

RHEUMARENE & Prostaglandins

Rheumarene is a non-steroidal anti inflammatory preparation with analgesic and antipyretic properties. It acts by inhibition of prostaglandin synthesis. Rheumarene combats inflammation, relieve pain, tenderness and oedema.

What is prostaglandin?

Prostaglandins were first discovered and isolated from human semen in the 1930s by Ulf von Euler of Sweden. Thinking they had come from the prostate gland, he named them prostaglandins. It has since been determined that they exist and are synthesized in virtually every cell of the body.

Prostaglandins, are like hormones in that they act as chemical messengers, but do not move to other sites, but work right within the cells where they are synthesized.

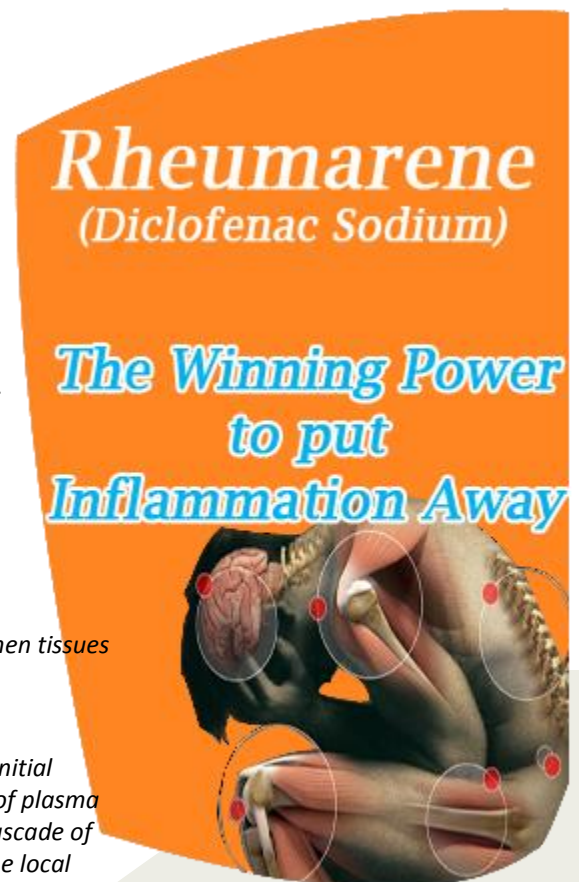
Prostaglandins are unsaturated carboxylic acids, consisting of a 20 carbon skeleton that also contains a five member ring. They are biochemically synthesized from the fatty acid, arachidonic acid. See the graphic on the left.

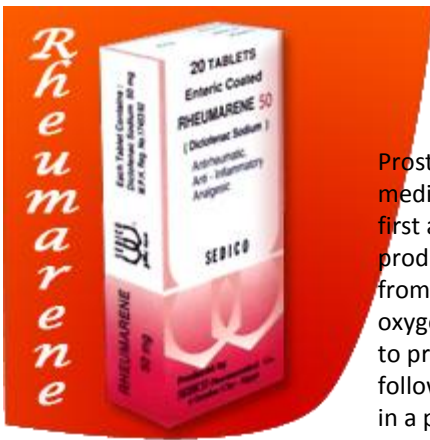
In 1971, it was determined that aspirin-like drugs could inhibit the synthesis of prostaglandins. The biochemists Sune K. Bergström, Bengt I. Samuelsson and John R. Vane jointly received the 1982 Nobel Prize in Physiology or Medicine for their research on prostaglandins.

What is an Inflammation?

Prostaglandin activate the inflammatory response, production of pain, and fever. When tissues are damaged, white blood cells flood to the site to try to minimize tissue destruction. Prostaglandins are produced as a result.

Inflammation can be classified as either acute or chronic. Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes (especially granulocytes) from the blood into the injured tissues. A cascade of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system, and various cells within the injured tissue. Prolonged inflammation, known as chronic inflammation, leads to a progressive shift in the type of cells present at the site of inflammation and is characterized by simultaneous destruction and healing of the tissue from the inflammatory process.





Prostaglandins and NSAIDs

Prostaglandins are potent mediators of inflammation. The first and committed step in the production of prostaglandins from arachidonic acid is the bis-oxygenation of arachidonate to prostaglandin PGG₂. This is followed by reduction to PGH₂ in a peroxidase reaction. Both these reactions are catalyzed by cyclooxygenase, also known as PGH synthase.

Cyclooxygenase (COX) is inhibited by the family of drugs known as non-steroidal anti-inflammatory drugs or NSAIDs.

Aspirin, ibuprofen, flurbiprofen and acetaminophen (trade name Tylenol) are all NSAIDs.

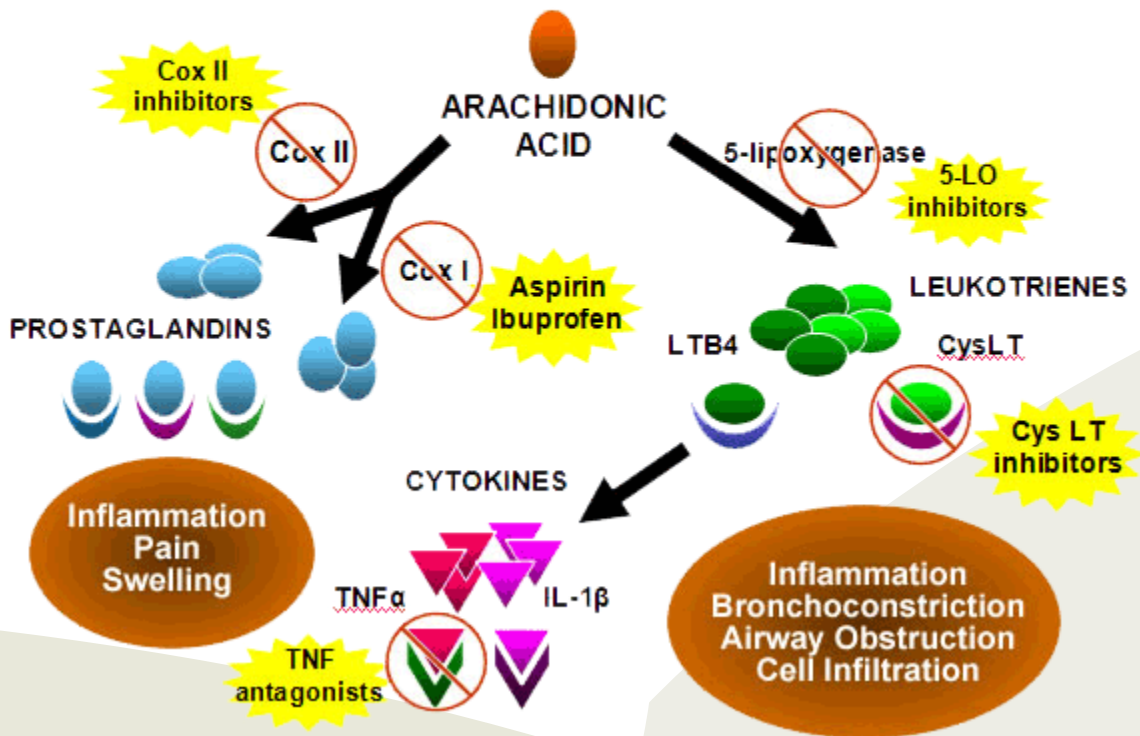
When you see that prostaglandins induce inflammation, pain, and fever, what comes to mind but aspirin. NSAIDs blocks an enzyme called cyclooxygenase, COX-1 and COX-2, which is involved with the ring closure and addition of oxygen to arachidonic acid converting to prostaglandins. This has the effect of blocking the channel in the enzyme and arachidonic can not enter the active site of the enzyme.

By inhibiting or blocking this enzyme, the synthesis of prostaglandins is blocked, which in turn relieves some of the effects of pain and fever.

Aspirin is also thought to inhibit the prostaglandin synthesis involved with unwanted blood clotting in coronary heart disease. At the same time an injury while taking aspirin may cause more extensive bleeding.

How NSAIDs Blocks the inflammation process?

Arachidonic acid is metabolized to produce inflammatory mediators. Many current anti-inflammatory and pain medicines are inhibit some portion of the arachidonic acid pathways.



What are the types & the functions of Prostaglandins?

The following is a comparison of different types of prostaglandin, prostaglandin I₂ (PGI₂), prostaglandin E₂ (PGE₂), and prostaglandin F_{2α} (PGF_{2α}).

Type	Receptor	Function
Thromboxane	TP	<ul style="list-style-type: none"> • Blood clots form when a blood vessel is damaged since thromboxane stimulates constriction and clotting of platelets.
PGI₂	IP	<ul style="list-style-type: none"> • Vasodilation • Inhibit platelet aggregation • Bronchodilatation
PGE₂	EP1	<ul style="list-style-type: none"> • Bronchoconstriction • GI tract smooth muscle contraction
	EP2	<ul style="list-style-type: none"> • Bronchodilatation • GI tract smooth muscle relaxation • Vasodilatation
	EP3	<ul style="list-style-type: none"> • ↓ gastric acid secretion • ↑ gastric mucus secretion • Uterus contraction (when pregnant) and has been used to induce labor • GI tract smooth muscle contraction • lipolysis inhibition • ↑ autonomic neurotransmitters • ↑ platelet response to their agonists and ↑ atherothrombosis in vivo
	Unspecified	<ul style="list-style-type: none"> • Hyperalgesia • Pyrogenic
PGF_{2α}	FP	<ul style="list-style-type: none"> • Uterus contraction • Bronchoconstriction

Rheumarene (Diclofenac Sodium)

Rheumarene is rapidly & almost completely absorbed. Peak plasma concentration is attained after 2-3 hours & significant concentration in the synovial fluid within 2-4 hours. The drug is 99% to plasma protein. Given parent rally the peak blood level is twice that of the same dose administrated orally Hepatic impairment does not affect the pharmacokinetic of Rheumarene. The terminal half life time is 1-2 hours. It is excreted primarily in the form of metabolites mainly in the urine but also in the bile.

Indications:

- ▶ [Rheumatoid arthritis](#), [osteoarthritis](#), ankylosing spondylitis.
- ▶ Acute [gout](#), juvenile rheumatoid arthritis.
- ▶ Various rheumatic diseases : Bursitis, myalgia, [sciatica](#), tendinitis.
- ▶ Acute soft tissue injuries: [sprain](#), [strain](#).
- ▶ Dysmenorrhea, headache, [migraine](#).
- ▶ Postoperative & postpartum pain.
- ▶ Dental pain, renal & biliary colics.