

# BCH 202 (CHEMISTRY OF LIPIDS cont'd)

## EICOSANOIDS

- **Prostaglandins** and the related compounds **thromboxanes** and **leukotriens**, are collectively known as **eicosanoids**.
- Eicosanoids are synthesized from **arachidonic acid**. A polyunsaturated fatty acid containing 20-carbon atoms from which they take their general name (Greek: eikosi means twenty).

### Prostaglandins

- Prostaglandins are a group of 20-carbon compounds derived from **arachidonic acid** (Figure 1).
- They derive their name from the tissue in which they were first recognized (the prostate gland) but they are now known to be present in almost all tissues.
- Chemically, the prostaglandins are derivatives of the hypothetical parent compound **prostanoic acid**, having cyclopentane (5 carbon) ring and two aliphatic side chains  $R_1$  and  $R_2$  (Figure 1).
- Prostanoic acid does not occur naturally but is regarded as the parent compound of the prostaglandins and thromboxanes for the purpose of classification and carbon numbering.
- In addition to cyclopentane ring, each of the biologically active prostaglandin has a hydroxyl group at carbon 15, a double bond between carbons 13 and 14, and various substituents on the ring.

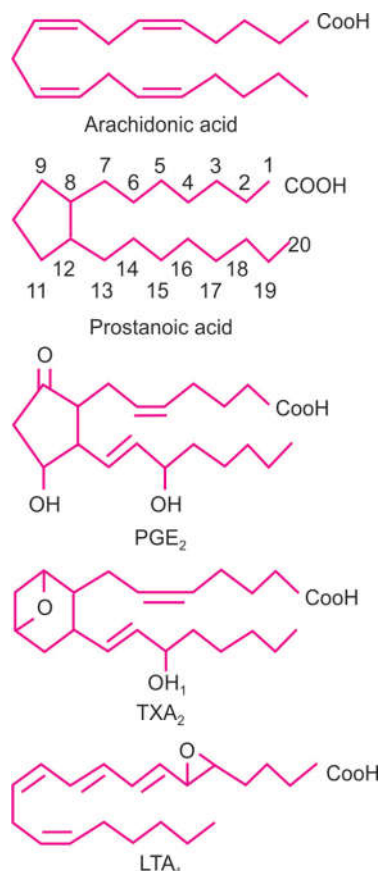
### Classification of prostaglandins

- By convention, prostaglandins are abbreviated as PG.
- They are classified into groups designated by a capital letter (A, B, C, D, E, F, G, H and I) depending on the substituents on the cyclopentane ring.
- These are subclassified by a subscript number 1, 2, or 3 corresponding to the number of double bonds in the side chains but not in the cyclopentane ring.
- Sixteen naturally occurring prostaglandins have been described but only seven are found commonly throughout the body. These are  $\text{PGE}_1$ ,  $\text{PGE}_2$ ,  $\text{PGF}_1\alpha$ ,  $\text{PGF}_2\alpha$ ,  $\text{PGG}_2$ ,  $\text{PGH}_2$ ,  $\text{PGI}_2$ .
- Prostaglandins are not stored, instead the precursor  $\text{C}_{20}$  arachidonic acids are stored in tissues.

### Functions of prostaglandins

- Prostaglandins and other eicosanoids have hormone like actions.
- Prostaglandins in many tissues act by regulating the synthesis of cyclic AMP (cAMP). As cAMP mediates the action of many hormones, the prostaglandins affect a wide range of cellular and tissue functions. Some of these are:
  - **Smooth muscle contraction and relaxation:** For example, in pregnancy  $\text{PGF}_{2\alpha}$  are produced in response to oxytocin and act to promote uterine contraction. Because of this effect, they have been used to terminate unwanted pregnancies.  $\text{PGE}_2$  are involved in relaxation of bronchial smooth muscle.

- **Inflammatory response:** PGs are involved in inflammatory response causing pain, edema, swelling and prolonged erythema (abnormal flushing of skin) by increasing capillary permeability.
- **Platelet aggregation:** Prostaglandins have an effect on platelet aggregation.  $\text{PGE}_2$  promote aggregation and are thus, involved in the blood clotting.
- **Regulation of Blood pressure:**  $\text{PGE}_2$  decrease blood pressure. It can lower systemic arterial pressure through their vasodilator effect.
- **Body temperature:** Prostaglandins elevate body temperature producing fever and cause inflammation, resulting in pain.
- **Gastric secretion:**  $\text{PGE}_2$  suppress gastric secretion.
- PGs are involved in  $\text{Na}^+$  and *water retention* by kidney tubules.



**Figure 1:** The structure of arachidonic acid, prostanoic acid, common prostaglandin ( $\text{PGE}_2$ ), thromboxane ( $\text{TXA}_2$ ) and leukotrienes ( $\text{LTA}_4$ )

## Thromboxanes

Thromboxanes were first isolated from blood platelets, thrombocytes—hence the name. They have six membered oxane ring (**Figure 1**) that includes an oxygen atom.

### Nomenclature of thromboxanes

- Thromboxanes are abbreviated as TX. Different capital letters are used to designate different substituents of the ring (like prostaglandins).
- A subscript, if present, denotes the number of unsaturated bonds (double bonds), e.g. the most common thromboxane TXA<sub>2</sub> having two double bonds.

### Functions of thromboxanes

- TXA<sub>2</sub> is produced by platelets, promotes platelets aggregation. Platelet aggregation initiates thrombus formation at sites of vascular injury.
- TXA<sub>2</sub> causes contractions of the smooth muscles of the arterial wall and therefore, raises blood pressure.

## Leukotrienes (LT)

Leukotrienes were so named because they were initially described in leucocytes and are characterized by a conjugated **triene** system but no such ring structure that is found in prostaglandins and thromboxanes.

### Nomenclature of leukotrienes

- All leukotrienes are abbreviated as LT.
- These are grouped into five classes (A to E) based on the type of substituents attached to the parent compound.
- The LTs found in humans have a subscript four to denote that they contain four double bonds (**Figure 1**).

### Functions of leukotrienes

- The LTs facilitate chemotaxis, inflammation and allergic reactions.
- LTC<sub>4</sub>, LTD<sub>4</sub> induce contraction of muscle of the lung and constrict pulmonary airways. Overproduction of LT causes asthmatic attacks.
- LTD<sub>4</sub> has been identified as the *slow reacting substance of anaphylaxis (SRS-A)* which causes smooth muscle contraction.
- LTB<sub>4</sub> attracts neutrophils and eosinophils to sites of inflammation.