UNIT – 1

Impurities in Pharmaceutical Substances:

History of Pharmacopoeia:

- Pharmacopoeias are official compendia of drug standards and specifications. They have a long history, dating back to ancient civilizations. Notable pharmacopoeias include the Indian Pharmacopoeia, British Pharmacopoeia, United States Pharmacopeia (USP), and European Pharmacopoeia (Ph. Eur.), among others. These compendia provide guidelines for the quality and purity of pharmaceutical substances.

Sources and Types of Impurities:

1. **Extrinsic Impurities:** These are contaminants that are not part of the drug's composition but can be introduced during manufacturing, storage, or handling. Examples include dust, microorganisms, and cross-contaminants from equipment.
2. **Intrinsic Impurities:** These impurities are inherent to the drug substance and may include degradation products, residual solvents, and related substances.
3. **Foreign Impurities:** Substances that are not intended to be present in the drug product but may be introduced from various sources.
4. **Degradation Products:** Impurities formed due to drug decomposition over time, often related to factors like temperature, humidity, and exposure to light.
5. **Residual Solvents:** Solvents used in the drug's manufacturing process that may remain in the final product.
6. **Related Substances:** Compounds that are structurally related to the drug and are present in the formulation.

Principle Involved in the Limit Test for Specific Impurities:

- Limit tests are analytical tests designed to determine whether a specific impurity in a pharmaceutical substance or product exceeds a predefined acceptance criterion. These tests are based on specific chemical reactions or color changes. Here are some examples of limit tests:

1. **Chloride Limit Test:**
    - Principle: This test involves the reaction between chloride ions and silver nitrate to form a white precipitate of silver chloride.
    - Acceptance Criterion: The sample's chloride content should not exceed a specified limit.
2. **Sulphate Limit Test:**
    - Principle: This test is based on the reaction between sulphate ions and barium chloride to form a white precipitate of barium sulphate.
    - Acceptance Criterion: The sample's sulphate content should not exceed a specified limit.

3. **Iron Limit Test:**
    - Principle: Iron is reacted with a reducing agent, such as hydrochloric acid and stannous chloride, to form a blue color complex.
    - Acceptance Criterion: The iron content in the sample should not exceed a specified limit.
4. **Arsenic Limit Test:**
    - Principle: Arsenic impurities can be detected using various methods, including the Gutzeit test, which involves the generation of arsine gas and its reaction with silver nitrate to form a brown or black precipitate.
    - Acceptance Criterion: The sample's arsenic content should not exceed a specified limit.
5. **Lead Limit Test:**
    - Principle: Lead impurities can be detected using various methods, including the formation of a yellow color complex when reacted with potassium chromate.
    - Acceptance Criterion: The sample's lead content should not exceed a specified limit.

Modified Limit Test for Chloride and Sulphate:

- Modified limit tests involve specific procedures that may differ from the traditional methods but are designed to achieve the same objectives. For chloride and sulphate limit tests, modifications may include using alternative reagents or techniques while maintaining the fundamental principles outlined above.

Understanding and implementing limit tests for specific impurities is critical in pharmaceutical quality control to ensure that drug substances and products meet safety and efficacy standards. Limit tests help identify and quantify impurities within acceptable limits to safeguard patient health and product quality.