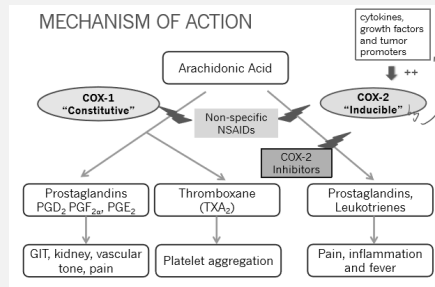


MOA



Enzyme targets by NSAIDs

NSAIDs targets these enzymes:
CYCLOOXYGENASE (COX)

COX-1	COX-2
<ul style="list-style-type: none"> Always present in tissues for homeostatic purposes produces physiologically important prostaglandins (PGs) Constitutively expressed in <ul style="list-style-type: none"> Kidney, gastric mucosa, vascular endothelium, platelets maintenance of GI mucosal lining kidney vasoregulation platelet aggregation 	<ul style="list-style-type: none"> An inducible enzyme that is not normally present in tissues other than the kidney and brain (where COX-2 is constitutive) Induced by cytokines, growth factors and tumor promoters produces PGs that are primarily pathophysiological mediate inflammatory and pain

REMEMBER

COX-2

= C = K = Kidney
= 2 = B = Brain

COX-1 = 1 = Number 1 so good at affecting everything else

Chemical mediators of inflammation

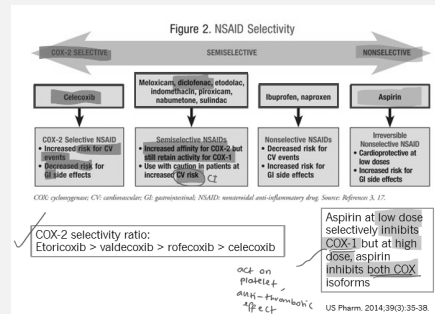
CHEMICAL MEDIATORS OF INFLAMMATION

Mediators	Sources	Actions
Histamine	Mast cells, basophils, platelets	Vasodilation, ↑vascular permeability, endothelial activation
Serotonin	Platelets	Vasoconstriction
Prostaglandins	Mast cells, leukocytes	Vasodilation, pain and fever
Leukotrienes	Mast cells, leukocytes	↑vascular permeability, chemotaxis, leukocyte adhesion & activation
Platelet-activating factor (PAF)	Leukocytes, mast cells	Vasodilation, ↑vascular permeability, chemotaxis, leukocyte adhesion, degranulation, oxidative burst
Cytokines (TNF, IL-1, IL-6)	Macrophages, endothelial cells, mast cells	Local: endothelial adhesion Systemic: fever, metabolic abnormalities, hypotension
Bradykinin	Plasma	Vasodilation, pain, ↑vascular permeability

Lysosomal constituents (collagenases, proteases, free radicals), Nitric oxide (NO)

extra information

Common NSAIDs



NOTES:

- * Cannot take other NSAIDs before taking aspirin because they may prevent aspirin action
- * COX-2 selective has less AE of GI
- * Naproxane less CVS effect dt antithromboxane

REMEMBER:

"ABCDiN"

- Aspirin
- iBuprofen, Naproxen
- COX-2 selective
- Diclofenac

COX-2 Selective, remember "-coxib"
main: Celecoxib

Beneficial effects of inhibition PG synthesis

Analgesia

↓ Bradykinin, 5-HT (serotonin)

Antipyretic

↓ IL-1, reset thermostat

Anti-inflammatory

↓ PGE2, PGI1

Antithrombotic

by aspirin at low dose (permanent acetylation, inhibit platelet activation)

Arteriosus (NSAIDs for closure of patent ductus arteriosus)

Adverse effect

nSAIDs

- Allergy
- Impaired Renal function
- Damage stomach wall (ulcer)

Contraindication

Bleeding

- Avoid in patient:
 - Anticoagulants
 - Pregnancy 3rd trimester (premature close DA, risk bleeding)
- Inhibit platelet cyclooxygenase (COX), thereby **blocking the formation of thromboxane A2 (TXA2)** and impairing TXA2 dependent platelet aggregation

Asthma

Inhibition of COX pathway shifts the arachidonic acid metabolism to **Lipoxygenase (LOX) pathway** leading to **increased leukotriene synthesis**

Allergy

Stomach (Peptic ulcer, gastritis)

- Mucosal damage by –
- COX-1 inhibition: Reduced blood flow
- Topical irritation: Epithelial damage
- COX-2 inhibition: Leukocyte adherence
- *Can prescribe PPI for gastro-protection

CVS event

angina, recent cardiac bypass usrgery, MI, any CV events

REMEMBER

CBARS