CLASSIFICATION OF NSAIDs

1) COX-1 SELECTIVE INHIBITORS
   - acetylsalicylic acid at low dosage
2) NONSELECTIVE COX INHIBITORS
   - acetylsalicylic acid at high dosage
   - diclofenac
   - ibuprofen
   - ketoprofen
   - flurbiprofen
   - indomethacin
   - piroxicam
   - naproxen
3) MORE COX-2 SELECTIVE INHIBITORS
   - nimesulid
   - etodolak
   - meloxicam
   - nabumeton
4) COX-2 SELECTIVE INHIBITORS
   - celecoxib
   - etorcoxib
   - valdecoxib

ANTI-INFLAMMATORY EFFECTS OF NSAIDs

This effect of NSAIDs is due to the inhibition of the enzyme COX, which converts arachidonic acid to prostaglandins, TXA2 and prostacyclin.
Acetylsalicylic acid irreversibly inactivates COX-1 and COX-2 by acetylation of a specific serine resideu.
Other NSAIDs reversibly inhibit COX-1 and COX-2
Additional anti-inflammatory mechanism may include:
- interference with the potentiative action of other mediators of inflammation – bradykinin, histamine, serotonin
- modulation of T-cell function
- stabilization of lysosomal membranes
- inhibition of chemotaxis

ANALGESIC EFFECT OF NSAIDs

This effect of NSAIDs is thought to be related to the peripheral inhibition of prostaglandin production, but it may also be due to the inhibition of pain stimuli at a subcortical site.
NDAIDs prevent the potentiating action of prostaglandins on endogenous mediators of peripheral nerve stimulation (e.g. bradykinin)

ANTIPYRETIC EFFECT OF NSAIDs

This effect is believed to be related to inhibition of the interleukin-1 and interleukin-6 induced production of prostaglandins in the hypothalmus and the „ resetting „ of the termoregulatory system, leading to vasodilation and increased heat loss

CLINICAL USES O NSAIDs

1) analgesia
2) inflammation
3) antipyresis
4) antiplateled effect
5) cancer preventive agents

ADVERSE EFFECTS OF NSAIDs

1) gastrointestinal effects: abdominal pain, gastric and duodenal ulcer, diarrhea, pancreatis gastrointestinal hemorrhage, hepatotoxicity
2) renal effects
   - disturbances of renal function with water and sodium retention
3) inhibition of platelet aggregation
4) central symptoms: headache, decreased hearing, tinnitus, dizziness, confusion, dpression
5) allergic reactions: asthma, rashes, photosensitivity

PHARMACODYNAMIC INTERACTION NSAIDs WITH OTHER DRUGS

NSAIDs + hypotensive drugs (β-blockers, ACE-inhhibitors, diuretics) = ↓ hypotensive effect
NSAIDs + ehanol = ↑risk of bleeding from gastrointestinal tract
NSAIDs + ticlopidine or clopidogrel = ↑risk of bleeding
NSAIDs + lithium = ↑lithium toxicity
NSAIDs + cylosporine or ACE-inhibitors or takrolimus= ↑nephrotoxicity of drugs
NSAIDs + fluoroquinolons = ↑ toxic action of fluoroquinolons on CNS
NSAIDs +oral antidiabetic drugs =↑ risk of hypoglycemia
NSAIDs + cumarines = ↑risk of bleeding from gastrointestinal tract

PHARMACOKINETIC INTERACTION NSAIDs WITH OTHER DRUGS

NSAIDs + oral antidiabetic drugs = ↑ risk of hypoglycemia
NSAIDs + cumarines =↑risk of bleeding
NSAIDs + corticosteroids = ↑risk gastropathy and bleeding from gastrointestinal tract
NSAIDs + aminogycosides = ↑ ototoxicity and nephrotoxicity of aminogycosides
NSAIDs + fenytoine or valproinic acid = ↑action of fenytoine or valproinic acid
NSAIDs + metotrexat or digoxin = ↑action and ↑ toxicity metotrexat or digoxin
NSAIDs + tricycles antidepressive drugs neuroleptics or antiarrhytmic drugs or selective serotonin reuptake inhibitors (SSRI) = ↑ action of drugs