PHARMACEUTICAL INORGANIC CHEMISTRY- BP104T

UNIT: 1 (IMPURITIES IN PHARMACEUTICAL SUBSTANCES)

CLASS: 2

TOPIC: HISTORY OF PHARMACOPOEIA

EUROPEAN PHARMACOPEIA

- EP commission started working since 1964 to prepare EP
- 1st edition: published 1967
- 2nd edition: published 1980
- 3rd edition: published 1997
- 4th edition: published 2001, valid from 1 January 2002
- 5th edition: published 15 June 2004, valid from 1 January 2005
- 6th edition: published 16 July 2007, valid from 1 January 2008
- 7th edition: published June 2010, valid from 1 January 2011
- 8th edition: published June 2013, valid from 1 January 2014

Based on the published information, Pharmacopoeia is divided into three different major parts. Each part is comprised of several chapters

Part I: Generally the drugs that have similar actions are bringing together by part I of pharmacopoeia.

Part II: Monographs of new drugs, drugs under investigation, drugs which are not easily classified and obsolescent drugs still of interest are presented in part II of pharmacopoeia. It also provides details regarding effects of required drug therapy.

Part III: Composition of proprietary medicines that are advertised to the public in different countries is documented with omission of herbal medicine in part III of pharmacopoeia.

PHARMACOPOEIAL DESCRIPTION

Most of the Pharmacopoeias including Indian Pharmacopoeia consist of the three major sections namely:

A. Introduction including general notices
B. Monographs of the official drugs
C. Appendices.

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(A). Introduction: It is a useful pointer to pharmaceutical progress since last edition. It summarizes the different changes including additions/deletions in the current edition compared to last edition. To avoid misinterpretation and misunderstanding of later parts of the text, attention should be paid to general notices at the outset.

(B) Monographs: The general monographs for dosage forms of active pharmaceutical ingredients (APIs) are grouped together at the beginning of volume II of Indian Pharmacopeia 2010. They are followed by the monographs for the APIs, pharmaceutical aids and individual dosage forms all in alphabetical order. Monographs for other articles of a special nature such as vaccines and immunesera for human use, herbs and herbal products, blood and blood related products, biotechnology products, veterinary products are given in separate sections in volume III of Indian Pharmacopeia 2010

The written study of a subject was implied by the word "monograph". These are considered as very important because medicinal substances are used for the cure and/or prevention of diseases. Therefore their written studies appear as monographs in the Pharmacopoeia. These monographs are arranged in the alphabetical order of their names and are somewhat stereotyped in style. The following information about the drugs and pharmaceutical aids are described in Pharmacopoeial monographs.

INDIVIDUAL MONOGRAPHS:

1. Title: The main title for a drug substance is the International Non-proprietary Name (INN) approved by World Health Organization (WHO). The official name of the compound in English is stated in the title. In place of the main title, sometimes sub titles are given which are synonyms/subsidiary names; where included, they have the same significance as the main title. For example: calcium carbonate can also be called precipitated chalk; iron and ammonium citrate can also be called ferric ammonium citrate and milk of magnesia can also be called magnesium hydroxide mixture.

2. Chemical formulae: When the chemical structure of an official substance is known or generally accepted, the graphic and molecular formulae are normally given at the beginning of the monograph for information. To specify the absolute stereo chemical configuration International Union of Pure and Applied Chemists (IUPAC) systems have been used. If the substance is enantiomer, the sign of optical rotation has been attached to the systematic name.

3. Atomic and molecular weight: The atomic and molecular weight is shown, as and when appropriate at the top right hand corner of the monograph. For example, magnesium chloride (Molecular weight: 202.30) and potassium permanganate (Molecular weight: 158.03). In general if the correct chemistry is not known or the compound is of indefinite composition these two items are not provided.

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4. Definition: The opening statement of a monograph is one that constitutes an official definition of the substance, preparation or other article that is the subject of the monograph. In some monographs of pharmaceutical preparations the statement is given in terms of principle ingredient(s). In monographs on vegetable drugs, the definition indicates whether the subject of the monograph is, for example, the whole drug or the drug in powdered form. Certain pharmaceutical substance and other articles are defined by reference to a particular method of manufacture.

5. Statement of content: The limits of content stated are those determined by the method described under assay.

6. Category: This part of monograph expresses the pharmacological or therapeutic or pharmaceutical application of the compound. Although the compound may have other applications usually this part describes the main application. Analgesics, antibiotic, antacid, laxative etc. are some of the main categories for inorganic pharmaceuticals in the Pharmacopoeia.

7. Dose: Dose mentioned in the Pharmacopeia is intended merely for general guidance and represent, unless otherwise stated, the average range of quantities which are generally regarded as suitable for adults when administered by mouth. It provides the quantity guidance to the prescriber or the physician to achieve the desired therapeutic effects in adults. The dose can be altered as and when required. For example the dose of calcium carbonate is 1-5 gm.

8. Usual strength: It indicates the strength(s) usually marketed for information of the pharmacist and the medical practitioner.

9. Description: This part of monograph is not to be interpreted in a strict sense and is not to be regarded as official requirements. It illustrates a physical description of the substance such as amorphous nature or crystalline, odor, color and taste etc. In the preliminary evaluation of the integrity of an article these properties help and not themselves the standards or tests or purity. For example, Calcium carbonate is a fine white microcrystalline powder, odorless and tasteless.

10. Solubility: The solubility mentioned in Indian Pharmacopeia is the approximate solubility at a temperature between 15 ℃ and 30 ℃, unless otherwise stated, and are not to be considered as official requirements. In the Pharmacopoeia under general notices solubility is described. The solubility of a substance in water, hot or boiling water, alcohol, glycerol, other organic solvent, acid and alkali were given.

11. Test methods: References to general methods of testing are indicated by test method numbers in brackets immediately after the heading of the test or at the end of the text.

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12. Identification: These identification tests are not a proof of identity. This usually involves specific chemical test or tests for identifying the substance. It provides a means of verifying that the identity of the material under examination is in accordance with the label on the container. In certain monographs alternative series of tests are given; compliance with either one or the other set of tests is adequate to verify the identity of the article. In general for inorganic pharmaceuticals color reactions, precipitation reactions and gas evolving reactions are used. For example, Phenol gives violet color with ferric chloride

13. Tests and assay: These are the official methods upon which the standards of Pharmacopoeia depend. The requirements are not framed to take into account all possible impurities. Tests and assay are prescribed for the minimum sample available on which the attributes of the article should be measured. Assurance of quality must be ensured by the manufacture by the use of statistically valid sampling and testing programs.

14. Tests: In general the assays and test are carried out at a temperature between 20 °C and 30 °C unless otherwise stated. Precaution should be taken to avoid exposure to direct sunlight or other strong light where it is directed that an analytical operation is to be carried out "in subdued light". Similarly precaution should be taken to exclude actinic light by the use of low actinic glassware, working in a dark room or similar procedures.

15. Other tests: In the monographs on dosage forms and certain preparations, under the sub heading "other tests" it is stated that an article complies with the tests stated under the general monograph of the relevant dosage form or preparation. Details of such tests are illustrated in the general monographs.

16. Limits: The limits given are based on data obtained in normal analytical practice. They take into account normal analytical errors, of acceptable variations in manufacture and of deterioration to an extent that is acceptable. No further tolerances are to be applied to the limits for determining whether or not the article under examination complies with the requirements of the monograph.

17. Quantities: Unless otherwise stated, in tests with numerical limits and assays, the quantity stated to be taken for testing is approximate. Volumes stated in microliters (pl) are measured using a micropipette or micro syringe. The term "transfer" is used generally to indicate a quantitative operation.

18. Apparatus: Measuring and weighing devices and other apparatus are described in the chapter entitled "apparatus for tests and assays". Unless otherwise stated, comparative tests are carried out using identical Nessler cylinders.

19. Reagents and solutions: The reagents required for the tests and assays of the drugs in the Pharmacopoeia are defined in the various chapters showing their nature, degree of purity and the strengths of the solutions to be made from them.

20. Indicators: Where the use of an indicator solution is mentioned in an assay or test approximately 0.1 ml of the solution shall be added, unless otherwise directed.

21. Reference substances: These are the authentic specimens chosen and verified on the basis of their suitability for intended use as prescribed in the Pharmacopoeia and not necessarily suitable in other circumstances.

22. Test animals: Unless otherwise directed, animals used in test or assay shall be healthy and are drawn from a uniform stock, and have not been previously treated with any material that will interfere with the test or the assay.

23. Calculation of results: The results should be calculated to one decimal place more than the significant figures stated and then rounded up or down as follows; if the last figure calculated is 5-9, the preceding figure is increased by 1; if it is 4 or less, the preceding figure is left unchanged.

24. Storage: These directions are useful in preserving the activity of the chemical. Specific directions are given in some monographs with respect to the temperatures at which Pharmacopoeial article should be stored, where it is considered that usage at a lower or higher temperature may produce undesirable results.

The storage conditions are defined by the following terms:

a) Store in a dry, well ventilated place at a temperature not exceeding 30 °C
b) Store in a refrigerator (2 °C to 8 °C) and do not freeze
c) Store in a freezer and
d) Store in a deep freezer (below -18 °C).

The storage conditions not related to temperature are indicated in the following terms;

a) Store protected from light and
b) Store protected from light and moisture.

Where no specific storage directions or limitations mentioned, it is to be understood that the storage conditions include protection from moisture, freezing and excessive heat (any temperature above 40 °C). For example insulin injection store in multiple dose containers at a temperature between 2°C to 8 °C. It should not be allowed to freeze.

25. Storage containers: The storage containers in the Pharmacopoeia are indicated in the following terms:

a) Well closed containers: This implies the substance is stable and gets protected from dust, dirt, insects etc, getting into the container
b) Tightly closed container: The substances in such cases get affected by atmospheric oxygen or moisture or carbon dioxide. For example, reducing agents, hygroscopic substances, strong bases etc. must be stored in tightly closed containers. It may also include such compounds are volatile or contain dissolved gases etc.
c) Light resistant container: Substances which are affected by light are stored in amber or dark colored containers,
d) Single dose containers: This is generally prescribed for some injectable which once opened should not be used again. For example, ferrous fumarate (Store in a light resistant container)

26. Labeling: The labeling of drugs and pharmaceuticals is governed by the Drugs and Cosmetics Rule, 1945. The statements that are given in the monographs under the side heading "labeling" are not comprehensive. Only those that are necessary to demonstrate compliance or otherwise with the monograph have been given and they are mandatory. For example, in the monograph on betamethasone sodium tablets the labeling statement is "The label states the strength in terms of the equivalent amount of betamethasone". Any other statements may also include as recommendations.

(C). Appendices: A comprehensive section of appendices are presented followed by the general notices and monographs.

- The apparatus that are needed for various Pharmacopoeial tests and assays are described in the appendix 1.
- Biological tests and assays are described in appendix 2.
- The details of various chemical tests and assays are included in appendix 3.
- The details of microbiological tests and assays are included in appendix 4.
- In the appendix 5, some physical tests and determinations like loss on drying determination of pH, melting range etc are described.
- Appendix 6 includes the useful directions on cleaning glassware.
- Appendix 7 describes the reagents and solutions needed for the various tests and assays, their method of preparation, standards etc.
- Appendix 8 describes reference substances.
- Appendix 9 have been described fully the names, symbols used in the Pharmacopoeia for weights and measures and of elements and their atomic weights have been described.

2 MARKS QUESTIONS

1. Define a Monograph

5 MARKS QUESTIONS

1. What is a monograph and list out the contents of monograph
2. Write a note on European Pharmacopoeia

10 MARKS QUESTIONS

1. Describe the contents of monograph in detail
2. Write a note on Pharmacopoeial description in detail