USES of NSAID –

1) **Analgesia** – Blocks the pain sensiting mechanism by inhibiting COX-2 primarily. It constitute peripheral component of analgesic action. ∴ more effective against inflamat^n associated pain.

2) **Antipyretic** – It lowers body temp. in fever, but do not cause hypothermia in normo thermic individual

Fever during infect^n & tissue injury is produced when the generat^n of pyrogens including ILs, TNFα, interferons etc which induce PGE_2 product^n in hypothalamus & raise its temp set point.

NSAIDs block the action of pyrogen bt not dat of PGE_2 injected in hypothalamus

3) **Antinflammatory** → The most imp. mechanism of antinflamatory action of NSAID is inhibition of COX-2 mediated enhanced PG_I synthesis at site of injury. Inhibition of COX-1 also contributes to supression of inflamat^n, espacially in initial stages. *(Nimuselide is potent antinflamatory bt weak COX inhibitor.)

* Inflamat^n is result of particpat^n of large no. of vasoactive, chemotactic & prolferative factors at diff. stages & there r many target for antinflamatory action. Activated endothelial cells express adhesion mol. [ELAM-1, ICAM-1] on their surface & play a key role in directing circulating leucocytes to the site of inflat^n (chemotaxis).

Similarly, inflammatory cells express selectins & integrins. Certain NSAID may act

by additional mechanism including inhibition of expression of some of these mol. & generatn of free radicals.

4) **Dysmenorrhoea** – Involvement of PGs in dysmenorrhoea has been clearly demonstrated: level of PG in menstrual flow, endometrial biopsy & $PGF_{2\alpha}$ raise in circulatn of dysmenorrhoeic women.

NSAID lowers uterine PG levels – c excellent relief in 60-70% patient. Headache, muscle ache & nausea ralso relieved along c normalising excess flow.

5) **Antiplatelet aggregatory** → Inhibits platelet aggregatn & prolong bleeding time. Aspirin is highly active as it acetylate platelet COX irreversibly (Act. thru COX-1) in the portal circulatn before getting deacetylated by first pass metabolism in liver.

Small dose of aspirin is therefor able to exert antithrombotic effect for many days. Risk of surgical & anticoagulant associated bleeding is enhanced

6) **Parturition** – Sudden PG synthesis by uterus occurs just before labour begins. It is believed to trigger labour as well as facilitates it's progression.

Also. NSAID have the potential to delay & retard labour.

7) **Gastric mucosal damage** – Inhibition of COX-1 mediated synthesis of gastroprotective PGs (PGE_2, PGI_2) is clearly involve in erosion/ulceration of gastric wall. Deficiency of PGs reduces mucus & HCO_3^- secretn, tends to increase acid secretn & may produce mucosal ischaemia

PCM is a very weak inhibitor of COX (selective COX-2 inhibitors) & is practically free of gastric toxicity & is relatively safer.

Renal – Na^+ retention & oedema can occur

Diuretic & antihypertensive drug effects r blunted