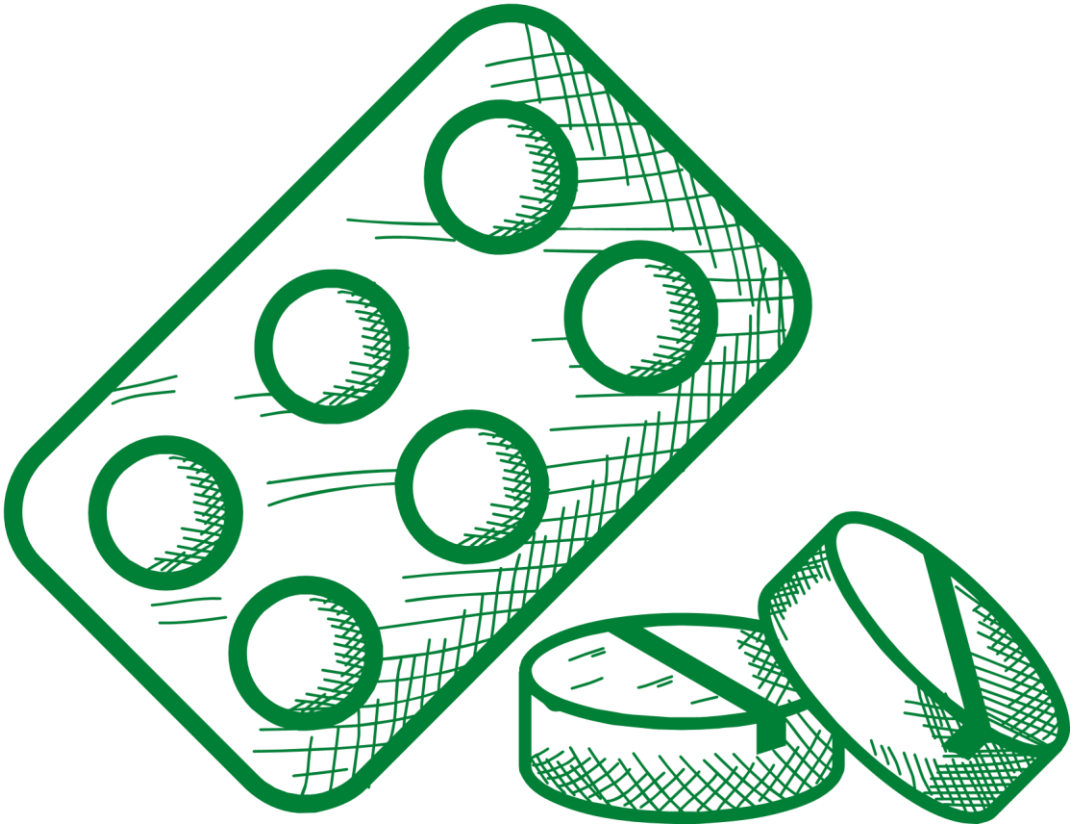
MSS

Sheet no.

Pharmacology



NSADs:

Writer: Yamama al lemon
Corrector: Alia shatnawi
Doctor: jana zaidan- Yamama al lemon

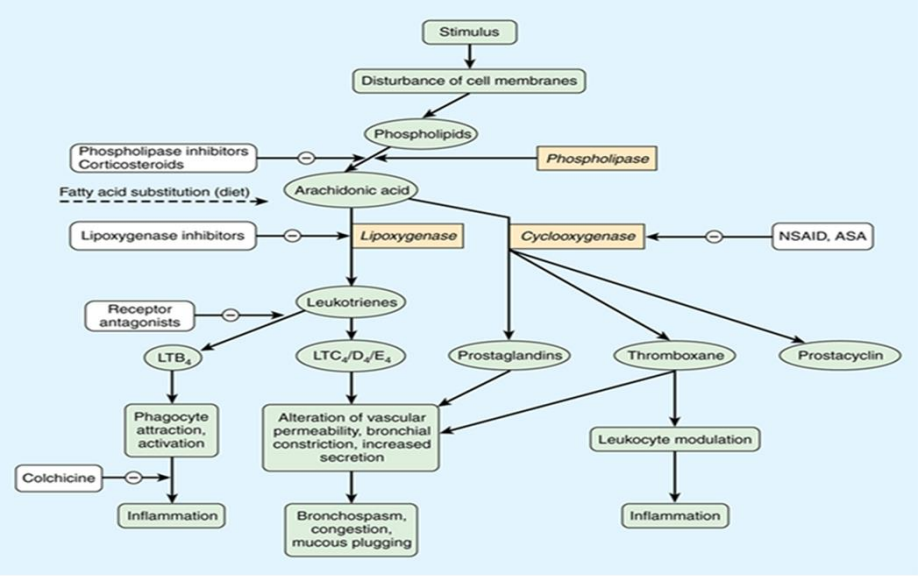
Universal, Complex, Subjective experience

- No. 1 Reason people take medications.

People seek medical treatment.

- Generally is related to some type of tissue damage and serves as a warning signal. Pain is alarming sign so there is something wrong on our body, it's usually tissue damage, its warning signal for the person to take action related to the damage .

A lot of pain associated with cytokines released from our body in response to a trigger like prostaglandins.



when any stimulus disrupt plasma membrane (in injuries) , the phospholipase c will convert certain kind of phospholipids to produce arachidonic acid (the corticosteroids is inhibitors of phospholipase c , so that's why they are antinflamatory drugs , they blockage the central step of inflammatory pathway) , the arachidonic acid have two pathways ; either by cyclooxygenase enzyme or lipoxygenase enzyme , the first one (cox) is responsible for production of prostaglandins which control the action of inflammatory system (NSADs work by cox pathway) , the another pathway is continued later .

Pain killers

Pain is unpleasant sensation that can either be acute or chronic, usually related to some type of tissue damage and serves as a warning signal

- Derived from Greek an- "without" & -algia "pain". So make the person not to feel the pain.

- An analgesic, or painkiller, is any member of the group of drugs used to achieve analgesia — relief from pain .

- Drugs that relieve pain selectively without blocking

the conduction of nerve impulses, markedly altering

sensory perception, or affecting consciousness.

local anesthetics : its mechanism unlike analgesic , it prevent conduction of pain , they affect nerne endings by blocking voltage gated channel like sodium channels .

- Act in various ways on the peripheral and central nervous systems

The drugs that work on central nervous system are called Narcotic (or opioids), on the other hand Non-Narcotic drugs (nonopioids) belong to a group of drugs called non-steroidal anti-inflammatory drugs (NSAIDs).

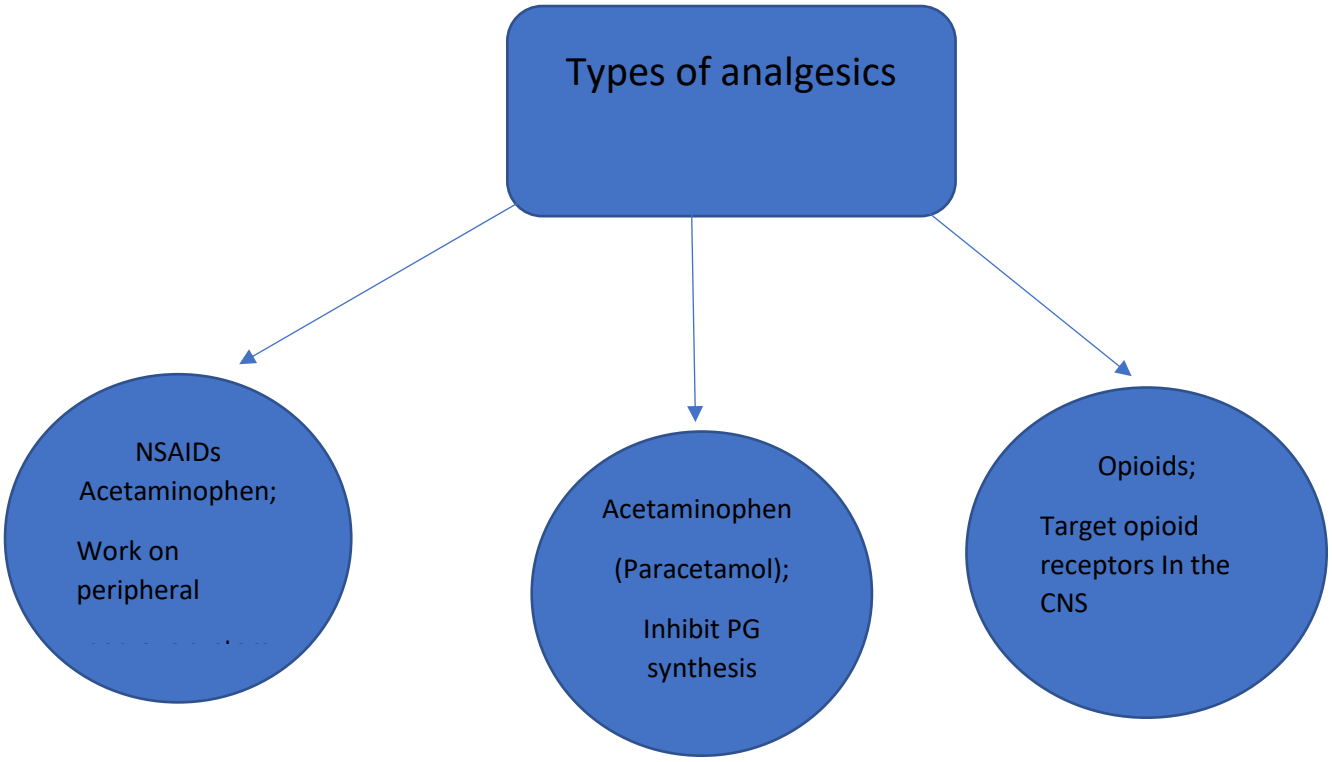
Feature	Narcotic (Opioids)	Nonnarcotic (nonopioid)
	One of these drugs is opium , natural drug , and we rely on it for categorizing this group	
Efficacy	Strong	Weak
Prototype	Morphine	Aspirin
Pain Relieved	Any Type	Musculoskeletal
Site of Action	Central	Peripheral and Central
Mechanism	Specific Receptors	PG Synthesis
	Opioid receptor	prostaglandin
Danger	Tolerance & Dependence	G.I irritation
Anti-inflammatory	No	Yes
Antipyretic	No	Yes
		خافض للحراره
		Like paracitamol
Antiplatelets	No	Yes
		Like aspirin , we give it prophylactically
		To reduce thromboembolic diseases

For visceral pain like in cancers and surgeries. We don't give it often for migraine because it causes abuse because migraine is chronic condition.

At such drugs like ibupofen Doctors advice not to take it at empty Stomach , especially if those pepole

Have chronic disease like rhumatid arthritis and they have to take pills continusly or for peptic ulcer , because the food forms protection layer from high exposure of somach to the drugs

هاد الكلام للصندوق اللي عليه نقطه اصفر , ما قدرت احطو فيه



Why we separate paracitamol from NSAIDs group and why its useage is very common , because its inflammatory effects is minimal so when suffer just from headache or any pain doesn't relates to inflammation ;it's the best option , also it doesn't have that effect on stomach , because it works more centrally than peripherally , centrally doesn't mean at center receptors but block cox pathway at CNS ,so it would be advised for peptic people .

NSADs is not advised for people have been infected of COVID 19, because some issues of concerns didn't advice to use.

NSAIDs;

The NSAIDs are a group of chemically dissimilar agents that differ in their antipyretic, analgesic, and anti-inflammatory activities. Chemically dissimilar it mean that they belong to different chemical group

Inhibiting the cyclooxygenase enzymes that catalyze the first step in prostanoid biosynthesis. The mechanism of action is the same in these drugs

>>>> decreased prostaglandin synthesis with both beneficial and unwanted effects

Inflammatory pathways

Cyclooxygenase (COX) pathway of arachidonate metabolism produces prostaglandins

Effects on blood vessels, on nerve endings, and on cells involved in inflammation.

The lipoxygenase pathway of arachidonate metabolism yields leukotrienes.

have a powerful chemotactic effect on eosinophils, neutrophils, and macrophages and promote bronchoconstriction and alterations in vascular permeability

lipoxygenase pathway;

which is involved in inflammatory conditions, they use arachidonic acid to produce different kinds of leukotrienes involved in inflammation, cause phagocyte attraction , alteration of vascular permeability , increased secretion ,bronchoconstriction , which lead to bronchospasm , congestion , mucus plugging .

(some drugs like atropine (phenylephrine family) can treat congestion at nose which happen due the inflammation and then edema when person gets rhinitis, these drugs will eases the signs and symptoms of inflammation.) but when we talk about anti-inflamatory drugs we try to block the problem centrally , preventing the production of inflamatory cytokines.

Another thing leukotrienes do they cause bronchial constriction , increase secretion , bronchospasm , congestion and mucus plugging which involved

in inflamatory conditions like viral rhinitis , also another condition like asthma , they have B.C and sometimes congestion.

Drugs target this pathway (lox);

like lipooxgenase inhibiters ; like luton , used to treat inflamatory conditions like asthma

antagonist receptors: target luekotriens receptor , used for asthma and inflammatory conditions associated with B.C and excessive mucus production like Singulair.

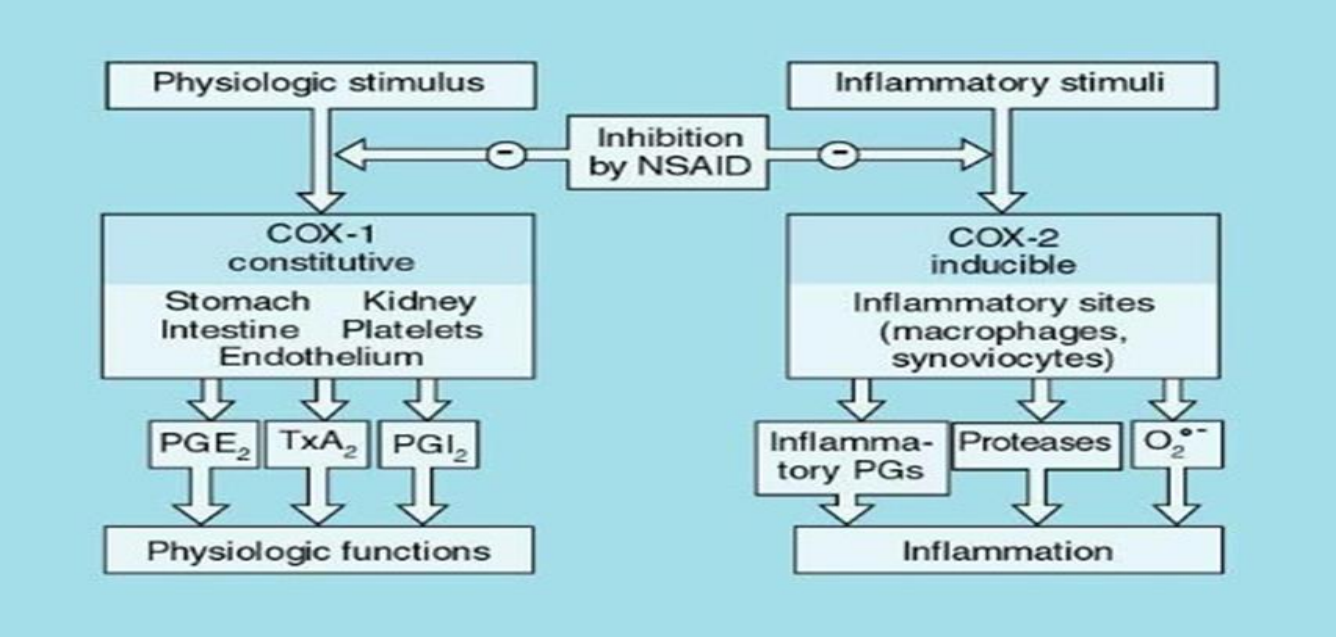
We don’t have to use these newly drugs like singulair more times , because these expensive drugs have high efficacy sometimes , causing our bodies unresponsive to lower efficacy drugs .

Why NSAIDs don’t be used for COVID 19?

Because when block one arm of pathway; the another will take over (lipoxygenase) which associated with Respiratory system infections , so it will exaggerate the problem Also some study would find that it have thrombotic effect (except aspirin) so it induce susceptible thromboembolic events .

Contraindication for NSAIDs: asthma patients, except if the benefit risk ratio is high.

Cyclo-oxygenase (COX)



Exists in the tissue as constitutive isoform (COX-1).

At site of inflammation, cytokines stimulates the induction of the 2nd isoform (COX-2).

Inhibition of COX-2 is thought to be due to the anti-inflammatory actions of NSAIDs.

Inhibition of COX-1 is responsible for their GIT toxicity.

It's available all time and functioning in our body , unlike cox2 (inducible) which is get increases at inflammatory response which is macrophages , synoviocytes .

The cox1 is present in stomach ,kidney, intestine, platelets, endothelium , usualy cox1 produces PGE2,TxA2 ,PGI2 which give its physiologic functions , on the other hand cox2 produces inflammatory PG ,proteases, and superoxide which are more associated with inflammations.

Most currently used NSAIDs are somewhat selective for COX-1, but selective COX-2 inhibitors are available.

both drug are non selective , even though have slight preference for one isoform.

Cyclooxygenase is part of arachidonic acid metabolism which produces PG, so NSAIDs will decrease PG synthesis with both beneficial and unwanted effects

Remember that we have 2 types of cyclooxygenase enzyme: -cyclooxygenase 1 which exist in the tissue as constitutive form (physiological response). -cyclooxygenase 2 the inducible form which found in the site of inflammation. >>inhibiting these enzymes will inhibit the production of their products which are PG (for both) & prostacyclin and thromboxane (for COX-1).

when we inhibit these PGs we not only inhibit the inflammation but also we will lose important function that they do.. Ex: in the stomach PG-E2 protect the stomach from the excessive acid secretion (it increases the mucus production and lower the acid secretion from parietal cells), so inhibiting PG-E2 will lead to over secretion of HCl and lower the protection of mucus layer and because of that these drugs cause GI irritation

Gastrointestinal effects:

we will not take much details about function of PG but some, that we interest of it for side effects of NSADs

PGE2 stimulate synthesis of protective mucus in both the stomach and small intestine. It also decrease acid synthesis in stomach

In the presence of aspirin, these prostanoids are not formed, resulting in increased gastric acid secretion and diminished mucus protection.

Agents used for the prevention of gastric and/or duodenal ulcers include proton-pump inhibitors (PPIs); esomeprazole, lansoprazole, omeprazole ; it prevent secretion of HDL .

Voltaren: its painkiller belong to NSADs , given in forms of cream ,injection ,pales , and if it given in the form injection it will reach stomach by blood and could cause gastric irritation , doctors' advice to take drugs with filled stomach ; because food will represent protective layer against more exposure to drugs and from excessive acid secretions

Non-steroidal anti-inflammatory drugs (NSAIDs)

pain

fever

Inflammation

By inhibition of cyclo-oxygenase enzymes COX1 & COX2.

COX-1 is involved in tissue hemeostasis, platelet aggregation, gastric cytoprotection.

COX- 2 is responsible for the production of mediators of inflammation

Aspirin in small dose act more selective at cox 1 so prevent aggregation of thrombosis , as we increase the dose in general drugs will lose their selectivity