

# PHARMACOGNOSY – 1

## LECTURE 2

1 Drug Monographs

2 Medicinal Plant Cultivation

3 Drying and Stabilization of Drugs

4 Medicinal Plant Trade

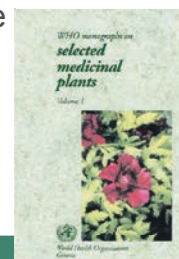
5 Primary and Secondary Metabolism in Plants

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## Drug Monographs

❖ Drug monographs were special reference documents that provide information about the description, identification, quality control (QC) and standardization of drugs. These monographs can be found in the following resources;

- “Pharmacopoeia”s,
- “Compendium”s (e.g. **USP Dietary Supplement Compendium**),
- **ESCOP** (The **E**uropean **S**cientific **C**ooperative **O**n **P**hytotherapy) **M**onographs or
- **WHO Monographs on Selected Medicinal Plants**



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## Drug Monographs

❖ Information provided in the monographs include;

- **Description;** Latin name of the plant source and section of the plant that used as drug. For example dried fruits of *Pimpinella anisum* L. yield **Anisi fructus** drug
- **General properties;** Specific information about the drug such as
  - the state of the source plant material:
    - Fresh or dried?
    - Coarsely divided or pulverized?
    - Growth stage of Plant Source (e.g. during blooming), etc.

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## Drug Monographs

❖ Information provided in the monographs include (contd.);

- **Organoleptic characters;** color, smell, taste, etc. (characters that could be discerned using sensory organs).
- **Identification;** Macroscopic or microscopic features of drug that could provide specific information for the identification of drug (e.g. epidermal hairs, glands, druse, etc.), chemical tests or chromatographic procedures (TLC, GC or HPLC) for the specific secondary metabolites of drugs also could help in identification of drug.

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## Drug Monographs



❖ Information provided in the monographs include (contd.);

- **Purity testing (quality control);** water content, heavy metal and pesticide amount, ash determination, microbiologic testing, microbiologic testing, radioactive isotope impurity level
- **Chemical (or Chromatographic) Quantification;** Using specific chemical or physicochemical tests (e.g., color reactions, titrations, spectrophotometric measurements), or chromatographic analyses amount of active substance(s) were determined to confirm the suitability of drug for the intended use (i.e., standardization)

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## Medicinal Plant Cultivation




❖ Drugs harvested from the wild plants when;

- Drug consumption is limited
- Availability of the wild source plant is high or
- Cultivation of the source plant is very difficult

❖ The source medicinal plant is cultivated when;

- Drug consumption is high
- Availability of the source plant is very limited or
- Cultivation of the source plant is easy


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## Medicinal Plant Cultivation

- ❖ Examples of the drugs harvested from wild plants; chamomile (*Matricariae flos*), galls (*Gallae quercinae*)
- ❖ Examples of the drugs obtained from the cultivated medicinal plants; *Opium* or *Papaveri fructus* (papaver fruit –capsule-), *Anisi fructus* (anason), etc.

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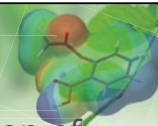
## Medicinal Plant Cultivation

- ❖ **Medicinal Plant Cultivation**
  - Advantages;**
    - Large quantity of drug can be harvested from a small area.
    - Drug collection can be completed in a short time.
    - Collection time can be controlled as desired.
    - If needed, drying process og t
    - In comparison with the wild medicinal plant sourced drugs, drugs obtained from the cultivated plants has better purity.
    - By selection of high quality varieties, the yield and active substance content of drug can be improved.
  - Disadvantages;**
    - Since cultivation is limited to small areas, parasite or disease infestation of cultivated plants can spread quickly.

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## Medicinal Plant Cultivation



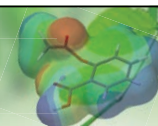
❖ Similar to the other plant products, application of good agricultural principles improve the yields and quality of medicinal plants;

- **Soil selection:** Selection should be performed according to the medicinal plant species; for example while *Lavandula spicata* does not grow well in wet and calcareous soil *Mentha piperita* grows extremely well.
- **Soil preparation;** In order to increase the quality of cultivated medicinal plant, the soil should be prepared in fall by tillage, cleaning (from wild rhizomes, weeds, etc.) and fertilization. This preparation improves the yield of cultivated medicinal plant.

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## Medicinal Plant Cultivation



❖ **Sowing:** Ripe and clean seeds of medicinal plant should be sown by row cultivation, this would improve the yield of medicinal plant as well as allow the easy collection of drug from the field.

❖ **Watering and Hoeing;**

- In order to improve the yield, the medicinal plant needs a moist soil while rapidly growing in June-July. A good irrigation system could establish such moist soil and improve the drug yield.
- Frequent hoeing would improve the purity of drug by removing the weeds, this procedure also reduce the watering need due to the removal of wild weeds.

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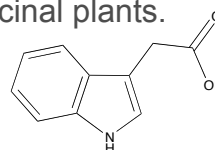
## Plant Growth Hormones



- ❖ Higher plants contain certain compounds known as the growth hormones which increase the growth rate, differentiation (e.g. rooting, etc.) and maturation of plants that could help in the cultivation of medicinal plants.

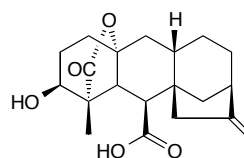
These compounds;

- Auxins (indol derivatives)



Indol-3-acetic Acid

- Gibberellins (Diterpene structure)

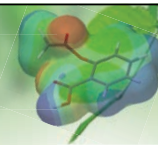


Gibberellic Acid

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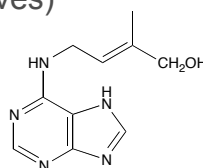


## Plant Growth Hormones

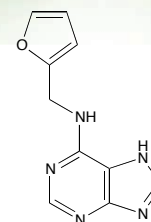


- ❖ Growth compounds;

- Cytokinins (Adenine derivatives)

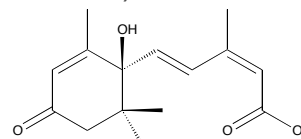


Zeatin



Kinetin

- Absciscic Acid (ABA, Sesquiterpen derivative)



Absisik Asit

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## Collection of Medicinal Plants

- ❖ The **structure of active drug substance** (qualitative) and/or **their amount** (quantitative) in medicinal plants could change by seasons even this change could take place in different time periods of a day. For example;
  - The alkaloid biosynthesis of *Papaver somniferum* starts with **thebain**, it changes into **codein** and later to **morphine**.

CN1CCC23C4C1CC5=C3C(=C(C=C5)OC)OC2C(=O)CC4     $\rightarrow$     CN1CCC23C4C1CC5=C3C(=C(C=C5)OC)OC2C(=O)CC4O     $\rightarrow$     CN1CCC23C4C1CC5=C3C(=C(C=C5)O)OC2C(=O)CC4O

Tebain                                      Kodein                                      Morfin

The codein amount of *P. somniferum* latex (opium) reaches to its highest level at noon.

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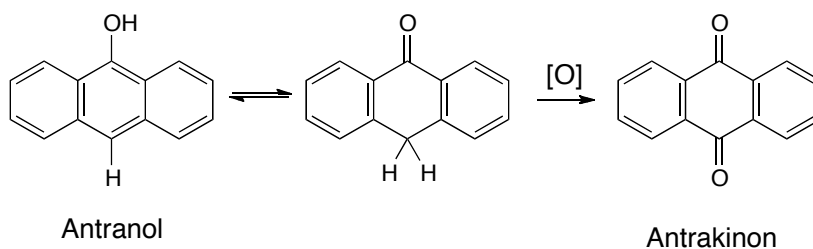
## Collection of Medicinal Plants

- ❖ The alkaloid content of *Ephedra* plant doubles in Fall-Winter seasons in comparison with the Summer, thus, it should be harvested in Fall-Winter period.
- ❖ The cardiotonic glycosides in *Digitalis* (yüksükotu) leaves get hydrolized to the sugars and aglycone components during night-time, the glycoside synthesis resume as the photosynthesis process begin in the morning. Since cardiotonic activity requires glycoside structure, *Digitalis* leaves should be collected in the afternoon.

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## Collection of Medicinal Plants

❖ *Rhizoma rhei* (ravent) contain **anthranol** derivatives in the winter, this compound acts as severe irritant in the gut. Anthranols oxidize to **anthraquinones** in the Summer which act as mild laxative in the GI system, thus the drug should be collected in the Summer.



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## Collection of Medicinal Plants

❖ The medicinal plants should be collected according to the followin rules;

1. Leaves; should be collected when the plant starts blooming.
2. Flowers; should be collected before full development while they're in bud stage.
3. Underground portions; should be collected after the full drying of overground (stem, leaves, flowers, etc.).
4. Bark; should be collected after the plant sheds its leaves.
5. Fruits and seeds; if there is no specific instructions they should be collected after full maturation.
6. Leaves, flowers and overground portions should not be collector durin rainy periods, this will make drying process extremely difficult and cause spoilage of plant material.
7. Roots, rhizomes and tubers as well as barks should be collected in rainy periods.

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## Drying of Drugs

- ❖ Drugs rarely used in fresh state (e.g., some essential oil containing drugs such as rose petals, etc.), however, vast majority of drugs used after drying.
- ❖ In order to store drugs for a long period of time they should be dried, dried drug loss about 75% of its weight and could be easily stored and transported.
- ❖ **Since the drying process remove the majority of plant's water content, it will stop the enzymatic activity in the plant material that could cause degradation or structural change of the active drug substances.**

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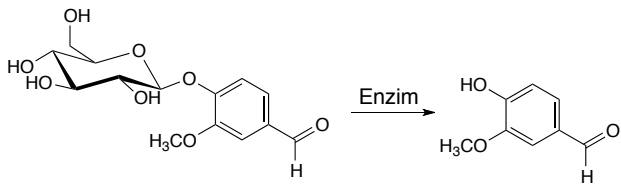
## Drying of Drugs

- ❖ **Drying:** Is a process of the reduction of water content of plant material without changing the quality or quantity of active drug substance(s).
- ❖ Drying process does not degrade the enzymes, however, it reduces the water content which is a required media for enzyme activity. Drying process reduce the water content of drugs to %5-10 that will reduce/stop enzymatic reactions in the drug material.
- ❖ The drying process should be carried out as fast as possible, otherwise the structure of active drug substance (e.g., glycosides) could be changed by enzymes (e.g. hydrolysis of glycosides) which will render them into less- or inactive-form.
- ❖ In order to prevent such changes, the water content of drugs should be removed as soon as possible, using a stream of air with **over or under 35-50°C temperature** (i.e. the highest enzymatic activity temperature range) or drugs should be stabilized by the inhibition of enzymatic activity.

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## Drying of Drugs

- ❖ Sometimes continuation of enzymatic activity desired for example natural vanillin is produced by the enzymatic hydrolysis of vanillin glycoside in Vanilla fruit



Vanillin glikoziti                      Vanillin

- ❖ Drugs containin essential oils should be dried in the shade and essential oil should be extracted or steam/water distilled ASAP.
- ❖ Some plant materials should be processed before drying (e.g. *Liquiritiae radix*), otherwise, removal of their bark or cutting becomes very difficult.

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## Drying of Drugs

- ❖ **Drying Procedures:**
  - 1. Drying in Open Air;**
    - a. Under the Sun;**

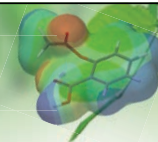
The plant material spread on a large surface under the sunlight. Based on the quantity of water content, the drying process may be completed within couple hours or few weeks. Such procedure can be used with the drugs that could withstand exposure to sun, drying of leaves or flowers is not suitable for this process.  
*Gallae, Valonea, Tubera salep, Liquiritiae radix, Chinae cortex, Cinnamomi cortex* could be dried under the sun.
    - b. Drying in the shade;**

A light impenetrable nylon cover could be stretched over the plant material with a few inches distance between the material and cover, and sideways also left open. This process provides a rapid drying in open air without exposure to the sunlight.

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## Drying of Drugs



### ❖ Drying procedures (Contd.):

#### 2. In the closed & shaded area;

Plant material was dried by spreading as a thin layer on drying racks or hanging in a well ventilated drying rooms. If the ventilation in the drying room was not sufficient, an aspirator could be used to provide it.

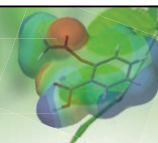
*Digitalis folium*, *Stramonii folium* and essential oil containing drugs could be dried by this method.



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## Drying of Drugs




### ❖ Drying procedures (Contd.):

#### 3. Mixed Drying;

Drying under open air removes ca. 60% of the water content of plant materials in a short time, however, it takes a very long time for the removal of remaining water content. Thus, following the initial open air drying period plant material was subjected to hot air drying procedure to remove the remaining moisture rapidly.

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## Drying of Drugs

❖ Drying procedures (Contd.):

**4. Drying with hot air;**

- a. Drying Cabinet:** It is suitable for the rapid drying of small quantity of plant material. In order to dry the plant material, it should be spread on the racks that made of screens (with at least 15 cm distance between them) and depending on the stability of plant material a hot air (50-120°C) should be circulated around the plant material.
- b. Drying Room:** It is suitable for the drying of large quantities of plant material. The plant material should be spread on the drying racks as a thin layer (as described above) and again depending on the stability of plant material a hot air (ca. 80°C) should be circulated around them. Time to time, plant material should be mixed to ensure an even drying process. In order to evacuate the moisture saturated air from the drying room, two windows with a powerful aspirator should be installed.

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## Drying of Drugs

❖ Drying procedures (Contd.):

**4. Drying with hot air (contd.);**

- c. Drying tunnel:** It is suitable for drying a large quantity of plant material. The plant material is moved in to the drying tunnel in wagons while a stream of hot air sent into the tunnel from the opposite direction. This procedure allow the even exposure of plant material to the hot air stream which enables the drying of plant material in a relatively short period of time.

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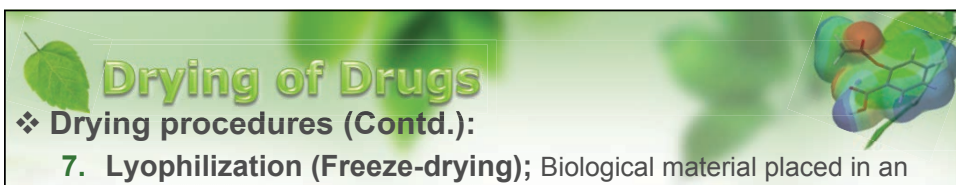


## Drying of Drugs

❖ **Drying procedures (Contd.):**

- 5. Drying with Infrared (IR) Lamps;**  
 Plant material is spread on the racks in an oven equipped with IR lamps (made of tungsten filament) that will dry the plant material within 5-10 minutes at 120-160°C. The plant material should be stable at the drying temperature, it's an expensive procedure.
- 6. Vacuum aided drying;** The plant material is spread on the racks of a vacuum drying oven, upon evacuation of the air from the drying oven moisture of the plant material will start to evaporate. This procedure does not require application of high temperature to dry the plant material and suitable for the drying of heat-sensitive plant material.

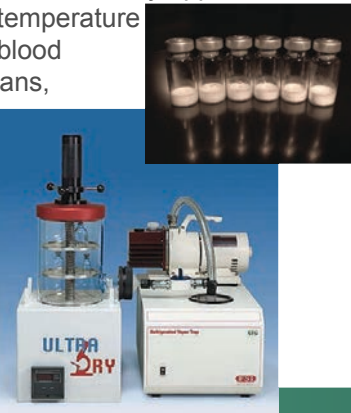
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## Drying of Drugs

❖ **Drying procedures (Contd.):**

- 7. Lyophilization (Freeze-drying);** Biological material placed in an extremely cold refrigerator (i.e., -40°C to -80°C), the water content of material becomes frozen. The frozen material is placed in a high-vacuum chamber, that will trigger the evaporation of frozen water without melting (by sublimation). This procedure usually applied to the materials that are sensitive to high drying temperature or to prolonged exposure to heat such as blood fractions, serum, enzymes, extracts of organs, vitamins, antibiotics, etc. The equipment used for the lyophilization is called freeze-drier. The material dried by freeze-drying can be stored at room temperature in a tightly closed vessels. This material has a porous appearance and easily dissolves in water.




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## Drying of Drugs

❖ Drying procedures (Contd.):

**8. Mikrodalga ile Kurutma;**  
Çok yüksek frekanslı (900 ile 5000 Mhz) güç kaynağı kullanılır. Kurutma kısa sürede gerçekleşir. Kurutulacak materyal ince bir tabaka halinde yayılmalıdır.



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## Drying of Drugs

❖ Storage of Dried Plant Material:

❖ In order to avoid deterioration of dried plant material by humidity, heat or light, it should be stored in a dry, cool and dark place. It may be stored in a paper or canvas bag, cardboard box, tin box or glass jar.


**Enzyme Inhibition;**

- Cold treatment
- Sugar solution treatment
- Application of salt solution
- SO<sub>2</sub> vapor, formol vapor treatment
- Buffer treatment

Enzyme inhibition treatment temporarily stops the chemical activity, it does not change the chemical structure of enzyme.

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## Stabilization of Drugs

❖ **Stabilization;**

- Stabilization is a process where enzyme activity permanently stopped via degradation of enzyme chemical structure.
- Enzyme inhibition with the material drying process is reversible, enzymes become activated when dried material exposed to humidity and heat.
- In order to stop the enzyme activity permanently, following the collection of plant material chemical structures of enzymes must be destroyed.
- Since enzymes chemical structure is protein, they could be denatured by exposure to heat, boiling alcohol or alcohol vapor.

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## Stabilization of Drugs

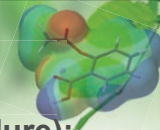
**1. Boiling Alcohol Procedure (Bourquelot Procedure);**

- The first application of this procedure was performed by Bourquelot to stabilize Colae semen in 1896.
- The plant material is boiled in 80% ethanol (5 times more than the material amount) under reflux for one hour to inactivate enzymes. The only draw back of this procedure is compounds that dissolve in ethanol will be extracted by the boiling ethanol.
- This procedure is suitable if the simultaneous extraction and stabilization of the plant material is desired (for example during the phytochemical investigations).

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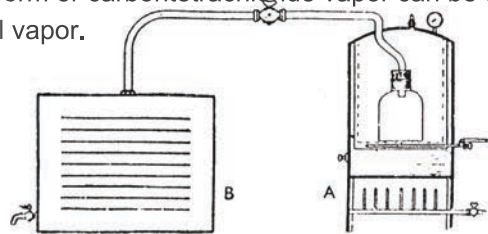


## Stabilization of Drugs



### 2. Alcohol Vapor Procedure (Perrot-Goris Procedure);

- The fresh plant material is placed on to the screen racks in a double walled cabinets, the ethanol vapor generated in an autoclave is directed in to the cabinet which stabilizes the plant material via short vapor exposure.
- This procedure is suitable for the stabilization of unstable plant material such as *Digitalis folium*.
- Chloroform or carbontetrachloride vapor can be used instead of ethanol vapor.

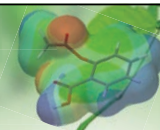


Perrot - Goris stabilizasyon âletinin şeması.  
A - otoklav, B - stabilize edilecek materyelin konulacağı  
raflı dolap (Wattiez ve Sternon'dan).

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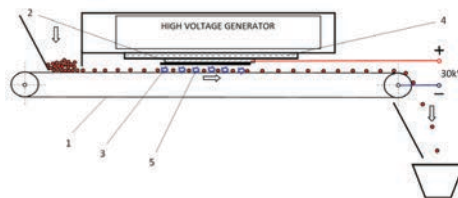
## Stabilization of Drugs



### 3. Dry-Hot Air Procedure:

Stabilization achieved by the application of dry heat around 400° C. An example of this procedure is the preparation of Green Tea, fresh tea leaves were dried on hot pans which will destroy the enzymes and preserve the green color of tea leaves.

- ### 4. Ozonation Procedure;
- Plant material is placed on a conveyor belt as a thin layer that moves under a high voltage ozone generator, the ozone gas stabilizes the plant material by denaturing its enzyme content.



The scheme of the equipment used for  
stabilizing medicinal plants, by ozonation

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## Turkish Medicinal Plant Trade

### Principal Drugs Exported by Turkey (in 2009)

Lauri folium (Defne)	Origani herba, Thymi herba (Kekik)
Carvi fructus, Cumini fructus (Kimyon)	Ceratoniae fructus (Keçiboynuzu)
Anisi fructus (Anason)	Salviae trilobae folium (Adaçayı)
Rhus coriariae fructus (Sumak)	Foeniculi fructus (Rezene)
Rosmarini folium (Biberiye)	Liquiritiae radix (Meyan kökü)
Menthae piperitae folium (Nane)	Tiliae flos (Ihlamur)
Trigonellae semen (Çemen)	Mahaleb semen (Mahlep)
Coriandri fructus (Kışniş)	Nigellae semen (Çörekotu)

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## Turkish Medicinal Plant Trade

### Principal Drugs Imported by Turkey (in 2009)

Cinnamomi cortex (Tarçın)	Vanillae fructus (Vanilya)
Salviae folium (Adaçayı)	Fungi (Mantarlar)
Thymi herba (Kekik)	Anisi stellati fructus (Yıldız Anasonu)
Curcumae rhizoma (Zerdeçal)	Cardamomi fructus (Kakule)
Caryophylli flos (Karanfil)	Myristicae fructus (Küçük Hindistan Cevizi)
Sinapis semen (Hardal tohumu)	Saponariae albae radix (Çöven)

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