

Pharmacology





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:**

◆ Stomach ↑ Gastric mucosal integrity ↓ HCl secretion Prevention of peptic ulcer	◆ Kidney 💯 Renal vasodilation (VD) Maintains renal blood flow (RBF) Controls renal filtration rate (RFR)	◆ Platelets 💙 Produces TXA ₂ ↑ 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

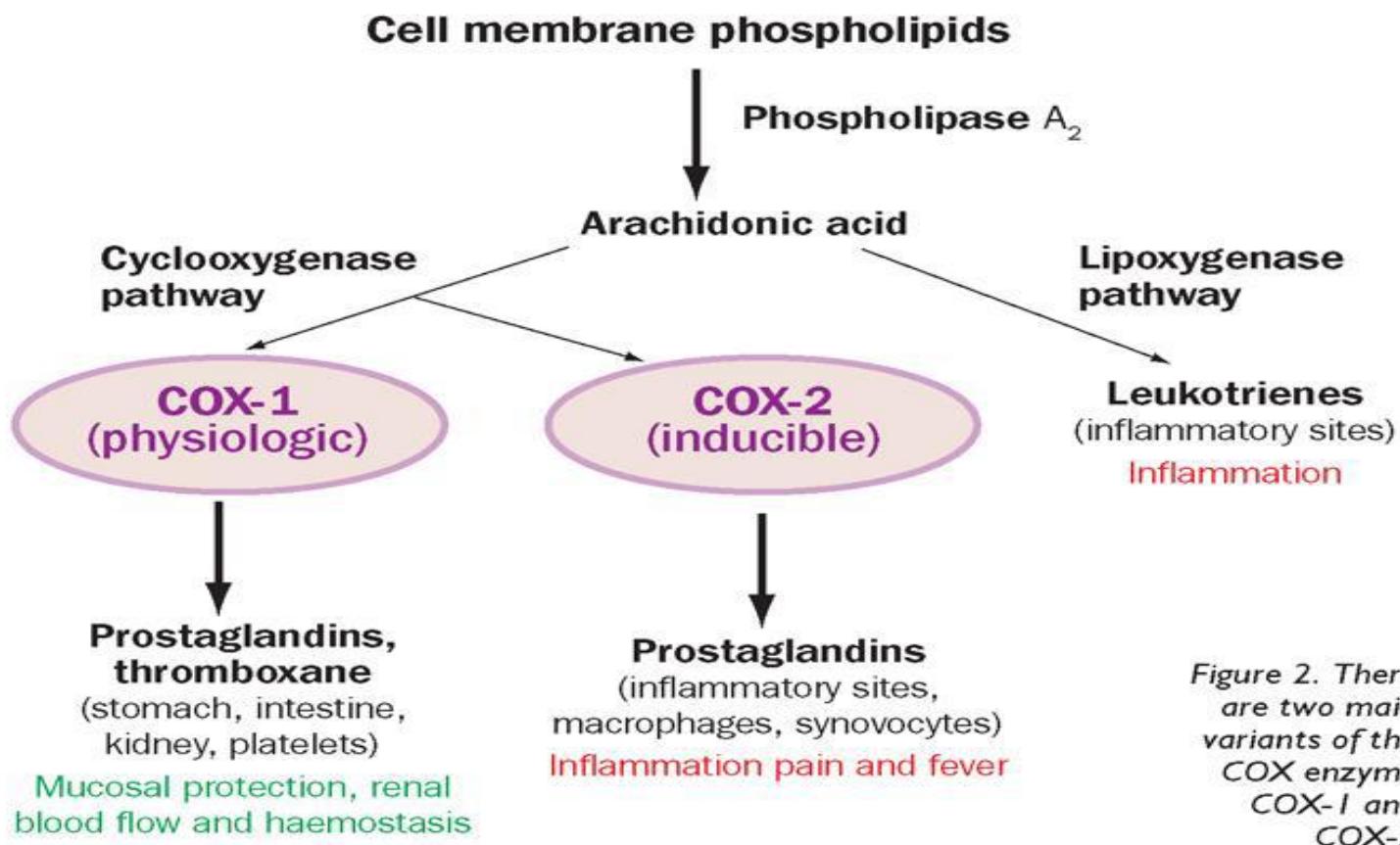


Figure 2. There are two main variants of the COX enzyme, COX-1 and COX-2.

💊 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 ↓ TXA₂ → ↓ 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

 **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

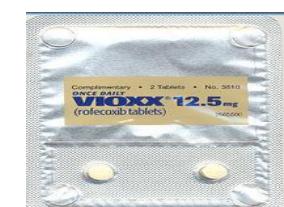
➡ Indications:

- Acute pain
- Osteoarthritis
- Patients at high GIT risk

- ⚠ Selective COX-2 → ↑ TXA₂
- ↑ 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 → GIT upset 🤢 ➡ (حرقان - تهيج المعدة)

➤ 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 (PGE₂ & PGI₂)

➡ ↓ Renal Blood Flow (RBG)

➡ ↑ Renin–Aldosterone system

➡ ↑ Na⁺ & H₂O 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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