1st Year MBBS

CVS Module
Lecture on Eicosanoids
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بسم الله الرحمن الرحيم

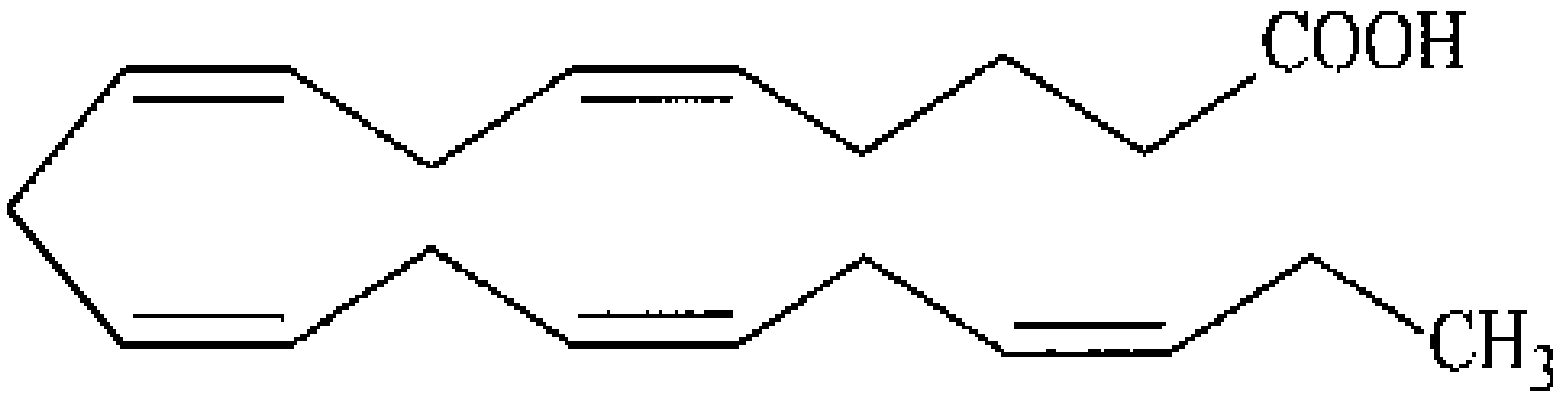
EICOSANOIDS

LEARNING OBJECTIVES

- To understand
- Eicosanoids
- Functions of Eicosanoids
- Classification
- Prostaglandins/Prostacyclins & their functions
- Leukotrienes & their functions
- Lipoxins & functions

Eicosanoids:

- These are derived from eicosapolyenoic FA.
- Eicosanoids are derived from either omega-3 (ω-3) or omega-6 (ω-6) EFAs. The ω-6 eicosanoids are generally pro-inflammatory; ω-3s are much less so.



EPA (5,8,11,14,17-Eicosapentaenoic Acid)

- Eicosanoids are signaling molecules made by oxidation of twenty-carbon essential fatty acids, (EFAs). They exert complex control over many bodily systems, mainly in inflammation or immunity, Eicosanoids function in these diverse physiological systems and pathological processes by mounting or inhibiting inflammation, allergy, fever and other immune responses

- Other important functions include……
- contributing to the perception of pain
- regulating cell growth
- controlling blood pressure
- and modulating the regional flow of blood to tissues.
- regulating the abortion of pregnancy and normal childbirth
- and as messengers in the central nervous system.

- The networks of controls that depend upon eicosanoids are among the most complex in the human body.

CLASSIFICATION

- They are classified mainly into TWO groups:

- PROSTANOIDS (PGs)
- LEUKTRIENES (LT's) & LIPOXINS (Lxs)

Eicosapolyenoic FA

Prostanoids

- Prostaglandins (PGs)
- Prostacyclins (PGI)
- Thromboxanes (Tx)

- Leukotrienes LTs
- Lipoxins LXs

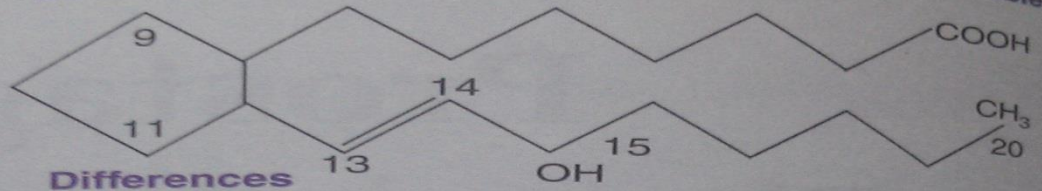
- According to structures the PGs can further be classified into FOUR main groups:
- (a) PG-E group: PGE-1,PGE-2,PGE-3
- (b) PG-F group: PGF 1^{α}, PGF 2^{α}, PGF 3^{α}
- (c) PG-A group: PG-A1, PG-A2, 19-OH PG-A1,19-OH PG-A2
- (d) PG-B group: PG-B1, PG-B2, 19-OH PG-B1 19-OH PG-B2

CHARACTERISTIC FEATURES OF STRUCTURES

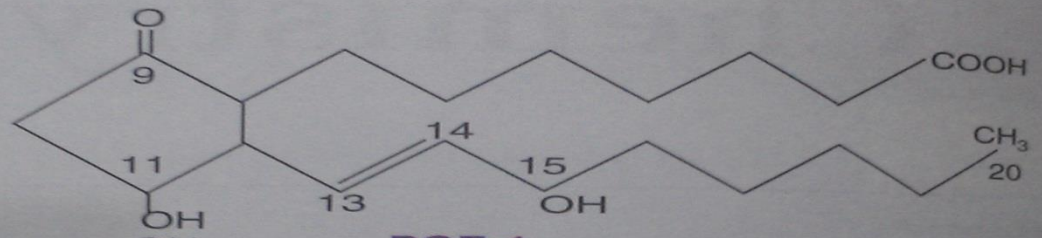
- All naturally occurring PGs are 20C fatty acids contain a cyclopentane ring
- -OH group at 15 position
- Trans double bond at 13 position
- Difference in the four main groups is due to difference in structure of cyclopentane ring.

A. **Similarities**

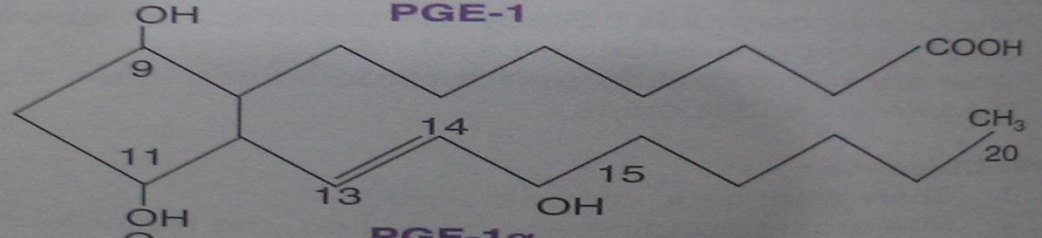
All have one-OH group at 15 and a "trans" double bond at 13



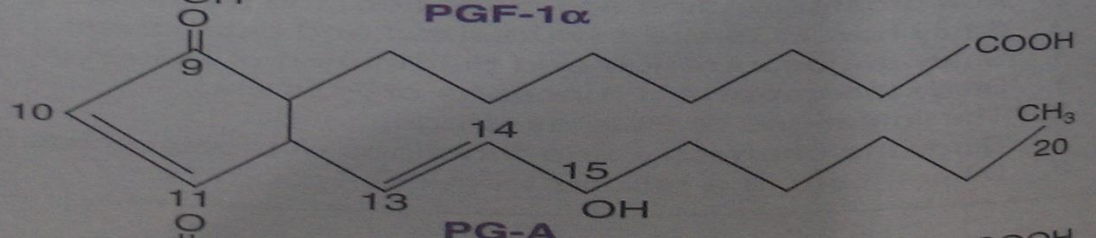
B. **Differences**



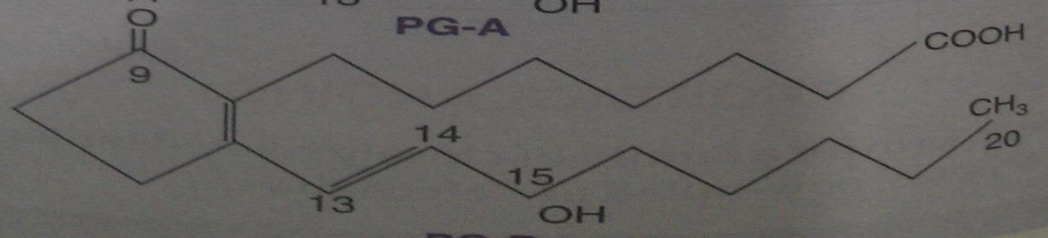
PGE-1



PGF-1α



PG-A



PG-B

FIG. 5.3: SHOWING THE STRUCTURAL SIMILARITIES AND DIFFERENCES OF PGS

Release: A...

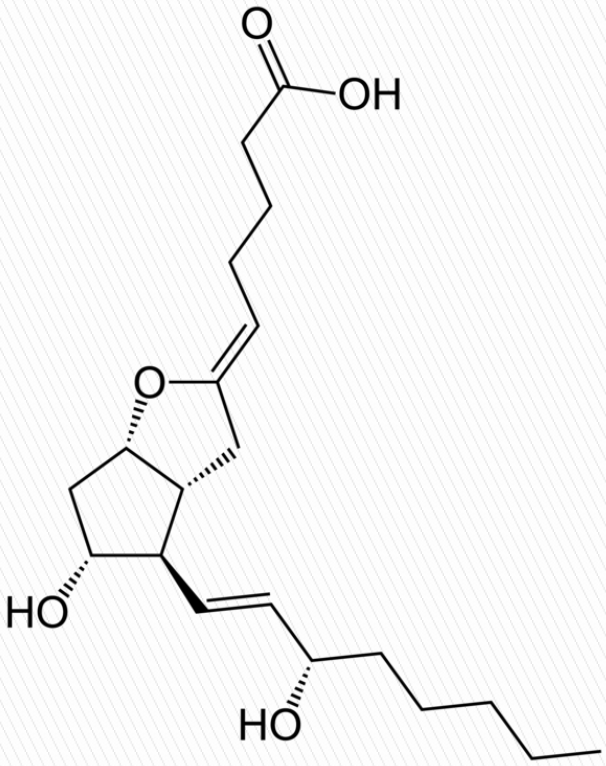
FUNCTIONS OF PROSTAGLANDINS

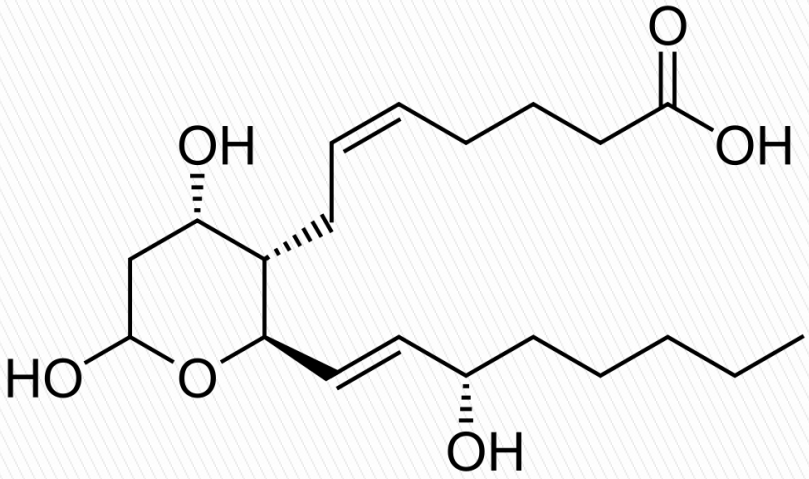
- Antihypetensive : lowers BP
- Inhibits platelets aggregation
- Inhibits gastric secretion
- Stimulates GI musculature (purgative action)
- Bronchodilation,used in treatment of bronchial asthma
- Increase uterine contraction,can be used as abortifacient
- Renal action:increases Renal plasma flow {RPF},increase in GFR,diuresis,natriuresis,kaliuresis

- Stimulates renin secretion from JG cells
- Metabolic effects:
- Decreases lipolysis
- Insulin like effect
- PTH like effect:produces hypercalcemia
- TSH like effect
- Steroidogenesis
- Luteolysis:(also known as luteal regression) is the structural and functional degradation of the corpus luteum (CL), which occurs at the end of the luteal phase of menstrual cycle in the absence of pregnancy.

CHEMISTRY AND FUNTIONS OF PROSTACYCLINS & THROMBOXANES

- Structure:cyclopentane ring
- Oxane ring





PROSTACYCLINS

THROMBOXANES

- Formed in vascular endothelium,heart & kidneys
- Inhibits platelet aggregation
- Produces vasodilatation
- These 2 features prevent thrombus formation

PROSTACYCLINS

- Formed in platelets,neutrophils,lungs,brain,kidney & spleen
- Enhance platelet aggregation
- Produces vasoconstriction
- These 2 features favors thrombus fromation

THROMBOXANES

Clinical aspects of Prostacyclins

- 1) Asprin as effective anti-platelet aggregator:
- Asprin—acetyl salicylic acid is the most effective drug which prevents platelet aggregation
- CLINICAL USES:
- Treatment and Management of angina and evolving Mycocardial Infarction
- Prevention of stroke and death in patients with transient ischeamic attacks

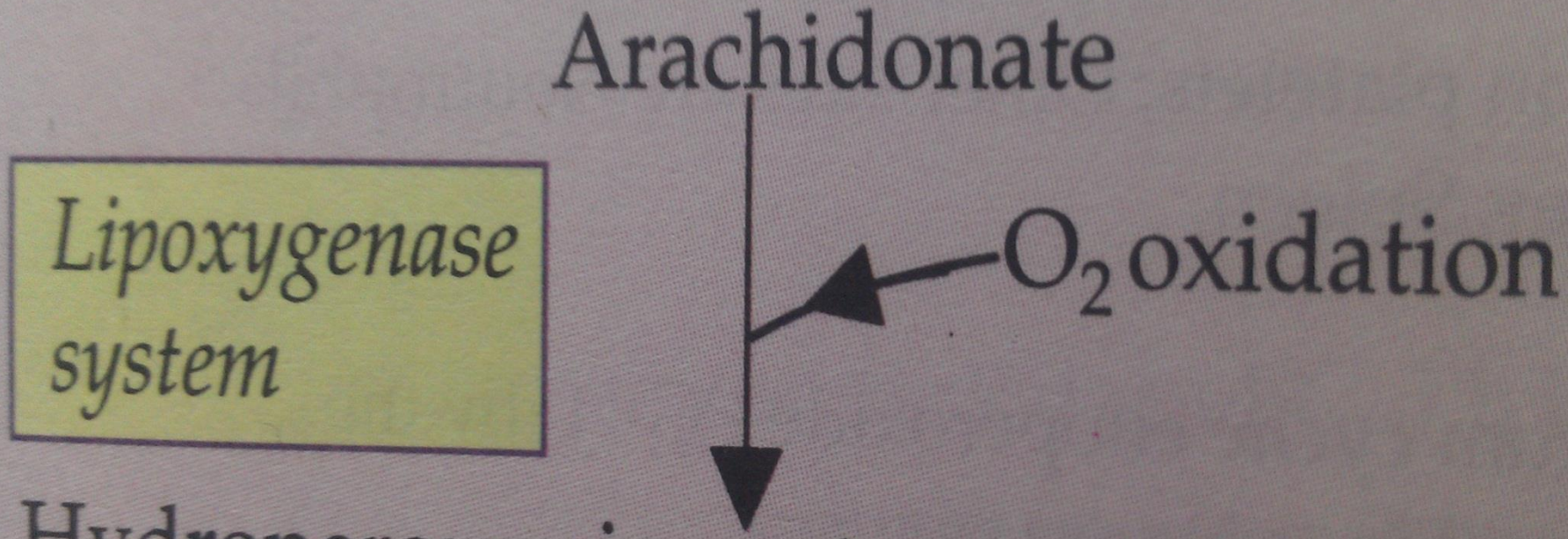
- 2) Role of MARINE FISH LIPIDS:
- Most predominant UFA in fish food is eicosapentanoic acid,which
- Decreases plasma cholesterol
- Decreases triacylglycerol
- Inhibits synthesis of thromboxane--------low levels of thromboxane-------reduced platelet aggregation-----reducing thrombus formation---------lowering risk of MYOCARDIAL INFARCTION.

LEUKOTRIENES

- THESE are formed from eicosanoic acids in leukocytes ,mast cells and macrophages by the lipo-oxygenase pathway,in response to both immunologic and non-immunological stimuli.
- LTs are synthesized by addition of hydroperoxy groups to arachidonic acid and produces hydroperoxy eicosa-tetraenoates (HPETE)

ent types of HPETE. Depending on the p

on, *three types* of HPETE have been fou



types of HPETE are:

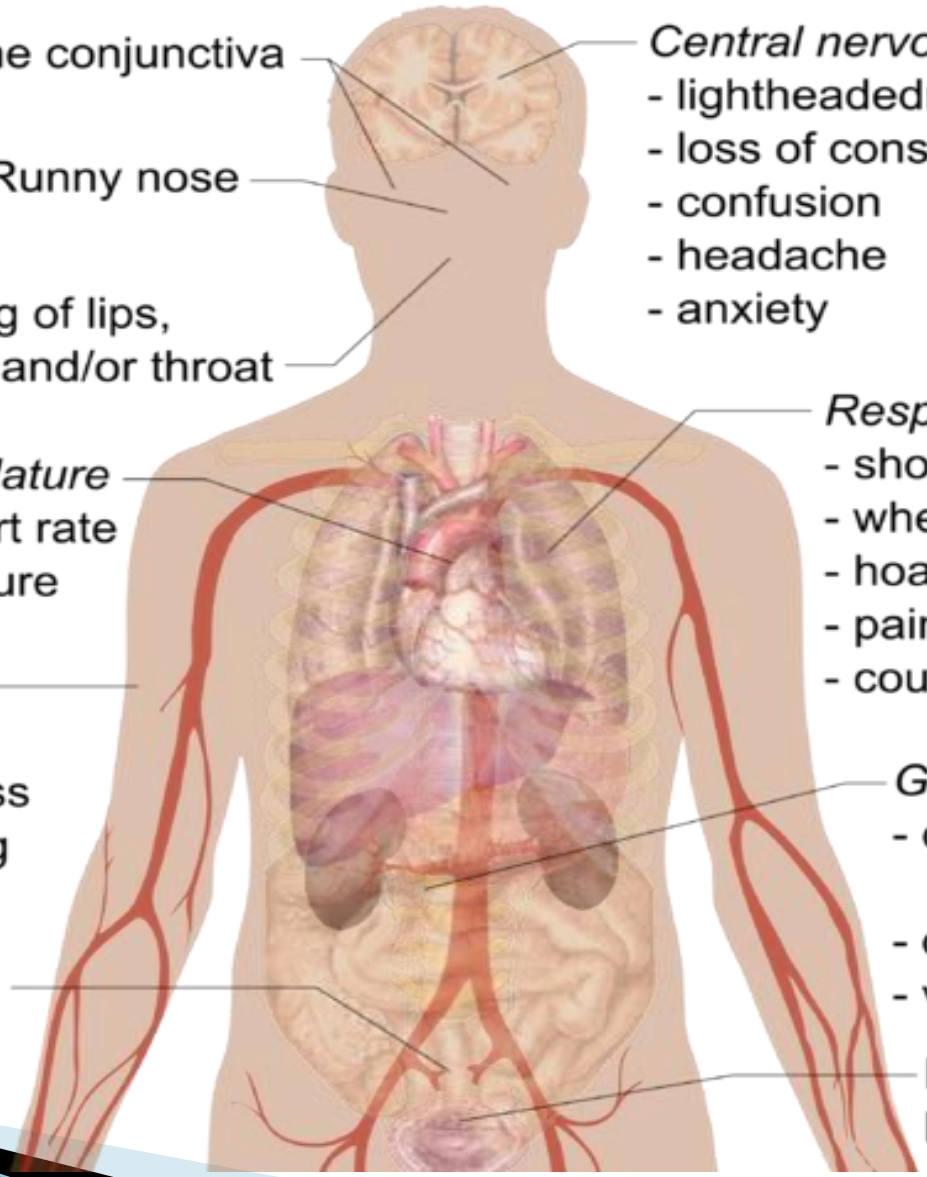
HPETE: Most

FUNCTIONS OF LTs

- Mediators in inflammation and anaphylaxis
- Capillary dilatation and vascular permeability
- Causes bronchospasm
- Increases mucous secretion
- Stimulates chemotaxis of neutrophils and eiosinophils at the site of inflammation

Signs and symptoms of

Anaphylaxis



Swelling of the conjunctiva

Runny nose

Swelling of lips, tongue and/or throat

Central nervous system
- lightheadedness
- loss of consciousness
- confusion
- headache
- anxiety

Respiratory
- shortness of breath
- wheezes or stridor
- hoarseness
- pain with swallowing
- cough

Heart and vasculature
- fast or slow heart rate
- low blood pressure

Skin
- hives
- itchiness
- flushing

Gastrointestinal
- crampy abdominal pain
- diarrhea
- vomiting

Pelvic pain

Loss of bladder control

LIPOXINS

- LIPOXINS arise in leukocytes by lipooxygenase pathway
- Lipoxins are derived enzymatically from arachidonic acid,
- Has immunoregulatory effect.

- The **lipoxins** are believed to **function** as anti-inflammatory agent and promoting resolution of inflammation by reducing excessive tissue injury and chronic inflammation.
- They control the entry of neutrophils to sites of inflammation and the affected organs.
- They are chemo-attractants for monocytes, i.e. cells that are required for wound healing.

THE END