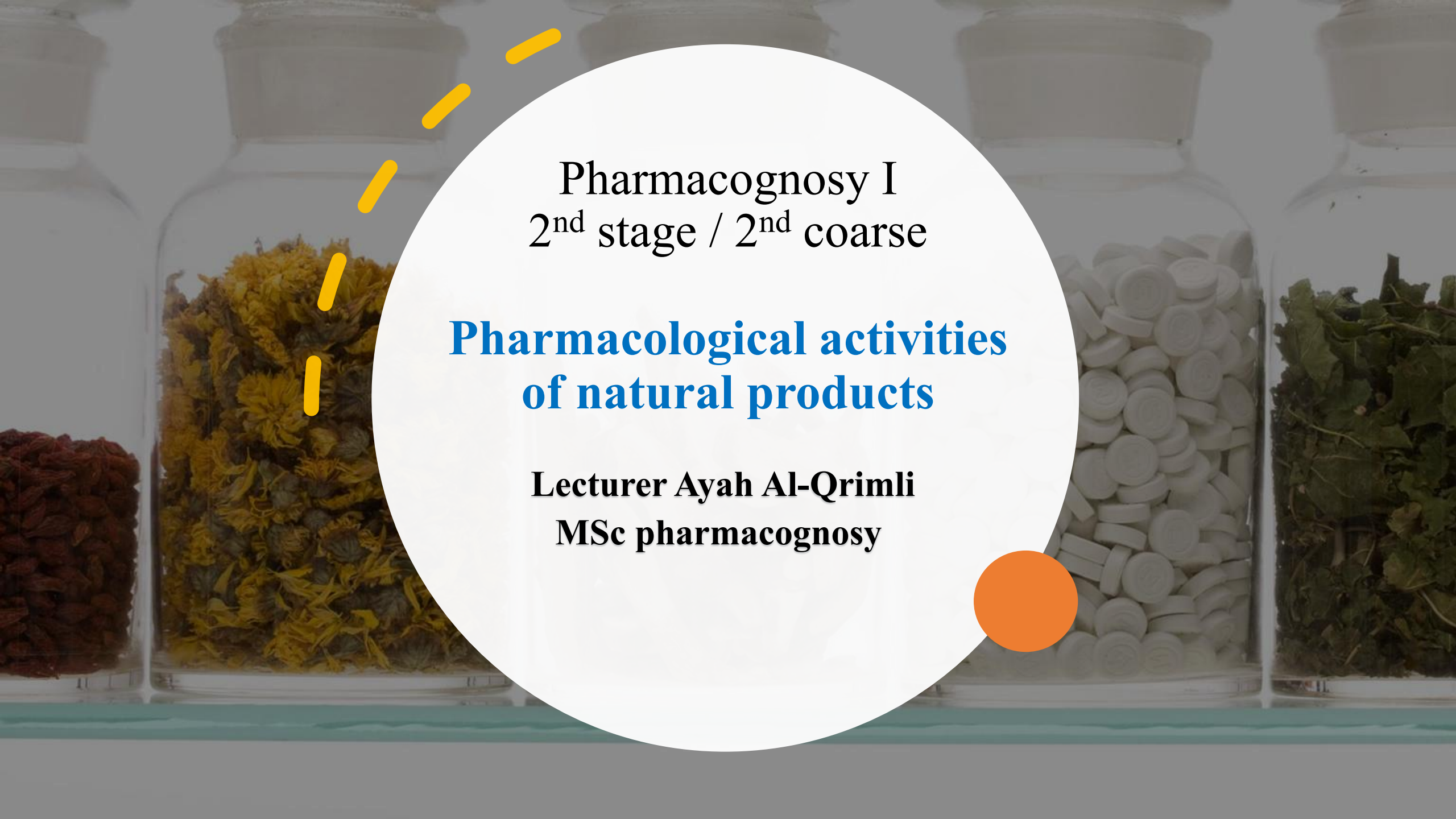


Pharmacognosy I

2nd stage / 2nd coarse

Pharmacological activities of natural products

Lecturer Ayah Al-Qrimli

MSc pharmacognosy

Pharmacological and Therapeutic classification:

- This classification involves the grouping of drugs according to the **pharmacological action** of their most important constituent.
- **Advantage**: More relevant and mostly followed method.
- **Disadvantage**: Drugs having different action get classified separately in more than one group that causes confusion.







1. Drugs acting on G.I.T.

- **Carminative** → Fennel, Cardamom, Mentha
- **Emetic** → Ipecac
- **Laxative** → Senna, Castor oil.
- **Antispasmodic** → **Datura, Hyoscyamus, Opium**.











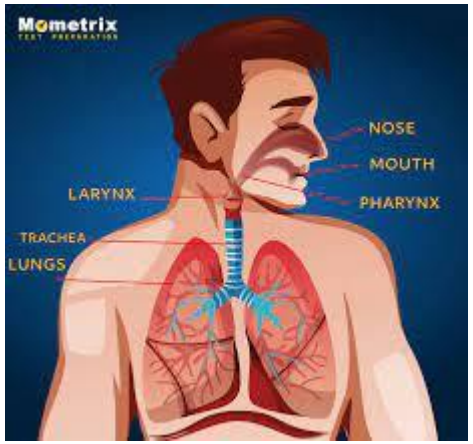












2. Drugs acting on Respiratory System

- **Antitussive** → *Opium* (codeine)
- **Bronchodilators** → *Ephedra*, Tea
- **Expectorant** → Liquorice, Ivy

3.Drugs acting on Central Nervous System

- **Central analgesic** → Opium (morphine)
- **CNS depressant** → Belladonna, Opium
- **CNS stimulant** → Tea, Coffee

4.Drugs acting on Autonomic Nervous System

- **Adrenergic** → Ephedra
- **Cholinergic** → Pilocarpus
- **Anticholinergic** → Belladonna.

5.Drugs acting on Cardiovascular System

- **Cardiotonic** → Digitalis,
- **Cardiac depressant** → Cinchona (quinidine).
- **Vasoconstrictor** → Ergot
- **Antihypertensive** → Rauwolfia.

6. Anticancer → Vinca (vincristine)



7. Antirheumatic → Colchicum



8. Astringent → Witch hazel



9. Antimalarial → *Cinchona* (quinin)

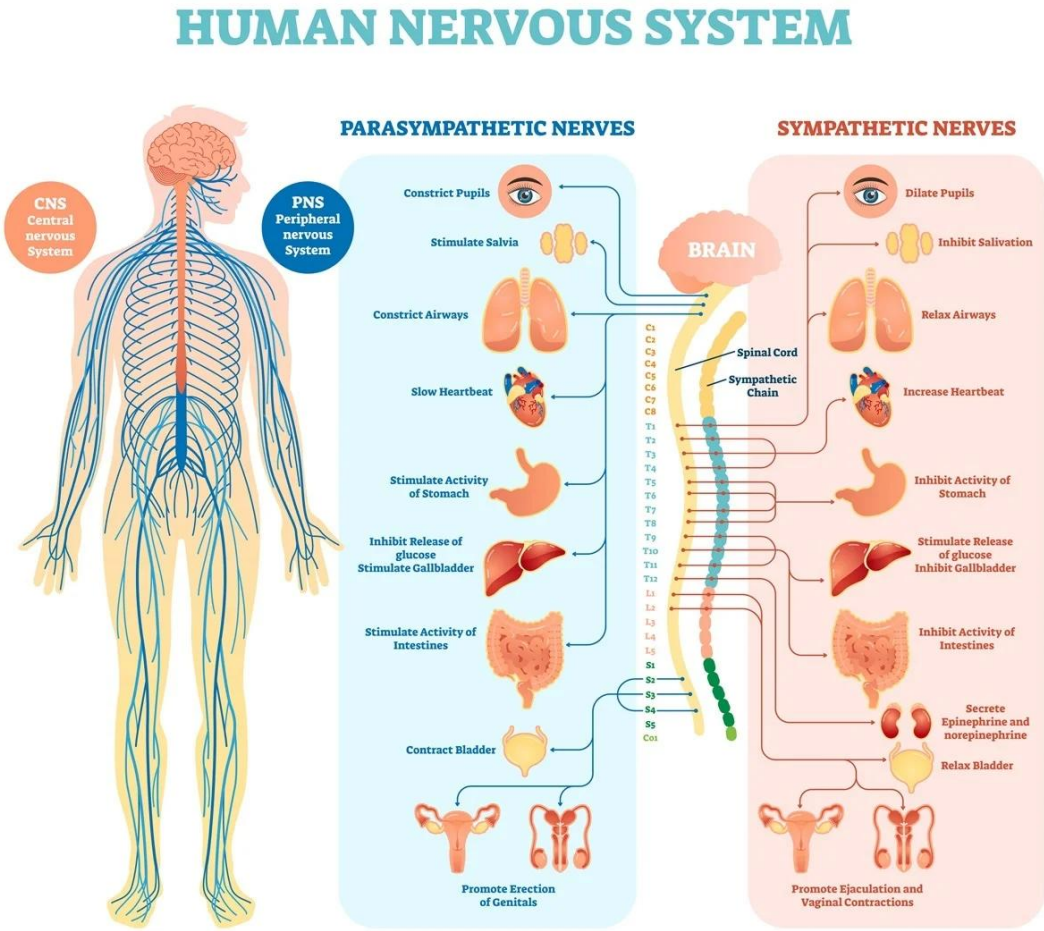
Pharmacological activities of natural products

- Some major pharmacological groupings involve drugs which act on the **nervous systems**, **heart** and blood vessels, **gastrointestinal tract, kidneys, liver, reproductive organs, skin and mucous membranes.**

1. Drugs acting on the **nervous system**
2. The **heart, circulation and blood**
3. Action on the **gastrointestinal tract**

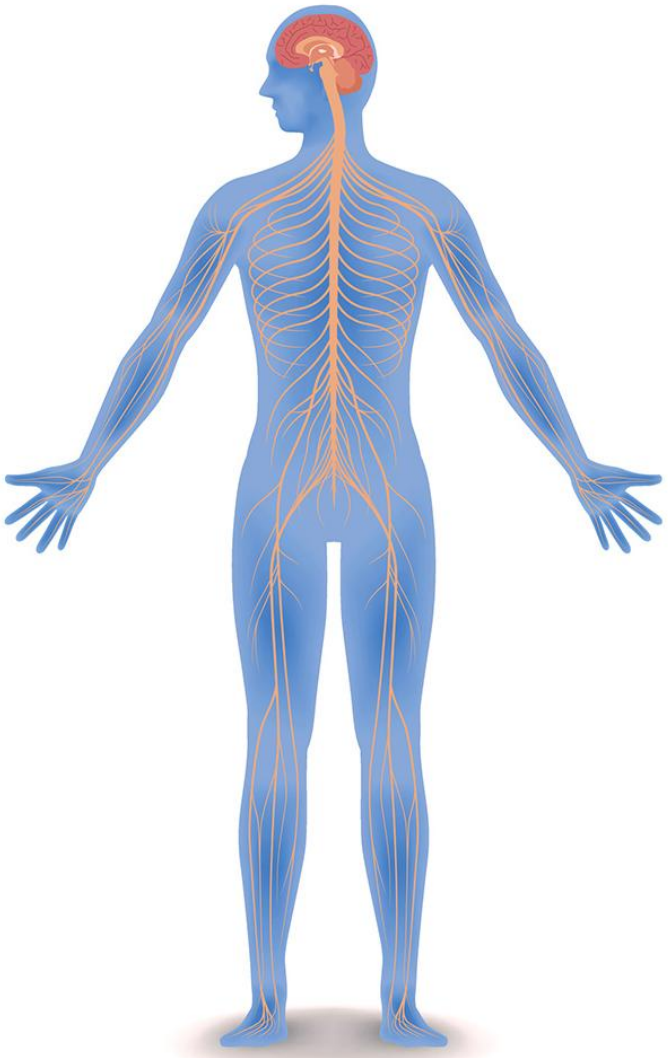
1. Drugs acting on the Nervous system

- The nervous system coordinates and regulates the various voluntary and involuntary activities of the body and is conveniently considered under two headings:
- The central nervous system **(CNS)** → **brain & spinal cord**
- **Consciousness, mood, behavior, sleep, pain**
- The autonomic nervous system **(ANS)** → **smooth muscle & glands**
- **Heart rate, GIT motility, secretions, pupils**



A. The central nervous system

- The CNS comprises the **brain** and the **spinal cord**.
- CNS-active natural products are **among the most potent crude drugs.**
- They **cross the blood–brain barrier** due to **lipophilicity.**
- Mainly are **alkaloids, terpenoids,** and **methylxanthines.**
- Drugs involved with the CNS can be broadly classified according to whether they have a general **stimulatory** or **depressant** action with further subdivision regarding specific actions such as:
- **CNS stimulants,**
- **CNS depressants (sedatives),**
- **Hallucinogens,**
- **Adaptogens & cognitive enhancers**



Drugs acting on CNS



- **Cannabis-marijuana leaves of *Cannabis sativa:* Hallucinogenic , altered perception and analgesia**
- Active constituents: **THC tetrahydrocannabinol** (responsible for "high" effect) is **the psychoactive cannabinoid responsible for the central nervous system effects of cannabis.**
- THC is **Lipophilic cannabinoid binds strongly to CB1 receptors in the brain**
- Cannabis and Pain : Cannabinoids share mechanisms of action with many common medications including **NSAIDs, Pregabalin (Lyrica), Gabapentin (Neurontin)**
- After examining all the available data, the National Academy of Sciences released a report in 2017 which found "substantial and conclusive evidence" **for the effectiveness of cannabis in treating chronic pain**





Purine bases
Caffeine & Theophylline



- Source: **coffee beans (*Coffee arabica*) and tea leaves (*Thea sensis*).**
- Chemical class: **Methylxanthines**
- Mechanism: **Adenosine receptor antagonism (adenosine is responsible for sleep)**
- Effect: **CNS stimulation, alertness**



Cocaine

- Source: **leaves** of ***Erythroxylum coca***
- Chemical class: **Tropane alkaloid**
- Mechanism: **Blocks monoamine reuptake (enhance their action)**
- Effect: strong **Mental stimulant** , produces **addiction**

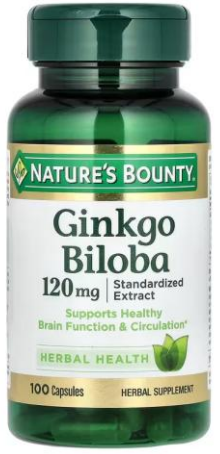


Reserpine

- Source: **roots** of ***Rauwolfia serpentina***
- Chemical class: **Indole alkaloid**
- **Depletes monoamines Depresses mental activity** , used in **psychiatric treatment**
- **CNS depressant**



Ginkgo biloba





- Source: **leaves of *Ginko biloba***
- Active constituents: **Flavonoids, terpenes**
- Improves **short term memory** (Used in **Alzheimer's disease**)
- **Improves cerebral blood flow and Antioxidant neuroprotection**

Ginseng

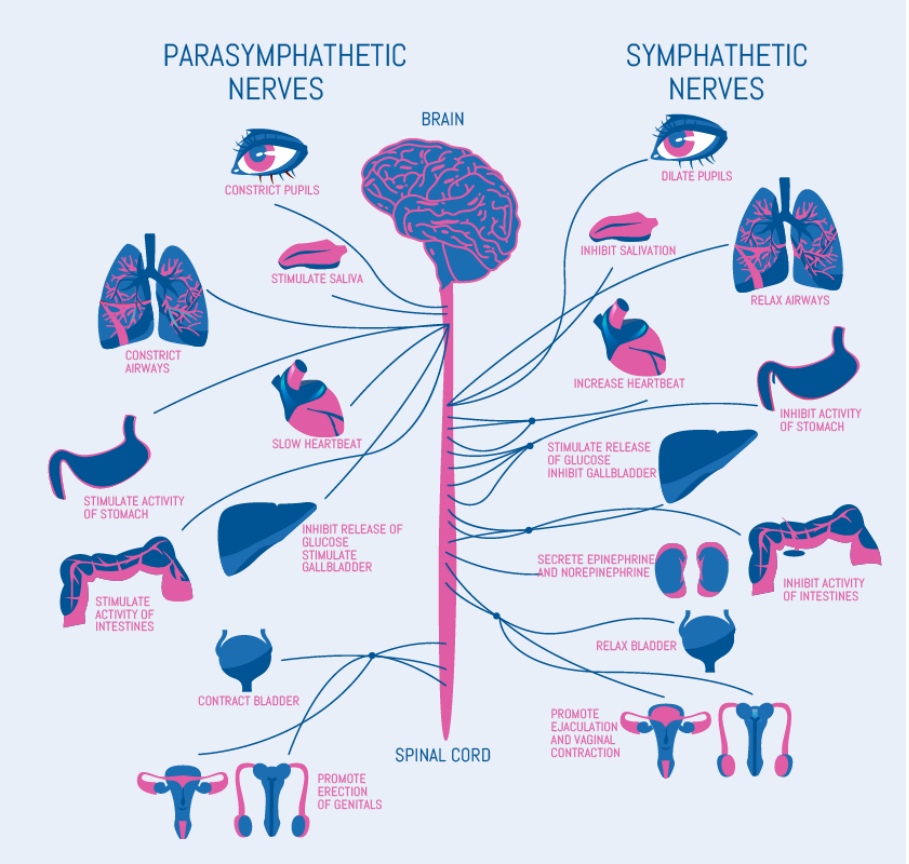




- Source: **Roots of *Panax ginseng***
- Active constituents: glycoside (Ginsenosides)
- **Adaptogenic effect**
- **Improves mental concentration**
- **Reduces fatigue**

B. The Autonomic nervous system

- The autonomic nervous system supplies the **smooth muscle tissues** and **glands** of the body. It is composed of two divisions, the **sympathetic** division, and the **parasympathetic**.
- Two important neurotransmitter substances of the autonomic nervous system are **acetylcholine** and **noradrenaline** and its derivatives.
- Drugs acting on the autonomic nervous system are summarized in the following table.



Acetylcholine like drugs (Cholinergic Drugs) : Alkaloids

Pilocarpine	 	From the **leaves** of ***Pilocarpus microphyllus*** for **glaucoma.** **Muscarinic agonist**

Acetylcholine Antagonist (blockers) Anticholinergic Drugs

Tropane alkaloids (hyoscine, atropine)	• Members of **Solanaceae** family (***Atropa belladonna***) • Block muscarinic receptors • They have many uses involving their **gastrointestinal, bronchial, Genito-urinary and ophthalmic effects (Reduce secretions, relax smooth muscle) in addition to the CNS activity** at high dose

Adrenaline like drugs (Adrenergic alkaloids)

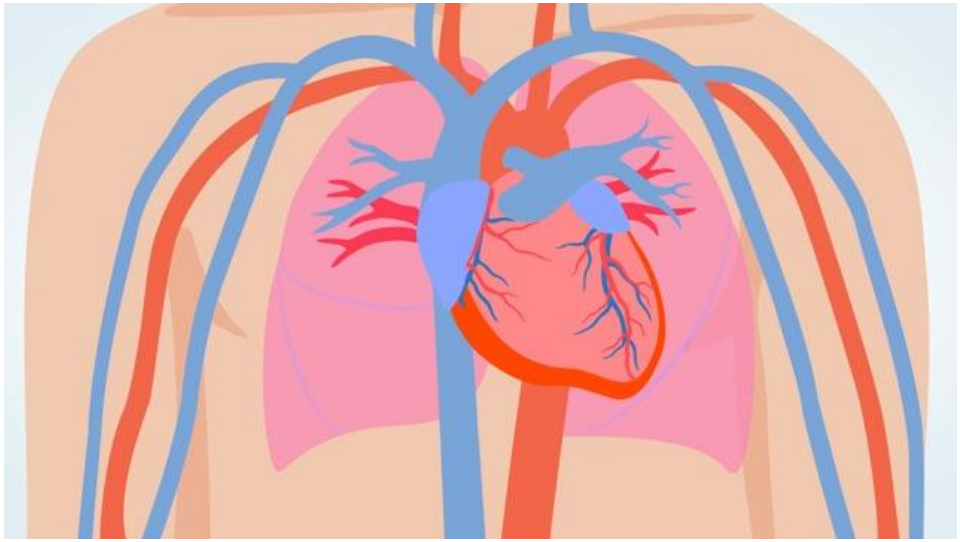
Ephedrine	From the **stems** of ***Ephedra*** **species Sympathomimetic action** **• Bronchodilator and CNS stimulant**

Adrenaline antagonist (Adrenergic Antagonists)

Ergot alkaloids (ergotamine)		From the ***Claviceps*** spp. **Fungus** **Vasoconstrictor effect , Used in migraine**

2. The heart, circulation and blood

- Cardiovascular diseases are among the **leading causes of mortality worldwide.**
- Therefore, this is an area of intensive research, not entirely devoted to **treatment**, but also to the **prevention** of these diseases.
- Natural products act on the **heart, blood vessels, and blood**.
- Activities include:
- **cardiotonic,**
- **antihypertensive,**
- **antiarrhythmic,**
- **anticoagulant, and**
- **antiplatelet effects.**



A. Anti arrhythmic

Digoxin and Quinidine







- **Digoxin** in **leaves** of ***Digitalis lanata*** is a **Cardiac glycoside** used in cases of congestive heart failure is to **increase the force of myocardial contraction** (**the positive inotropic effect**).
- Mechanism: **Na+/K+ ATPase inhibition → ↑ Ca2+**
- Uses: **Heart failure, arrhythmias**
- **Quinidine** from ***Cinchona*** **bark is an alkaloid**
- Mechanism: **Sodium channel blockade to** Stabilizes cardiac rhythm
- Uses: **Supraventricular & ventricular arrhythmias**





B. Antihypertensive drugs

- Hypertension is a major risk factor for cardiovascular disease.

- The control of hypertension is an important element in the management of cardiovascular disorders.
- Hypotensive plant drugs ***Rauwolfia*** and its principal **indole alkaloid Reserpine**
- **Mechanism: Depletes catecholamines from nerve endings**
- **Effect: Reduction in blood pressure (*refractory cases*)**
- Together with ***Veratrum*** extracts were recognized in the early 1950s.
- They are **Steroidal alkaloids**
- **Mechanism: Reflex vasodilation and bradycardia**
- **Effect: Decrease in blood pressure *(risk of toxicity)***



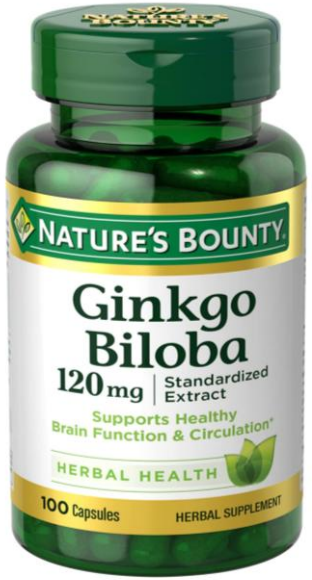




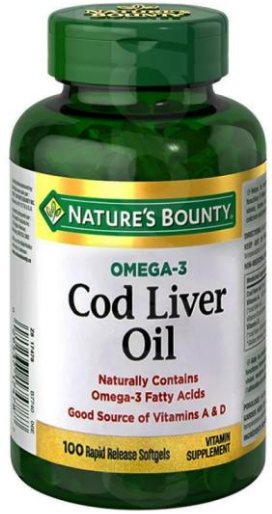
C. Platelet-activating factor (PAF) antagonists



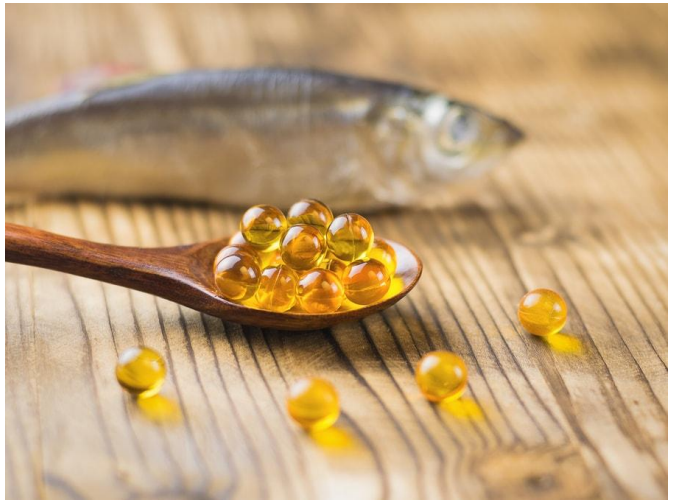
- In the circulatory system **Platelet aggregation and clot formation contribute to thrombosis**
- This platelet aggregation is triggered by the **platelet activating factor which is released from activated basophils.**
- Many plants have been screened for **anti- PAF activity (reduce platelet aggregation or blood clotting)**. Which are important in prevention of cardiovascular events.
- **Ginkgo biloba** have proved especially interesting and are commercially available in Europe for the treatment of **various circulatory disorders to improve blood flow.**
- **Mechanism:** **Platelet-activating factor (PAF) antagonism**
- **Effect:** **Improves blood flow, reduces platelet aggregation**

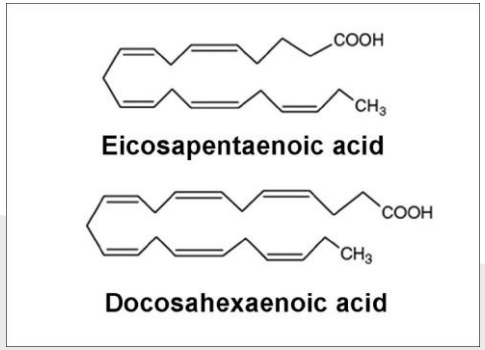


Fish oil (omega-3)



- Certain fish oils (e.g. **cod-liver oil)** once employed solely for their vitamin contents together with 'oily fish' body oils have recently received a resurgence in popularity as dietary supplements.
- One favorable response is that they **decrease the ability of platelets to aggregate** by virtue of their high **eicosa-pentaenoic-acid content**; **EPA**
- This acid tends to favor the **biosynthesis of thromboxane A3**, a **weaker stimulator of platelet aggregation** than thromboxane A2.





D. Drugs acting on blood vessels

- These drugs are essentially either **vasoconstrictor** or **vasodilator** substances.

Peripheral vasoconstrictor drugs	
Ergotamine	Produces a **direct** **constrictor effect in vascular smooth muscles.**
Ephedrine	it has a **vasoconstrictor** effect by promoting the **release of the vasopressor adrenaline**
Vasodilator drugs	
Papaverine (**opium** alkaloids)	Acts **directly** on blood vessels by causing **relaxation of smooth muscles**
Reserpine	Vasodilation by **peripheral** and **central** action

Reserpine

- **Reserpine works by irreversibly blocking VMAT (vesicular monoamine transporter).** This leads to depletion of monoamines such as: Noradrenaline, Dopamine, Serotonin from nerve endings.
- **Depletion of dopamine and serotonin in the brain leads to:**
- CNS depression
- Sedation
- Reduced mental activity
- **That is why reserpine is classified as a CNS depressant and was used in psychiatric disorders.**
- **Depletion of noradrenaline in sympathetic nerve endings causes:**
- Vasodilation
- Decrease in heart rate and cardiac output→ Result: Lower blood pressure
- **Reserpine appears in more than one classification because its single mechanism of monoamine depletion produces effects on both the central nervous system and the cardiovascular system."**



E. Oral anticoagulants

- These compounds **inhibit the clotting mechanism** of the blood and are of value in arterial thrombosis; they have **no effect on platelet aggregation**.
- **Warfarin** (**coumarin**) is one of the most widely used drugs. Mechanism: **Inhibits vitamin K–dependent clotting factors**



F. Hypolipidemic drugs

- Natural products having a beneficial action include fish oils containing high quantities of **omega-3-marine triglycerides** (eicosapentaenoic acid and docosahexaenoic acid)EPA/DHA
- The suggested beneficial properties of **garlic** (***Allium sativum***) that garlic **lowers serum total cholesterol and improves the lipid profile**.
- Active constituents: **Sulfur-containing compounds**



3. Action on the gastrointestinal tract



- **Antispasmodic drugs**: In this capacity **hyoscine and hyoscyamine** help disturbances caused by gastric mobility and **muscle spasm** particularly with some ulcer patients.(*Atropa belladonna*)



- **Laxatives and purgatives**: Purgatives may be classed according to their mode of action :
- **Bran** an ***indigestible*** vegetable **fiber** which **absorbs water** and provides bulk.(bulk forming)
- **Senna** (leaves) Contains **anthraquinone** derivatives which are hydrolyzed in the bowel to **stimulate bowel movement.**
- **Castor oil** Contains glycerides which on hydrolysis yield **riconoleic acid,** irritant to the small bowel.



- **Antidiarrheal drugs**: **Morphine and codeine** act by increasing the smooth muscle tone of the bowel and by reducing its mobility.


The End