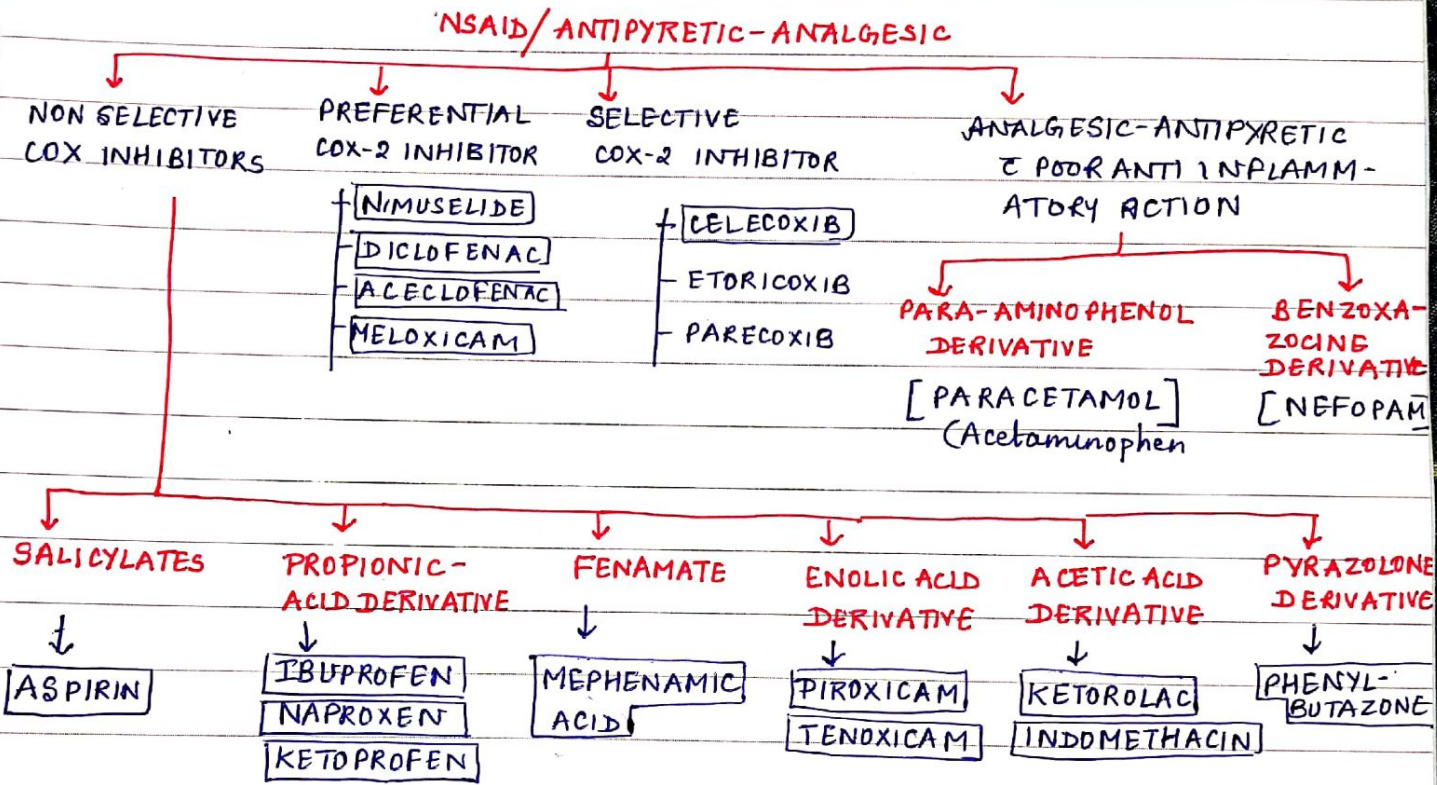


NSAID & ANTI-PYRETIC- ANALGESICS

It is a class of drug with analgesic, antipyretic & anti-inflammatory action in different measures. In contrast to morphine they do not depress CNS, do not produce physical dependence, no abuse liability & is particularly effective in inflammatory pain.

They act mainly on peripheral pain mechanism, but also in CNS to raise pain threshold.

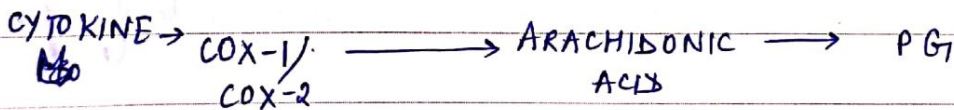


M/A → ① NSAID blocks PG_1 (prostaglandin) synthesis.

② Cytokines & other signal molecules at the site of inflammation induce COX-1 & COX-2 enzyme (inducible isoform) (housekeeping function)

③ These enzymes act on arachidonic acid to produce enzyme prostacyclin (PGI_2) & thromboxane A_2 (TXA_2).

④ This leads to generation of PG_1 s locally which mediate many inflammatory changes.



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Most NSAID inhibit COX-1 & COX-2 nonselectively, but now some selective COX-2 inhibitors have been produced.

ASPIRIN inhibits COX irreversibly, return of COX activity depends on synthesis of fresh enzyme.

Other NSAIDs are competitive & reversible inhibitors of COX, return of activity depends on their dissociation from enzyme (depending on pharmacokinetic characteristics of comp.)

USES of NSAID -

1) **Analgesia** - Blocks the pain sensing mechanism by inhibiting COX-2 primarily. It constitutes peripheral component of analgesic action. \therefore more effective against inflammation associated pain.

2) **Antipyretic** - It lowers body temp. in fever, but does not cause hypothermia in normothermic individual.

Fever during infection & tissue injury is produced thru the generation of pyrogens including ILs, TNF α , interferons etc which induce PGE₂ production in hypothalamus & raise its temp set point.

NSAID block the action of pyrogen but not that of PGE₂ injected in hypothalamus.

3) **Anti-inflammatory** \rightarrow The most important mechanism of anti-inflammatory action of NSAID is inhibition of COX-2 mediated enhanced PG synthesis at site of injury. Inhibition of COX-1 also contributes to suppression of inflammation, especially in initial stages. * (Mefenamic acid is potent anti-inflammatory but weak COX inhibitor.)

* Inflammation is result of participation of large no. of vasoactive, chemotactic & proliferative factors at different stages & these are many targets for anti-inflammatory action. Activated endothelial cells express adhesion molecules [ELAM-1, ICAM-1] on their surface & play a key role in directing circulating leucocytes to the site of inflammation (chemotaxis).