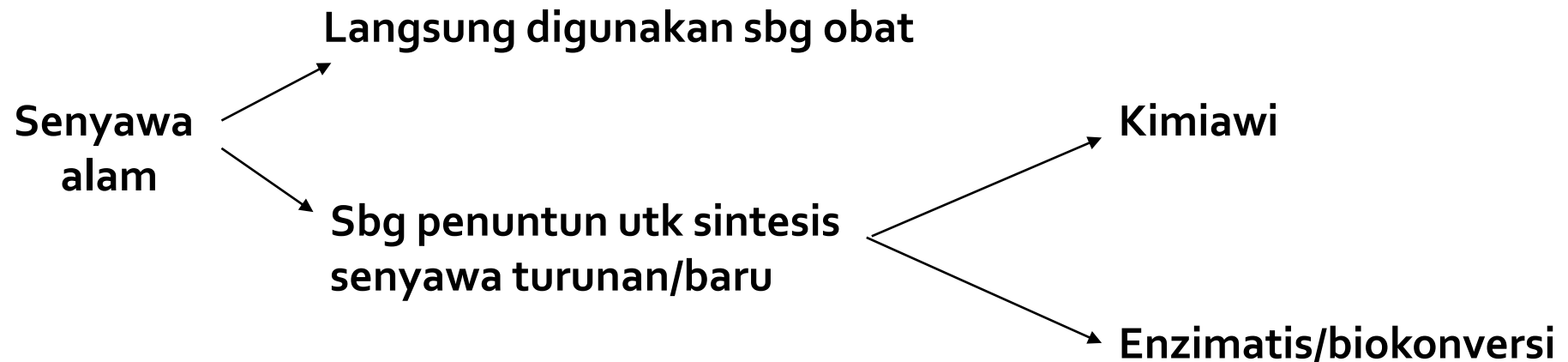


SENYAWA ALAM SEBAGAI ANTIBAKTERI

Purwanto
Fakultas Farmasi UGM

Pendahuluan

- Lebih dari 4000 senyawa alam telah ditemukan aktivitasnya..
- Tanaman adalah kaya dengan metabolit sekunder yg berkhasiat obat, termasuk sbg antibakteri
- **PENTING** : tidak selamanya senyawa dari alam adalah sepenuhnya aman/bebas efek samping



ALKALOIDS

- Largest group of secondary chemical constituents
- Made from ammonia compounds
- Basically of nitrogen bases synthesized from amino acid



Morphine

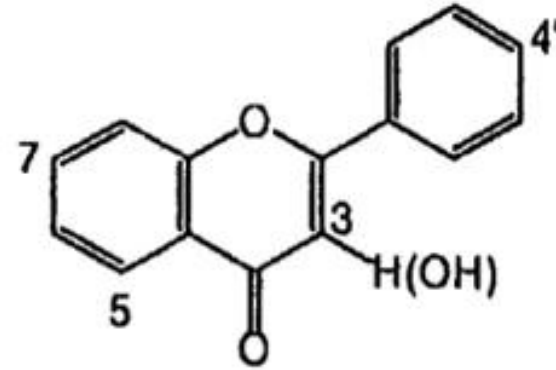
GLYCOSIDES

- Condensation products of sugars
- Colorless, crystalline carbon, hydrogen and oxygen- containing water-soluble phytochemicals
- Found in cell

Continued

Flavonoids

- Important group of polyphenols
- Widely distributed among the plant flora



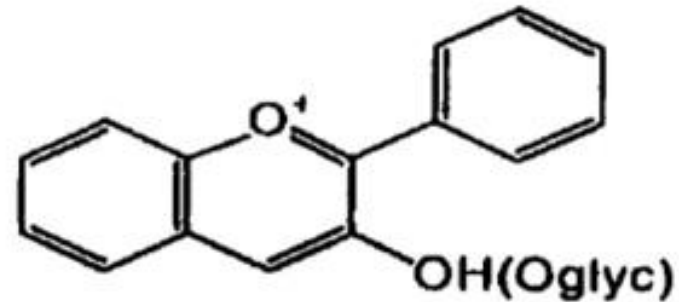
- Found in almost all plant based food and beverages
- Level depending in degree of ripeness, variety and processing
- >4000 distinct flavonoids identified

Nearly present in 70% of plants.

- Quercetin, Kaempferol and Quercitrin

Other group include

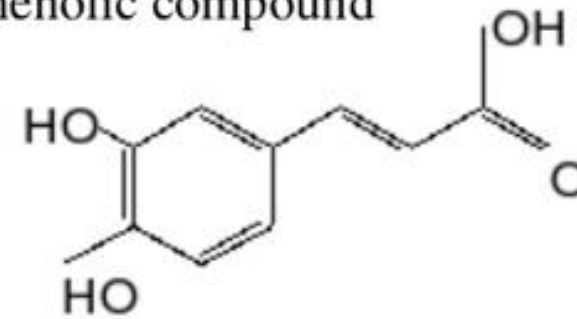
- Flavans
- Flavonoids
- Anthocyanidins
- Catechin



Anthocyanidin

Phenolics

- Chemical compounds occur as natural color pigments
- Responsible for the color of fruits of plants
- Have multiple functions
- **Caffeic acid** is regarded as most common phenolic compound distributed in plant flora.



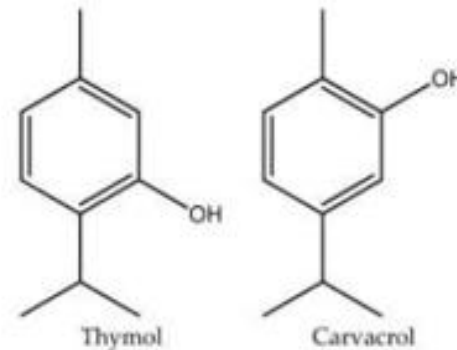
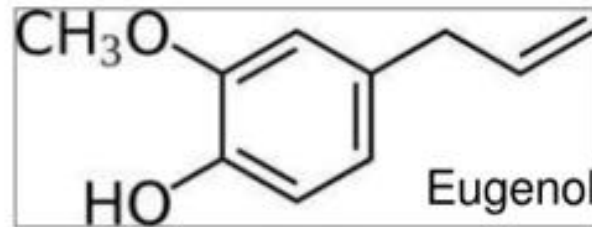
Caffeic acid

Essential oils

- Odorous and volatile products

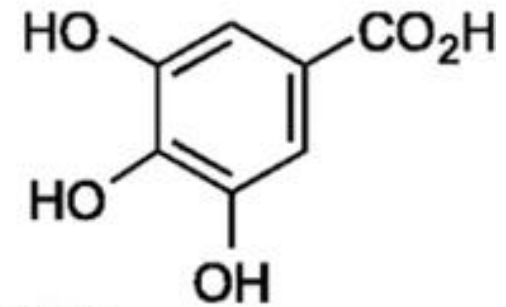
Major plant derived are-

- Eugenol
- Thymol
- Carvacrol



Tannins

- Widely distributed in plant flora
- Phenolic compounds of high molecular weight
- Found in root, bark, stem and outer layers of plant tissues
- **Gallic acid**- plant derived



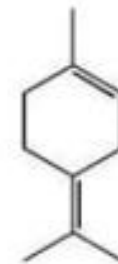
gallic acid (GA)

Terpenes

- Most widespread
- Chemically diverse group of natural products
- Major plant derived-
- Linalool
- Pinene
- Terpinolone



α -pinene



terpinolene

Senyawa alam sbg antibakteri

Phytochemicals	Activity	Mechanism of action
Quinones	Antimicrobial	Binds to adhesins, complex with cell wall, inactivates enzymes
Flavonoids	Antimicrobial Antidiarrhoeal	Complex with cell wall, binds to adhesins Inhibits release of autocooids and prostaglandins, Inhibits contractions caused by spasmogens, Stimulates normalization of the deranged water transport across the mucosal cells, Inhibits GI release of acetylcholine
Polyphenols and Tannins	Antimicrobial Antidiarrhoeal Anthelmintic	Binds to adhesins, enzyme inhibition, substrate deprivation, complex with cell wall, membrane disruption, metal ion complexation Makes intestinal mucosa more resistant and reduces secretion, stimulates normalization of deranged water transport across the mucosal cells and reduction of the intestinal transit, blocks the binding of B subunit of heat-labile enterotoxin to GM ₁ , resulting in the suppression of heat-labile enterotoxin-induced diarrhea, astringent action Increases supply of digestible proteins by animals by forming protein complexes in rumen, interferes with energy generation by uncoupling oxidative phosphorylation, causes a decrease in G.I. metabolism

Senyawa alam sbg antibakteri

Phytochemicals	Activity	Mechanism of action
Coumarins	Antiviral	Interaction with eucaryotic DNA
Terpenoids and essential oils	Antimicrobial Antidiarrhoeal	Membrane disruption Inhibits release of autocoids and prostaglandins
Alkaloids	Antimicrobial Antidiarrhoeal Anthelmintic	Intercalates into cell wall and DNA of parasites Inhibits release of autocoids and prostaglandins Possess anti-oxidating effects, thus reduces nitrate generation which is useful for protein synthesis, suppresses transfer of sucrose from stomach to small intestine, diminishing the support of glucose to the helminthes, acts on CNS causing paralysis
Lectins and Polypeptides	Antiviral	Blocks viral fusion or adsorption, forms disulfide bridges
Glycosides	Antidiarrhoeal	Inhibits release of autocoids and prostaglandins
Saponins	Antidiarrhoeal Anticancer Anthelmintic	Inhibits histamine release in vitro Possesses membrane permeabilizing properties Leads to vacuolization and disintegration of teguments
Steroids	Antidiarrhoeal	Enhance intestinal absorption of Na ⁺ and water

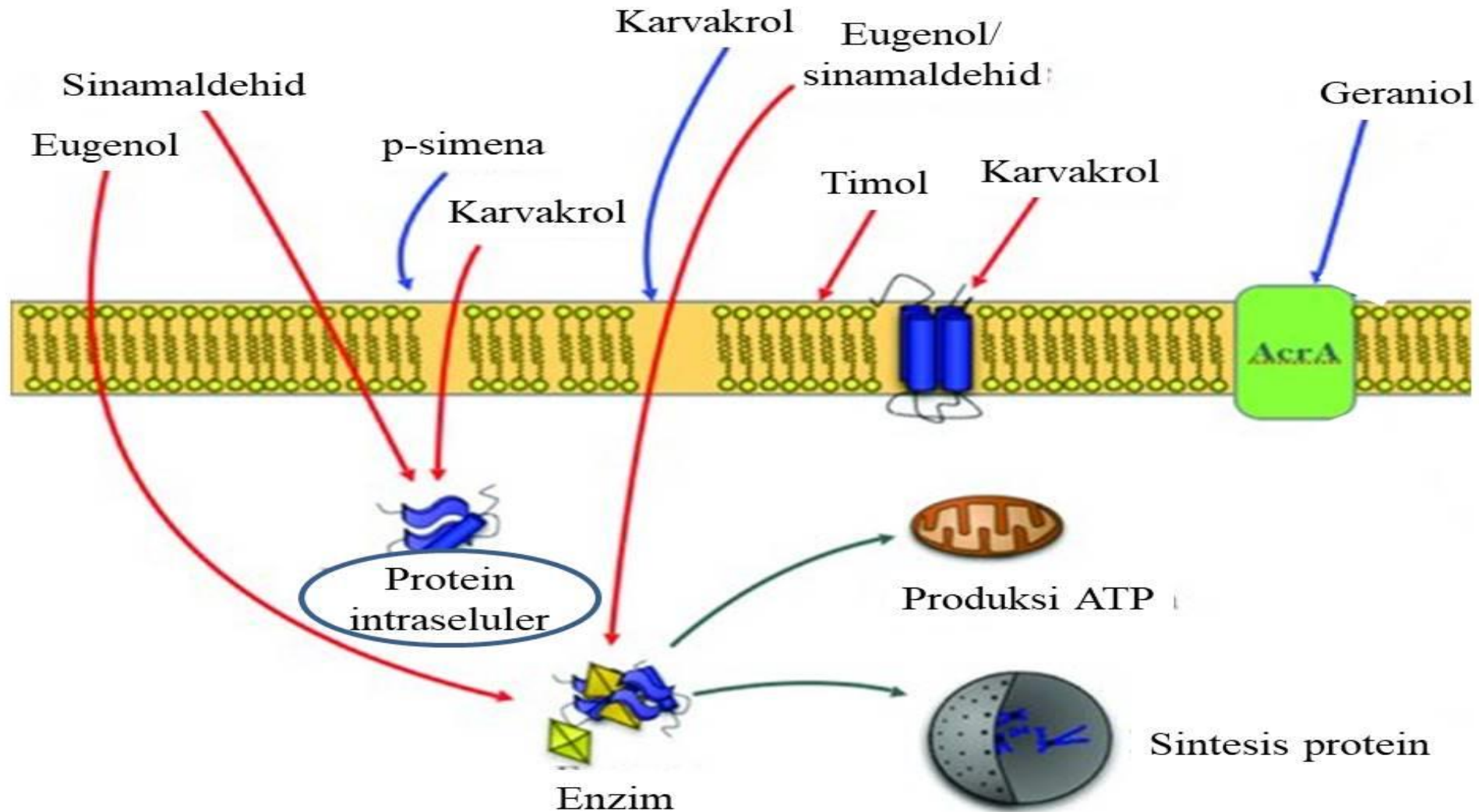
Sinergi senyawa alam dg antibiotik sbg antibakteri

No.	Metabolit aktif	Sumber tanaman	Antibiotik yang dipengaruhi	Mekanisme aksi
1.	Asam karnosat	<i>Rosmarinus officinalis</i>	Tetrasiklin, eritromisin	Inhibisi pompa efluks antibiotik
2.	Karnosol			
3.	Reserpin	<i>Rauwolfia serpentina</i>	Fluorokuinolon, tetrasiklin	Inhibitor pompa efluks antibiotik
4.	Berberin	<i>Berberis sp.</i>	Ampisilin, oksasiklin	Interkalasi di DNA, meningkatkan permeabilitas membran
5.	5-metoksi hidnokapin	<i>Berberis sp.</i>	Berberin, norfloksasin	Inhibisi Nor A
6.	Fenorbid A			
7.	Feruginol	<i>Chamaecyparis lawsoniana</i>	Norfloksasin, eritromisin, oksasiklin, tetrasiklin	Inhibisi efluks EtBr
8.	5-epipisiferol			
9.	Katekin galat	<i>Camelia sinensis</i>	Beta laktam, norfloksasin, karbapenem, tetrasiklin	Inhibisi beta laktamase, inhibisi sintesis PBP2a, bereaksi dengan peptidoglikan, Inhibisi efluks EtBr
10.	Epikatekin galat			
11.	Epigalo katekin galat			
12.	Piperin	<i>Piper longum</i>	Siprofloksasin	Inhibisi efluks EtBr
13.	Timol	<i>Thymus vulgaris</i>	Banyak antibiotik	Meningkatkan permeabilitas membran
14.	Karvakrol			
15.	Baikalein	<i>Scutellaria sp.</i>	Tetrasiklin, beta laktam, gentamisin, siprofloksasin	Inhibisi PBP ₂ , bereaksi dengan peptidoglikan, inhibisi Nor A

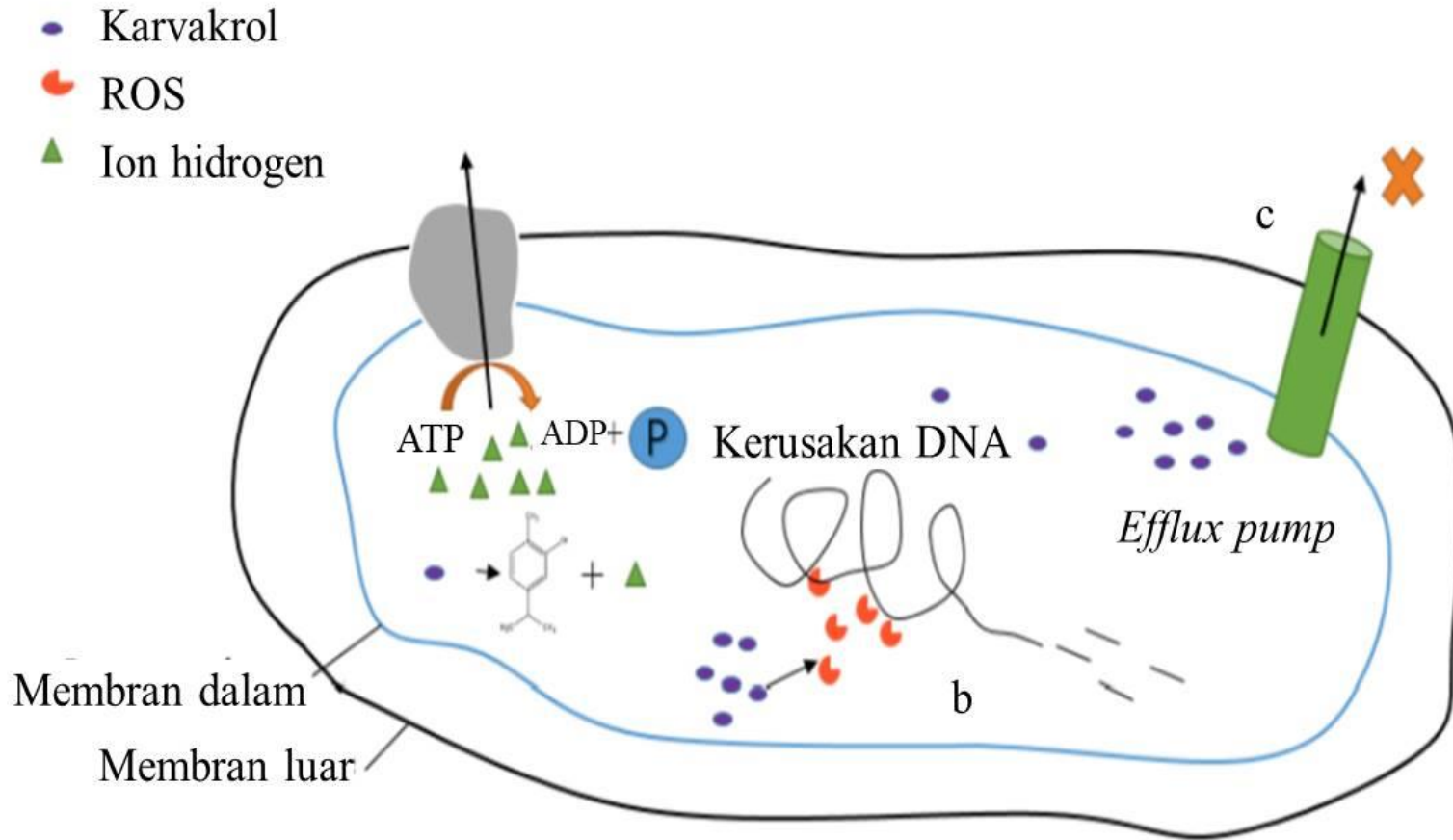
Terpenoid

Tanaman dan Suku	Bagian tanaman dan nama daerah	Bakteri Uji	Aktivitas antibakteri	Sumber Pustaka
Syzygium aromaticum (Myrtaceae)	Bunga cengkeh	E.coli	Daya hambat 3,4±0,7 mm (35 µg/disk)	Pavesi dkk., 2018
		S.aureus	3,0±0,6 mm (35 µg/disk)	
Cinnamomum zeylanicum (Lauraceae)	Kulit kayu manis ("True cinnamon")	S.aureus, S.epidermidis, S.pyogenes, P.aeruginosa, dan E.coli	KHM : 0,5 mg/mL Tiap bakteri uji	Firmino dkk., 2018
Zingiber cassumunar Sin. Zingiber montanum (Zingiberaceae)	Rimpang bengle	Acinetobacter baumannii galur resisten antibiotik	Daya hambat: 20,33±1,98 mm (10 mg/mL); KHM : 8,67±1,93 mg/mL	Boonyanugomol dkk., 2017

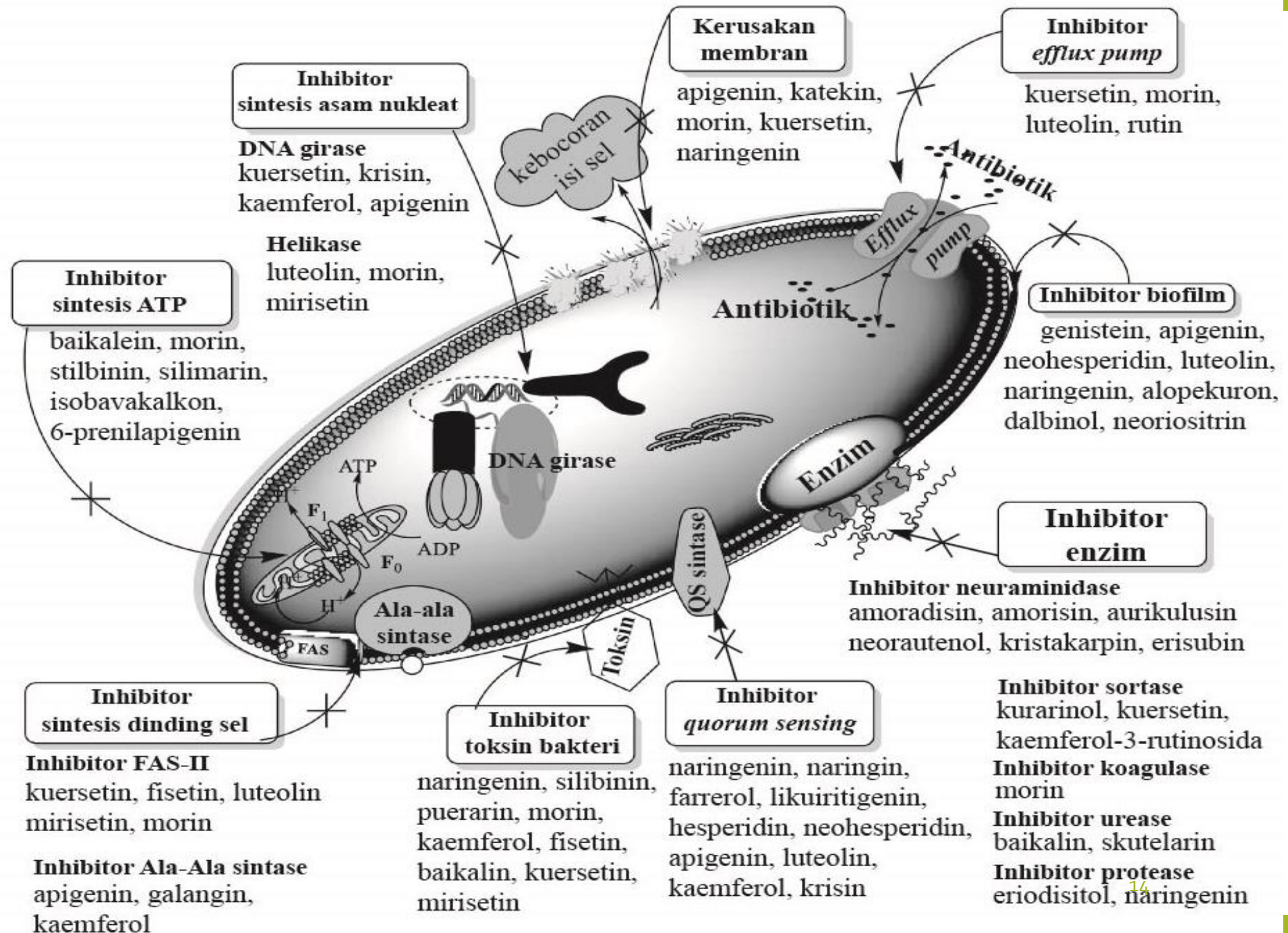
Terpenoid dan target aksi sbg antibakteri



Karvakrol juga mengurangi ATP intraseluler



Flavonoid sbg antibakteri



1. CLOVE

Scientific Name: *Eugenia caryophyllus*

Family : *Myrtaceae*

Plant part used : Bud and flower

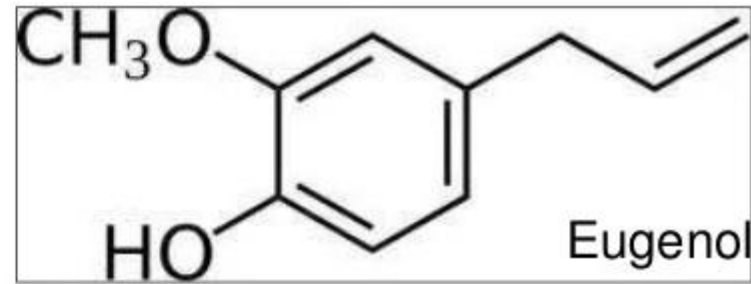
Common Name: Clove flower ,clove bud ,
caryophyllus



Geographical source:

The clove plant grows in warm climates and is cultivated in Tanzania, Sumatra and South America, India.





Chemical Constituents

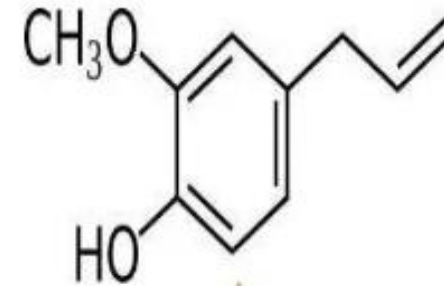
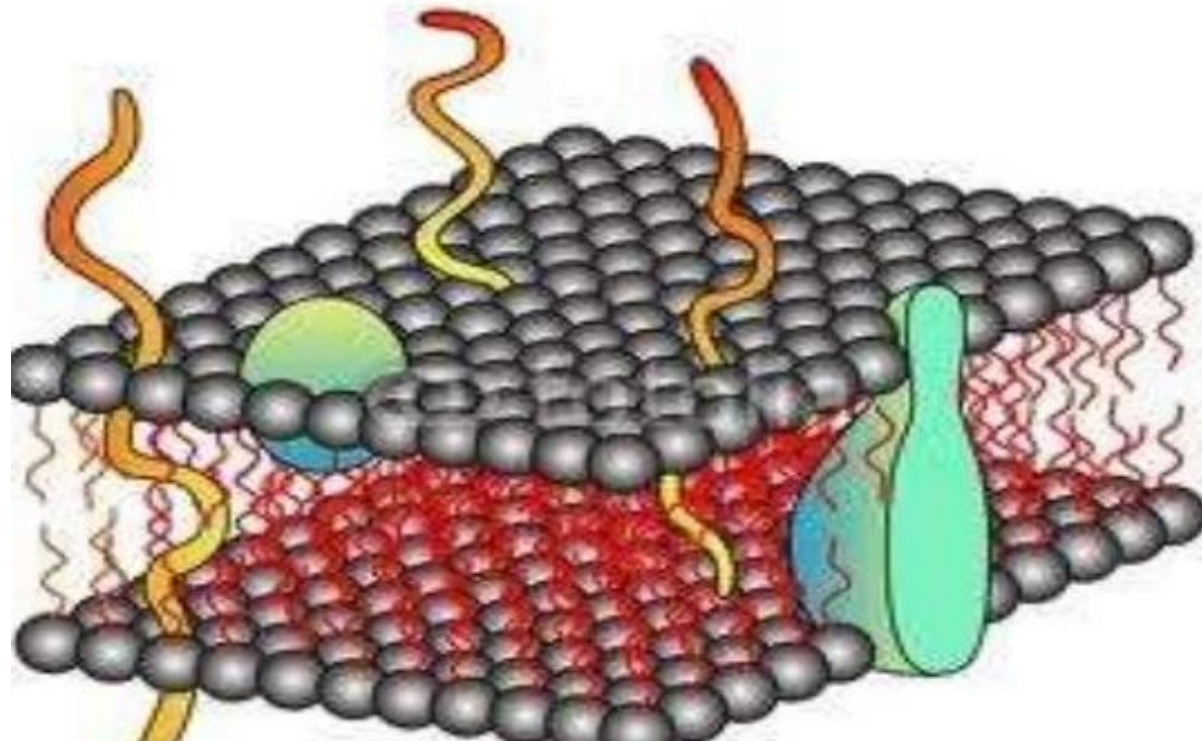
- 15% to 20% of a volatile oil
- Tannins, gum and resin, and sterols.
- The principal constituent of distilled clove bud oil (60% to 90%) is eugenol (4-allyl-2-methoxyphenol).
- The oil also contains about 10% acetyleneugenol and small quantities of gallic acid, sesquiterpenes , etc.
- Other constituents - Flavonoids, carbohydrates, lipids and vitamins.

Uses of Clove

- Antiseptic and Analgesic effects
- treatment of toothaches
- healing stomach ulcers.
- has anthelmintic properties.
- Effective in treating topical fungal, ringworm infections.

- It is react with the phospho lipid of the cell membrane and mitochondria .

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2. GARLIC

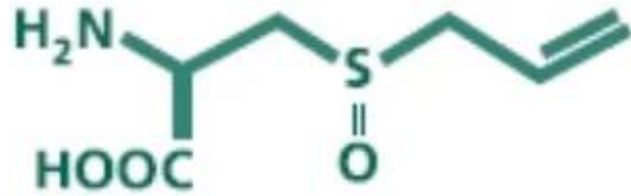


- **Scientific Name:** *Allium sativum*
- **Family :** *Liliaceae*
- **Plant part used :** Bulb
- **Common Name:** Garlic, allium, stinking rose,

Geographical source:

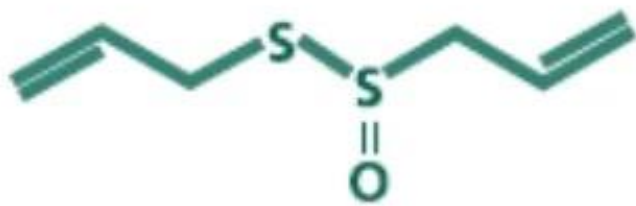
Central Asia, Europe , Asia , USA, INDIA

Formation of Allicin from Alliin upon crushing Garlic

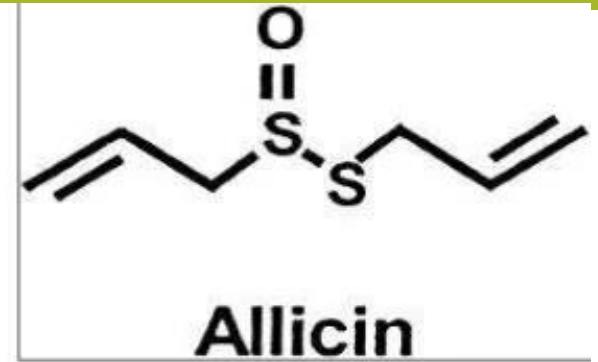


Alliin

Alliinase



Allicin



Chemistry

- Carbohydrates- 29%.
- Garlic contains about 0.5% of a volatile oil composed of sulfur-containing compounds (diallyldisulfide, diallyltrisulfide, methylallyltrisulfide).
- Allicin gives the pungent characteristic odor to crushed garlic and is believed to be responsible for some of the pharmacologic activity of the plant.

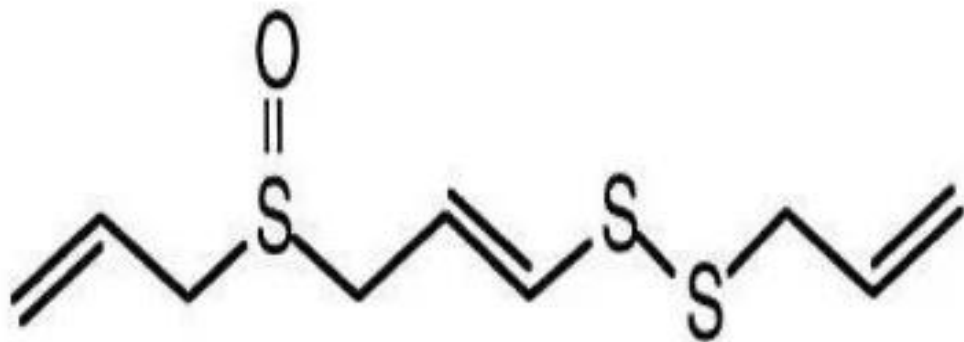
- Antimicrobial effect of garlic is possible because of Organosulfur compounds.
- Allicin react with enzyme containing thiol. so it is inhibit the
 - ❖ Acetyl co A forming system
 - ❖ DNA synthesis & protein synthesis

Other Antimicrobial compounds in garlic :

Ajoene

DATS

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3.GINGER



Scientific Name: *Zingiber officinale*

Family : Zingiberaceae

Plant part used : whole or cut , dried scrapped or unscrapped rhizome

Common Name: Ginger , ginger root, Sunthi , zingiberis rhizoma

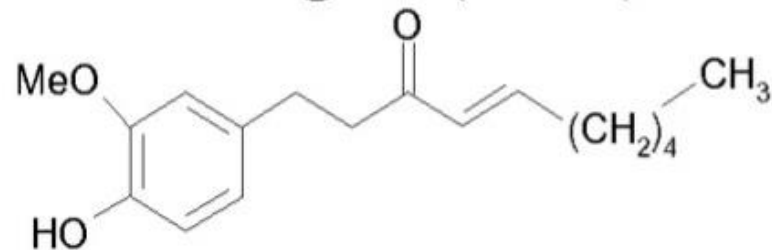
Geographical Source:

- A native of tropical Asia, this perennial is cultivated in tropical climates such as Australia, Brazil, China, India, Jamaica, West Africa, and parts of the US.

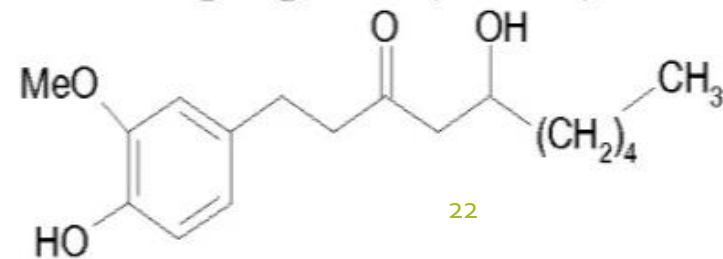
Chemical Constituents

- Pungent principles -responsible for its activity.
- Aroma of ginger - due to the zingiberol .
- Carbohydrates -50 to 70%, which are present as starch.
- Oleoresin provides 4 to 7.5% of pungent substances as gingerol , shogaol , zingerone, and volatile oils.
- Volatile oils -1 to 3% consist mainly of the sesquiterpenes and zingiberene; other sesquiterpenes include zingiberol and zingiberenol; numerous monoterpenes are also found.
- 6-gingerol and 6-shogaol are the main components

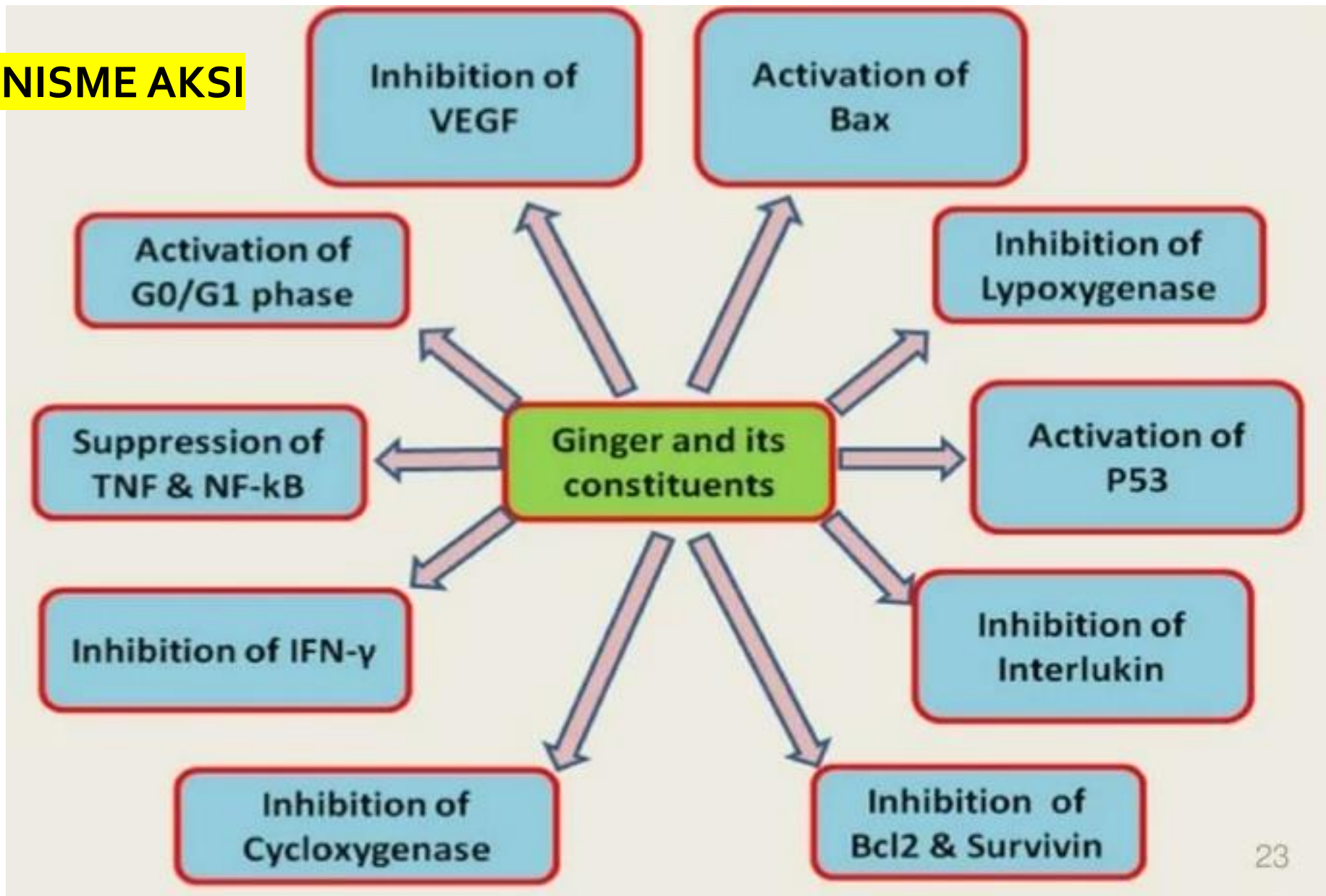
6-shogaol (“6-S”)



6-gingerol (“6-G”)



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4. CINNAMON

Scientific Name: *Cinnamomum verum*, *C. zeylanicum*.

Family: *Lauraceae*

Plant part used : dried inner bark of shoots.

Common Name: Cinnamon bark, Kalmi-Dalchini, Ceylon cinnamon.

Geographical source:

- The plant is native to Sri Lanka, southeastern India, Indonesia, South America, and the West Indies.

Chemistry

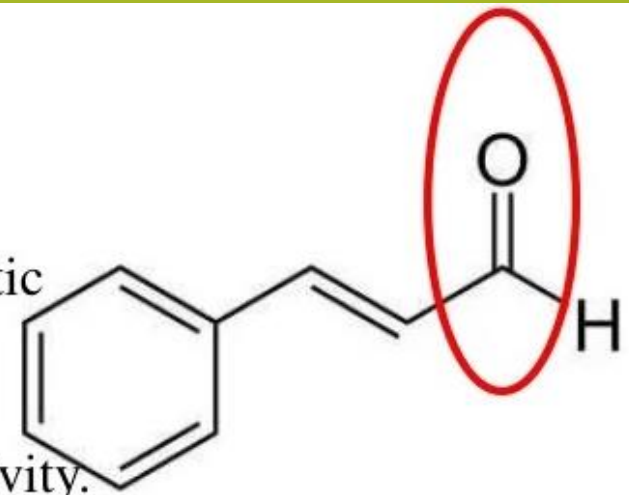
- Essential oil - 65% to 80% cinnamaldehyde and lesser amounts of other phenols and terpenes, including eugenol, trans-cinnamic acid, hydroxycinnamaldehyde, o-methoxycinnamaldehyde, cinnamyl alcohol, limonene, α -terpineol,
- tannins, mucilage, and trace amounts of coumarin.



Uses of Cinnamon

- As a spice and an aromatic.
- The bark or oil has been used to combat microorganisms, diarrhoea and other GI disorders, and dysmenorrhea.
- An anti-inflammatory agent, an antioxidant, and an antimicrobial substance.
- Carminative
- Mild astringent
- Antiseptic

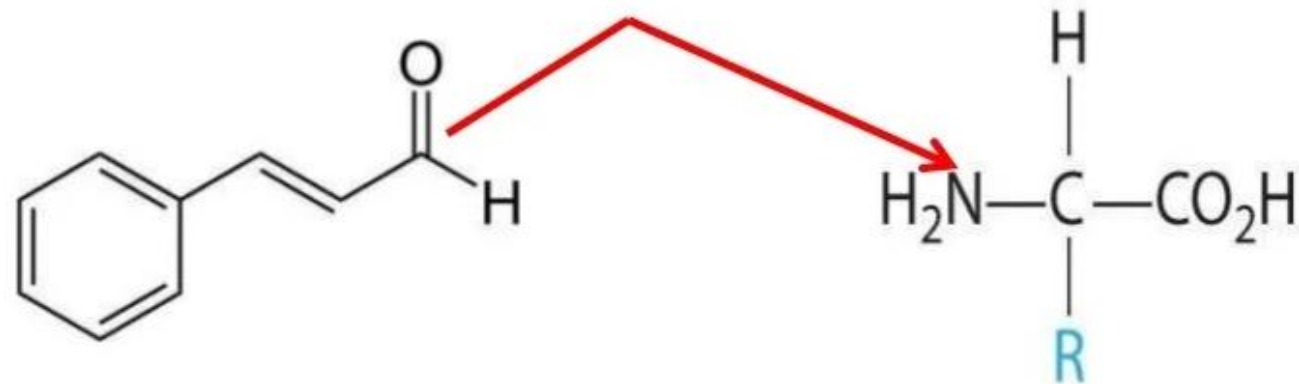
Cinnamaldehyde has electro- negative characteristic



These characteristic is cause for antimicrobial activity.

Electro-negative compounds interfere in biological processes involving electron transfer and react with nitrogen-containing components .

- They deform amino acid after then protein
- Cause damages to enzymes
- They destroy nucleic acid



5.ONION



- **Scientific Name(s):** *Allium cepa*
- **Family :** *Liliaceae*
- **Plant part used :** Bulb
- **Common Name:** Onion, wild onion, garden onion

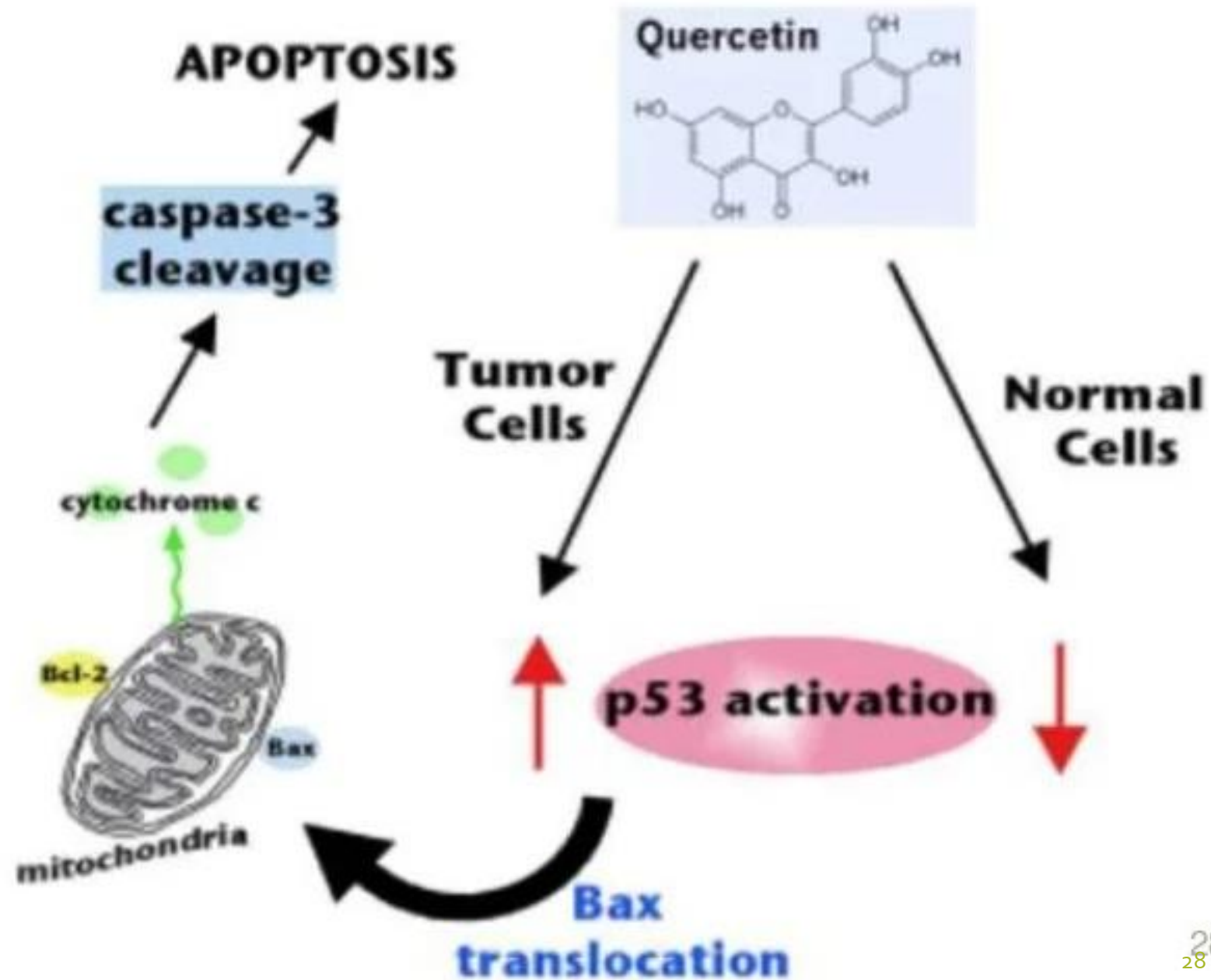
Chemical Constituents:

- 89% water, 1.5% protein, and vitamins, including B1 , B2 , and C, along with potassium.
- Polysaccharides such as fructosans , saccharose
- peptides, flavonoids, and essential oil.
- **Quercitin** is aslo predominantly present.
- Onion contains allicin and similar sulfur compounds, including allylalliin and methyl and propyl compounds of cysteine sulfoxide.
- Prostaglandins.

Antimicrobial effects

- The antibacterial, antiparasitic, and antifungal actions of onion is believed to be due to a number of sulfur containing compounds such as allicin , allylalliin , diallyl disulfide and the methyl and propyl compounds of cysteine sulfoxide.

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6. NUTMEG

Scientific Name: *Myristica fragrans*

Family : *Myristicaceae*

Plant part used: Dried Kernels of the seeds

Common Name: Nutmeg, mace, Nux Moschata , myristica oil

Geographical Source:

- India, Ceylon, Malaysia, and Canada, Indonesia, etc.

Chemical constituents:

- 20% to 40% of a fixed oil known as nutmeg butter. This oil contains myristic acid, trymiristin, and glycerides of lauric,, stearic, and palmitic acids.
- 8% to 15% of an essential oil . The essential oil contains myristicin, elimicin, eugenol, and safrole.
- Geraniol , terpineol etc.



7. TURMERIC

Scientific Name: *Curcuma longa*

Family : *Zingiberaceae*

Plant part used: Fresh rhizomes

Common Name: Indian Saffron, Curcuma, Haridra, Haldi .

Geographical Source:

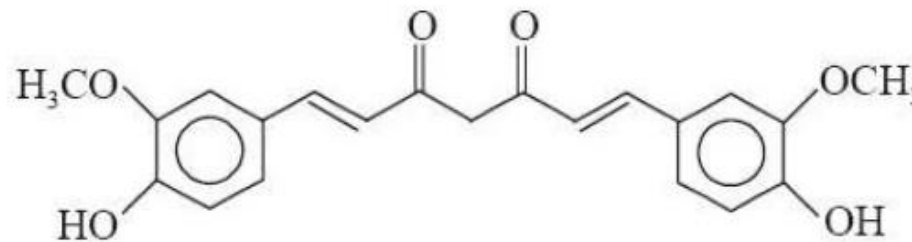
- India, China, Thailand, Italy, Malaysia, etc.

Chemical constituents:

- 5%-Volatile oils, Resin, Zingiberaceous starch grains , curcuminoids.
- Curcumin - 50-60%.
- Demethoxy curcumin , bisdemethoxy curcumin.

Uses:

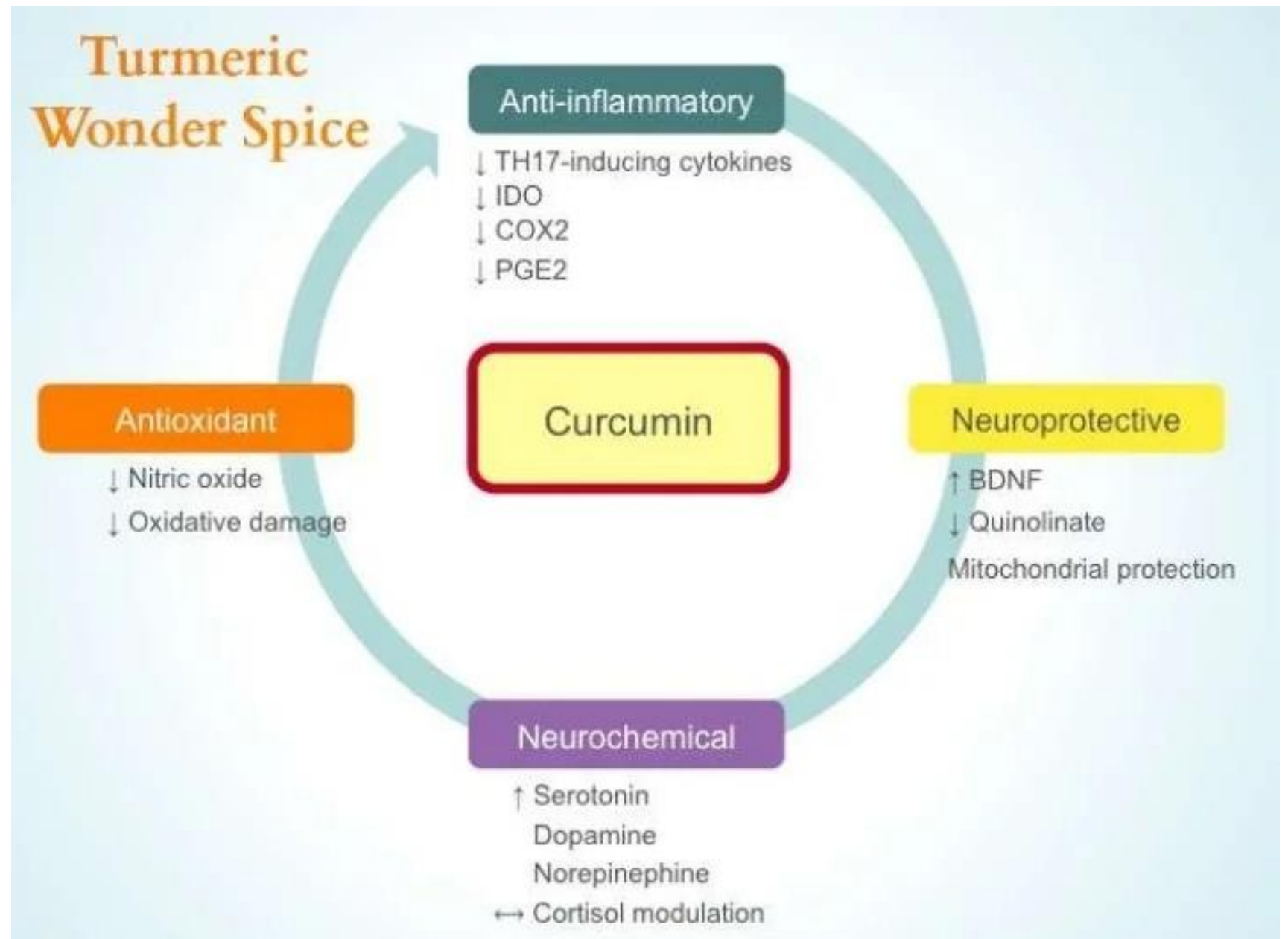
- Condiment or spice.
- Colouring agent .
- Antiseptic.
- Anti inflammatory.
- Anti-oxidant.
- HIV-1 and HIV-2 protease inhibitory activity.



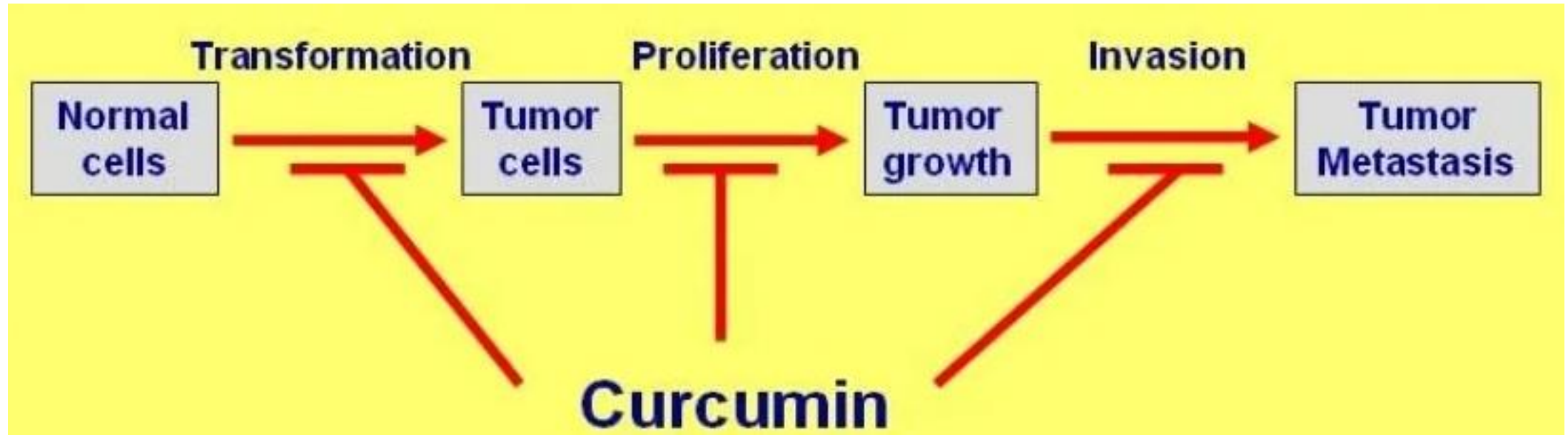
Curcumin

(Orange-yellow crystalline powder, mp 183°C)

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THANK YOU!

