Pharma Team - 430 - MSB

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Non-Selective Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Are group of drugs that induce the following effects:

- **Analgesic** (مسكنات): Drugs that relieve pain.
- **Antipyretic** (مخفض حرارة): Drug that lower the elevated body temperature **<u>to normal</u>**
- **Anti-inflammatory**
- **Anti-platelet**

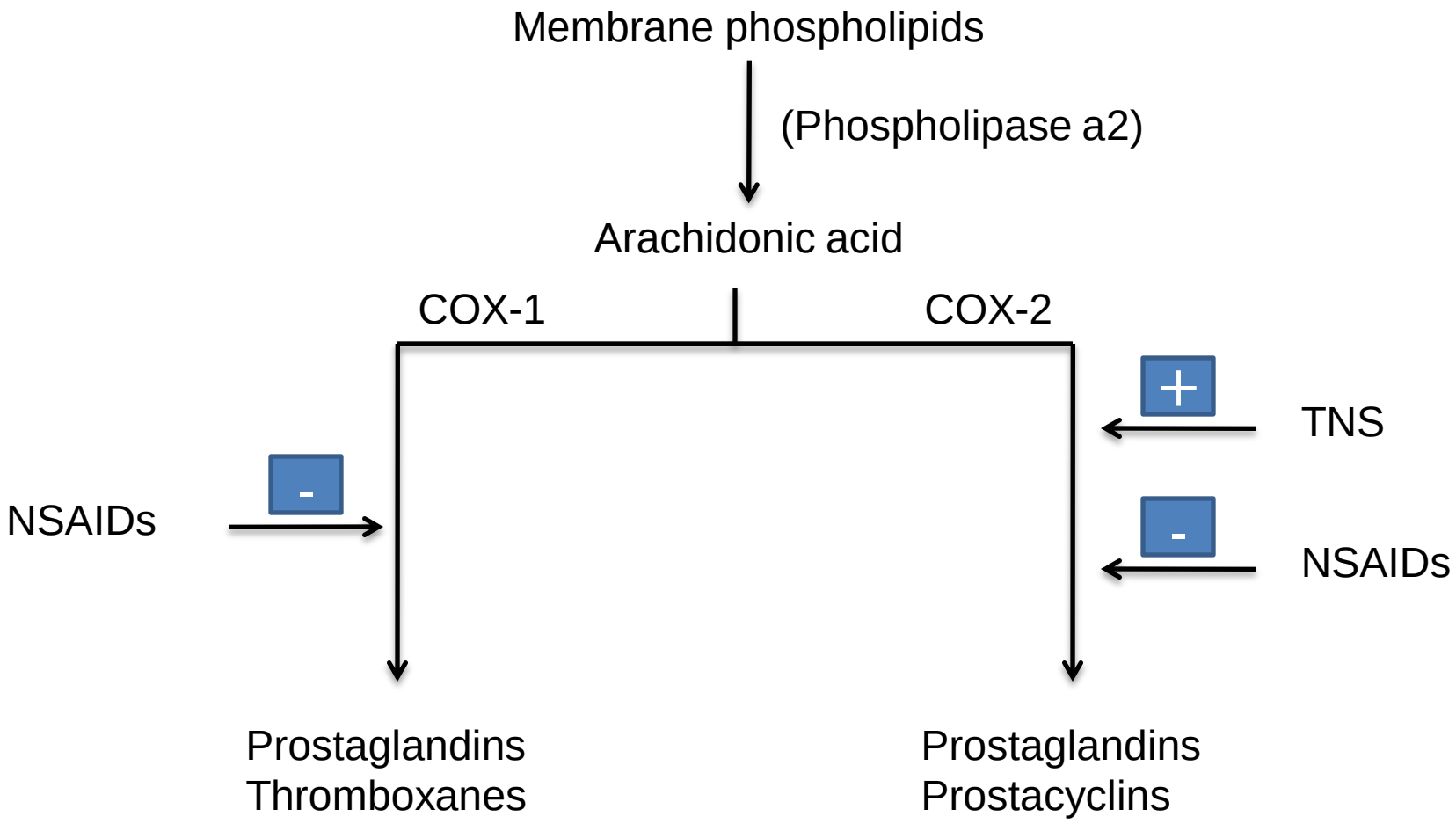
They inhibit both COX-1 & COX-2

Classification of NSAIDs

- **Non-Selective COXs Inhibitor (Aspirin)**
- **Selective COXs Inhibitor**

Pharmacokinetic

- Oral administration
- Acidic drugs (best absorbed in stomach)
- 95% bound to plasma protein (High bioavailability)
- Metabolized in liver (oxidation & conjugation)



IMPORTANT NOTE:

Aspirin is **IRREVERSIBLE** inhibitor to COX enzymes

Prostaglandins are inflammatory mediators

يتم إنتاج الـ Arachidonic acid من الـ phospholipids الموجود على غشاء الخلية بمساعدة الأنزيم Phospholipase a2 ، هذا الأنزيم يتفرع إلى COX-1 و COX-2.

Mechanism Of Action

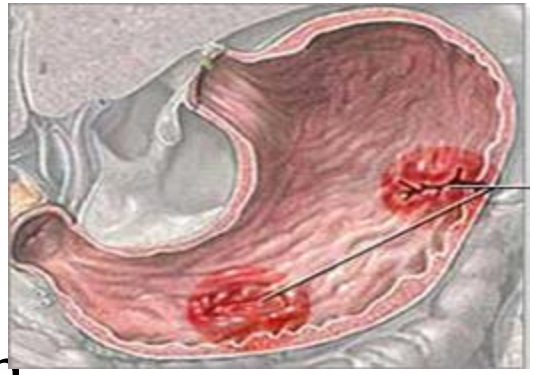
Analgesic	Antipyretic	Anti-Inflammation	Anti-platelet
•Inhibition of COX enzymes in CNS •Anti-Inflammatory action	•Inhibition of COX enzymes in CNS. •Inhibition of IL-1 •Heat regulation center at Hypothalamus	Inhibition of COX enzymes in CNS	Inhibition of platelet COX_1 enzyme & TXA_2

Therapeutic Uses Of Non-Selective NSAIDs:

- Fever. (**Antipyretic**)
- Headache, Migraine, Dental pain, **NOT** visceral pain. (**Analgesic**)
- Common cold.
- Rheumatic / Rheumatoid arthritis / myositis or other forms of inflammatory conditions. (**Anti-inflammatory**)
- Dysmenorrhea (by decreasing uterine contraction)

Adverse Effects of Non-Selective NSAIDs:

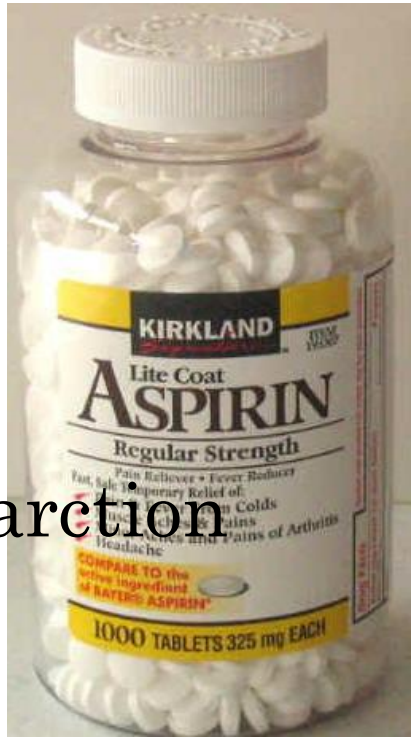
- GIT upsets (nausea, vomiting)
- GIT bleeding & ulceration
- Bleeding
- Hypersensitivity reaction
- Inhibition of uterine contraction
- Salt & water retention **(Edema)**



Stomach ulcer


ASPIRIN

Clinical uses



- Acute rheumatic fever
- Reducing the risk of myocardial infarction (cardioprotective)
- Prevention of pre-eclampsia
- Chronic gouty arthritis with large doses
- Chronic use of small doses , reduce the incidence of cancer colon

Adverse Effects of Aspirin

Therapeutic doses	Large doses
Gastric irritation	Salicylism (ringing of ear, vertigo)
Hypersensitivity (Aspirin asthma)	Hyperthermia
Acute Gouty arthritis	Gastric ulceration & bleeding
Reye's syndrome	

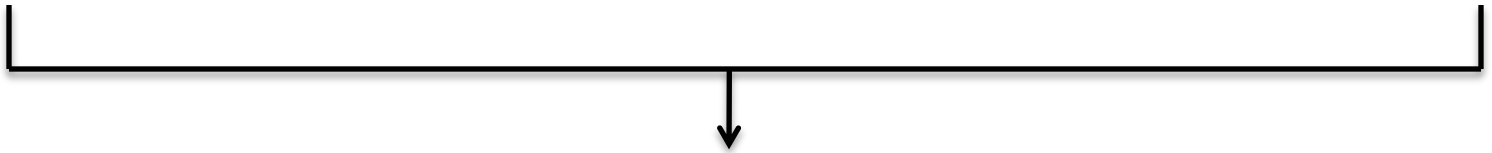
Contraindications

- Peptic ulcer
- Pregnancy
- Hemophilic patients
- Patients taking anticoagulants
- Children with viral infections
- Gout التهاب المفاصل (small doses)

Paracetamol

Used as **Analgesic Antipyretic** **(NO anti-inflammatory)** instead of Aspirin in case of:

- Peptic or gastric ulcers.
- Pregnancy.
- Bleeding tendency (Hemophilic patients).
- Children with viral infections.
- Allergy to Aspirin.



Aspirin الـ حقت Contraindications هي نفس الـ

Adverse Effects of Paracetamol

- Mainly on liver due to its active metabolite
- Therapeutic doses elevate liver enzymes
- Large doses cause liver & kidney necrosis

Treatment:

by **N-Acetylcysteine** to neutralize the toxic metabolite in case of high doses.

Diclofenac

Clinical uses

- Anti-inflammatory
- Analgesic
- Antipyretic
- Acute gouty arthritis
- Locally to prevent post-opthalmic inflammation

Selective COX-2 inhibitors

General advantages :

- Potent anti-inflammatory
- Antipyretic & analgesic
- Lower incidence of gastric upset
- NO effect on platelet aggregation (COX-1)

General adverse effects

- Renal toxicity
- Dyspepsia & heartburn
- Allergy
- Cardiovascular (do not offer the cardioprotective effects of non-selective group).

General clinical uses

- Rheumatoid arthritis
- Osteoarthritis
- Acute gouty arthritis
- Acute musculoskeletal pain
- Ankylosing spondylitis
- Dysmenorrhea

Celecoxib

- Half-life 11 hours
- Food decrease its absorption
- Highly bound to plasma proteins

Summary

- NSAIDs are group of drugs that have **Analgesic**, **Antipyretic**, **Anti-platelet** & **Anti-inflammatory** effects.
- They are classified into:
  - non-selective: inhibit both COX-1 & COX-2.
  - Selective: inhibit only COX-2 enzymes.
- Their therapeutic uses are:
  - Relieving of mild to moderate pain (not visceral pain).
  - Reducing high body temperature.
  - Preventing clot formation.
  - Anti-inflammatory in rheumatic, rheumatoid arthritis, Desmenrrhea & other inflammatory conditions including muscles or bones.

So Aspirin can be used as prophylaxis in ischemic heart disease.

Summary

- The common adverse effects includes:
  - Gastric upset (nausea, vomiting ,gastric ulceration or bleeding).
  - Allergy.
  - Edema.
- They are contraindicated mainly in patients with:
  - Peptic ulcer.
  - Bleeding tendency.
  - Pregnancy.
- Selective COX-2 inhibitors as Celecoxib are potent anti-inflammatory & analgesic ,but have no anti-platelet effect & less gastric upset.
- They can be used in patients with gastric ulcer, haemophilia.
- Their common adverse effect is mainly on kidney & cardiovascular system.

Aspirin

Clinical uses	Adverse effect		Contraindications
Acute rheumatic fever	Therapeutic doses	Large Doses	Peptic ulcer
(cardioprotective)	Gastric irritation	Salicylism (ringing of ear, vertigo)	Pregnancy
pre-eclampsia	Hypersensitivity (Aspirin asthma)	Hyperthermia	Hemophilic patients or patients taking anticoagulants
Chronic gouty arthritis (large doses)	Acute Gouty arthritis	Gastric ulceration & bleeding	Children with viral infections
reduce the incidence of colon cancer (Chronic small doses)	Reye's syndrome		Gout (small doses)

Paracetamol

Clinical uses	Adverse effect		Contraindications
Peptic or gastric ulcers	Therapeutic doses	Large Doses	NONE
Bleeding tendency	Liver	liver & kidney necrosis	
Allergy to aspirin			
Viral infections in children	elevate liver enzymes		
Pregnancy			

Diclofenac

Clinical uses	Adverse effect		Contraindications
Acute gouty arthritis	Therapeutic doses	Large Doses	NONE
post-opthalmic inflammation	NONE		

Celecoxib (Selective)

Advantages	Clinical uses	Adverse effect
Potent anti-inflammatory	Rheumatoid arthritis	Renal toxicity
Lower incidence of gastric upset	Osteoarthritis	Dyspepsia & heartburn
NO effect on platelet aggregation (COX-1)	Acute gouty arthritis	Allergy
	Acute musculoskeletal pain	Cardiovascular
	Ankylosing spondylitis	
	Dysmenorrhea	

Questions

Prescribe a suitable analgesic for patient who:

- Developed repeated attacks of simple headache:
  All 4 drugs
- Simple headache and suffering from bleeding or peptic ulcer:
  Paracetamol + Selective NSAIDs
- Simple headache and pregnant women:
  Paracetamol
- Child with rheumatic arthritis & viral infection:
  Paracetamol
- Child with rheumatic arthritis:
  Aspirin
- Rheumatic arthritis but allergic to aspirin:
  Paracetamol
- Patient suffer from rheumatic arthritis & peptic ulcer:
  Celecoxib

Questions

1. Common mechanism shared by NSAIDs?
   Inhibition of COXs enzyme
2. Advantage of selective NSAIDs:
   Potent anti-inflammatory, Lower gastric upset
3. Aspirin is used in myocardial infraction for its:
   Anti-platelet effect