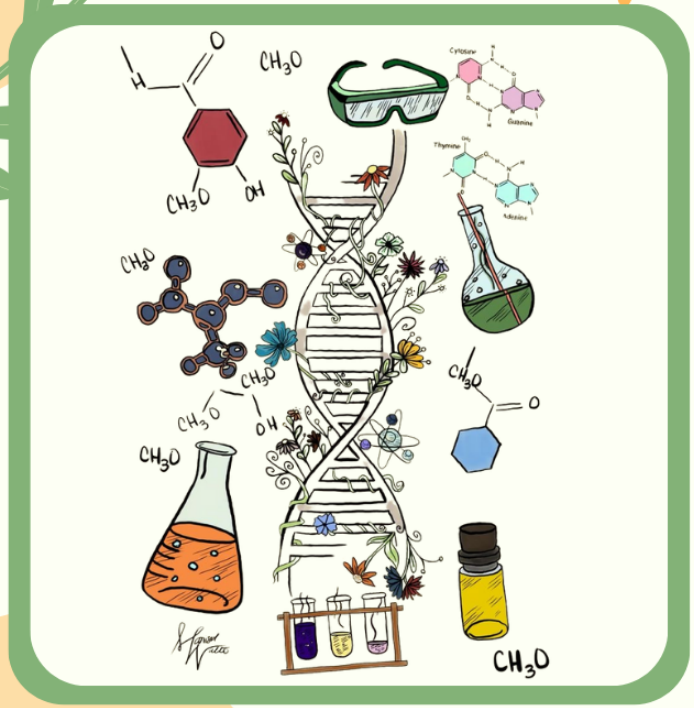
تفريغ عقاقير



اسم الموضوع: Chapter 6 part two

إعداد الصيدلاني/ـة: لؤي المجدلاوي

Soul Academy

لجان الدُّفعات

Linseed- Flax seed بذر الكتان

- Linum usitatisimum L. Family: Linaceae.

- They're the best plant source of omega-3 fatty acids.
- Flaxseeds are also a powerful source of fiber, protein, magnesium, iron, and potassium.
- Flaxseeds are also the leading source of a class of compounds called lignans, which are phyto-estrogens, or plant estrogens. Lignans influence the balance of estrogens in the body and help protect against breast cancer.
- **The seeds must be ground, as the nutrients are difficult to absorb from the whole seeds**. Since the oil in flaxseed spoils quickly, it's best to grind them as needed. Some people use a grinder dedicated to flaxseeds, grind them in small amounts, and keep the ground portion in the fridge in a small glass jar.
- Sprinkle ground flaxseeds on oat-meal, cereal, and yogurt, and use it in smoothies, pancakes, muffins, and quick breads. **One to two tablespoons of ground flaxseed a day is all you need.**

* من ملعقة لملعقتين كبار يوميا للحماية من الاصابة بالسرطان و للحصول على فوائد بذور الكتان

اللهم صل على سيدنا محمد

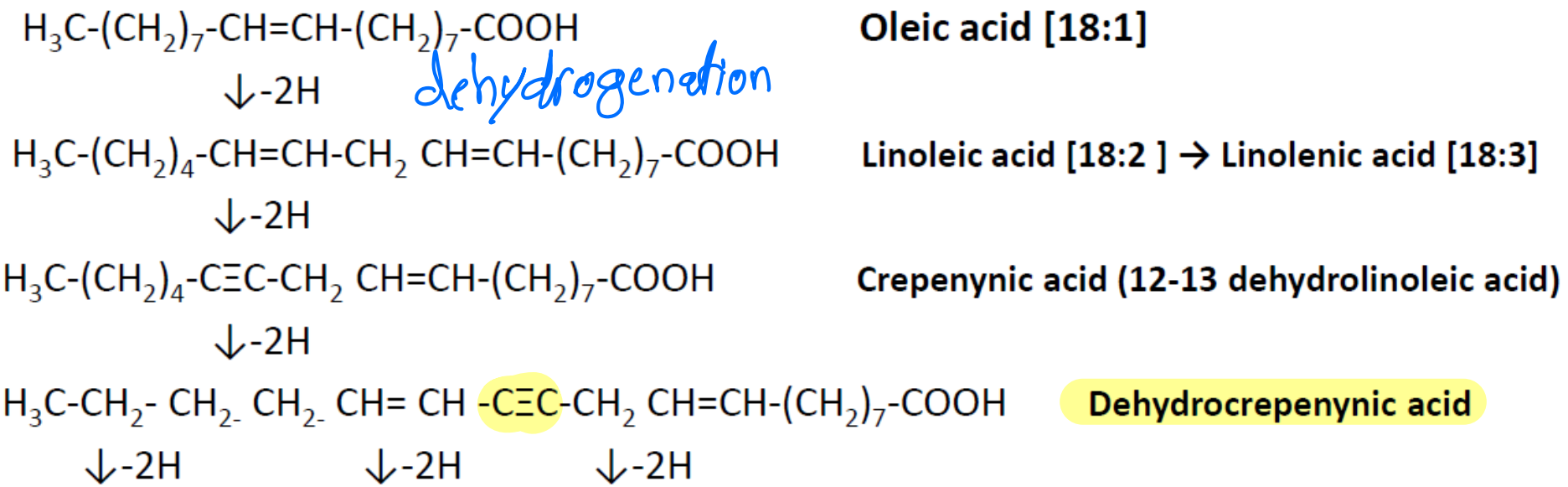
Linseed- Flax seed بذر الكتان

- **Active constituents:** مشتقات الـ carb
- **Mucilages:** including arabinoxylans, galactans, rhamnogalacturonans. مواد زي الجلي
- **Cyanogenic glycosides:** Linamarin, linustatin, neolinustatin (yielding under optimal conditions 30-50 mg HCN per 100 gm). $C \equiv N$
- Linmarin (may play a role in cancer treatment)
- **Fatty oil** (30-45%): chief fatty acids linolenic acid , linoleic acid ,oleic acid. اكثر واحد omega-3
- **Proteins**.
- **Gluten: Flax is gluten-free**.
- •**Lignans:** secoisolariciresinol-diglucoside SDG
- **lignans**: Flax is a very rich source of a lignan called secoisolariciresinol diglucoside (SDG), which is found in amounts ranging from 1 mg/g of seed to nearly 26 mg/g of seed.
- **lignans** are natural antioxidants that may reduce the activity of cell-damaging free radicals, slow the aging process, and increase overall wellness.
- Besides acting as antioxidants, lignans are phytoestrogrens
- Lignans are especially important for women as studies have shown them to decrease the risk of breast cancer. In addition, lignans have been proven to reduce breast cancer symptoms and reduce the spread and growth of breast cancer after diagnosis.

* يؤخذ للوقاية و للعلاج

Biogenesis of natural acetylenes

The precursor of the acetylenic substances is oleic acid

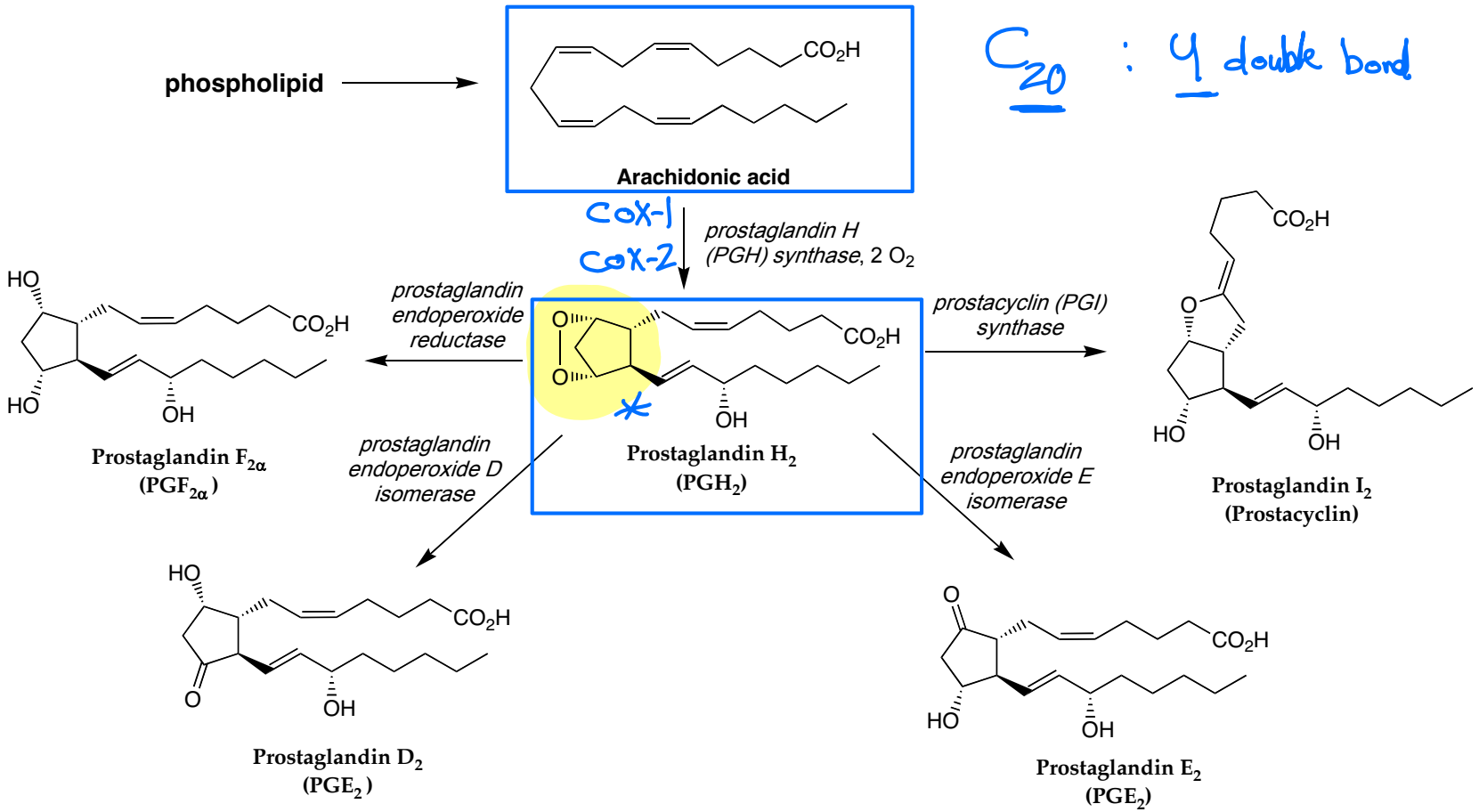


Ref.:
Prof. Sulaiman Khalil

Prostaglandin

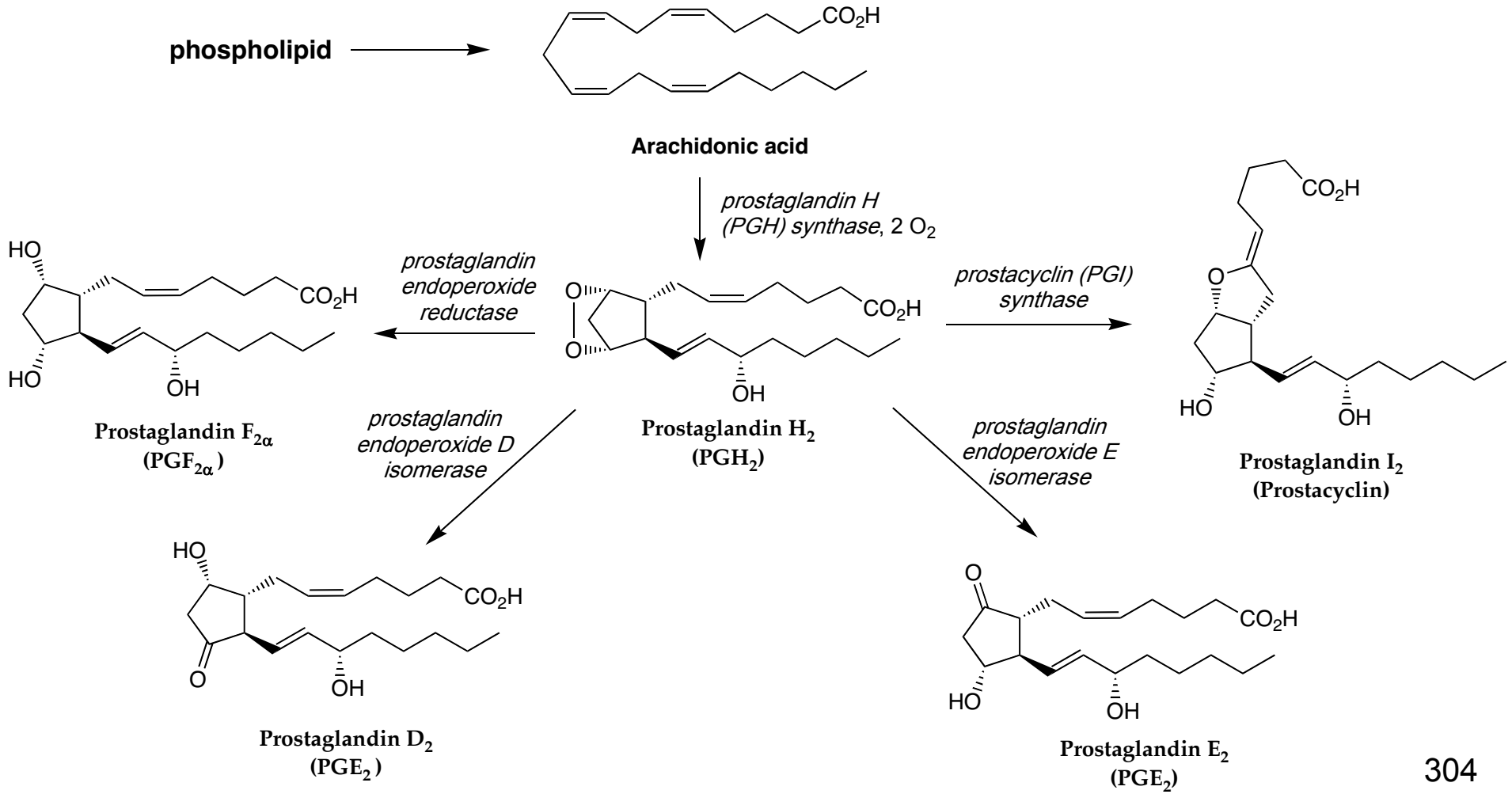
يسبب ألم واحمرار وحرارة

- The **prostaglandins** (PG) are a group of physiologically active lipid compounds having diverse hormone-like effects in animals.
- Prostaglandins have been found in almost every tissue in humans and other animals. They are derived enzymatically from fatty acid (Arachodonic acid). Every prostaglandin contains 20 carbon atoms, including a 5-carbon ring

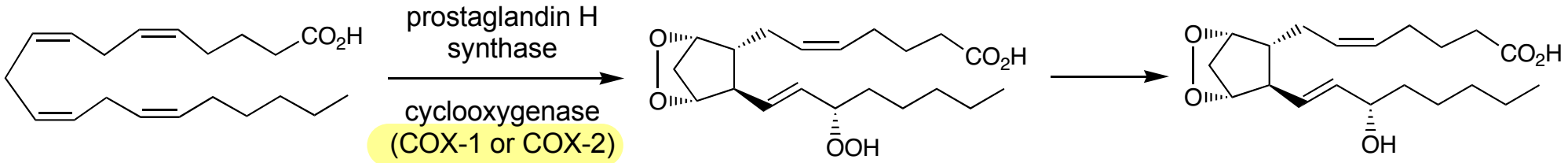


Prostaglandins. (eicosanoids) C_{20} compounds derived from arachidonic acid and related fatty acids

hormone: (Greek, *horman*, to set in motion) chemical messengers from one cell to another, that acts as a signal for a biochemical event.



Prostaglandin biosynthesis

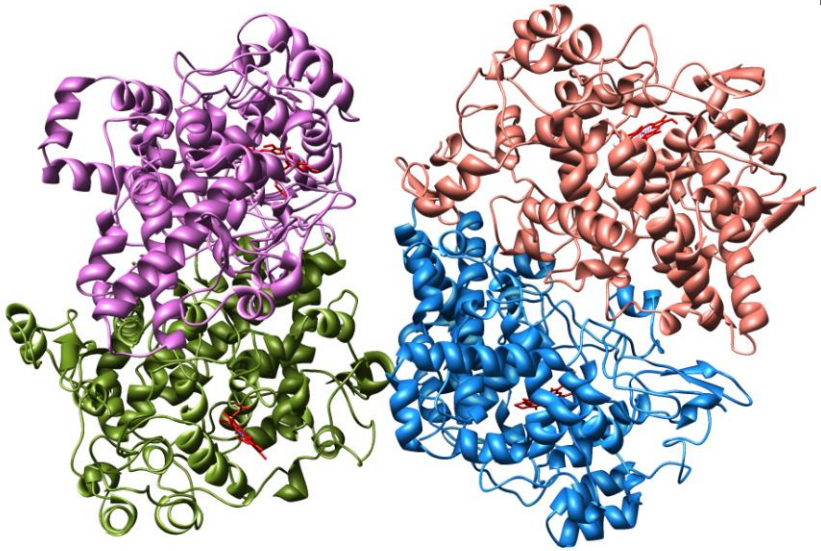


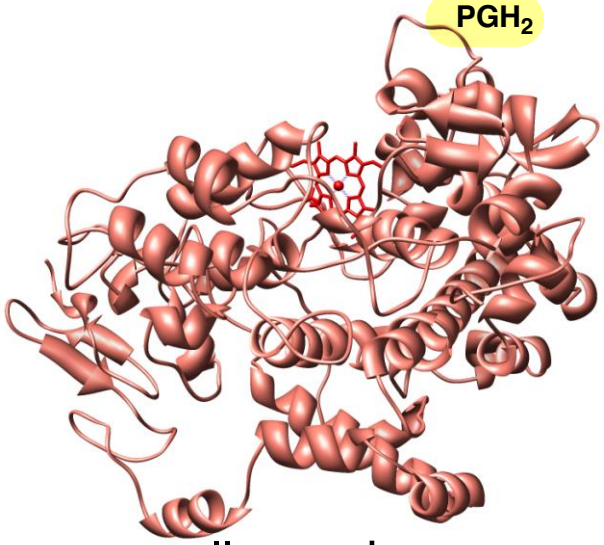
Arachidonic acid

PGG_2

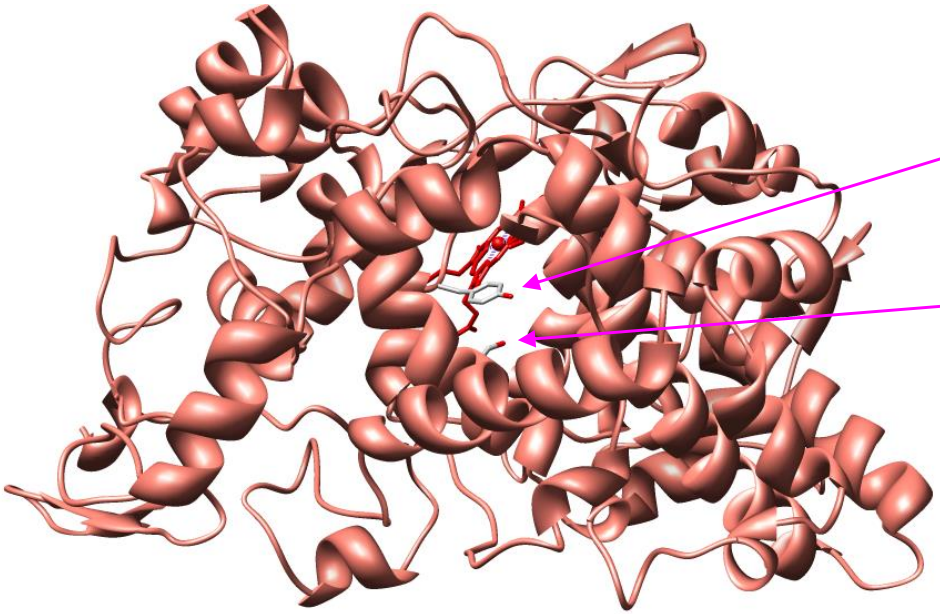
PGH_2

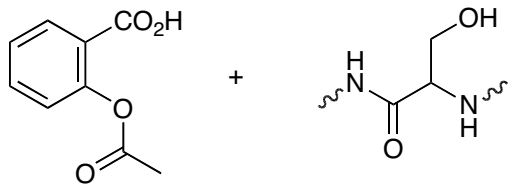
COX-2





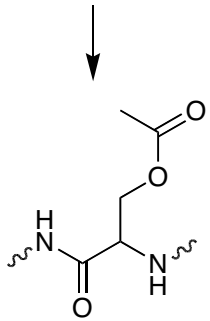
cell membrane





acetylsalicylic acid

Ser-530 COX



covalently modified enzyme

COX-1 is a constitutive enzyme that is expressed in virtually all mammalian cells Protection of GI mucus

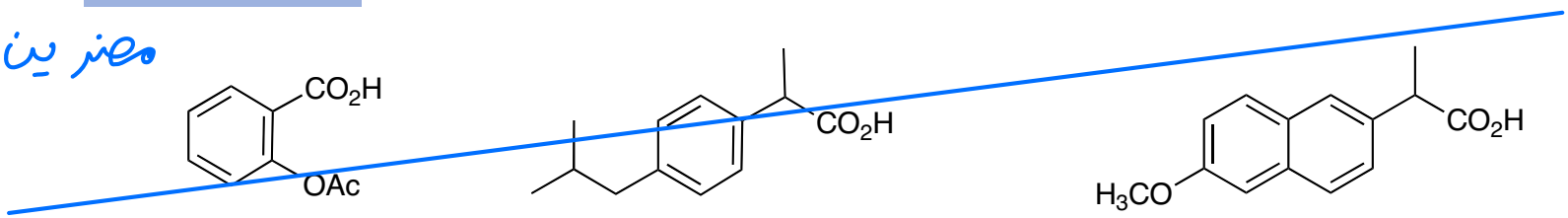
COX-2 is an inducible enzyme that is expressed as a results of a biochemical response; expressed in phagocytes WBC (macrophages) as part of an inflammation response.

* NSAIDs: non-steroidal anti-inflammatory drugs

Aspirin, ibuprofren, and naproxen are non-selective inhibitors of COX

cox-2 و cox-1 کل

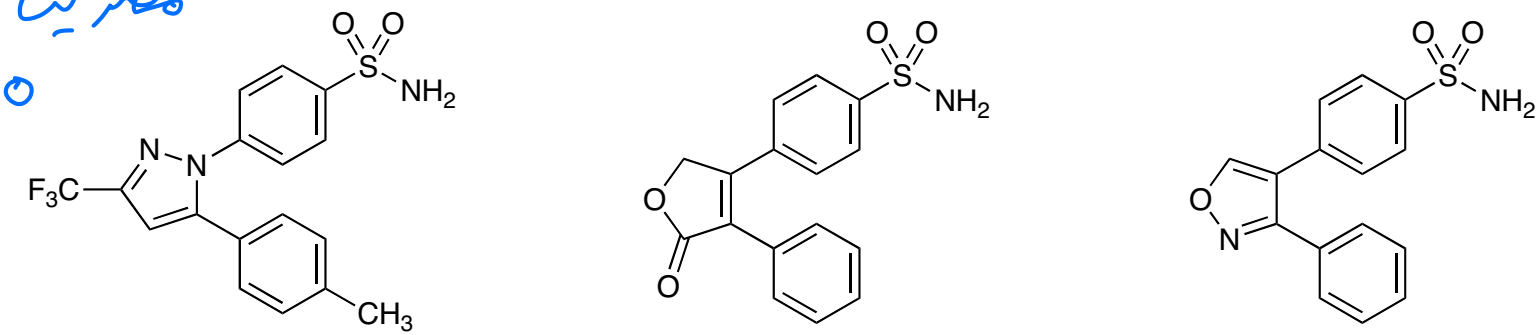
مضر ین بال GI



Celebrex, vioxx, and brextra are selective inhibitors of COX-2 (coxibs)

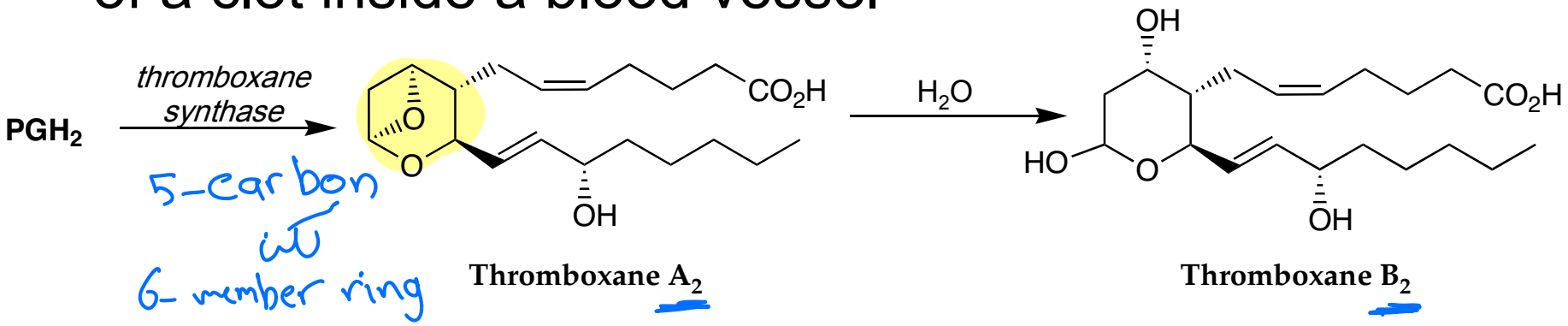
cox-2 کل

مضر ین بال Cardio



Another eicosanoids types

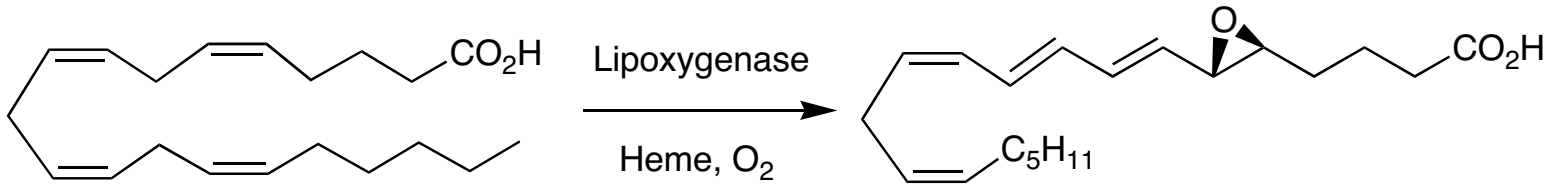
Thromboxanes: named for their role in thrombosis, the formation of a clot inside a blood vessel



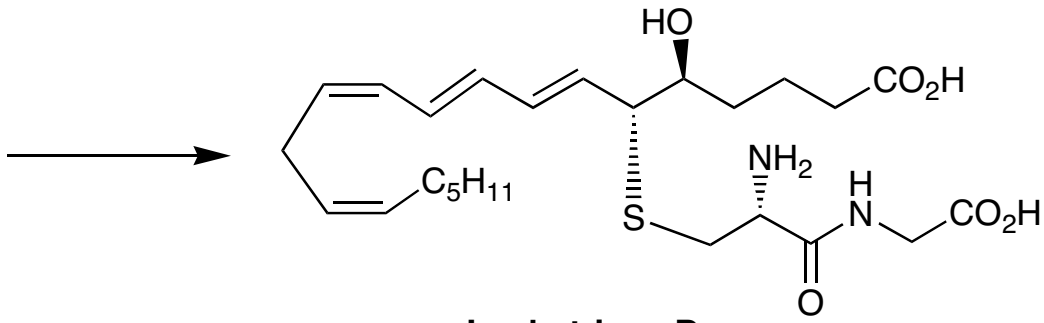
5-carbon in 6-member ring

Thromboxane A_2 | Thromboxane B_2

Leukotrienes: a family of eicosanoid inflammatory mediators produced in leukocytes by the oxidation of the essential fatty acids arachidonic acid



Aracidonic acid | **Leukotriene A_4**



Leukotriene D_4

مضادات حيوية

Antibiotics Derived from Acetate Malonate Pathway

Professor Suleiman OLIMAT

Antibiotics derived from the acetate metabolism

1- Antibiotics with fused ring system:

- -Griseofulvin
- -Tetracyclines
- -Anthracyclines

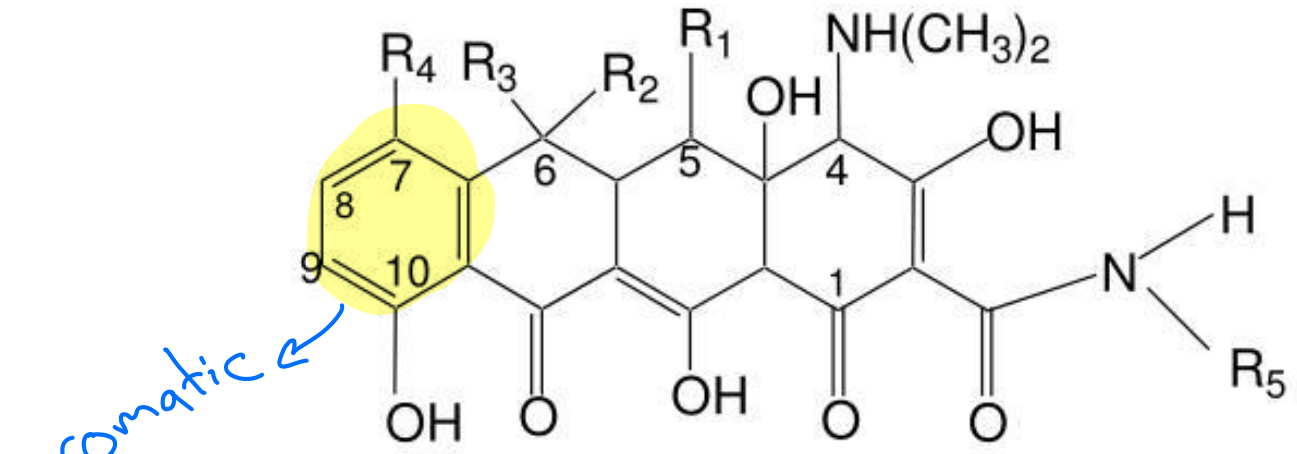
2-Macrolide antibiotics

3-Polyene antibiotics

اللهم صل على سيدنا محمد

Tetracyclines

4 - cyclic



aromatic

Tetracyclines

- **Biosynthesized from 1 MalonamylCoA + 8 MalonylCoA**

  ($1NH_2$-CO-CH_2-CO-SCoA +8 HOOC-CH_2-CO-SCoA)→C-19 Polyketide → → →cyclisation →C-6 methylation →OH at C-4 →dearomatization → 4-keto derivative → Cl^- at C-7 → amination and stepwise methylation at C-4 → hydroxylation C-6 →reduction of double bond in ring B

- Biosynthesized in *Streptomyces* spp. (*S. aureofaciens, S. rimosus,…)*
- Broad spectrum activity
- Protein synthesis inhibitor
- Side effects!

3C 2×8 C

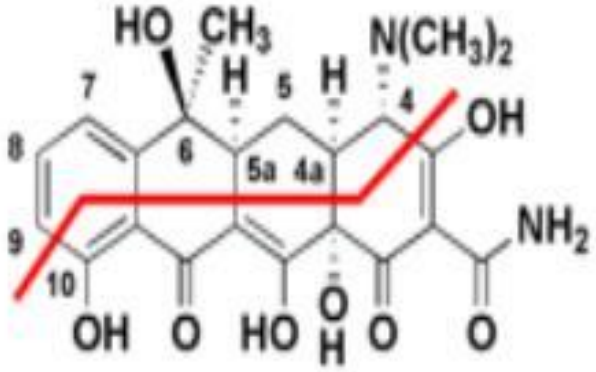
نوع بكتيريا

في البكتيريا

chelating agent

Tetracyclines

Positions amenable to modification

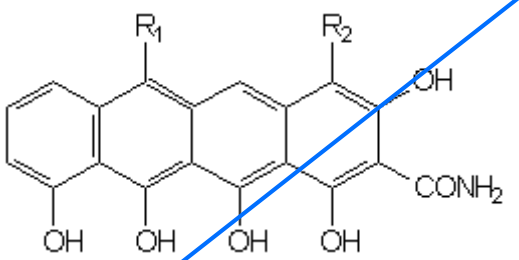


Positions believed to be key to ribosomal binding

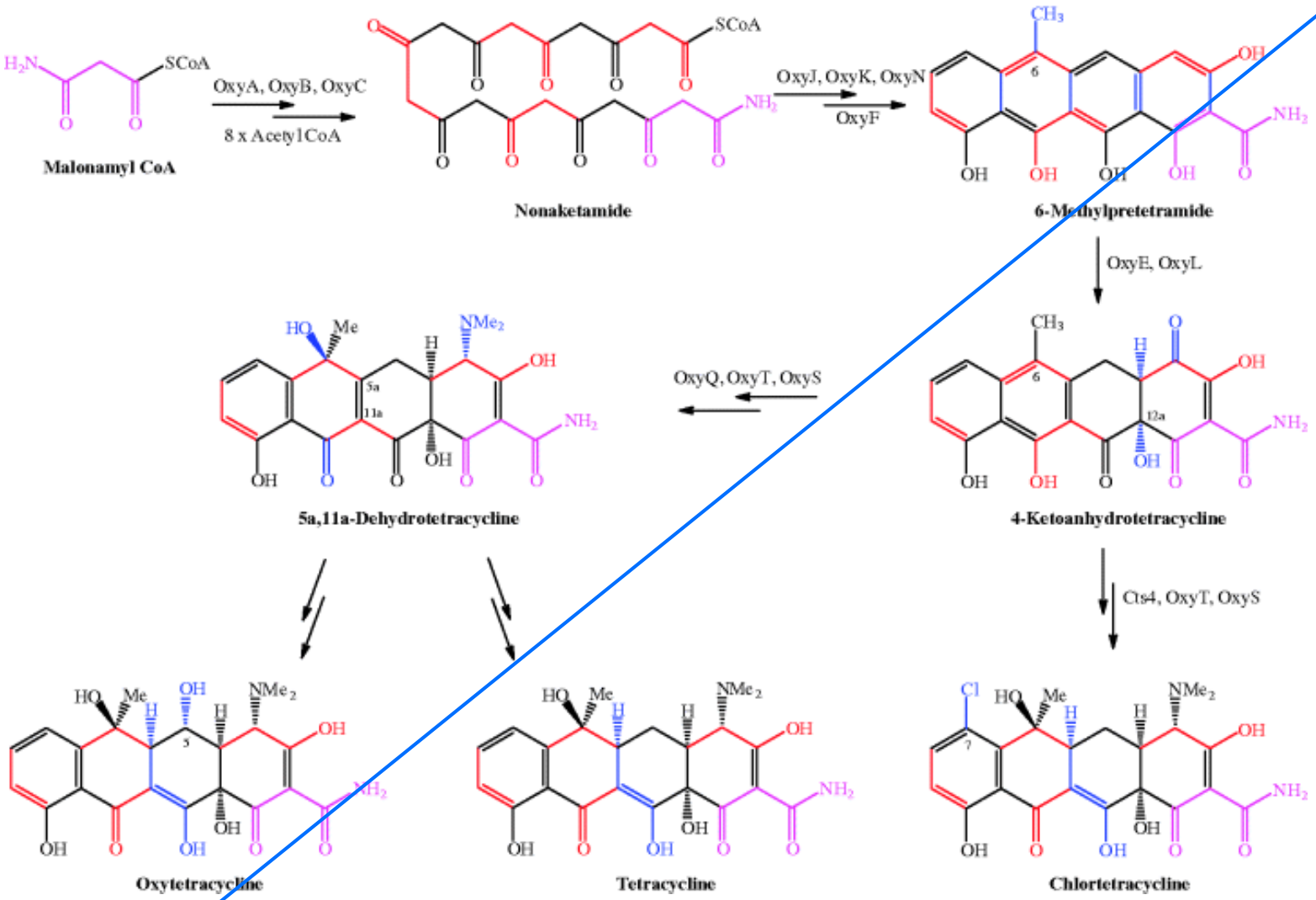
protein synthesis يمنع ال
في البكتيريا

Biosynthesis

- A biosynthesis of tetracycline, particularly in its latter stages, has been studied with the use of mutant cultures. It has been established that the so-called **pretetronids**:



- are intermediates, convertible by non-mutated *Streptomyces aureofaciens* into tetracyclines. Cosynthesis, by use of blocked mutants, has demonstrated that 4-hydroxy-6-methylpretetranid (R_1 = Me, R_2 = OH) is a transformable intermediate and the precursor to the 6-methyltetracyclines. The complete biosynthesis is as follows :


Malonamyl CoA
OxyA, OxyB, OxyC
8 x Acetyl CoA
Nonaketamide
OxyJ, OxyK, OxyN
OxyF
6-Methylpretetramide
OxyE, OxyL
4-Ketoanhydrotetracycline
OxyQ, OxyT, OxyS
5a,11a-Dehydrotetracycline
Cts4, OxyT, OxyS
Oxytetracycline
Tetracycline
Chlortetracycline

From bacteria without modification

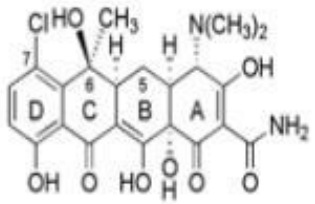
Naturally occurring: Tetracycline, Chlorotetracycline, Oxytetracycline, Demeclocycline

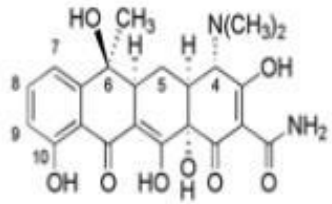
for acne

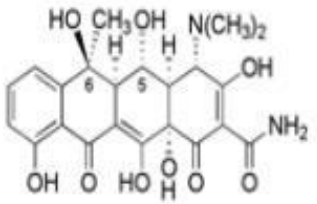
Semi-synthetic: Doxycycline, Meclocycline, Methacycline, Minocycline, Tigecycline,…

modificated

Natural Tetracyclines:

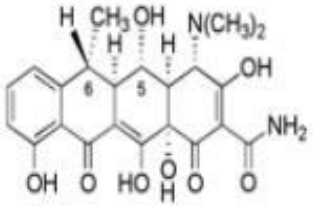


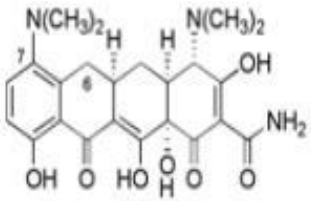


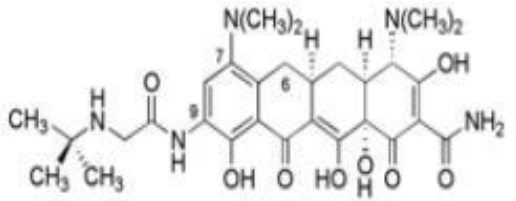


US FDA Approval: ~~1950~~ Chlorotetracycline | ~~1953~~ (–)-Tetracycline | ~~1964~~ Oxytetracycline

Semi-Synthetic Tetracyclines:







~~1967~~ (–)-Doxycycline | ~~1971~~ (–)-Minocycline | ~~2005~~ (–)-Tigecycline

Anti cancer + Anti bacterial

Antineoplastic anthracycline derivatives

Produced by cultures of *Streptomyces* spp.; inhibit DNA dependent RNA synthesis

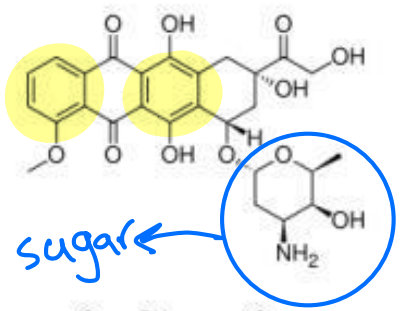
side Effect SE: nausea, bone marrow depression, hair loss, local tissue necrosis;

Biosynthesis: 1 PropionylCoA + 9 MalonylCoA

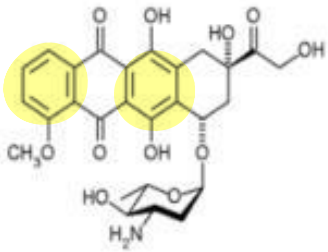
3C 2x9 C

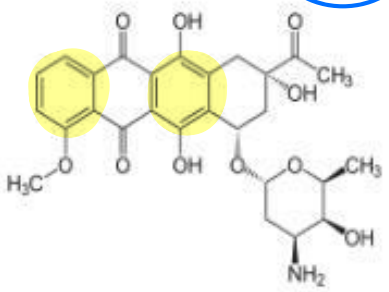
- 4 cyclic
- 2 aromatic
- N sugar

Doxorubicin

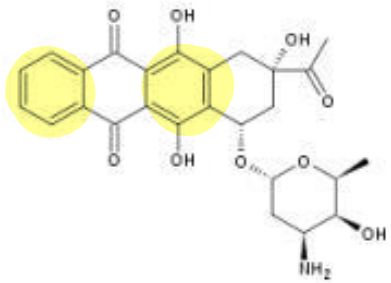


Epirubicin





Daunorubicin

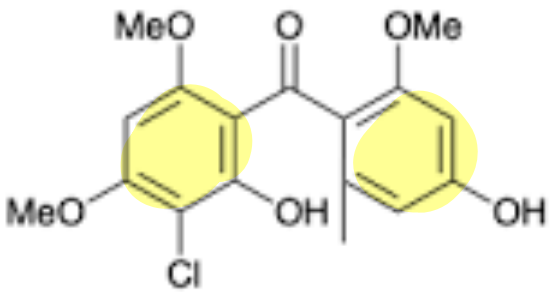


Idarubicin

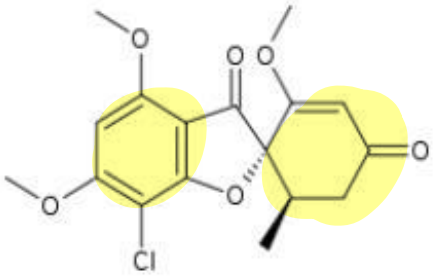
Griseofulvin:

Produced by *Penicillium* spp (*P. griseofulvum*, ….)

1 AcetylS-CoA + 6 MalonylS-CoA → Polyketide → Griseophenone C →B →A →Dehydrogriseofulvin → Griseofulvin



griseophenone A (8)



Griseofulvin

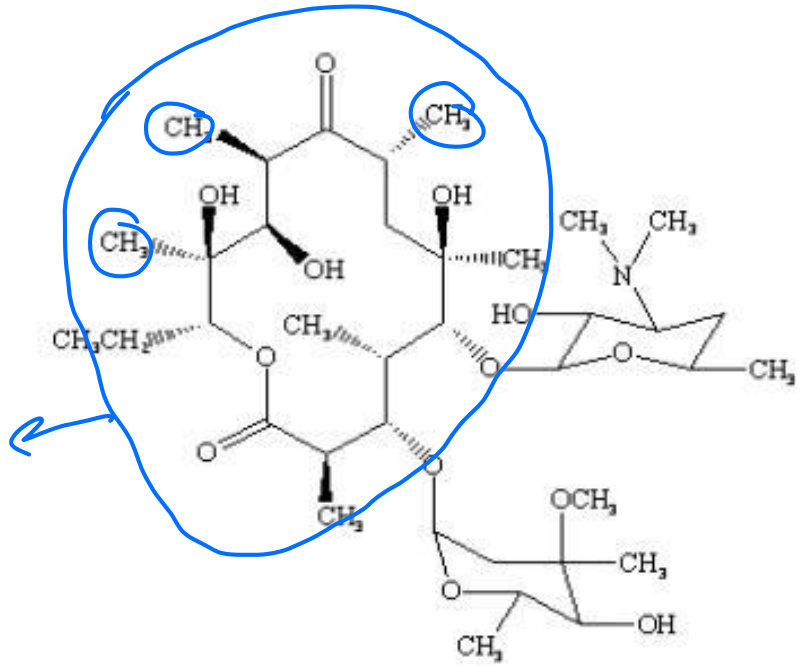
Macrolide antibiotics

upper respiratory infection

- Synthesized from acetate units
- Produced by *Streptomyces* spp.
- Large lactone ring (12, 14, 16 or ~~17~~ atoms)
- Numerous CH_3 substituents in lactone ring
- 1-3 deoxy-sugar/sugar moieties attached to the ring
- Erythromycin A, B as examples
- Mainly active against Gram-positive bacteria and *Mycoplasma* spp.; useful in pat. with penicilline allergy
- Protein synthesis inhibitors
- SE: few, mainly GI symptoms

Erythromycin A: 1 [PropionylCoA] + 6 [2-MethylmalonylCoA] →Poly-keto-acid →condensation →Erythronolide ring (14 atoms)→glycosidation →Erytrhromycine (Azithromycine is its semi-synthetic analog)

[1 CH_3-CH_2-CO-SCoA + 6 HOOC-CH-(CH_3)-CO-SCoA]



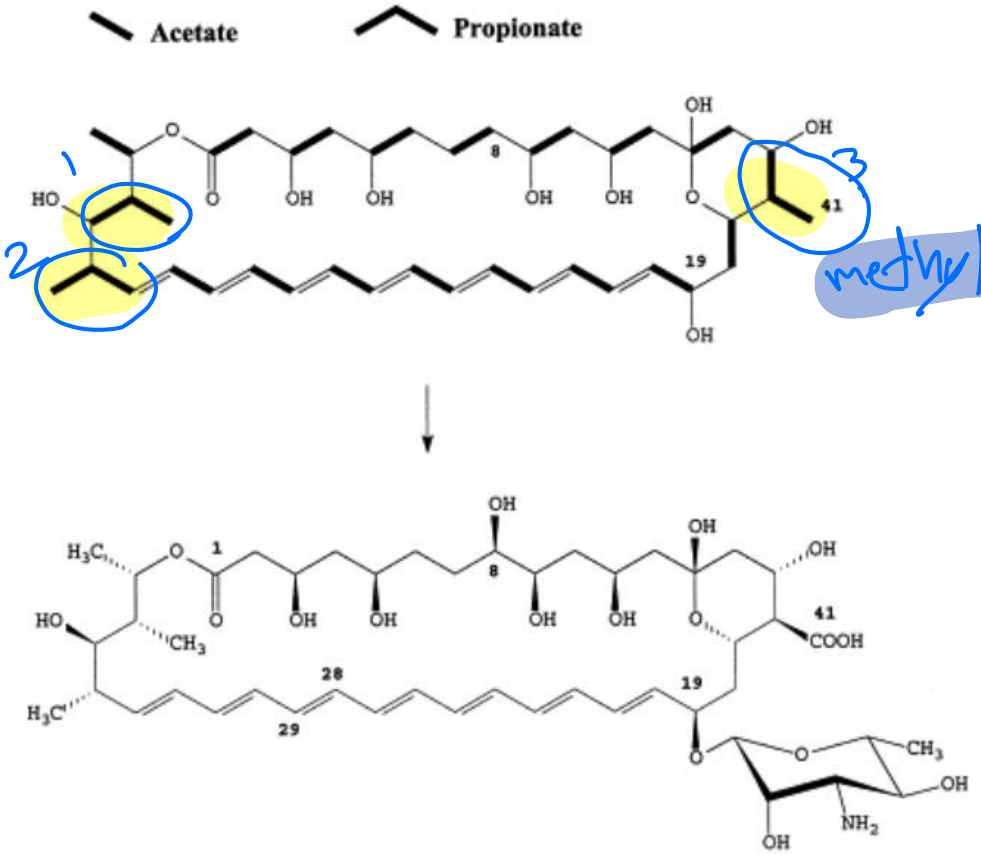
lactone ring

- numerous CH_3
- 1-3 sugar

Polyenes

- The group of antibiotics known collectively as polyenes is characterized by a large lactone ring (20–44 membered) containing a series of conjugated double bonds.
- The macrolide ring is often linked via a hydroxyl group to an aminosugar unit
- The macrolide ring is probably derived from acetate and propionate.
- They are often mixtures of closely related compounds.
- *Streptomyces* are the usual producing organisms, and to date over *200* polyenes have been claimed
- *Candida albicans* is susceptible to the polyenes
- Cutaneous, intestinal and vaginal infections of *Candida*

Amphotericin B: formed of 16 acetate units (1 AcetylCoA + 15 MalonylCoA + 3 MethylmalonylCoA); macrolactone ring followed by glycosidation withD-mycosamine via OH at C-19



2C

2x15C

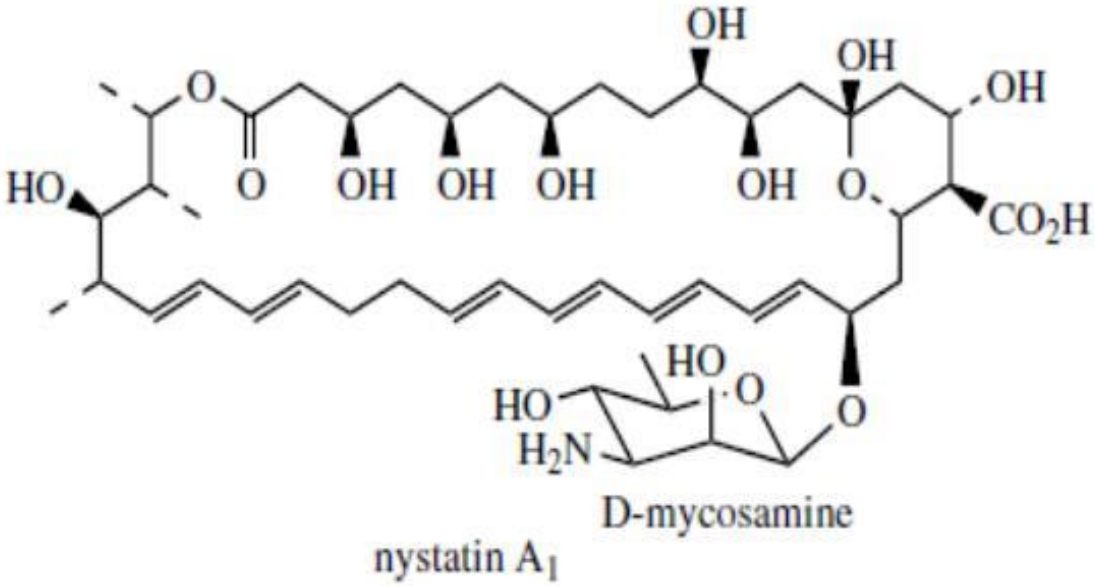
3x3 C

Anti fungal

methylmalonyl

Nystatin A_1

Anti fungal strong



D-mycosamine

nystatin A_1