

# Evaluation of Non Steroidal Anti-Inflammatory Drugs (NSAIDs)

By

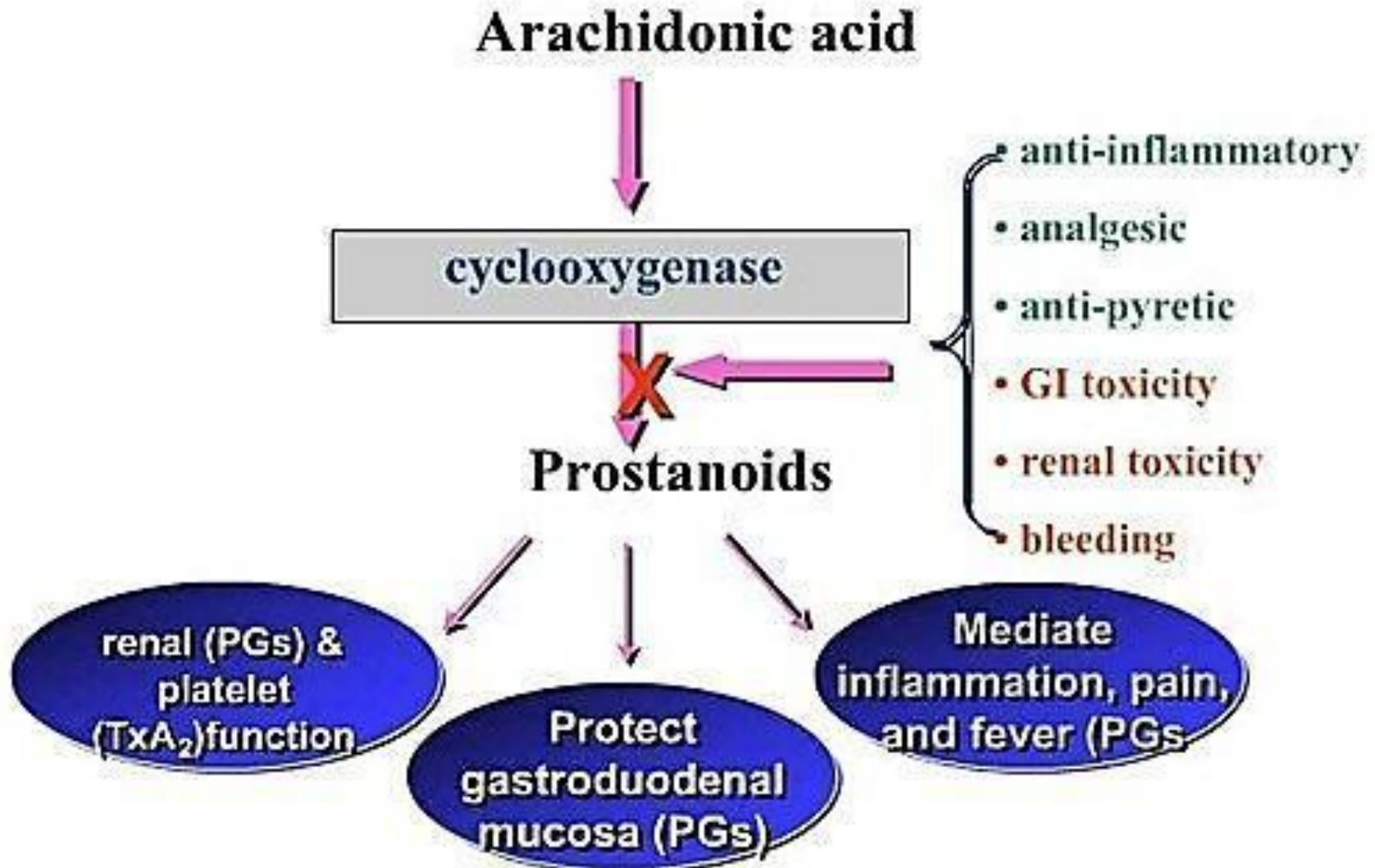
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# NSAIDS

The **NSAIDs** are a group of **chemically dissimilar agents** that differ in their **antipyretic, analgesic, and anti-inflammatory** activities. They possess a **single** common mode of action: inhibition of cyclo-oxygenase enzyme, thereby reducing prostaglandin synthesis.

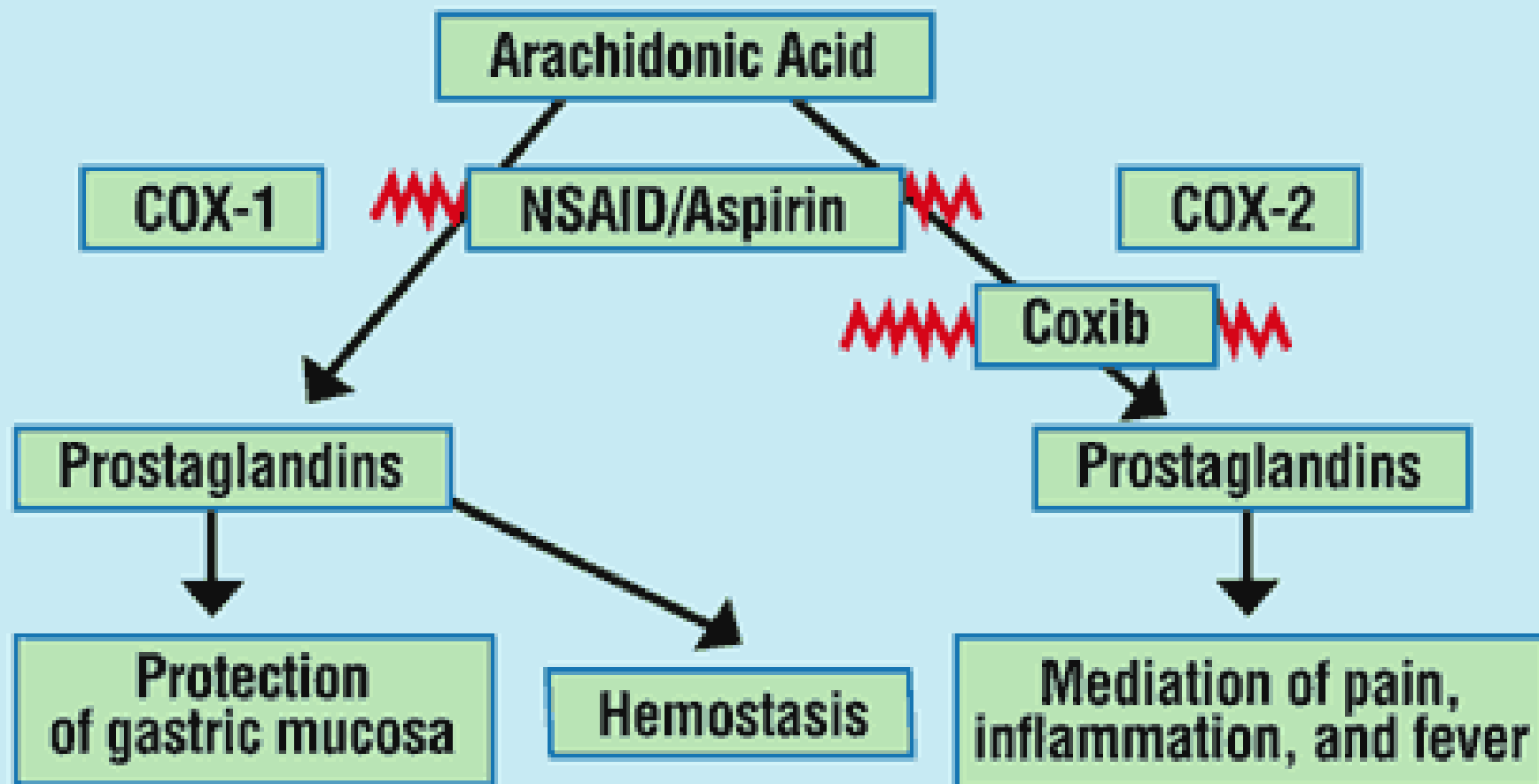
# Mechanism of action



# There are two isoforms of cox enzyme

- **COX-1** : constitutive enzyme is involved in tissue homeostasis it is a process that maintains the stability of the human body (internal environment in response to changes in external condition)
- **COX-2** : inducible enzyme is responsible for the production of prostanoid mediators of inflammation

## Figure 7. Comparison of NSAIDs and Coxib Mechanisms of Action



Source: Wolfe et al. *N Engl J Med.* 1999;340:1888.

# Classification of NSAIDs

The NSAIDs can be sub-classified on the basis of chemical structure as follows:

- salicylic acid derivatives: aspirin
- Para-aminophenol: acetaminophen (paracetamol)
- Propionic acid derivatives: ibuprofen, naproxen
- Acetic acid derivatives: diclofenac, sulindac, indomethacin.
- Enolic acid derivatives: piroxicam, meloxicam.
- Fenamic acid derivatives: mefenamic acid (ponstan).
- Selective cox 2 inhibitors: celecoxib, rofecoxib

# Pharmacokinetics of NSAIDs

- **Absorbed** completely from the gastro-intestinal tract,
- **highly protein bound**
- **T<sup>1/2</sup> values** in plasma grouped in to short ex: Ibuprofen (1-2 hrs) and long ex: Piroxicam (20-50 hrs)
- **Renally excreted.**

# Uses of NSAIDs


1. Anti-inflammatory actions
2. Analgesic actions
3. Antipyretic actions: Reduce cytokine-induced prostaglandin synthesis in the hypothalamus, thus reducing fever.
4. Antiplatelet actions



# Side effects

## 1. Gastro-intestinal effect

- Include gastric discomfort, dyspepsia, diarrhea, nausea, vomiting, gastric ulceration, bleeding, and serious perforation and hemorrhage can occur.
- These adverse effects are due to inhibition of COX1 in the gastric intestinal tract.

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- Selective cox2 inhibitors are associated with lower risk of serious GI side effects than non-selective NSAIDs.
  - Patients at risk of GI ulceration (including the elderly) who need NSAIDs treatment should receive gastroprotective treatment.

## 2. Cardiovascular effects

- MI and stroke (with selective cox2 inhibitors)
- Increased risk of bleeding (antiplatelet effect of aspirin)( cox1 inhibition)

## 3. Actions on the kidney:

Reversible renal insufficiency in susceptible patients, sodium and water retention.

- ## 4. Other side effects:
- skin reaction, increase the risk of exacerbations of asthma.

# Pregnancy:

- Most NSAIDs are pregnancy risk **category C** in the **first two** trimesters.
- ( **Acetaminophen** is preferred if analgesic or antipyretic effects are needed during pregnancy)
- In the **third** trimester, NSAIDs should generally be **avoided** due to the risk of **premature closure of the ductus arteriosus**.

# Aspirin ( acetyl salicylic acid)

## Therapeutic uses

### 1. Anti-inflammatory and analgesic uses

Only at **higher doses** these drugs show anti-inflammatory activity.

### 2. Antipyretic uses:

3. **Cardiovascular uses** (antiplatelet) Aspirin is used to inhibit platelet aggregation. **Low-dose** aspirin inhibits COX-1-mediated production of TXA<sub>2</sub> thereby reducing TXA<sub>2</sub> mediated **vasoconstriction and platelet aggregation** and the subsequent risk of cardiovascular events

Medicinal form  
tablet, vial



- **Side effects**

Blood disorder, bronchospasm, confusion, GI haemorrhage , increased bleeding time, tinnitus.

- **Pregnancy:** use antiplatelet doses with caution in 3rd trimester.

- **Breast feeding:** avoid possible risk of Reye 's syndrom

- **Contraindication**

Active peptic ulceration, bleeding disorder, children under 16 years (risk of **Reyes syndrome**), haemophilia, previous peptic ulcer.

# Acetaminophen (paracetamol)

**Therapeutic uses** antipyretic and analgesic

Inhibits prostaglandin synthesis in the **CNS**.

**safe** in pregnancy, breast feeding, children and old age



## Medicinal form

Tablet, oral solution, oral suspension, solution for injection, and suppositories.



# Adverse effects

- At normal therapeutic doses, acetaminophen is free of adverse effects
- **hepatotoxicity** a very serious and potentially life-threatening condition occur with large doses (7.5-10 gm in adult)

# Ibuprofen

Is a propionic acid derivative with anti-inflammatory, analgesic and antipyretic properties. It has **fewer side effects** than other non-selective NSAIDs but its anti-inflammatory properties are **weaker**.

## **Therapeutic uses**

Rheumatoid disease, dysmenorrhea, post-operative, migraine and dental pain.

## Medicinal form

tablet, capsule, oral suspension, gel.



# Diclofenac sodium

Is acetic acid derivatives, is good choice because it combine **good efficacy** and **fewer** incidence of side effect (but **more** than ibuprofen).

## Therapeutic uses

Pain and inflammation in musculoskeletal disorder, acute gout, post operative pain, ureteric colic, prevention of postoperative pain.

## Medicinal form

Tablet, solution for injection, suppositories, gel



# Mefenamic acid

Fenamic acid derivative, has **minor** anti-inflammatory properties .it has occasionally been associated with **diarrhea** and **haemolytic anaemia** which require **discontinuation** of treatment.

## Therapeutic uses

Pain and inflammation in rheumatoid arithritis, osteoarthritis post operative pain.

# Medicinal form

Tablet, capsule and oral suspension





# Indomethacin

Enolic acid derivatives, it has efficacy **equal** to or **superior** to that of **diclofenac** but with a **high** incidence of **side effects** including headache, dizziness and GI disturbances.

## Therapeutic uses

Pain and moderate to severe inflammation in rheumatic disease and other musculoskeletal disorder., acute gout and dysmenorrhoea.

# Medicinal form

## Capsule ,suppositories.



# Selective cox2 inhibitors

## Celecoxib

Is as **effective** as **non selective** NSAIDs such as diclofenac sodium, evidence appears to indicate that the risk of **upper GI events** is **lower** with selective inhibitors than **non selective** NSAIDs.

# Therapeutic uses

Pain and inflammation in OA and RA

## Side effects

Renal toxicities, **high** incidence of cardiovascular thrombotic events

**Medicinal form** (Capsule).





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