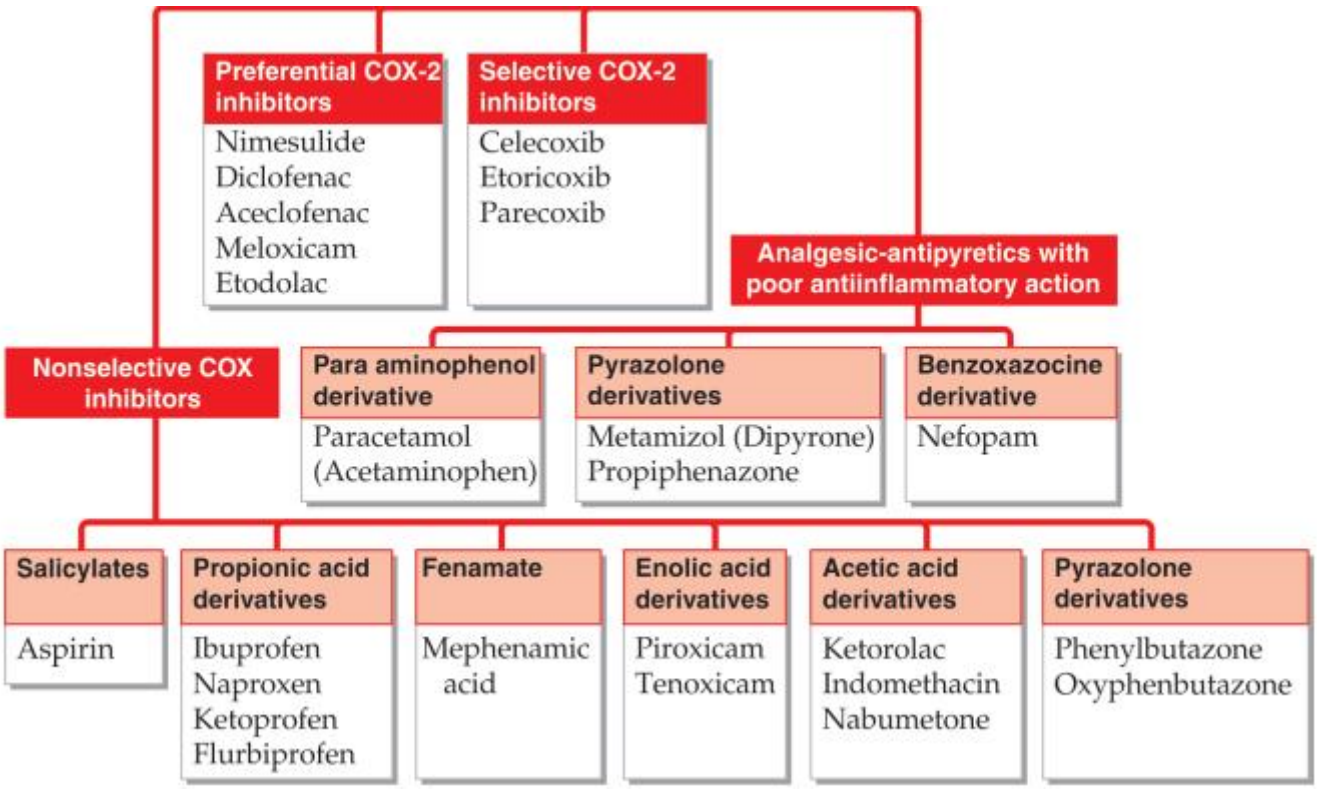
NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)

These drugs act as antipyretic, analgesic and anti-inflammatory agents, i.e. these drugs provide symptomatic relief from fever, pain and swelling in chronic joint disease such as occurs in osteo- and rheumatoid arthritis, as well as in more acute inflammatory conditions such as fractures, sprains, sports and other soft tissue injuries. They are also useful in the treatment of postoperative, dental and menstrual pain, as well as headaches and migraine. Several NSAIDs are available OTC and are widely used to treat minor aches and pains and other ailments. There are also many different NSAID formulations available, including tablets, injections and gels.

Important NSAIDs include aspirin, ibuprofen, naproxen, indometacin, piroxicam and paracetamol. Newer agents with more selective inhibition of COX-2 (and thus fewer adverse effects on the gastrointestinal tract) include celecoxib and etoricoxib.

CLASSIFICATION of NSAIDs



Source: KDT

Therapeutic effects of cyclo-oxygenase (COX) inhibitors

These drugs inhibit COX enzymes, and therefore prostanoid synthesis, in inflammatory cells. Inhibition of the COX-2 isoform is probably crucial for their therapeutic actions which include:

• An anti-inflammatory action: the decrease in PGE2 and prostacyclin reduces vasodilatation and, indirectly, oedema. Accumulation of inflammatory cells is not directly reduced.

• An analgesic effect: decreased prostaglandin generation means less sensitisation of nociceptive nerve endings to inflammatory mediators such as bradykinin and 5-HT. Relief of headache is probably a result of decreased prostaglandin-mediated vasodilatation.

• An antipyretic effect: IL1 releases prostaglandins in the CNS, where they elevate the hypothalamic set point for temperature control, thus causing fever. NSAIDs prevent this.

Salicylates

Aspirin is the only irreversible inhibitor of COX enzyme (other salicylates are reversible inhibitors).

Apart from antipyretic, analgesic and anti-inflammatory effects, aspirin has several other indications:

• At low doses (40-325 mg), it acts as an antiplatelet drug and is useful in the prophylaxis of myocardial infarction and stroke. It acts by inhibiting COX enzyme and thus decreasing the synthesis of TXA2 (platelet aggregator). It also inhibits PGI_2 (anti-aggregatory) synthesis. But net effect is to decrease TXA2 synthesis

• Aspirin is used to inhibit niacin induced flushing (it is PG mediated).

• COX-2 inhibitory action is responsible for decreased incidence of colorectal carcinoma in patients on long term aspirin therapy

General unwanted effects of COX inhibitors

Unwanted effects, many stemming from inhibition of the constitutive housekeeping enzyme COX-1 isoform, are common, particularly in the elderly, and include the following:

• Dyspepsia, nausea, vomiting and other GI effects. Gastric and intestinal damage may occur with chronic use, with risk of haemorrhage, ulceration and perforation which can be life-threatening. The cause is suppression of gastroprotective prostaglandins in the gastric mucosa.

• Adverse cardiovascular effects. These can occur with many NSAIDs and coxibs and may be related to inhibition of COX-2 in the kidney or elsewhere leading to hypertension.

• Skin reactions. Mechanism unknown.

• Reversible renal insufficiency. Seen mainly in individuals with compromised renal function when the compensatory prostaglandin I2/E2-mediated vasodilatation is inhibited.

• Bronchospasm. Seen in 'aspirin-sensitive' asthmatics. Uncommon with coxibs.

• 'Analgesic-associated nephropathy'. This can occur following long-term high-dose regimes of NSAIDs and is often irreversible.

• Liver disorders, bone marrow depression. Relatively uncommon.