IMPURITIES

An impurity in pharmaceuticals is classified as any component that is not the entity defined as the drug substance. In addition, for a drug product, any component that is not a formulation ingredient is considered an impurity.

The Different Types of Impurities Commonly Occurring in Drugs

1. Impurities which have a toxic effect and cause unpleasant reactions in the body when present beyond certain limits,

e.g. lead and arsenic.

2. Impurities which, though otherwise harmless, are present in such proportions that is not desirable. The presence of sodium bromide in the more expensive potassium bromide is not likely to cause harm to the patient. However medicinal quality potassium bromide should contain only potassium bromide and not contain large quantities of sodium bromide.

3. Impurities which lessen the keeping properties of the substances.

For example a small amount of moisture may cause many substances to be easily oxidised or to undergo hydrolysis._

4. Impurities which render the substanee incompatible with other substances.

5. Impurities which cause technical difficulties in the use of substance.

6, Impurities which impart a different odour on colour to the main substance and so are not desirable, Sodium salicylate is often discoloured due to phenolic Impurities, Sodium chloride becomes damp due to the presence of traces of deliquescent magnesium salts,

SOURCES OF IMPURITIES IN PHARMACOPOEIAL SUBSTANCES

Impurities in pharmacopoeial substances may be due to the

following sources:

(a) Raw Materials Used in Manufacture

A good example is the presence of tin, lead, silver, copper, gold in bismuth salts, These metals occur along with bismuth in bismuth ores, Rock salt contains small amounts of calcium sulphate and magnesium chloride so that sodium chloride prepared from this source will almost certainly contain traces of calcium and magnesium compounds.

(b) The Method of Manufacture

Contaminatio by reagents and solvents at various stages of manufacturing process may give rise to impurities.

(i) Reagents employed in the process:

Lead as an impurity may result from the sulphuric acid used as reagent.

(ii) Reagents Added to Remove Other Impurities

Potassium bromide is liable to contain traces of barium which is added in the course of the manufacturing process to remove excess sulphate,

(iii) Solvents

Water is the solvent easily available and cheap and is used in the manufacture of inorganic chemicals. This can give rise to trace impurities such as sodium, calcium, magnesium, carbonate, chloride and sulphate ions, These difficulties do not arise in the use of Purified Water (distilled or demineralised water).

(iv) The Reaction Vessels

The vessels used in the manufacturing process are made of metals like copper, iron, aluminium, zinc, nickel and tin though these days many of these metals are replaced by stainless steel. The above metals are introduced as impurities due to the solvent action of the raw materials on the material of the plant. Glass vessels may pay rise to traces of alkali, though this is unlikely if the vessels are made of neutral glass.

(c) Atmospheric Contaminants

Atmospheric contamination may take place through dust, Sulphur dioxide, hydrogen sulphide etc. Carbon dioxide and water vapour are possible contaminants of substances which are affected by their action.

(d) Decomposition of the Product During Storage

Many chemical substances undergo changes due to careless storage, Ferrous sulphate is slowly changed into insoluble ferric oxide by air and moisture.

(e) Deliberate adulteration with spurious or useless materials:

One has to be vigilant and purchase drugs only from reputed manufacturers

Impurities in Pharmaceuticals

Raw material used in manufacture

Impurities known to be associated with these chemicals may be carried through the manufacturing process and contaminate the final product.

E.g: Rock salt contains $CaSO_4$ & $MgCl_2$. So, NaCl prepared from this will contain Ca & Mg.

Reagents used in the manufacturing process

If reagents used in manufacturing process are not completely removed by washing, these may find entry into the final products.

E.g.: Precipitate of NH_2HgCl contains NH_4OH. If not removed by washing, the final product may contain NH_4OH as impurity.

Method or the process used in the manufacture

Many drugs & chemicals are manufactured from different raw materials & by using different methods or processes. Some impurities are incorporated into materials during the manufacturing process.

E.g: Reagents employed in the process, reagents added to remove impurities, action of solvents & reagents on reaction vessels.

Chemical process used in the manufacture

For the synthesis of drugs, many chemical reactions such as Nitration, Halogenation, Oxidation, reduction, hydrolysis are involved & different chemicals are used.

E.g: Tap water is used in the various processes & is having Cl^-,Mg^{2+},Ca^{2+} ions, which are found in the substances being manufactured.

Sources

Atmospheric contamination during the manufacturing process

Atmosphere is contaminated with dust particles & gases like H_2S, SO_2 & black smoke. During manufacture/purification, these may enter the final products.

E.g NaOH absorbs atmospheric CO_2.

Defects in the manufacturing process

Defects like imperfect mixing, incompleteness, nonadherence to proper temperature, pressure, pH or reaction conditions, which may give chemical compounds with impurities in them.

E.g: ZnO is prepared by heating metallic Zn in current of air. But if there is air,Zn metal is not completely converted to ZnO. Thus it has metallic Zn as impurity.

Manufacturing hazards

Particulate contamination, process errors, cross contamination & microbial contamination

E.g Metal particles which have been found in eye ointments packed in metal tubes.

Intermediate products in the manufacturing process

Some intermediates are produced during manufacturing process & are carried to final product as impurity.

E.g: KI is prepared by reacting I_2 with KOH. In this process if the intermediate product (KIO_3) is not completely converted into KI & becomes an impurity.

Storage conditions

Filth, Chemical instability, Reactions with container materials, Physical changes & Temperature effect.

E.g: Contamination with dust, bodies of insects &excreta. Decomposed by light,acid/alkali, air, water vapour & traces of metal ions. Physical changes occur if not stored at proper temperature.

Decomposition of the product during storage

Separation of a chemical compound into elements or simpler compounds. It is often an undesired chemical reaction.

E.g: Deliquescent substances, absorb water from the atmosphere and get liquefied.

Accidental substitution/deliberate adulteration with spurious/useless materials

Pharmaceutical chemicals are adulterated with cheaper substances.

E.g The expensive potassium may be adulterated with sodium bromide.

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