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Environmental Science and Health Department

Lec. 4 How do plant medicines work? Modes of action

Dr. Badr Qader Surchi
Assist. Professor

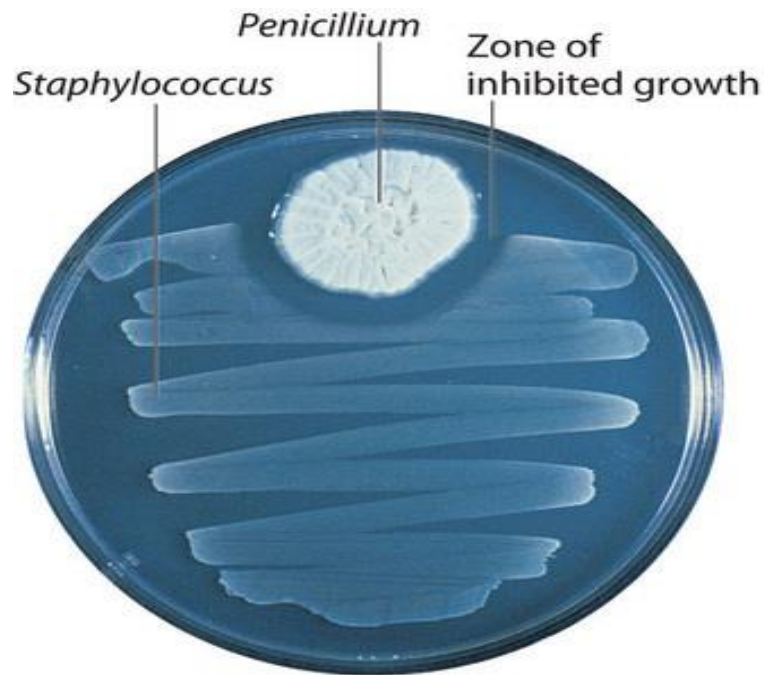
How do plant medicines work? Modes of action of secondary metabolites.

Several secondary metabolites have been used by mankind for thousands of years as **dyes** (e.g. indigo, shikonine), **flavours** (e.g. vanillin, capsaicin, mustard oils), **fragrances** (e.g. rose oil, lavender oil and other essential oils), **stimulants** (e.g. caffeine, nicotine, ephedrine), **hallucinogens** (e.g. morphine, cocaine, scopolamine, tetrahydrocannabinol), **insecticides** (e.g. nicotine, piperine, pyrethrin), **vertebrate and human poisons** (e.g. coniine, strychnine, aconitine) and, most importantly, as **therapeutic agents** (e.g. atropine, quinine, cardenolides, codeine).



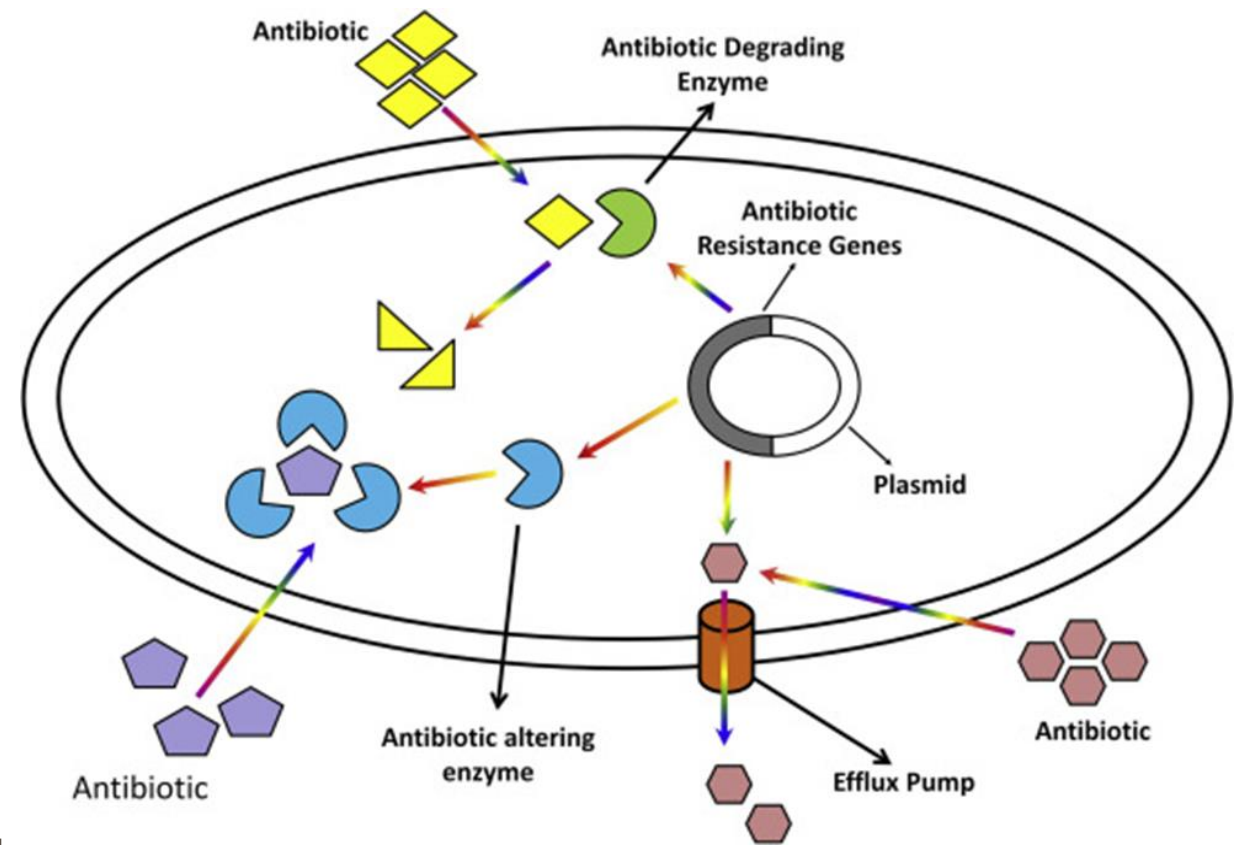
Golden age of antibacterials

In 1928, Fleming's major medical breakthrough came about as he serendipitously discovered **penicillin**, later to be claimed as the miracle drug of the 20th century. "The discovery and development of penicillin 1928-1945"



Mode of action

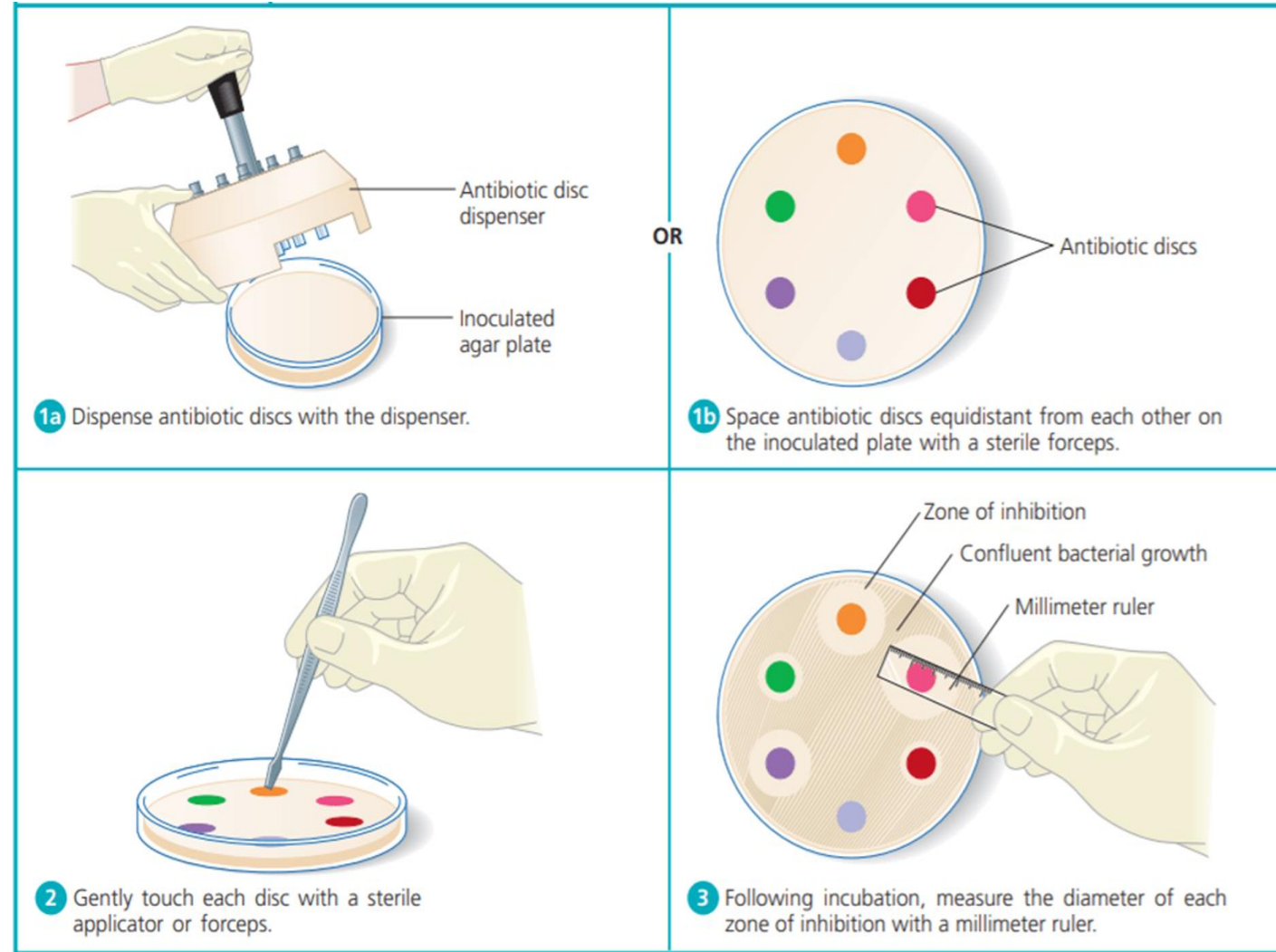
- Inhibitors of cell wall synthesis.
- Inhibitors of cell membrane function
- Inhibitors of protein synthesis.
- Inhibitors of nucleic acid synthesis
- Inhibitors of other metabolic processes



Antibiotics Versus Antimicrobials

- An **Antibiotic** is a low molecular substance produced by a microorganism that at a **low concentration inhibits** or **kills** other microorganisms.
- An **Antimicrobial** is any substance of **natural**, semisynthetic or synthetic origin that **kills** or **inhibits** the growth of microorganisms but causes little or no damage to the host. All antibiotics are antimicrobials, but not all antimicrobials are antibiotics.

- **Susceptible:** means they **can't grow** if the drug is present. This means the antibiotic is **effective** against the bacteria.
- **Resistant:** means the bacteria can grow even if the drug is present. This is a sign of an ineffective antibiotic.
- **Intermediate:** means a higher dose of the antibiotic is needed to prevent growth.



Antimicrobial

In order to be effective as a therapeutic agent, a secondary metabolite must **interfere with an organ, tissue, cell and ultimately with a molecular target** in the human body. Secondary metabolites usually are **multifunctional compounds** because most of them **carry more than one pharmacologically active** chemical group. In addition, secondary metabolites usually occur in **complex mixtures**. In consequence, the extract of a medicinal plant affects more than one molecular target (so-called **multi target drugs**) and it is likely that several targets are affected concomitantly when taking **phytomedicines**. In complex disorders the application of such extracts increases the chances of **“hitting” one or several relevant targets**. In general, we find a series of related compounds in a given plant species; often a few major metabolites and several minor components, which differ in the position of their chemical groups.



The profile usually varies between plant organs, within developmental periods and sometimes even diurnally. Also, marked differences can usually be seen between individual plants of a single population, even more so between members of different populations.

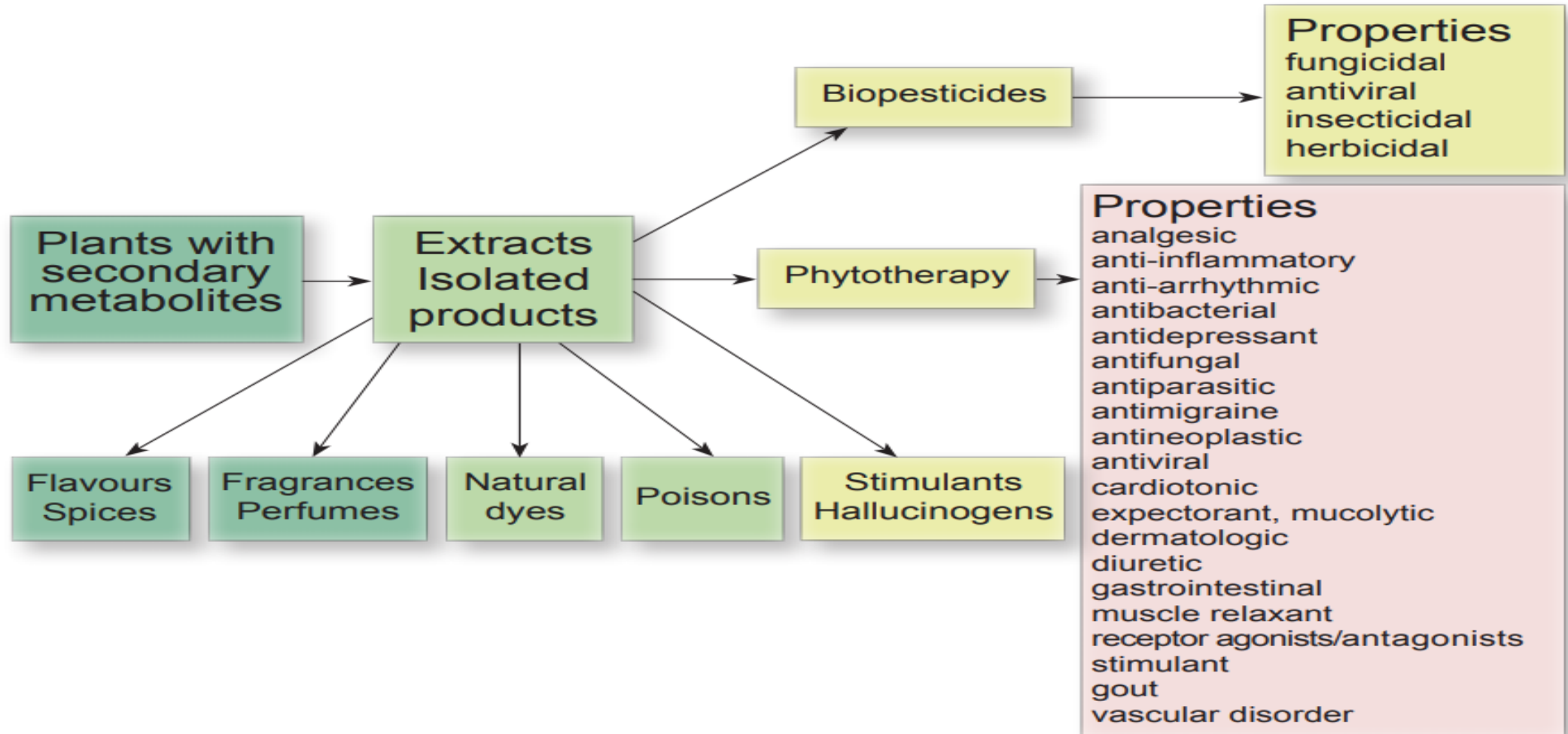
Even small changes in chemistry can be the basis for a new pharmacological activity. This aspect is important for quality control in phytotherapeutics. On the opposite page a human cell is shown together with an overview of all the main molecular targets that are modulated by plant medicines. Structures of allelochemicals appear to have been shaped during evolution in such a way that they can mimic the structures of endogenous substrates, hormones, neurotransmitters or other ligands; this process can be termed “evolutionary molecular modelling”.



Other metabolites intercalate or alkylate DNA, inhibit DNA- and RNA-related enzymes and protein biosynthesis, modulate metabolically **active enzymes** or they disturb membrane stability. As a consequence of such interactions, plant medicines can interfere with organ malfunctions (heart and circulation, stomach and intestines, lung, liver, kidney, CNS disorders, gonads), inflammation and infections.

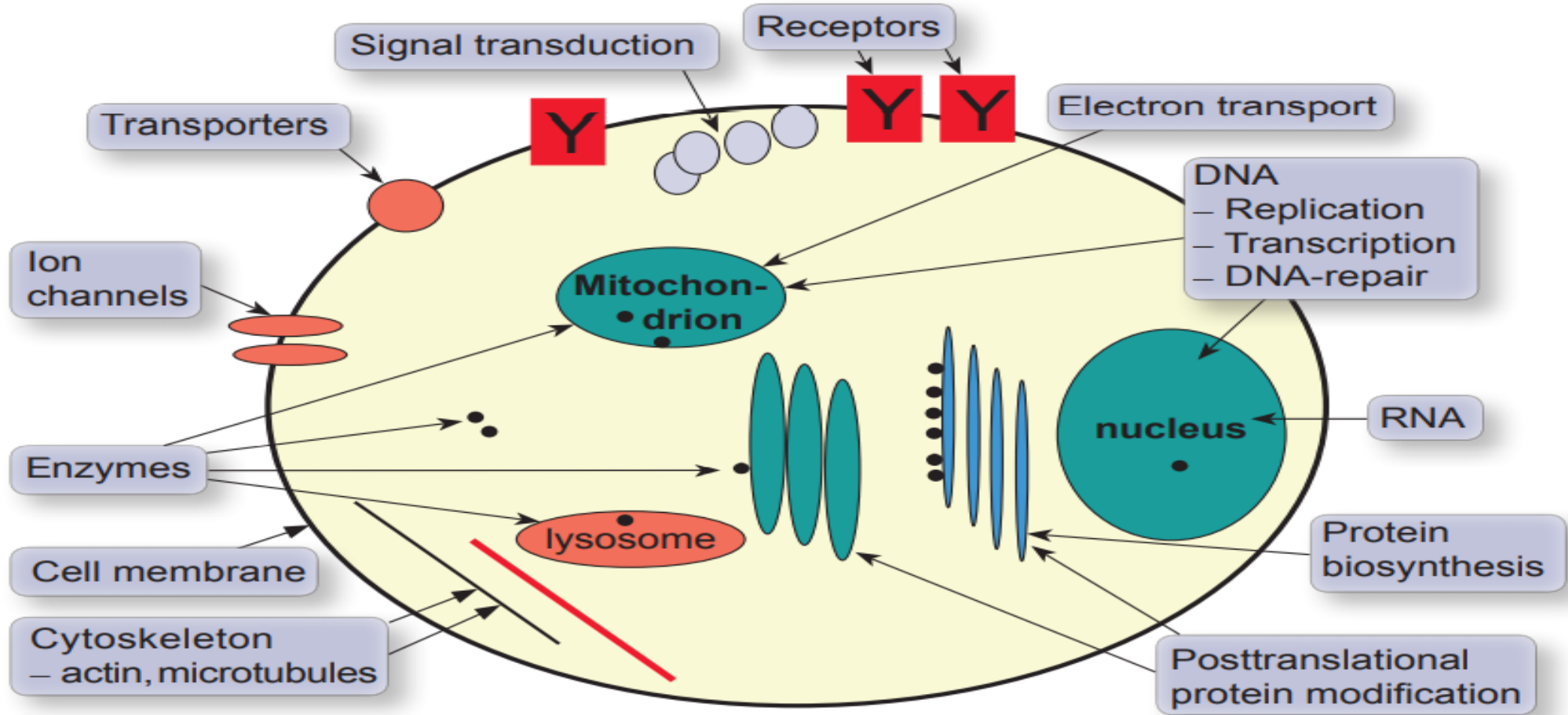
In conclusion, phytotherapy is a traditional approach to use the right plants in the right concentrations to restore health or to relieve symptoms of disorders and disturbances.





The diversity of natural products and their biological properties

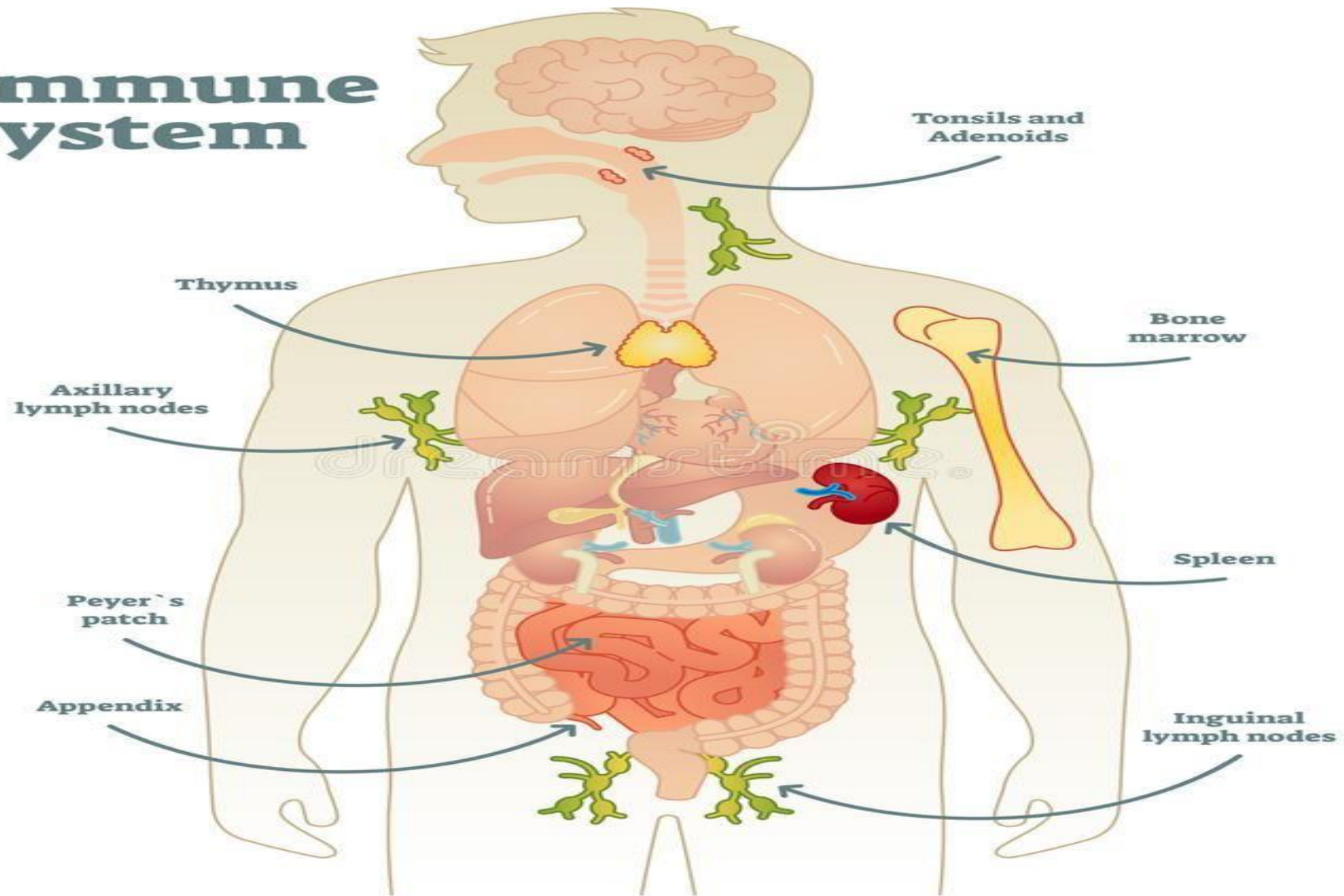




Overview of the main molecular targets that are modulated by plant medicines



Immune system



Description Rosemary is an aromatic evergreen shrub (about 1 m) bearing narrow leaves that are bright green above, with rolled-in margins and densely hairy below, and small, pale purple or bluish flowers.

Origin Mediterranean region; widely cultivated as a culinary herb; commercially in the Mediterranean.

Parts used Dried leaves (Rosmarini folium), essential oil (Rosmarini aetheroleum).

Therapeutic category General tonic, antimicrobial, spasmolytic.

Rosemary - اكليل الجبل - گهلاپهژم

***Rosmarinus officinalis* L.**

Lamiaceae



Uses and properties Rosemary is a carminative and stomachic (often part of final medicinal products) to treat stomach cramps and flatulence, and to stimulate appetite and the secretion of gastric juices. It is considered to be useful against headache and nervous complaints. When used externally (in ointments and bath oils), the oil stimulates blood circulation and has **antibacterial, antifungal, antiparasitic** and mild analgesic activity (it provides some **relief** from **muscle aches** and **joint pains**).

Preparation and dosage

A tea made of 2 g of dry herb is taken three times per day. For internal use, a maximum of 20 drops of oil (1 ml) should be taken per day, in doses of no more than 2 drops. For preparing a bath, 50 g of the herb is boiled in a liter of water.



Active ingredients:

Essential oil is present (2.5%), with 1,8-cineole, α -pinene, and camphor as main components, and smaller amounts of β -pinene, borneol, isobornyl acetate, limonene, linalool, 3-octanone, terpineol and verbinol. Also reported in leaves are phenolic acids (rosmarinic acid), bitter diterpenes (carnosol, rosmanol), triterpenes (oleanic and ursolic acid), triterpene alcohols (α amyryl, β -amyryl, betulin), as well as several flavonoids and their glycosides (diosmetin,

Pharmacological effects:

Animal and laboratory studies have confirmed the reported antibacterial, antifungal, antiviral, spasmolytic, antioxidant, smooth muscle modulating, analgesic, anti-inflammatory and venotonic effects. The herb acts as mild cholagogue and choloretic.

Notes: Rosemary is an ingredient in cosmetics and in liqueurs such as b nedictine.

Status: Traditional medicine; PhEur8; Comm.E+; ESCOP; WHO 4; HMPC.

