4.Evaluation of Drugs

- A natural substance is considered as food if it fills stomach in every day life without any harmful effect.
- A substance becomes a drug if it changes a pathological or disease state of human/ animal to normal physiological condition having no undesirable effect in specific dose.
- A long-term studies (chemical, biological and physical etc) are required to establish whether a substance will be considered as drug or food or eliminate for consumption. Those studies are referred to as evaluation.

Evaluation of drug means –

- Identification
- Determination of quality
- Determination of purity
- Identification

✓ Cultivation

✓ The identification can be established by careful observational study of the collected drug, and then compared with authentic specimen by the collector.

✓ Therefore, for proper identification of a drug from plant or animal sources, a collector must be educated about plant taxonomy and very much experienced with his/her job.

✓ Therefore, drugs from plants/animals are identified by –

- o A qualified, specialized & experienced person
- o Comparison with the authentic sample specimen.

✓ In every country, there is a national herbarium where most of plants specimen are preserved. A number of specialists are working on plant identification there.

Quality

- The word “quality” refers to the intrinsic value of the drug, i.e., the amount of medicinal principles or active constituents present. These principles are classified as carbohydrate, alkaloid, glycoside, volatile oil, lipid, antibiotics and steroids etc.
- A high grade of quality in a drug is of primary importance. An effort should be made to obtain and maintain high quality.
- To maintain high quality products one should do the following:

1. Select proper source (wild or cultivated)
2. Appropriate time of collection
3. Collection of required parts of plants (bark, leaf, stem, rhizome, root)
4. Preparation of the collected drug by proper cleaning, drying.
5. Proper preservation to avoid contamination by microorganisms and moisture, heat, air and light.

Purity

- The purity of drug can be achieved by –

1. Proper identification
2. Quality assurance.

Evaluation Method

- The evaluation of a drug involves a number of methods, which may be classified as follows:

1. Organoleptic
2. Microscopic
3. Biological
4. Chemical
5. Physical

1. Organoleptic evaluation of drug:

- Organoleptic evaluation means the study of a drug with the help of organs of sense.
- It includes any drug's macroscopic or external appearance, color, odor, taste & sounds of its fracture etc.
- Aromatic odour of umbelliferrous fruits and sweet taste of liquorice are examples of this type of evaluation. The ovoid tears of gum acacia, ribbon shaped characteristics of tragacanth, disc shaped structure of nux-vomica etc are important diagnostic characters.
- The wavy shape of rauwolfia, pungent taste of capsicum and ginger, brown colour of cinnamon, odour and taste of spice drugs like asfoetida, black pepper, nutmeg, caraway, cumin, etc are important diagnostic organoleptic characteristics.
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- The macroscopic or external characteristic of a drug may be divided into 7 headings -

1. Shape
2. Size
3. Color
4. Internal color
5. Fracture
6. Odor
7. Taste

2.Microscopic evaluation of drug:

- Microscopic evaluation of drug can be done in the laboratory by the use of microscopes and utilizes various microscopic characters of the drugs, such as types and arrangement of various cells and tissues.

3. Chemical evaluation of drug:

- Chemical evaluation of drugs involves both qualitative and quantitative determination of their active principles.
- In this method characteristic qualitative chemical tests are employed to identify crude drugs and their constituents.

4. <u>Biological evaluation of drug:</u>

- The biological evaluation of crude drugs is very useful in determining the pharmacological activity of the drug.
- Since living organism or their isolated living tissues are used, this method is also called the biological method or bioassay.
- Many drugs, particularly the antibiotics, toxins and toxoids and also vitamins are assayed by this method.
- ***5. <u>Physical evaluation of drug:</u>***
- The physical evaluation of crude drugs is accomplished by the determination of various physical characteristics using various physico-chemical techniques, for example, specific gravity (of fats and volatile oils), melting points (of alkaloids), optical rotation (of alkaloid and volatile oils), etc.

<u>Adulteration of Crude Drug</u>

- ✓ The term 'adulteration' or debasement of an article covers a number of conditions, which may be deliberate or accidental. Usually in crude drugs, this practice includes substitution of the original crude drugs partially or fully with other substances which is either free from or inferior in therapeutic and chemical properties.
- ✓ ***<u>Inferiority</u>*** is a natural substandard condition (e.g. where a crop is taken whose natural constituent is below the minimum standard for that particular drug) which can be avoided by more careful selection of the plant material.

- ✓ ***Spoilage*** is a substandard condition produced by microbial or other pest infestation, which makes a product unfit for consumption, which can be avoided by careful attention to the drying, and storage conditions.
- ✓ ***Deterioration*** is an impairment of the quality or value of an article due to destruction or abstraction of valuable constituents by bad treatment or aging or to the deliberate extraction of the constituents and the sale of the residue as the original drugs.
- ✓ ***Admixture*** is the addition of one article to another through accident, ignorance or carelessness e.g. inclusion of soil on an underground organ or the co-collection of two similar species.
- ✓ ***Sophistication*** is the deliberate addition of spurious or inferior material with intent to defraud; such materials are carefully produced and may appear at first sight to be genuine e.g. powder ginger may be diluted with starch with addition of little coloring material to give the correct shade of yellow color.
- ✓ ***Substitution*** is the addition of an entirely different article in place of that which is required e.g. supply of cheap cottonseed oil in place of olive oil.

- **Types of Adulteration Of Crude Drugs**
- *Adulteration may be :*
- *Intentional*
- *Unintentional*

Different methods used for adulteration may be grouped as follows:

1) ***SUBSTITUTION:***

A) Substitution by exhausted drugs.

B) Substitution by superficially similar but cheaper natural substances.

C) Substitution with inferior commercial varieties.

2) ***Adulteration by artificially manufactured substitutes.***

3) ***Adulteration by addition of worthless heavy materials.***

4) ***Addition of synthetic principles.***

5) ***Usage of vegetative matter from the same plant.***

1.A. Substitution by Exhausted Drugs

Here the same plant material is mixed which is having no active medicinal components as they have already been extracted out. This practice is most common in case of volatile oil containing materials like clove, fennel etc., where the dried exhausted material resembles the same like original drug (similarly with drugs like *Cascara sagrada* and ginger). Sometimes when coloring matters have been extracted or removed during exhaustion, the residue is re-colored with artificial dyes as is done with saffron and red rose petals.

1.B. Substitution by Superficially Similar but Cheaper Natural Substances

Usually here the adulterated product has no relation with the genuine article, may or may not have any therapeutic or chemical component desired, e.g. leaves of species - *Ailanthus* are substituted for belladonna, senna, mint etc.; Leaves of *Phytolacca* and *Scopolia* for belladona; Leaves of *Xanthium* for *stramonium* and dandelion for henbane; Indian dill with European dill or caraway etc.

1. ***C. Substitution with Inferior Commercial Varieties***

Due to morphological resemblance to the authentic drugs, different inferior commercial varieties are used as adulterant which may or may not have any chemical or therapeutic potential as that original natural drug e.g. Arabian Senna (*Cassia angustifolia*), dog Senna (*Cassia obovata*) and avaram (*Cassia auriculata)* have been used to adulterate Senna (*Cassia senna)*; Japanese ginger (*Zingiber mioga*) to adulterate medicinal ginger (*Zingiber officinale*).

2. ***Adulteration by Artificially Manufactured Substitutes***

To provide the general form and appearance of various drugs, some materials are artificially manufactured and are used as substitute of the original one, e.g. artificial invert sugar for honey; paraffin wax after yellow coloration substituted for bees wax.

3. ***Adulteration by Addition of Worthless Heavy Materials***

A large mass of stone mixed with Liquorice root, pieces of limestone are found in asafoetida and lead shot has occurred in pieces of opium etc.

4. ***Addition of Synthetic Principles***

Sometimes to fortify inferior natural products, synthetic principles are added e.g. adding citral to oil of lemon; benzyl benzoate to balsam of Peru etc.

5. ***Usage of Vegetative Matter from the Same Plant***

This is done by mixing adventitious matters or naturally occurring with the drug in excessive amount or parts of plant other than that which constitutes the drugs. For example liver warts and epiphytes growing in bark portion are mixed with Cascara or Cinchona*;* stems of buchu are sometimes cut into short lengths and added to the drug.

Unintentional Adulteration Of Crude Drugs

In this case unwanted substances may be admixed with the drugs accidentally i.e. due to carelessness and ignorance.

This type of adulteration may be due to

1. Faulty collection,
2. Imperfect preparation and incorrect storage.

It is also called as admixture.

1. ***Faulty collection***

Faulty collection of drugs is due to ignorance or carelessness by the collectors during the time of collection. The collectors either collect the drug at inappropriate season or collect another drug identical to the genuine one e.g. official source of digitalis is Digitalis purpurea which resembles in shape to Verbascum thapsus or Verbascum officinale.

Sometime undesirable parts of the plant are collected due to ignorance and not removed after collection. In this way the drug becomes adulterated.

1. ***Imperfect Preparation***

In this case the drug is not prepared properly which results in adulteration e.g. neglecting of proper conditions for drying leads to adulteration. E.g. when digitalis leaves are left in a moist condition for long time, the glycosides are decomposed due to the action of enzymes. Similarly when the leaves are dried above 60 degree centigrade, hydrolysis of the glycosides takes place and drug becomes adulterated.

- **Deterioration of Crude Drugs**
- Besides being adulterated by different means as discussed earlier, the crude drugs are prone to deterioration on storage. The shelf-life of crude drugs are influenced by many factors which include not only the quality of storage conditions but also the stability of the secondary (2°) metabolites present therein. Several factors are to be considered for the detrimental effects on the stored products.
- Several primary environmental factors relating to storage can produce detrimental effects on stored products e.g.

    1) Light,
    2) Moisture / humidity,
    3) Temperature &
    4) Oxygen etc.

But more deterioration usually results from a combination of these factors, which leads to the development of living organism including molds, mites, bacteria etc.

- **Primary Factors for Deterioration**

1. **Light**

Photo-decomposition occurs with santonin, the principal constituents of wormseed, which on exposure to light darkens and eventually becomes black. In general, drugs should be protected by suitable light-proof wrapping or by the use of amber colour containers. Powdered rhubarb stored in clear glass jars rapidly changes as the exposed surfaces turning from yellow to more reddish colour.

For these detrimental effects, WHO has specified that medicinal plant materials requiring protection from light should be maintained in a light resistant container that shields the contents from the effects of light. Alternatively, the container maybe placed inside a suitable light resistant (opaque) covering and/or stored in a dark place.

2. Moisture/Humidity

Moisture present in drugs depends largely upon the amount of moisture in the atmosphere, which is usually expressed in the terms of humidity. When the atmosphere is completely saturated, the humidity is 100%, when half saturated it is 50% and so on. Drugs stored in non-airtight containers are termed air-dry and contain about 10-12% of water depending on the humidity of the atmosphere. This amount of water is sufficient to activate the enzymes present in some dried plant materials, such as Digitalis and bring about the decomposition of the active glycosides. Such drug should therefore be stored with a dehydrating agent or in sealed containers immediately after drying.

Squill contains a hygroscopic mucilage and the powder there from, if exposed to the atmosphere, will pickup moisture and become a sticky mass.

Therefore strict humidity control is necessary while storing; low moisture may be maintained, if necessary by the use of desiccant in the container provided that direct contact with the product is avoided.

3. Temperature

It has a marked effect which is sometime unsuspected. Many enzymatic changes in the plant secondary metabolites proceed more rapidly at the slightly raised temperature up to about 45°C. Obviously those drugs containing volatile constituents in unprotected structures, e.g. plants belonging to Labiatae family and the petals of rose and chamomile all loose oil with an increase in temperature. Absorbent cotton wool contains a small amount of fatty material which is the residual component from the natural fiber. At a raised temperature these molecules become re-oriented, spreading themselves over the surface of the fiber to form an impervious layer. Thus cotton wool, once fully absorbent will gradually become completely non-absorbent because of the effect of temperature.

4. Air Oxidation

Direct oxidation of the constituents of crude drug is sometime brought about by the oxygen of the air, e.g. Linseed oil rapidly become resinified as like the oil of Turpentine and oil of Lemon. Usually this conversion is applied to the essential oil with terpenoid derivatives and we can find the resinous deposit build-up around the stoppers used in dispensing bottle containing this oil. Beside this, the rancidification of fixed oils e.g. cod-liver oil, which involves the formation of unstable peroxides, is also an oxidative process. Thus, these types of materials require storage in a well-filled, airtight container.

- **Secondary Factors for Deterioration**
- Living organisms usually develop in stored drugs where the conditions are satisfactory for them. From a hygienic point of view, such contaminated material should be destroyed irrespective of whether or not the active principles of drug have been effected. The more common of such organisms belongs to the groups of bacteria, moulds, mites, nematodes, worms, insects etc.

    1) Bacteria and Moulds
    2) Mites and Nematode Worms
    3) Insects/Moths
    4) Coleoptera or Beetles

1. Bacteria and Moulds

Dried herbs are particularly liable to be contaminated with the spores of the bacteria and moulds, which are always present in the air. Under satisfactory storage conditions their presence causes no problem, but it is generally accepted that *the viable count permissible for crude drugs should be the same as that for the food stuff*. The effect produced by bacteria are not always very visible with the exception of some chromogenic species of bacteria, e.g. *Bacillus prodigious*, which produces red patches in starchy materials. However, bacterial growth is usually accompanied by the crude drug by growth of moulds whose presence is quickly evident by the characteristic smell and by the mass of clinging particles entrapped in the mycelial hyphae.

Dusty cotton wool, which is formed by bacterial attack causing the trichomes to break into short length, rendered it to be very brittle. In order to identify a particular mould or bacteria, which is proliferating in a stored product, it is necessary to culture it on a suitable medium with a view to obtain fruiting bodies for examination. However, if the drug to be examined is infested rapidly, then it may be possible to make microscopic preparation directly from the sample. Usually the moulds encountered with poorly stored drugs include the genera *Mucor* (e.g. grey mould, *M. mused), Rhizopus* (e.g. black mould, *R. nigricans), Penicillium* (e.g. blue mould, *P. glaucum), Aspergillus* (e.g. green mould, *A. repens)* and *Saccharomyces.*

2. **Mites and Nematode Worms**

If found in stored drugs, mites are usually present in countless numbers upto 1.0 mm in length. Different mites found usually include *Tyroglyphces siro* (Cheese mite); *Aleurobius farinae* (Flour mite) and *Glycyphagus spinipes* (Cantharides mite). All these mites can be examined microscopically by clearing the sample of powder containing them with chloral hydrate reagent. The best known examples of nematode worms are "Vinegar eel" – *Turbatrix aceti, Anguillula aceti, Anguina tritici* which are found in wheat flour or in the crude drug containing starchy materials. These worms are visible to the unaided eye as minute threads continually curling and twisting in the medium they inhabit.

3. **Insects/Moths**

A few species of the *Lepidiptera* attack the stored crude drugs and cause damage at the larval stage, where the infestation can spread rapidly due to the mobility of the adults. The moths involved are unspectacular in appearance, 22-30 mm in length with off-white wings e.g. *Ephestia kuehniella* (Flour moth); *E. ellutella* (Cocoa moth). Besides this some other insects, cockroaches, ants and others are sometimes found to cause deterioration to the stored products.

4. **Coleoptera or Beetles**

These are the insects that constitute the largest order of the animal kingdom comprising about 2,50,000, species of which about 600 have been found to be associated with stored food product or drugs. *Stegobium paniceum* is one beetle, which is found in many drugs including gentian, liquorice and rhubarb as well as leafy drugs and seeds. Belonging to the same family is

Lasioderma serricorne (tobacco or cigar beetle) which is reddish brown in colour, 2 to 2.5 mm in length and found in many stored crude drugs including ginger and liquorice.

- **Control Measures for Deterioration**
- The container used for storage and its closure must not interact physically or chemically with the material within in any way which would alter its composition.
- A well closed container must protect the contents from extraneous matter or from loss of the material while handling and a tightly closed container must protect the material from efflorescence, deliquescence or evaporation under normal condition of handling or storage.
- Storage area should be kept clean and spillages not allowed to enter cracks or in accessible crevices.
- Periodic spraying of the premises with insecticides will help to prevent the spread of infestation.
- The principles, which apply to the control of infestation in warehouses, are equally applicable to small-scale storage.
- Good house keeping is utmost essential.
- Each stock should be inspected regularly and the material found to be contaminated is best to be destroyed by burning. In this respect a quick turn over to eliminate the effects of deterioration due to both the primary and secondary factors as mentioned above are desirable.
- Cool, dry condition is the most suitable for the retardation of living organisms. As all living organisms require water for the development, perfectly dry drugs should be immune from secondary deterioration. Sometimes the crude drugs purchased by the herbalist may already have been sterilized, which is most commonly achieved by treatment of the bulk consignment with ethylene oxide or methyl bromide under controlled conditions.
    - *Drugs so treated, should comply with an acceptable limit for toxic residues e.g. for Senna pods 50 ppm of ethylene oxide is the limit.*