IMPURITY

• A compound is said to be impure if it is having foreign matter. Pure chemical compound refer to that compound which is having no foreign matter i.e., impurities.

• Purification of chemicals is an expensive process, substances should not be purified more than required as it brings about waste of time, material and money.

• Sugarcane, dextrose, inorganic salts 99% purity while many other only are having traces of impurity.

• Pure Relative term Pharmacopoeia of India and BP has been prescribed test for purity.

The standards demanded for chemicals for pharmaceutical use may be determined by a number of factors, which take account of impurities likely to arise because of all known method of manufacture.

The pharmaceutical preparation should be free from toxic and other impurities. Pharmacopoeia prescribe limits for harmful compound present in substances.

**Impurities commonly found in Medicinal preparations:**

1. Activity depressing impurities.
2. Due to colouring or flavouring substances, *e.g.*, Sodium Salicylate.
3. Humidity.
4. Decrease shelf life.
5. Physical and chemical properties.
6. Impurities due to which substances become incompatible.

**SOURCES OF IMPURITIES**

A list of impurities which are likely to be present in a given pharmaceutical substance can be easily compiled from the knowledge of the raw materials employed, the manufacturing process and stability of the final product. Impurities may also arise from physical contamination and improper storage conditions. The various sources of impurities in pharmaceutical substances are as follows:
1. Raw Materials Employed in the Manufacturing of the Pharmaceutical Substance

Pharmaceutical substances are either isolated from natural sources or synthesized from chemical starting materials. The natural sources include mineral sources, plants, animals, and microbes. It is essential to verify the identity of the source material and to establish its quality otherwise impurities associated with the raw materials may be carried through the manufacturing process to contaminate the final product. In nature minerals rarely occurs in a reasonably pure form. Almost always mixtures of closely related substances occur together e.g., aluminum ores are usually accompanied by alkali and alkaline earth compounds, barium and magnesium impurities are found in calcium minerals, zinc accompanies magnesium or iron compounds, lead and heavy metals are found as impurities in many sulphide ores, among the acid radicals or anions, bromides and iodides are often found as impurities in chlorides, bismuth salts contains silver copper and lead as impurities.

Rock salt used for the preparation of sodium chloride is contaminated with small amounts of calcium and magnesium chlorides, so that sodium chloride prepared from rock salt will definitely contain traces of calcium and magnesium compounds impurities.

2. Method of Manufacture

The process or method of manufacture may introduce new impurities into the final product arising due to contamination by reagents, catalysts and solvents employed at various stages of the manufacturing process. The new impurities may also arise from the reaction vessels and reaction intermediates.

(A) **Reagents employed in the manufacturing process:** Calcium carbonate contains ‘soluble alkali’ as impurity which arises from the sodium carbonate (Na₂CO₃) employed in the process. Calcium carbonate is prepared by the interaction of a soluble calcium salt with a soluble carbonate. Therefore, the final product (CaCO₃) is liable to contain small amount of ‘soluble alkali’ as impurities which were not removed by the washing process.

\[
\text{CaCl}_2 + \text{Na}_2\text{CO}_3 \rightarrow \text{CaCO}_3 \downarrow + 2 \text{NaCl}
\]

Anions like Cl⁻ and SO₄²⁻ are common impurities in many substances because of the use of hydrochloric acid and sulphuric acid respectively in processing. Barium ion may be an impurity in hydrogen peroxide so, hydrogen peroxide employed as reagent in the manufacturing process can contaminate the final product.

(B) **Reagents used to eliminate other impurities:** Barium is used in the preparation of potassium bromide to remove sulphate which in turn arise form the bromine used in the process. It is likely that potassium bromide will now be contaminated by traces of barium.

(C) **Solvents:** Most of the pharmaceutical substances are prepared in solvated crystalline form. Small amounts of solvents employed in preparation, and purification of reaction intermediates or the final product may also result in the contamination of the pharmaceutical substances. Water is the cheapest solvent available and is used quite frequently in the preparation of inorganic pharmaceuticals. Water can be the major source of impurities as different types of water containing different types and amount of impurities are available. Various types of water which are available are
(i) **Tap water:** Containing impurities of Ca$^{2+}$, Mg$^{2+}$, Na$^+$, Cl$^-$, CO$_3^{-2}$ and SO$_4^{-2}$ in trace amounts. The use of tap water on large scale will lead to the contamination of the final product with these impurities because the impurities will remain in the product even after washings.

(ii) **Softened water:** It is almost free from divalent cations (Ca$^{2+}$, Mg$^{2+}$) but contains more of Na$^+$ and Cl$^-$ ions as impurities because of the usual chemical water softening process. Therefore, the final products obtained using softened water as solvent will not have Ca$^{2+}$ and Mg$^{2+}$ impurities but still contain Na$^+$ and Cl$^-$ impurities.

(iii) **Demineralized water:** It is prepared by means of ion-exchange and is free from Na$^+$, Ca$^{2+}$, Mg$^{2+}$, Cl$^-$, SO$_4^{-2}$ and CO$_2^{-2}$ etc. It may have pyrogens, bacterias and organic impurities. So, it is a better solvent than tap water or softened water but the economic factors discourage its use on large scale.

(iv) **Distilled water:** It is free from all organic and inorganic impurities and is therefore the best as a solvent but it is quite expensive. As it is free from all impurities, it does not pass on any impurities to the final products.

(D) **Reaction vessels:** The reaction vessels employed in the manufacturing process may be metallic such as copper, iron, cast iron, galvanized iron, silver, aluminium, nickel, zinc and lead. Glass and silica are also used in the construction of the chemical plants but these days many of these are replaced by stainless steel and variety of other alloys. Some solvents and reagents employed in the process may react with the metals of reaction vessels, leading to their corrosion and passing traces of metal impurities into the solution, contaminating the final product. Similarly, glass vessels may give traces of alkali to the solvent. Lead (Pb) may be found as impurity in commercial sulphuric acid which has been manufactured by lead chamber process. Also, substances prepared by same electrolytic process, may contain electrode material as an undesirable impurity e.g., antimony, bismuth etc.

(E) **Intermediates:** Sometimes, an intermediate substance produced during the manufacturing process may contaminate the final product e.g., Sodium bromide is prepared by reaction of sodium hydroxide and bromine in slight excess.

$$6 \text{NaOH} + 3 \text{Br}_2 \rightarrow \text{NaBrO}_3 + 5 \text{NaBr} + 3 \text{H}_2\text{O}$$

The sodium bromate an intermediate product is reduced to sodium bromide by heating the residue (obtained by evaporating the solution to dryness) with charcoal.

$$\text{NaBrO}_3 + 3 \text{C} \rightarrow \text{NaBr} + 3 \text{CO}$$

Sodium bromate Sodium bromide

If sodium bromate is not completely converted to the sodium bromide then it is likely to be present as an impurity.

(F) **Atmospheric contamination during the manufacturing process:** Atmosphere may contain dust (aluminum oxide, sulphur, silica, soot etc.) and some gases like carbon dioxide, sulphur dioxide, arsine and hydrogen sulphide. These may contaminate the final product during the manufacturing process. Some substances which are susceptible to action by atmospheric carbon dioxide and water may get contaminated with them during
their preparation e.g., sodium hydroxide readily absorbs atmospheric carbon dioxide when exposed to atmosphere.

\[ 2\text{NaOH} + \text{CO}_2 \rightarrow \text{Na}_2\text{CO}_3 + \text{H}_2\text{O} \]

Calcium hydroxide solutions can absorb carbon dioxide from the atmosphere to form calcium carbonate.

\[ \text{Ca(OH)}_2 + \text{CO}_2 \rightarrow \text{CaCO}_3 + \text{H}_2\text{O} \]

(G) **Manufacturing hazards:** If the manufacturer is able to control and check impurities from the all above mentioned sources there exists certain manufacturing hazards which can lead to product contamination. The various manufacturing hazards can lead to:

(i) **Contamination from the particulate matter:** The unwanted particulate matter can arise by a number of ways, such as accidental inclusion of dirt or glass, porcelain, plastic or metallic fragments from sieves, granulating, tabletting and filling machines and the product container. The particulate contamination mainly arises from the wear and tear of the equipments. It may also arise from the bulk materials used in the formulation or from dirty or improperly maintained equipments e.g., metal particles found in eye ointments packed in metal tubes made up of tin and aluminum.

(ii) **Cross-contamination of the product:** This manufacturing hazard has to be considered in the preparation of solid dosage forms. Cross-contamination of product can occur by air-born dust arising out of handling of powders, granules and tablets in bulk. Cross-contamination is dangerous particularly in case of steroidal and other synthetic hormones and therefore, it should be carefully controlled. Precautions, such as use of face mask and special extraction equipment can minimize these undesirable contaminations.

(iii) **Contamination by microbes:** Many products, like liquid preparations and creams intended for topical applications are liable to contamination by microbes from the atmosphere during manufacturing. For all products intended for parenteral administration and ophthalmic preparations, sterility testing is done and it provides an adequate control for microbial contaminations in such preparations. Microbial contamination can be controlled by adding suitable antimicrobial and antifungal agents.

(iv) **Errors in the manufacturing process:** Sometimes in a liquid preparation, there is incomplete solution of the solute. This ought to be detected by the normal analytical methods as it can lead to major error. A proper check on the efficiency of mixing, filling, tabletting, sterilization etc. should be exercised in order to obtain a product of maximum purity and desired quality. Special precautions are required to be observed to avoid mixing and filling errors in the preparation of low dosage forms (e.g., tablets and capsules containing highly potent medicaments).

(v) **Errors in the packaging:** Similar looking products, such as tablets of the same size, shape and colour, packed in similar containers can result in mislabeling of either or both of the products. Adequate care should be taken to avoid the handling of such products in the close proximity.
3. Instability of the Product

(A) Chemical instability: Impurities can also arise during storage because of chemical instability of the pharmaceutical substance. Many pharmaceutically important substances undergo chemical decomposition when storage conditions are inadequate. This chemical decomposition is often catalyzed by light, traces of acid or alkali, traces of metallic impurities, air oxidation, carbon dioxide and water vapours. The nature of the decomposition can easily be predicted from the knowledge of chemical properties of the substance. All such decompositions can be minimized or avoided by using proper storage procedures and conditions. The photosensitive substances should be protected from light by storing them in darkened glass or metal containers thereby inhibiting photochemical decomposition. Materials susceptible to oxidation by air or attack by moisture should be stored in sealed containers and if necessary the air from the containers can be displaced by an inert gas such as Nitrogen. Oxidation can also be prevented by adding suitable antioxidants which are capable of undergoing oxidation at the expense of the substances.

(B) Changes in physical properties: Pharmaceuticals may undergo changes in physical properties during storage. There can be changes in crystal size and shape, sedimentation, agglomeration and caking of the suspended particles. These physical changes are not always avoidable and may result in significant changes in the physical appearance, pharmaceutical and therapeutic effects of the product. Particle size and consequently surface area is a critical factor in determining the bioavailability of the low solubility drug such as griseofulvin. Physical changes such as sedimentation and claying in case of multidose suspension may constitute a safety hazard leading to the possibility of under dosage and later to overdosage of the drugs. Similarly increase in the globule size of the injectable emulsions on storage may lead to fat embolism.

(C) Reaction with container material: The possibility of reaction between the container material and the contents cannot be ruled out as it constitutes a safety hazard. Preparations susceptible to reaction with metal surfaces e.g., salicylic acid ointment must not be packed in metal tubes. Solutions of substances which are alkali-sensitive e.g., atropine sulphate injection must be packed in glass ampoules which comply with the test of hydrolytic resistance therefore such preparations must not be packed in containers made from soda glass. Plastic containers and closures must be carefully evaluated because of their tendency to give undesirable additives, such as plasticizers, particularly in the presence of non-aqueous solvents. Plastic containers intended for injectables should be sufficiently translucent to allow visual inspection of the contents and if they are having higher than 500 ml capacity, they must also comply with the test limiting animal toxicity in the cat, ether-soluble extractive and metal additives with special reference to barium and heavy metals like lead, tin and cadmium. Rubber closures are more susceptible to absorb medicaments, antioxidants and bactericides from solution, unless they are appropriately pretreated by immersion in solutions of the concerned compounds.

(D) Temperature: The rate of chemical decomposition and physical changes of stored products depends upon the temperature. The susceptible substances may have temperature storage requirements assigned to them in order to protect them against undesirable decomposition.
CONTROL OF IMPURITIES

Pharmacopoeial Methods

Official monographs for pharmaceutical substances provide description and 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**: It is the official name of the substance. Sometimes the common names or synonyms are also mentioned.

2. **Chemical formulae**: When the chemical structure of the compound is known, the graphic and molecular formulae and the molecular weight are given following the title. A chemical formula refers to the chemically pure substance and is not an indication of purity of the substance.

3. **Chemical names**: Sometimes the IUPAC name of the substance is also given.

4. **Category**: It is indicative of the medical or pharmaceutical application of the substance. It is generally the more common application, representing the main pharmacological action of the substance or its active ingredient and the substance may possess other uses or activities also.

5. **Dose**: The doses mentioned in the pharmacopoeia are for the general guidance and represents the average range of quantities regarded suitable for adults when administered orally.

6. **Description**: It gives information regarding the general physical and organoleptic properties of the substance. It helps in the preliminary evaluation of the integrity of the article and should not be considered as the analytical requirements.

7. **Solubility**: The solubility of the substance given in the monograph is primarily for information and should not be regarded as standards or test for purity but if a quantitative solubility test is given under ‘STANDARDS’ then the substance should comply with the given requirement. If the exact solubility of the substance is not known, the approximate solubility of the substance is indicated by the descriptive terms. Following table gives the meaning of such descriptive terms for substances at 20 to 30°C.

<table>
<thead>
<tr>
<th>Descriptive term</th>
<th>Approximate volume of the solvent for 1 part of the solute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very soluble</td>
<td>less than 1 part</td>
</tr>
<tr>
<td>Freely soluble</td>
<td>from 1 to 10 parts</td>
</tr>
<tr>
<td>Soluble</td>
<td>from 10 to 30 parts</td>
</tr>
<tr>
<td>Sparingly soluble</td>
<td>from 30 to 100 parts</td>
</tr>
<tr>
<td>Slightly soluble</td>
<td>from 100 to 1000 parts</td>
</tr>
<tr>
<td>Very slightly soluble</td>
<td>from 1000 to 10,000 parts</td>
</tr>
<tr>
<td>Insoluble or practically insoluble</td>
<td>more than 10,000 parts</td>
</tr>
</tbody>
</table>
8. **Storage:** It contains information regarding the storage conditions of pharmaceutical substances so that they can be guarded against possible contamination and deterioration. The precautions need to be taken regarding the effect of atmosphere, moisture, heat and light are also indicated where appropriate in the individual monograph. The temperature conditions related to the storage of pharmaceutical substances are specified in some monographs. The following terms are used in the IP for defining the conditions of temperature.

   (a) **Cold:** Any temperature not exceeding 8°C and usually between 2°C and 8°C. A refrigerator is a cold place in which the temperature is maintained thermostatically between 2°C and 8°C.

   (b) **Cool:** Any temperature between 8°C and 25°C. An article directed to be stored in cool place, may, alternatively be stored in a refrigerator, unless otherwise specified in the monograph.

   (c) **Room temperature:** The temperature prevailing in the working area.

   (d) **Warm:** Any temperature between 30°C and 40°C.

   (e) **Excessive heat:** Any temperature above 40°C.

   (f) **Protection from freezing:** The label of container bears this instruction where, in addition to the risk of breaking of the container, freezing results in a loss of strength or potency or in destructive alteration of the characteristics of an article.

   (g) **Storage under non-specific conditions:** When no specific storage conditions are indicated in the monograph, the storage conditions include protection from moisture, freezing and excessive heat.

9. **Standards as determined by the assay:** It specifies the quantitative purity of the official compound. If an article does not complies with all the stated requirements it is not of pharmacopoeial quality. These requirements are applicable only to those articles that are intended for medicinal use and not to articles that may be marketed under the same name for other purposes.

10. **Identification test:** It includes various chemical tests to verify the identity of the substance. They are not absolute proof of identity.

11. **Test for purity including limits tests:** Different limits for impurities are prescribed for different substances. Test for purity are tests for the presence of impurities in the substance and fix the limits of tolerance for undesirable impurities.

12. **Assay:** It describes the official method for the quantitative determination of the active ingredient of the pharmaceutical substance and its preparation.

**IDENTIFICATION TEST**

The purpose of identification test is to ensure the correct labeling of the substances. Identification tests are specific but they are not necessary sufficient in establishing the absolute proof of identity of the substances. If an articles taken from a labeled container do not meet to the requirements of a prescribed identification test indicates that the articles is either mislabeled or substituted. In same monographs, more than one identification tests are
given. In such cases, if the articles complies with the either one or the other identification test, in sufficient to verify the identity of the article.

Identification tests are generally based upon the combination of simple chemical test and measurement of the appropriate physical constants. There is considerable overlap between identification tests and the limit tests. Limit tests are designed to ensure that the undesirable impurities are within the prescribed limits. Identification tests whether physical or chemical, provided they are sufficiently specific, can be used as the basis of a quantitative estimation or in the design of specific limit tests. Practically, a single identification test may contribute to identification as well as standardization of the substance.

Chemical tests, used for identification are basically qualitative confirming to the presence of the substance under investigation. They may be far too general or lack specificity but can be considered sufficiently specific when used in conjunction with the other requirement of the monograph.

Physical constants such as melting point, boiling point, solubility, weight per ml, refractive index, optical rotation, viscosity etc., have characteristic values for a given substance. They can be used in identification, checking quality and maintaining standard of purity.

**TEST FOR PURITY**

'Test for purity' for substances have been prescribed by the pharmacopoeias of the various countries in order to ensure reasonable freedom from the undesirable impurities. The so-called 'Test for purity' are infact the tests for the presence of impurities in the substance and fix the limits of tolerance for these undesirable impurities. Test for purity are not framed to guard against all the possible impurity rather they provide appropriate limitation of the potential impurities only.

The guiding factor for fixing a limit of tolerance for the various impurities is the amount of impurity that is likely to be harm. Arsenic and lead are quite dangerous even in trace amounts therefore very small limits of tolerance have been fixed for their presence in all pharmaceutical substances. Another factor is the practicability of the commercial method of production of the substance meeting the requirements of a particular standard of purity. It would be useless to fix the limits of tolerance which can only be attained at a very high cost. There are cases in which the limits fixed in the pharmacopoeia were later relaxed because they were found to be too difficult to attain by the available methods of manufacturing.

The ultimate objective is that the pharmaceutical substances if not completely free from the undesirable or toxic impurities should be of reasonable good purity ensuring therapeutic safety. The presence of sodium bromide (NaBr) in the more expensive potassium bromide (KBr) is not likely to cause any harm to the patient but at the same time the KBr should be of sufficiently good pharmaceutical quality and purity not containing excess amount of sodium bromide. Some of the tests which may be undertaken to ascertain the purity of a substance are:

(a) **Clarity of solution:** The degree of clarity or opalescence of solution is measured by direct comparison with a reference solution having standard opalescence. The comparison is against a black background by viewing vertically downward under diffused light. A solution
SOURCES OF IMPURITY

is considered clear if its clarity is the same as that of water or of the solvent employed in the preparation of the solution being examined.

(b) **Colour of solution:** In Indian Pharmacopoeia, the colour standards are based on three primary colorimetric solutions: yellow, red and blue prepared from ferric chloride, cobaltous chloride and cupric sulphate respectively. These primary solutions are mixed in various proportions with or without 1% w/v hydrochloric acid to give five reference colour solutions which are yellow (YS), greenish yellow (GYS), brownish yellow (BYS), brown (BS), and red (RS). The colour of the solution is compared with reference colour solution by viewing vertically downwards through the columns of liquids in diffused light. A solution may be considered as colourless if it has the same appearance as water or as the solvent employed in the preparation of the solution being examined.

(c) **Acidity or alkalinity:** Pharmaceutical substances prepared using chemical reactions involving acids and alkalis may possess some degree of acidity or alkalinity resulting from improper purification by inadequate washings after their separation. The limits for acid or alkali impurities are fixed for various pharmaceutical substances and the test for acidity and alkalinity is of great help in determining the extent of such impurities.

(d) **Loss on ignition:** It is the loss of weight in % w/w resulting from a volatile part of any test material that is driven off under specified conditions. It is applied to thermostable substances which contain thermolabile impurities that decompose and lose a volatile product e.g., zinc carbonate decomposes losing carbon dioxide. The substance is heated, cooled and weighed repetitively until a constant weight is attained. The loss on ignition in this case should not be more than 2% w/w.

(e) **Loss on drying:** It is the loss of weight in % w/w resulting from water and volatile matter that is lost under specified conditions. The temperature to which the substance is subjected varies considerably according to the nature of the substance. The temperature applied should not be so high as to cause decomposition of the substance but at the same time it should be sufficiently high to produce the desired results within a reasonable time. It is usually applied by drying the substance to constant weight at 105°C.

(f) **Moisture content:** Sometimes the determination of the moisture content of the substance is a good measure of the purity of the substance especially in case of crude drugs.

(g) **Ash values:** The determination of ash values in crude drugs, organic compounds and certain inorganic compounds provides valuable information regarding the extent of heavy metals and minerals impurities.

**ASSAY**

An assay method should be specific for the substance or chemical species being examined. Nevertheless non-specific assay methods are quite commonly employed particularly in acid-base titrations. Many inorganic salts are assayed by simply determining the content of one of the ions present e.g., sodium sulphate to assayed by determining its sulphate content by precipitating the sulphate as barium sulphate. Although non-specific an assay method can be considered as sufficiently specific when used in conjunction with other requirement of the monograph.
**Assay Tolerances**

Assay tolerances play an important role in fixing standards for pharmaceutical substances. They include the limits of error of the actual assay process for the active pharmaceutical ingredients, the limits of tolerance of manufacturing process for the particular dosage form and the sampling errors. The limits of error of the assay process depend upon the method employed.

Volumetric and gravimetric methods are very accurate and have quite narrow limits of error whereas spectrophotometric assays are not that accurate and have much wider limits of error.

**SOURCES OF CONTROL OF IMPURITIES**

- Washing
- Drying
- Re-crystallization
- Sublimation.

**Washing:** When water soluble substance has to be washed away and water insoluble substances is needed.

Chalk from native CaCO₃, water soluble substances are washed with water and dried and is required to have NLT 97% CaCO₃ on dry basis while precipitate CaCO₃ as water insoluble subs. is required to have NLT 98.5% of CaCO₃ after drying in a manner which is similar to that used for prepared chalk.

**Drying:** Generally dried in air Anhydrous chemicals—Vacuum drying has been an impurified unit operation and needs care and precaution so that chemicals may not deteriorate due to oxidation, caking or mould growth.

**Re-crystallization of solid substances from water:** Re-crystallization is most common method of purifying soluble salts.

With a few exceptions, the solubility of salt in a solvent get ↑ with ↑ in temperature and hence a saturated. Solution is allowed to cool slowly after which crystals of a greater purity could be obtained.

**Sublimation:** Applicable to very few substances e.g., AS₂O₃, I₂, HgCl₂, sublimed sulphur. The organic compounds purified by this process are camphor and benzoic acid.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Impurities</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin-B</td>
<td>Tetraenes</td>
<td>Ultra Violet Spectroscopy</td>
</tr>
<tr>
<td>Atropine Sulphate</td>
<td>Apo Atropine</td>
<td>Ultra Violet Spectroscopy</td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>N,N dimethyl aniline</td>
<td>Gas Chromatography</td>
</tr>
</tbody>
</table>
### SOURCES OF IMPURITY

<table>
<thead>
<tr>
<th>Substance</th>
<th>Impurity</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextrose</td>
<td>5 Hydroxy Methyl Furfural</td>
<td>Ultra Violet Spectroscopy</td>
</tr>
<tr>
<td>Doxorubicin hydrochloride</td>
<td>Acetone and ethanol</td>
<td>Gas Chromatography</td>
</tr>
<tr>
<td>Ethambutanol Hydrochloride</td>
<td>2-Amino butanol</td>
<td>Thin layer Chromatography</td>
</tr>
<tr>
<td>Fluorescence Sodium</td>
<td>Dimethyl Formamide</td>
<td>Gas Chromatography</td>
</tr>
<tr>
<td>Framycetin Sulphate</td>
<td>Neamine</td>
<td>Thin layer Chromatography</td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td>Hypoxanthine</td>
<td>Ultra Violet Spectroscopy</td>
</tr>
</tbody>
</table>

### QUESTIONS

1. Illustrate the sources of impurities in pharmaceutical substances. *(U.P.T.U., 2007)*
2. Types of Impurities. *(R.G.P.V., 2009)*
4. Explain Control of Impurities.
5. Describe briefly the impurities in storage for pharmacopeial substances.
6. Explain the importance of impurity for pharmacopeial substances.