Subject :- Pharmaceutical Inorganic chemistry
Sub code :- BP304TP.

Chapter- 1

(1) Write an information note on pharmacopoeia & pharmacopoeial monograph ?

→ Pharmacopeia

→ pharmacopeia is a government official book that include standard of drug test by identification, Efficacy & potency to be maintained strictly

→ It consist all information about medicine, their preparation, their assays, about drug other dosage forms available of drug. their respective

→ Their are different types of p'copoeia published by different country such as.

1) I.P (Indian p'copoeia)
2) B.P (British p'copoeia)
3) U.S.P (United state of p'copoeia)
4) E.P (European p'copoeia)
5) martindale

It consists of three different mainly parts.

1) Appendix and general notices
2) Monograph
3) Introduction, Index

→ pharmacopeial monograph.

- It is an important part of p'copeia consisting all information about drugs.

The p'copeeial monograph consists of :-

1) main title :- The name of API or their formulation

2) Synonyms :- The common name of dry substance.

3) Chemical Formul & Molecular weight :- It provide The IUPAC name of compound as well as its mol. weight

4) Category :- It indicate the use of drug in medicine & p'centRelated E.g :- Antibacterial, antimalarial, diuretics, Emetics, Expectorants Etc.

5) Dose :- Represents the Avg. range of Quantity Suitable for adults.

6) Description :- This includes the general characteristics of p'central Subst. Eg :- physical state, odour, byte, Smell, type of compound etc.

7) Solubility :- Give the type of solubility in the Standards.

8) Standards :- Prescribes the Standard of purity & strength

9) Identification :- This includes some specific & some non-specific test for Identification of Compound

10) Test for Purity :- These tests include melting point, boiling point; limit test of chlorides, sulphate, iron Heavy metals, lead & Arsenic, etc.

11) Method of Assay :- The term 'Assay' is used in pharmacopoeia for Quantitative determination of percentage purity of compound or substance

12) Storage :- Prescribes some conditions for the storage

2 Give a brief note on Indian pharmacopoeia

Indian pharmacopoeia

→ It is an government official book which provide standard of drug test by identification, Efficacy & potency to be maintained strictly.

→ It is an official medicinal preparation book consisting all information of drugs, medicines, dosage forms & other products published by legislative Authority named as "Indian Pharmacopoeia Commission", (IPC)

→ The First edition of I.P was published in 1955 by IPC under the chairmanship of Dr. B.N Ghosh.

→ The second Edition of I.P was published in 1966 by IPC

→ The third edition of I.P was published in 1985 by I.PC in which Indigenous drugs were removed, only Quality std. drugs were included.

→ The Fourth Edition of I.P was published in 1996 by IPC.

→ The Fifth edition of Indian pharmacopeia was published in 2007 by I.Pc which includes herbal medicines & preparations
- It also includes newer methods of analytic techniques such as I.R Spectroscopy HPLC etc.

- The 6th edition of IP was published in 2010 by IPc in which pyrotoxic test was replaced by bacterial endogenic test and Abnormal toxicity test was removed

- The 7th edition of IP was published in 2014 by IPC

- The 8th edition of I.P was published in 2018 by IPC which is classified from volume-I to volume-4

- The 4th ics well as latest edition of Indian pharmacopeia is published in oct-2022 by IPC which is also available in the form of CD's & DVD's.

3. Discuss the source of impurity in pharmaceutically OR Enlist the source of impurities in pharmaceutical & dicuss the manufacturing hazards as source of imp

→
- reagents used
- reagents used to eliminate
- solvents used impurit
- Atmospheric contamination

4. manufacturing process

1. Raw materials → 2. Intermediate → 3. Final product.

packaging

5. manufacturing hazards.

- Contamination from matter
- cross contamination
- contamination by microbes

6. Storage
↓
instability
↓
physical, chemical, temp., light

- Manufacturing hazards.

- The manufacturing hazards are the main sources of impurities, which is classified as follows.

i) Particulate contamination

- The presence of unwanted particulate matter such as dust, dirt glass or metal fragments present in our pharmaceutical is known as particulate contamination

E.g:- metal particles found in eye ointments packed in metal tubes

ii) Error in process :-

- It may occur due to incomplete or inappropriate process followed during manufacturing

iii) Cross-contamination :-

- The mixing of unwanted excipients / API of the other pharmaceutical with a particular pharmaceutical preparation is called as cross cont.

E.g:- mixing of Paracetamol dust in Penicillin during manufacturing.

(iv) microbial contamination :-

- The presence of unwanted microbes or any other microorganisms may result into microbial contamination
- It is an imp. step for parenteral & opthal. prep. to pass the check test for microbial prep. as they have to prepared sterile soln.

Eg :- Acacia, tragacanth should be controlled for Salmonella a type of bacteria.

(v) Packaging errors :-

→ Products of similar appearance such as Tablet of same size, shape, colour packed in similar containers can constitute a potential source of danger

→ Improper labelling or destruction of stable of also constitutes a major packaging error

→ Instability of product in pharmacy

→ different types of pharmacy, when prepared have to be stored in diff. types of containers depending upon

nature of material
Batch size
Quantity

Date
Page

→ many types of materials are used for storage purpose like Plastic, Polythene, iron vessels, stainless steel & aluminium

- reaction of these subst. with materials of storage vessels, the products which are formed are found as impurities in stored materials

Leaching Out Effect :-

- Alkalies stored in ordinary glass containers, it will extract lead from it, which is found as impurity in final product.

- Strong chemicals react with iron containers and extract Iron as impurity in final product

- In adequate storage & their effects are as follows :-

a) Filth :-

Stored products may become contaminated with dust, bodies of insects, Animal & insect Excreta

b) Chemical instability :-

→ decomposition, base of right types of acids or alkali, air oxidation, water vapour, CO_2 & traces of metallic ions.

E.g :- light sensitive materials should be stored in amber coloured bottle

c) physical instability :-

→ The occurence of changes in physical form of drug like change in crystal size can lead change in Efficacy of the product.

d) Reaction with container :-

E.g :- salicylic Acid ointments must not be stored in metal tubes

e) Temperature Effect :-

- Chemical & physical changes occur if materials are not stored at proper temperature

Sources of impurities

1. Raw materials
2. Method of manufacturing
   - Reagents used
   - Reagents used to eliminate impurities
   - Intermediate products
   - Solvents used
   - Atmospheric contamination
3. Manufacturing hazards
   - Contamination with matter
   - Contamination with microbes
   - Cross contamination
   - Error in Storage & Packing
   - Error in manufa
4. Instability of Products
   - chemical instability
   - physical instability
   - Temp.
   - R×n with container

4 Discuss the limit test of chloride in detail.

→ **limit test :-** limit test are quantitative or semiquantitative test designed to identify & control small Amt. of impurity which are likely to present in the Subst

limit test of chlorides :-

- **principle :-**

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

white ppt.

→ dissolve sp
Amt of
Nessler's
- Add 5ml
- make u
up to 50
Water in
- Add
- Keep
- Obser

Procedure

- The limit test of chloride is based on the rxn of chloride ion with chloride free silver nitrate soln in presence of dilute Nitric Acid

** - dilute Nitric Acid is used to make the Acidic medium to the products formed by chloride & silver nitrate Rxn i.e. AgCl

- This is silver chloride formed in the products as white insoluble ppt. which produces the opalescence / Turbidity

- $AgNO_3$ is used to precipitate chloride ion in the form of silver chloride.

Procedure:

Test sample	Std. sample
→ dissolve specified weighed Amt of sample in water Nessler's cylinder	Take 1ml of 0.05 % w/v of NaCl in Nessler cylinder
- Add 1ml of HNO_3	"
- make up the vol. upto 50ml with water in N. cylinde	"
- Add 1ml of $AgNO_3$	"
- Keep it aside for 5 min	"
- Observe the Turbidity	"

observation :-

- If the turbidity observed in test sample is less than the standard sample, then the limit test of chloride is passed.

5 Define limit test : give the principle, Chemical rxn involved in L.T. of sulphate.

→ Limit test :-

Limit Test is Quantitative or semi-Quant. test used to identify & control the small amt. of impurity present in the substances. 6

→ Limit test of sulphate.

Principle :-

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

Sulphate — Barium chloride — Barium Sulphate (white ppt).

- The L.T of sulphate is based on Reaction betn sulphate ion and Sulphate Free Barium Chloride in the presence of dilute HCl
- This produces the Barium Sulphate as the product in the form of white ppt.

Barium sulphate Reagent :- Alcohol (sulphate free), Potassium sulphate, added to prevent & supersaturation added to increase Barium chloride the sensitivity of test. uniform turbidity which give turbidity / opalescence in soln

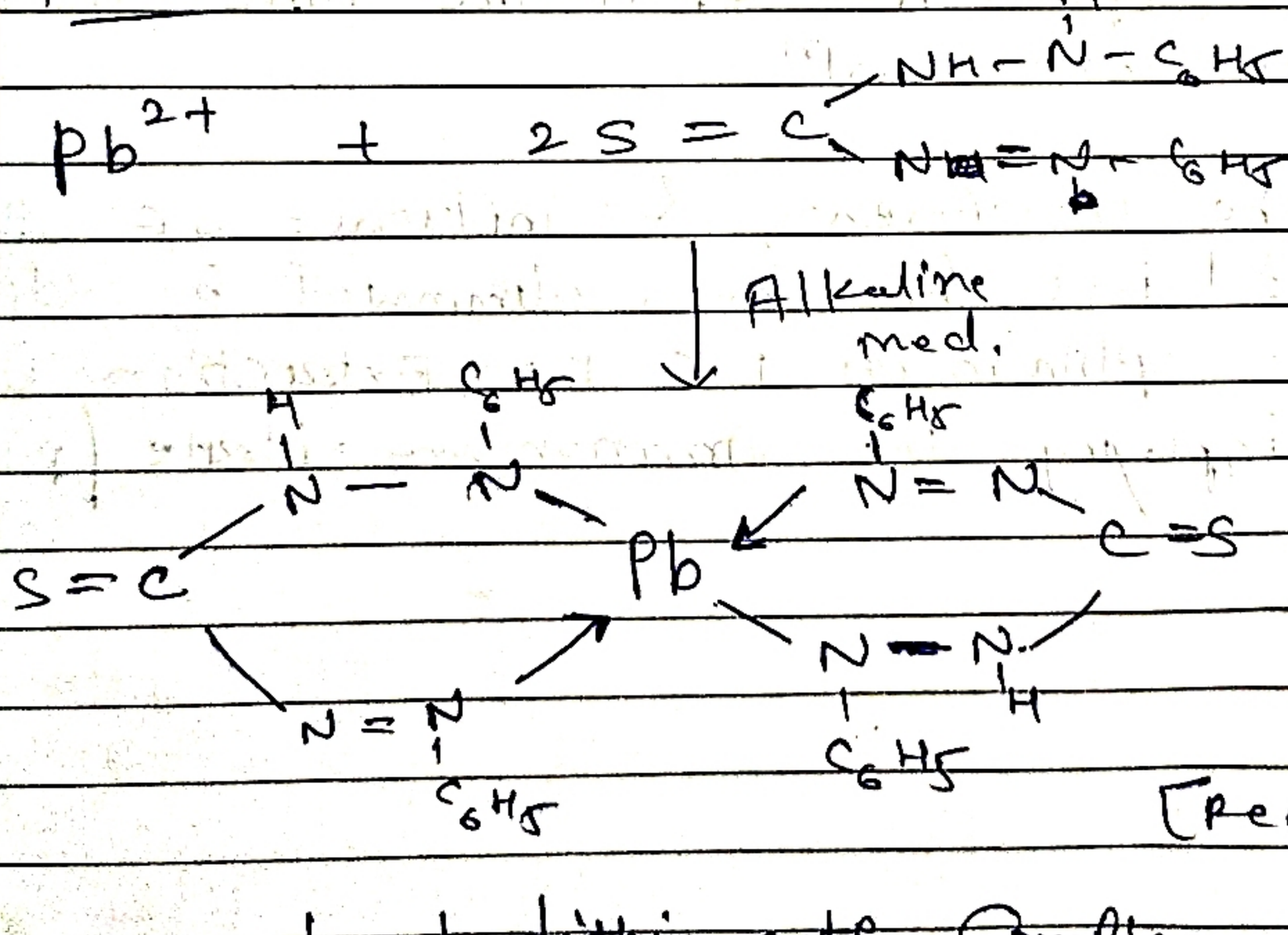
- The turbidity of both test & std. soln is compared to check the Amt. of sulphate present in both the soln,

- In recent times barium chloride is replaced with Barium sulphate reagent. consisting of Alcohol, soln of potassium sulphate & barium chloride.

6 Write a short note on "limit test for lead"?

→ Limit test for lead.

- Principle



[Red colour]

Lead dithizonate Complex

→ L.T of Lead is based on Rxn betn Lead ion & di phenyl thio carbazone (dithizone) in Alkaline medium to form lead dithizon complex which is Red in colour.

→ The dithizone in chloroform helps to leach lead & forms a complex of lead dithizone which is red in colour.

→ The dithizone in chloroform is green in colour which after Rxn changes to Red colour.

→ The intensity of the colour of complex is dependent upon the Amt. of lead in the soln.

→ The interference & influence of other metal ions they been eliminated by adjust the optimum ph for the Extraction by Employing the Ammonium citrate / potassium cyanide

Procedure

Test sample	Standard sample
A known Qnty. of Sample. Soln is transferred in a Separatry funnel	A Std. lead soln is Prepared Equivalent to Amt. of lead permitted in the Sample under Consider
- Add 6ml of Ammonium citrate	"
→ Add 2ml of KCN & 2ml of Hydroxylamine hydrochloride [$HONH_2.HCl$]	"
- Add 2 drops of phenol red as indicator	"
- make the Sol. Alkaline by adding ammonia Solution,	"
→ Extract with 5ml of dithizone untill it becomes green	1.
→ Combine, dithizone Extract are shaken for 30 min with 30 ml HNO_3, Thus Chloroform layer discarded.	1.
→ To Acid soln, Add 5ml of Std. dithizone soln.	1
→ Add 4ml of Ammonium cyanide	1
→ Shake for 30 min → Observe the colour.	1

Q. Discuss the limit test of Arsenic in detail. Draw a neat diagram of Gutzeit App

→ Limit test of Arsenic.

- Arsenic is a well known undesirable and harmful impurity which is present in medicinal substance.

- ~~All pharmacopeia prescribe a L.T~~ -

- All the special reagents used in the Limit Test for Arsenic are marked and distinguished by letter 'AS T' which means they all should be Arsenic free & should themselves confirm the Test for Arsenic.

Principle $As^{3+} \xrightarrow{HCl} H_3AsO_3$ [Arsanious Acid]

$As^{5+} \xrightarrow{HCl} H_3AsO_4$ [Arsenic Acid]

Substance + dil. HCl → H_3AsO_4
[containing as impurity] Arsenic Acid

$H_3AsO_4 + H_2SnO_2 \longrightarrow H_3AsO_3$

Arsenic Acid | Stanous Acid | Arsenious Acid

$H_3AsO_3 + 6[H] \longrightarrow AsH_3 + 3H_2O$

Arsenic Acid — nascent hydrogen — Arsine gas

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

Diarsinomercury.

→ limit test of As is based on the yellow stain produced on the mercuric paper.

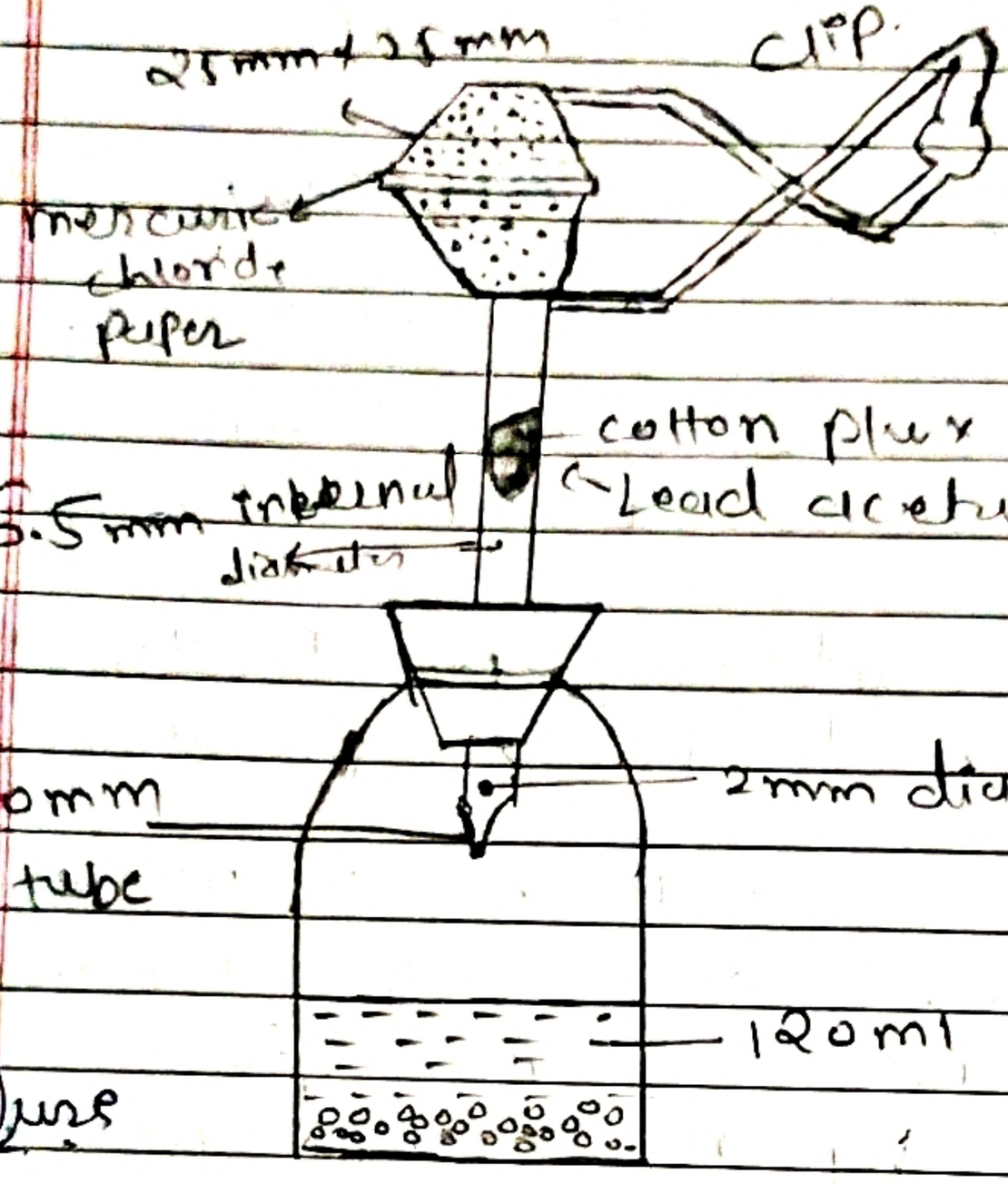
→ The subst. containing As as an impurity reacts with dil. HCl to produce Arsenic acid.

- This Arsenic Acid further reacts with stannous acid which is reducing agent to produce Arsenous Acid. It is further reduced by nascent hydrogen to form Arsine gas.

- This Arsine gas passes through Gutzeit test Apparatus to mercuric paper producing yellow stain.

- This stain of Std. & Test Sample Compared. The amt. of As can be estimated by the intensity of the colour produced.

(*) Gutzeit test apparatus :-



Procedure

Test Sample	Stand. comp.
→ The test sol. is prepared by dissolving specific amnt. in water & std. HCl (Arsenic Free) & kept in a wide mouth bootle.	A known Qnt. of Arsenic soln in water with stanned HCl (As free) which kept in wide mouth bottle
Add 1 gm of KI	"
5 ml of Stannous chloride soln.	"
10 g of zinc granulate	"
- Keep soln aside for 40 min	- Keep the soln as

→ The stain obtained on mercuric chloride paper is compared with standard soln. It must be freshly prepared as it fades on keeping.

Observation :-

- If the stain produced by of test soln is less than of standard soln. So, The L.T of AS. is passed

8 Explain principle of limit test of Iron and Arsenic.

→ Principle of Limit Test of Iron

Fe^{2+} + 2 CH_2SH (COOH) —citric Acid→ Iron Thioglycolate (pale pink to deep reddish purple colour) + $2H^+$

Thioglycolic Acid.

→ The limit test of Iron is based on the Rxn of Iron with thioglycollic Acid to produce ferrous Thioglycolate in Alkaline medium.

→ this ferrous thioglycolate complex produces purple colour in Alkaline medium, thus Ammonia is used,

→ but, Ammonia may form complex with Iron of ferrous hydroxide, to prevent this complex formation, we are using citric Acid,

- Thioglycollic acid is used to form complex with Iron as well as it also reduces Ferric ion into Ferrous ions.

→ The intensity of the colour depends on the Amt. of Iron present in Sample which is compared between test & Standard sample.

→ Principle of Limit Test of Arsenic

Substance + dil. HCl ⟶ H_3AsO_4
(containing as a impurity) Arsenic Acid

H_3AsO_4 + H_2SnO_2 ⟶ H_3AsO_3
Arsenic acid — Stannous Acid — Arsenious Acid

H_3AsO_3 + 6 [H] ⟶ AsH_3
Arsenious Acid — Nascent Hydrogen — Arsine gas

$2AsH_3$ + $HgCl_2$ ⟶ Hg[$(AsH_2)_2$] + 2HCl
Di Arsinomercury.
↓
give yellow stain

The limit test of Arsenic is based on the rxn of Arsine gas on the mercuric chloride paper to produce Yellow Stain

- The substance which contains Arsenic as an impurity is reacted with dilute HCl to produce Arsenic acid.

- This Arsenic Acid is further reduced by Stannous Acid to produce Arsanious Acid. which further reduced by nascent hydrogen to produce Arsine gas.

- This Arsine gas then passed through cotton test apparatus to produce yellow stain on the Mercuric chloride paper.

- The strength of yellow stain produced is compared bet^{n} sample & std. sample.

Q Diff. Assay & Limit test.

Assay	Limit Test.
- Assay is an quantitative method to determine the percentage purity of any comp.	Limit test is an semi Quantitative method used to determine the traces Amount of Impurity Present in the subst.
- It is Quantitative method of Analysis.	→ It is semi-Quantitative method of Analysis
- The main component of the sample is analyzed in Assay	Impurities present in the sample is analyzed in Limit Test

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10 Answer the Following Comments:

(i) Aqueous Ammonia is added in Limit Test of lead ?

→ The above stated statement is true, Bcoz it provides Alkaline medium for the stability of lead dithizone, which gives red colour at alkaline pH.

(ii) Citric Acid is added in limit test of Iron or pH plays an important role in limit test of Iron ?

→ The Above stated statement is True, Bcoz citric Acid is added in limit Test, of Iron to prevent the rxn of Ammonium hydroxide with Iron to form Ferrous Hydroxide Complex, thus citric acid binds with ammonia to form ammonium citrate

(iii) Hydrogen Sulphide is added in L.T of Heavy metals ?

→ The Above stated statement is true, Bcoz Hydrogen Sulphide reacts with metal ions to form colouration in acidic medium, which

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· gives results for all heavy metals.

iv) Dilute Acetic Acid is used in Limit Test for Lead ?

→ The above stated statement is False. The correct statement is that nitric Acid is used in limit test of lead Bcoz Nitric Acid acts as a buffer for the Stabilization of Ammonium citrate & potassium cyanide

(v) Granulated zinc is Used in Limit Test of Arsenic

→ The above stated statement is True, Bcoz as The Function of Granulated zinc in the limit test of Arsenic is high & prolong Evolution of Nascend Hydrogen gas.

(vi) Comment : Limit test is Semi-Quantitative Analysis.

→ The Above stated statement is True, Bcoz, it determine truly Amount of impurities but not Exact conc of impurities could be determined by L.T, Thus it is Semi-Quantitative Analysis.