



# NSAIDs



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

- ◆ **Definition & Main Effects**

Non-steroidal anti-inflammatory drugs (NSAIDs) are drugs that have:

- **Analgesic effect** 😌 → Relieve pain *centrally without narcosis*
  - **Antipyretic effect** 🔥 ↕ → Reduce elevated body temperature to **normal**
  - **Anti-inflammatory & Anti-rheumatic effects** 🔥
- Present in **most NSAIDs** ✗ *except Paracetamol*

### Types of Cyclooxygenase Enzymes (COX)

#### A COX-1 (Constitutive – Physiological)

- Expressed normally in the body
- **Sites:** Stomach 🍔 | Intestinal endothelium | Kidneys ☐
- **Functions:**

◆ <b>Stomach</b> ↑ Gastric mucosal integrity ↓ HCl secretion Prevention of peptic ulcer	◆ <b>Kidney</b> 💯 Renal vasodilation (VD) Maintains renal blood flow (RBF) Controls renal filtration rate (RFR)	◆ <b>Platelets</b> 💙 Produces TXA <sub>2</sub> ↑ Platelet aggregation First step in thrombus
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#### B COX-2 (Inducible – Pathological)

- Induced during inflammation
- Uregulated by **pro-inflammatory mediators:** IL-1, IL-2, TNF-α, oncogenes ⚠
- **Effects:**

- Vasodilation 💯 ↑ → Edema 💧
- Inflammation 🔥 → Pain 😌 → Fever 🔥

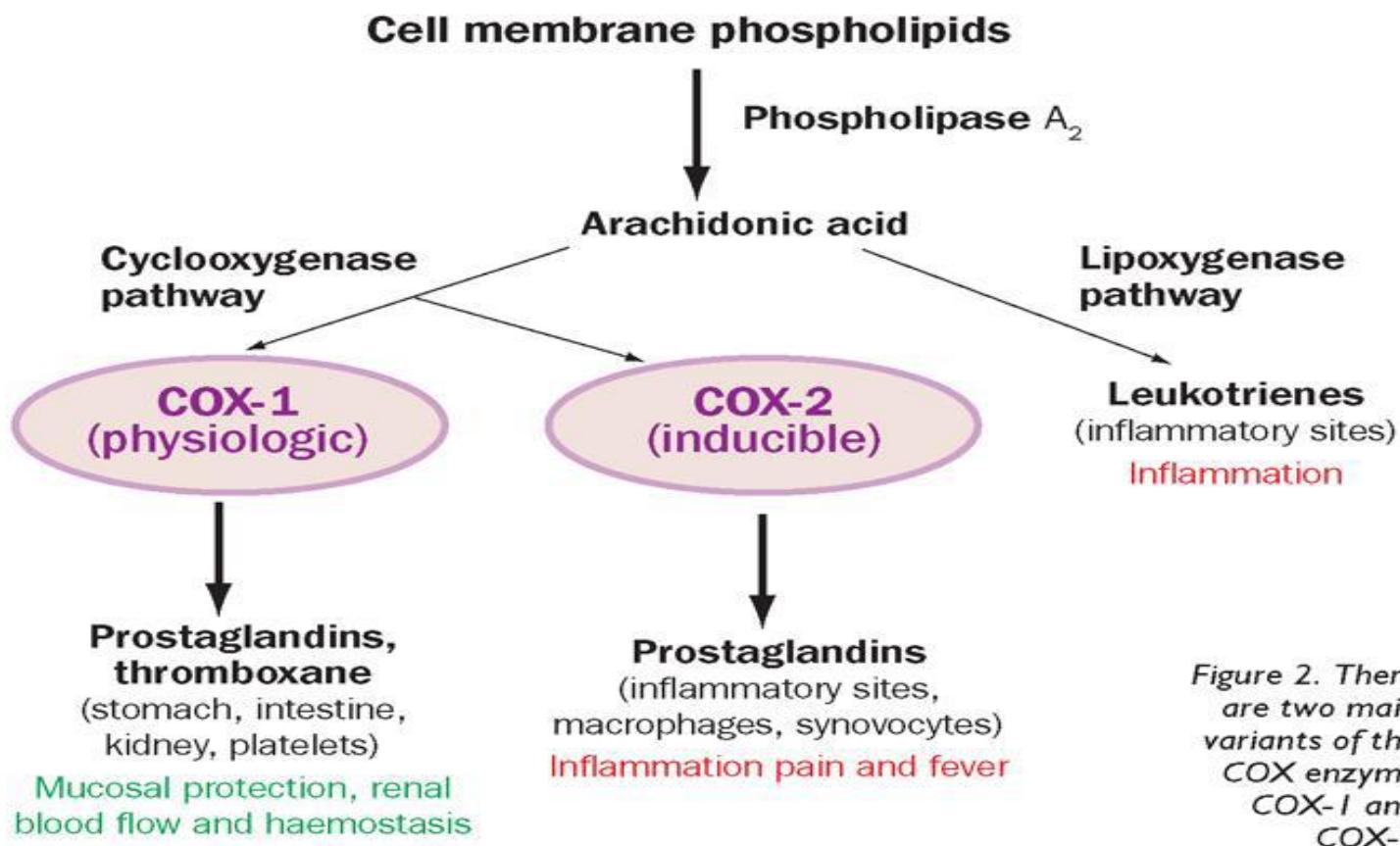
## C COX-3 (Central)

🧠 Located in CNS & Heart

➡ Responsible for:

- Analgesic effect
- Antipyretic effect

✗ No anti-inflammatory activity



## 💊 Mechanism of Action of NSAIDs

➡ NSAIDs inhibit conversion of **arachidonic acid** ➡ **Prostaglandins & Thromboxane**

➡ By inhibition of:

**Cyclooxygenase enzyme (COX)** 🔪

◆ Most NSAIDs inhibit:

- COX-1 ✗
- COX-2 ✗

◆ Exception:

➡ **Selective COX-2 inhibitors** ⚪



## 1. Salicylates

### Aspirin (Acetylsalicylic Acid)

Uses 

- Analgesic 
- Antipyretic 
- Anti-inflammatory  (only at high doses – rarely used)
- Antiplatelet 

 Dose: 75–150 mg/day → Prophylaxis against thromboembolic diseases

#### Mechanism:

→ Irreversible ↓ TXA<sub>2</sub> → ↓ Platelet aggregation

#### Important Note (NB)

 Aspirin is NOT indicated in:

→ Children & adolescents

#### ! Risk of Reye's syndrome:

-  Encephalopathy (brain damage)
-  Liver damage
-  Occurs after viral infections (influenza, chickenpox)

→ Aspirin inhibits COX-1 more than COX-2

## 2. Indole Derivatives

### Indomethacin (Indocid®)



→ Potent COX inhibitor: → Central: COX-3  → Peripheral: COX-1 & COX-2

Best used as: → Anti-inflammatory → Anti-rheumatic

 NOT preferred as: → Analgesic for mild pain → Antipyretic

#### Most toxic NSAID



## Diclofenac

- One of the **most potent NSAIDs** 💪
- Better tolerated
- Mechanism: → Inhibits COX-1 & COX-2 → ↓ Prostaglandins
- Additional action:  
→ Inhibits **Lipoxygenase (LOX)** → ↓ Leukotrienes (LTs) → ↓ Asthma risk 
- Recommended in **asthmatic patients**

 Dosage Forms:

12.5 – 25 – 50 – 75 – 100 mg  
 Tablets (enteric coated, SR, dispersible)  
 Capsules – Suppositories – I.M – Gel – Eye drops

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 **Common Adverse Effects (NSAIDs)**

- GIT irritation  → Reduced by enteric-coated tablets → Taken after meals 
  - Nephropathy  
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## Propionic Acid Derivatives

- **Ibuprofen (Brufen)**   
 100–600 mg (tablet, pack, suppository, syrup)
- **Ketoprofen (Ketofan)**   
 12.5–200 mg (tablet, capsule, suppository, syrup, parenteral)
- **Fenoprofen (Nalfon)**
- **Naproxen (Naprosyn)** 250–500 mg
- **Flurbiprofen (Froben)** 50 mg



◆ **Ibuprofen**

→ Used for:

Fever | Pain | Inflammation  
Rheumatoid arthritis | Pericarditis



◆ **Ketoprofen**

→ Used for:

Arthritis pain  
Gingival inflammation   
Dysmenorrhea



◆ **Naproxen**

→ 20× stronger than Aspirin

→ Used for:  
Pain – Fever – Inflammation – Dysmenorrhea



## 🎯 Selective COX-2 Inhibitors

- Strong anti-inflammatory & anti-rheumatic effects
- Less gastric toxicity
- Less platelet inhibition

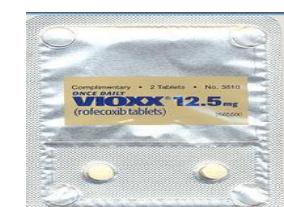
➡ Indications:

- Acute pain
- Osteoarthritis
- Patients at high GIT risk

- ⚠ Selective COX-2 → ↑ TXA<sub>2</sub>
- ↑ Platelet aggregation
- ↑ Vasoconstriction
- ↑ Thrombosis risk ! # Aspirin.

### 💊 Examples

- Celecoxib (Celebrex®) 100–200 mg
- Rofecoxib (Vioxx®) 12.5–25–50 mg
- Minimal GIT effects
- Used for long-term pain management



## ⚠ Side Effects of NSAIDs

➤ NSAIDs 🥗 💧

➡ يُفضل تناولها مع الطعام أو السوائل ➡ (حرقان - تهيج المعدة) GIT upset 🚩 ➡

➤ High GI risk patients ⚠

➡ يُستخدم معها Proton Pump Inhibitors (PPIs) 🥃

✓ Omeprazole

✓ Pantoprazole

➡ أو ✓ Synthetic Prostaglandin E analogue ➡ Misoprostol

🎯 الهدف: ➡ Prevention of NSAIDs-induced gastric ulcers 🌟 💯

➤ NSAIDs

➡ ↓ COX-1 & COX-2

➡ ↓ Prostaglandins (PGs)

➡ ↑ HCl secretion 🧪 ➡ Damage of gastric mucosa ➡ 💯 Gastric ulcer

➤ Renal adverse effects ⚡ ⚠

➡ NSAIDs ➡ ↓ COX-1 & ↓ COX-2 ➡ ↓ PGs (PGE<sub>2</sub> & PGI<sub>2</sub>)

➡ ↓ Renal Blood Flow (RBG)

➡ ↑ Renin–Aldosterone system

➡ ↑ Na<sup>+</sup> & H<sub>2</sub>O retention 💧

➡ Edema + Renal vasoconstriction

➡ ✗ Renal failure

➡ with chronic or prolonged use

➡ Analgesic nephropathy

➤ Cardiovascular risk ❤️ ⚠

➡ Patients with cardiovascular disease

➡ Taking NSAIDs

➡ Especially Selective COX-2 inhibitors 🎲

➡ Higher risk of Myocardial Infarction (MI) 💥

➡ Compared to patients not taking NSAIDs



## II. Aniline Derivatives

### Phenacetin

→ Prodrug → Liver metabolism → Paracetamol

### Paracetamol (Acetaminophen)

(Stopian – Panadol)

#### Dosage Forms:

Tablets – Syrup – Drops – Suppository – I.V

✓ Dose: 250–500 mg

→ NOT a true NSAID ✗

#### Effects:

- ✓ Analgesic 😊
- ✓ Antipyretic 🔥

(central COX-3 inhibition)

✗ Minimal / No anti-inflammatory effect

#### ✓ Safe in:

Pregnancy 💫

Peptic ulcer

Asthma

Children with viral infections

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