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Commerce & production

- The crude drug which reaches the pharmaceutical manufacturing line will have passed through various stages , all can influence the nature & amount of active constituents. These headings are :

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- **Source Materials**
 - **Environmental conditions.**
 - **Cultivated & wild plants.**
 - **Collection**
 - **Drying**
 - **Storage**


Source Materials

- It is imperative that correct identification of the source material is made. Adulteration may be accidental, particularly if collection is made from wild plants, or it may be deliberate. Failure in this area can result in poisoning (e.g. hemlock fruits mistaken for other umbelliferous fruits) or inactive products (e.g. substitution of St John's wort with other vegetable material when demand exceeds supply).
- For pharmacopeial drugs, precise macroscopic and microscopic characters are available.



Environmental conditions

- plant growth , development & sometimes the nature & quantity of secondary metabolites are affected by temperature , rainfall , length of day & quality of light & altitude. Such effects have been studied by growing particular plant in different climatic areas & observing variations

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- **A-Temperature** : It is a major factor controlling the development & metabolism of plants. Although each species has become adapted to its own natural environment , plants are frequently able to exist in a considerable range of temperature. Many tropical & subtropical plants will grow in temperate region during summer months , but lack frost resistance to withstand the winter. An example of the effect of temperature on plants is the formation of volatile oils appear to be enhanced at higher temperature , although very hot days may lead to physical loss of oil.




- **B-Rainfall :**


The important effects of rainfall on vegetation must be considered in relation to the annual rainfall , its distribution throughout the year , its effect on humidity & its effect coupled with the water-holding properties of the soil ex: different results have been reported for the production of volatile oils under different conditions of rainfall & sometimes it is coupled with the development of glandular hairs. Some times continuous rain can lead to loss of water soluble substances from leaves & roots by leaching this is known to apply to some plants producing alkaloids, glycosides and even volatile oils , this gives the main reason for low yield of some active constituents in wet seasons from plants although its general condition is good..



- **C-Day-length & radiation characteristics :**

- Plants differ in both the amount & intensity of the light they require. Wild plants will be found where its shade requirement is met & under cultivation similar shade must be provided. In certain cases research has shown that light is a factor which affect the amount of some substances produced ex : glycosides or alkaloids.

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- It has been shown that under long day conditions peppermint leaves contain menthon , menthol & traces of menthofuran; while plants grown under short-day conditions contains menthofuran as a major component of the volatile oil.

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- Type of radiation had been studied in respect to morphological development of the plant , but little information had been reported concerning medicinal metabolites ex: many plants initiate flowers only in certain day length , therefore when flowering is essential this factor must be carefully considered before planting in a new region. Presence or absence of light , together with wave length range have a marked effect on the secondary metabolite production of some plants in tissue culture




- **D-Altitude :**

- Plants differ greatly in their altitude requirement ex: tea , coffee, cocoa , medicinal rhubarb , & cinchona require elevation , there fore changing or lowering the altitude with such plants will affect its metabolites production ex: Cinchona succirubra the plant grows well at low levels but produce practically no alkaloids



E-Soils

- Different plant species vary enormously in their soil and nutritive requirements, and this aspect has received considerable attention with medicinal plants. Three important basic characteristics of soils are their physical, chemical and microbiological properties.
- Variations in particle size result in different soils ranging from clay, via sand, to gravel. Particle size is one factor influencing water holding capacity, and some plants (e.g. *Althaea officinalis*) which produce mucilage as a water retaining material contain less mucilage when grown on soil with a high moisture content.

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- The effect of nitrogen containing nutrients on alkaloid production has received considerable study (solanaceous drugs including Nicotiana, opium); generally nitrogen fertilizers increase the size of the plants and the amounts of alkaloids produced
 - Although particular species have their own soil pH tolerances (Datura stramonium 6.0–8.2) no marked influence of pH value within the tolerance range has been demonstrated alkaloids (D. stramonium).





F-Propagation from seeds

Time of seeds sowing may affect the active constituents, as illustrated by *Chamomilla recutita*—for 17 cultivars investigated most gave a significantly higher yield of oil if they were spring sown rather than autumn sown and the oil composition also varied

Cultivated & wild plants


- Certain drugs are now obtained almost exclusively from cultivated plants ex: Cardamon , Ginger , Peppermint & Spearmint for oil production .Cultivation is essential in the case of drugs such as Indian hemp & Opium , which are subjected to government control & in many cases it is advisable because of the improved quality of the drug which is possible to produce. The improvement may be due to the following:


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- **a-**The power to confine collections to species , varieties , or hybrids which have the desired characters ex: Cinnamon , Fennel , Cinchona.
 - **b-**The better development of the plants owing to improved conditions of the soil , control of insects , pests , fungi etc.
 - **c-**The better facilities for treatment after collection ex : drying at a correct temperature in cases of Digitalis , Belladonna & the peeling of Cinnamon & Ginger.


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- For success in cultivation it is necessary to study the conditions under which the plant flourishes in the wild state & produce these conditions & / or improve them.

Collection

- Drugs may be collected from wild or cultivated plants & the task may be undertaken by unskilled or skilled workers depending on the plant to be collected. There are many points that should be taken in consideration during collection to have a good yield & quality of the plant , these are:

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- a-The season at which each drug is collected is usually important because the amount & sometimes the nature of the active constituents is not constant through out the year.
 - b-The age of the plant is also important & governs not only the total quantity of the active constituents produced but also the relative proportions of the components of the active mixture.

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- c-The time of collection whether it is day or night because there are evidence that the composition of a number of secondary metabolites varies through out the day & night.
 - d-Generally , leaves are collected as the flowers are beginning to open , flowers are collected just before they are fully expanded & underground organs as the aerial parts die down.

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- e-Leaves , flowers & fruits should not be collected when covered with dew or rain , barks are usually collected after a period of damp weather as they then separate more readily from the wood. For the gums , gum resins etc., dry weather is required & care should be taken to exclude vegetable debris as far as possible.
 - f-Any parts which are discolored or attacked by insects or slugs should be rejected.
 - g- Under ground organs must be freed from soil . Shaking the drug before, during & after drying or brushing it may sufficient to separate a sandy soil, but in the case of a clay or other heavy soil washing is necessary.


Pause





Rest time


Drying


- prevent molding, the action of enzyme, the action of bacteria, and chemical or other possible changes. Drying fixes the constituents, facilitates grinding and milling, and converts the drug into a more convenient form for commercial handling


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- If enzymic action is to be **encouraged** , **slow drying at moderate temperature** ex : Vanilla pods is necessary , but if enzymic action is not desired, drying should take place as soon as possible after collection. Drugs containing volatile oils are liable to lose their aroma if not dried or if the oil is not distilled from them immediately , & all moist drugs are liable to develop mould. For these reasons drying apparatus should be situated as near to the growing plants as possible.


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- The duration of the drying process varies from a few hours to many weeks, & in case of open-air drying depends very largely on the weather. In suitable climates open-air drying is used for drugs such as Clove , Cardamon & Cinnamon. Even in warm & dry climates arrangements have to be made for getting the drug under the cover of sheds at night or during wet weather .


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- Compact samples of fresh plant material with little air circulation may experience fungal infestation & fermentation if left to stand for several days, hence well-ventilated places & homogeneous distribution of the material should be ensured.

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- **Drying in sheds the drugs (open-air drying) may be done by :**
 - suspended in bundles from the roof
 - placed on trays made of sacking or tinned wire-netting .
 - Paper spread on a wooden framework are also used especially for fruits from which it is required to collect the seeds.
 - In all drying sheds there must be a space of at least 15 Cm between super imposed trays , & air must circulate freely.

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- **Artificial drying is done by:**
 - Belt driers which are used for large crops .
 - Alternatively heat may be applied by means of open fires.
 - Stoves
 - hot- water pipes.


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- **Note** : Drying by artificial heat is more rapid than open-air drying & is often necessary in tropical countries where the humidity is very high.
 - **Rapid drying** helps flowers & leaves to retain their colour & aromatic drugs their aroma , but the temperature used in each case must be governed by the constituents & the physical nature of the drug.


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- Generally leaves , herbs & flowers may be dried between 20-40 C & barks & roots between 30-65 C . If leaves & other delicate structures are over dried , they become very brittle & tend to break in transit , while drugs such as aloes & opium may require further drying after importation.


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- The plant material may also be frozen with liquid nitrogen, & pound in a chilled mortar or thick polyethylene bag, even with fresh material. The grinding process assists the penetration of the solvent to the cellular structure of the plant tissues , thereby helping to dissolve the secondary metabolites & increase the yields of extraction. Generally , it has been found that the smaller the particle size of the plant material the more efficient the extraction.

Storage

- Drugs stored in the usual containers ex: sacks , bales , wooden cases , cardboard boxes & paper bags , reabsorb about 10-12% or more of moisture. They are termed “air dried” . Plastic sacks will effectively seal the contents. The combined effects of moisture & temperature on humidity & the subsequent water condensation when the temperature falls , must be considered in drug storage.

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- Drugs such as Digitalis & Indian hemp should never be allowed to become air dried or they lose a considerable part of their activity . They may be kept in a sealed containers with a dehydrating agent . For large quantities the bottom of a case may be filled with quicklime & separated from the drug by a perforated grid or sacking. If the lime becomes moist , it should be renewed .

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- Volatile oils should be stored in a sealed well filled containers in a cool , dark place. Similar remarks apply to fixed oils .

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- Air – dried drugs are always susceptible to the attack of insects & other pests , so they should be examined frequently during storage & any showing mould or worminess should be either rejected or treated, & sometimes to reduce undesirable microbial contamination & to prevent the development of other living organisms , materials may require sterilization before storage , but drugs so treated should comply with an acceptable limit for toxic residue.



- **Deterioration :**


- The primary factors which must be considered in relation to drug deterioration are moisture content , temperature , light & presence of oxygen , when these conditions are suitable , living organisms ex : bacteria , mould , insects will rapidly multiply using drug as a source of nutrient.




- Humidity :

humidity in 10-12 % moisture may be sufficient to activate enzymes present in the leaves & bring about decomposition of the glycosides.

Other drugs which contain mucilage quickly absorb moisture & become a sticky mass .

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- **Temperature** : an increase in temperature in combination with moisture may
 - accelerate enzyme activity .
 - large temperature rise will lead to a loss of volatile constituents ex: volatile oils.
 - In case of absorbent cotton wool cause a reorientation of the small amount of fatty material present leading to non or lower absorbency.

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- Sun-light : direct sunlight can cause :
 - Produce bleaching of leaves & flowers.
 - Decomposition of certain constituents ex: vitamins in cod-liver oil
 - Oxygen : this factor assists in the resinification of volatile oils & in the rancidification of fixed oils.
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The End

