

EICOSANOIDS

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WHAT ARE EICOSANOIDS ?

- Eicosa: (Greek) = 20.

They are compounds which are derived from polyunsaturated fatty acids with 18, 20 & 22 carbon skeletons.

- **Needs receptors:** either plasma membrane or intracellular binding protein.

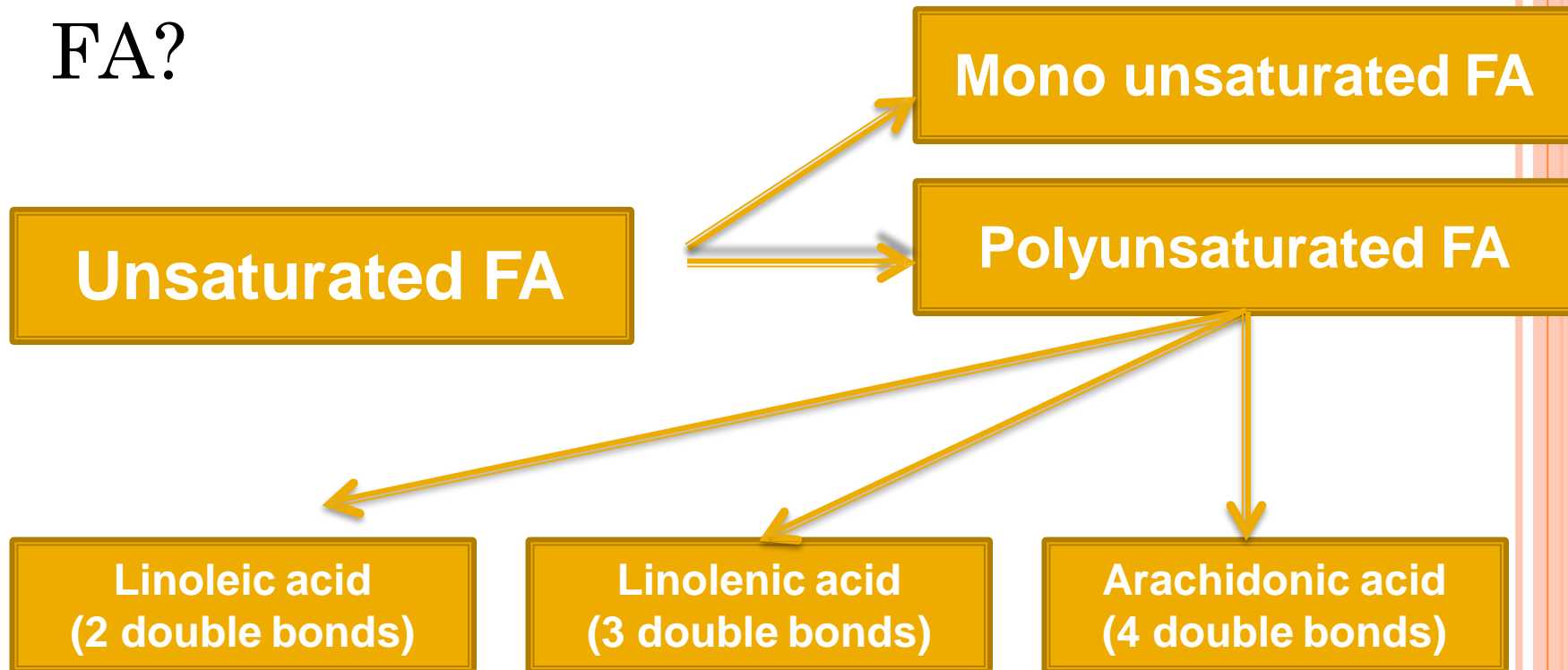
○ **Eicosanoids** is a Generic term for the 20 Carbon related compounds like:

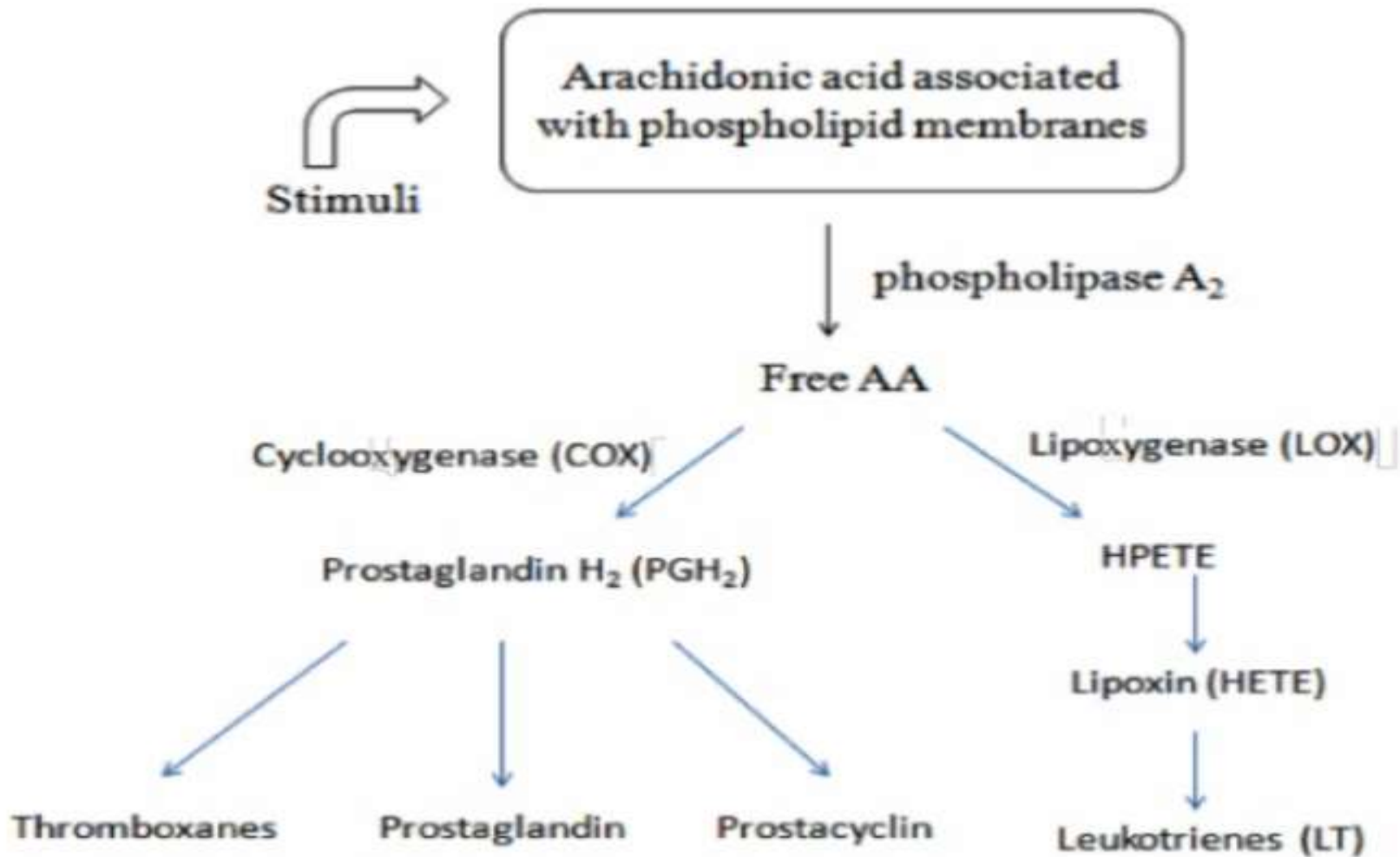
- I. **Prostaglandins (PGs)**
- II. **Prostacyclins (PGI₂)**
- III. **Thromboxanes (TX)**
- IV. **Leukotrienes (LT)**
- V. **Lipoxins (LX)**



FATTY ACIDS

- LOWER FA VS. HIGHER FA?

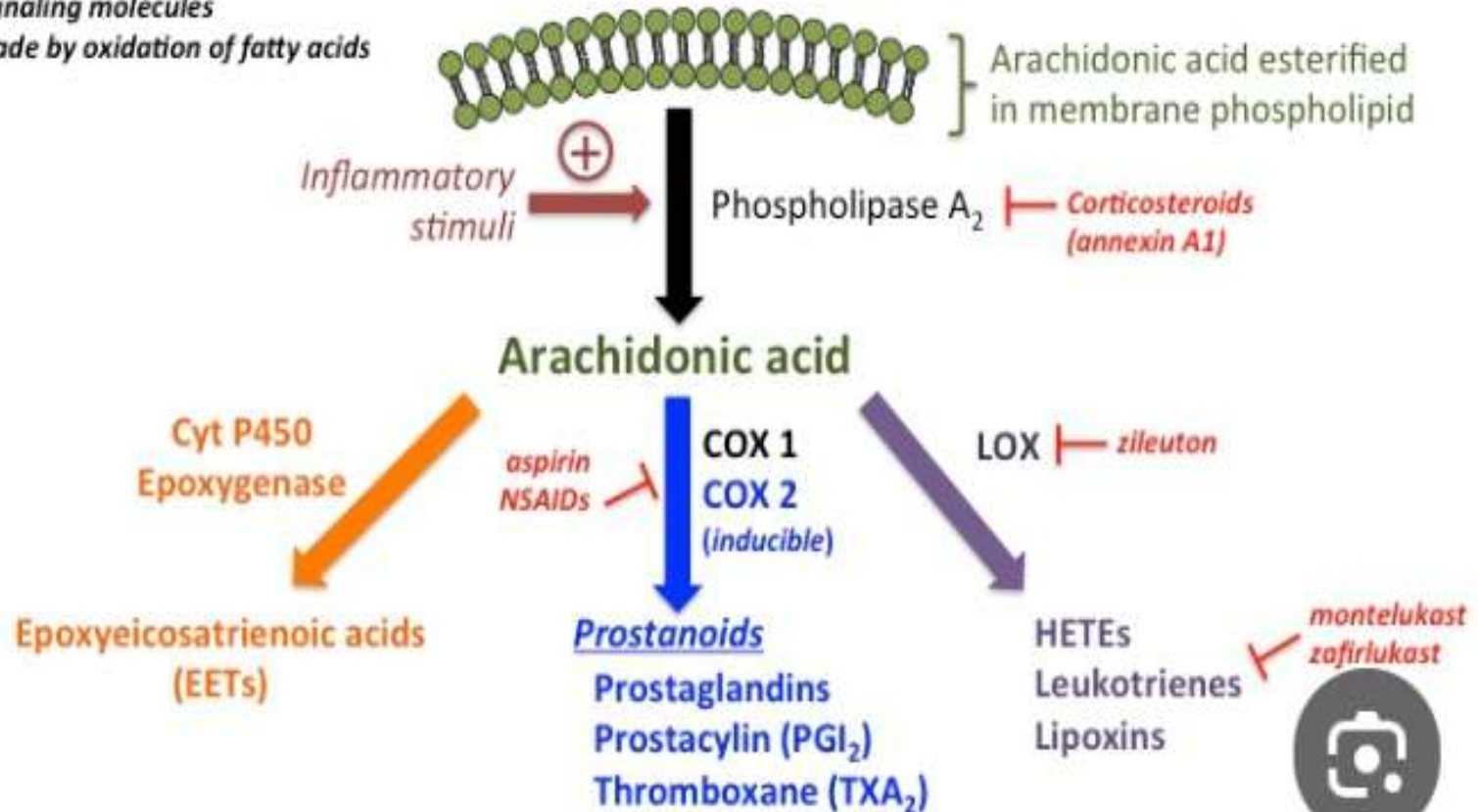




INHIBITION OF PG SYNTHESIS

Eicosanoids

signaling molecules
made by oxidation of fatty acids



INHIBITION OF PG SYNTHESIS

- Inhibited by structurally unrelated compounds
 - E.g. Corticosteroids (Cortisol)
- Non-steroidal anti-inflammatory drugs
- Aspirin inhibits PG synthesis
 - **Aspirin** – irreversibly blocks synthesis of cyclooxygenase
 - **Indomethacin & Phenylbutazone** – reversibly blocks synthesis of cyclooxygenase.

Biological effects

1- PGE₁, E₂, I₂

- **-VD.**
- **Lung:** Bronchodilation.
- **GIT:** ++ mucus production.

- **Ut:** Cont. of pregnant uterus.
- Relax non pregnant uterus.
- **Kid:** ++ RBF. promotes urine formation and urine output.
- Thus helps in **removing waste out of the body.**
- PGI₂:--Platelet aggregation.



Biological effects

2-PGF_{2a}, TXA₂, LTb₄:

- **-VC.**(LTs produce inflamm. VD).
- **Lung:**Bronchospasm.
- **GIT:** ++ mucus production.
- **Ut:** Cont. of pregnant uterus.
- **Kid:** --RBF. promotes urine formation and urine output.
- .
- TXA₂:++Platelet aggregation.
- **LTs:**chemotaxis.



7- Role Of PGs In Immunity And Inflammation

- Prostaglandins are produced in more amounts at the time of :
 - **Fever**
 - **Pain**
 - **Nausea and Vomiting**
 - **Inflammation**



Uses:

1. PGE₁

- i.v to produce controlled **hypotension**.
- Intracavernous in cases of **impotence**.
- Tried as vasodilator in **peripheral vascular diseases**.
- TGV.
- Misoprostol (cytotec) PGE₁ analogue used orally in **peptic ulcers**.

3-Epoprostenol (PGI₂) **antiplatelet aggregation**.

4PGE₂ tried in **bronchial asthma** but it is irritant.

5-PGE₂ & PGF_{2a} for induction of **abortion and labor**.

6- PGs in Kidneys **increases GFR** and **promotes urine formation and urine output**. Thus helps in **removing waste out of the body**.

7-Latanoprost is PGF_{2a} used topically in treatment of **glaucoma**.

8-PGE₂ is used in organ transplantation **to reverse rejection**

2. Prostacyclins (PGI₂)

Prostacyclins are type of **Eicosanoids/ Prostanoids**.

Principally **formed in vascular endothelium**

They are Platelet Aggregation Inhibition Factors

Biosynthesized by enzyme **Prostacyclin Synthetase**.

ROLES OF PROSTACYCLINS

- Prostacyclins are **Vasodilators**.
- Prostacyclins like Prostaglandins **inhibit platelet aggregation**.
- Prostacyclins **prevent Thrombus/clot formation**.

THROMBOXANE

- Are produced by platelets (**called thrombocytes**)
- Act in formation of blood clot
- And reduction of blood flow to the site of clot

Increases

Vasoconstriction

Platelet aggregation

Lymphocyte proliferation

Bronchoconstriction

LEUKOTRINES

Types of Leukotrienes:

LTB₄, LTC₄, LTD₄ and LTE₄

Drugs affecting:

-An **Antiasthmatic drug** Prednisone inhibits **Leukotriene biosynthesis**.

-Montelukast and Zafirlucast: block receptors.

Ziluton : inhibit lipooxygenase enz.

Mechanism of action:

Kinins act by stimulation of 2 subtypes of Gq coupled receptors

.That increases intracellular calcium through increasing I3P and DAG:

Effect Of Leukotrienes

1-Leukotrienes are biologically active **components of Slow Reacting Substances (SRS-A)**. causes fluid leakage from blood vessels to an inflamed area

2-Leukotrienes are **100-1000 times more potent** than **Histamine** during **allergic reactions**

SRS-A are released during **Allergic reactions/Anaphylaxis**.

3-LTB₄ is a potent **chemotactic agent**.

(chemical substance which mediates movement of cells).

4-Leukotrienes by action are:

Bronchoconstrictors

Vasoconstrictors -

**Levels Of Leukotrienes Increased In:
Allergies**

Allergic rhinitis

Asthma

Overproduction: **Anaphylactic shocks**.

LIPOXINS

- **Lipoxins** are Eicosanoids produced in Leukocytes of human body.

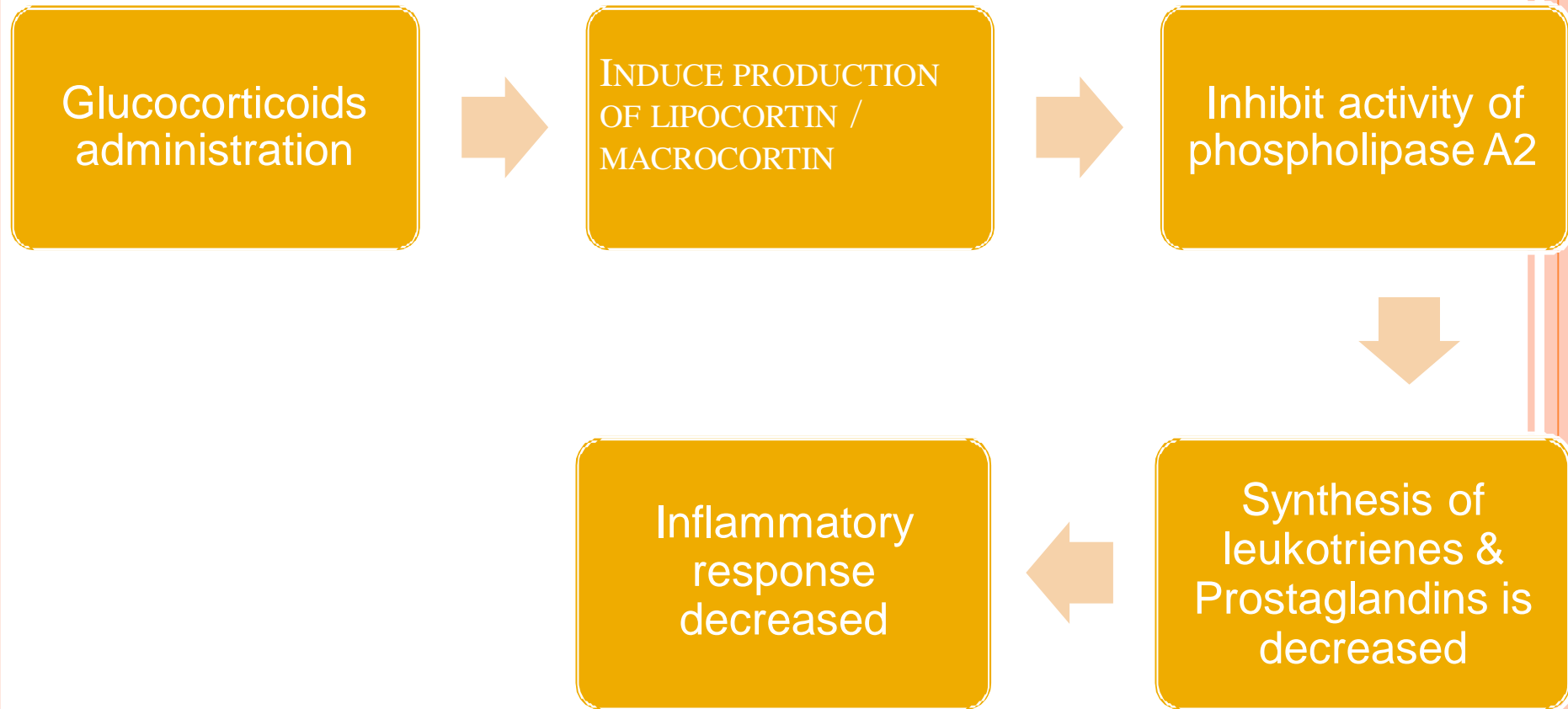
Lipoxins are essential in **maintaining tissue homeostasis and resolve inflammation.**

- **Lipoxins are:**

- Vasoactive/Vasodilators
- Anti-inflammatory
- Anti-proliferative
- Pro-resolving
- Immunoregulatory
- Chemotactic substances



ROLE OF DRUGS



Pharmacological applications of Eicosanoids

1. Cardiovascular use- pulmonary arterial hypertension, peripheral vascular disease. for keeping the ductus arteriosus open until surgery in neonates carrying certain cardiac malformations and platelet anti-aggregating agents.
2. Digestive Uses- indicated in the treatment of gastro duodenal ulcer and for the prevention of NSAID-induced ulcers.
3. Gynecological and obstetrical uses - They induce cervical dilatation and uterine contractions, particularly in late pregnancy. Used for medical termination of pregnancy and induction of labour.



Pharmacological applications of Eicosanoids

4. Ophthalmologic Use- lower intraocular pressure.
5. Anti- inflammatory use-Inhibitors of cyclo-oxygenases have anti-inflammatory properties and include nonsteroidal anti-inflammatory drugs or NSAID. The useful effects in therapeutics are-

anti-inflammatory effect

analgesic effect

antipyretic effect

inhibition of platelet aggregation and decrease of

thromboembolic risk (well-known with aspirin at low doses)



THANK YOU