etc are removed) and compressed into liquid state. It is subjected to fractionation by distillation to get O_2 which is then filled under pr in metallic cylinders.

2. Direct current is passed between iron and steel electrode immersed in 10% aqueous solution of potassium or Sodium Hydroxide O_2 is liberated at the anode and hydrogen at cathode. O_2 liberated is suitably collected and stored.

Assay :

By gas measurement method.

Apparatus specified by I.P is used.

Gas is introduced into apparatus and is allowed to come in contactwith absorbing liquid. After most of the gas is absorbed, the residual gas is brought back to the burette by adjusting mercury reservoir and the volume of residual gas is measured. It should not exceed 1% v/v.

Storage :

Stored in metallic cylinders under pressure

Labelling :

Shoulder of the cylinder is painted white and the remainder painted black. The name and symbol of O_2 is stencilled on the shoulder of cylinder.

Uses :

1) Used in the treatment of Hypoxia.

2) Used in the treatment of aroxia.

3) Used in the treatment of carbon monoxide poisoning.

4) Industrially used in oxy-acetalene flame required for welding and cutting metals.

5) Liquid O_2 used as a fuel in rocket technology.

b) Nitrous Oxide :

FORMULA N_2O

MOLECULAR WEIGHT 44.01

Synonym : LAUGHING GAS - because of its exhilaration effect when inhaled.

Contains not less than 95% v/v of N_2O.

Properties :- colourless gas with slight sweetish taste and odour. It decomposes at high temperature.

$N_2O \longrightarrow N_2 + (O)$ liberated O_2 assists in burning.

Preparation :

By thermal decomposition of ammonium nitrate. Gas is purified by washing with sodium chromate, Sodium Hydroxide and water, then filled in cylinder.

$NH_4NO_3 \longrightarrow 2H_2O + N_2O$

Assay :

Using special apparatus described in official. pharmacopoeia.

The apparatus consists of burettes connected to a condenser- Manometer. Here volume of liquid nitrogen is measured. Not less than 95% v/v is condensed.

Storage :

Stored in metallic cylinder under compression and at the temperature not more than 37°C.

Labelling :

Cylinder is painted blue and carries a label stating the name and symbol of gas stencilled in paint.

Uses :

1) Used by inhalations for operations of short duration like dental extractions minor operations of boils and obsesses.

2) Produces anesthesia with analgesia.

3) Also effective in calming excited mental patients.

– X –

EMETICS, RESPIRATORY STIMULANTS AND EXPECTORANTS

INTRODUCTION :

Respiratory stimulants belongs to the class of central nervous system stimulants. The (CNS-stimulants) drugs which increase the various activities and functions in central nervous system are called C.N.S. stimulants or stimulants or 'analeptics'. One of the important stimulation is 'Respiratory stimulation' brought through the stimulation of chemo-receptors and vasomotor centres.

The mechanism of action is different for different drugs or chemicals. The role of gases and also pH of blood and various chemicals which alter the pH also effect respiration. The compounds mainly stimulates the epithelial cells of Trachea, bronchial and bronchiole which in turn leads to the respiratory stimulation.

Ammoniacal salts and preparation- in general considered as respiratory stimulants. They give off ammonia gas which irritates respiratory tract and act as reflux stimulant.

'Expectorants' drugs or substances which remove sputum from the respiratory tract. They either increase the fluidity of sputum or increase the volume of fluids that are to be expelled from respiratory tract by coughing.

Classified into 2 categories according to their mode of action.

1. Sedative type

2. Stimulant type.

Sedative type- They are stomach irritants, produce their effect through stimulation of gastric reflexes. Bitter drugs like Ipecac, Squill, Senega and compounds like Ammonium chloride, Sodium citrate, Antimorry potassium tartrate, KI are sedative type.

Stimulant type- These drugs directly or indirectly brings out the stimulation of senctory cells of the respiratory tract, more fluid is produced in Respiratory tract and there by sputum is diluted. Turpenoid oils like lemon, Eucalyptus, Anise and active constituents of oil like terpine hydrate, Anithole,are stimulants

Emetics- drugs or substances which remove fluid from respiratory tract. Some of the inorganic compounds act directly by stimulating the Respiratory tract secretions. These are added in small quantities in the preparation of cough syrups.

Q.1 : Give the method of preparation, uses, properties and assay of :

a) Ammonium chloride b) Antimony potassium tartrate. c) KI

Ans :

a) Ammonium chloride :

FORMULA. NH_4Cl.

MOLECULAR WEIGHT 53.5.

Contains not less than 99.5% NH_4Cl calculated with reference to the substance dried over silica gel for 4 hours.

Properties :

Colourless or white, crystalline or coarse powder. Odourless, has a cooling, saline taste. Slightly hygroscopic solubie in water, sparingly in alcohol but freely in glycerin.

Freshly prepared aqueous solutions are neutral but quickly becomes acidic due to hydrolysis. (on standing)

$$NH_4Cl + 2H_2O \longrightarrow NH_4OH + H_3O^+ + Cl^-$$

Ammonium salts are incompatable with alkalis, carbonates of alkaline earths and lead salts.

Preparation :

1) By interaction of Ammonia gas with HCl solution is evaporated to dryness.

$$NH_3 + HCl \longrightarrow NH_4Cl.$$

Salt is purified by crystallization and sublimation salt is mixed with 5% calcium phosphate, during purification, to prevent the sublimation of any volatile iron salts, sublimation is carried out in cast iron pots.

2) Also by treating ammonia gas liquors with lime and the liberated ammonia is passed into HCl.

Assay :

By volhards method- precipitation titration.

Excess of silver nitrate solution is added to the sample solution residual $AgNO_3$ is determined by titrating it with standard ammonium thiocyanate using ferric ammonium sulphate as indicator.

Now is based on formal titration principle.

The formaldehyde added to the sample solution endows acidic properties to the compound and hence can be titrated with standard alkali solution using phenolpthalin as indicator.

Storage :

Stored in a tightly closed container.

Uses :

Exhibits three important phsycological actions. All are dose dependent.

1) acts in maintaining acid-base equilibrium of body fluids.

2) Diuretic effect due to the utilization of ammonium cation in conversion into urea. On repeated use cause metabolic acidosis.

3) acts as mild expectorant and Diaphorotic- in small doses.

b) Antimony Potassium tartrate.

FORMULA $C_4H_4KO_7Sb$

Synonym : Tarter Emetic

Properties :

Odourless, colourless, has sweetish taste. Soluble in water and insoluble in alcohol.

Preparation :

Mix 5 parts of antimony trioxide with 6 parts of potassium acid tartrate in a fine paste and leave it aside for a day. Boil with water for 15 minutes with stirring. Liquid is filtered hot and the filtrate is left for crystallisation. crystals are collected and dried.

Assay:-

Based on oxidation - reduction reaction.

Here I_2-solution is used as Oxidising agent. It converts antimony to antimonic state (Sb_2O_5). This titration is done in the presence of excess of sodium potassium tartrate and borax. Sodium potassium tartrate prevents the precipitation of antimonious hydroxide. In the reaction hydroidic acid is neutralised by borax used in the analysis. Strong alkalis like NaOH is not used, as it may react with I_2 to form Hypoiodate.

$$2NaOH + I_2 \longrightarrow NaOI + NaI + H_2O.$$

$$2C_4H_4O_7SbK + 3H_2O + 2I_2 \longrightarrow 2KHC_4H_4O_6 + Sb_2O_5 + 4HI.$$

This antimany sodium tartrate acts similarly as emetic agent.

Uses :

1) Used as expectorant- emetic.

c) Potassium Iodide :

FORMULA-KI

MOLECULAR WEIGHT 166.0.

Contains not less than 99% KI, calculated with reference to the substance dried to constitute water at 105°c.

Properties :

Colourless, opeque or transparent salt, has saline bitter taste, Odorless, soluble in water, alcohol and glycerine. Aquous solution of KI take up iodine and forms poly iodide complex, KI_3, KI_4 etc., When water is added to KI to prepare its aqueous solution the temp. of the solution gets lowered.

Preparation :

2 different process.

1) By the action of I_2 on moist Iron filing to form ferro ferric iodide which is then decomposed with potassium carbonate.

$$Fe + I_2 \longrightarrow FeI_2 \quad ; \quad 3FeI_2 + I_2 \longrightarrow -FeI_2.2FeI_3,$$

$$FeI_2.2FeI_3 + 4K_2CO_3 \longrightarrow 8KI + FeOFe_2O_3 + 4CO_2$$

Here ferro-ferric oxide is filtered out. KI is obtained by the recrystallisation of the concentrated filtrate.

2) By adding excess of I_2 to KOH solution. KI and iodate are formed. Potassium iodate is reduced to KI with carbon.

$$6KOH + 3I_2 \longrightarrow 5KI + KIO_3 + 3H_3O$$

$$KIO_3 + 3C \longrightarrow KI + 3CO\,.$$

Assay :

By titrating with potassium iodate which acts as oxidising agent. Weighed quantity of sample dissolved in water acidified with HCl and the contents are titrated with standard potassium iodide solution using chloroform as indicator solvent.

Chloroform is used to detect the disappearance of Iodine.

Storage :

Store in a well closed container.

Uses :

1. used as expectorant.
2. used as source of iodine and potassium.
3. used as stabiliser in preparation of I_2 solutions.
4. used as reagent in pharmacy.

d) Copper sulphate :

FORMULA $CuSO_4 . 5H_2O$

MOLECULAR WEIGHT. 249.7

Contains not less than 98.5% and not more than 101% $CuSO_4$ $5H_2O$

Properties :

Occurs as triclinic crystals of pentahydrate or as blue crystalline granules or powder. Soluble in water, almost insoluble in alcohol. Aqueous solution are acidic and produces blue green colour.

Preparations :

By roasting copper containing sulphide ore in the presence of air or by heating copper with sulphur in a furnace. In this process the mixture of $CuSO_4$ and copper oxide is obtained and is treated with dil H_2SO_4. Resultant solution is filtered, concentrated and crystallised.

$$2Cu + 2H_2SO_4 + O_2 \longrightarrow 2CuSO_4 + H_2O$$

-another method of preparation.

Assay :

Red ox titration method :

Weighed amount of sample dissolved in specified volume of water. The solution is treated with 3g (excess) of KI and 5ml acetic acid and the liberated I_2 is titrated with standard 0.1N $Na_2S_2O_4$ using starch solution as indicator. Titration is continued to get a faint blue colour. Add 2g potassium thiocyanate and stirred well. Titrate until the blue colour disappears.

Each ml of 0.1N $Na_2S_2O_3$ ≡ 0.002497g of $CuSO_4.5H_2O$

Storage :

Store in a well closed container protected form air, heat and moisture.

Uses :

1. used as emetic, in chemical poisoning.
2. used externally as astringent.
3. used externally as fungicide.
4. used in the preparation of Benidict and Fehling's reagents.

Q. 2 : Give the method of preparation assay properties and uses of Aromatic spirit of Ammonia.

Ans :

Aromatic spirit of Ammonia.

Contains 1.12-1.25% w/v of free ammonia and 2.76-3.24% w/v of ammonium carbonate.

Syn :– Spirit Of Sal Volatile.

Composition/ingredients	**Quantity for 1000ml.**
Ammonium bicarbonate	25G.
Strong ammonia solution	70ml.
Lemon oil	5.1ml.
Nutmeg oil	3ml.
90% Alcohol	750ml.
Purified H_2O quantity sufficient	1000ml.

Preparation :

Nutmeg oil, lemon oil, alcohol and 375 ml of water placed in distillator and about 875 ml of distillate is collected. In addition,, 35ml of distillate is separately collected and ammonia and ammonium bicarbonate are added. The contents are warmed on a water both at 60^{o}c, stirred, filtered. Gradually

add filtrate to the first distillate. Sufficient quantity of water is added to obtain the desired volume.

Assay :

Assayed for alcohol, ammonium carbonate and for free ammonia.

1) For alcohol content- the method according to I.P is followed .

2) For ammonium carbonate - 20ml of the preparation in a flask with stopper . Add 25ml of 1N NaOH , 40ml of barium chloride solution to the flask. The contents are heated on a water bath for 15 minutes and cooled. Add 10ml of previously neutralised formaldehyde and excess of alkali is titrated with standard 1N HCl using thymol blue as indicator till grey colour is obtained.

Each ml of 1N NaOH ≡ 0.04805g of ammonium carbonate.

3) For free ammonia :

Add 50ml of 1N HCl to 20ml of preparation mixture is boiled, cooled and the excess of acid is titrated with standard 1N NaOH using methyl red as indicator.

The free ammonia is calculated by subtracting the number of ml equivalent to 1N NaOH in ammonium carbonate from number of ml of 1N HCl used.

Each ml of 1N HCl ≡ 0,01703 g of ammonia.

Storage :

Stored in a well filled, tightly closed container in a cool place.

Uses :

1. Used as respiratory stimulant.

Q.3. : Give the properties, preparations, uses and assay of Ammonium chloride

Ans : Ammonium chloride :

FORMULA NH_4Cl.

MOLECULAR WEIGHT . 53.5.

Contains not less than 99.5% of ammonium chloride calculated with reference to the dried substance over silica gel for 4 hours.

Properties :

Odourless, colourless or white crystalline or coarse powder. Has cooling effect and saline taste. Slightly Hygrascopic, soluble in water, sparingly soluble in alcohol and freely soluble in glycerin.

Freshly prepared solutions are neutral but quickly becomes acidic on standing due to the process of hydrolysis.

$$NH_4Cl + 2\,H_2O \longrightarrow NH_4OH + H_3O^+ + Cl^-$$

Preparations :

By interaction of ammonia gas with Hydrochloric acid solution is evaporated to dryness.

$$NH_3 + HCl \longrightarrow NH_4Cl.$$

Salt is purified by the process of crystallisation and sublimation. The salt is mixed with 5% calcium phosphate to prevent the sublimation of any volume of iron salts during sublimation process.

2) Also by treating ammonia gas liquors with lime and the liberated ammonia is passed into HCl.

Assay :

By volhards method- precipitation titration :

Excess of silver nitrate solution is added to the sample solution. Residual $AgNO_3$ is determined by titrating it with standard ammonium thiocyanate using ferric ammonium sulphate as indicator.

Now is based on formal titration principle.

The formaldehyde added to the sample solution endowed acidic properties to the compound and hence can be titrated

with standard alkali solution using phenolpthalin as indicator.

Storage :

Stored in a tightly closed container.

Uses :

Exhibits three important phsycological actions. All are dose dependent.

1) acts in maintaining acid-base equilibrium of body fluids.

2) Diuretic effect due to the utilization of ammonium cation in conversion into urea. On repeated use cause metabolic acidosis.

3) acts as mild expectorant and Diaphorotic- in small doses.

– X –

ANTIDOTES

INTRODUCTION :

Poisoning may be due to various reasons like contamination of food, water, contamination of heavy metals etc. In most of the cases these metals are leached from the utensils, cookwares which can lead to poisoning. Some times poisoning is also due to pesticides and insecticides or excessive dose of drugs.

Here the discussion is restricted to heavy metal and cyanide poisoning and the use of antidotes in poisoning.

Q.1 : What are antidotes ? Give this classification with examples.

Ans : Antidotes are those agents or drugs or substance used to reverse, stop or counteract the action of poisons.

Based on their mechanism of action, classified into

1. Physiological antidote - It produces the effect opposite to that of poison or to counteract the poison effect physiologically.

Ex: Mg. Sulphate in Barium or lead poisoning.

2. Chemical antidote : It combines with the poison chemically and thereby changes its chemical nature rendering the poison inactive.

Ex: Sodium Phosphate in iron poisoning.

3. Mechanical Antidote : It prevents the absorption of poison in the body or expels the poison out by emisis or eliminates the poison through urine.

Ex : Copper Sulphate, Kaolin.

Q. 2. : Give a brief account of the antidotes used in heavy metal poisoning.

Ans : The common heavy metals causes poisoning are salts of mercury, lead, Arsenic, Iron and Cadmium. Poisoning may be due to over dosage (excess intake) or incomplete metabolisms in body. The most widely accepted and adopted method to treat heavy metal poisoning is use of such heavy metal antagonists which will specifically combine and form chelate or complex with the heavy metal.

The treatment involves :

1) Administration of activated charcoal to absorb the poison or heavy metal.

2) Administration of compounds which produces emesis - eliminates any poison remained in the stomach.

3) In case of poison being absorbed, same effective organic antidotes are used in systemic heavy metal poisoning.

The inorganic compounds used as antidotes are :

1) **Activated charcoal -** in the ratio of 5:1 or 10:1 (antidote to poison) - in the form of tablets.

2) **Kaolin -** As an adsorbent in the treatment of food and alkoloidal poisoning.

3) **Copper Sulphate** - As an emetic, antidote in phosphorous poisoning.

4) **$MgSO_4$** - in the treatment of Barium and lead poisoning.

5) **Sodium phosphate** - as an antidote for iron poisoning.

6) **D- Pencillamine** - in Cu, Mg and lead poisoning by forming complex with Cu, Hg, Zn and Pb, it promotes elimination through urine.

7) **Deferoxamine** - form of injections in iron poisoning.

8) **Dimereaprol** - Injections - in arsenic, gold and mercury poisoning - form complex with metals and the complex is rapidly excreted.

9) **Calcium Disodium Edetale** - Infusions - effective in systemic poisoning and heavy metals.

10) **Succimer** - In the treatment of mercury, lead and Arsenic poisoning.

Q 3. Discuss the method of preparation, uses and assay of sodium nitrite used in Cyanide poisoning.

Ans : Cyanide poisoning occurs accidentally or especially when taken intentionally. The cyanide ion combines with the ferric ion of cytochrome oxide enzyme responsible for electron transfer and thus stops the cellular respiration and metabolic reaction. Poisoning with cyanide is usually fatal if untreated immediately.

Here Sod. nitrite reacts with ferrous ion and converts into ferric form and thus reduces the availability of ferric ions to cyanide ions. This inturn reduces the concentration of cyanide poisoning.

Sodium. Nitrite.

FORMULA $NaNO_2$

MOLECULAR WEIGHT 68.99

Contains not less than 97% and not more than 101%. $NaNO_2$ calculated with reference to the substance dried over silica gel.

Properties :

Has saline taste, available as white crystals or white granular powder. Soluble in water, sparingly soluble in alcohol when exposed to air, slowly oxidises into Sod. Nitrate. Easily decomposed with the acidification by dilute sulphuric acid.

Chemically acts as reducing agents and gets oxidised in acedic medium.

Preparation :

Suitable method of preparation is absorbing Nitrogen oxide gas (NO) obtained during catalytic oxidisation of ammonia

and oxygen in sod. carbonate solution. The solution. is concentrated. Product is crystallized out.

$$2Na_2CO_3 + 4NO + O_2 \longrightarrow 4NaNO_2 + 2CO_2$$

Assay :

Based on the oxidisation of nitrite to nitrate.

10 ml solution. of the sample is slowly added to 50ml of 0.1N potassium permanganate solution acidified with 5ml H_2SO_4. Nitrous acid which is formed, in contact with acid, immediately oxidised to nitric acid by $KMnO_4$ solution. Since Nitrous acid is volatile, the tip of the pipette is kept below the level of the solution while adding the solution of sodium Nitrite.

Add excess of known quantity of oxalic acid (25ml) and the mixture is heated to 80^oC and the excess of oxalic acid is back titrated with standard $KMnO_4$ solution.

$$NaNO_2 + H_2SO_4 \longrightarrow NaHSO_4 + HNO_2$$

$$HNO_2 + O \longrightarrow HNO_3$$

Each ml of 0.1N $KMnO_4 \equiv 0.00345$ g of $NaNO_2$.

Storage :

Stored in a well tightly closed container in a cool dry place.

Uses :

1) Antidote in cyanide poisoning

2) As food preservative

3) Prevents the rusting of surgical instruments.

– X –

ELECTROLYTES

In the body there are various body fluids present. The various body fluids include cytoplasm (Intracellular fluid), interstitial fluid (present between the cells), Plasma (an vascular fluid). Various organic and inorganic compounds are present in the body fluids and the concentration of each organic or inorganic compounds is balanced in such a way that the body cells and tissue always have the same environment. These organic or inorganic compounds are responsible in turn for the various regulatory mechanisms like ionic balance, PH, Osmotic balance etc. Generally (in the body), if the body does not maintain or correct the electrolysis balance, this is done by external administration of the same which is known as replacement therapy. Various electrolytes, acids, bases, carbohydrates, proteins and same blood products are used in replacement therapy as per the patient's need.

Here the electrolytes used in replacement therapy for the correction of various regulatory mechanisms as said above are of much importantance.

For the discussion, the body fluids are broadly classified as

(a) Cytoplasm - the fluid present inside the cell, an intracellular fluid

(b) Plasma -and interstitial fluid are extracellular fluids present outside the cell.

Examples for anionic electrolytes are bicarbonate (HCO_3),Chlorides (Cl^-), Phosphates (H_3PO_{4-}) ,Sulphates (SO_{4--}) and for cationic electrolytes are Sodium, Potassium, Magnesium, Calcium, etc,.

The concentration of some of the important electrolytes in the body fluids are given in the table (* values are ranged for adults).

Ions	Intracellular 1	Extracellular 2	Plasma
Cations			
1. Mg^{++}	58	1.2	1.5 - 3.0
2. K^{+}	140	4	4.5 - 5.5
3. Ca^{++}	0.0001	2.4	2.1 - 2.6
4. Na +	1	142	135 - 145
	Values in mEq / L		
Anions			
1. Sulphates	2	1	0.3 - 1.5
2. Chlorides	4	103	98 - 105 *
3.Bicarbonates	10	28	25 - 31*
4. Phosphates	75	4	1.2 - 3.0*

The concentration of electrolytes is expressed in terms of mEq/L. i.e., milli equivalent per litre and usually electrolytes are given in the form of salt solutions which is expressed in w/v. It is very easy to convert the w/v to mEq/L and viceversa. The equation for the purpose is

$$mEq/L = \frac{\text{mg of substance / L}}{\text{Equivalent Weight}}$$

Equivalent weight = Molecular weight / Equivalent weight

Ex : 1. Calculate the number of mEq of sodium chloride in one litre of 0.57% w/v of solution.

Data - 0.57% Nacl = 5.7g of Nacl in one litre.

$$\text{Formula. mEq/L} = \frac{\text{Molecular weight}}{\text{Equivalent weight}}$$

$$= \frac{5.7\text{gm or } 5700\text{mg}}{58.5 \text{ mg}} \text{ mg}$$

$$= 97.44 \text{ mEq NaCl/L.}$$

As the number of sodium ions is necessarily equal to the number of chloride ions thus concentration of each ion is equal to i.e., 97.44 mEq Na^{+}/L and 97.44 mEq Cl^{-}/L

In the same way, the weight of the substance required to prepare the solution in terms of mEq can be calculated by the equation,

$$\text{Mg/ lt} = \frac{\text{mEq}}{\text{L}} \text{(Eq.wt.)} \qquad \text{Eq. Wt.} = \frac{\text{mol.wt.}}{\text{valency}}$$

$$= \frac{\text{mEq}}{\text{L}} \left[\frac{\text{mol.wt.}}{\text{valency}}\right]$$

For example How many calcium chloride will be needed to prepare one lt. solution containing 12 mEq. Ca^{++} / lt

$$\text{mg/lt} = \frac{(12)\ (147)}{1} \times 2 = 882 \text{ mg}$$

Q .1. : Discuss the importance of Sodium, Magnesium and Potassium ions in the body.

Ans :

Sodium –

Human body contains about 1.8 g/kg of sodium ions and is normally supplied in the diet. Good sources of sodium are table salt, baking powder, meat, milk and same vegetables. The daily requirement is about 3–5g for an adult.

Major cation present in the extracellular fluid is sodium ions which is associated with chlorides, bicarbonates and maintains acid-base equilibrium. It also maintains Osmotic pressure of various body fluids and thereby protects the body from excess of fluid loss. It even plays an important role in preserving normal irritability of muscles and cell permeability.

Conditions where high sodium serum level is exercised includes severe dehydration, Hyper adrenalism, certain cases

of brain damage and excessive intake of sodium and its salts.

Conditions where low sodium serum level is exercised includes Addison's diseases diarrhoea, vomiting, excess fluid loss and excessive sodium excretion.

Magnesium :

Human body contains about 0.5 g/kg and 70% of it is present in the form of complex and calcium or phosphorus in bones- Remaining 30% present in body fluids and soft tissues. Good source includes various nuts, sea foods, whole grains and soya beans. Daily requirement is about 350 mg.

Major functions of magnesium are, a cofactor for phosphate transferring enzymes, constituent of teeth and bones, decreases the neuro muscular irritability very much essential for the normal and smooth functioning of neuromuscular systems and for protein synthesis.

Reasons for magnesium depletion :

Include malnutrition, dietary restriction, chronic alcoholism and gastro intestinal diseases and faulty absorption may result in muscular tremor, confusion vasodilation, hyper irritablilty etc,.

Potassium :

Human body contains about 2.6 g/kg body weight. About 1.5-4.5g is required daily. Good sources of potassium are food, milk, meat, whole grains and some vegetables.

It is the principal cation in intracellular fluid and also constitutes an important constituent of excellular fluids. It influences the cardiac muscle activity, influences acid base balance, Osmotic pressure and the water retention.

Elevated levels are resulted with renal failure, dehydration, shock, Addison's disease, which results in mental confusion, weakness of Respiratory muscles and flacid paralysis of extremities.

Depleted levels are seen in prolonged illness, malnutrition, diarrhoea, metabolic alkalosis, use of diuretics like acetozolamide and chlorothiazide which increases potassium excretion in urine, heart diseases, dehydration or acidosos or alkolisis with sodium and water.

Q .2. : Give the importance of chloride and bicarbonate ion in human body.

Ans :

Chloride :

The total amount of chloride present in the body is about 50 mEq/kg body weight. The daily requirement ranges 5-10g. Good source of chlorides is the common salt or table salt used in cooking. It is the major anion present in all body fluids.

It serves two important functions. It is responsible for maintaining the Osmotic balance between different body fluids and is also responsible for maintaining the charge balance between the body fluids. Chloride ions involve in the formation of Gastric HCl.

When Carbon-di-oxide enters from an actively metabolising tissue to RBC and gets converted into bicarbonate, meanwhile equivalent amount leaves the cell and thus charge neutrality is maintained.

Bicarbonates :

Second largest anion present in the extracellular body fluid. Along with Carbonic acid acts as one of the important buffer system in maintenance of acid-base balance. Excess of bicarbonate leads to metabolic alkalosis and depletion causes metabolic acidosis.

Q .3.: Enumerate sodium chloride formulations used in Electrolyte replacement therapy.

Ans :

1. Sodium chloride
2. Sodium chloride lotion

3. Sodium chloride solution
4. Sodium chloride injection I.V
5. Sodium chloride Tablets
6. Sodium Chloride Hypertonic solution
7. Sodium Chloride & Dextrose injection I.V.
8. Mannitol and Sodium Chloride injection.

Q .4.: Give the method of preparation, properties, Assay and uses of KCl.

Ans : Potassium Chloride:

FORMULA KCl

MOLECULAR WEIGHT - 74.55

Contains not less than 99% KCl calculated with reference to the dried substance.

Properties :

Colourless, Prismatic or cubical crystals or white granular powder. Posses saline taste and is odourless. Freely soluble in water and in qualitative analysis the chloride is precipitated by silver, Mercury and lead ions as insoluble chlorides.

Preparation :

Obtained from natural mineral Carnallite-Raw salt is grinded and treated with hot water and Potassium chloride crystrallises out from mother liquor.

In laboratory scale prepared by potassium carbonate or bicarbonate treated with Hydrochloric acid.

$$K_2CO_3 + 2HCl \longrightarrow 2KCl + H_2O + CO_2$$

$$KHCO_3 + HCl \longrightarrow KCl + H_2O + CO_2$$

Assay :

As per Indian Pharmacopoeia by Mohr's method.

Aqueous solution is directly titraed with standard silver nitrate solution using potassium chromate as indicator.

As per British Pharmacopoeia analyzed as sodium chloride but exception that,the nitrobenzene is replaced by dibutyl pthalate.

Uses :

1 Used for oral replacement of potassium in the form of solution.

2 Used in treatment of myasthenia gravis as an adjuent.

3 Used as the constituent of oral dehydration salt

4 Used as a constituent of Ringer's injection and solution.

5 Used as a constituent of Sodium Chloride, Potassium Chloride I v infusion, sodium and potassium chloride, glucose I.v. infusion

Q.5 : Give a brief account of electrolyte combination therapy.

Ans : Usually before or after surgery if the patient is not able to take the normal diet then the electrolyte combination therapy is recommended. As per the need of the patient variuos electrolytes are combined and given to replace the same. Various combinations of electrolytes are commercially available.

This combinations is divided into two categories.

1. Used for fluid maintenance. 2. For replacement therapy.

In this first case, the electrolytes are administrated intravenously and provides the normal requirement responsible for the maintenance of various regulatory mechanisms. All fluid maintenance of electrolytes infusion contains 5% glucose which helps to reduce metabolics like ketone bodies phosphate usually associated with Starvation. In the later case, due to excess fluid lose, diarrhoea vomiting, prolonged fever the depleted electrolytes are replaced.

Various commercially available electrolyte combination in the form of dry powders dissolved in specified amount of water and administrated in the form of oral electrolyte solution.

Some example include sodium lactate injection, compound sodium chloride compound sodium lactate injection, compound sodium tartrate I V infusion oral dehydration salts etc.

Q .6 .: How is acid base balance is maintained in the body?

Ans : The acid-base balance is regulated by intricate mechanisms like number of chemical reactions take place in the cell,activity of cell and the pH. pH of blood of a normal healthy person is constant which is about 7.35 If pH of blood is low it results in acidosis and if high it results in alkalosis.

The pH is regulated mainly by three mechanisms.

1. Buffering systems :

a) Carbonic acid /bicarbonate buffer mainly in plasma & kidney.

b) Mono hydrogen phosphate/Dihydrogen phosphate found in cells & kidney.

c) Protein buffer systems.

2 The other important regulation is through the regulation of respiratory center.i.e.,through the rate of breathing,removal of carbon-di-oxide from body fluid leads to changes in pH of blood.

3. By the elimination of some ions through urine by kidney.

Q.7. : Explain the terms metabolic acidosis and alkalosis ? How are they corrected ?

Ans : Metabolic acidosis is the condition where excess of acid will be present in the body, it may be due to a) failure to excrete metabolic acids by kidney b)formation of excess of metabolic acids c)Administration or absorption excess of metabolic or other acids.

This may be due to the result of diarrhoea dysentery,vomiting,diabetes mellitus etc.

Metabolic alkalosis is the condition where alkalinity in the body increases. This may be because of administration of

diuretics or excess administration of alkaline drugs, due to loss of chloride ions.

Following are the drugs used for the treatment.

1)Potassium acetate.
2)Potassium citrate.
3)Sodium acetate.
4)Sodium bicarbonate.
5)Sodium citrate.
6)Sodium phosphate.
7)Ammonium chloride etc.

Q.8 . : Give the method of preparation, properties and assay of Potassium acetate and Sodium citrate.

Ans :

Potassium acetate

FORMULA $C_2H_3O_2K$

MOLECULAR WEIGHT 98.14.

Contains 99-101% of C_2H_3O2K,calculated with reference to the dried substance.

Properties :

Odourless, colourless or white crystalline powder has slightly alkaline taste, when exposed to air,rapidly absorbs moisture. soluble in water and alcohol, insoluble in others.

When heated strongly leaves residue of potassium carbonate.

$$2CH_3COOK + 4O_2 \longrightarrow K_2CO_3 + 3H_2O + 3H_2O + 3CO_2$$

Preparation :

By neutralizing Acetic acid and Potassium carbonate or bicarbonate till the effervescence ceases.Evaporate the solution to dryness and allow to solidify.It is immediately powdered and packed/bottled.

$2CH_3COOH + K_2CO_3 \longrightarrow 2CH_3COOK + H_2O + CO_2$

Assayed :

Assayed by non – aqueous method.

Dissolve the sample in glacial acetic acid and titrate with standard perchloric acid using crystal violet as indicator.

Uses :

1) Used as urinary alkaliser.

2) Used as diuretic

3) Used as systemic alkaliser.

4) Used as antacid.

Sodium citrate :

FORMULA : $C_6H_5Na_3O_72H_2O$

MOLECULAR WEIGHT 294.10

contains not less than 99% and not more than 101% of $C_6H_5Na_3O_7$,calculated with reference to anhydrous substance.

Properties :

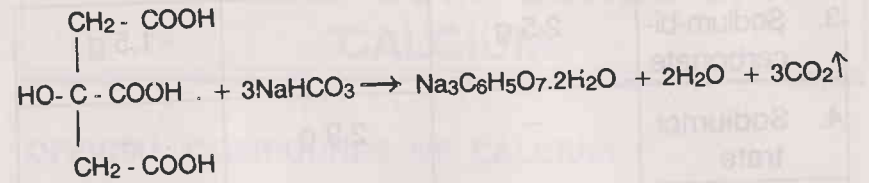
Colourless or white,crystalline or powder. Freely soluble in water insoluble in alcohol and ether.Has saline taste.

When heated to about 150°C becomes anhydrous.further heating chars and the residue of Sodium carbonate is left.

$2Na_3C_6H_5O_7\ 2H_2O + 9O_2 \longrightarrow 3Na_2CO_3 + 9CO_2 + 9H_2O$

Preparation :

By neutralizing citric acid solution and sodium carbonate/bicarbonate. After the cessation of effervescence the solution is evaporated for crystallization



$$HO\text{-}C(CH_2\text{-}COOH)(CH_2\text{-}COOH)\text{-}COOH + 3NaHCO_3 \longrightarrow Na_3C_6H_5O_7.2H_2O + 2H_2O + 3CO_2\uparrow$$

By non-aqueous method.

Dissolve the sample in glacial acetic acid and titrate with standard perchloric acid.Here end point is determined potentiometrically.

Uses :

1) Used as buffer.

2) Used as systemic alkaliser.

3) Used as an anti-coagulant and sequestering agent.

Q. 9. : Give the brief account of oval dehydration salt.

Ans : A number of formulations are available commercially which contains glucose, Sodium Chloride, Potassium Chloride either sodium bi-carbonate or sodium citrate. They are in the form of dry powders, mixed with specific quantity of water and used for oval dehydration therapy.In addition they may also contain flavouring agent and other agents for the free flow of powder.

Commonly used 3 formulations are given,for preparing 1 Lt solution.

INGRIDIENTS	FORMULA I	FORMULA II	FORMULA III
1. Sodium Chloride	3.5 g	3.5 g	1.0 g
2. Potassium Chloride	1.5 G	1.5 G	1.5 g

3. Sodium-bi-carbonate	2.5 g	–	1.5 g
4. Sodiumci trate	–	2.9 g	–
5. Anhydrous glucose.	20 g	20 g	36.4 g
or glucose	22 g	–	40 g

Formula I and II recommended by WHO and UNICEF for the control and treatment of diarrhoel diseases.

Note – When glucose is used,sodium bicarbonate is packed separately.

– X –

OFFICIAL COMPOUNDS OF CALCIUM

OFFICIAL COMPOUNDS OF CALCIUM :

INTRODUCTION :

Calcium is one of the very important and essential element required for various functions of the body. 90% of the total body calcium is found in bones in the form of calcium carbonate and calcium phosphate. Daily body requirement of calcium is about 450mg calcium is absorbed from the upper intestinal tract and is excreted through urine and feces. As the upper portion of the intestine is acidic, it favours the absorption of calcium and its salts since as in acidic medium they have the better solubility.Alkaline medium precipitates the calcium and there by its absorption is retarded. The meal containing higher fatty acid contents also reduces the absorption of calcium as it forms calcium salts of fatty acids which are insoluble.

Calcium and its derivatives/salts are essential for the maintenance of various important Body functions like Cardial function, Coagulation of blood, growth and development and also repair of tissues and Bones.etc.

When there is deficiency of Calcium the condition is known as "Hypocaleemia" may be due to various reasons and produces syndromes known as letany and related phenomenon, which is characterised by increased neuromuscular activity (excitability), convulsions etc.

Administration of excess of Calcium can cause **"Hypercalcemia"** the condition in which high concentration of Calcium is present in Blood It is Characterised by loss of weight, bradicardia, muscular pain, arrhythmia and kidney impairment etc. The condition may be associated with various clinic conditions like Hyperthyroidism, excess of milk and alkalinising agent (milk alkali syndromes), excess of Vitamin D administration, etc. A number of drugs are used in the

treatment of various hypercalcemic conditions, such as Indomethacin (used in hypercalcemia resulted from excess production of prostaglandons,) Calcitonin and phosphates, Prednisolone and other steroids etc.

Calcium compounds in general given in Calcium deficiency state or as dietory replacement These are useful in immediate treatment of low Calcium tetany and are best controlled by intravenous admn. If the tetany symptoms are milder and in case of latent tetany salts are orally administered.

Q.1. : Give the list of official compounds.of Calcium and their formulates.

Ans :

a. Calcium acetate (B.P)
b. Calcium Carbonate Synonym.Precipitated chalk.
c. Calcium Chloride.
d. Calcium Gluconate
e. Calcium gluconate injection
f. Calcium hydroxide solution Synonym lime water
h. Calcium Lactate
i. Calcium lactate Tablets
j. Calcium levulinate injection (I.P)
l. Calcium pentathonate
m. Dibasic Calcium phosphate (I.P)
n. Tribasic Calcium phosphate
o. Calcium sodium lactate (B.P)
p. Calcium sulphate dried (B.P) Synonym Plaster of paris: Exsiccated calcium sulphate
q. Sodium Calcium Edetate (B.P)
r. Sodium Calcium Edetate I.V. infusion (B.P)

s. Calcium amino salicylate (I.P) Synonym Calcium PAS (Para amino Salycilic acid)
t. Chlorinated lime synonym Bleaching powder remains no more official.

Q.2. : Give the method of preparation and uses of :
(a) Calcium acetate. (b) Calcium carbonate.
(c) Dibasic Calcium phosphate (d) Calcium Sulphate.

Ans : (a) Calcium acetate :

FORMULA $C_4H_6CaO_4$

MOLECULAR WT. 158.2

Contains not less than 98.0% and not more than 100.5% of $C_4H_6CaO_4$ Calculated with reference to dried substance.

Properties :

Almost colourless, white powder Hygroscopic in nature soluble in water Slightly soluble in alcohol Aqueous solution are slightly alkaline in nature.

Preparation :

Prepared by neutralizing acetic acid with suitable Calcium salts like Calcium hydroxide or Calcium carbonate

$$CH_3COOH + CaCO_3 \longrightarrow (CH_3COO)_2Ca + CO_2 \uparrow + H_2O$$

Storage :

Stored as it is hygroscopic should be kept in well closed container in a cool dry place.

Uses: (i) one of the ingredient of solutions used for haemodialysis and peritoneal dialysis.

(B) Calcium Carbonate :

FORMULA $CaCO_3$

MOLECULAR WT. 100.09.

Contains not less than 98% and not more than 100.5% of $CaCO_3$ Calculated with respect to dried salts. Most abundantly and widely used Calcium Salt.

Occurs as Chalk, lime stone, marble, aragonite and Calcites and Chief constituents of Pearls, shells and corals.

Properties :

Fine tasteless, odourless, white micro crystalline powder Stable in air, almost insoluble in water and alcohol The solubility in water can be increased by the presence of CO_2 an also by ammonium salts.

$CaCO_3 + H_2CO_3 \longrightarrow Ca(HCO_3)_2$

$CaCO_3 + 2NH_4 \longrightarrow Ca^{++} + 2NH_3 + H_2O + CO_2 \uparrow$

Calcium Carbonate neutralizes acids

$CaCO_3 + 2HCl \longrightarrow CaCl_2 + CO_2 \uparrow + H_2O$

Preparation :

Commercially prepared by the interaction of Sodium Carbonate and Calcium Chloride. The precipitate resulting from the interaction is filtered and washed.

$Na_2Ca_3 + CO_3Cl_2 \longrightarrow CaCO_3 \downarrow + 2NaCl$

Uses :

(1) used as non systemic antacid.

(2) used in the Calcium deficiency as a supplement.

(C) Dibasic Calcium Phosphate :

FORMULA. $CaHPO_4$

MOLECULAR Weight. 136.06

FORMULA. $CaHPO_4.2H_2O$

MOLECULAR WT. 172.09

Contains not less than 30.9% and not more than 31.7% of Calcium calculated with reference to the ignited substance

Properties:

White, Odourless, tasteless powder, practically insoluble in water and alcohol. Easily soluble in dilute HCl and HNO_3

Preparation :

It is prepared from animal bones. Usually bones are calcined until white, produced and digested with Sulphuric acid. Calcium Sulphate is precipitated and phosphoric acid is formed Calcium Sulphate is filtered off calculated and of Calcium hydroxide is added to the filtrate to form dibasic salt

$Ca_3(PO_4)_2 + 3H_2SO_4 \longrightarrow 2H_3PO_4 + 3CaSO_4$

Uses :

(1) Used as the salt supplies both calciums and phosphorus administered orally to children for growth and development.

(2) Used for pregnant women and lactating mothers.

(3) Used In tablets used as excepients.

(D) Calcium sulphate dried :

FORMULA- $CaSO_4$ 1/2 H_2O.

MOLECULAR. WT 145.1

Calcium sulphate with 2 molecular of water, actually found as **"Gypsum" and "Selinite"** The granular masses called **"Alabastar".**

Properties :

Odourless, white powder, Hygroscopic in nature Sparingly soluble in water Soluble in dilute mineral acids.

Preparation :

By heating Gypsum at controlled temperature of about 150°c. or as heated till 3 quarters of the water for crystallization is lost.

Calcium Sulphate di hydrate is prepared by adding soluble sulfates like sodium sulphate to Calcium Chloride solutions. The precipitate is filtered washed thoroughly and dried.

$Na_2SO_4 + CaCl_2 + 2H_2O \longrightarrow CaSO_4\ 2H_2O + 2NaCl$

Uses:

(1) Used in dentistry.

(a) Used in surgery for making casts.
(b) Used for taking impressions.

(2) Used To fix the bone fractures as Plaster of paris

(3) Also used as plaster of Paris bandages

Storage : Stored in a tightly closed container, protect from moisture and heal because of its hygroscopic nature.

Q.3.: Outline the principle and essay procedure for :

(a) Calcium Hydroxide.
(b) calcium amino salicylate
(c) Sodium Calcium lactate.
(d) Dibasic Calcium phosphate

Ans :

(A) Calcium Hydroxide

Assay:

Principle : Acid base titration.

Procedure :

To about 1.5 gm of substance moistened with 5ml previously neutralized alcohol and added about 250ml of previously neutralized sucrose solution shaken vigorously at 5 mts regular intervals for 4 hrs The volume is made 500ml with sucrose solution and filtered.

Sucrose solution helps to solubilise Calcium hydroxide 250ml of the filtrate is titrated 1N Hydrochloric acid using Phenolpthaline as indicator.

Each ml of 1N HCl ≡ 0.03705gms $Ca(OH)_2$

(B) Calcium amino Salicilate –

Assay :

Principle : Nitrate titration.

The assay was carried out by diazatisation method using sodium nitrate as titrant and starch iodide paper as an external indicator. At the end point slight excess of nitrous acid turns this starch iodide paper blue.

Now, this method is modified according to new pharmacopoeial edition. The end point is detected potentiometrically.

Procedure-

Weigh about 0.5 of sample dissolve in 75ml water + 10ml Hydrochloric acid + 1g Potassium bromide. Cool at 15^{o}c. Carryout the titration as described under "Nitrite titration" method.

Each ml of 0.1M Sodium nitrite ≡0.01722g of
$C_{14}\ H_{12}\ Ca\ H_{12}\ Ca\ N_2\ O_6$
(Calcium.amino salicilate).

(C) Sodium Calcium lactate :

Assay :

Here it is assayed for its calcium and sodium content.

Calcium is directly titrated by complexametric titration method.

For the determination of sodium, first the sample is carbonized. The residue contains both calcium and sodium in the form of oxide which is taken in known volume of standard acid and excess of acid is back titrated using standard Sodium hydroxide solution using methyl orange as indicator.

(A) Dibasic calcium Phosphate :

Method-Complexometric titration

Accurately weighted specified quantity of the substance is dissolved in a mixture of Hydrochloric acid and water small quantity of triethanolamine is added and titrated 0.05M di sodium editate using hydroxynapthal blue as indicator nearing end point.

Then the PH is adjusted with Sodium hydroxide till the colour of the indicator changes from red to blue.

Titration is continued till colour changes to violet then again blue which persists for 60 seconds.

Each ml of 0.05 M disodium ediatate ≡ 0.002004g of calcium.

Q.4. : Discuss briefly about calcium gluconate:

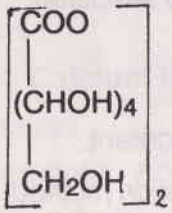
Ans :

Calcium gluconate-

FORMULA – $C_{12}H_{22}O_{14}CaH_2O$

MOLECULAR.WT-448.4

Structural formula :



Contains not less than 98% and not more than 102% of $C_{12}H_{22}O_{14}CaH_2O$ **Properties :**

White crystalline or granular powder-odourless, tasteless,stable in air. Sparingly soluble in water, freely soluble in boiling water and insoluble in alcohol.

Gluconic acid is formed which is again converted to D-glucolactone when the aqueous solution is treated with HCl.

Preparation : can be prepared by two ways.

(a) By the oxidation of glucose to gluconic acid in presence of calcium carbonate. The oxidation of glucose is effected either by Bromide or by electrolytic oxidation in presence of sodium bromide.

(b) By first preparing gluconic acid and then adding calcium carbonate to form the salt. Here the gluconic acid usually obtained by the action of various moulds/bacteria on glucose.

Assay : By direct complexometric method.

The salt is dissolved by boiling in sufficient water and cooled (as it has low solubility in water). The PH is adjusted using Sodium hydroxide solution and titrated with standard disodium editate solution using calcon carboxylic acid mixture as indicator (as per B.P).

According to I.P-it is assayed by complexometric titration involving replacement with magnesium, using 5ml standard Magnesium sulphate solution the PH is adjusted with Ammonia-Ammonium Chloride buffer. The volume of disodium edetate equivalent to Magnesium sulphate solution is subtracted from total disodium edetate used and then results are calculated.

Each ml of remainder of 0.05M disodium edetate ≡ 0.02242g of $C_{12}H_{22}CaO_{14}.H_2O$

The other official formulations of calcium gluconate includes.

(a) Calcium gluconate injection.

(b) Calcium gluconate tablets also.

Uses :

(1) Used as source of calcium in Calcium deficiency.

(2) Used as Drug of choice in severe hypocalcemic tetany.

(3) Also used in supplementing diet of convalscent and expectant mothers (tablets form is used)

Note :

Injections used Intravenously Intra muscular route should not be used particularly in children as it causes abscess at the site of injection.

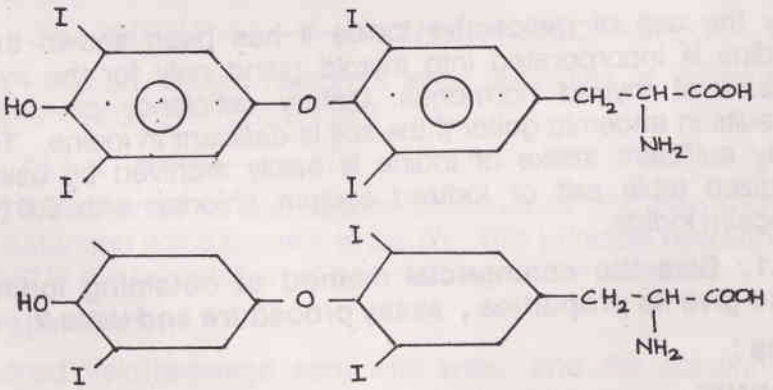
– X –

OFFICIAL COMPOUNDS OF IODINE

INTRODUCTION :

Iodine used as Iodide is one of the essential trace element. Iodine and its preparations are used for topical applications as discussed under topical agents. Now we will discuss about its systemic use and biochemical role.

Iodine play an important role in the synthesis of the two important Thyroid gland hormones secreted by thyroid off and known as thyroxine and Triiodo thyroxine which are essential for the normal growth and development and plays an important role in energy metabolism.



TRI -- IODO THYROXINE

It is evident that the tri-iodothyroxine is the circulating form whereas the thyroxine is the storage form of the hormone.

The deficiency of these hormones causes Hypo thyroidism in which all the metabolic processes are slowed down and enlargement of the thyroid gland (known as goiter), characterized by swelling of neck. Cretinism (mental retardation and dwarfinisum) is clinical condition of deficiency of thyroid hormone since birth.

Excessive secretion of the hormone results in hyper-thyroidism and the severe form of this is manifested by enlargement of eyeballs. Termed: "Exopthalmas" to treat both these condition thyroid hormones of suitable concentration and anti-thyroid drugs like carbimazole and methimazole are used.

Usual requirement of iodine in an average man is about 140 mg and in female about 100 mg which is daily obtained from diet. Since iodine is insoluble, the salts of iodine like sodium iodide are preferred for internal administration. The iodide form is normally utilized for the synthesis of thyroid hormone.

The iodine administered in the form of iodide is converted into Mono.-iodo and di-iodo thyroxine. There are then converted in tri-iodo and tetra-iodo thyroxine by the coupling reaction.

By the use of radioactive iodide it has been shown that iodine is incorporated into thyroid gland only for the synthesis of thyroid hormones. Dietary deficiency of iodine results in endemic goiter if the soil is deficient in iodine. Today sufficient intake of iodine is easily archived by using iodized table salt or iodized sodium chloride with 0.01% sodium iodide.

Q.1.: Give the commercial method of obtaining iodine and give its properties , assay procedure and uses ?

Ans :

IODINE –

MOLECULAR FORMULA : I_2

MOLECULAR.WT – 253.8

It contains 99.5-100.5% of iodine.

Properties :

Occurs as heavy, bluish black, rhombic prism or plates with metallic luster. Has a peculiar odour & volatalises at ordibnary temperature. It melts at high temperature. It is in-

soluble in water but soluble in alcohol freely soluble in chloroform and ether.

The clinical properties.

(a) reacts directly with same non-metals and with many metals giving their corresponding Iodides.

(1) $Fe + I_2 \longrightarrow FeI_2$

(2) $2P + 3I_2 \longrightarrow 2PI_2$

(b) Reducing agents get oxidized when the iodine reacts with reducing agents.

$H_2S + I_2 \longrightarrow 2HI + S$

$2Na_2S_2O_3 + I_2 \longrightarrow 2Na_2 + NaIO_3 + 3H_2O$

(c) Iodine with alkali forms iodide and iodate when especially heated.

$3I_2 + 6NaOH \longrightarrow 5NaI + NaICO_3 + 3H_2O$

(d) Potasium Iodide dissolves large quantities of iodine by the formation of I3 (iodate ion)

$KI + I_2 \longrightarrow KI_3$

(e) Iodine adds to unsaturated compounds and also to the unsaturated acids present in the oil. This principle reaction is used in the preparation of non-staining Iodine ointment.

Preparation :

Extract kelp(seaweed ash) with water and the solution is concentrated, the sulphate or chloride of sodium and potassium are crystallised out, leaving freely soluble sodium and potassium iodides in the mother liquor. Sulphuric acid is added to mother liquor and sulphate which is liberated from small amount of thiosulphate and sulfide is allowed to settle. Mother liquors decanted and to the Manganese-di-oxide is then added to and the iodine distilled out.

$2NaI + 3H_2SO_4 + MnO_2 \longrightarrow MnSO_4 + 2NaHSO_4 + I_2 + 2H_2O$

By heating oxide iodine with potassium iodide impurities like Iodo chloride IBr and ICN can be removed.

$$ICl + KI \longrightarrow KCl + I_2$$

Assay :

Oxidation-reduction titration

About 0.5g of substance dissolved in a solution of potassium iodide in 5ml of H_2O in an iodine flask diluted with 50ml water, acidified with 1ml acetic acid and titrated with 0.1N sodium thiosulphate solution using starch solution as indicator

Each ml of 0.1N sodium thiosulphate ≡ 0.01269g of Iodine

Storage :

Stored in amber coloured bottles with tight glass stopper and kept in cool place.

Uses :

(1) Used in the form of its aqueous and alcoholic solutions as germicides and fungicides.

(2) Used in the treatment of thyrotoxicosis to reduce the metabolic rate.

(3) Elemental iodine is effective in purification of drinking water

(4) Both bactericide and amoebicidal.

(5) Iodine precipitates alkaloids and therefore tincture of iodine used as a chemical antidote in alkoloidal poisoning.

(6) In TLC (thin layer chromatography) elemental iodine is used as locating agent.

(7) Also finds application in oxidation reduction titrations.

Q.2.: Give the method of preparation, properties uses and assay procedures for :
(1) Sodium.iodide or Potassium Iodide.

Ans : Sodium iodide :

FORMULA – NaI

MOLECULAR Weight – 149.9

Contains not less than 90% and not more than 100.5% NaI calculated with reference to the dried substance.

Properties :

Colourless or white crystalline powder. It is odourless, Hygroscopic in nature and stable in dry air and may decompose on storage and develops brown colour oxidation or presence of air causes liberation of free iodine-soluble in water, alcohol Aqueous solution gives yellow precipitate with silver nitrate and oxidizing agents liberate iodine in acidified solution.

$$NaI + AgNO_3 \longrightarrow AgI + NaNO_3$$

$$2NaI + H_2SO_4 + H_2 \longrightarrow I_2 + 2H_2O + Na_2SO_4.$$

Assay :

Involves oxidation the direct titration with potassium Iodate.

Principle :

When sodium iodide is treated with potassium iodate- solution in acidified media, free Iodine is liberated. Under high concentration of acid (HCl) liberated iodine is converted into iodine monochloride. The end point of this titration is indicated by disappearance of iodine colour form chloroforrn layer.

Procedure :

About 1.3g substance dissolved in 100ml water. Put 20ml of this solution to an iodine flask, add 40ml concentrated Hydrochloric acid and the contents are titrated with 0.05M potassium iodate until the colour changes to yellow. 5ml of chloroform is added and titration is continued with shaking against Potassium iodate till chloroform layer is colourless.

Each ml of 0.05 M KIO3 ≡ 0.01499 g of NaI.

Storage :

Store in a well closed containers/preferably bottles in a dry cool place. Due to their deliquency in moist air and oxidised giving yellow/brown colour due to liberation of iodine.

Potassium Iodide :

FORMULA - KI

MOLECULAR WEIGHT - 166.00

Contains not more than 99% KI calculated with reference to dried substance.

Properties :

White or colourless crystalline powder, odourless, taste is saline or slightly bitter. Salt in deliquesent in moist air. Soluble in water, alcohol and glycerine.

When added into water, dissolves and the solution becomes cool. Iodine gets dissolved in aqueous solution of potssium iodide by forming poly iodide complex (KI_3).

Preparation :

By two methods :

(i) Prepared by the action of iodine on moist Iron filings to form ferro ferric iodide (FeI_3 or FeI_2, $2FeI_3$ .....) which is then decomposed with potassium carbonate.

$Fe + I_2 \longrightarrow FeI$; $3Fe; I_2$.

$3FeI_2 + I_2 \longrightarrow FeI_2.2FeI_3$.

$FeI_2.2FeI_3 + 4K_2CO_3 \longrightarrow 8KI + FeO.Fe_2O_3 + 4\,CO_2$

Ferro ferric oxide is filtered off and is filtrated. It is concentrated to obtain KI. The salt, KI is purified by crystallization.

(ii) Slight excess of iodine is added to the solution of potassium hydroxide when potassium iodide and iodate are formed. So formed potassium iodate is reduced to potassium iodide with carbon.

$6\,KOH + 3\,I_2 \longrightarrow 5\,KI + K\,IO_3 + 3\,H_2O$

$KIO_3 + 3C \longrightarrow KI + 3\,CO\uparrow$

Assay :

Principle is similar to that of sodium iodide.

Procedure - dissolve about 0.5 g of substance in 10 ml water, 35 ml of con. Hydrochloric acid, 5 ml Chloroform is added and the contents are titrated with 0.05 M potassium iodate as described under sodium iodide.

Each ml of 0.5 M $KIO_3 \equiv 0.0166$ g of KI

$2KIO_3 + KI + 6\,HCl - 3\,KCl + ICl + 2H_2O$

Storage :

As it is deliquesent in moist air and oxidised giving brown/yellow colour because of the liberation of iodine is stored in a well closed containers and kept in cool dry place.

Q .3. : Outline the importance of Radioactive sodium iodide.

Ans : There are several radioactive isotopes of iodine available Out of which 131_I is abundantly used.

Radio active sod iodide solution is an aqueous solution containing ^{131}I in the form of sodium iodide and it contains a reducing agent like sodium thio sulphate and may be suitably buffered. The content of ^{131}I activity is not less than 90 and not more than 110 of the stated amount on the label at that date and hour stated on the label.

Properties :

Clear, colourless solution ^{131}I has an half life of 8.04 days & emits β and g radiations. The solution has a PH between 7 to 10.

Assay :

Activity is determined by comparison with a standard ^{131}I solution using any suitable counting intsrument besides, this

is also tested for Radio chemical purity and radio nuclide purity.

Uses :

1) Widely used for the purpose of diagnosis in disorders of thyroid and in the treatment of hyper thyroidism. In diagnostic studies, radio active iodine helps in the measurement of thyroidal accumulation of tracer dose

2) It helps in the diagnosis of hyper thyroidism and goiter and also the response to thyroid to thyrotropic hormone an also be evaluated.

Therapeutic Uses :

1) Considered as the choice of treatment in hyperthyroidisum.

2) Used in the course of grave's disease.

3) In metastatic thyroid cancer,used to prolong the life particularly of a young patient as the accumulation of iodine is very little.

I–123 has the half life of only 13 hrs, emits x – rays because of brief exposure to radiation, it is used for thyroid scans.

Q.4 . : Write short notes on,

a) Uses of sodium or potassium iodide.

b) Incompatibilities with respect to iodine is its preparations.

Ans :

a) Uses of sodium or potassium iodide :

1) Sodium or potassium iodide the oldest remedy for the disorders of thyroid gland.

2) Iodide acts as fibrolytic agent in syphilis leprosy.

3) Due to its fibrolytic action, the use is contraindicated in TB. However claimed that iodides improves the accessibility of anti-tubercular agents to the caustic organic.

4) Potassium iodide present in many cough mixtures as expectorant.

5) As potassium iodide liquify tenaciuos secretins, they find use in asthma and chronic bronchitis.

Note - If the iodides are used in excess toxic symptons like irritation of skins and mucous membrane occurs known as 'Iodism' which is characterized by Coryza, Headache rashes, laryngitis. It may also causes g.I. effects like Nausea and Vomiting. If this is observed, the iodide treatment is discontinued and Sodium chloride is administered for rapid removal of iodide.

(b) In computabilities with respect to iodine and its preparations.

Iodine is an oxidizing agent. It oxidizes hypo phosphates, sulfites, some metals and reducing agents and itself gets reduced into Iodide form. Reaction with turpentine is violent. Iodine reacts with ammonia or ammoniated mercury to form explosive iodide of nitrogen. iodine reacts with alkali hydroxides and carbonates to form iodides or iodate. Iodine treated with aqueous solution of alkaloidal salts, alkaloids gets precipitated.

Both potassium and sodium iodides get decomposed in the presence of acid. with the liberation of iodine. Sugar slows down this reaction. oxidizing agent also liberate iodide with the simultaneous reduction of the agent. The iodides also precipitate many alkaloids.

Sodium and potassium iodides are deliquescent in moist air and are oxidized giving yellowish / brown colour due to the liberation of Iodine.

– X –

OFFICIAL COMPOUNDS OF IRON

IRON COMPOUNDS :

The iron is used in the form its compounds as Ferric salts Fe^{+++}, Ferrous salts Fe^{++} and complexed iron compounds such as Ferric ammonium citrate.

Iron is one of the essential constituent of body which plays an important role in carrying out various body functions. Iron usually associated with specific proteins like Haemoproteins and transport proteins. Haemoproteins are responsible for carrying Oxygen in the process of respiration. In cytochrome 'C' - a protein – iron is (present) complexed in Porparin ring system and function as electron carrier as Fe^{+++} or Fe^{++}. It can take up or loose electron in the process of electron transfer. Haemoglobin and myoglobin are the other important haemoproteins which stores and or carrys/transports oxygen. In Haemoglobin, iron is present in ferrous form and it complexes with molecular oxygen.

The other category of proteins Ferritin and Hemosidirin are the important ironstore proteins found in Liver, spleen and bone morrow.

The amount of Iron present in the body is controlled by regulating the absorption and not by excretion. Because body recycles the iron obtained from break down by Red Blood Corpuscles and thus daily requirement iron is very low.

The requirement of iron increases during pregnancy, growth and lactation. The iron loss is more in case of female as large amount of iron is lost during haemoorhage and in menstrual flow. Iron loss is still more during pregnancy as it is transported to placenta and therefore generally iron preparations are given during pregnancy.

Food is the common source of iron for most of us. A large number of iron preparations are available to treat the conditions (due to the deficiency of Iron) like Anemia. The oral

preparations sometimes cause constipation, G.I. irritation, leading to vomiting and diarrhoea. These adverse reactions can be controlled by controlling the dose and the time of admission.

Over doses may cause serious problems leading to death particularly for young patients.

Poisoning with iron usually treated with gastric leavage followed by administering Sodium-bi-carbonate and sodium dihydrogen phosphate which converts the iron into an insoluble salt.

Deferaxamine can also be used in the treatment of iron poisoning, if the patient does not have the evidence of kidney damage.

When administered parentally it causes chelation which passes through urine. It is used only when unbound Iron is found to be present in serum.

Q .1.: Give preparation, properties and uses of important Iron compounds.

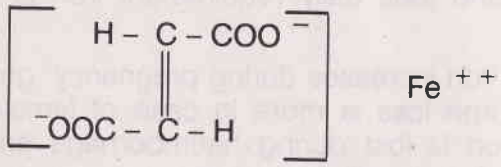
Ans :

Ferrous fumarate -

Molecular weight - 169.90

Molecular formula - $C_4H_2FeO_4$

Structural formula -



Contains not less than 93% of $C_4H_2FeO_4$-calculated with reference to the dried substance.

Properties :

Reddish orange/reddish brown powder. When crushed it may produce yellow streak. It has an astringent taste and light odour. It is slightly soluble in water and even less soluble in alcohol.

Ferric iron content test :

Dissolve about 3g of compound in 200ml H_2O and 20ml Hydrochloric acid by heating. To cooled solution add 3g of potassium iodide and allowed to stand for 15 minutes in dark and then the liberated iodine is titrated with 0.1N sodium thio sulphate using starch as indicator.

Again, a blank filteration is carried out. The difference gives the amount of iodine liberated by ferric iron.

Each ml of 0.1N sodium thio sulphate ≡ 0.005585g of ferric iron.

Preparation :

Prepared by double decomposition method. Hot aqueous solution of ferrous sulphate added to a solution of sodium fumarate with constant stirring. Sparingly soluble ferrous fumarate separated which is filtered and dried.

Assay :

Principle- an oxidation – reduction titration –

About 0.3g sample dissolved in 15 ml dilute. Sulphuric acid by gently warming, cooled. Add 50 ml H_2O and immediately titrated with 0.1M ceric ammonium sulphate using ferroin sulphate solution as indicator.

Reaction – $Fe^{2+} + Ce^{4+} \longrightarrow Fe_{3+} + Ce^{3+}$

Each ml of 0.1 M Ceric ammonium sulphate ≡ 0.01699g of ferrous fumarate

Storage :

Store in a well closed container,protected from light.

Uses :

1) Used as haematinic.

2) When other preparations of iron is not tolerated,the salt gives better result.

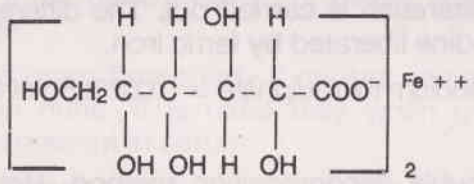
This is administrated in the form of tablets.

Ferrous gluconate-

MOLECULAR FORMULA-$C_{12}H_{22}O_{14}Fe.2H_2O$

MOLECULAR WEIGHT 482.7

Structural formula :



Contains not less than 95% of $C_{12}H_{22}O_{14}Fe$ calculated with reference to dried substance.

Properties :

Pale greenish yellow or yellowish grey fine powder, has odour of burnt sugar. Soluble in water,more soluble in boiling water and insoluble in alcohol. The aqueous solution is acidic in nature.

Preparation :

1)When glucose is fermented it gives rise to gluconic acid.

$$\underset{\text{(glucose)}}{C_6H_{12}O_6} \xrightarrow[\text{Fermentation}]{O_2} \underset{\text{(gluconic acid)}}{C_6H_{12}O_7}$$

2)When gluconic acid reacts with ferrous carbonate in the ferrous gluconate crystallizes out usually as dihydrate.

$$2C_6H_{12}O_7 + FeCO_3 + H_2O \longrightarrow Fe(C_6H_{11}O_7)2H_2O + CO_2\uparrow$$

Assay : Redox titration method.

About 1.5g of substane dissolved in a mixture of 75 ml water and 15ml of 2N sulphuric acid. About 0.75g of zinc powder is added flask is stoppered and set aside fill the solution is decolourised .It is filtered through sincered glass and wash the precipitate with 20ml water and the combined filtrate is titrated with 0.1m Ceric ammonium sulphate using ferroin sulphate as indicator. Colour change is from orange to green. A blank titration is carried out to make the necessary correction.

Equivalent of 0.1M Cerric ammonium sulphate ≡ 0.04461g of $C_{12}H_{22}FeO_4$

$$Fe^{3+} + Fe^{2+} \longrightarrow Fe^{3+} + Ce^{2+}$$

Uses :

Used as Haematinic-shows less side effects and is absorbed well.

C.Ferrous sulphate :

MOLECULAR FORMULA- $FeSO_4.7H_2O$

MOLECULAR WEIGHT 278

Contains not less than 98% and not more than 105% $FeSO_4$-$7H_2O$.

Properties:

Pale bluish green crystalline powder or transparent green crystals,odourless and has metallic astringent taste. On exposure to moist air undergoes oxidation rapidly and this is coated with brownish yellow basic ferrous sulphate freely soluble in water and insoluble in alcohol.

Ferrous sulphate when heated deccmposes to ferric oxide sulphur dioxide and sulphuric acid.

$$2(FeSO_4.7H_2O) \longrightarrow Fe_2O_3 + SO_2\uparrow + H_2SO_4 + 13H_2O$$

Preparation :

Prepared by dissolving excess of iron in dilute Sulphuric acid. The liquid is filtered, concentrated and cooled after effervescence is stopped the crystals formed are separated by filteration. In any operation undue exposure to air is avoided.

$Fe + H_2SO_4 + 7H_2O \longrightarrow FeSO_4.7H_2O + H_2$

Assay :

Red-Ox principle-It is titrated with ceric ammonium sulphate.

About 1g of substance is dissolved in the mixture of 30ml water and 20ml dilute.sulphuric acid and the contents titrated with 0.1M CAS.(Ceric Ammonium Sulphate) using ferroin sulphate solution as indicator.

Each ml kof 0.1M ceric ammonium sulphate ≡ 0.0278g of $FeSO_4.7H_2O$.

Storage :

Preserved in tightly closed contains, protected from moisture and atmospheric oxygen.

Uses :

A popular hematinic-used in the deficiency of Iron in anaemia.

Q.2. : Give the method of preparation, properties, assay and the uses of ferric ammonium citrate.

Ans :

Ferric ammonium citrate-

A complex salt containing not less than 20.5% and not more than 22.5% Iron. known as "Scale preparation of Iron"-no more official in I.P and B.P.

Properties :

Bright brownish red scaly with slight astringent taste. Freely soluble in water but insoluble in alcohol. Preparation is deliquesent in air and is affected by light.

Preparation :

Prepared by using ferrous sulphate,sodium hydroxide, ammonia and citric acid.

I Step –

Ferric hydroxide is prepared freshly by adding ferric salt solution to sodium hydroxide by constant stirring (Not be prepared by adding alkali to ferric salt as it may result in precipitate containing basic ferric salt, which substantially prevent the formation of transparent scales)

$Fe_2(SO_4)_3 + 6NaOH \longrightarrow 2Fe(OH)_3 + 3Na_2SO_4.$

II Step –

Precipitate of ferric hydroxide is collected,washed and added as such (without drying) with stirring into the solution of citric acid. Most of it gets dissolved. Slight excess of ammonia is then added and any undissolved ferric hydroxide is filtered out the clean reddish brown filtrate is evaporated to a syrup-little ammonia is added in this process to maintain any loss during evaporation. The syrup is then painted on glass plates and dried at 40^oC. The dried scales are scrapped off and packed.

The characteristic brownish-red colour is due to basic complexes of variable composition which maybe represented by.

$FeC_6H_5O_7 \times Fe(OH)_3$ where "x" is more than 1 and lesser than 2.

Assay :

Based on oxidation-reduction titration.

About 0.5g and dissolved in 15ml water- acidified with sulphuric acid and warmed until the colour becomes yellow. To the cooled solution 0.1N Potassium permanganate is added drop by drop (to oxidize any small quantity of ferric to ferrous when the pink colour of potassium permanganate persists for few seconds, an excess of Hydrochloric acid (15ml) and Potassium iodide (2g) are added and kept aside for 3mts. The liberated iodine is titrated with 0.1N Sodium thiosulphate solution using starch solution as indicator.

$2FeCl_3 + 2HI \longrightarrow 2FeCl_2 + 2HCl + I_2$

$2Na_2S_2O_3 + I_2 \longrightarrow Na_2S_4O_6 + 2NaI.$

Each ml of 0.1N Sodium thiosulphate ≡ 0.005585g of Fe.

Storage :

In a well closed container, protected from light and moisture.

Uses :

Used as a source of Iron in Iron deficiency. Has less constipating action and less irritant action than other Iron-salts.

Q.3. : Mention the method and give the procedure for the assay of
(a) Ferrous sucinate (b) Ferrous sulphate tablets.

Ans :

(a) Ferrous succinate-

Principle :

Involved is that of redox titration.

Procedure :

Similar to that of ferrous fumarate.

(b) Ferrous sulphate tablets :

Principle :

Redox titration.

Procedure-

Weigh and powder 20 tablets.

Accurately weight about 0.5g of powder and carryout the assay as described under ferrous sulphate.

Q.4. : Give brief account of the following-

(a) Iron and dextron injection.

(b) Incompatibilities of Iron compounds.

Ans : (a) Iron and dextron injection (I.P,B.P) :

It is a sterile, colloidal solution containing a complex of ferric hydroxide with dextrons of low molecular weight (B.P 1980 specifis the dextrons of the molecular weight between 5000-7000) in water for injection.

Contains not less than 4.75% and not more than 5.25% W/V of Iron sterilized by heating in an autoclave.

Administered by deep I.M injection and usual dose is 1-2ml daily.

(b) Incompatibilities and storage of Iron salts / preparation :

Most of the Iron preparation are oxidized by air and therefore stored in air tight containers in a cool and dark place. Ferric ammonium citrate is incompatible with mineral acids, alkali, alkali carbonates and tannates.

Ferrous gluconate solution incompatible with ascorbic acid, glycin and pyridoxine. With vitamin-C and glycin the preparation develop a dark colour where as in presence of pyridoxine solution becomes greenish. In alkaline and neutral solutions they undergo rapid oxidation.

Ferrous sulphate incompatible with alkali and gets oxidized in air easily in presence of arsenate and mercuric salts. Also incompatible with phosphates, tanntes, and benzoate, sugar, glycine and alkali citrates prevents the precipitation of ferric salts.

Q.5. : Mention all the official compounds of ferrous and ferric ions.

Ans : The official compounds of ferrous and ferric ions are-

1. Ferrous fumarate.
2. Ferrous fumarate tablets
3. Ferrous gluconate
4. Ferrous gluconate tablets
5. Ferrous sulphate

6. Ferrous sulphate tablets
7. Ferrous sulphate mixture for pediatric
8. Ferrous succinate
9. Ferrous succinate tablets and capsules
10 .Iron and dextran injection
11. Iron sorbital injection

Q.6. : The limit test for iron cannot be carried out in presence of oxidizing agent explain.

Ans : The limit test for iron is based on the principle that, the co-ordination compound ferrous thioglycollate is formed by reducing the ferric ion into ferrous state using the reagent thioglycollic acid.

It is impossible to carryout the limit test for iron in presence of an oxidizing agent where the ferrous ion is oxidized to ferric state (by the oxidizing agent present).

– X –

RADIO PHARMACEUTICALS

RADIOACTIVITY :

INTRODUCTION :

The substance having the property of emitting radiations/particles spontaneously which affect photographic plates even when protected from visible direct light (also discharge the electrified bodies) are called **"Radioactive Substances"**

The phenomenon by which the Radioactive substances emits the radiations spontaneously or continuously is called **"Radioactivity".**

NOTE :

About 40 radioactive elements are there which are arranged into families like Uranium Series, Thorium Series, Actinium series & so on.

FUNDAMENTALS OF RADIOACTIVITY :

Every atom is composed of Nucleus containing Protons, Neutrons surrounded by Electrons

If the atom is electrically neutral, means that the number of protons in the Nuclear is the same number of Electrons.

The number of protons in the Nucleus is the atomic number of the atom which determines the characteristics of that atom.

Various atomic species are known as Nucleides and are often represented simply by the name/symbol

Ex. Carbon (Atomic number) 6 $^{C12\text{--(mass number)}}$

Isotopes – Elements of the same atomic number but different atomic weight or masses are called Isotopes.

Isotopes of particular element have same physical and chemical properties but different kinetics and rate of reactions as these depends on atomic mass.

Two types (major) of isotopes.

1. Stable Isotopes which do not decompose into other isotopic form of the element.

2. Unstable or Radioactive Isotopes :

I. Which undergo decomposition or decaying process by emitting the radiations or particles into the other isotopic form.

The phenomenon of undergoing this type of Nuclear reaction/decay is called **Disintegration** or **Radioactive decay**.

II. The element (Nucleides which undergo spontaneous Nuclear change in order to attain Stability by emitting radioactivity (radiations or particular) are called **Radio-isotopes or Radio-neuclides**.

Types :

A Natural Radio nucleides : available naturally constitutes about 40

Example : Uranium 238, Radium 226, (Ex for higher atomic weight elements) Potassium 40, Rubidium 87 (example for Moderate atomic weight elements)

B. Artificial Radio nucleides:

These are produced synthetically by the bombardment of atomic Neuclei with Neutrons or Electrons to produce unstable Neuclei of the same Element or different element.
Ex:- Cobalt 60, Phosphorous 32, Iodine 131 etc.
Have wide applications in the field of chemistry Medicine Geology etc.

Radio Active Decay :

Radio active subjects disintegrates or decays with the emission of certain particles or radiations which are always Characteristic of the Isotopes or substances.
They emit α, β, γ -radiation or particles

Unit of Radiation :

Unit of **Radioactivity is 'Curie'** symbolised 'C' defined as the quantity of any radioactive substance undergoing the

same number of disintegrations in unit time as of 1 g of Radium which is equal to 3.7×10^{10} disintegrations/sec.
Sub unit, Millicuric (mc) = 3.7×10^{7} disintegrations/sec

Micro Curie (μc) = 3.7×10^{4} disintegrations/sec.

Half Life Of Radioactive Substance :

Radio active substances continue to decay for a particular period. During the specific time, a particular number of atoms originally present decays.

The Half life is used to designate that period of time during which half the number of atom originally present decays or undergoes Disintegration.

$$\text{Half life } (t_{1/2}) = \frac{0.693}{\lambda}$$

Where λ = Disintegration constant/ sec

PROPERTIES OF RADIATIONS :

1. Radiations emitted by atoms is a form of energy which can be divided into a. particulate and b. Electromagnetic. which are interchangeable

2. Can be deflected by Electrical or Magnetic fields

3. Can penetrate the matter.

4. Can ionise matter (eg: Gases) through which they pass.

5. Causes certain subjects to emit flashes of light (Scintillation)

6. Cause darkening of Photographic (Film) plate.

Q.1. : Give the properties of α, β and γ radiations.

Ans:

Properties of α -radiations/particles.

1. Posses Positive charge (2 units).

2. When the Radio Active element emits α–radiations the resulting nucleus will have two '+'ve charges less than the original Nucleus and thus it will correspond with element having its atomic number less than 2 units.

Since α -particles are similar to Helium Nuclei with a mass of 4 amu , the mass number of New nucleus will be 4 amu less than that of original.

Ex : – $_{88}Ra^{226} \xrightarrow{\alpha\text{-}P} {}_{86}Rn^{222} + {}_{2}He^{4}$

3. Heaviest and slowest of Radioactive emissions.

4. Since Penetration power is least (they cannot penetrate tissue and have no medicinal application)

5. Speed -1/10 th of the speed of light (varies from element to element)

6. Affected by strong Magnetic field.

Properties of β–radiations/particles.

1. Negatively charged (described as the electrons of Nuclear origin).

2. They have the mass $\frac{1}{836}$ th of H_2 negligible and charge is -1.

to Hydrogen.

3. Since radiation are lighter, they travel with the velocity little less of light.

4. More penetrating power than α -Particles (they can penetrate Aluminium sheet up to 3mm thick).

5. Affected by strong Magnetic field.

6. Emission of β-particles do not alter the atomic mass but atomic number alters and converted to the element of next highest at number.

Ex : – $_{6}C^{14} \xrightarrow{\beta\text{-}P} {}_{7}N^{14} + \beta^{-}$

Properties of γ – radiations / particles.

1. Does not posses any charge.

2. Have proportion of both of wave and particles.

3. Do not have mass and charge but very high energy and thus have excellent penetrating power. (Thick lead sheet or concrete should be required to protect from these radiations).

4. They are of very short wave length resembling x-rays travel with the speed of light.

5. Since uncharged has poor ionising power but can interact with molecules and atoms in specific media and can produce ions and free radicals by dislodging electrons from orbits.

6. When γ-rays are emitted their lowering of Nuclear energy level but no elemental change is noted.

Q.2. : How is radioactivity is measured and explain the principle and working of ionisation Chamber, scintillation counter and Geiger Muller Counter.

Ans :

Measurement of Radioactivity :

Ionisation chamber:

Available in various shapes & sizes.

Consists of Chambers filled with gas fitted with 2 electrodes kept at different electrical potential (50–100) volts for each cm of distance between the 2 electrodes which a measuring instrument to indicate the flow of electric current.

Radiations causes ionisation of gas molecules or ions which results in emission of electrons and in turn shows changes in Electrical Current.

2. Proportional Counters modified ionisation method is used,

3. Geiger muller Counters : - or GM Counter.

Best known of all radiation detectors

Consists of a cylinder of stainless steel or glass coated with silver on inner side which acts as cathode.A fine wire is co-axially mounted inside the tube which acts as Anode.Space in the chamber filled with special gas mixture.

Radiations enters the tube through the thin section of outer wall called 'window' and cause the ionisation of the gas.

A high voltage (800-1300v) is maintained between the electrode.Due to the ionisation of gas the electrons are at-

tracted by anode and positively charged ions by cathode.The passage of these ions through the tube constitute the flow of current.

Each particle of radiation causes a brief flow or pulse of current - recorded by 'scaler' which shows the total number of pulses.

4. Scintillation Counters :

When radiation strikes certain substances like phosphorus a flash of light is given out,. thus it is possible to measure , $\alpha, \beta,$ or γ radiations with scintillation detectors if the detector is suitably modified for the type of radiation to be measured.

The counter consists of a cell and for example a photo multiplier tube coupled with phosphor or flour to convert scintillations into electric pulses,) an amplifier and a scaler.

For eg :- For γ - radiations the flour used is a crystal of sodium iodide activated with 1% of Thalium to enhance the degree of fluorescence.The - radiations pass through a small window enter the crystal where it produces the small flash of light,This is brought into photo multiplier tube which in turn detects the flash,amplifies and converts into an electrical impulse which is recorded directly by means of scaler.

5. Auto radiography :

More useful in determining and detecting the γ - radiations in physiological studies of plants and animals.

Q.3. : What are the various precautions to be taken in storing and handling of Radio pharmaceuticals ?

Ans :

Storage and Handling :

Precautions that are necessary to protect the personnel handling the radioactive substances from the harmful effects of the radiations given out.

1. Radioactive emitter should never be touched with hand but handled by means of forceps or with suitable instruments.

2. Smoking, Drinking, Eating and such other activities should be avoided in the area where the radioactive substances are stored and handled.

3. Sufficient shielding must be provided for Radioactive substances while storage and handling.

4. Suitable protective clothing should be wear the personnel handling the Radioactive substances.

5. Areas, where Radioactive substances are stored should be monitored and tested for radioactivity regularly.

6. Radioactive substances should be kept (with) in suitable labeled containers,shielded by lead breaks preferably in a remote corner.

7. Disposal of Radioactive substances should be done with great care.

Q.4.: Give the applications of radio isotopes listing the various radio isotopes giving their uses in medicine.

Ans :

Applications of Radio Isotopes : –

Two ways

i) As a Source of radiation in therapy.

ii) As a Radioactive traces in diagnosis.

Some of the important radio isotopes used in medicine are,

1.Calcium(Ca^{44},Ca^{45})-Study the bone structure and used in the treatment bone cancer.

2. C^{14}-most widely used in Structural Activity Relationship studies of Alkaloids,glycosides and other plant products.

3. B_{12}(Co^{57})-Vitamin B_{12} containing Co^{57}-used in the diagonsis of Pernicious Anemia.

4.Gold(Au^{198}) solution-Used as Neoplastic suppressant used in recteculoendothelial activity estimation.

5. H^2 & Fe^{59} - Duterium & Tritium - used in determination of total body water.

5. Sodium chromate(Cr^{51}) Solution-To study the red cell volume and survival time.

7. Sodium Iodide(I^{131}) Capsule and solution-used as Diagonistic agent and as therapeutic agent in thyroid conditions and Myxedema.

8. Iron(Fe^{55} & He^{59}) - Research studies about utilisation and absorption of Iron salts.

Q.5 . : What are Radio opeque compounds?Give the method of preparation and uses of Barium sulphate.

Radio opaque substances are those,both organic and inorganic that have the properties of casing a shadow on x-ray films.Radio opaque substances have the ability to stop the passage of x-rays and thus appear opaque on x-ray examination.Preparations are thus also called **'x-ray contrast media'.**

Ex:-Barium sulphate,Bismuth compounds,organic iodinated compounds etc.

Barium sulphate –

Formula:-$BaSO_4$

Molecular Weight : - 233.4

Contains 97.5 to 100.5% w/w Barium sulphate.

Properties :

Fine,white,odourless,colourless,bulky powder.

Salt is insoluble in water,organic solvents,diluted acids and alkalies,soluble in concentrated Sulphuric acid.

It can be solubilised with concentrated Sulphuric acid. or fusing it with alkali carbonates.Once it is converted into carbonate it reacts with acids easily.

Preparation :

For x-ray purpose, prepared by precipitating barium ions from cold dilute solutions of Barium salt with dilute Sulphuric acid..

$$Ba(OH)_2 + H_2SO_4 \longrightarrow BaSO_4 + 2H_2O$$

$$BaCl_2 + H_2SO_4 \longrightarrow BaSO_4 + 2HCl$$

Action and Uses :

1) Used for the preparation of Barium sulphate compound powder and also as a contrast medium for x-ray examination of alimentary tract.

2) Administered orally in enema forms for examination of colon.

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IDENTIFICATION TEST FOR CATIONS AND ANIONS AS PER INDIAN PHARMOCOPOEIA

Qualitative tests of some common substances, radicles and ions.
A large number of inorganic compounds are tested for their identity on the basis of the qualitative reactions given by the radicles and by the sustance obtained through special treatments. These reactions , as given official under the appendix are reproduced herewith.

These tests are commonly termed 'Identification tests.'

CHEMICAL TEST	OBSERVATIONS
1. ACETATES	
i. Sample + Oxalic Acid (warm)	Acetic acid odour is produced
ii. Sample + Suiphuric acid + small quantity of alcohol (warm)	Ethyl acetate odour is produced
iii. Sample + Ferric Chloride Solution.	Gives deep red colour. Reddish brown ppt produced Red solutions turns yellow.
iv. Samples + CaO – heat.	Acetone produced. detected by indigo, blue colour obtained (placing the paper dipped in O–Nitro benzaldehyde, in alcohol, dried and moistened with NaOH soln.
2. ALUMINIUM	
i. Sample soln. + dil Ammonium soln. or Ammonium sulohide soln.	White gelatanous precipitate soluble in HCl, acetic acid and NaOH soln.
ii. Sample Solution + 5 drops of freshly prepared 0.05% W/V Quinalizarine soln. in 1% W/V NaOH soln. boiled, cooled, Acidified with excess of Acetic acid.	Reddish Violet colour.
iii. Sample in 5ml H_2O few drops Ammonium acetate + 0.1% modrant blue.	Intense purple colour is produced.

3. AMMONIUM	
i. Sample + NaOH Soln. (heat) a) moist red litmus on the evolving gas.	Ammonia gas evolves. Red litmus turns blue.
b) With Paper impregnated with mercurous nitrate soln.	Black stain is produced.
4. ANTIMONY	
i. Acidic soln. + H_2S	Orange red colour ppt. soluble in NaOH soln., Amm sulphide soln.
ii.. PPt. from (i) + Amm. carbonate soln.	PPt is insoluble.
5. ARSENIC	
i. Sample soln. + HCl + H_2Ssoln.	Yellow pprecipitate soluble in NaOH soln. Amm. sulphide soln. and amm Carbbonate Soln.
ii. Soluble ppt from (i) + HCl	Repptd.
iii. Sample soln. + Stannous Chloride soln.	Brown precipitate.
iv. Soln. of sample + hypophosphorous reagent (equal vol)	Brown precipitate.

6. BARIUM	
i. Sample soln. + dil H_2SO_4	White ppt insoluble in HCl & HNO_3
ii. Sample held in non-luminous flame	Yellowish green in colour.
When viewed through green glass	Appears blue.

7. BENZOATE	
i. Sample soln. + H_2SO_4 (heat)	White sublimate on the walls of the tube
ii. Sample soln. + dil. Hcl	White crystalline ppt readily soluble in sovent either in chloroform
iii. Neutral Sample soln. + Ferric chloride	Buff coloured ppt - soluble in HCl - Simultaneously seperates the white crystalline ppt of benzoic acid.
8. BISMUTH	
i. Sample soln. + H_2S	Brownish black precipitate soluble in HNO_3
ii. Sample soln. + Excess dil. NaCl soln.(not too acidic) + tartaric acid soln.	White ppt is produced.
iii. Sample soln. + KI soln. a. ppt + excess KI soln. b. Soln. from a + Excess of H_2O.	Dark brown ppt. Yellow brown soln. is obatined Orange ppt is obtained
iv. Sample soln. + dil HNO_3 + 10% w/v Thiourea soln.	Deep yellow colour is produced

9. BROMIDES	
i. Sample + H_2SO_4 and MnO_2 or $K_2Cr_2O_7$ (Heat)	Bromine vapour produced (detected by orange yellow colour of the filter paper which is poistured with starch solution.
ii. Sample solution + $AgNO_3$ solution.	Curdy yellow ppt is obtained
a) ppt from (ii) + Ammonia solution.	ppt partly soluble.

b) ppt from (ii) + dil. HNO_3 or dil NH_3 solution.	ppt is insoluble.
iii. Sample Solution + Chlorine solution.	Bromine is liberated. Soluble in a few drops of Carbon-di-sulphide or Chloroform. giving reddish solution.
iv. Aqueous solution containing bromine + saturated phenol solution.	White ppt.

10. CALCIUM

i. Sample solution + Amm Carbonate solution	White ppt.
Boil & Cool the mixture.	Insoluble in Amm Chloride.
ii. Sample solution + Amm. Oxalate solution.	White ppt. soluble in HCl and insoluble in Acetic acid.
iii. Sample solution + Pot Chromate solution.	Yellow crystalline ppt (Soluble in acetic acid or well diluted with H_2O)
iv. Sample solution + Excess pot ferro cyanide solution + Excess Amm. Chloride.	white ppt.

11. CARBONATES AND BICARBONATES

i. Sample + dil. acids	CO_2 gas is liberated
a) Gas produced from (i) passed through $Ca(OH)_2$ solution.	White ppt. obtained.
ii. Sample solution + Mercurric Chloride solution.	Brownish red ppt (if carbonates) White ppt. (if bicarbonate)
iii. Carbonate solution + $AgNO_3$ solution	white ppt.
a) ppt from (iii) + Excess reagent	Becomes yellow
b) Boil the mixture.	Turns brown colour.

iv. Carbonate solution + Magnessium sulphate solution.	White ppt.
a) bicarbonate + Magnessium sulphate boiling	White ppt.

12. CHLORIDES

i. Sample + MnO_2 + H_2SO_4	yields chlorine gas.
a) Gas passed through KI + Starch solution.	Blue colour is produced.
ii. Sample solution + $AgNO_3$ solution.	White, curdy ppt. soluble in dil. Ammonia and insoluble in nitric acid.

13. CITRATES

i. Smaple + H_2SO_4 - Heat on boiling H_2O bath.	Pale yellow colour & CO_2 & CO i.e. evolved.
ii. Neutral solution of Sample + Excess cal. Carbonate solution.	White granular ppt. . Soluble in Acetic acid.
iii. Neutral solution of Sample + Excess $AgNO_3$ solution.	White ppt. - soluble in HNO_3 & dil. NH_3 solution.
iv. Sample solution + Excess mercurric sulphate solution - boiled + few drops $KMnO_4$ solution.	Decolourlises the agent & gives white ppt.
v. Sample solution + $HgSO_4$ solution in Excess - boiled. Filter. Filtrate + few drops $KMnO_4$ solution Sodium nitro prusside + Sulphonic acid + Alkaline with strong Ammonia solution.	Violet colour turns blue.

14. COPPER	
i. Solution sample + H_2S	Brownish black ppt. insoluble in dil. HCl & NaOH solution.
ii. Sample solution + NaOH solution on boiling.	Light blue ppt. Becomes brownish black.
iii. Sample solution + KI solution	Brownish ppt.
a) Above solution + Starch solution.	Deep blue colour.
vi. St. Solution + Amm. thiocyannate solution	black ppt.
a) ppt. from (iv) + Sulphurous acid.	Becomes white.
v. Sample solution + dil. HNO_3 solution.	Greenish blue ppt.
vi. Sample solution + pot. ferrocyanide solution.	Reddish brown ppt.

15. CYANIDES	
i. Sample solution + $AgNO_3$ solution.	white curdy ppt. soluble in KI solution or dil. NH_3 solution.
ii. Sample solution + few ferrous sulphate crystals + NaOH solution. Boil the mixture acidify with dil. HCl.	Blue coloured ppt. is produced.
iii. Sample solution - evaporated to dryness with Amm. polysulphide solution. Acidify the residue with few drops of HCl + $FeCl_3$ solution.	Blood red colour.

16. GOLD	
i. Sample solution + H_2S	Black ppt. insoluble in dil HCl & soluble Amm. polysulphide solution.

ii. Neutral / weak acidic solution of sample + Stannous chloride	Purple colour.
a) Sample solution + H_2O_2 solution & NaOH solution (neutral or weakly acidic.)	ppt.
i. Under reflected light	ppt appears brownish black.
ii Under transmitted light.	ppt appears bluish green.

17. IRON	
i. Smaple solution + $KMnO_4$ solution (till faint pink + amm. thiocyanate solution.	Blood red colour is produced.
a) Resultant solution + Phosphoric acid or $HgCl_2$ solution.	Blood red colour is discharged.

Note : This test is common to ferrous & ferric salts.

18. FOR FERRIC SALTS	
i. Sample solution + Amm. nitrophenyl hydroxylamine + dil Hcl.	Reddish brown ppt. soluble in solved ether.
ii. Sample solution + ppt. ferricyanide	Reddish brown colour but no. ppt.
iii. Sample solution + NaOH solution (in absence of Citrates & tartrates)	Reddish brown ppt. soluble in citric acid & tartaric acid.

19. FOR FERROUS SALTS	
i. Sample solution + ppt ferricyanide solution	White ppt. turning blue. insoluble in dil. HCl.

ii. Sample solution + ppt ferricyanide solution.	Dark blue ppt. - decomposed by NaOH solution.
iii. Sample Solution + NaOH sloution.	Dull green ppt.
a) Resultant ppt. when exposed to atmosphere.	Colour.changes to brownish colour.

20. MERCURY	
i. Sample solution + H_2S	Black ppt insoluble in Amm. sulphide & in boiling dil. HNO_3.
ii. Sample + Excess stannous chloride solution	White ppt.
a) Add excess of reagent.	Colour rapisly turns grey.

*** Tests for mercuric & mercurous are common**

21. FOR MERCURROUS SALTS	
i. Sample solution + NaOH solution	Balck ppt.
ii. S. Solution + HCl	white ppt. insoluble in water
a) Above solution + dil. Ammonia.	Colour is blackened.
iii. S.Sloution + KI solution	Greenish yellowish ppt.

22. FOR MERCURIC SALTS	
i. Sample Solution + NaOH solution	Yellow ppt. obtained
ii. Neutral Sample Solution + KI solution.	Scarlet ppt.

23. IODIDES	
i. Sample solution + H_2SO_4 & MnO_2 or $K_2Cr_2O_7$ heat	Evolves vapours of I_2
ii. Sample Solution + pot. iodide solution + dil. CH_3COOH	Iodine is liberated.
a) Liberated iodine + Chloroform	Gives reddish violet colour.
b) Liberated iodine + starch solution.	gives deep blue colour.
iii. S.Solution + $HgCl_2$ solution.	Scarlet obtained - soluble in excess reagent or with KI solution.

24. LEAD	
i. Sample sloution + HCl	white ppt.
ii. Sample Solution + H_2S	black ppt - insoluble in dil. HCl & Amm. sulphide solution - soluble in hot & dil. HNO_3
iii. Sample Solution + dil. H_2SO_4	white ppt.
iv. Sample Solution + pot chromate solutin	yellow ppt - soluble in NaOH solution.
v. Sample Solution + pot cyanide solution + NH_3 solution + diphenyl thiocarbazone	The lower layer becomes brick red colour.

25. NITRITES	
i. Sample Solution + H_2SO_4 - heat	red fumes are given out.
ii. Sample Solution + few drops of dil. H_2SO_4 + KI solution + starch solution.	blue colour is produced

iii. Sample solution + ferrous sulphate solution.	Deep brown colour
iv. Sample Solution + Urea + dil. H_2SO_4	gives CO_2 gas - produces white ppt in Calcium hydroxide solution.

26. NITRATES	
i. Sample Solution + H_2SO_4 + copper - warm	gives out red fumes
ii. Sample Solution + H_2SO_4 + ferrous sulphate solution	Brown colour formed at interface of two liquids.
iii. Sample Solution + H_2SO_4 + crystal of brucine.	gives red colour.

27. PHOSPHATES (ORTHO)	
i. Sample Solution + Silver ammonia solution	light yellow ppt -soluble in dil. NH_3 solution & cold dil. HNO_3 solution.
ii. Sample Solution + Mg ammonio nittrate solution.	white crystalline ppt.
iii. Sample Solution + amm. molybdate & HNO_3 in equal volumes - warm.	yellow ppt.
28. OXALATES	
i. S. Solution + $CaCl_2$ solution	white ppt is obtained
ii. S. Solution + dil H_2SO_4 + few drops $KMnO_4$ solution - heat.	Pink colour of the permanganate is discharged.
29. POTASSIUM	
i. Sample moistered with HCl^- introduced to bunsen burner on platinum wire.	gives violet colour in the flame.

ii. S. Solution + dil CH_3COOH in H_2O + SoCL cobalt nitrate solution.	yellow ppt is obtained.
iii. S. Solution + Sod. Carbonate solution + tartaric acid.	white crystalline ppt is obtained.

30. SODIUM	
i. Sample moistered with HCl^- introduced to bunsen burner on platinum wire.	gives golden yellow colour to the flame
ii. S. Solution + Uranyl Zinc acetate solution	gives yellow crystalline solution.
31. SILVER	
i. S. Solution + Chloride soln. / HCl	white curdy ppt is pbtained
ii. S. Soln. + pot chromate soln.	Red ppt obtained . solble in HNO_3
iii. S. Soln. + pot iodide.	Cream coloured ppt - insoluble in dil.- NH_3 soln and nitric acid.

32. SALICYLATES	
i. Sample + Excess soda lime	Evolves phenol - recognised its characteristic odour.
ii. Neutral Sample Soln. + few ferric chloride solution.	Reddish - violet colour obtained
iii. Sample Soln. + 2ml. Bromine soln.	Cream coloured ppt. obtained.

33. SULPHATES	
i. Sample Soln. + $BaCl_2$ Soln.	White ppt insoluble in Hcl
ii. S. Soln. + lead acetate solution	white ppt - soluble in NaOH solution

34. SULPHITES & BISULPHITES	
i. Sample + HCl - heat	Evolves H_2SO_4 with pungent smell
ii. Sample Soln. + I_2 soln.	Colour of I_2 decolourised - soln. give as tests for sulphates
iii. Sample Soln + $KMnO_4$ soln + few drops of H_2SO_4	Pink colour of $KMnO_4$ decolourised

35. PROTEINS	
i. S. Solution + Mercurric nitrate solution - heat	gives brick red ppt.
ii. S. Soln. + NaOH soln. + few drops $CuSO_4$ soln.	Pinkish violet colour is obtained

36. TARTRATES	
i. Neutral S. Soln. + excess Cal. Chloride soln.	gives white granular ppt. soluble in CH_3COOH
ii. Sample + H_2SO_4 - HCal on H_2O bath	Chass rapidly evolving CO & CO_2 gas.
iii. S. Soln. + CH_3COOH + $FeSO_4$ soln. few drops + H2O2 soln. 2 drops + exxcess NaOh soln.	gives purple violet colour.

37. THIOSULPHATE	
i. S. Solution + HCl	gives white ppt. of sulphur which soon turns yellow and evolves SO2
ii. Strong S. Soln. + BaCl2 soln.	white ppt. - soluble in HCl.

iii. S. Soln. + I2 soln.	Colour is decoloured - soln. does not give reaction for sulphates
iv. S soln. + bromine soln.	Colour is decolourised - solution gives reaction to sulphates
v. S. Soln. + lead acetate soln.	white ppt. - soluble in excess reagent
a) On boiling the resultant ppt from (v)	black ppt obtained.

38. ZINC	
i. Neutral S. Soln. + H_2S gas + drops of NaOH soln.	white ppt soluble in HCl & insoluble in acetic acid is obtained
ii. S. Soln + pot ferrocyanide soln.	white ppt insoluble in dil Hcl
iii. S. Soln. + phosphoric acid + 0.05 ml of 0.1% $CuSO_4$ + mercurricammoniumthiocyanate soln.	violet ppt is obatained

– X –

APPENDIX – I

Here for the convenient of students,the inorganic substances used as therapeutic and diagnostic agents and pharmaceutical aids are classified here under.Though some of the inorganic substances,specially those used therapeutically having 2 or more uses,they are categorized based on their main use.However in few instances prominent and secondary use and action is given in the brackets.

1. **ACIDIFIERS –**

   Hydrochloric acid
   Sodium acid phosphate

2. **ABSORBENTS-**

   Activated charcoal
   Light Kaolin
   Soda lime(CO_2 absorbent)

3. **ANTI-COAGULANTS-**

   Sodium citrate

4. **ANALGESICS AND ANTI-PYSETICS-**

   Sodium salycilate

5. **ANTIFUNGAL,ANTIMICROBIAL,ANTIPROFOZOAL AND ANTISEPTIC AGENTS**.

   Ammoniated mercury-as an antiinfecteve
   Ammoniated mercury - as anointment
   Borax-as a bacteriostatic.
   Borax glycerine
   Boric acid-as a local anti-infective.
   Calcium mandalate-as an antibacterial
   Hydrogen Peroxide
   Iodine as a Germicide, Fungicide and local anti infective.
   yellow mercuric oxide-Antibacterial opthalmic agent.
   Potassium Permanganate -as an oxidant
   Silver nitrate-as an local anti infective.

Mild silver protein-local anti infective.
Strong silver protein-local anti infective.
Sodium benzoate-as a fungistatic.
Precipitated sulphur-as a seabicide.
Sublimed sulphur-as a seabicide.

6. ASTRINGENTS-

Alum
Bismuth sub carbonate
Bismuth subgallate
Calamine - as an Protective
Calamine lotion - as a Protective
Calamine hydroxide - as a Protective
Copper sulphate
Lead acetate
Zinc oxide
Zinc sulphate.

7. CATHARETICS (PURGATIVES AND LAXATIVES)-

Magnesium sulphate
Dried magnesium sulphate
Mercurous chloride.
Mercury with chalk.
Potassium acid tartrate.
Sodium phosphate.
Sodium Potassium tartrate.

8. DIAGNOSTIC AGENTS-

– Barium sulphate.
Sodium benzoate.

9. DIURETICS –

Ammonium chloride.

Potassium citrate.

10. ELECTROLYTES AND REPLENISHERS

Hydrated calcium chloride.
Calcium gluconate.

Calcium lactate.
Dibasic Calcium-phosphate.
Potassium chloride.
Sodium Chloride

11. EMETICS-

Zinc sulphate.

12. EXPECTORANTS AND ANTI TUSSIVES.

Ammonium chloride.
Potassium iodide.
Sodium iodide.

13. GASTRIC ANTACIDS.

Aluminium hydroxide gel.
Bismuth sub carbonate.
Bismuth sub-gallate.
Heavy and light magnesium carbonate.
Heavy and light magnesium oxide.
Magnesium trisilicate.
Milk of magnesia
Potassium bicarbonate.
Sodium bi carbonate.
Sodium carbonate.
Sodium citrate.

14. GENERAL ANESTHETICS.

Nitrous oxide.

15. HAEMATINICS –

Ferrous gluconate.
Ferrous sulphate.
Iron
Iron and Ammonium citrate.

16. RESPIRATORY STIMULANTS-

Aromatic spirit of ammonia.
Carbon-di-oxide
O

17. SEDATIVES AND HYPNOTICS-

Potassium bromide.

Sodium bromide.

18. PHARMACEUTICAL AIDS

Alum

Strong and dilute ammonia solution.

Ammonium bicarbonate.

Bentonite

Boric acid

Calcium phosphate

Dried ferrous sulphate.

Hypophosphoric acid.

Kaolin

Mercury

Phosphoric acid.

Plaster of paris.

Potassium hydroxide.

Sodium hydroxide.

Sodium nitrate.

Sodium perborate.

Sodium thiosulphate.

Purified talc.

Zinc oxide.

Zinc stearate and many others.

APPENDIX – II

Assays of some important chemical compounds.

1.Ammoniated Mercury :

I.P and B.P has the same procedure for the assay

Principle :

By stirring up potassium iodide and water, together with ammoniated mercury, the compound is reduced.Mercuric iodide formed any converted to Potassium mercury iodide by potassium iodide.The liberated alkali (Ammonia and potassium hydroxide) is titrated with 0.1n HCl using methyl orange as indicator.

Reactions involved-

$NH_2HgCl + 2KI + H_2O \longrightarrow HgI_2 + NH_3 + KOH + KCl$

$HgI_2 + 2KI \longrightarrow K_2HgI_4$

Each ml of 0.1N HCl ≡ 0.01261g of NH_2HgCl

Procedure :

Accurately weighed quantity of the sample is transferred to a stoppered flask containing 50ml water.Add 3g of potassium iodide and shaken occasionally, liberated alkali is titrated with standard 0.1n HCl using methyl orange as indicator.

2. Ammonium Chloride :

Ammonium chloride is a salt of weak base and strong acid. Therefore its aqueous solution is acidic.Due to this reason the reaction with silver nitrate is an incomplete process and hence Back titration method(Volhard's method) is adopted.

Principle :

In this assay,excess of silver nitrate solution is added to the ammonium chloride solution and the residual silver nitrate is determined by titrating it with standard ammonium thiocyanate solution using ferric ammonium sulphate as indicator.

I.P indicates the use of nitro benzene before titration in order to avoid the interaction between precipitated silver chloride and ammonium thio cyanate as nitrobenzene forms a layer over precipitated silver chloride.

When all the silver is precipitated as silver thiocyanate,because of the formation of ferric thiocyanate, a permanent red colour is developed.

Reactions involved.

$NH_4Cl + AgNO_3 \longrightarrow AgCl + NH_4NO_3$

Excess $AgNO_3 + NH_4SCN \longrightarrow AgSCN + NH_4NO_3$

End point $-Fe^{3+} + SCN^- \longrightarrow [Fe(SCN)]^{2+}$ Red colour

Each ml of 0.1N $AgNO_3 \equiv 0.005349$ g of NH_4Cl

Procedure :

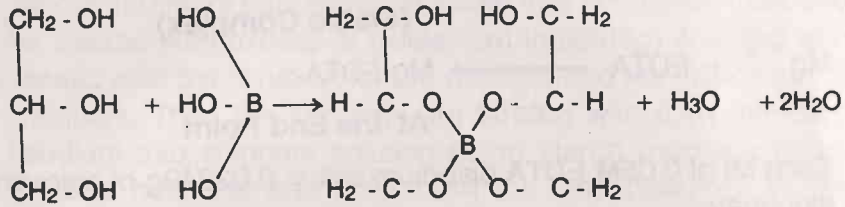
Accurately weigh about 0.2g of sample and dissolve in 40 ml water in a flask.Add 3 ml Nitric acid,5 ml nitrobenzene and 50 ml 0.1N $AgNO_3$ solution and shake vigorously.The solution then titrated with 0.1N standard 0.1N ammonium thiocyanate solution using ferric ammonium sulphate as indicator.

3. Boric acid :

Since, Boric acid in aqueous solution is a weak acid it cannot be titrated directly and accurately against standard alkali.Therefore, it is dissolved in glycerine-water mixture where it acts like a strong monobasic acid and can be

titrated against standard alkali, using phenolpthalein as indicator. Here the compounds like mannitol also acts in the similar way as of polyhydric glycerine compounds.

Reaction involved.



(Glyceroboric Acid)

Each ml of 1N NaOH solution $\equiv 0.06183$ g of H_3BO_3

Procedure :

Accurately weigh about 2g of sample,dissolved in the mixture of 50 ml water and 100 ml glycerine, which is previously neutralised to phenolpthalein and titrated with 1N standard NaOH solution using phenolpthalein as indicator.

4. Calcium gluconate :

Assayed by complexometric titration method

Principle and Procedure :

Calcium ions forms stable complex with EDTA-disodium salt.In the assay to the calcium gluconate solution known volume of M/20 Mg sulphate is added and the mixture is made alkaline with a buffer solution and the titration is carried out using M/20 EDTA sodium salt as titrant.

Initially there is a complex formation between magnesium ions and disodium EDTA salt.As calcium ions forms much stable complex,the magnesium ions are liberated.These ions are titrated with disodium EDTA salt using moderant black as indicator.

From the volume of M/20 disodium EDTA solution required,a volume of M/20 magnesium sulphate solution is substrated.

Reactions involved-

Ca^{++} + Mg-EDTA ⟶ Ca-EDTA + Mg^{++}

(Stable Complex)

Mg^{++} + EDTA ⟶ Mg-EDTA

At the End Point

Each Ml of 0.05M EDTA disodium salt ≡ 0.02249g of calcium gluconate

5.Chlorinated lime :

Chlorinated lime or bleaching powder is analysed by the titration which involves oxidation - reduction reaction.

Principle :

Chlorinated lime liberates chlorine slowly when added to water. On tritration and shaking with purified water, the available chlorine of the sample treated with acetic acid in presence of potassium iodide. The acetic acid liberates chlorine from sample which displaces an equivalent amount of iodine from potassium iodide. The liberated iodine is titrated with 0.1N standard sodium thio sulphate solution using starch mucilage as indicator near the end point.

Reactions involved :

$Ca(OCl) + 2CH_3COOH \longrightarrow (CH_3COO)_2Ca + HOCl + HCl$

$HOCl + HCl \longrightarrow Cl_2 + H_2O$

$2KI + Cl_2 \longrightarrow 2KCl + I_2$

$I_2 + 2Na_2S_2O_3 \longrightarrow Na_2S_4O_6 + 2Na\,I$

Each ml of 0.1N sodium thio sulphate ≡ 0.003545g of available chlorine.

Procedure :

Accurately weigh about 4g of sample triturated with small quantity of water and transferred to 1 litre flask and the volume is made upto the mark. A measured quantity of about 100 ml of suspension is taken into stoppered flask and is treated with excess of potassium iodide(3g).Acidified with acetic acid 5 ml,shaken for 2-3 minutes and kept aside for 15 minutes. Then the contents are titrated with 0.1N standard sodium thio sulphate solution using starch mucilage as indicator near the end point untill the disappearance of the blue colour.

6. Hydrogen Peroxide :

The titration with potassium permanganate solution is very convenient,easy and official method.

Principle :

Based on oxidation - reduction reaction. As a matter of fact hydrogen peroxide is an oxidising agent as it liberates oxygen readily. However,when it is titrated in an acidic medium against potassium permanganate, Hydrogen peroxide acts as a reducing agent.

Reaction involved :

$2KMnO_4 + 3H_2SO_4 + 5H_2O_2 \longrightarrow K_2SO_4 + 2MnSO_4 + 8H_2O + 5O_2$

Each ml of 0.1N $KMnO_4$ solution ≡ 0.001701 g of H_2O_2

Procedure :

10 ml of the sample is diluted to 250 ml in a volumetric flask with purified water. To 25 ml of solution add 10 ml 5N sulphuric acid and the contents are titrated against 0.1N standard potassium permanganate solution till a faint pink colour appears.

7. Iodine :

Principle:- Based on oxidation - reduction reaction, I_2 acts as mild oxidising agent.I_2 , under suitable conditions oxidises a variety of reducing agents like sodium thio sulphate is oxidised to sodium tetrathionate. I_2 has poor water solubility and therefore potassium iodide is added to effect the solution.The end point is detected using starch solution as indicator.

Reaction involved :

$$2NaS_2O_3 + I_2 \longrightarrow Na_2S_4O_6 + 2\,Na\,I$$

Each ml of 0.1N sodium thiosulphate ≡ 0.01269 g of I_2.

Procedure :

Accurately weigh about 0.5g of I_2, dissolved in a solution of 1g potassium iodide in 5 ml water in Iodine flask.

Diluted to 50 ml with water, acidified with 1 ml acetic acid and the contents titrated with 0.1N standard sodium thiosulphate solution using starch solution as indicator.

8. Potassium Permanganate :

Principle :

Potassium permanganate is a strong oxidising agent.Oxalic acid is used for the standardisation of Potassium permanganate solution.

A known quantity of pure oxalic acid is dissolved in water and the solution is acidified with dilute sulphuric acid, as Hydrochloric acid and acetic acid get oxidised by $KMnO_4$. The solution is warmed to 70°C it is titrated with KMno4 solution until a permanent pale pink colour is obtained.

Since oxalic acid - potassium permanganate reaction tends to slow down, warming to 70°C is required.

Reaction involved :

$$5H_2C_2O_4.2H_2O + 2KMnO_4 + 5H_2SO_4 \longrightarrow K_2SO_4 + 2MnSO_4 + 8H_2O + 10CO_2$$

Each ml of 0.1N oxalic acid ≡ 0.00316g of Potassium permanganate .

Procedure :

Accurately weighed about 3.2 g of potassium permanganate dissolved in 1000 ml distilled water by boiling 10-15 minutes.Solution is cooled, filtered through glass wool and kept in bottle. About 0.2 g of oxalic acid is weighed and dissolved in 25-30 ml water,25 ml dilute H_2SO_4 is added. Warm the contents to 70°C and titrated against potassium permanganate solution keeping the temperature constant till pale pink colour persists at least for 30 seconds.

9. Yellow Mercuric Oxide :

Method : Precipitation titration method.

Principle :

Mercuric oxide dissolved in nitric acid to give mercuric nitrate. This is titrated with 0.1N ammonium thiocyanate solution. The precipitation of mercuric thiocyanate gives red colour with ferric ammonium sulphate solution, which is used as indicator.

Reactions involved.

$$HgO + HNO_3 \longrightarrow Hg(NO_3)_2 + H_2O$$

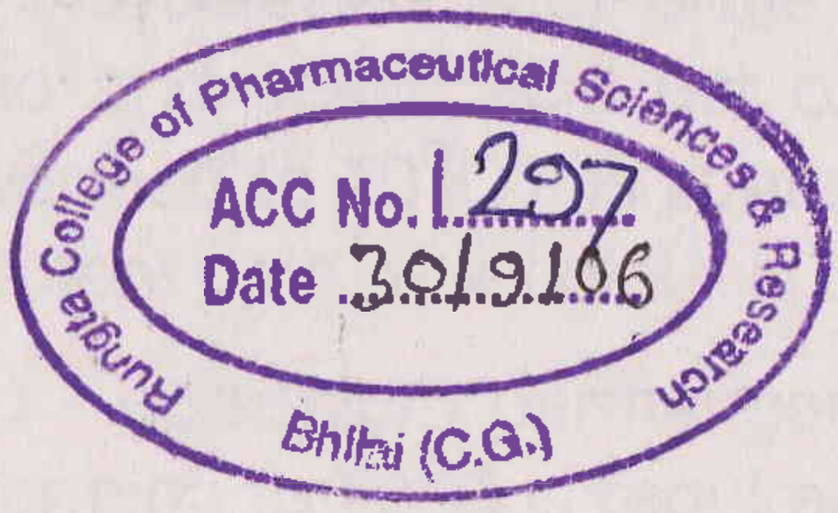
$$Hg(NO_3)_2 + 2\,NH_4\,SCN \longrightarrow Hg(SCN) + 2NH_4NO_3$$

Each ml of 0.1N NH_4 SCN ≡ 0.01083 g of Mercuric Oxide

Procedure :

Accurately weighed about 0.4 g of sample dissolved in the mixture of 5 ml nitric acid and 10 ml water. Dilute it to 150 ml with water.It is then titrated with 0.1N ammonium thiocyanate solution using solution of ferric ammonium sulphate as indicator.

– X –



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