

NSAIDS

Classification

- ① Nonselective COX inhibitors →
 - ① Salicylates: Aspirin, diflunisal
 - ② Propanoic Acid derivatives: Ibuprofen, ketoprofen, niflumate
 - ③ Benzoic Acid: Naproxen Acid, ~~ibuprofenic~~ Acid
 - ④ Acetic Acid derivatives: Ketorolac, indomethacin
 - ⑤ Enolic Acid derivatives: Piroxicam, tenoxicam, benoxicam
- ② Preferential COX-2 Inhibitors: Diclofenac, meloxicam, nimesulide
- ③ Highly selective COX-2 Inhibitors: Etoricoxib, parecoxib, celecoxib
- ④ Analgesic And Antipyretics: Paracetamol, mefenam.

MECHANISM OF ACTION:

COX is responsible for biosynthesis of prostaglandins.
two isoforms of COX: COX-1 & COX-2.

— COX-1 is physiological — found in most tissue such as blood vessel, stomach, kidney.

— COX-2 is induced during inflammation by cytokines & endotoxins.

- Aspirin & most of NSAIDs inhibit both COX-1 & COX-2 thereby ↓ PGI₂ & thromboxane
- ↳ Thromboxane inhibition COX-1 activity, Rest of NSAIDs are Reversible

ASPIRIN: (Acetylsalicylic Acid)

Analgesic, Anti-inflammatory effect duration of Action

① ANALGESIC EFFECT: useful for Relieving pain associated with inflammation or tissue damage.

↳ due peripheral Inhibition of PGI₂ Production

This prevent sensitization of peripheral nerves by inflammatory mediators.

(75-150 mg/day)

3) ANTIPLATELET EFFECT: ↓ blood clots, ↓ possibility of Thrombosis, ↓ Thrombosis
↓
↓ synthesis by platelets → ↓ risk of platelet aggregation

All higher Thromb + both PGI₂ (vasodilation & Thromb + PA) of TXA₂ (vasoconstriction & Thromb)
Aspirin should be withdrawn 1 week prior to elective surgery. (Risk of bleedg.)

6) Acid-base electrolyte balance: In Metabolic acidosis cause Resp alkalosis
compensated by excretion of bicarbonate.
Thrombosis → Resp Acidosis
uncompensated by H⁺ Acidosis

7) CVS: Prolonged use of Aspirin & other NSAIDs cause sodium & water retention.
↓
precipitate CHF.

8) Urate excretion: salicylate Thromb (high doses) the Reabsorption of urate.
→ ↑ RAARF, ↑ Thrombosis & discase, ↑ Thrombosis cause.
PK: Rapidly absorbed from upper GI tract
metabolised in liver by glycine and glucuronide conjugation
low doses → 1st dose kinetics
high doses → zero order kinetics.

ADR: GIT: Nausea, Vomiting, epigastric pain
ulcerogenic effect → mgs. decrease
↓ prevent by: NSAIDs after food
Buffered Aspirin
PPID with NSAIDs.
Selective COX-2 Inhibitors.

Hypersensitivity → skin rash, Rhinitis, bronchospasm,
Aspirin induced Asthma due to a leukotrienes

→ DSSP deficiency → Adrenoleukodystrophy - haemolytic anaemia

→ D prolonged use interfere with Acth of vit E.

↓ synthesis of clotting factors.

Bleeding.

Pe = P411

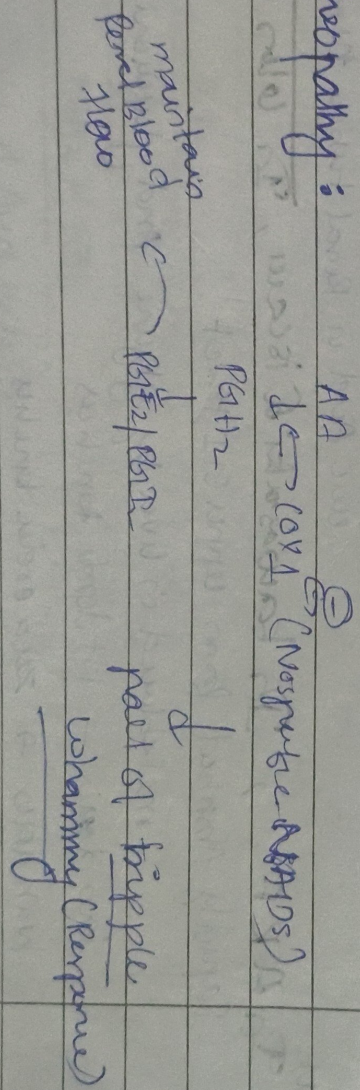
→ Reye's syndrome? Use of salicylates in children with viral infection
may cause hepatic damage.

↓

with fatty infiltration of encephalopathy.

→ Pregnancy → Disturb in synthesis delay onset of labour
↑ chance of PPH.

→ Analytic nephropathy:



X PGL synthase
without HPG MS2

PARLETAHOL:

→ It is para-immunophenol derivative.

→ Antipyretic, Analgesic with poor Anti-inflammatory Activity.

→ It mainly inhibit COX-3 in brain.

↓ so does not produce gastric irritation

As they don't interfere with COX & Pathway

→ It does not affect Acid-Base balance

does not effect CVS.

does not effect platelet function or clotting factors and not interfere

PK → well Absorbed orally.

It → liver E → urine

ADR → Nausea, Rashes.

ACUTE PARLETAHOL POISONING:

750 mg
toxic

occurs in small children with low hepatic glucuronide conjugation.

→ 150 mg/kg - fatal

Symptoms:

Abdominal Pain & liver tenderness (early)
↓

Centrilobular necrosis & necrosis

Renal tubular necrosis; hypoglycemia → coma.

MECHANISM OF TOXICITY:

Antipyretic, N. Analgesic, 100 mg/kg