Prostaglandins (eicosanoids) are found in almost every tissue and body fluid in a sequence of enzymatic reactions starting with cyclooxygenase (COX). Cyclooxygenases have 2 distinct activities: an endoperoxide synthase activity that forms PGG and a peroxidase activity that converts PGG to PGH. The fate of these intermediates varies in each tissue and depends on other specific synthase enzymes present and their relative abundance. Prostaglandins contribute to multiple physiological and pathological processes including inflammation, smooth muscle tone, hemostasis, thrombosis, parturition, and gastrointestinal secretion. Several classes of drug, most notably the NSAIDs, owe their therapeutic effects to blocking formation of eicosanoids and inhibiting their cellular effects by blocking COX.

- COX exists in two isoforms, COX-1 and COX-2:
  - COX-1 is constitutively expressed in most cells
  - COX-2 is induced by pro-inflammatory stimuli and shear laminar forces in endothelial, leukocytes, and plaque-associated cells

- Most currently available nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit both COX-1 and COX-2 activities to variable degrees and synthesis of prostaglandins and thromboxane

- The inhibition of COX-2 is thought to have a role in mediating the antipyretic, analgesic, and anti-inflammatory action of NSAIDs. Simultaneous inhibition of COX-1, however, results in unwanted renal side effects (e.g., fluid retention, renal insufficiency, and hypertension) and gastroenterological irritation and ulcers from the removal of cytoprotective effects.

- Selective COX-2 inhibitors (except for celecoxib (Celebrex®) have been withdrawn from market due to adverse cardiovascular effects related to an increased risk of thrombosis. To some degree, all NSAIDS share the potential for adverse cardiovascular events from COX-2 inhibition.