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Prostaglandins

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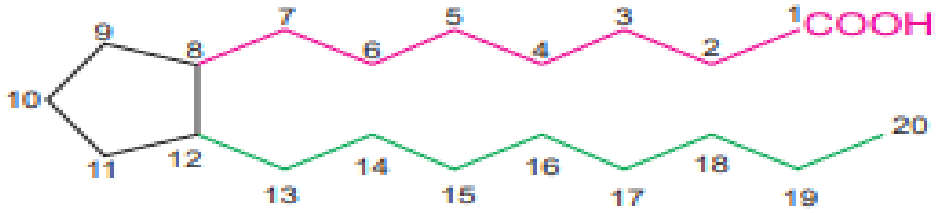
Prostaglandins

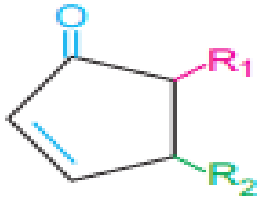
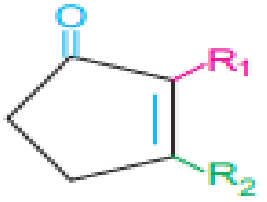
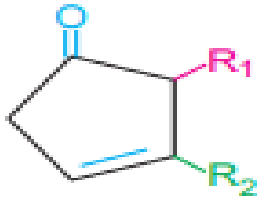
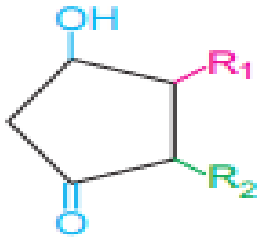
prostaglandins and their related compounds prostacyclins (PGI), thromboxanes (TXA), leukotrienes (LT) and lipoxins are collectively known as **eicosanoids**.

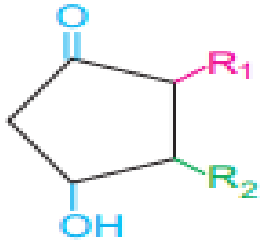
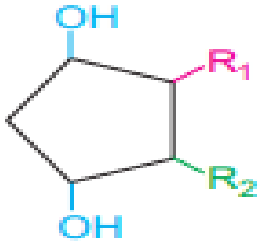
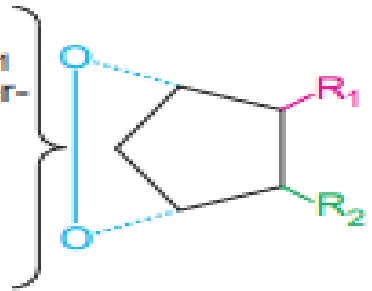
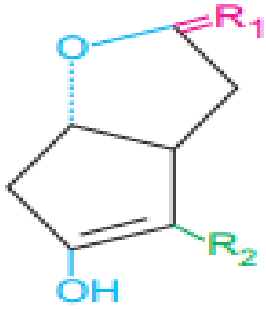
Structure of prostaglandins :- Prostaglandins are derivatives of a hypothetical 20-carbon fatty acid namely **prostanoic acid**, hence known as **prostanoids**.

This has a cyclopentane ring (formed by carbon atoms 8 to 12) and two side chains, with carboxyl group on one side. Prostaglandins differ in their structure due to substituent group and double bond on cyclopentane ring. The structures of the most important prostaglandins (PGF2 and PGF2D), prostacyclins (PGI2), thromboxanes (TXA2) and leukotrienes (LTA4) along with arachidonic acid .



Prostanoic acid

Prostaglandin	Substituent group	Structure
PGA	Double bond $C_{10} - C_{11}$ Keto group C_9	
PGB	Double bond $C_8 - C_{12}$ Keto group C_9	
PGC	Double bond $C_{11} - C_{12}$ Keto group C_9	
PGD	—OH group at C_9 Keto group at C_{11}	

Prostaglandin	Substituent group	Structure
PGE	Keto group at C_9 —OH group at C_{11}	
PGF	—OH group at C_9 and at C_{11}	
PGG	Two oxygen atoms present at C_9 and C_{11} are bonded; hydroperoxide group at C_{15}	
PGH	Ring the same as in PGG; —OH group at C_{15}	
PGI	Attachment of oxygen between C_6 and C_9 forming another 5-carbon ring	

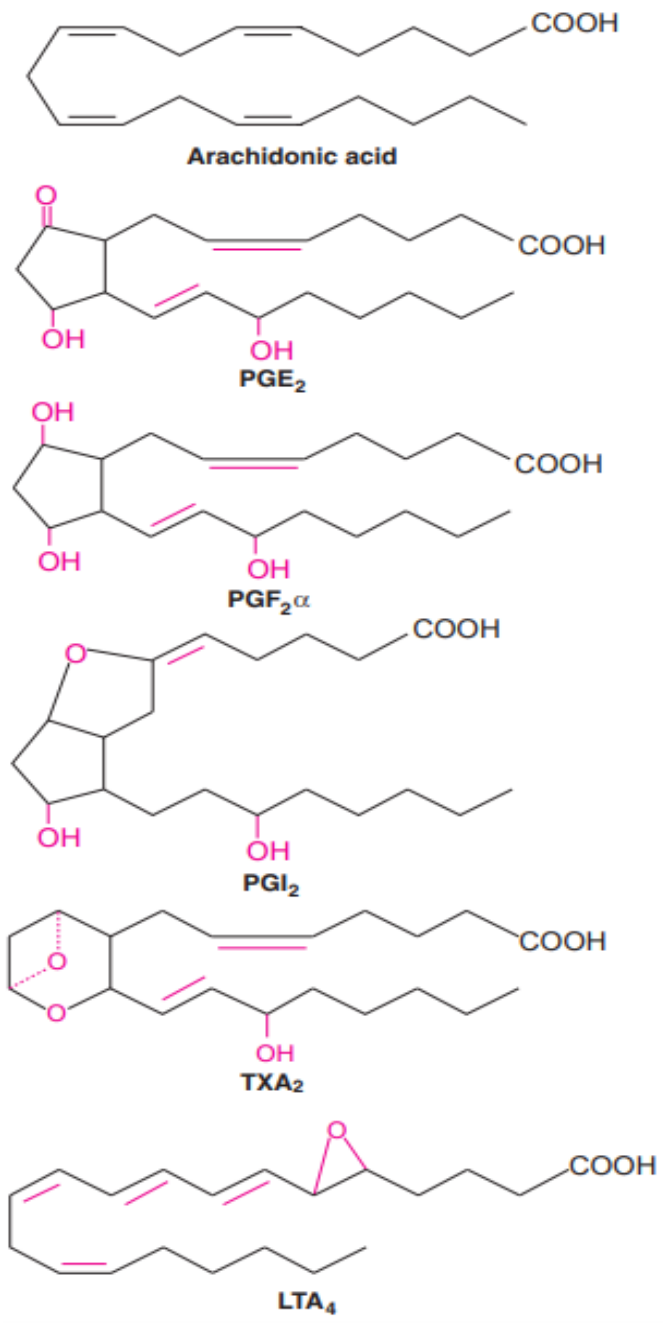
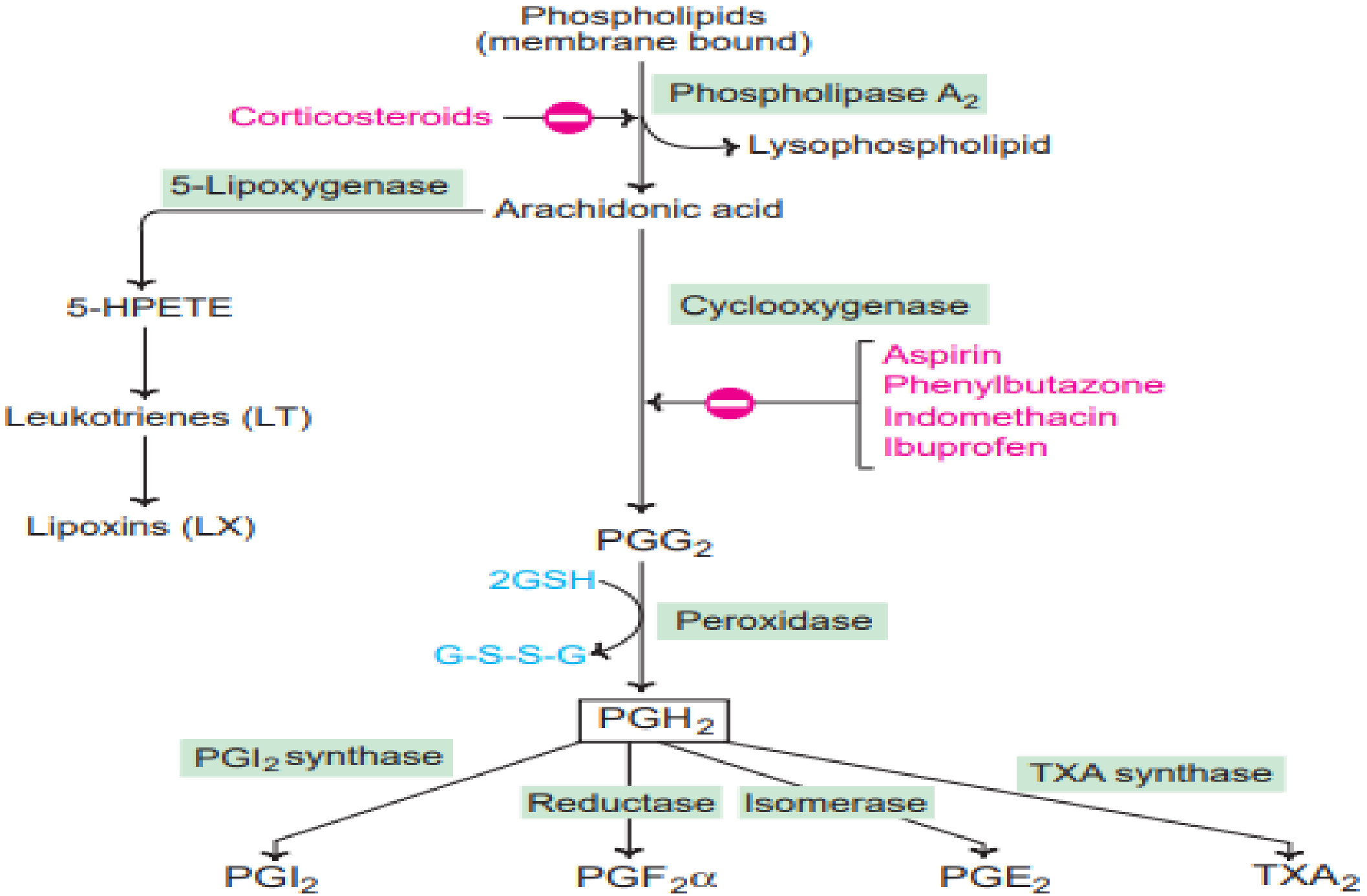


Fig. 32.2 : *The structures of arachidonic acid, common prostaglandins (PGE_2 and $PGF_2\alpha$), prostacyclins (PGI_2), thromboxanes (TXA_2) and leukotrienes (LTA_4).*

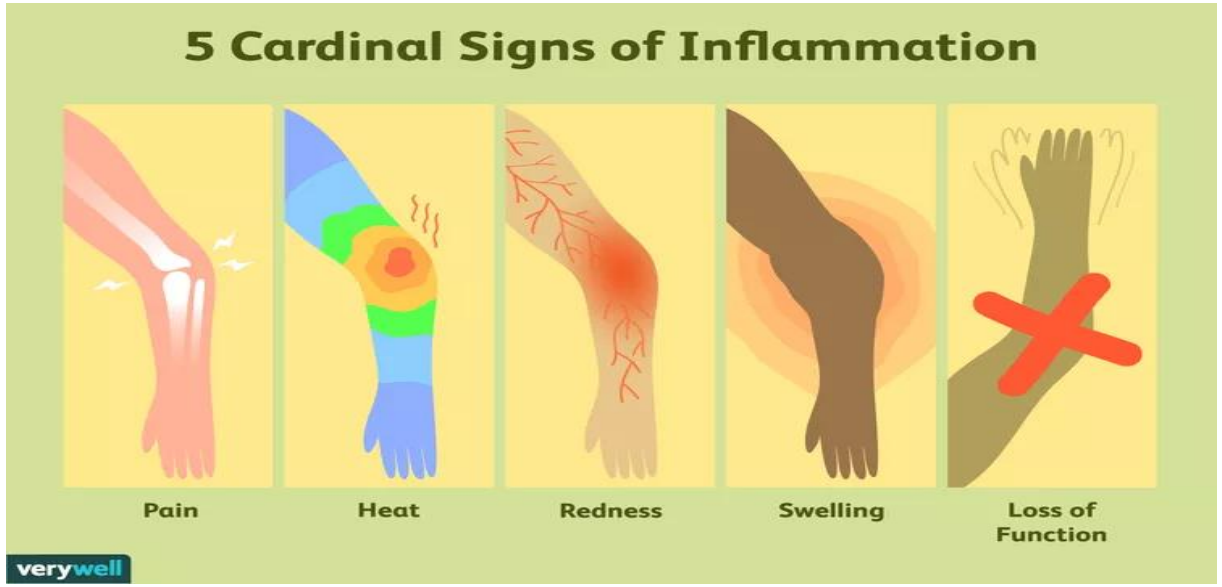

Phospholipids
(membrane bound)
Phospholipase A2
Corticosteroids
Lysophospholipid
5-Lipoxygenase
Arachidonic acid
5-HPETE
Cyclooxygenase
Aspirin
Phenylbutazone
Indomethacin
Ibuprofen
Leukotrienes (LT)
Lipoxins (LX)
PGG2
2GSH
Peroxidase
G-S-S-G
PGH2
PGI2 synthase
TXA synthase
Reductase
Isomerase
PGI2
PGF2α
PGE2
TXA2

Prostaglandins functions

Prostaglandins act as local hormones and are involved in a wide range of biochemical functions. In general, PGs are involved in the

- ✓ lowering of blood pressure
- ✓ induction of inflammation
- ✓ medical termination of pregnancy
- ✓ induction of labor
- ✓ inhibition of gastric HCI secretion
- ✓ decrease in immunological response
- ✓ increase in glomerular filtration rate
- ✓ Thromboxanes (TXA2) and prostaglandin E1 promote while prostacyclins (PGI2) inhibit platelet aggregation.

1. **Regulation of blood pressure :** The prostaglandins (PGE, PGA and PGI2) are vasodilator in function. This results in increased blood flow and decreased peripheral resistance to lower the blood pressure. PGs serve as agents in the treatment of hypertension.
2. **Inflammation :** The prostaglandins PGE1 and PGE2 induce the symptoms of inflammation (redness, swelling, edema etc.) due to arteriolar vasodilation. This led to the belief that PGs are natural mediators of inflammatory reactions of rheumatoid arthritis (involving joints), psoriasis (skin), conjunctivitis (eyes) etc. Corticosteroids are frequently used to treat these inflammatory reactions, since they inhibit prostaglandin synthesis.


5 Cardinal Signs of Inflammation
Pain
Heat
Redness
Swelling
Loss of Function
verywell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Rheumatoid Arthritis
Symptoms and Physiotherapy Treatments
WWW.PHYSIOTATTVA.COM


psoriasis

3. Reproduction : PGE2 and PGF2 are used for the medical termination of pregnancy and induction of labor. Prostaglandins are administered to cattle to induce estrus and achieve better rate of fertilization.

4. Pain and fever : It is believed that pyrogens (fever producing agents) promote prostaglandin biosynthesis leading to the formation of PGE2 in the hypothalamus, the site of regulation of body temperature. PGE2 along with histamine and bradykinin cause pain. Aspirin and other non-steroidal drugs inhibit PG synthesis and thus control fever and relieve pain.

5. Regulation of gastric secretion : In general, prostaglandins (PGE) inhibit gastric secretion. PGs are used for the treatment of gastric ulcers. However, PGs stimulate pancreatic secretion and increase the motility of intestine which often causes diarrhea.

6. Influence on immune system : Macrophages secrete PGE which decreases the immunological functions of B-and T-lymphocytes.

7. Effects on respiratory function : PGE is a bronchodilator whereas PGF acts as a constrictor of bronchial smooth muscles. Thus, PGE and PGF oppose the actions of each other in the lungs. PGE1 and PGE2 are used in the treatment of asthma.

8. Influence on renal functions : PGE increases glomerular filtration rate (GFR) and promotes urine output. Excretion of Na+ and K+ is also increased by PGE.

9. Effects on metabolism : Prostaglandins influence certain metabolic reactions, probably through the mediation of cAMP. PGE decreases lipolysis, increases glycogen formation and promotes calcium mobilization from the bone.

10. Platelet aggregation and thrombosis : The prostaglandins, namely prostacyclins (PGI2), inhibit platelet aggregation. On the other hand, thromboxanes (TXA2) and prostaglandin E2 promote platelet aggregation and blood clotting that might lead to thrombosis. PGI2, produced by endothelial cells lining the blood vessels, prevents the adherence of platelets to the blood vessels. TXA2 is released by the platelets and is responsible for their spontaneous aggregation. Thus, prostacyclins and thromboxanes are antagonists in their action. In the overall effect PGI2 acts as a vasodilator, while TXA2 is a vasoconstrictor. The balance between PGI2 and TXA2 is important in the regulation of hemostasis and thrombosis. PGE increases cAMP levels whereas PGF elevates cGMP.

Dr. Sagar Dhanraj