INORGANIC CHEMISTRY

UNIT 1 NOTES

INORGANIC CHEMISTRY

- INTRODUCTION
- IMPURITIES
- PHARMACOPOEIA
- LIMIT TEST

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PHARMACEUTICAL CHEMISTRY

- Pharmaceutical chemistry is defined as branch of chemistry that deals with those chemical compounds that are basically used in manufacturing / development of drugs / medicines.
- It basically deals with chemical / biochemical and pharmacological aspect of drugs.

BRANCHES OF PHARMACEUTICAL CHEMISTRY

Pharmaceutical chemistry can be further sub divided into following parts :

① Pharmaceutical Inorganic Chemistry
② Pharmaceutical Organic Chemistry
③ Analytical Chemistry
④ Medicinal Chemistry

Pharmaceutical Inorganic Chemistry

Pharmaceutical inorganic chemistry deals with the study of all the elements and their compounds except hydrocarbons that are used in synthesis, manufacturing and development of drugs.

PHARMACOPOEIA

- Pharmacopoeia is derived from two greek words 'Pharmakon' means drugs and poeia means 'to make'.
- It is a legal and official book of standards for drugs issued by recognized authorities appointed by Government of each country.
- It contains list of pharmaceutical substances, formulae along with their description and standards.
- Pharmacopoeia is nothing but the collection of Monographs.

MONOGRAPHS

A monograph is a collection of detailed information on a particular drug its dosage form and method of analysis.

- A monograph contains :
- Chemical Name
- Formulae
- Solubility
- Identification
- pH
- Assay
- Loss On Drying
- Dose

Importance Of Pharmacopoeia

- To maintain uniformity and control standard of drugs available in the market.
- Avoid adulterated drugs.
- Complete information of drugs and dosage form.
- Reference for laboratory , industry and academic institutions.

History Of Pharmacopoeia

- The term 'Pharmacopoeia' was first used by ancient greek physician Pedanius Dioscorides in the 1st century.
- In 1820 first united states pharmacopoeia was published.
- In 1864, first british pharmacopoeia was published.
- Todays Pharmacopoeias mainly focus on assurance of quality of products by various tools of analytical sciences.

Pharmacopoeias Of Different Countries

- Indian Pharmacopoeia
- British Pharmacopoeia
- United states Pharmacopoeia
- European Pharmacopoeia
- French Pharmacopoeia
- Japanese Pharmacopoeia

Indian Pharmacopoeia

- It is official book of standard for drugs to define identity, purity and strength for the drugs imported, manufactured for sale, stocked or distributed in India.
- Indian Pharmacopoeia is published by 'IPC'.

Indian Pharmacopoeia Commission

- Indian Pharmacopoeia Commission is an autonomous institution of the ministry of health and family welfare that sets standard for all the drugs that are manufactured, consumed and sold in India.
- Its head office is in Ghaziabad, Uttar Pradesh, India.
- The IPC was established in 1956.

History Of Indian Pharmacopoeia

In Pre-idependence days, British Pharmacopoeia was used in India.
In 1946 Government of India issued 'The Indian Pharmacopoeia List'.
Committee under chairmanship of Sir R.N. Chopra along with other nine members prepared the 'Indian Pharmacopoeia List'.
It was prepared by department of Health Government of India, Delhi in 1946.
In 1948 Government of India appointed an Indian Pharmacopoeia Committee for preparing Indian Pharmacopoeia.
Indian Pharmacopoeia Committee under chairmanship of Dr. B.N. Ghosh published first edition of IP in 1955.

List Of Indian Pharmacopoeia

Editions	Year	Addendum / Supplement	No Of Volumes	Monographs
1st Edition	1955	Supplement 1960	2	986
2nd Edition	1966	Supplement 1975	3	890
3rd Edition	1985	Addendum 1989 Addendum 1991	2 –	261 –
4th Edition	1996	Addendum 2000 Addendum 2000 Addendum 2002 Addendum 2005	3 – – –	1149 208 19 –
5th Edition	2007	Addendum 2008	3	271
6th Edition	2010	Addendum 2012	3	52
7th Edition	2014	Addendum 2015 Addendum 2016	4 –	577 –
8th Edition	2018	Addendum 2019	4	220

IMPURITIES

- Impurity can be simply defined as any substance or material that affect the purity of material of interest.
- Presence of impurity may produce toxic effect.
- It may lower the strength & quality of pharmaceutical substances.
- Common impurities include Lead, Arsenic, Iron, Chloride etc.

TYPES OF IMPURITIES

Impurities can be divided into three following types :

① Organic Impurities
② Inorganic Impurities
③ Residual Solvents

Organic Impurities

- Organic impurities basically arise during synthesis, purification and storage of drug substances.
- They may be identified or non-identified.
- They mainly include starting material, by-product, intermediate, reagent etc.

Inorganic Impurities

- They often derive during manufacturing process.
- They are generally identified.
- It mainly includes reagents, catalyst, heavy metals, inorganic salts etc.

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Residual Solvents

- These impurities are mainly arise during manufacturing process.
- These are the impurities that are basically present in solvents used in pharmaceutical manufacturing.

Sources Of Impurities

There can be various sources of impurities as follows :

- Raw Materials
- Reagent Used
- Method or Process
- Solvents
- Atmospheric Contamination
- Reaction With Vessel
- Packaging Error
- Storage Conditions

Raw Materials

- Impurities from raw materials may be carried through manufacturing process and contaminate the final product.
- Example : Rock salt (contains $CaSO_4$ + $MgCl_2$) = NaCl Prepared
- Rock salt contains small amount of Calsium Sulphate & Magnesium Chloride, Now NaCl prepared from this source (rock salt) may contain Magnesium and Calcium traces.

Reagent Used

- If the reagent used in manufacturing process are not completely removed by washing, then it may find entry into the final product.
- Example : $HgCl_2 + 2NH_4OH \longrightarrow NH_2HgCl + NH_4Cl + H_2O$
- In above reaction Ammoniated Mercury Chloride (NH_2HgCl) contains some amount of 'Ammonium Hydroxide', now if this ammonium hydroxide is not removed by washing it may contaminate the final product.

Method / Process

- There are various method/ process used for manufacturing of pharmaceutical products.
- In certain drugs, a multiple step synthesis process is used that produces intermediate compounds.
- Now it is very important to purify this intermediate compounds otherwise it will contaminate the final product.

Packaging Errors

- Products of similar appearance such as tablets of same shape & size may sometimes packed in similar containers that can leads to potential source of danger.
- Improper labelling may also cause major packaging error.

Storage Conditions

- After preparation of final product it should be stored in appropriate container depending upon :

- Nature of Material
- Batch Size
- Quantity

- Generally materials like plastic, iron, stainless steel & aluminium are used for storage, improper storage leads to reaction with these material & contamination of final product

Limit Test

- Limit test are quantitative or semi-quantitative test designed to identify and control small quantities of impurities that are present in the substance.
- Limit : Certain or Fix Value
- Test : To examine / To investigate

- It basically involves small comparison of opalescence, turbidity or colour with fixed standards.
- Generally it is carried out in Nessler's Cylinder.

Limit Test Of Certain Compounds

In our syllabus we have to study about following Limit Test.

- Limit Test For Chloride
- Limit Test For Sulphate
- Limit Test For Iron
- Limit Test For Arsenic
- Limit Test For Lead
- Limit Test For Heavy Metals.

CHLORIDE

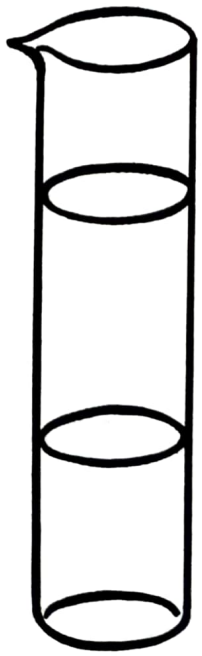
PRINCIPLE

The principle of limit test of chloride is based on the reaction of soluble chlorides with silver nitrate in the presence of dilute nitric acid to form Silver Chloride which appears as turbidity / opalescence.

$$Cl^- + AgNO_3 \xrightarrow{dil.\ HNO_3} AgCl + NO_3^-$$

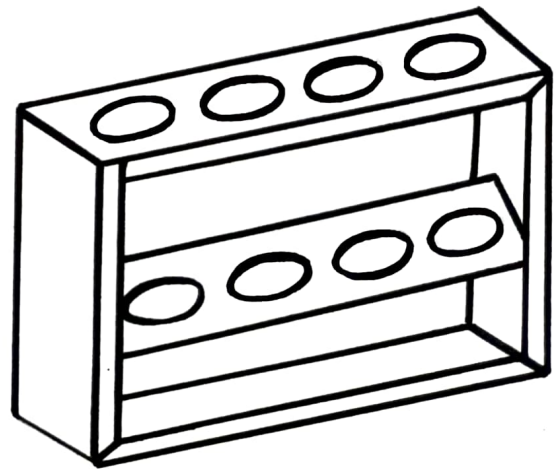
APPARATUS REQUIRED

- Nessler Cylinder
- Glass Rod
- Stand



NESSLER CYLINDER

GLASS ROD



STAND

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Chemical Required

- Dilute Nitric Acid (10%)
- Silver Nitrate (5%)
- Sodium Chloride

Use Of Nitric Acid

- Nitric acid is added in the solution to make solution acidic.
- It helps to dissolve other impurities.
- Provide common ion effect & help silver chloride precipitate to make solution turbid at the end of process.

Procedure

Test	Standard
• Specific amount of substance dissolved in nessler cylinder as directed in pharmacopoeia.	• Take 1 ml of 0.0585% w/v solution of Nacl in a nessler cylinder.
• Add 10 ml dilute HNO_3	• Add 10 ml dilute HNO_3
• Dilute the solution to 50 ml with water.	• Dilute the solution to 50 ml with water.
• Add 1 ml Silver Nitrate solution.	• Add 1 ml Silver Nitrate solution.
• Observe the opalescence/ turbidity.	• Observe the opalescence / turbidity.

OBSERVATIONS

- If turbidity of test solution is less than turbidity of standard solution then sample passes the limit test.
- If turbidity of test solution is greatre than turbidity of standard solution sample fails the limit test.

SULPHATE

PRINCIPLE

The principle of limit test of sulphate is based on the reaction of soluble sulphates with barium chloride to form barium sulphate in the presence of dilute hydrochloric acid which appears as turbidity / opalescence.

$$SO_4^{2-} + BaCl_2 \xrightarrow{HCl} BaSO_4 \downarrow + 2Cl^-$$

APPARATUS REQUIRED

- Nessler Cylinder
- Glass Rod
- Stand

CHEMICAL REQUIRED

- Dilute Hydrochloric Acid
- Standard Potassium Sulphate Reagent
- Barium Sulphate Reagent

ROLE OF HCl

- Provide acidic medium
- Prevent precipitation of other radicals

PROCEDURE

TEST	STANDARD
• Dissolve specific amount of substance in nessler cylinder as directed in pharmacopoeia.	• Take 1 ml of 0.1089 % w/v solution of K_2SO_4 in nessler cylinder
• Add 2 ml dilute HCl	• Add 2 ml dilute HCl
• Dilute the solution to 45 ml with water	• Dilute the solution to 45 ml with water
• Add 5 ml barium sulphate reagent	• Add 5 ml barium sulphate reagent
• Observe the opalescence	• Observe the opalescence

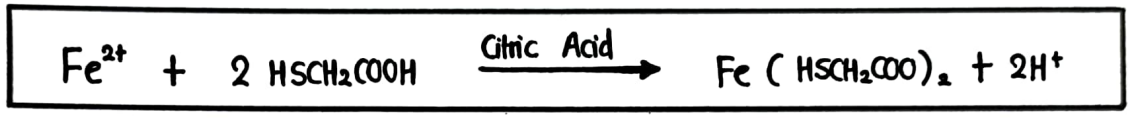
OBSERVATION

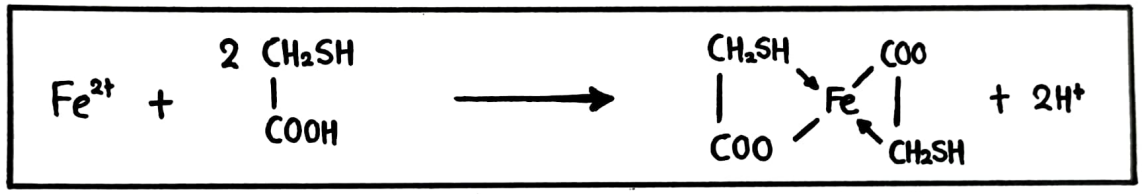
- If turbidity of test solution is less than turbidity of standard solution then sample will pass the limit test.
- If turbidity of test solution is greatre than turbidity of standard solution sample will fails the limit test.

IRON

PRINCIPLE

The principle of limit test of iron is based on the reaction between Ferrous Ions and Thioglycolic Acid in the presence of Ammonia & Citric Acid to form Ferrous Thioglycolate Complex which appears as Pale Pink to Deep- Reddish Purple colours.





APPARATUS REQUIRED

- Nessler Cylinder
- Glass Rod
- Stand

CHEMICALS REQUIRED

- Standard Iron Solution
- Iron Free Citric Acid
- Thioglycolic Acid
- Iron Free Ammonia Solution

PROCEDURE

TEST	STANDARD
• Dissolve specific amount of sample in nessler cylinder as directed in pharmacopoeia	• Dissolve 2 ml standard iron solution in nessler cylinder.
• Dilute to 20 ml with water	• Dilute to 20 ml with water
• Add 2 ml iron free citric acid	• Add 2 ml iron free citric acid
• Add 0.1 ml Thioglycolic Acid	• Add 0.1 ml Thioglycolic Acid
• Make solution alkaline with Ammonia	• Make solution alkaline with Ammonia
• Observe the intensity of colour After the dilution to 50 ml with water.	• Dilute the solution to 50 ml with water & observe intensity of colour produced

OBSERVATIONS

- If the intensity of colour of test solution is less than intensity of colour of standard solution, sample passes the limit test.
- If the intensity of colour of test solution is greater than intensity of colour of standard solution, sample fails the limit test

ARSENIC

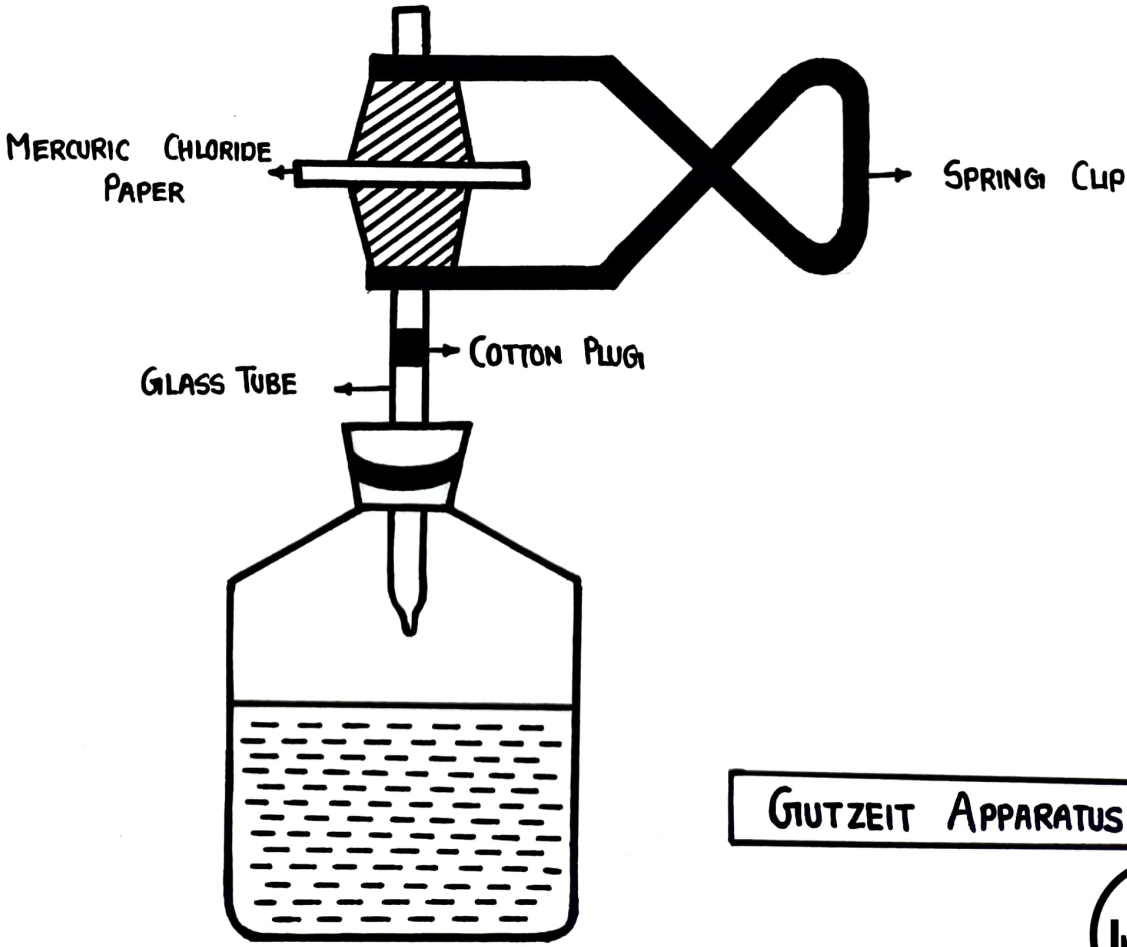
PRINCIPLE

The principle of limit test for Arsenic is based on the fact that arsenic in the arsanious taste easily gets reduced into Arsine Gas which on reaction with mercuric chloride gives yellow stain.

$$2AsH_3 + HgCl_2 \longrightarrow Hg(AsH_2)_2 + 2HCl$$

APPARATUS REQUIRED

- Gutzeit Apparatus
- Glass Rod
- Stand



GUTZEIT APPARATUS

Chemicals Required

- Standard Arsenic Solution
- Potassium Iodide
- Zinc
- Stannous Chloride
- Stannated HCl & Lead Acetate

Role Of Reagents

- Zn / KI / $SnCl_2$: As Reducing Agents
- HCl : To make solution acidic
- Lead Acetate : To trap any hydrogen sulphide (if present)

Procedure

Test	Standard
• Add specific amount of test sample along with stannated HCl in gutzeit apparatus	Dissolve known quantity of standard Arsenic solution with HCl in gutzeit apparatus
• Add 1 gm of Potassium Iodide	Add 1 gm of Potassium Iodide
• To this add 5 ml $SnCl_2$	Add 5 ml $SnCl_2$
• Add 10 gm Granulated Zinc	Add 10 gm Granulated Zinc
• keep the solution aside for 40 minutes	keep the solution aside for 40 minutes.

OBSERVATION

- If stain produced by test is less than stain produced by standard, sample passes the limit test.
- If stain produced by test is greater than stain produced by standard, sample fails the limit test.

THANK YOU

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