

# NSAIDS EPIDEMIOLOGY

NSAIDs amounts to 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

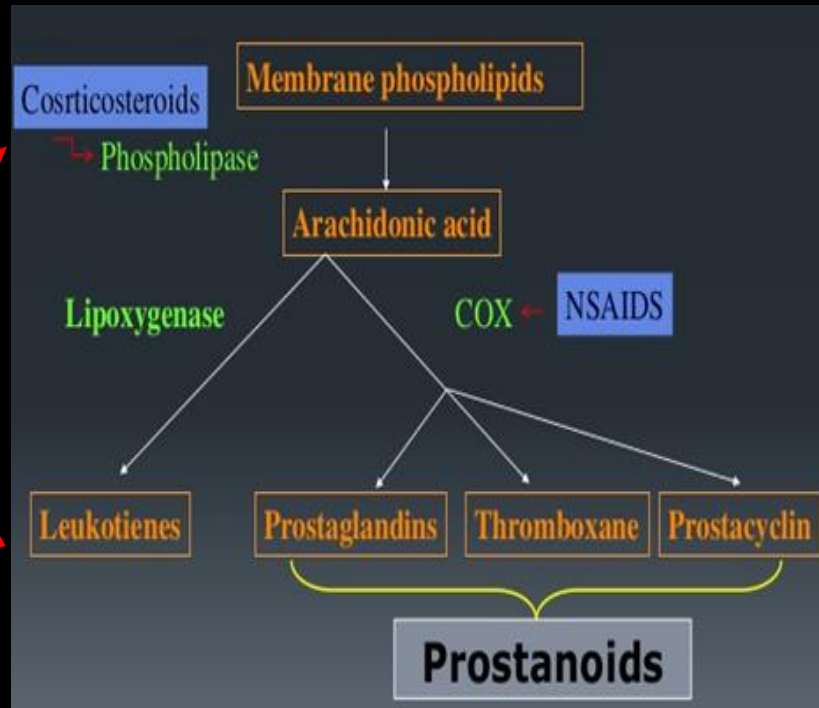
To classify NSAIDs on basis of their specificity to COX isoenzymes

To outline the common pharmacodynamic effects and ADRs of NSAIDs

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

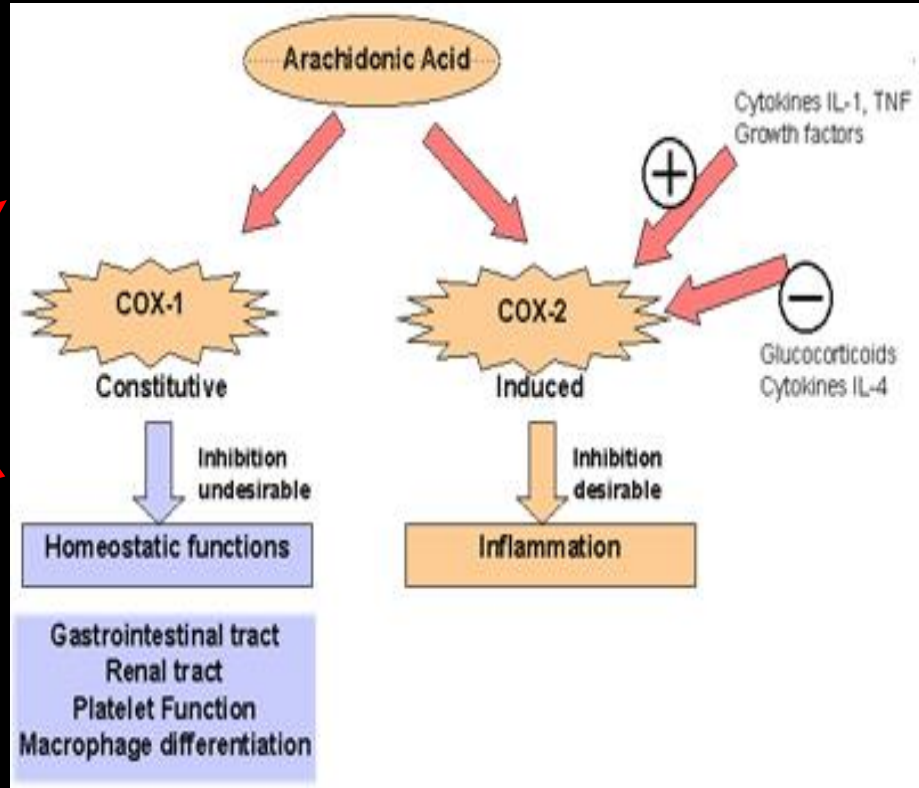
# MECHANISM OF ACTION OF NSAIDS

NSAIDs  
inhibit cyclo  
oxygenase  
enzyme



# COX ISOFORMS

**COX<sub>3</sub> is  
found in  
the brain**



# CLASSIFICATION OF NSAIDS

Nonselective COX-1/COX-2  
Inhibitors

Aspirin, Diclofenac

Selective COX-2  
Inhibitors

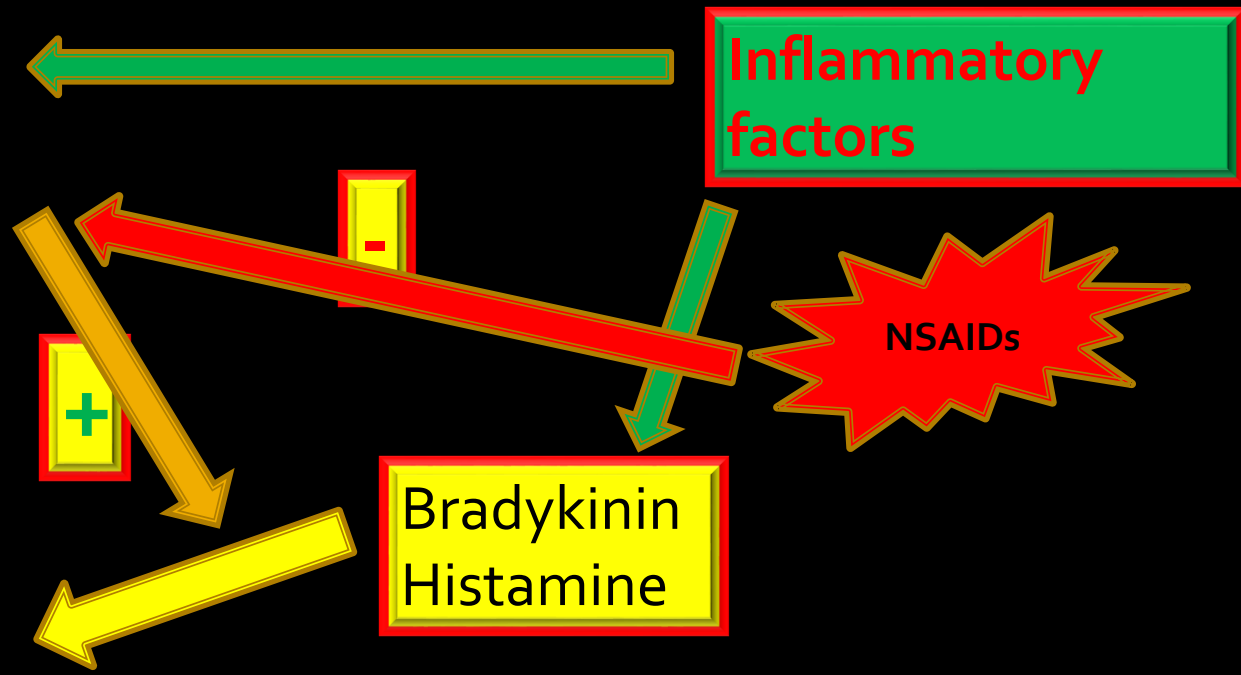
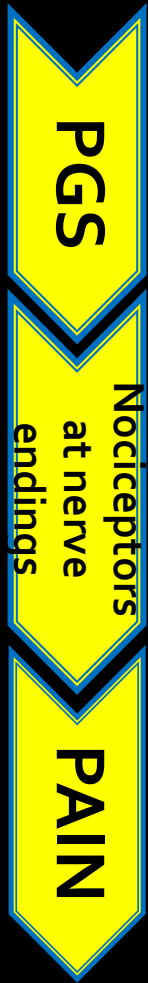
Coxibs

Preferential COX-2  
inhibitors

Meloxicam

COX-3 inhibitors

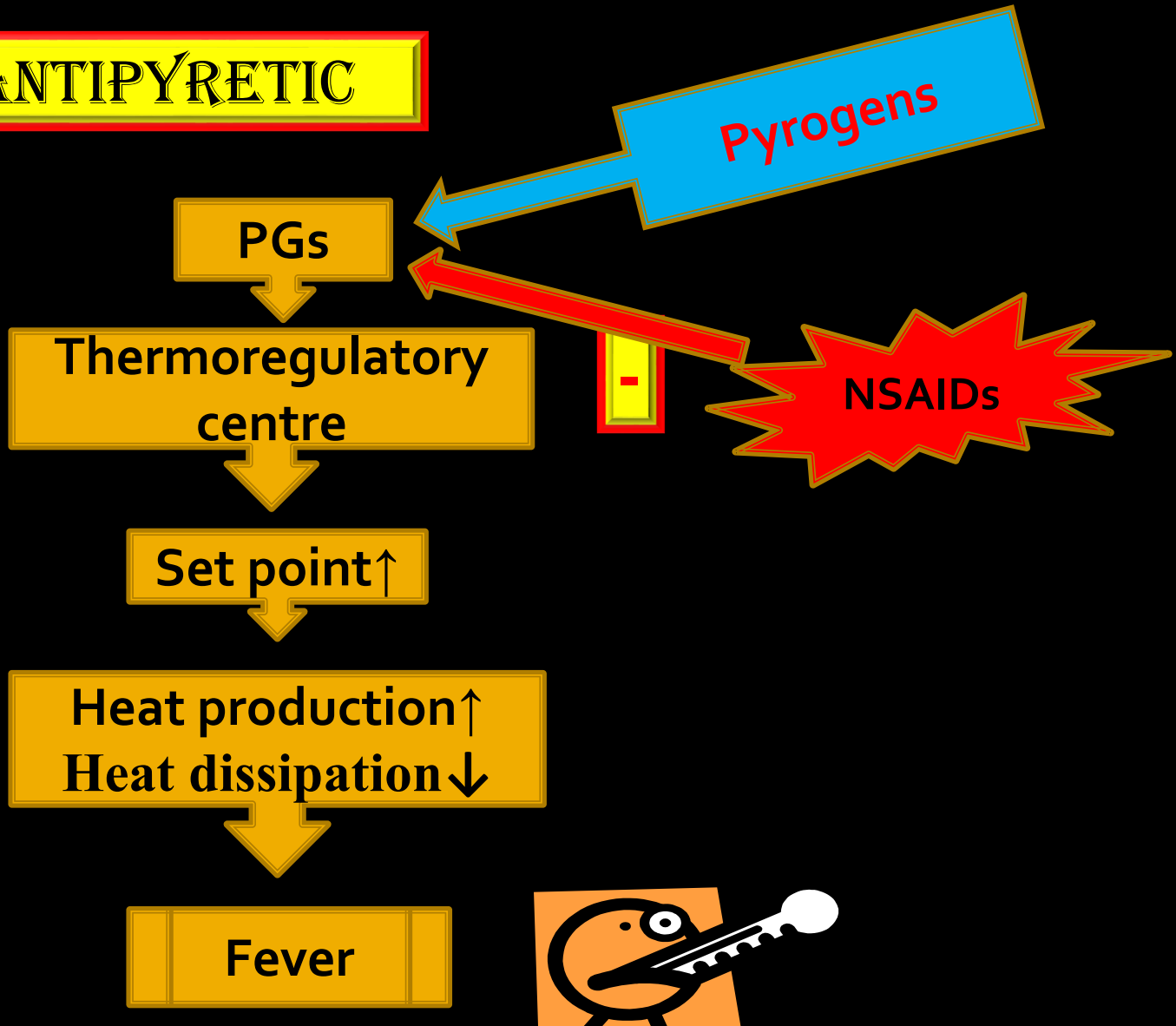
Paracetamol



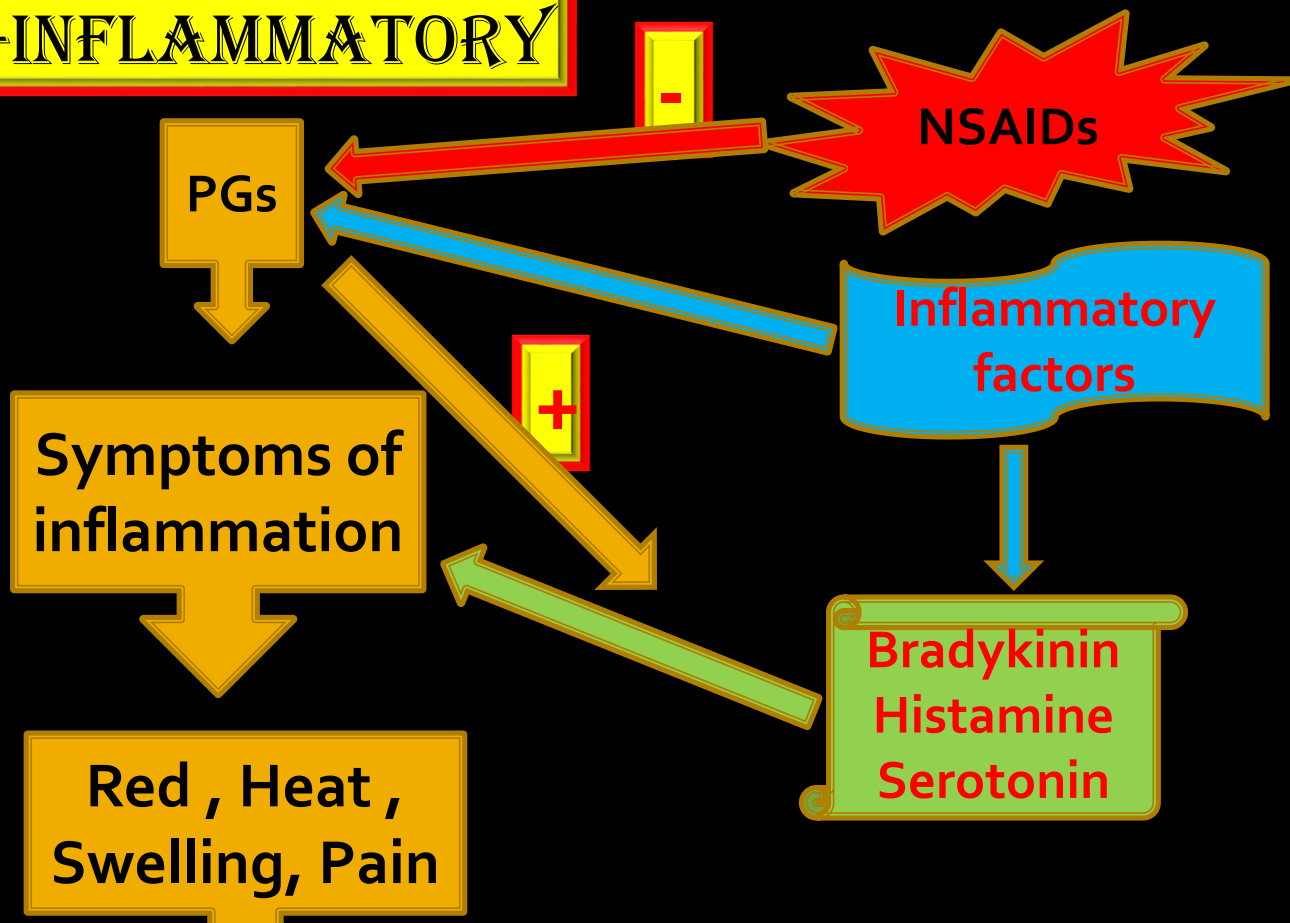
PHARMACODYNAMIC EFFECTS

1-ANALGESIC

# 2-ANTIPYRETIC



# 3-ANTI-INFLAMMATORY





# CLINICAL USES

Fever

Headache, Migraine,  
Dental pain, Dysmenorrhea

Common cold

Rheumatoid  
arthritis / myositis

# ADRS

GIT upsets (nausea, vomiting)

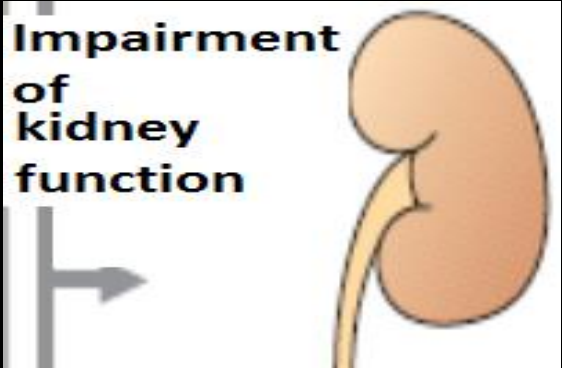
GIT bleeding & ulceration

Hypersensitivity reaction

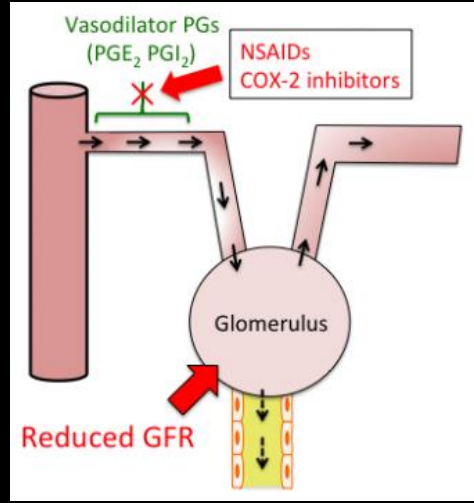
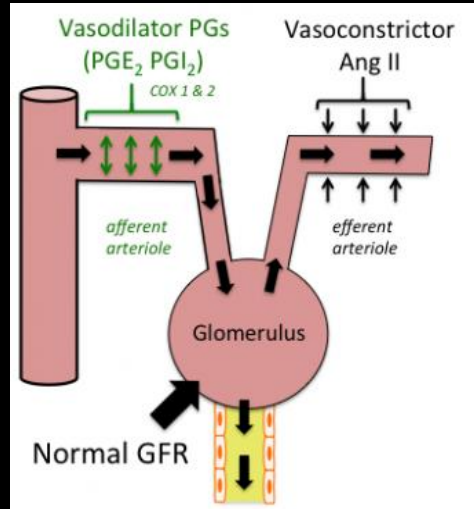
Inhibition of uterine contraction

Salt & water retention

# ADRS



NSAIDs cause hemodynamically-mediated acute renal failure



# NON SELECTIVE COX INHIBITORS

Aspirin

Diclofenac

Ibuprofen

Ketoprofen

Naproxen

Piroxicam

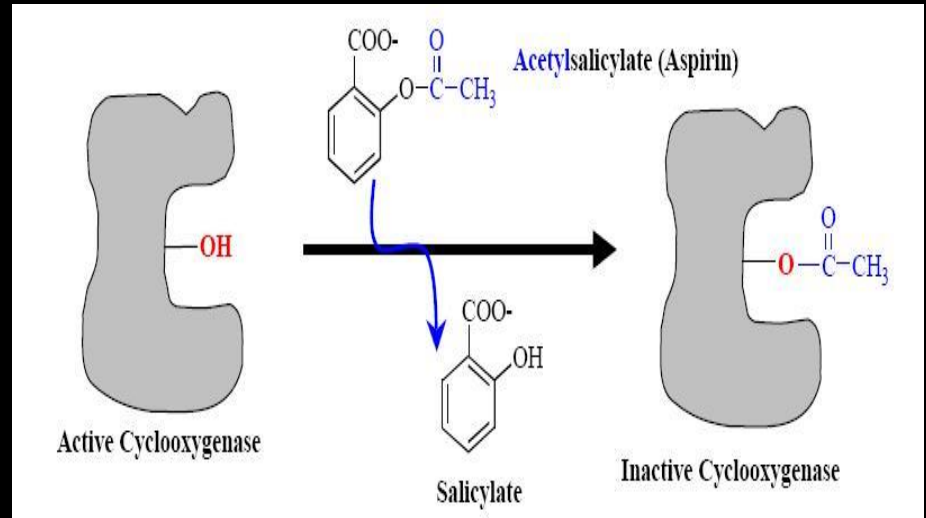
Indomethacin

# NON SELECTIVE COX INHIBITORS



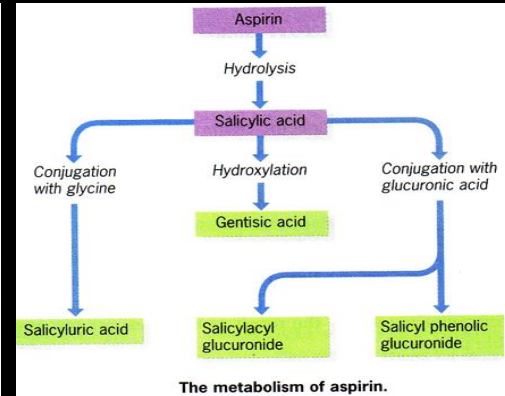
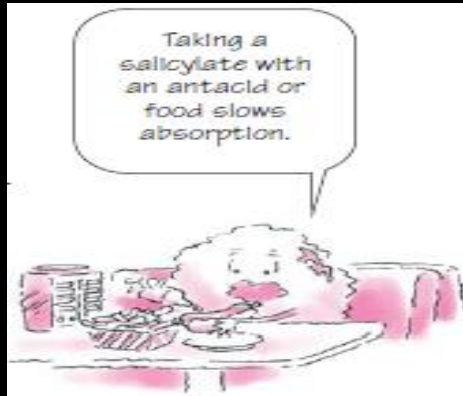
## MECHANISM OF ACTION

Aspirin  
inhibits COX  
irreversibly

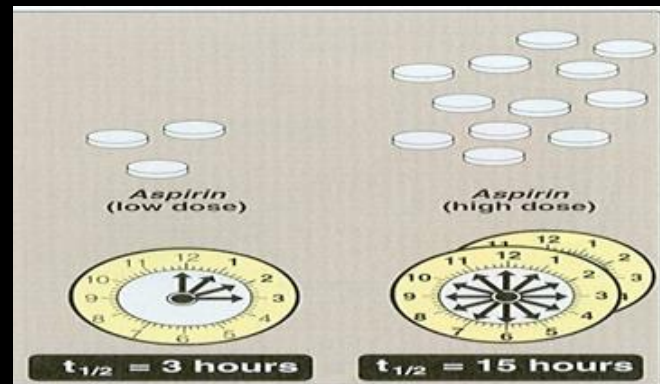


# PHARMACOKINETICS

Metabolized by hydrolysis and then conjugation



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



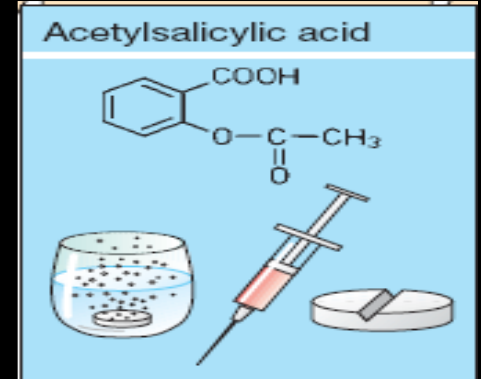
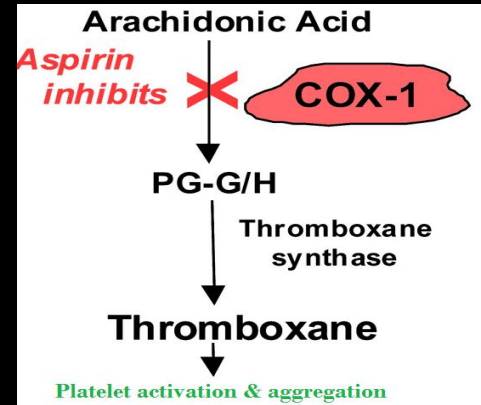
# CLINICAL USES

Acute rheumatic fever

Reducing the risk of myocardial infarction (cardioprotective)

Prevention of pre-eclampsia

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



Because they relieve muscle ache and reduce temperature, salicylates help treat symptoms of colds and influenza.



# ADRS AT CLINICAL DOSES

Hypersensitivity

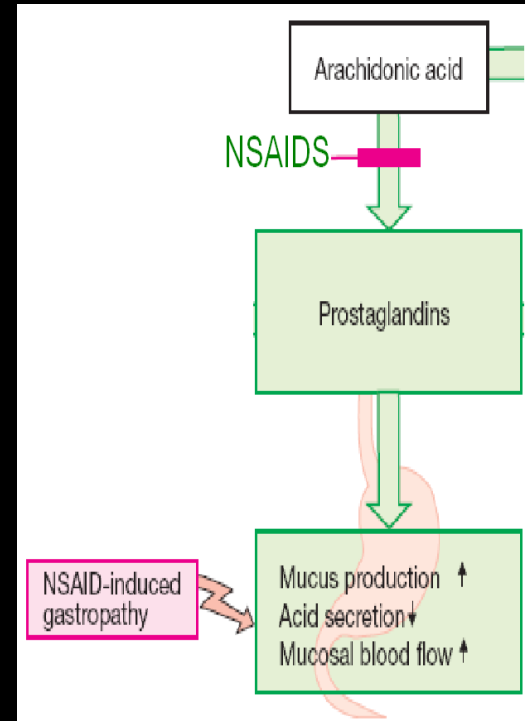
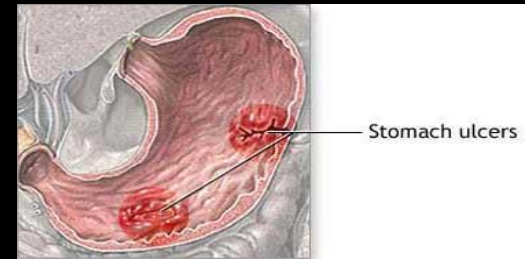
Acute Gouty arthritis

Reye's syndrome

Impaired haemostasis

🌐 GIT side effects, dyspepsia, nausea, vomiting

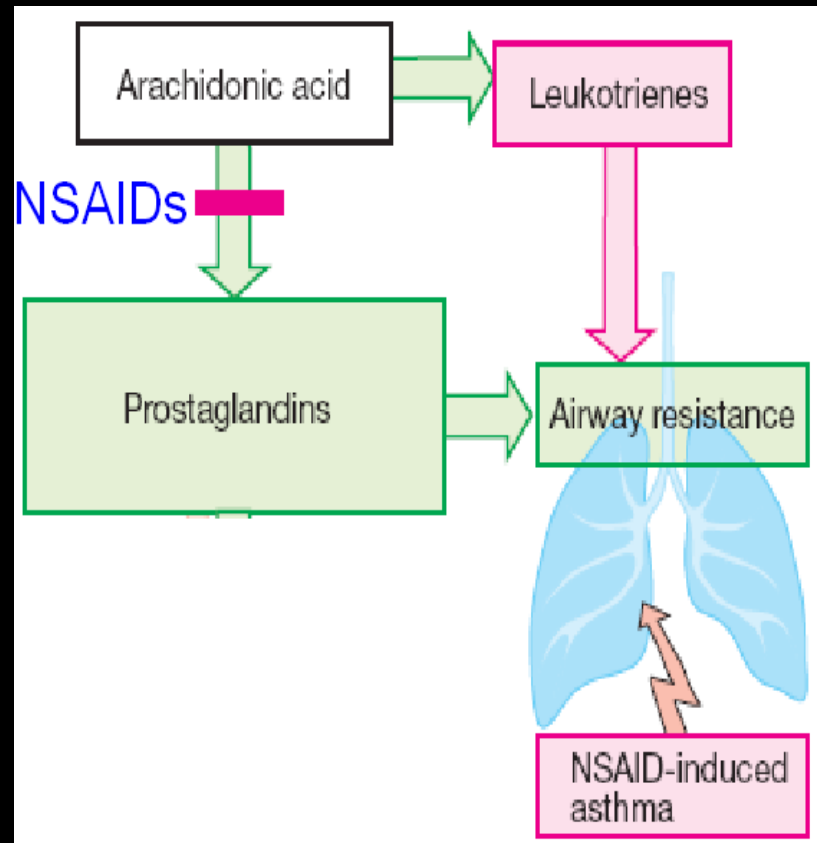
Mucosal damage → hemorrhage





# ADRS AT CLINICAL DOSES

■ Bronchospasm in aspirin-sensitive asthmatics

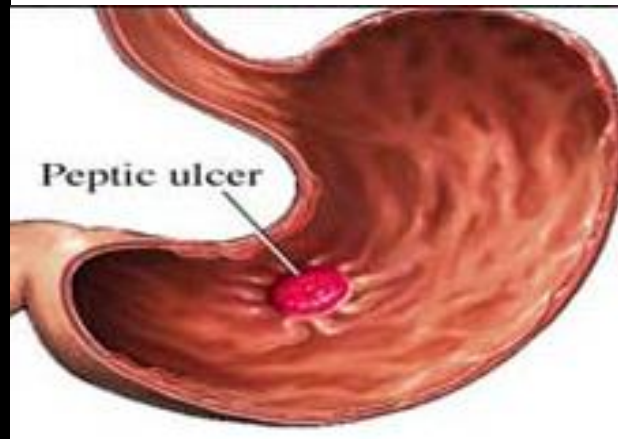


# ADRS AT OVERDOSE

Salicylism ( ringing of ear , vertigo)



Hyperthermia



Gastric ulceration & bleeding



# CONTRAINDICATIONS

Peptic ulcer

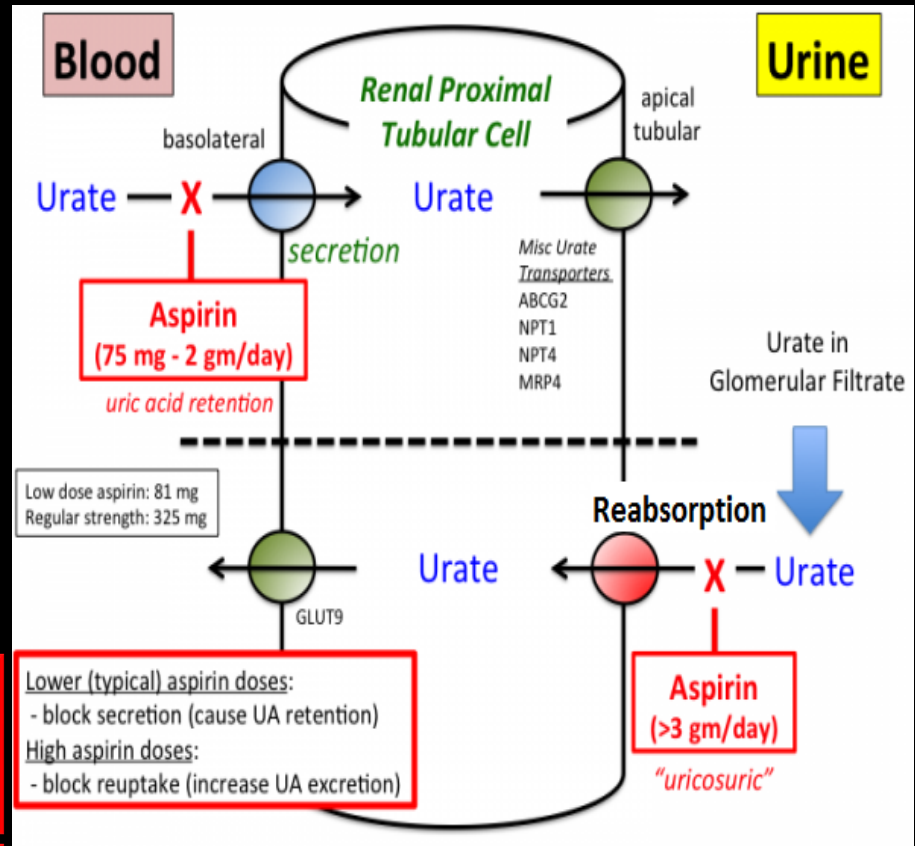
Pregnancy

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



Withdrawn  
because of  
risk of  
myocardial  
infarction &  
stroke

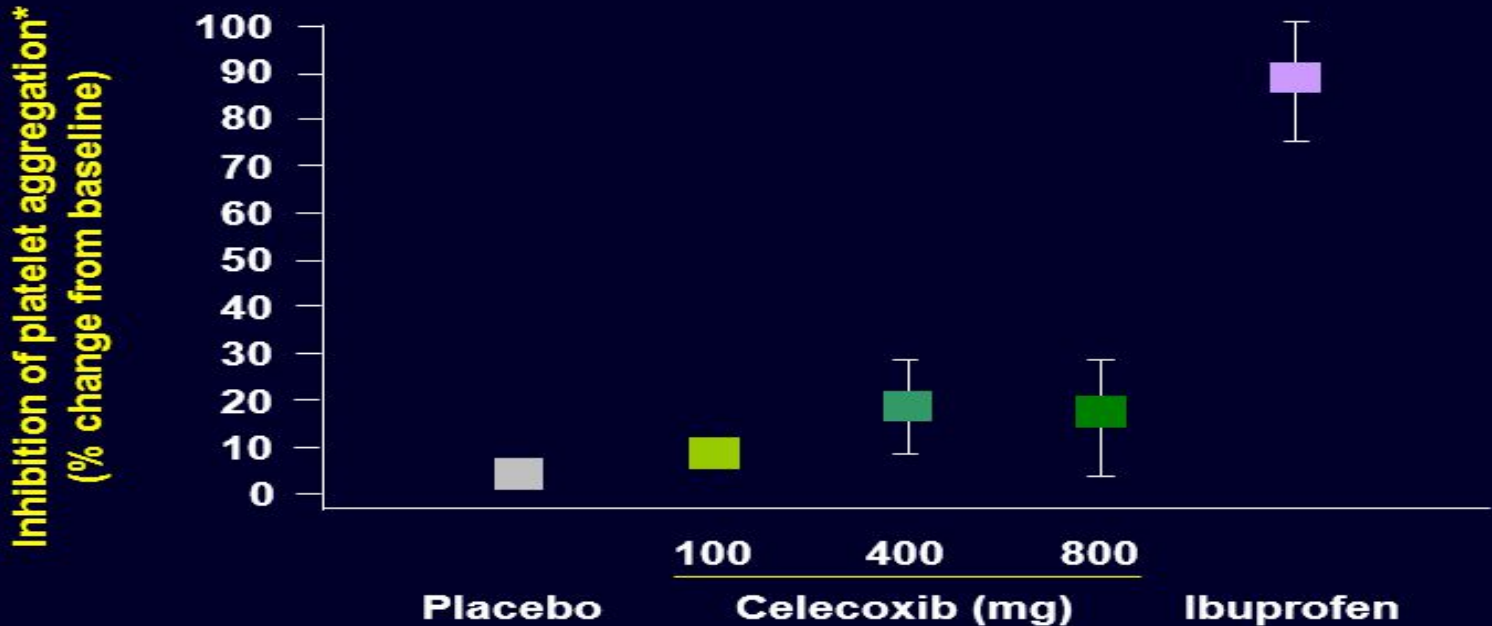
# SELECTIVE COX-2 INHIBITORS

- Potent anti-inflammatory

- Antipyretic & analgesic

- Lower incidence of gastric upset

# SELECTIVE COX-2 INHIBITORS



○ No effect on platelet aggregation (COX-1)



# GENERAL ADRS

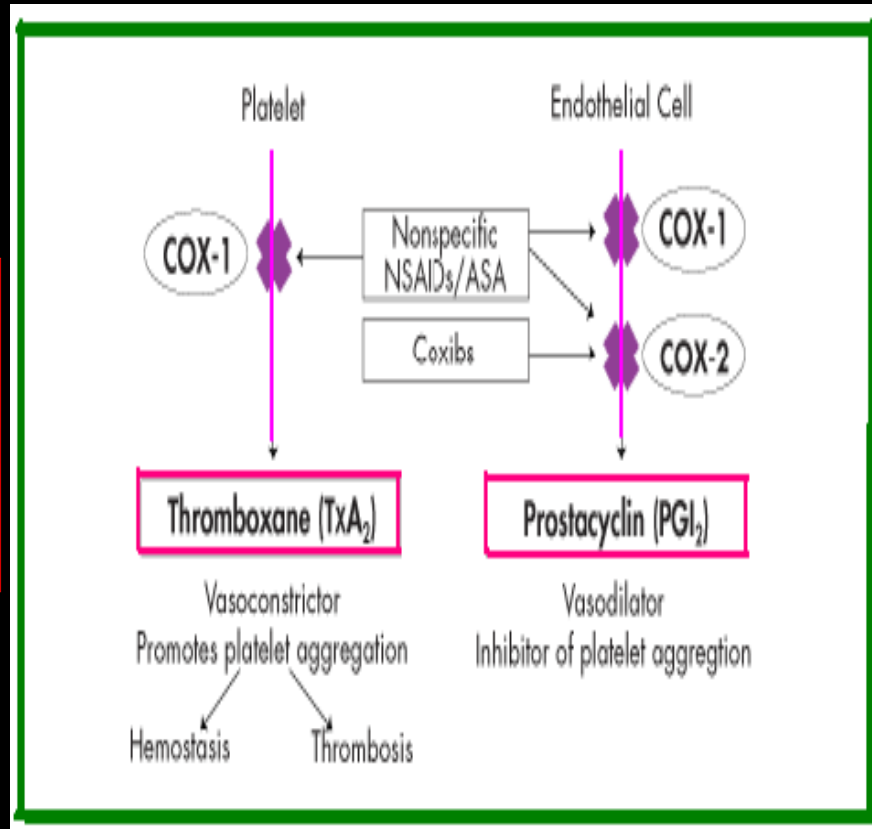
Renal toxicity

Dyspepsia & heartburn

Allergy

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

Should not be given to a patient with CV disease



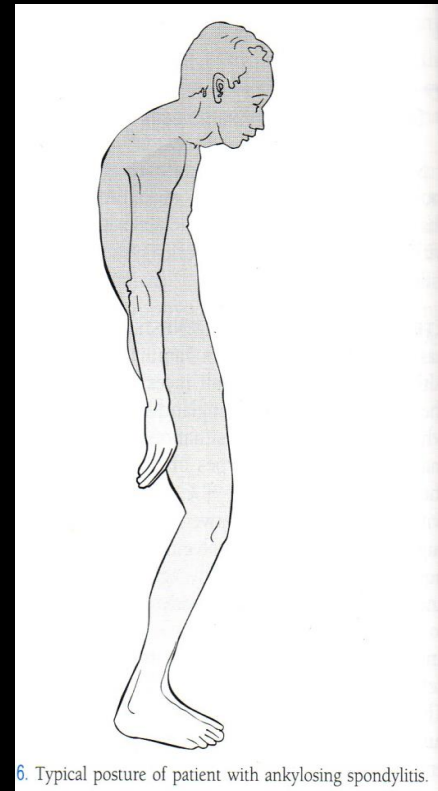
# GENERAL CLINICAL USES

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

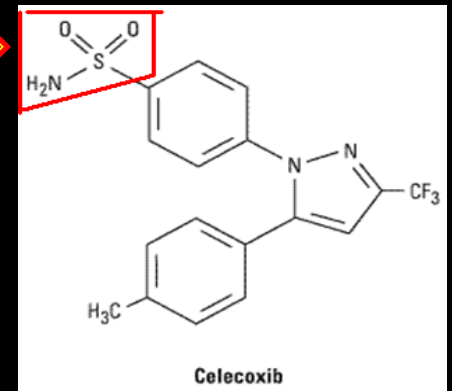


Half-life 11 hours

Food decrease its absorption

Highly bound to plasma proteins

Contra indicated in patients allergic to sulphonamides



# PREFERENTIAL COX-2 INHIBITORS

○ Meloxicam, nimesulide, nambumetone



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

○ Associated with lower GIT symptoms & complains, compared to non-selective COX inhibitors

○  $t_{1/2} = 20$  hours

○ Used for osteoarthritis & rheumatoid arthritis

# COX-3 INHIBITORS

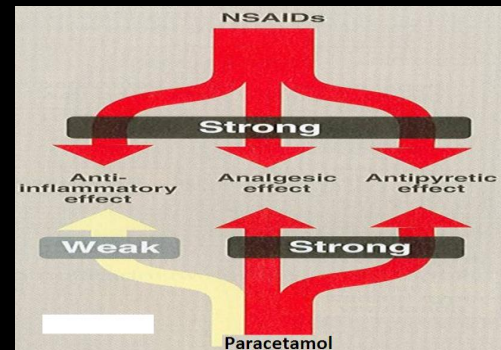
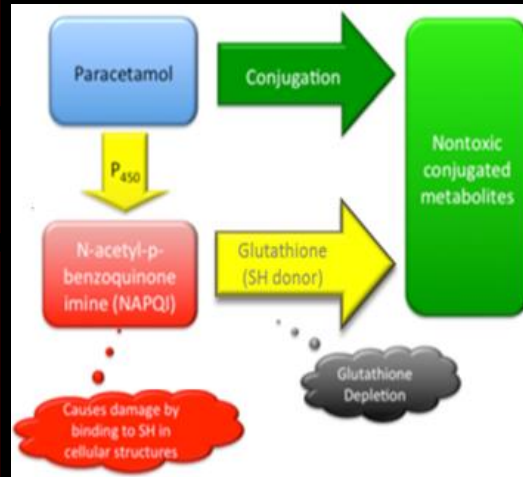
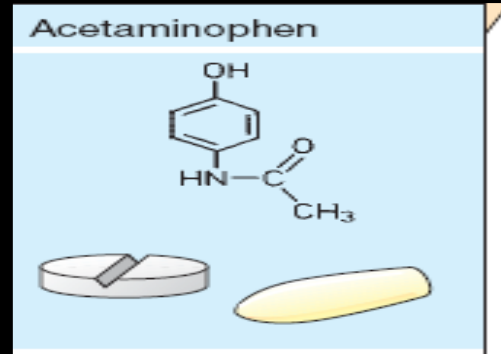


Weak anti inflammatory effect

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:-

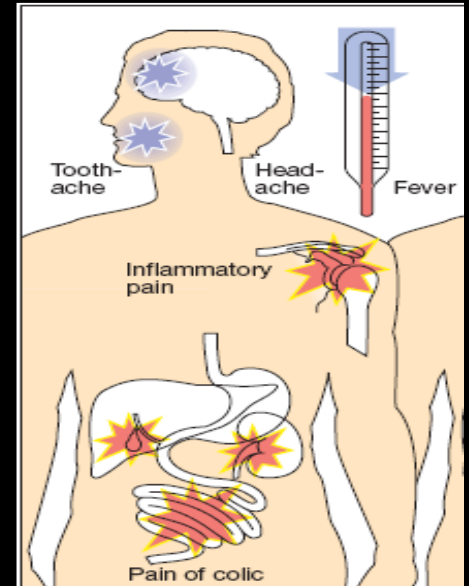
Peptic or gastric ulcers

Bleeding tendency

Allergy to aspirin

Viral infections in children

Pregnancy



Acetaminophen is the drug of choice to treat fever and flu-like symptoms in children.



# ADRS

*Binding of paracetamol to COX is inhibited by peroxides produced in inflammatory sites.  
There is no evidence that COX<sub>3</sub> exists in humans.*

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

