PHARMACEUTICAL INORGANIC CHEMISTRY

COMPLETE UNIT 1 NOTES

Rx Pharma Education

PHARMACEUTICAL CHEMISTRY

In pharmaceutical chemistry we study about those chemical compounds that are basically used in manufacturing / development of drugs / medicines.

Pharmaceutical Chemistry

Inorganic Chemistry

In this we basically study about those inorganic compounds that are used in ph--armaceutical industry

Organic Chemistry

In this we basically study about organic compounds that are used in pharmaceut--ical industry

Medicinal Chemistry

In this we study about synthesis, identification & developm- of drugs / medicines.

Inorganic Compounds :-

Inorganic compounds will never contain carbon & hydrogen together. but indivisually C & H can contain any atom i.e CO_2, HCl, H_2O etc.

SYLLABUS

UNIT - I

- Impurities in pharmaceutical substances
- Limit Test

UNIT - II

- Acid, bases & buffers
- Major extra & intracellular electrolytes
- Dental Products

UNIT - III

- Gastrointestinal Agents
  - Acidifiers
  - Antacid
  - Cathartics
  - Antimicrobials

UNIT - IV

- Miscellaneous Compounds
  - Expectorants
  - Emetics
  - Hematinics
  - Poisons & Antidote
  - Astrigents

UNIT - V

- Radiopharmaceuticals

PHARMACOPOEIA

- Pharmacopoeia is derived from two greek words.
  Pharmakon → 'drug'
  Poeia → 'to make'

- It is legal and official book of standard of drugs issued by recognized authorities usually appointed by 'Government of each country'
- Pharmacopoeia contains :-
- List of drugs & related substances
- Sources
- Prescription
- Tests
- Formulas
- Uses
- Doses
- Storage conditions

Importance Of Pharmacopoeia

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

Pharmacopoeia of Different Countries

- Indian Pharmacopoeia
- British Pharmacopoeia
- US Pharmacopoeia
- European Pharmacopoeia
- French Pharmacopoeia

Indian Pharmacopoeia Commission

Indian pharmacopoeia commission is an autonomous institution of the ministry of health & family welfare which sets standard for all the drugs that are manufactured, sold & consumed in India.

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'
- Its head office is in Ghaziabad (UP)
- Indian pharmacopoeia is published by 'NISCAIR'

Full Form Of NISCAIR

National Institute Of Science Communication And Information Resources

History Of Indian Pharmacopoeia

- In pre-independence days, British pharmacopoeia was used in India.
- In 1946 Government of India issued 'The Indian Pharmacopoeial List'.
- Committee under chairmanship of Sir R.N. Chopra alongwith other nine members prepared 'The Indian Pharmacopoeial List'
- It was prepared by 'Dep. of Health Gov. of India, Delhi in 1946.
- In 1948 Gov. of India appointed an Indian pharmacopoeia committee for preparing 'Pharmacopoeia Of India'
- Indian pharmacopoeia committee under chairmanship of 'Dr. B.N. Ghosh' published first edition of IP in 1955

Father Of Indian Pharmacopoeia

Professor Manadeva Lal Schroff

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 is any material that affect the purity of material of interest
- Presence of impurity may produce toxic effect
- It may lower the strength of pharmaceutical substance
- Common impurities include lead, arsenic, iron, chloride etc.

Types

They are of basically 3 types

- Organic Impurities
- Inorganic Impurities
- Residual Solvents

Organic Impurities

- Organic impurities basically arise during synthesis, purification and storage of drug substances
- They may be identified or Non-identified
- They basically include starting material, by product, synthesis intermediate, reagants, ligand & catalyst.

Inorganic Impurities

- They often derive during manufacturing process
- They are generally identified.
- They basically include reagents, ligands, catalyst, heavy metals, inorganic salts.

Residual Solvents

- They arise during manufacturing process
- These are impurities that are basically present in solvents used in pharmaceutical manufacturing

Sources Of Impurities

- Raw Material
- Reagent
- Method
- 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 ($CaSO_4 + MgCl_2$) = NaCl

Rock salt contains small amount of calcium sulphate & magnesium chloride, Now 'NaCl' prepared from this source may contain calcium and magnesium traces.

Reagent Used :-

If the reagent used in manufacturing are not completely removed by washing, then it may find entry into the final product

Example: $HgCl_2 + 2NH_4OH \longrightarrow NH_2HgCl + NH_4Cl$

In above reaction ammoniated chloride prepared contains 'ammonium hydroxide', Now if it is not removed by washing with water then 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, which produces 'intermediate compounds'

Now it is very important to purify this intermediate compound otherwise it will contaminate the final product.

Solvents :-

Most of the pharmaceutical products manufactured using water as solvent. Now generally we used distilled or de-mineralised water, but sometime for reducing cost we use softened water that contains 'Na^+' & 'Cl^-' ions as impurity that can contaminate the final product.

- Tap Water :- Contain Ca^{2+}, Mg^{2+}, Na^+ as impurity
- Softened Water :- Contain Na^+, Cl^- as impurity
- De-mineralised water :- May contain organic impurity
- Distilled Water :- Best but costly

Atmospheric Contamination :-

In industrial area atmosphere is contaminated with dust particles and harmful gases. During manufacturing products can react with them & get contaminated

Example : NaOH reacts with atmospheric CO_2 & get contaminated that's why it should not kept open for long time

That's Why most of the industries build in outer areas (where pollution is very low)

Reaction With Vessel

During manufacturing process some of the vess solvents & reagents may undergo reaction with vessel and contaminate the final product

Example : Iron contain arsenic as impurity, now inorganic compounds that are manufactured in iron vessel may contain Iron and arsenic as impurities.

Packaging Errors

Products of similar appearance such as tablet of same shape, size and colour sometimes packed in similar containers lead 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 materials and contamination of final product.

LIMIT TEST

Limit test are quantitative or semi-quantitative test designed to identify and control small quantities of impurity 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 carried out in nessler's cylinder.

Limit test in our syllabus

- Limit test of chloride
- Limit test of sulphate
- Limit test of Iron
- Limit test of Arsenic
- Limit test of Lead
- Limit test of Heavy Metals

Limit Test For 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.

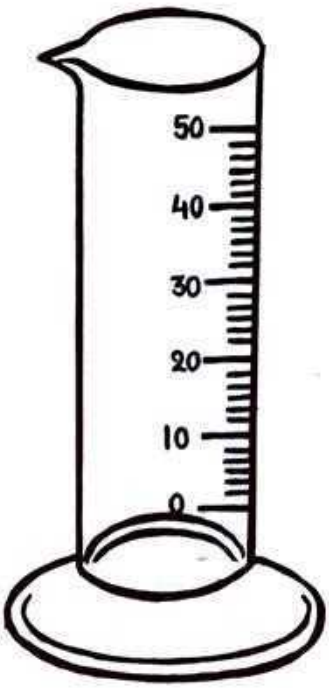
$$Cl^- + AgNO_3 \xrightarrow{dil.\ HNO_3} AgCl + NO_3^-$$

Why Nitric Acid ?

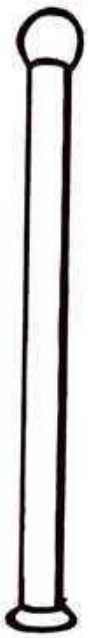
- Nitric acid is added in the solution to make solution acidic
- Dissolve other impurities
- Provide common ion effect and help silver chloride precipitate to make solution turbid at the end of process

Apparatus Required

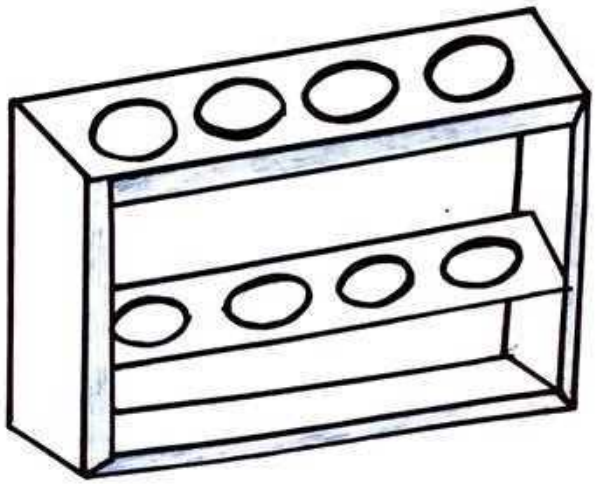
- Nessler Cylinder
- Glass Rod
- Stand



Nessler Cylinder



Glass Rod



Stand

Chemical Required

- Dilute Nitric Acid (10%) [106 ml conc. HNO_3 in 1000 ml water]
- Silver Nitrate (5%) [5g $AgNO_3$ in 100 ml water]
- Sodium Chloride [0.05845 g NaCl in 100 ml water]

Procedure

TEST	STANDARD
• Specific amount of subst. dissolved in nessler cylinder as directed in pharmacopoeia	• Take 1 ml of 0.0584S%. w/v solution of NaCl in a Nessler Cylinder
• Add 10 ml dil. 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

Observation

- If turbidity of test solution is les than turbidity of standard solution then sample will pass the limit test.
- If turbidity of test solution is greatre than turbidity of te standard solution limit test falls.

Limit Test For Sulphate

Principle :

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

Apparatus Required

- Nessler Cylinder
- Glass Rod
- Stand

Chemical Required

- Dilute Hydrochloric Acid
- Standard potassium sulphate sol.
- Barium sulphate reagent

  [Prepared by mixing 15 ml of 0.5 m $BaCl_2$ + 55 ml of water + 20 ml alcohol + 5 ml 0.0181 % w/v K_2SO_4 then diluted to 100 ml]

Role of HCl

- Provide acidic medium
- Prevent Ppt. of other radicals

Chemical Reaction

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

Procedure

TEST	STANDARD
• Dissolve specific amount of substance in nessler cylinder as directed in pharmacopoeia	• 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

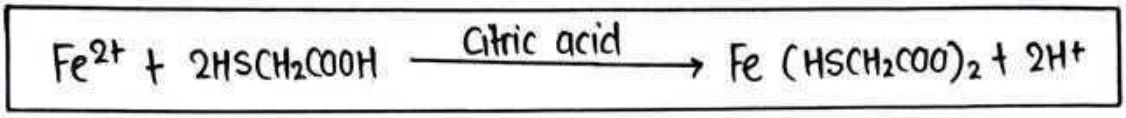
Observation

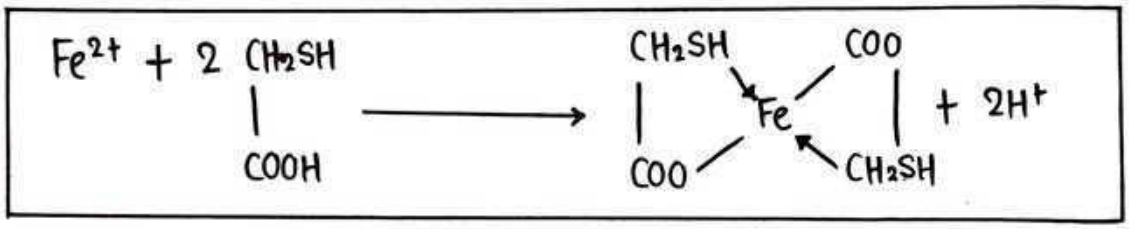
- If turbidity of test solution is less than turbidity of standard solution then sample will pass the limit test
- If turbidity of test solution > turbidity of standard solution limit test fails.

Limit Test For 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 and citric acid to form ferrous thioglycolate complex which appears as pale pink to deep-reddish purple colour





Apparatus Required

- Nessler Cylinder
- Glass Rod
- Stand

Chemical Required

- Standard Iron Solution (Ferric ammonium sulphate)
- Iron free citric acid
- Thyglycolic acid
- Iron free ammonia solution

Role Of Reagents

- Thipglycolic acid : Convert ferric (Fe^{3+}) ions into Ferrous (Fe^{2+}) ions
- Ammonia : Provide alkaline medium
- Citric acid : Prevent precipitation of Iron with ammonia

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 with 20 ml water	• Dilute with 20 ml 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
• Dilute the solution ~~with~~ 50 ml with water & observe.	• Dilute the solution to 20 ml with water

Observation

- If the intensity of colour of test solution is less than intensity of colour of standard solution then sample pass the limit test
- If Intensity of colour of test solution > Intensity of colour of standard solution, sample fails the limit test.

Limit Test For Arsenic

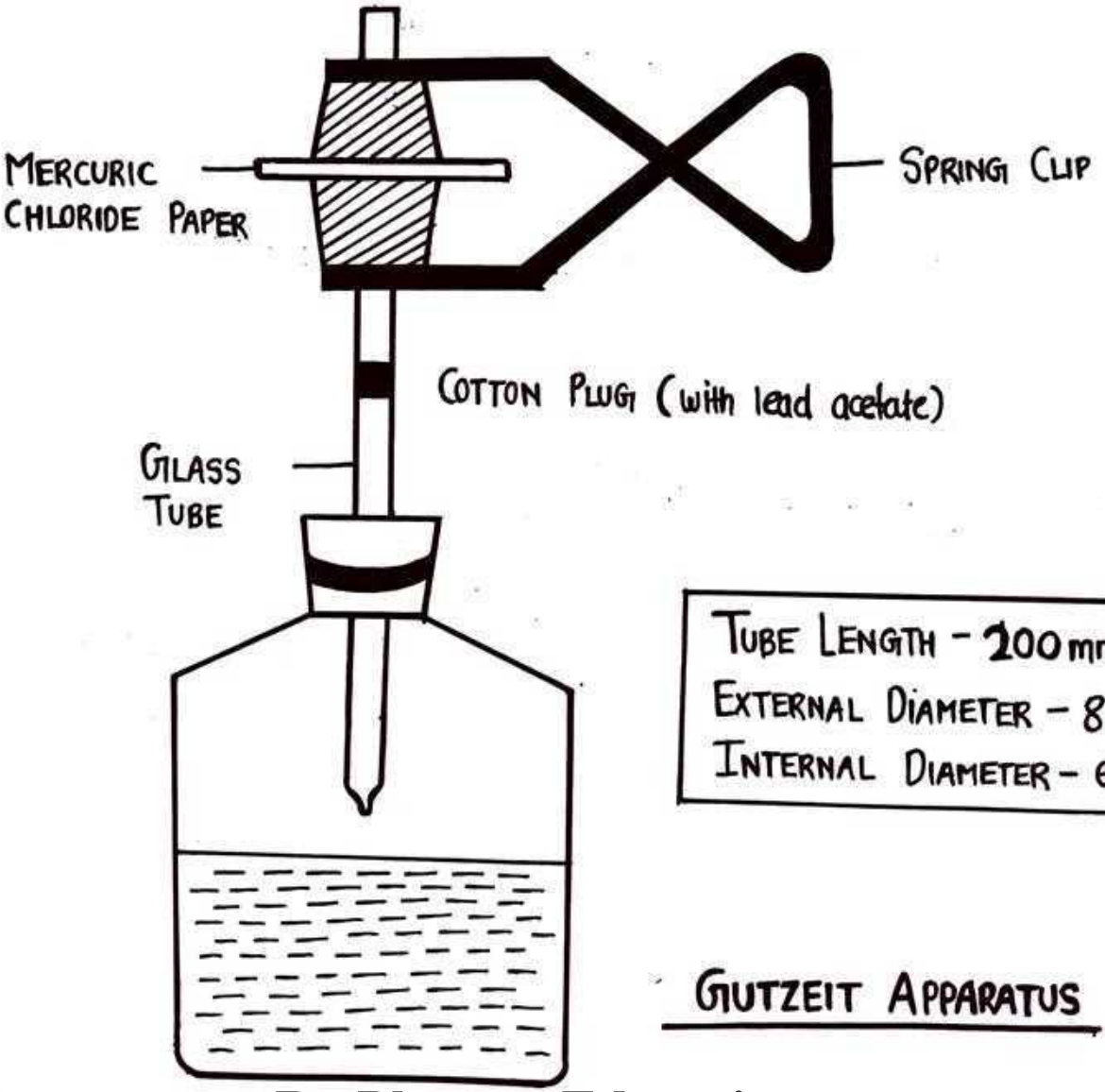
Principle :-

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

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

Apparatus Required

- Gutzeit Apparatus
- Glass Rod
- Stand



TUBE LENGTH - 200 mm
EXTERNAL DIAMETER - 8 mm
INTERNAL DIAMETER - 6·5 mm

GUTZEIT APPARATUS

Chemical 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 potassium Iodide
• To this add 5 ml $SnCl_2$	• Add 5 ml stannous chloride
• Now add 10g granulated zinc	• Add 10g granulated zinc
• keep the solution aside for 40 minutes	• keep the solution aside for 40 minutes.

Observation

- Stain produced by test < stain produced by standard, sample pass the limit test.
- Stain produced by test > stain produced by standard, sample fails the limit test.