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PHARMACOGNOSY AND PHYTOCHEMISTRY - II

UNIT 2

TOPIC :

- **Steroids, Cardiac Glycosides & Triterpenoids : Liquorice, Dioscorea, Digitalis**



Steroids

- Steroids are naturally occurring organic compounds containing a characteristic cyclopentanoperhydrophenanthrene ring system (four fused rings – three six-membered and one five-membered ring).
- They are biosynthesized from triterpenoids and play essential roles as hormones, vitamins, and structural components.

General Structure

- Basic nucleus: Sterane (gonane) – C_{17} skeleton.
- Commonly substituted with methyl groups at C-10 and C-13 and side chains at C-17.

Classification

1. Sterols (Alcoholic steroids):
 - Example: Cholesterol, Ergosterol.
2. Bile acids:
 - Example: Cholic acid, Deoxycholic acid.
3. Adrenocortical hormones:
 - Example: Cortisone, Hydrocortisone.
4. Sex hormones:
 - Male: Testosterone, Androsterone
 - Female: Progesterone, Estrogen.
5. Vitamin D group:
 - Example: Vitamin D_2 (Ergocalciferol), Vitamin D_3 (Cholecalciferol).

Chemical Nature

- Derived from isoprene units (C_5H_8).
- Contain oxygenated functional groups like hydroxyl, carbonyl, or carboxyl groups.

Biosources

- Found in plants, animals, and microorganisms.
- Cholesterol (animal source), stigmasterol (plants), ergosterol (fungi).

Therapeutic Uses

- Used as anti-inflammatory, antiallergic, anabolic, and hormonal agents.
- Important in contraceptive formulations and hormone replacement therapy.

Commercial Applications

- Used in pharmaceutical preparations (e.g., corticosteroids).
- Steroidal saponins from plants like *Dioscorea* are used as raw materials for semisynthetic steroids.

Cardiac Glycosides

- Cardiac glycosides are steroid glycosides that act on the heart muscle to increase the force of contraction (positive inotropic effect) and regulate heartbeat.
- They consist of a sugar (glycone) and a non-sugar (aglycone or genin) part.

General Structure

1. Aglycone (Genin):
 - Steroidal nucleus with an unsaturated lactone ring at C-17.
 - Two types:
 - Cardenolides → 5-membered lactone ring (e.g., Digitalis)
 - Bufadienolides → 6-membered lactone ring (e.g., Squill)
2. Glycone (Sugar):
 - Usually 1–4 molecules of sugars (glucose, digitoxose, etc.).

Chemical Classes

1. Cardenolides – Found in plants like *Digitalis*, *Strophanthus*.
2. Bufadienolides – Found in toad venom and *Urginea* (Squill).

Biosources

- *Digitalis purpurea* (Foxglove)
- *Digitalis lanata*
- *Strophanthus gratus*
- *Urginea maritima* (Squill)

Therapeutic Uses

- Used in the treatment of congestive heart failure (CHF) and atrial fibrillation.
- Example: Digoxin, Digitoxin, Ouabain.

Mechanism of Action

- Inhibits Na^+/K^+ -ATPase enzyme, increasing intracellular calcium → enhanced cardiac contractility.

Toxicity

- Narrow therapeutic index; overdose causes nausea, vomiting, arrhythmia.

Commercial Applications

- Used in cardiotonic preparations.
- *Digitalis* extracts used for standardized cardiac glycoside formulations.

Triterpenoids

Triterpenoids are terpenoid compounds composed of six isoprene (C_5H_8) units, forming a C_{30} skeleton.

They serve as precursors for steroids and saponins.

General Structure

- Derived from squalene, a linear C_{30} triterpene.
- May occur in cyclic or acyclic forms.
- Contain various oxygenated functional groups like alcohols, aldehydes, ketones, or acids.

Classification

1. Acyclic triterpenes – Squalene.
2. Cyclic triterpenes:
 - Pentacyclic: Oleanane, Ursane, Lupane types.
 - Tetracyclic: Lanostane, Cucurbitane.

Biosources

- Widely distributed in plants:
 - *Glycyrrhiza glabra* (Liquorice) – Glycyrrhizin
 - *Boswellia serrata* (Frankincense) – Boswellic acid
 - *Guggul* (Commiphora mukul) – Guggulsterone
 - *Digitalis* species – precursors for steroids.

Chemical Nature

- Neutral or acidic compounds.
- Soluble in organic solvents (chloroform, ether) and insoluble in water.

Therapeutic Uses

- Anti-inflammatory (Boswellic acids)
- Antiviral and antimicrobial
- Hepatoprotective
- Anticancer
- Expectorant and demulcent (Glycyrrhizin from Liquorice)

Commercial Applications

- Used in pharmaceutical formulations and cosmetics.
- Serve as precursors for steroid synthesis.
- Used in soap and shampoo formulations (due to foaming saponins).

Liquorice (*Glycyrrhiza glabra*)



- Common Names: Liquorice, Licorice, Mulethi (Hindi)
- Botanical Name: *Glycyrrhiza glabra* L.
- Family: Fabaceae (Leguminosae)
- Plant Type: Perennial herb
- Part Used: Roots and stolons (underground stems)
- Origin: Native to Southern Europe and Western Asia; cultivated in India, China, and Mediterranean countries.
- Description: Liquorice is a sweet-tasting root used as a flavoring agent and medicinal herb. It has been used since ancient times in Ayurveda, Unani, and Chinese medicine for cough, sore throat, and gastric problems.

Composition

Liquorice root contains many bioactive compounds, mainly triterpenoid saponins, flavonoids, and sugars.

Constituent	Percentage / Function
Glycyrrhizin (Glycyrrhizic acid)	6–14%; main active principle; sweet taste (50× sweeter than sugar)
Flavonoids (Liquiritin, Isoliquiritin, Liquiritigenin)	Antioxidant, anti-inflammatory
Sugars (Glucose, Sucrose)	Provide sweetness
Starch, Resin, Gum	Base materials
Volatile Oils	Responsible for aroma
Asparagine (amino acid)	Nutrient and soothing agent

Chemistry & Chemical Classes

- Main Chemical Classes:
 1. Triterpenoid Saponins: Glycyrrhizin (glycyrrhizic acid)
 2. Flavonoids: Liquiritin, liquiritigenin, isoliquiritin
 3. Polysaccharides: Starch, gums
- Chemical Nature:
 - Glycyrrhizin is a potassium and calcium salt of glycyrrhizic acid ($C_{42}H_{62}O_{16}$).
 - It hydrolyzes to glycyrrhetic acid and glucuronic acid.
 - Flavonoids are responsible for color and antioxidant effects.

Biosources

- Botanical Source: *Glycyrrhiza glabra* (true liquorice)
- Geographical Sources: Cultivated in India (Punjab, Jammu, Kashmir, and South India), China, Iran, Turkey, and Italy.
- Plant Part Used: Roots and underground stolons.
- Collection: Roots are collected in autumn when glycyrrhizin content is high, dried, and peeled before use.

Therapeutic Uses

Liquorice is widely used in both modern and traditional medicine due to its anti-inflammatory, demulcent, and expectorant properties.

Constituent / Action	Therapeutic Use
Glycyrrhizin	Anti-inflammatory, antiulcer, expectorant, and antiallergic
Flavonoids	Antioxidant, hepatoprotective, and antimicrobial
Asparagine and sugars	Soothing and nutritive effects

Pharmacological Actions:

- Anti-inflammatory: Similar to corticosteroids, helps in ulcers and allergies.
- Demulcent: Forms soothing film over mucous membranes, relieving irritation in the throat and stomach.
- Expectorant: Helps remove mucus from the respiratory tract.
- Antiviral: Shown activity against hepatitis and influenza viruses.

Commercial Applications

- Pharmaceutical Uses:
 - Used in syrups, lozenges, and cough mixtures.
 - Extracts used in anti-ulcer and anti-inflammatory formulations.
- Flavoring Agent:
 - Used in tobacco, toothpaste, chewing gum, confectionery, and beverages for its sweet flavor.
- Cosmetic Uses:
 - Used in skin creams for its anti-inflammatory and brightening effects.

Dioscorea

- Common Name: Yam, Wild Yam
- Botanical Name: *Dioscorea species* (mainly *Dioscorea composita* and *Dioscorea floribunda*)
- Family: Dioscoreaceae
- Plant Type: Twining herb (climbing plant with tuberous roots or rhizomes)
- Part Used: Tubers and rhizomes
- Origin: Native to tropical and subtropical regions of Asia, Africa, and Central America.
- Description: Dioscorea is a climbing vine with heart-shaped leaves and underground tubers rich in steroidal compounds.
- Significance: The plant is a major natural source of steroidal saponins, which are used in the synthesis of steroidal drugs such as cortisone, progesterone, and oral contraceptives.

Composition

Constituent	Type / Function
Diosgenin	Main active compound; used for synthesis of steroid hormones
Yamogenin	Steroidal sapogenin similar to diosgenin
Saponins (dioscin, gracillin)	Precursor of diosgenin; detergent and anti-inflammatory activity
Starch	Energy reserve
Resins and Sugars	Minor components

Chemistry & Chemical Classes

- Major Chemical Class: Steroidal Saponins
- Important Compound: Diosgenin (a sapogenin)
 - Chemical Formula: $C_{27}H_{42}O_3$
 - Structure: Spirostane type steroidal nucleus
 - Nature: Aglycone part of saponin (when sugar part is removed from dioscin, diosgenin remains).
- Chemical Reaction:
 - Hydrolysis of Saponins $\rightarrow$ Diosgenin + Sugars
- Properties of Diosgenin:



- Insoluble in water; soluble in organic solvents like alcohol and chloroform.
- Used as a starting material for synthesis of corticosteroids and sex hormones.

Biosources

- Botanical Sources:
 - *Dioscorea composita*
 - *Dioscorea floribunda*
 - *Dioscorea deltoidea*
- Geographical Sources:
 - Found in India, Mexico, China, Japan, and Africa.
 - In India, mainly cultivated in Himalayan regions and Southern states.
- Plant Part Used: Tuberous roots and rhizomes.
- Collection: Tubers are collected, cleaned, dried, and powdered for extraction of diosgenin.

Therapeutic Uses

Dioscorea and its active compound diosgenin are widely used in pharmaceutical and traditional medicine.

Active Compound	Therapeutic / Industrial Use
Diosgenin	Used in synthesis of steroid hormones (progesterone, cortisone, testosterone)
Saponins	Anti-inflammatory, antispasmodic, and antioxidant
Raw Extract	Used for relieving menstrual cramps, arthritis, and muscle pain
Traditional Uses	Used in Ayurveda and folk medicine for pain relief, digestive disorders, and hormonal balance

Pharmacological Actions

- Anti-inflammatory: Reduces inflammation and swelling.
- Antispasmodic: Relieves muscle cramps and uterine spasms.
- Hormonal activity: Acts as a precursor for steroid hormones (synthetic route).
- Antioxidant and Anti-arthritic: Reduces oxidative stress and joint pain.

Commercial Applications

- **Pharmaceutical Uses:**
 - Diosgenin from Dioscorea is used for semi-synthetic production of:
 - Corticosteroids (e.g., Cortisone, Hydrocortisone)
 - Sex hormones (e.g., Progesterone, Testosterone, Estrogens)
 - Oral contraceptives (e.g., Norethisterone)
- **Industrial Uses:**
 - Used as a raw material for steroid drug manufacturing.
- **Traditional Medicine:**
 - Used as a natural remedy for menstrual disorders, arthritis, and digestion issues.
- **Nutritional Uses:**
 - Some species of yams are used as food sources rich in starch and fiber (non-toxic varieties).

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Digitalis

- Common Name: Foxglove
- Biological Source: Dried leaves of *Digitalis purpurea* or *Digitalis lanata*
- Family: Scrophulariaceae (now Plantaginaceae)
- Part Used: Leaves
- Geographical Source: Mainly found in Europe, India, and North America
- Description:
Digitalis is a biennial herb (lives for two years). It has large, soft, green leaves and beautiful bell-shaped purple or white flowers.
The leaves are collected before the plant flowers because that's when they have the highest content of active glycosides.

Composition

Digitalis leaves contain cardiac glycosides — compounds that act on the heart.

Constituent	Type / Function
Cardiac Glycosides	Main active constituents
→ Digitoxin	Long-acting glycoside
→ Digoxin	Commonly used, short-acting glycoside
Gitoxin, Gitalin, and Digitalin	Other minor glycosides
Flavonoids, Sterols, and Sugars	Supportive components

Cardiac glycosides = Aglycone (genin) + Sugar (glycone)

→ Aglycone gives pharmacological activity

→ Sugar part helps in absorption and solubility



Chemistry & Chemical Classes

- Chemical Class: Cardiac glycosides (C-23 steroids)
- Chemical Nature: Steroidal compounds with lactone ring and one or more sugar units.
- Main Chemical Structure:
 - Aglycone (Genin): Steroid nucleus with unsaturated lactone ring at C-17.
 - Glycone (Sugar part): Digitoxose sugars (3 molecules in digitoxin).

Compound	Half-Life	Water Solubility	Remarks
Digoxin	1.5 days	Moderate	Commonly used
Digitoxin	5-7 days	Poor	Long-acting, more lipophilic

Biosources

- Plant Sources:
 - *Digitalis purpurea* — gives Digitoxin
 - *Digitalis lanata* — gives Digoxin
- Family: Scrophulariaceae
- Geographical Distribution:
 - Native to Europe
 - Cultivated in India (Nilgiri hills, Kashmir, Himachal Pradesh), Germany, England, and USA
- Part Used: Dried leaves (collected before flowering)

Therapeutic Uses

Digitalis is one of the most important cardiotonic drugs.

Use	Description
1. Congestive Heart Failure (CHF)	Increases the force of contraction of the heart, improving cardiac output.
2. Atrial Fibrillation / Flutter	Slows down heart rate by affecting AV node conduction.
3. Antiarrhythmic Agent	Used to maintain proper rhythm of the heart.
4. Diuretic Effect	Indirectly increases urine output due to better

Pharmacological Actions

- Positive inotropic effect: Increases the strength of heart contractions.
- Negative chronotropic effect: Decreases heart rate.
- Negative dromotropic effect: Slows down AV conduction.
- Overall: Improves efficiency of a weak heart.

Mechanism of Action

1. Digitalis inhibits Na^+/K^+ -ATPase enzyme in heart cells.
2. This increases intracellular Na^+ , which leads to increased Ca^{2+} inside the cells.
3. More calcium means stronger heart contractions.
4. It also slows the AV node conduction — reducing heart rate.

Result: Stronger, slower, and more efficient heartbeat.

Commercial Applications

- Pharmaceutical Uses:
 - Source of cardiac glycosides used in medicine (e.g., Digoxin tablets, injections).
 - Used in cardiotonic formulations for heart failure and arrhythmias.
- Industrial Uses:
 - Extraction of pure glycosides (digoxin, digitoxin) for drug manufacturing.
- Traditional Uses:
 - Historically used as a heart tonic, but now standardized due to toxicity risk