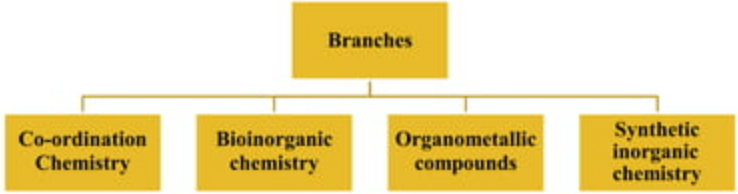
Inorganic Chemistry

- It is the study of all the elements and their compounds except carbon and its compounds (which studied under organic chemistry).
- It describes the characteristics of substances obtained from non-living things/matter and minerals which are found in the earth except the class of organic compounds.



- Application : Chemical industry- Synthesis of drugs, pigments, surfactant and agricultural products
- Examples: Sodium chloride(Nacl) used as table salt, Silicon dioxide(SiO_2) used in computer chips, Sulphuric acid (H_2SO_4) used in production of fertilizers.
- In short, Inorganic chemistry is the branch of chemistry that deals with inorganic compounds

- Inorganic chemistry is the study of all the elements and their compounds except carbon and its compounds (which is studied under organic chemistry).

- Inorganic chemistry describes the characteristics of substances such as nonliving matter and minerals which are found in the earth except the class of organic compounds.

- Branches of inorganic chemistry include coordination chemistry, bioinorganic chemistry, organometallic compounds and synthetic inorganic chemistry.

DIFFERENCE BETWEEN ORGANIC CHEMISTRY AND INORGANIC CHEMISTRY

Organic Chemistry	Inorganic Chemistry
1. Organic chemistry is the study of molecules that contain carbon compounds.	1. Inorganic chemistry is the study of all compounds that do NOT contain carbon compounds.
2. Organic compounds have much lower melting and boiling points	2. Inorganic compounds have much high melting and boiling points
3. organic compounds are less soluble in water	3. Inorganic compounds are soluble in water
4. Organic compounds are more inflammable (more volatile) but are poorer conductors of heat andElectricity.	4. Inorganic compounds are less inflammable Good conductors of heat and Electricity.
5. Organic compounds are derived from activities of living organisms	5. inorganic compounds are formed due to natural processes or are made in lab.

Organic Chemistry	Inorganic Chemistry
6. Organic compounds always contain carbon	6. Inorganic compounds contain metal and other elements.
7. Carbon-Hydrogen bonds are the characteristic of organic compounds	7. Carbon-Hydrogen bonds are not found in inorganic compounds
8. Organic compounds do not contain metal atoms.	8. Inorganic compounds contain metal atoms
9. organic compounds are biological in nature.	9. Inorganic compounds are mineral
10. Organic compounds can be a source of energy for living things.	10. inorganic compounds are catalysts.

DEFINITIONS

1.Abrasives: Drugs which are used for the cleaning and whitening of teeth. Example: Dibasic calcium phosphate.

2. Absorbents: Drugs which are used to absorb the toxins and bacteria in the GIT.

Example: Calcium carbonate.

3.Acidifiers: Drugs which are used to enhance the acidity temporarily in GIT. Example: Dilute hydrochloric acid.

4. Adsorbents: Drugs which are used in the treatment of mild dysentery or diarrhoea or other disturbances of GIT due to their ability to adsorb gases, toxins, and bacteria.

Example: Bismuth subcarbonate, Bismuth subnitrate.

5. Alkalizers: Drugs which are used to induce the alkaline condition or used in acidic condition of body. Example: Sodium citrate.

6. Anaesthetics: Drugs which are used to produce reversible loss of sensation.

Example: Nitrous oxide.

7. Analgesic: Drugs which are used to relieve pain.

8. Antacids: These are drugs which are usually alkaline substances, used for neutralizing excess acid in the stomach.

Example: Aluminium hydroxide gel, Calcium carbonate, Magnesium carbonate.

9. Anthelmintics: Compounds used for the treatment of worm infestations or schistosomiasis.

Example: Ammoniated mercury, Sodium antimony tartarate.

10. Antibacterial: Drugs which are used in the treatment of bacterial infections.

Example: Yellow mercuric oxide (ophthalmic).

11.Anticonvulsants: Drugs which are used for the treatment of epilepsy. Example: Potassium bromide.

12.Anti coagulants: Drugs which are used to prevent blood clotting. Example: Sodium citrate.

13. Anti depressants: Drugs which are used in the treatment of depression.

Example: Lithium carbonate.

14. Antidotes: Drugs which are used in the treatment of poison.

Importance of Inorganic Pharmaceuticals

Inorganic Pharmaceuticals are useful in any of the following ways:

1. For therapeutic purpose: e.g. Astringents, antimicrobials
2. As pharmaceutical aids: Bentonite, Talc
3. To change the reaction of body fluid either by acidifier or alkaliser. e.g. Antacids, alkalies
4. Replacing the normal content of body fluids. e.g. Sodium, potassium, calcium
5. As reagents to carry out the reactions. e.g. catalysts(platinum, nickel), oxidizing and reducing agents
6. In pharmaceutical analysis: Titrants such as potassium permanganate, EDTA

Introduction to Pharmacopoeia

Pharmacopoeia: the word derives from the ancient Greek word Pharmakon means Drug & Poeia means to make.

It is a legally binding collection, prepared by a national or regional authority & contains list of medicinal substances, crude drug & formulas for making preparation from them.

The pharmacopoeia contain-:

- ✓ List of drug and other related substances
- ✓ Sources
- ✓ Description
- ✓ Tests
- ✓ Formulas for preparation actions
- ✓ Uses
- ✓ Doses
- ✓ Storage conditions

Classification of compendia

► Drug compendia are classified as:

1. Official compendia

These are the complications of drug and other related substances which are recognized as legal standards for purity, quality and strength by a government agency of respective countries of their origin.

Examples:

- British pharmacopoeia(BP)
- British pharmaceutical codex(BPC)
- Indian Pharmacopoeia(IP)
- United state Pharmacopoeia(USP)
- National Formulary(NF)

2. Non-official compendia

The books other than official drug compendia which are used as secondary reference sources for drugs and other related substances are known as non-official drug compendia.

Contents of Pharmacopoeia

1. General Notice

General information of Pharmacopoeia and editions

2. Monographs

- Drug Name
- Synonyms
- Category
- Chemical structure & IUPAC name
- Description, solubility, Melting point, Boiling point
- Identification Tests
- Impurity test
- Packaging
- Storage condition

1. Appendices

- Apparatus used for testing
- Standards for Dosage forms
- Labelling Instructions

History of Pharmacopoeia

- The term pharmacopoeia first appears as a distinct title in a work published in Basel, Switzerland in 1561 by Dr.A. Foes, but does not appear to have come into general use until the beginning of the 17th century.

- On 15th December 1820, the first united state pharmacopoeia (U.S.P) was released.

- In 1864, the first british pharmacopoeia (B.P) was published with inclusion of monographs on benzoic acid , gallic acid, tartaric acid, camphor and seven alkaloids along with their salts.
- Todays pharmacopoeias mainly focus on assurance of quality of products by various tools of analytical sciences

INDIAN PHARMACOPOEIA

- **Indian Pharmacopoeia Commission (IPC)** is an autonomous institution of the Ministry of Health and Family Welfare which sets standards for all drugs that are manufactured, sold and consumed in India

- The set of standards are published under the title **Indian** Pharmacopoeia (IP)

- Vision: The IPC is committed to the promotion of the highest standards for drugs for use in the prevention and treatment of diseases in human beings and animals keeping in view the special features of the pharmaceutical industry in India.

- The process of publishing the first Pharmacopoeia started in the year 1944 under the chairmanship of R. N. Chopra

- In 1948 government of India appointed an Indian Pharmacopeia committee to prepare 'Pharmacopeia of India'

- 1st edition I. P. 1955 was published in the official gazette. Dr. B. N. Ghosh, Chairman
  – Supplement 1960

- 2nd edition I. P. 1966, Dr. B. Mukherji, Chairman, Shankar S.
  – Supplement 1975

- 3rd edition I. P. 1985, Dr. Nityanand, Chairman
  –I Addendum/Supplement 1989
  –II Addendum/Supplement 1991

- 4th Edition I. P. 1996 Dr. Nityanand, Chairman

III Addendum/ Supplement 2000

IV Addendum/ Supplement 2002

- 5th Edition I. P., 2007, Dr. Nityanand, Chairman
- 6th Edition I. P., 2010
- 7th Edition I. P. 2014

V Addendum/Supplement 2015

- 8th Edition I. P. 2018

IV Volumes

OVERALL PHILOSOPHY

- The Indian Pharmacopoeia is the official book of standards and medicines produced in India must comply with the specified standards

- Pharmacopoeial standards are the minimum ones with which a manufacturer must comply before release of a product for sale or distribution

Impurity

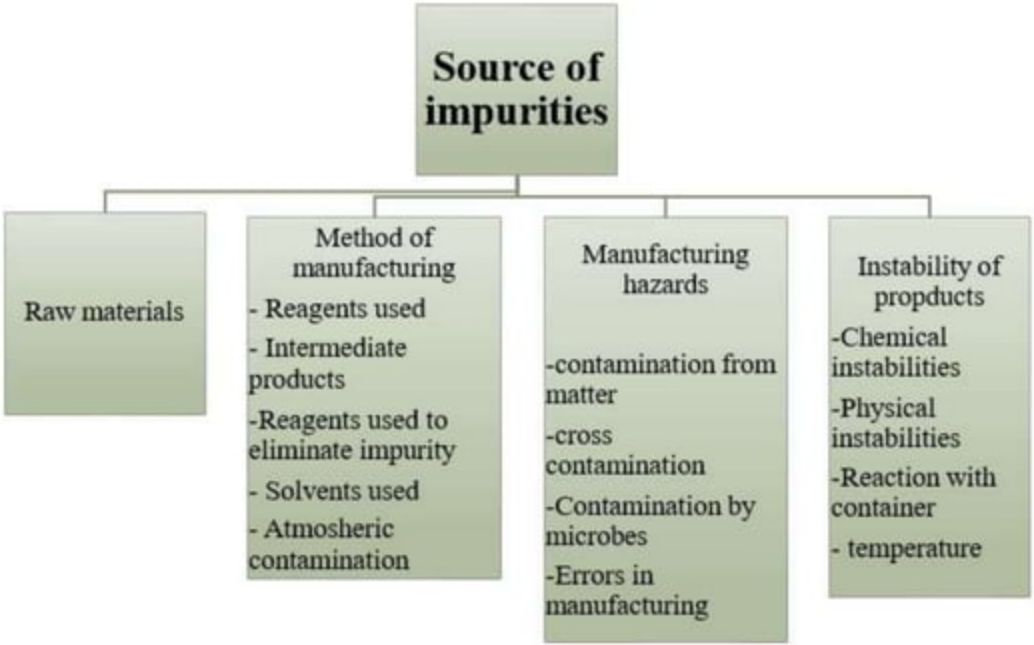
What is impurities.....?

- A foreign unwanted matter present in a compound which are differ from the actual molecular formula.
- According to ICH, an impurity in a drug substance is defined as "any component of new drug substance that is not the chemical entity defined as the new drug substance".
- Chemically a compound is impure if it contains undesirable foreign matter i.e. Impurities. Thus chemical purity is freedom from foreign matter.

Classification of Impurities

A] According to ICH guidelines, impurities associated with API's are classified into the following categories:

- Organic impurities
- Inorganic impurities
- Residual solvents


Source of impurities
Raw materials
Method of manufacturing
- Reagents used
- Intermediate products
-Reagents used to eliminate impurity
- Solvents used
- Atmosheric contamination
Manufacturing hazards
-contamination from matter
-cross contamination
-Contamination by microbes
-Errors in manufacturing
Instability of propducts
-Chemical instabilities
-Physical instabilities
-Reaction with container
- temperature

Sources of impurities

- Impurities are the substances, present in a confined amount of either in liquid, gas or solid preparation which differ from the original chemical compositionof material or compound. These either naturally occurring or added during synthesis of a chemical product.
- Impurities found in medicinal preparations can bring about the following changes:

1. Depress the activity of API.
2. Impart colouring or flavouring substances, e.g.sodium salicyalate.
3. Depressed shelf life of API.
4. Physical and chemical property changes in API.
5. Impurities cause incompatibility among ingredients.

A list of impurities which are likely to be present in a given pharmaceutical substance can be easily complied from the knowledge of the raw materials employed, the manufacturing process and stability of the final product.

The various sources of impurities in pharmaceutical substances are as follows:

Effects of impurities:

Most pure substance is difficult to prepare & that some amount of impurity always remain in the material. The impurities present in the substances may extent the following effects:

i. Impurities which are toxic can be injurious when present above certain limits.

ii. Impurities even present in traces may exert a cumulative toxic effect after some time.

iii. Impurities can cause incompatibility with other substances.

iv. Impurities may cause a change in physical and chemical properties of substances thereby making it medicinally useless.

v. Impurities are sometimes harmless. However if present in such large proportions that the active strength of the substance get lowered, its therapeutic effect gel decreased.

vi. Impurities though harmless in nature may cause changes in odour, thereby making the use of substance unhygienic.

vii. Impurities may decrease the shelf life of the product.

viii. Impurities may bring out the technical difficulties in the formulation, and use of the substance.

Tests for purity

- Pharmacopoeia prescribes the "test for purity" for pharmaceutical substances to check their freedom from undesirable impurities.
- Pharmacopoeia will decide and fix the limit of tolerance for these impurities.
- For certain common impurities for which pharmacopoeia prescribes the test of purity are:

- ✓ Colour, odour, taste
- ✓ Physicochemical constants(Iodine value, saponification value, melting point, refractive index)
- ✓ Acidity, alkalinity, Ph
- ✓ Humidity (estimation of moisture)
- ✓ Cations and anions
- ✓ Ash
- ✓ Arsenic or lead
- ✓ Loss on drying
- ✓ Loss on ignition

- Control of impurities

Pharmacopoeial method: official monographs for pharmaceutical substances provide description & information in addition to prescribing standards for the product and its storage conditions. An official monograph for a pharmaceutical substance generally includes the following:

1. Title
2. Chemical formula
3. Chemical names
4. Category
5. Dose
6. Description
7. Solubility
8. Storage
9. Standards as determined by the assay
10. Identification tests
11. Test for purity including limit tests
12. Assay

Limit Tests

Why Limit tests???

- ✓inorganic impurities are toxic at low levels, and these impurities should be monitored to ensure safety
- ✓Sources of inorganic impurities include those that are deliberately added to the process (e.g., catalysts),
- ✓undetected contaminants from starting materials or reagents
- ✓leaching from pipes and other equipment
- ✓from naturally derived plant or mineral sources
- ✓the level of each inorganic impurity should not exceed the limit defined in *or otherwise specified in the individual monograph.*

What is Limit Test.....?

Limit = A value or amount that is likely to be present in a substance. **Test** = to examine or to investigate

Impurities = a foreign matter present in a compound.

Limit test is defined as quantitative or semi-quantitative test designed to be identify and control small quantities of impurity which is likely to be present in the substance.

It is generally carried out to determine the inorganic impurities present in the compound. These is nothing but to identify the impurities present in the substance and but also to compare it with the standards.

Method use for limit tests

Comparison method

- ✓ Test of this type require a standard containing a definite amount of impurity, to be set up at the same time and under the same conditions as the test experiment.
- ✓ In this way the extent of the reaction is readily determined by direct comparison of the test solution with a standard of known concentration.
- ✓ E.g. limit test of chlorides, sulphates , arsenic etc.

► Limit test for Chlorides

Principle: Based on the simple reaction between simple nitrate and soluble chloride to obtain silver chloride which is insoluble in dilute nitric acid.

$$Cl^- + AgNO_3 \xrightarrow{\text{Dil } HNO_3} AgCl + NO_3$$

The silver chloride produced in the presence of dil.HNO_3 makes the test solution turbid, the extent of turbidity depending upon the amount of chloride present in the substance.

The standard solution prepared and compare with test solution.

Reasons: Nitric acid is added in the limit test for chloride to make solution acidic and helps silver chloride precipitate to make solution turbid at the end of process.

Apparatus required:

1) Nessler cylinder
2) Glass rod
3) Stand

Chemicals required:

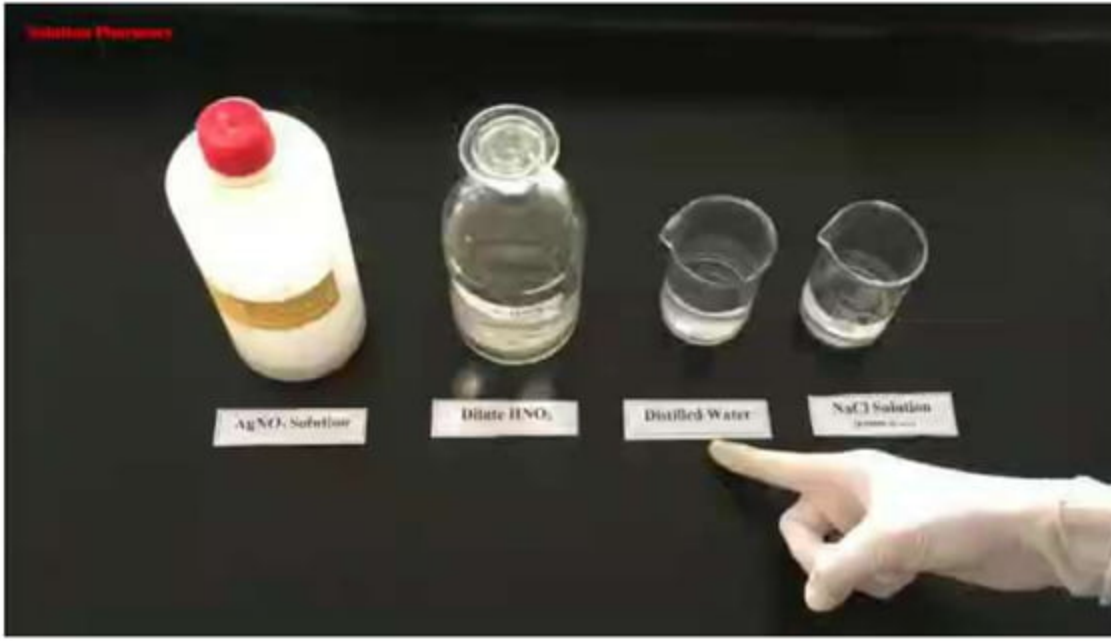
1) Dilute nitric acid
2) Silver nitrate
3) Sodium chloride

Procedure:

Test sample	Standard sample
1. Specific weight of compound is dissolved in water or solution is prepared as directed in the Pharmacopoeia and transferred in Nesseler cylinder	1. Take 1ml of 0.05845% w/v solution of sodium chloride in Nessler cylinder.
2. Add 1ml of dilute nitric acid	2. Add 1ml of dilute nitric acid
3. Dilute to 50ml in Nesseler cylinder	3. Dilute to 50ml in Nessler cylinder
4. Add 1ml of $AgNO_3$ solution	4. Add 1ml of $AgNO_3$ solution
5. Stir with glass rod and Keep aside for 5 min	5. Stir with glass rod and Keep aside for 5 min
6. Observe the opalescence/turbidity	6. Observe the opalescence/turbidity

The opalescence in the test and standard solution are compare.

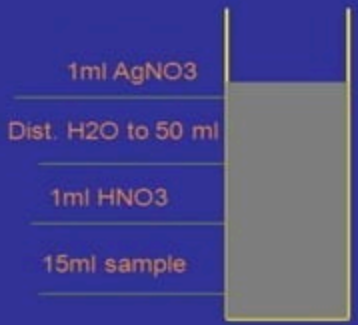

Nessler cylinder
50
50


AgNO3 Solution
Dilute HNO3
Distilled Water
NaCl Solution

Limit Test for Chloride

Principle:

$Cl^- + AgNO_3 \longrightarrow AgCl$



Observation :

The opalescence produced in sample solution should not be greater than standard solution. If opalescence produces in sample solution is less than the standard solution, the sample will pass the limit test of chloride.

Results and conclusion :

If the opalescence in the sample is less than the standard, it passes the test. If it is more than the standard, it fails the test.

For comparison opf turbidity for different substances to be used is varied, and not the standard turbidity. Pharmacopoeia do not give a numerical value to the limits, as is not practicable as its content will be influenced to great extent, by large quantities of other substances present.

Modified chloride limit test

Glassware's required:

1) Nessler cylinder
2) Measuring cylinder
3) Glass rod

Chemicals required:

1) Dilute nitric acid
2) 0.1M Silver chloride
3) Conc. HCl
4) Distilled water

Principle:

limit test of chloride is based on the precipitation reaction. The precipitates of chlorides develop on reaction of soluble chloride with silver nitrate in the presence of dilute nitric acid to form silver chloride, which appears as solid particles (opalescence) in the solution. The intensity of turbidity depends on the amount of chlorides present in test substance.

Procedure:

With reference to International Pharmacopoeia 6th edition 2016, the limit test of chloride has been modified in the context of standard solution preparation. Earlier the standard solution of chloride was prepared by dissolving sodium chloride(NaCl, known Cl^- impurity) but now it has been modified by using hydrochloric acid (HCl) instead of sodium chloride(NaCl).

Conclusion :

If opalescence produced in sample solution is less than the standard solution, the sample will pass the limit test of chloride.