

NSAIDS EPIDEMIOLOGY

NSAIDs amounts for 3.8 of all prescriptions

A significant quantity is sold over the counter(OTC)

Use increases with age

90% of all NSAIDs prescriptions are issued to patients at ages over 65 years

NSAIDs is the most prominent risk for gastric ulceration, hemorrhage and perforation

The prevalence of NSAID-induced ulcers is 10% to 30%

ILOS

To focus on the general mechanism of action of NSAIDs

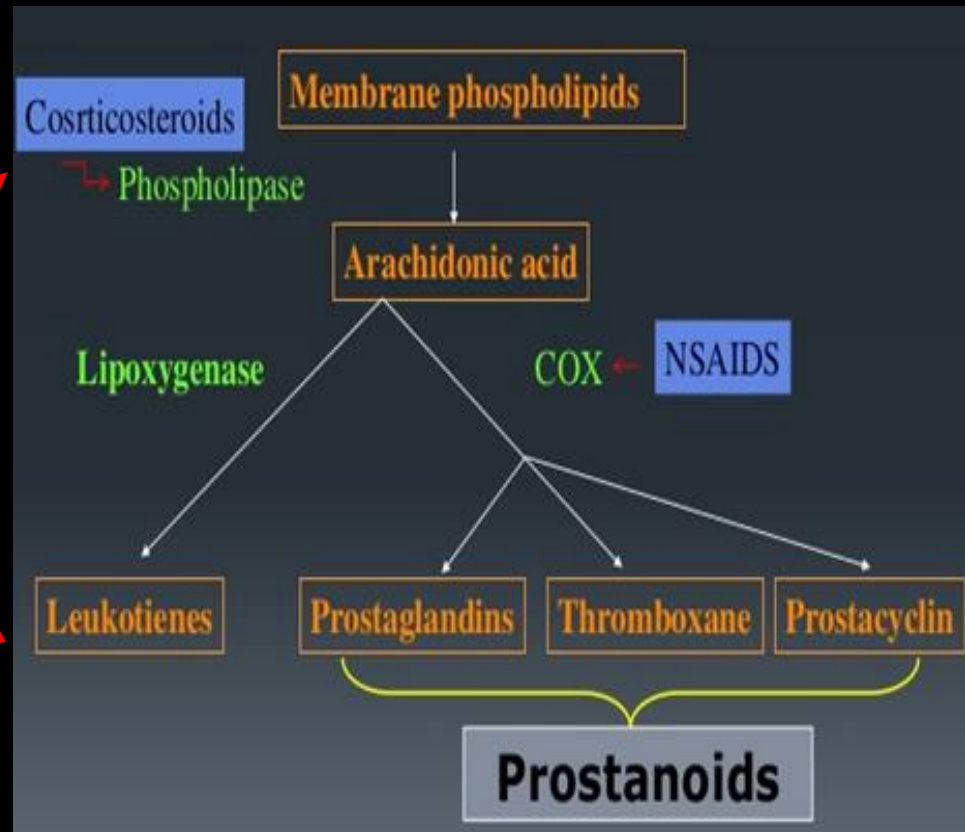
To outline the common pharmacodynamic effects and ADRs of NSAIDs

To classify NSAIDs on basis of their specificity to COX enzyme

To detail on the pharmacokinetic properties and pharmacodynamic effects of selected NSAIDs

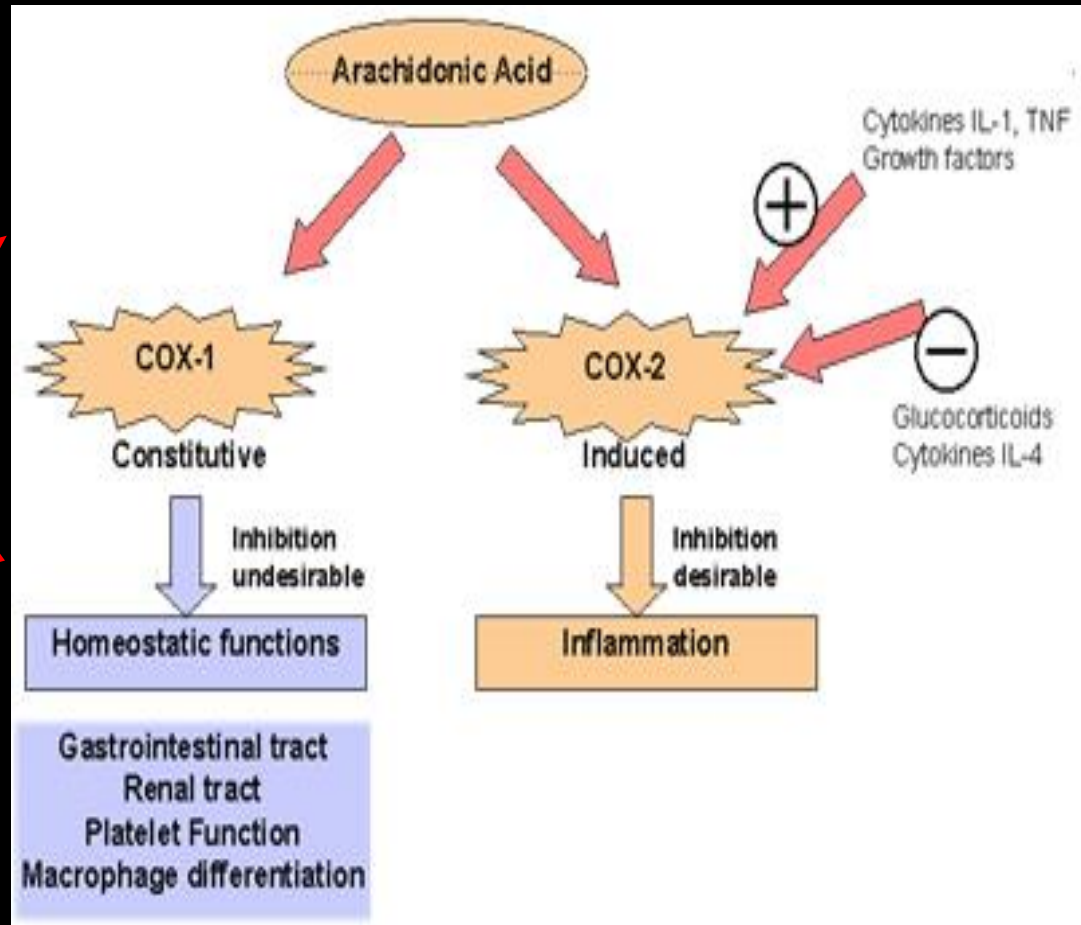
MECHANISM OF ACTION OF NSAIDS

NSAIDs
inhibit cyclo
oxygenase
enzyme



COX ISOFORMS

**COX₃ is
found in
the brain**



CLASSIFICATION OF NSAIDS

Nonselective COX-1/COX-2
Inhibitors

Aspirin, Diclofenac

Selective COX-2
Inhibitors

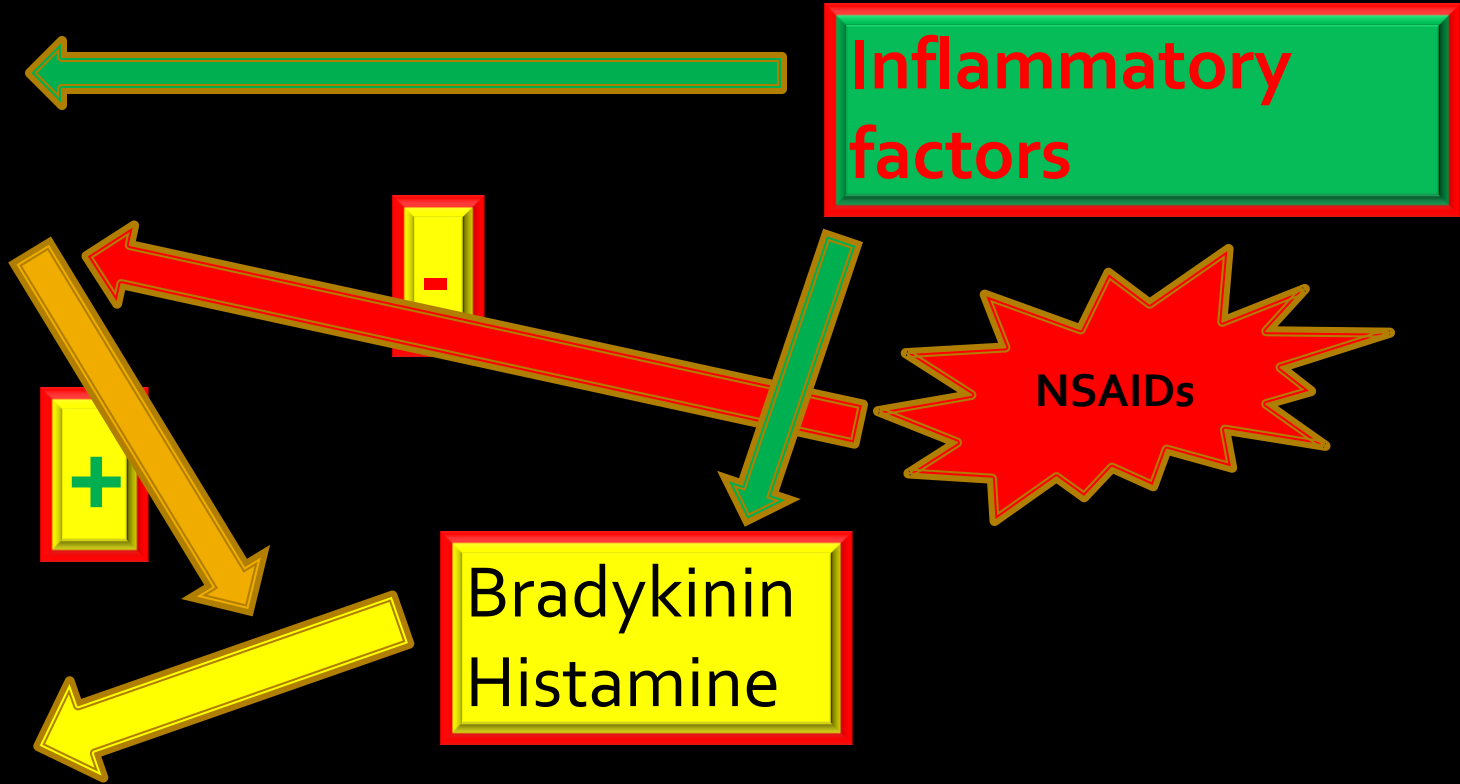
Coxibs

Preferential COX-2
inhibitors

Meloxicam

COX-3 inhibitors

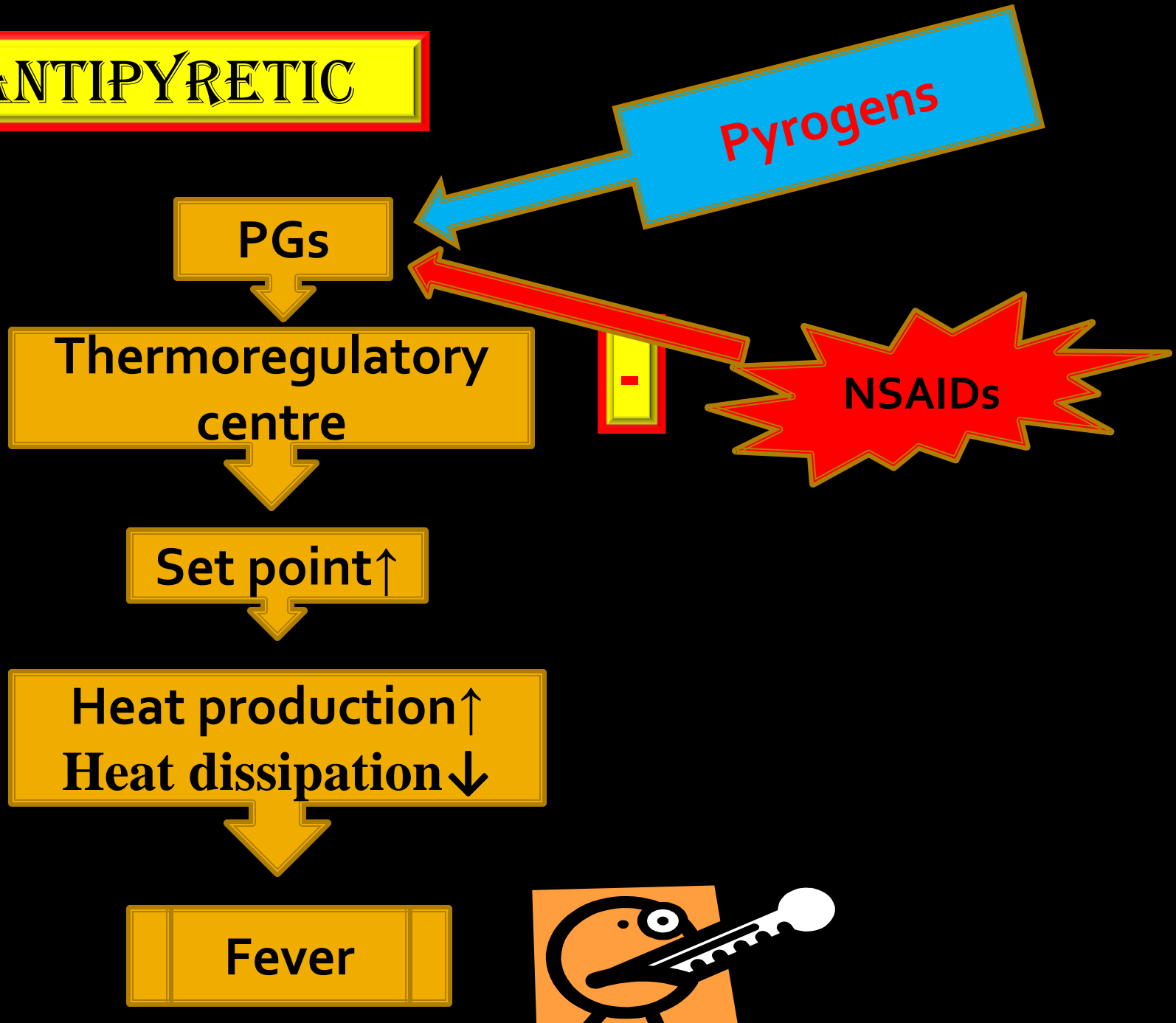
Paracetamol



PHARMACODYNAMIC
EFFECTS

1-ANALGESIC

2-ANTIPYRETIC



CLINICAL USES

Fever

Headache, Migraine,
Dental pain, Dysmenorrhea

Common cold

Rheumatoid
arthritis / myositis

ADRS

GIT upsets (nausea, vomiting)

GIT bleeding & ulceration

Hypersensitivity reaction

Inhibition of uterine contraction

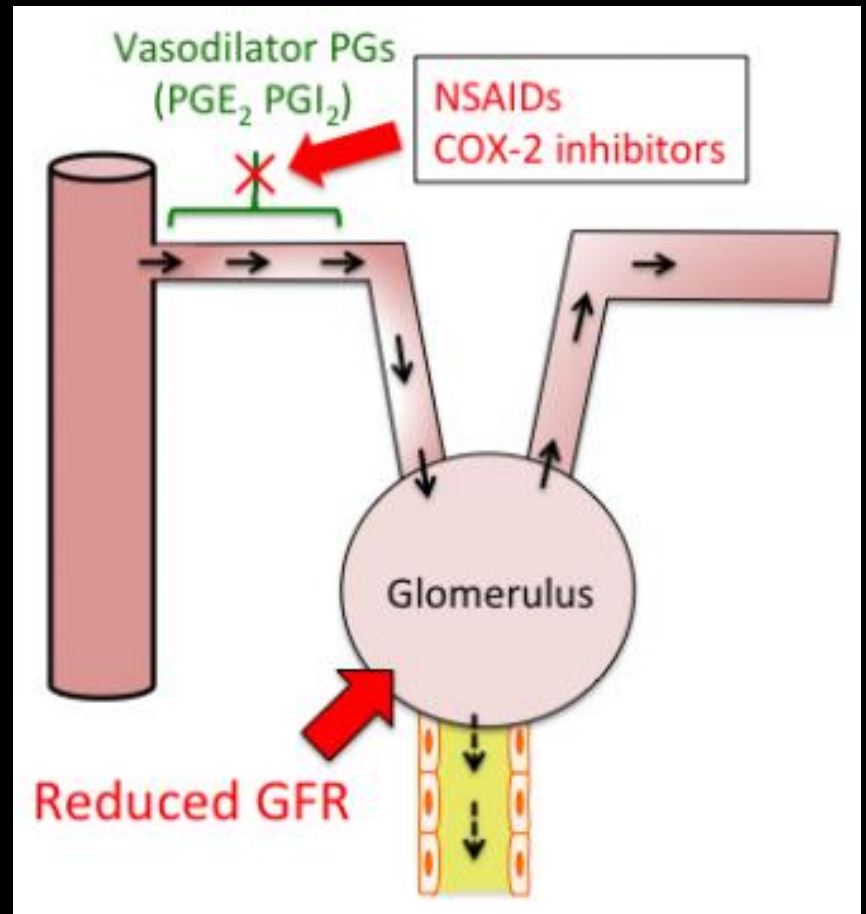
Salt & water retention

ADRS

Impairment
of
kidney
function



NSAIDs cause
hemodynamically-
mediated acute
renal failure



NON SELECTIVE COX INHIBITORS

Aspirin

Diclofenac

Ibuprofen

Ketoprofen

Naproxen

Piroxicam

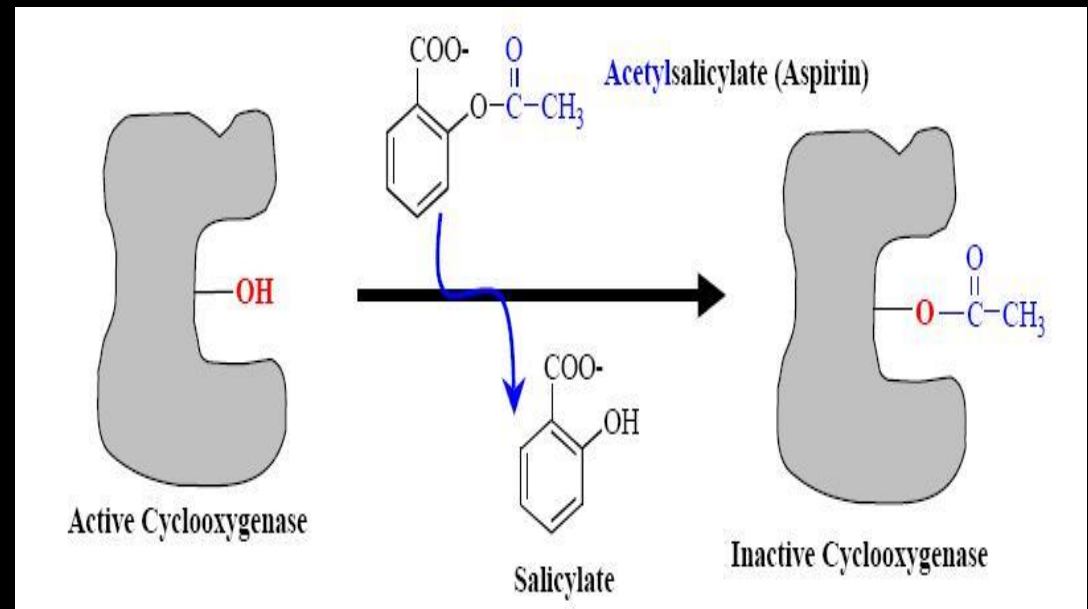
Indomethacin

NON SELECTIVE COX INHIBITORS



MECHANISM OF ACTION

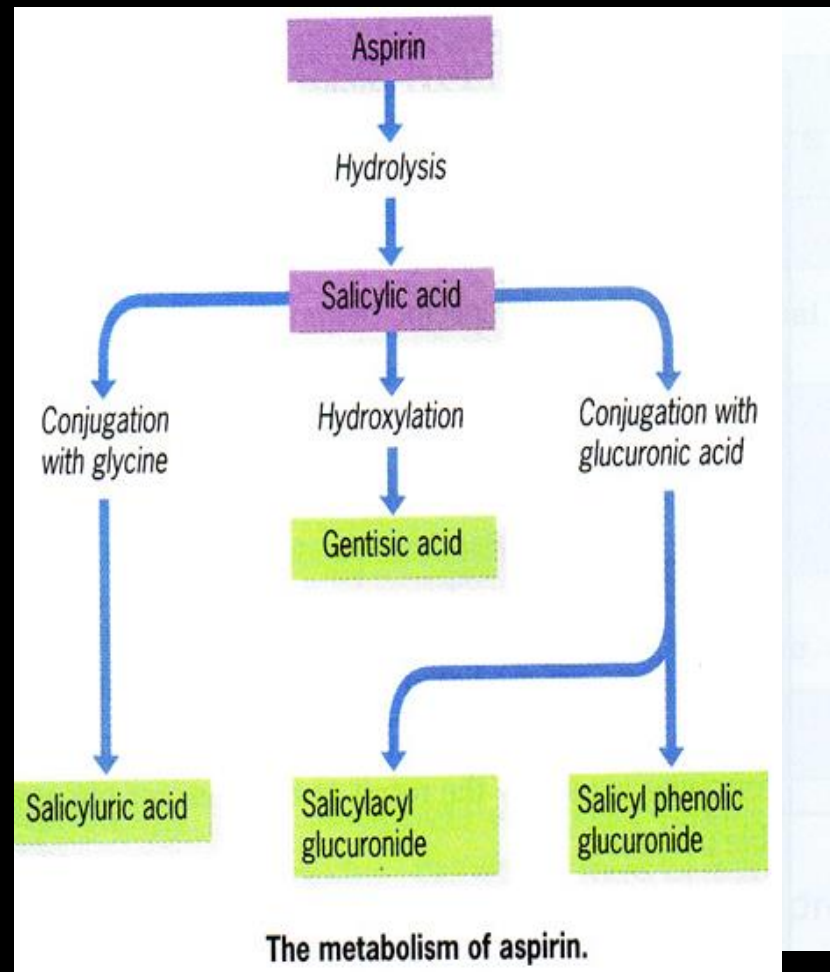
Aspirin
inhibits COX
irreversibly



PHARMACOKINETICS

Metabolized by hydrolysis and then conjugation

Why a high dose has a long plasma half-life?



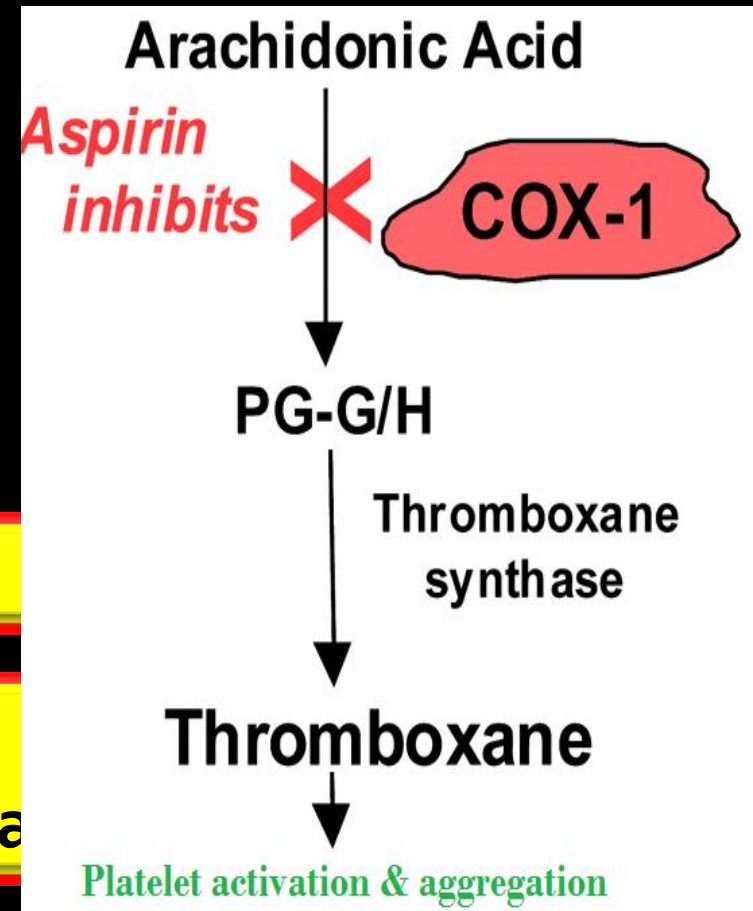
CLINICAL USES

Acute rheumatic fever

Reducing the risk of myocardial infarction (cardioprotective)

Prevention of pre-eclampsia

Chronic use of small doses ,
reduce the incidence of colon ca



ADRS AT CLINICAL DOSES

Hypersensitivity

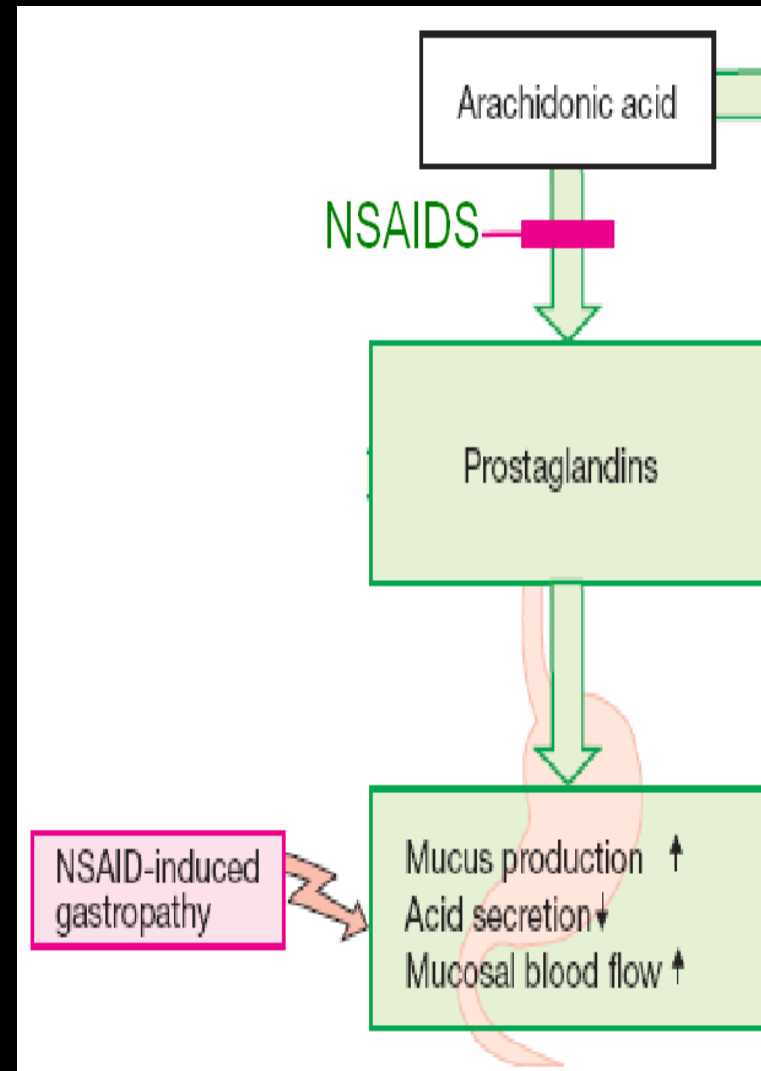
Acute Gouty arthritis

Reye's syndrome

Impaired haemostasis

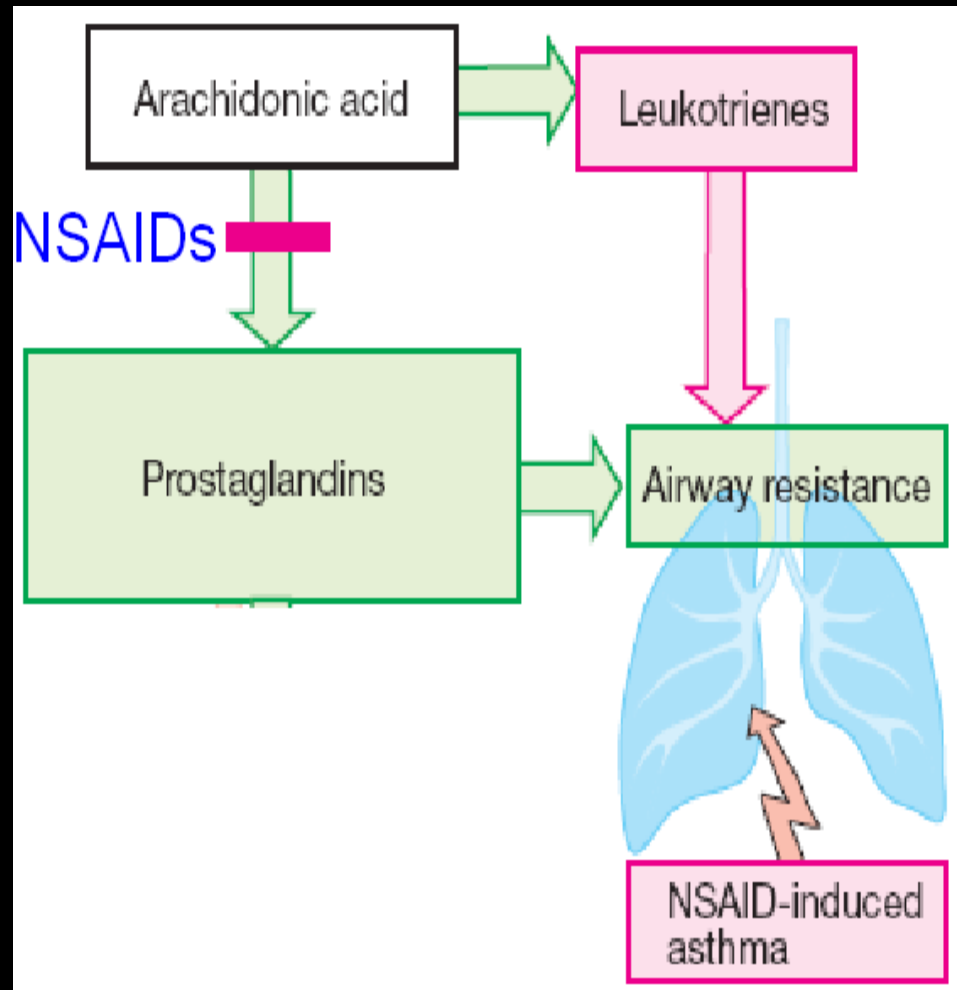
🌐GIT side effects, dyspepsia, nausea, vomiting

Mucosal damage → hemorrhage



ADRS AT CLINICAL DOSES

■ Bronchospasm in aspirin-sensitive asthmatics

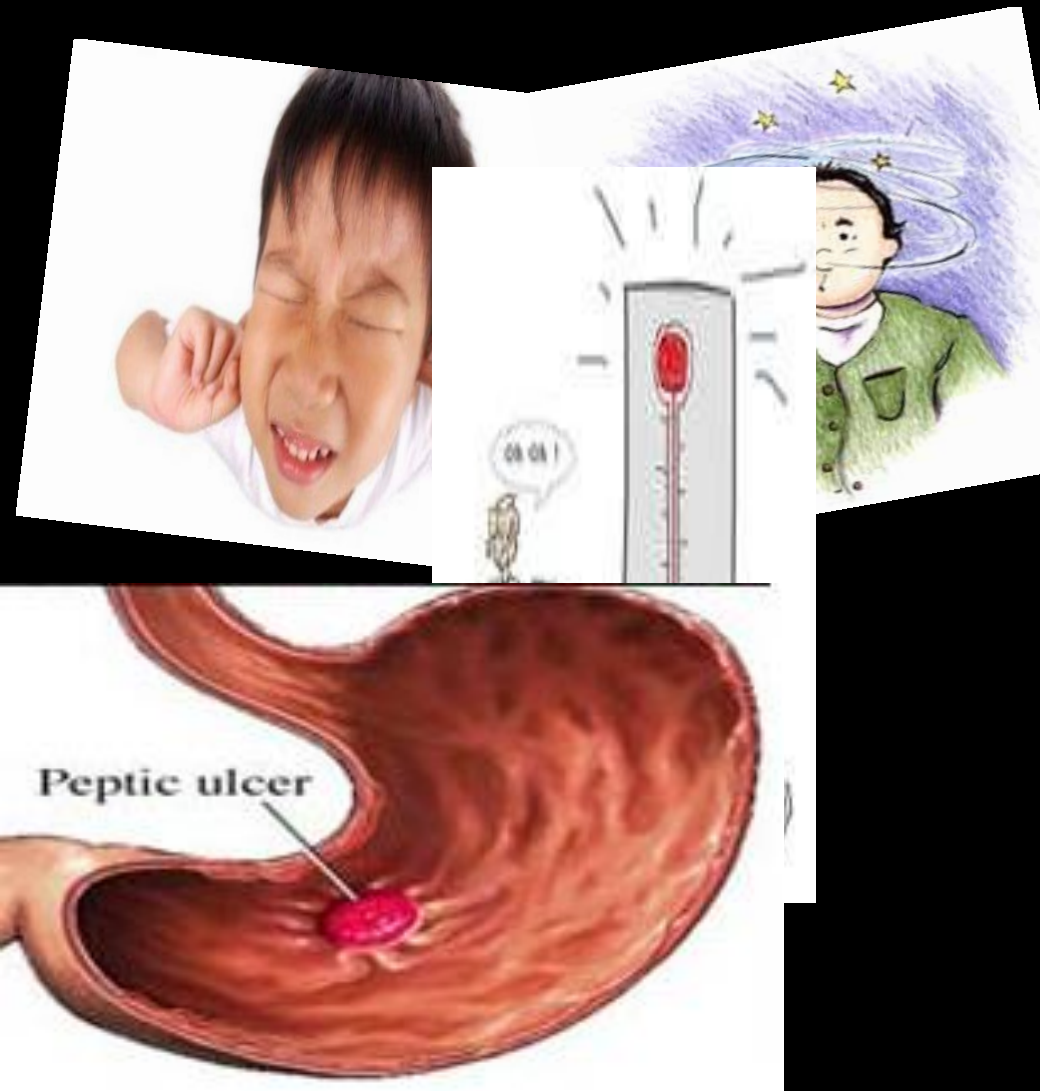


ADRS AT OVERDOSE

Salicylism (ringing of ear, vertigo)

Hyperthermia

Gastric ulceration & bleeding



CONTRAINDICATIONS

Peptic ulcer

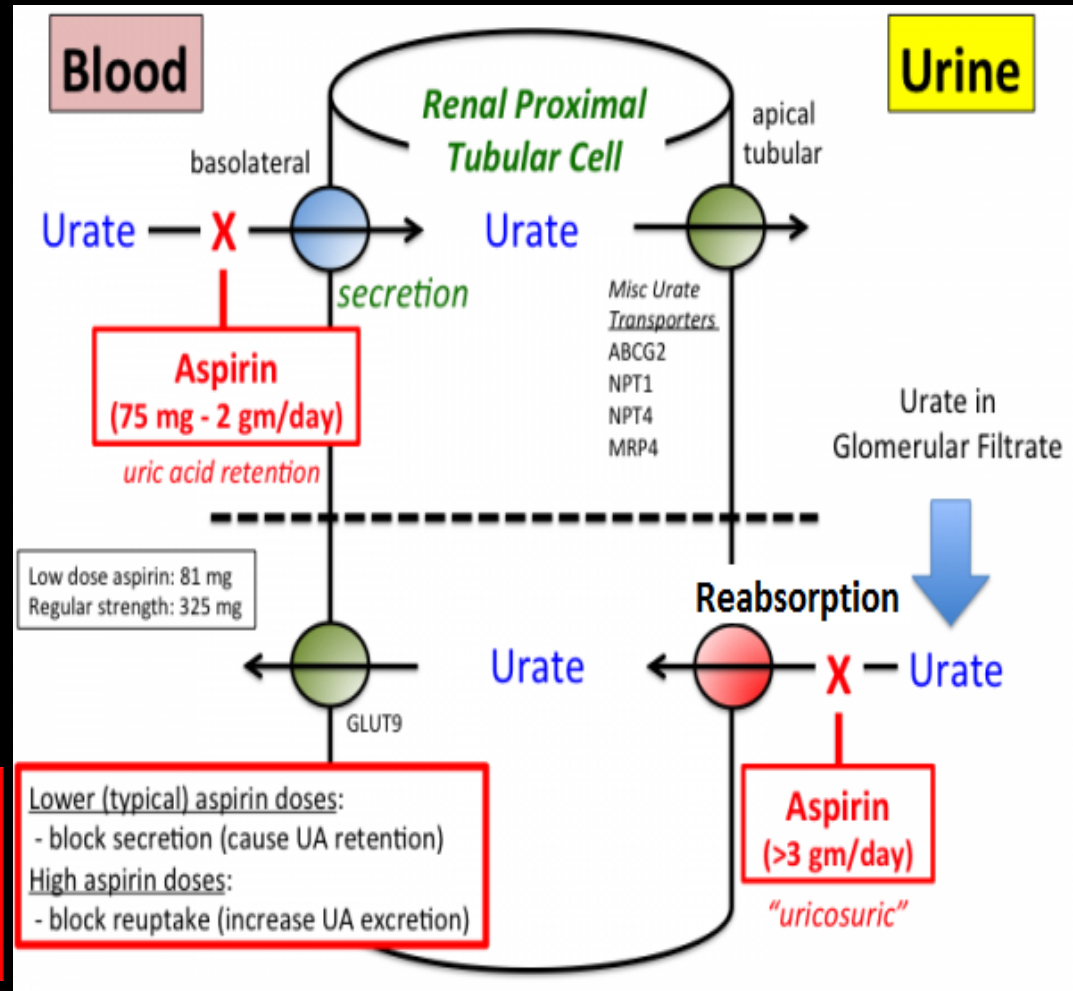
Pregnancy

Hemophilic patients

Patients taking anticoagulants

Children with viral infections

Gout (small doses)



NON SELECTIVE COX INHIBITORS



CLINICAL USES

○Analgesic

○Antipyretic

Anti inflammatory

○Acute gouty arthritis

○Locally to prevent post- operative ophthalmic inflammation (solution)

PREPARATIONS

Diclofenac with misoprostol decreases upper gastrointestinal ulceration, but results in diarrhea.

Diclofenac with omeprazole to prevent recurrent bleeding

0.1% ophthalmic preparation for postoperative ophthalmic inflammation.

A topical gel 3% for solar keratoses.

Rectal suppository as analgesic

Oral mouth wash.

Intramuscular preparations



SELECTIVE COX-2 INHIBITORS

○ Celecoxib

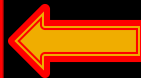
○ Etoricoxib

○ Paracoxib

○ Lumiracoxib

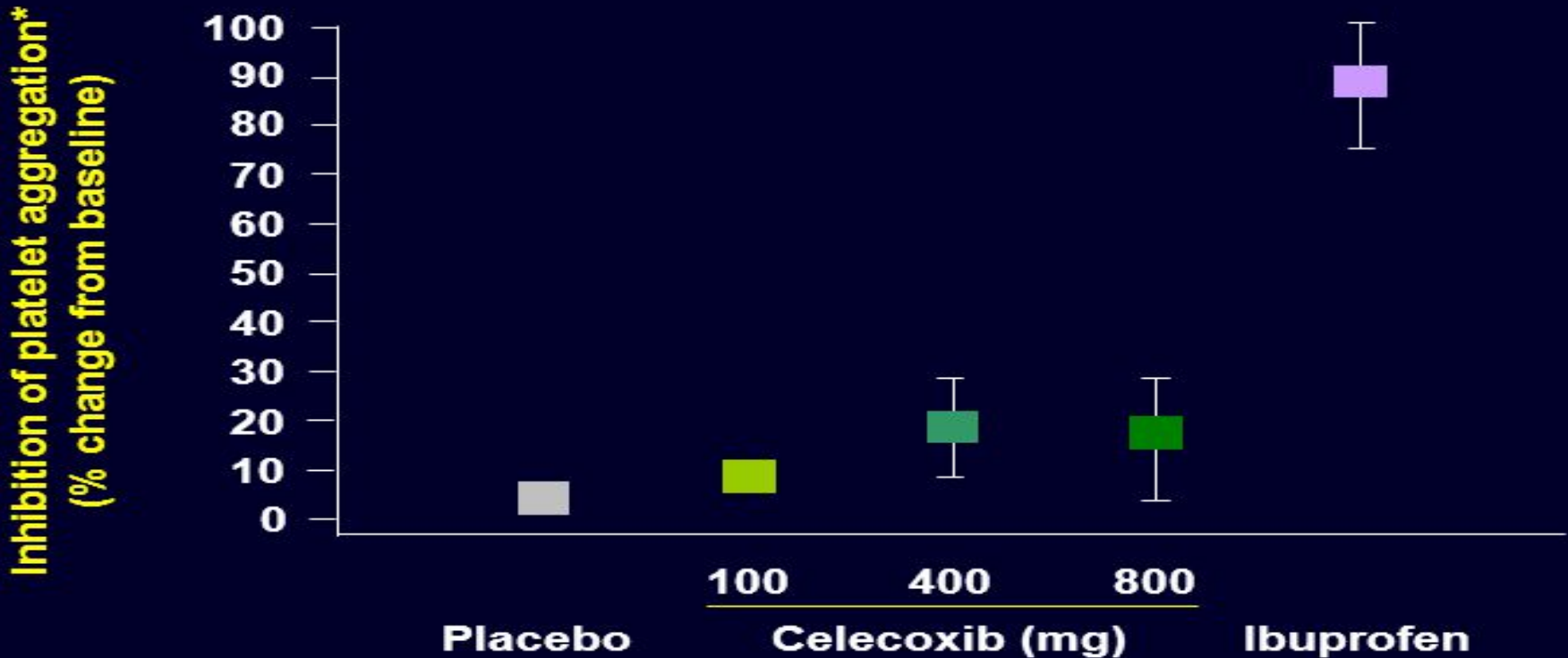
○ Rofecoxib

○ Valdecoxib



Withdraw
because of
risk of
myocardial
infarction &
stroke

SELECTIVE COX-2 INHIBITORS



○ No effect on platelet aggregation (COX-1)

GENERAL ADRS

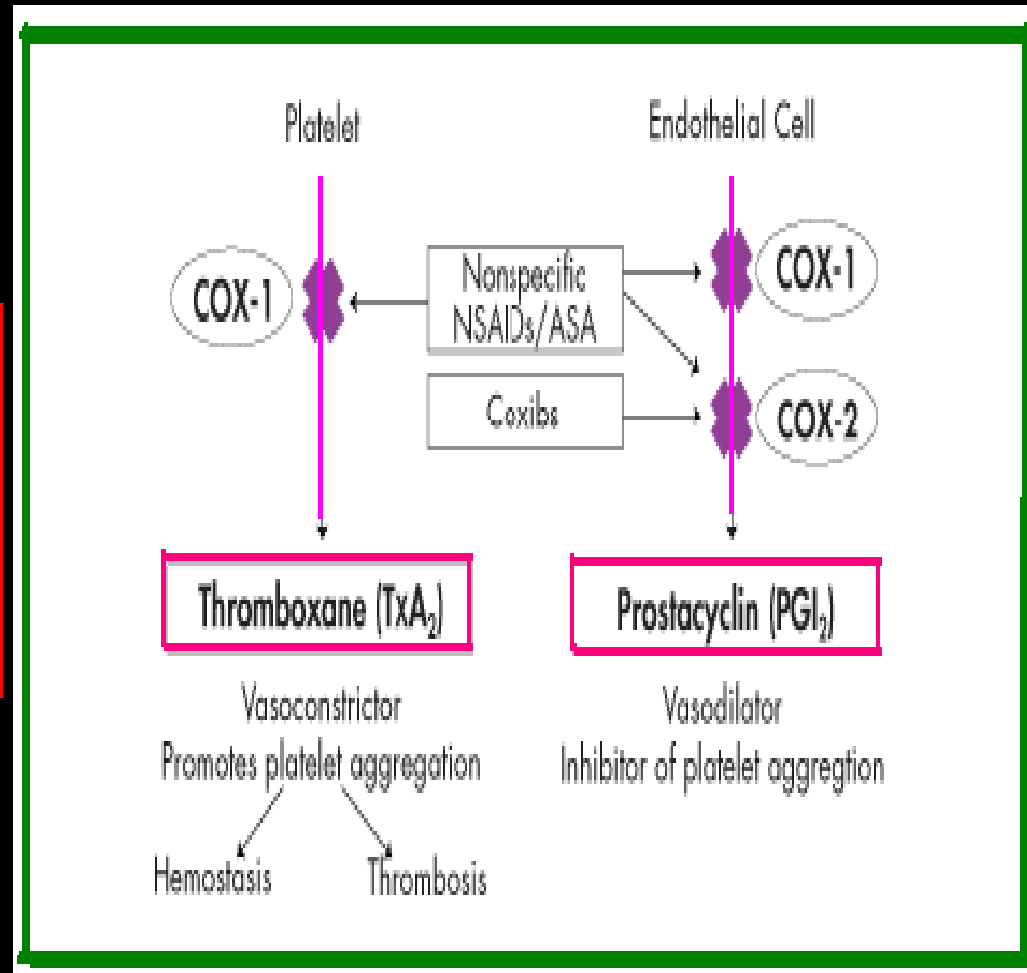
Renal toxicity

Dyspepsia & heartburn

Allergy

Cardiovascular (do not offer the cardioprotective effects of non-selective group).

Should not be given to a patient with CV disease



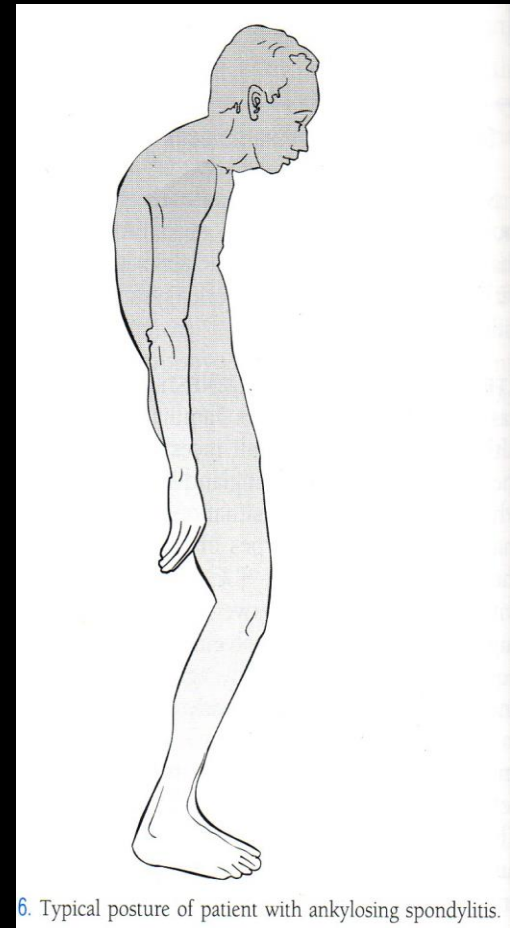
GENERAL CLINICAL USES

Short-term use in postoperative patients

Acute gouty arthritis

Acute musculoskeletal pain

Ankylosing spondylitis



6. Typical posture of patient with ankylosing spondylitis.

SELECTIVE COX-2 INHIBITORS

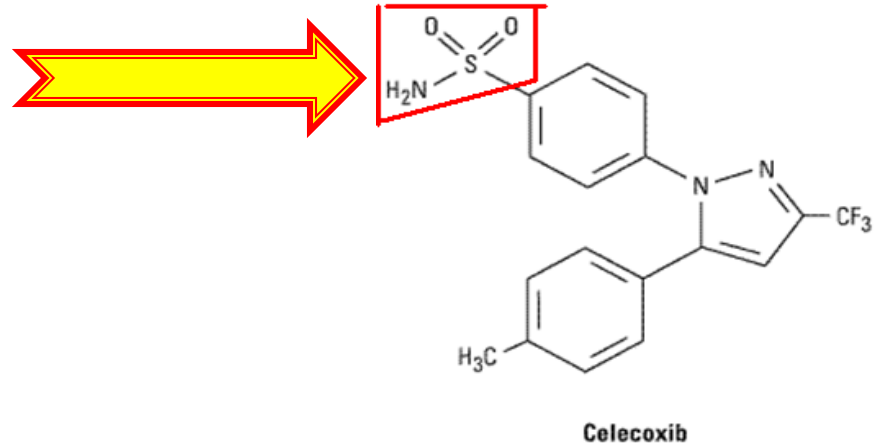


Half-life 11 hours

Food decrease its absorption

Highly bound to plasma proteins

Contra indicated in patients allergic to sulphonamides



PREFERENTIAL COX-2 INHIBITORS



- Preferentially inhibits COX-2 over COX-1, particularly at low dose

- Associated with lower GI symptoms & complaints, compared to non-selective COX inhibitors

- $t_{1/2} = 20$ hours

- Used for osteoarthritis & rheumatoid arthritis

COX-3 INHIBITORS

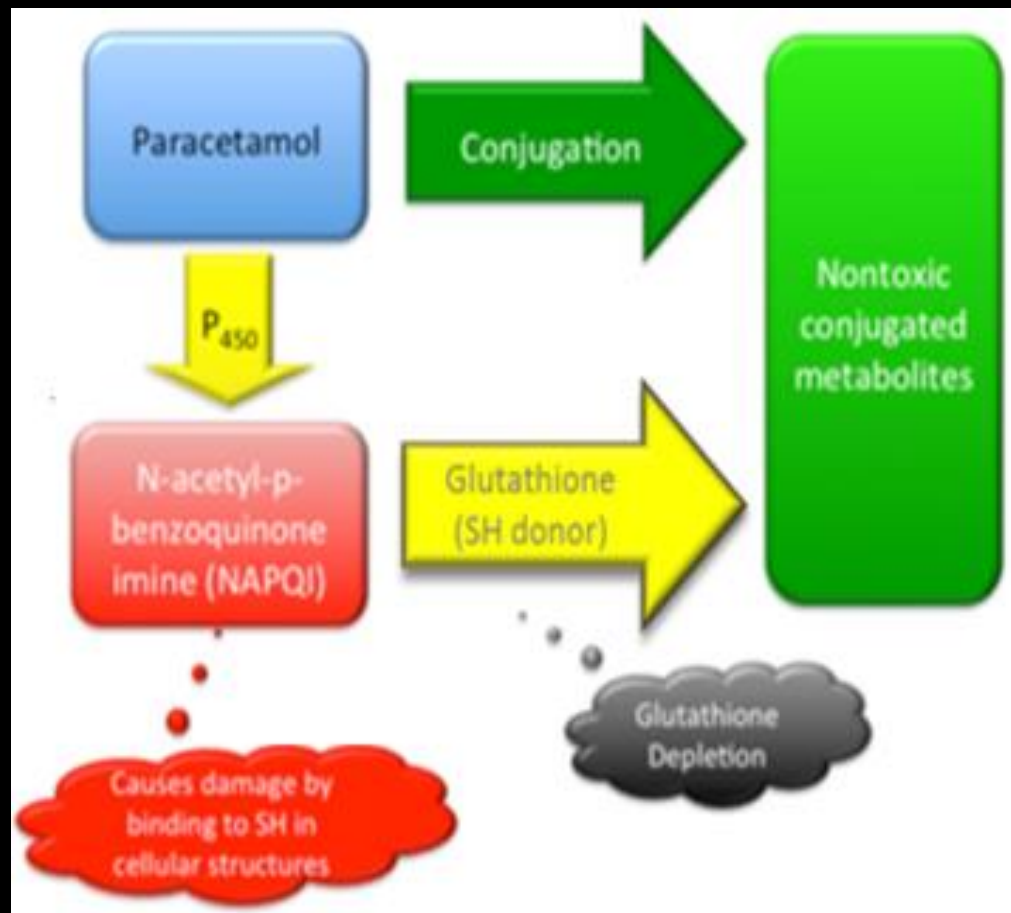


Weak anti inflammatory effect

Given orally , well absorbed.

$t_{1/2} = 2-4h$

Metabolized by conjugation at therapeutic doses



CLINICAL USES

Commonly used analgesic antipyretic instead of aspirin in cases of:-

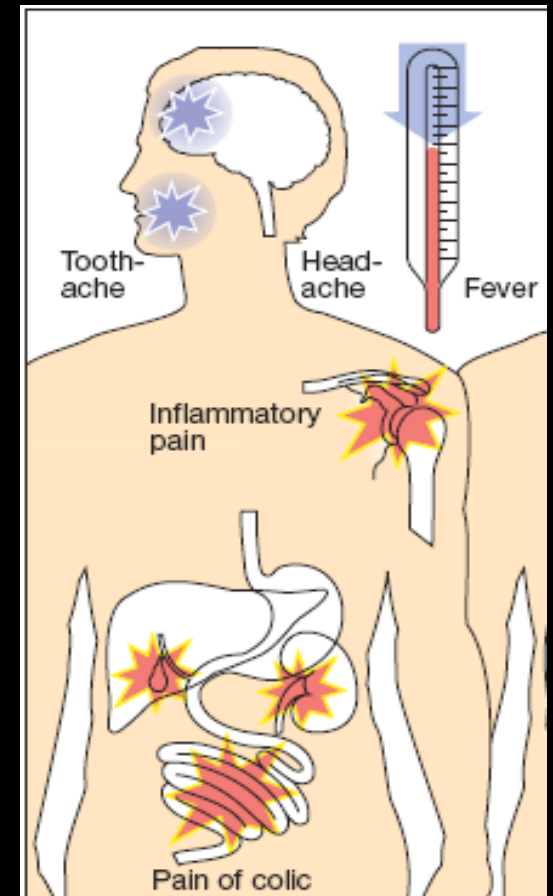
Peptic or gastric ulcers

Bleeding tendency

Allergy to aspirin

Viral infections in children

Pregnancy



ADRS

Mainly on liver due to its active metabolite

Therapeutic doses elevate liver enzymes

In large doses it is metabolized into N-acetyl-p-benzoquinone imine, which causes liver damage.

Treatment of toxicity of paracetamol is by **N-acetylcysteine** to neutralize the toxic metabolite

