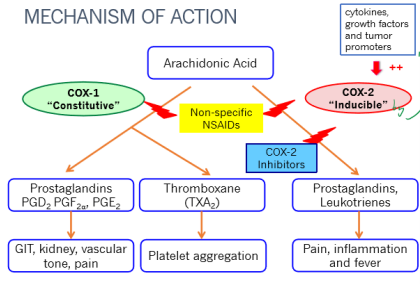


### MOA

#### MECHANISM OF ACTION



### Enzyme targets by NSAIDs

NSAIDs targets these enzymes:

#### CYCLOOXYGENASE (COX)

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

### REMEMBER

#### COX-2

= C = K = Kidney

= 2 = B = Brain

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

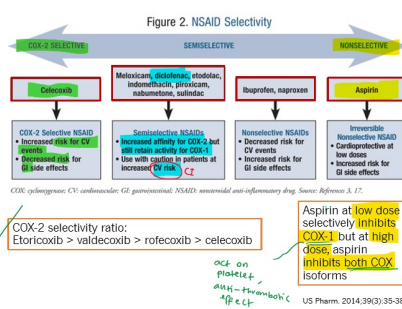
### Chemical mediators of inflammation

#### 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

↓ PGE<sub>2</sub>, PGI<sub>1</sub>

#### 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 A<sub>2</sub> (TXA<sub>2</sub>) and impairing TXA<sub>2</sub> 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