

PHARMACOGNOSY-II

Assoc. Prof. Dr. Sinem ASLAN ERDEM

TANNINS

- Tannins are polyhydroxy phenolic compounds, found in plants.
- Soluble in water, ethanol, acetone
- Less soluble in ether, chloroform
- Astringent, pungent taste
- Tannins can be found in plants as complexes → TANNOID (with alkaloid or protein)
- TANNOSIDE → tannin glycosides; tannin condensed with sugars.

TANNINS

- Common in plants.
- Can be found in wholeplant organs
 - Especially;
 - Cortex (C. Quercus, C. Granati)
 - Radix and Rhizoma (Radix Ratanhiae, Rhizoma Rhei)
 - Leaves (Foliae Rhois coriariae)
 - Flowers (Flores Rosae)
 - Fruits (Pericarp of walnut)
 - Seeds (Semen Colae)
 - Some pathological products (Gallae)

TANNINS

CLASSIFICATION

1) HYDROLYSABLE TANNINS

a) Gallitannins

b) Ellagitannins

2) CONDENSED TANNINS

3) PSEUDOTANNINS (Tannin like compounds)

TANNINS

1) HYDROLYSABLE TANNINS

- There is an ester linkage between phenolic acids and sugars.
- Hydrolisable tannin---hydr.---acid/enzyme---
gallic acid or ellagic acid
- Hydrolisable tannin---dry distillation---
Pyrogallols
- FeCl_3 reagent ---- blue colour

TANNINS

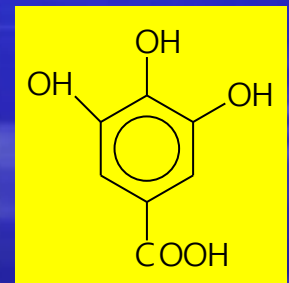
a) GALLITANNINS

Ester structure (between gallic or digallic acid and sugar)

Gallic acid derivatives

Sugar → glucose

Hydrolysis by acid and tannase enzymes result with gallic acid + sugar separation.



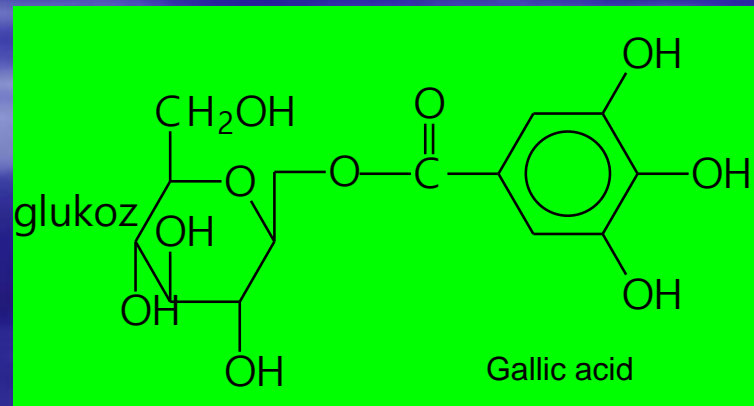
TANNINS

Examples:

1) Gallnut tannin → Galloyl-glucose (glucogallin)

Glucose + 5 mol hydroxy acid or 8-10 hydroxy acid bonding

2) Rh. Rhei (Rhubarb) tannin----Glucogallin

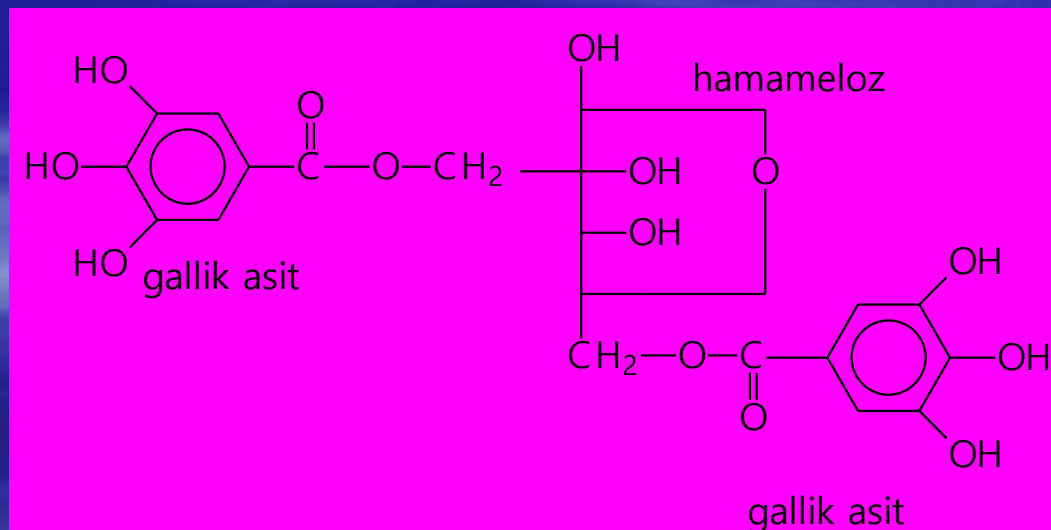


TANNINS

3) F. Hamamelidis-----Hamamelitannin

Crystalline form

Ester of 2 mol gallic acid and 1 mol hammamelose



TANNINS

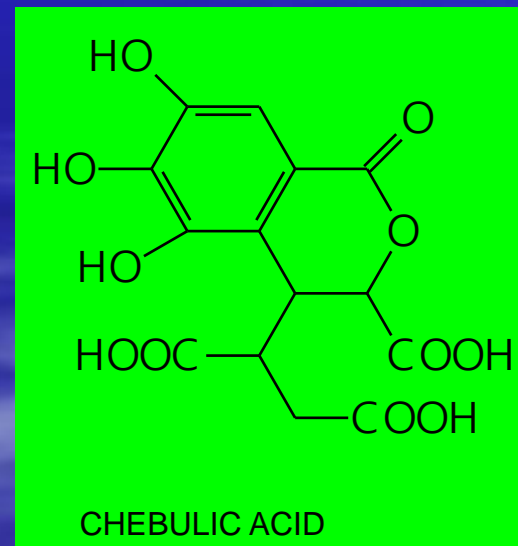
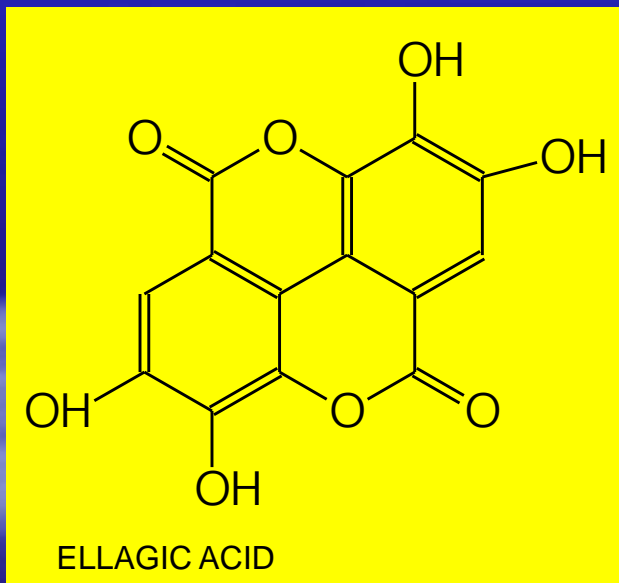
b) ELLAGITANNINS

Tannins in glycosidic form → Formation of hemiacetal bond between ellagic acid and sugars

Chebolic acid and luteic acid may also be found as acids.

TANNINS

- Ellagitannin \rightarrow acid/tannase \rightarrow ellagic acid / chebulic acid + sugar



TANNINS

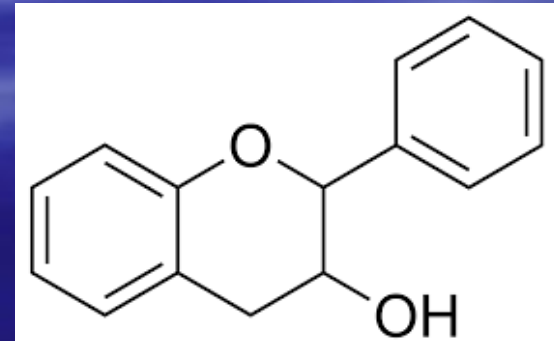
- Examples of drugs:
- Chestnut tannin
- Cortex Granati
- Gallae Quercinae
- Folia Eucalypti

TANNINS

2) CONDENSED (CATECHIN) TANNINS (PROANTHOCYANIDINS)

- Condensed tannins are polymeric flavans. They consist of flavan-3-ol units linked together by C-C bonds (4→8; 4→6). Flavonoid like compounds.
- They are not readily hydrolyzable

Flavan-3-ol



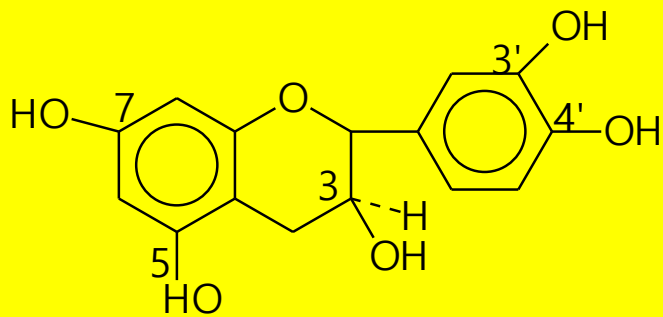
CONDENSED (CATECHIN) TANNINS (PROANTHOCYANIDINS)

- When treated with strong acids or enzymes, condensed tannins convert to phlobaphenes, -deep red coloured and insoluble compounds-

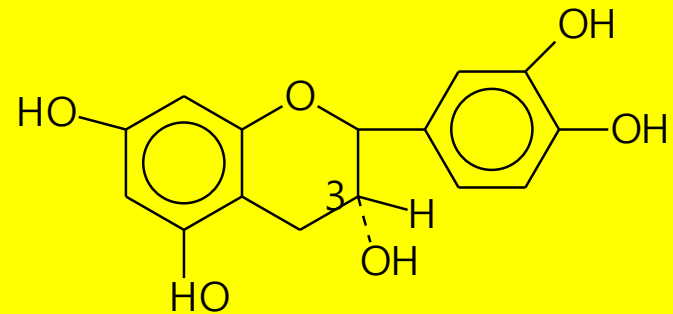
TANNINS

- Structure of condensed tannins

1) 5,7,3',4'-tetrahydroxy flavan-3-ol structure



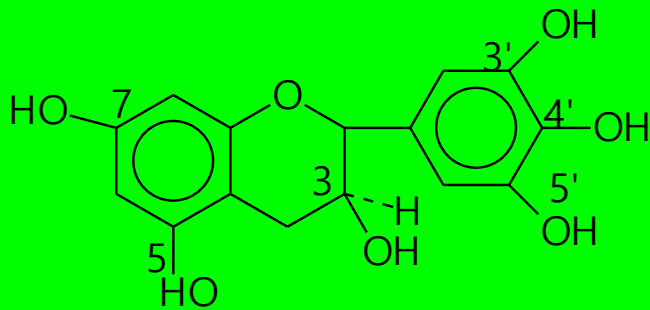
CATECHIN (CIS)



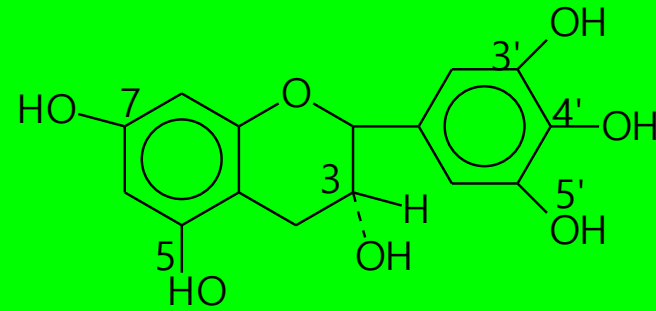
EPICATECHIN (TRANS)

TANNINS

- 2) 5,7,3',4', 5'-pentahydroxy flavan-3-ol



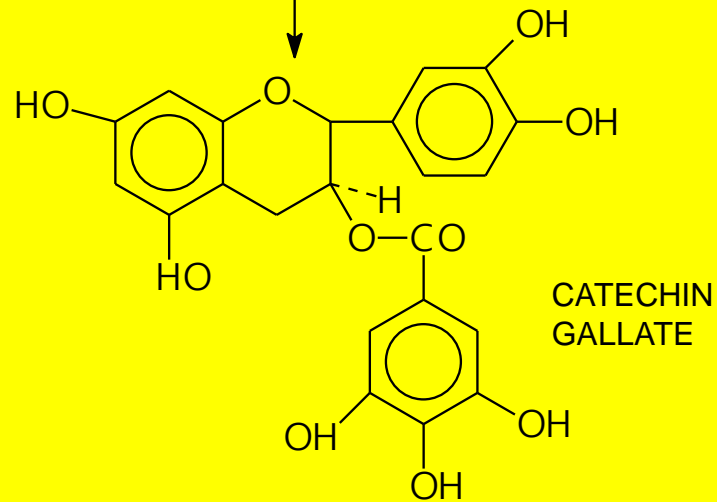
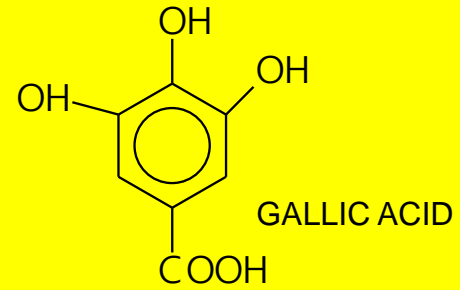
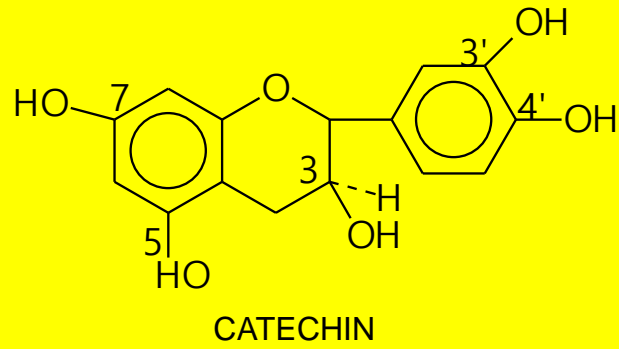
GALLOCATECHIN (CIS)



EPIGALLOCATECHIN (TRANS)

TANNINS

- These 4 compounds form ester with gallic acid from third position. :
- CATECHIN GALLATE
- EPICATECHIN GALLATE
- GALLOCATECHIN GALLATE
- EPIGALLOCATECHIN GALLATE



TANNINS

- Examples to drugs containing condensed tannins:
 - Semen Colae
 - Cotex Chinae
 - Radix Ratanhiae
- Phlobaphene amount (red colour) of these drugs increasing in time.

TANNINS

3) PSEUDOTANNINS (Tannin Like Compounds)

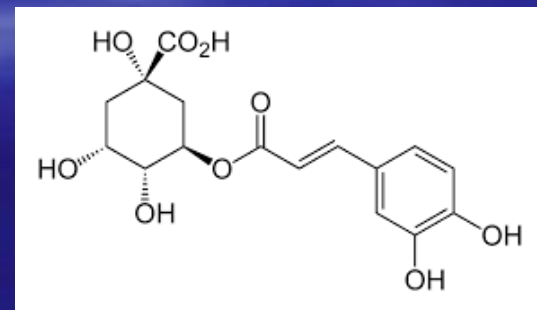
Their structure is different but they represent tannin properties; with low molecular weight.

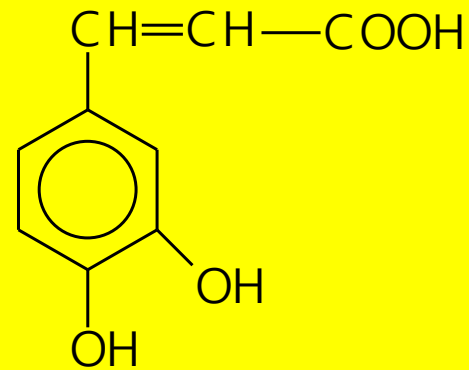
Example:

COFFEE TANNIN: chlorogenic acid

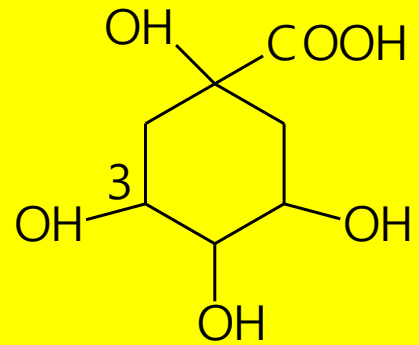
Found in coffee, tea, Strychnos seeds and Solanaceae leaves.

Ester of caffeic acid and quinic acid

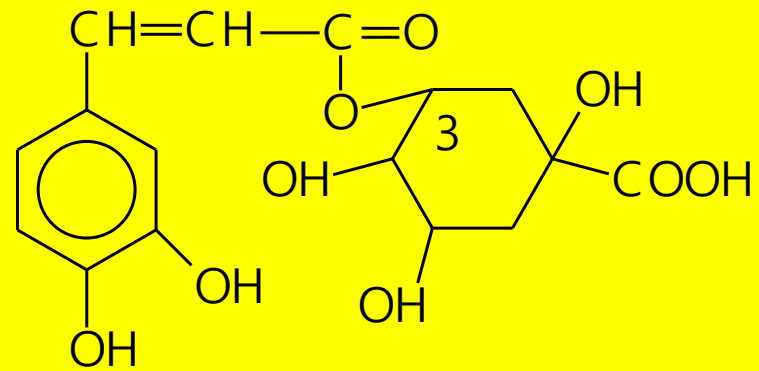




CAFEIC ACID



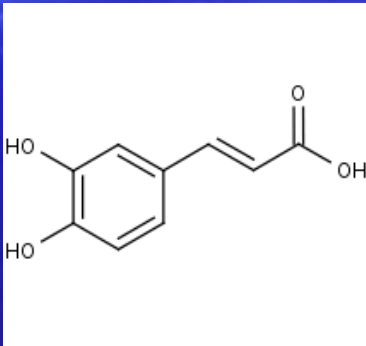
QUINIC ACID



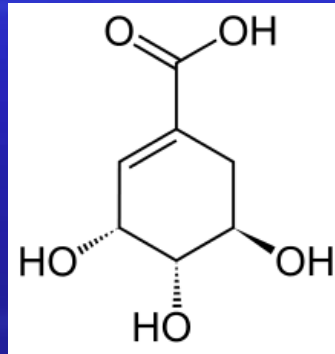
CHLOROGENIC ACID

TANNINS

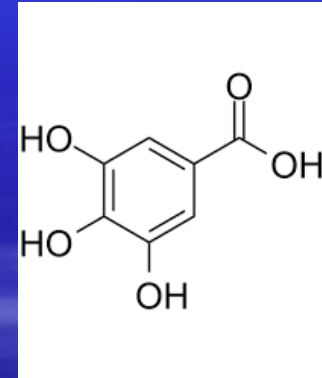
■ PSEUDOTANNINS



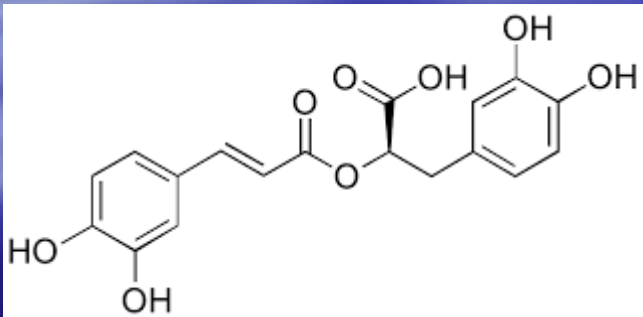
Caffeic acid



Quinic acid



Gallic acid



Rosmarinic acid

TANNINS

PROPERTIES

- Soluble in **water**, forming colloidal solutions
- Asidic reaction and sharp astringent taste
- Soluble in dilute alkalis, alcohol, glycerol and acetone but less soluble in other organic solvents
- Rarely crystallizable compounds
- Their solutions precipitate heavy metal salts (e.g. Cu, Fe, Zn, Hg, Pb), alkaloids and protein (e.g. gelatin)

TANNINS

- Tannins precipitate limewater ($\text{Ca}(\text{OH}_2)$), baryta-water ($\text{Ba}(\text{OH}_2)$)
- Tannin solution precipitate gelatin solution
- Oxidize easily in alkali medium
 - With iron(III) chloride (FeCl_3);
 - Hydrolysable tannins → blue-black
 - Condensed tannins → Brown-green (due to phenolic groups)

TANNINS

- Condensed tannins precipitate with Bromine water and Stiasny reagent
- Tannins reduce Fehling's solution

EXTRACTION

- The most suitable method is percolation with water-saturated EtOH: Ether mixture.

TANNINS

Quantitative Determination

1) Gravimetric Method: Precipitation with heavy metal salts then weight

2) Titrimetric (Volumetric) Method:

- Tannins are oxidized by using KMnO_4 , $\text{K}_2\text{Cr}_2\text{O}_7$ or I_2 and excess reagent is determined by reverse titration.

TANNINS

3) Absorbtion Method (Hide Powder Method):

- Tannins are precipitated/absorbed by addition of hide powder
- Total tannin amount is obtained by using this method (hydrolysable and condensed tannins amount).

TANNINS

- Tannin solution is prepared, divided to to equal portions; one portion is dried and weighed (A)
- Other portion is treated with hide powder; then filtered and solution is dried and weighed (B).
- Difference of the amounts A-B gives the amount of tannins.

TANNINS

5) Stiasny Method:

- Condensed tannin quantification.
- Water solution of drug (decoction 1%)
(completed to a certain volume)
- Divide to 2 equal portions.
- 1.portion+stiasny reagent---precipitate (A g)
(catechin + condensed tannin)

TANNINS

- 2. portion + gelatin salt solution ---- filter --- precipitate (condensed ve hydrolysable tannin)
- Filtrate + stiasny reak. --- precipitate (B g.) (catechin)
- CONDENSED TANNIN = A - B
- Stiany reagent = Formol + HCl

TANNINS

6) Biological Method:

- It is based on the fact that tannins form a combination with hemoglobin; non-precipitated hemoglobin can be estimated colorimetrically against a blank.

Tannin Quantification from European Pharmacopoeia

- Powdered drug/extract + water → heat 30min on waterbath
- Diluted and washed
- **Total polyphenol amount:**
- Filtrate + water → dilution + phosphomolybdotungstic reagent+ sodium carbonate → dilution → absorbance measurement at 760 nm (**A1**)

Polyphenols which are not absorbed to hide powder

- Filtrate + **hide powder CRS** → mix → filtrate → dilute
- Filtrate + phosphomolybdotungstic reagent + sodium carbonate → absorbance measurement at 760 nm (**A2**)
- **Pyrogallol** + phosphomolybdotungstic reagent + sodium carbonate → absorbance measurement at 760 nm (**A3**)

Tannin amount (on pyrogallol amount)

62.5 (A1-A2) M2

A3 X M1

M1: examined sample amount (g)

M2 : Pyrogallol amount (g)

TANNINS

EFFECT- USAGE

1) Externally;

- Astringent
- They make the skin surface less permeable
- Vasoconstriction on capillaries; used against hemorrhoids.
- They are used in burns → they form a mild antiseptic protective layer on the surface of the injured skin below which regeneration of new tissue takes place.
- Wound healing effect → antiinflammatory properties.
- Not suitable for uses in wide surfaces; they can be toxic

TANNINS

2) Internally;

- Antidiarrheal; reduces peristaltism of the large intestine.
- Antiseptic due to phenolic structure.
- Used as antiseptic in lung diseases (tuberculosis).
- Coagulates proteins → stop the development of certain microorganisms (antimicrobial)

TANNINS

- Gallic acid and chlorogenic acid---cholagogue
- Irritating in high doses → used as hair tonic.
- Antidot in alkaloid intoxication; non-soluble tannates occur.
- Provides easy intake of anthracene derivatives.
- Prevents hydrolysis of glycosides in drugs.
- Use in leather tanning.

TANNINS

- Catechins;
 - Show P vit. activity
 - Anticeptic
 - They delay and extend effect of caffeine

TANNIN CONTAINING DRUGS

DRUG	PLANT	TANNIN TYPE	%
Flos Caryophylli	<i>Jambosa caryophyllus</i>	Hydrolysable/Gallic	10-13
Flos Rosae	<i>Rosa gallica</i>	Hydrolysable/Gallic	10-25
Folia Hamamelidis	<i>Hamamelidis virginiana</i>	Hydrolysable/Gallic	8-10
Folia Juglandis	<i>Juglans regia</i>	Hydrolysable/Gallic	5
Folia Rhus coriariae	<i>Rhus coriaria</i>	Hydrolysable/Gallic	20
Gallae sinensis	<i>Rhus semialata</i>	Hydrolysable/Gallic	50-60
Gallae Turcicae	<i>Quercus infectoria</i>	Hydrolysable/Gallic	50-70
Rhizome Rhei	<i>Rheum sp.</i>	Hydrolysable/Gallic	15-25
Valonea	<i>Quercus macrolepis</i>	Hydrolysable/Gallic	27-30

DRUG	PLANT	TANNIN TYPE	%
Cortex Eucalypti	<i>Eucalyptus sp.</i>	Hydrolysable/Ellagic	10-50
Cortex Granati	<i>Punica granatum</i>	Hydrolysable/Ellagic	20-22
Cortex Quercus	<i>Quercus sp.</i>	Hydrolysable/Ellagic	10-15
Cortex Salicis	<i>Salix sp.</i>	Hydrolysable/Ellagic	5-17

DRUG	PLANT	TANNIN TYPE	%
Cortex Pini	<i>Pinus sp.</i>	Condensed/Catechin	5-16
Folia Theae	<i>Thea sinensis</i>	Condensed/Catechin	5-10
Gambir	<i>Ungaria gambir</i>	Condensed/Catechin	60
Catechu	<i>Acacia catechu</i>	Condensed/Catechin	5-35
Kino	<i>Pterocarpus marsupium</i>	Condensed/Catechin	25-80
Radix Ratanhiae	<i>Krameria triandra</i>	Condensed/Catechin	40
Rhizoma Filicis	<i>Aspidium filix-mas</i>	Condensed/Catechin	3-10
Semen Aracae	<i>Areca catechu</i>	Condensed/Catechin	13-27

GALLAE (GALLAE QUERCINAE)

Nut gall

- *Quercus infectoria* (Oak; Mazi meşesi) (Fagaceae)
- Galls are pathological outgrowth formed on twigs of tree. Galls form due to deposition of the eggs of insect *Cynips Gallae tinctoriae* (Hymenopterae).
- Common in Anatolia.
- 2 types of gall can be obtained.
- White Galls (Ak mazi) (Aegean Region)
- Black Galls (Kara Mazi) (Southeast Anatolia)

GALLAE (GALLAE QUERCINAE)

Nut Gall

- 1.5-2 cm diameter, spherelike, firm, with rough surface.
- The ones with short-stemmed and without a hole are called black-gall. Collected before the insects leave the gall.
- White-gall; yellowish, with a small hole. Collected after the insects leave the gall. It is lighter and second quality.

GALLAE (GALLAE QUERCINAE)

Nut Gall

- Galls obtained from Turkey is called Gallae Smyrnensis
- Galls obtained from Syria is called Gallae Halepensis.

GALLAE (GALLAE QUERCINAE)

- Chinese galls are known as Gallae Chinensis.
- These galls are occur on petiols of *Rhus semialata* ve *R. japonica* (Anacardiaceae) by the *Aphis chinensis* insect
- It is different morphologically
- Fragile, reddish-brown

GALLAE (GALLAE QUERCINAE)

- Turkish galls;
- 60-70% Gallotannins
- 2-4% free gallic acid and ellagic acid
- Chinese galls;
- 90% Gallotannins
- Turkish galls----- in tetragalloyl glucose structure

GALLAE (GALLAE QUERCINAE)

Pharmaceutical;

- Astringent and hemostatic (0.5-4 g dose)
- Externally--- use in skin infections as antiseptic
- Found in the composition of anti-hemorrhoidal medications
- Veterinary --- used to constipate
- Alkaloid intoxication----antidote
- Used to obtain tannins
- Mordant material in leather industry and textile industry
- Export product of our country

ACIDUM TANNICUM, Tannic Acid, Tanen

- Obtained from galls on Gallae or *Quercus* species
- Obtaining;
- Ground galls, percolated with water-saturated ethanol-ether (1:4) mixture
- Separated liquid part is in 2 layers; tannins found in the lower water phase; this layer is separated, and concentrated → tannin is obtained.
- Soluble in water, EtOH and acetone
- Non-soluble in Ether ve CHCl_3 .

ACIDUM TANNICUM, Tannic Acid

- Since it is strong irritant, its less soluble derivatives are prepared to use.
- If it is taken in free form side effects such as nausea and vomiting may be seen.
- TANNIGEN----Acetyltannic acid (USP XVII)
- TANNALBIN----Tannin albuminate (USP XVII)
- PROTAN----- Tannin caseinate (USP XVII)
- Bismuth subgallate - BIZMUT SUBGALLAT (TF)

ACIDUM TANNICUM, Tannic Acid

Tannic acid;

- Internally-----antidiarrheal
- Externally → used in 10% solution against small burns; not used in large burns since it will be toxic then.
- Bed wounds ---- pomade/spray
- Mouth and throat infections
- Antidote in alkaloid poisoning.

VALONEA, Valonia, Meşe Palamutu, Valonia oak

- *Quercus macrolepis* (Fagaceae)
- Fruits collected without fully matured.
- East Mediterranean region
- Turkey
- Obtained at Greece.

VALONEA, PALAMUT, MEŞE PALAMUTU

- Valonia fruit (Valonea);
- Pelit (Gland)----10% tannin
- Cup (Cupula)----30-35% tannin
- Trillo (Trillo)----40% tannin

VALONEA, PALAMUT, MEŞE PALAMUTU

- Contain gallotannins.
- Pelit is used Pharmaceutically. Roasted pelits, grinded (Semen Quercus tostum) and used to constipate.
- Cup and trillo-----leather industry.
- Export product.

CORTEX QUERCUS

- Bark of young branches of *Quercus* sp.
- Containing oligomeric proanthocyanidols --- catecin tannin
- Ellagitannin
- Gallotannin
- Monomeric and dimeric catechols and proanthocyanidins
- Tannic acid (12-16%)

CORTEX QUERCUS

- Astringent; internally antidiarrheal
- Antiinflammatory in gastrointestinal inflammations
- Externally used to treat dyshydrotic eczema as compress.
- Mouth and farynx inflammations → mouthwash.
- Virustatic effect.

FOLIA HAMAMELIDIS (TK) (EP)

Hamamelis, witch-hazel

- *Hamamelis virginiana* (cadı findığı)
(Hamamelidaceae)
- North America
- Grown in Mexico and Canada
- Hamamelitannin (hydrolysable tannin) (10%)---
hydr.---(acid/tannase)---2 mol gallic acid +
hamamelose
- Free gallic acid and quinic acid
- Oligomeric procyanidins, catechin
- Flavonoids: Kampherol, quercetin and
isoquercetin glycosides.

FOLIA HAMAMELIDIS (TK) (EP)

Due to tannin content;

- Astringent
- Vasoconstrictive---especially on peripheral veins
- Antiinflammatory
- Flavonoids----P vit. activity
- Used against hemorrhoids, varicosis, phlebitis.
- Used as haemostatic and astringent.
- Have preparations used externally.

FOLIA HAMAMELIDIS (TK) (EP)

- HAMETAN pomade/cream → In Burns and wounds; as diaper rash cream
- Dermocosmetically used against wrinkles.
 - ❖ Leaves alone used;
 - ❖ Mouth and farynx inflammations.
 - ❖ 2-3 g drug 150 ml decoction; mouthwash.

FOLIA HAMAMELIDIS (TK) (EP)

- Preparations sold abroad:
- DICKINSON'S----Hemostatic
- PREPARATION H---- Hemoroid
- EUCERIN-----Hemoroid
- PARKE DAVIS TUCKS+ALOE---Astringent,
skin cleanser

CORTEX HAMAMELIDIS

- Dried bark of young branches.
- %12 Hamamelitannin
- Oligomeric procyanidins
- Catechins
- Used with same purposes as leaves.
- Especially used as astringent, externally.

FOLIA RHOIS CORIARIAE

- *Rhus coriaria* (Anacardiaceae), sumac leaves
- Grown in Aegean, Mediterranean and East Anatolia.
- %15-20 GALLOTANNIN
- Astringent antidiarrheal usage.
- Mouthwash → tonsillitis and stomatitis
- Hemostatic
- Extracts are used for leather tanning and fabric dyeing.
- Export product due to tannin content.

SUMAC FRUITS

- 4% tannin
- Organic acid, essential oil
- Using as spice for its sour taste
- Hemostatic effect.

FRUCTUS ROSAE CANINAE (FRUCTUS CYNOBASTI), Rosehip Fruit, Kuşburnu

- *Rosa canina* (Rosaceae), red fruits of rosehip.
- 2-3% gallic tannin
- Vitamine C (based on dry weight %1-2)
- 20-25% pectin
- 30% carbohydrates
- Organic acids (malic, citric acid)
- Flavonoid and carotenoid derived dyeing compounds

FRUCTUS ROSAE CANINAE (FRUCTUS CYNOBASTI), Rosehip Fruit

- Tannin → astringent
- Flavonoid → diuretic, vitamin P activity
- Pectin and tannin → antidiarrheal
- Used as tea in respiratory diseases

CATECHU (TK), Cachou, Kateşu, Kaşu

- Dried water extract of body wood of *Acacia catechu* (Fabaceae).
- Ceylan, India, East Indian Islands and Burma; with 10-20 m height.
- It is a rigid mass.
- Outside Brown-black, inside red-brown
- Odourless
- Very astringent

CATECHU (TK), Cachou, Kateşu, Kaşu

- Composition;
- Cachou tannic acid (30%)---catechin tannin+catechol (condensed tannin)
- Catechin and Epicatechin (10%) (condensed tannin)
- Quercetin ---- Flavonoid

CATECHU (TK), Cachou, Kateşu, Kaşu

- Strong astringent-----antidiarrheal
- Found in composition of tooth powders.
- Catechols----P-vit. activity
- Used as food colouring

RADIX RATANHIAE (TK), Ratanya Kökü, Krameria root

- Dried roots of *Krameria triandra* (Fabaceae)
(Rhatany, ratany)
- Small trees growing in South America, Peru,
Bolivia, Chili mountains

RADIX RATANHIAE (TK), Ratanya Kökü, Krameria root

- Contains condensed tannins
- Catechol + catechin tannin (10-15%)
- Phlobaphen (ratanhia or Krameria red)
- Ratanhia tannic acid (20-40%) (condensed tannin)

RADIX RATANHIAE (TK), Ratanya Kökü, Krameria root

- Astringent
- Internally antidiarrheal
- Hemostatic effect; used against hemorrhage as dry extract (0.5-4 g) or as tincture (5-15g).
- Used for hemorrhoids and anal fissures as pomade and suppository
- Found in composition of toothwashes
- Used as mouthwash.