Autacoids

Objectives:

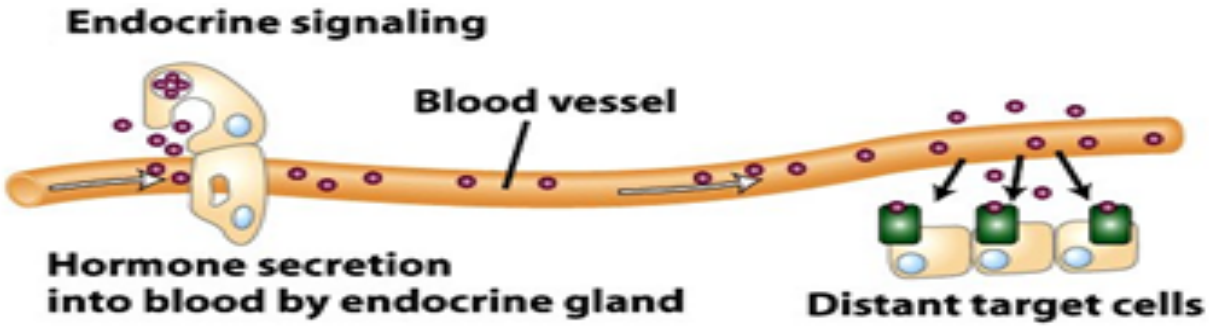
- To describe the synthesis, receptors and functions of histamine, eicosanoids ,nitric oxide , angiotensin, kinins & 5-HT.
- To study the agents which enhance or block their effects.

Titles
Very important
Extra information
Terms

Whoever guards his mouth preserves his life.

Autacoids features

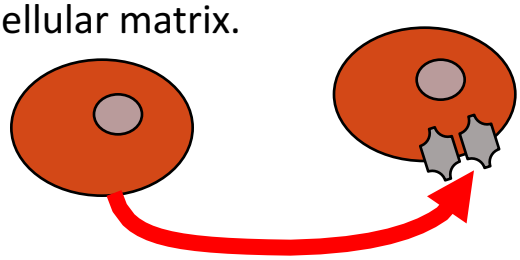
-Self remedy.
-Produced , act & metabolized locally.



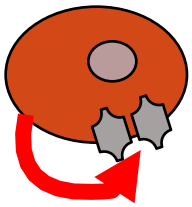
-**Have different biological actions including :**
1-modulation of the activity of smooth muscles.
2-glands.
3-Nerves.
4-platelets and other tissues.

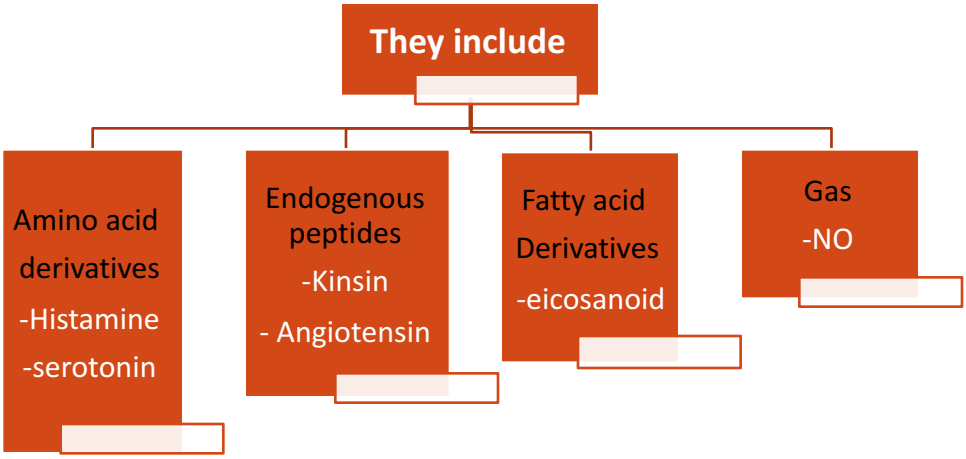
-**They have autocrine or paracrine effects :**

Paracrine: Secreted by one cell & acts upon adjacent cells or surrounding extracellular matrix.



Autocrine : Secreted from a cell and acts on the same cell.





Histamine :

It is an amine synthesized from L- histidine.

L- histidine. →	Decarboxylase → (Removing of CO_2)	Histamine

It is stored in:

1- Mast cells
2- Basophils
3- Lungs
4-Intestinal mucosa

Release by 2 ways:

1-During allergic reaction
2- Inflammatory reaction

Histamine receptors :

Receptor Type	Major Tissue Locations	Major Biologic Effects
H_1	smooth muscle, endothelial cells, brain	acute allergic responses
H_2	gastric parietal cells, Cardiac muscle, mast cells, brain	secretion of gastric acid
H_3	central nervous system	neurotransmission
H_4	mast cells, eosinophils, T cells	regulating immune responses

Actions:

- Stimulates gastric acid secretion through H2- receptors.
- Stimulation of H1-receptors contract smooth muscles, bronchioles ,uterus.
- Increases bowel peristalsis.
- Slow IV or SC injection which causes :
  - 1-Flushing of skin.
  - 2-Raise temperature.
  - 3-Increase blood flow to the periphery.
  - 4-Increase heart rate.
- Dilation of blood vessels which causes :
  - 1-Fall in blood pressure.
  - 2-An increase in CSF pressure.
  - 3-Headache.
  - 4-Dilation of blood vessels.

Histamine receptor blockers

H1 receptor blockers		
generation	**First generation**	**Second generation**
Name of the receptor blockers	• Diphenhydramine • cyclizine • promethazine	• Loratidine • Citrizine • Fexofenadine
effect	**Has a Sedating effect**	**Non-sedating effect**
Used for the treatment of:	• Allergic rhinitis. • Urticaria. • Insomnia. • Motion sickness.  Urticaria	*Allergic conditions such as:-* • Allergic rhinitis. • Conjunctivitis. • Urticaria.  Urticaria

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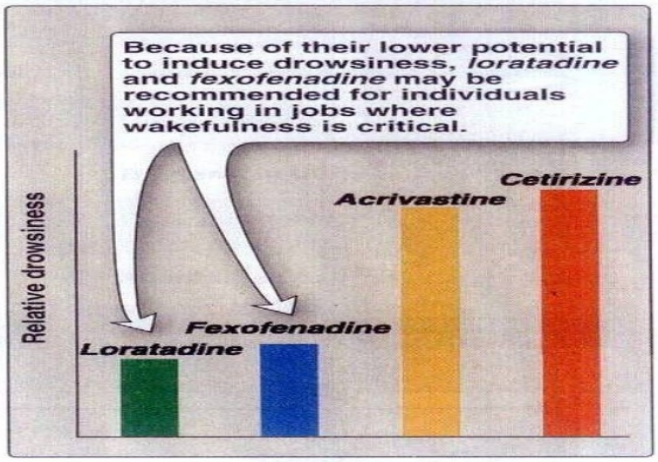
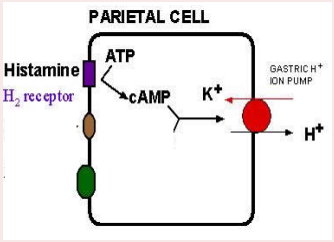
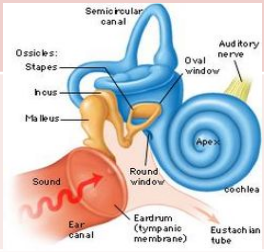


Loratidine and Fexofenadine
هذي النوعين من البلوكرز النعاس اللي تسببه بسيط مقارنة بالباقين عشان كذا تستخدم للأشخاص اللي عندهم أعمال تحتاج إلى تركيز كامل

H2 receptor blockers

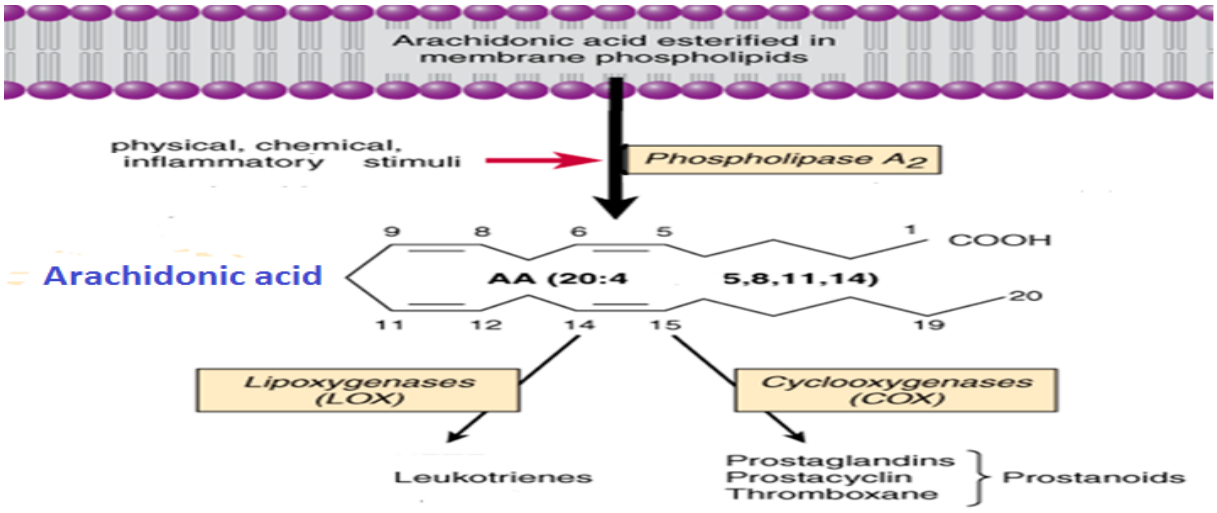
Name of the receptor blockers	Cimetidine, ranitidine, famotidine	
effect	Histamine plays an important role in the formation and secrtion of HCl (gastric acid) by the activity of H2 receptors **SO** Blockers of H_2 receptors inhibit gastric acid secretion	
Used for the treatment of:	• Gastritis • Peptic ulcers	

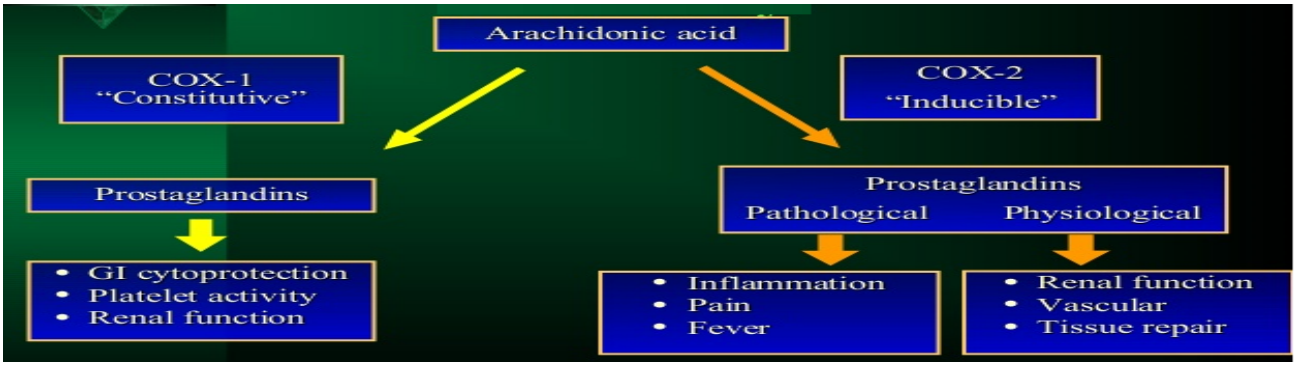
H3 receptor blockers

Name of the receptor blockers	betahistine	
effect	**It produces dilatation of blood vessels in inner ear**	
Used for the treatment of:	• **Vertigo and balance disturbances** **(May produce headache and insomnia)**	

Eicosanoid :

- Signaling molecules
- These are 20 carbon atom faby acids.
- Arachidonic acid (AA) found inside the phospholipids (PL). AA freed from PL by Phospholipase A2.
- Cyclooxygenase (COX) generate the Prostaglandins, Prostacyclins and Thrombaxane A2 (TXA2) from arachidonic acid
- Lipoxygenase (LOX) generate the Leukotrienes from arachidonic acid.
- Corticosteroids inhibit phospholipase A2.
- Zileuton inhibit lipoxygenase.
- NSAIDs inhibit cyclooxygenase





Prostaglandin (PG):

Major Characteristics :

• First found in semen, they have since been found in cells throughout the body and in menstrual fluid.

• Found In Almost Every Tissue In Humans.

• Contains 20 Carbon Atoms.

The Actions of PG :

• Causes Vasodilatation of Vascular Smooth Muscle Cells (Contrac6on of Uterus).

• Inhibit The Aggrega6on of Platelets.

• Sensitize Neurons To Cause Pain

• Induce Labor

• Decrease intraocular pressure, blood pressure

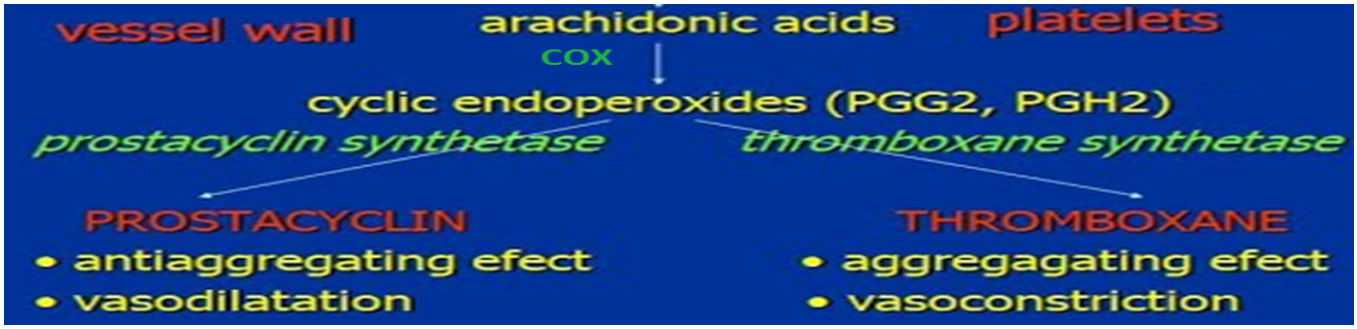
• Acts On Thermoregulatory Center of Hypothalamus To Produce Fever.

• Acts On Kidney To Increase Glomerular Filtra6on.

• Acts On Parietal Cells of Stomach To Prevent Gastric Mucosa.

• Control Cell Growth.

• Regulate Hormones, Calcium, Inflammation.



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Prostaglandins analogs	Treatment of
Carboprost	Induce abortion in first trimester
Latanoprost	Glaucoma
Misoprostol	Peptic ulcer
Alprostadil	Erectile dysfunction
Zileutonas	lipoxygene inhibitor
Zafirlukast (leukotreine receptor blocker)	Bronchial asthma

Nitric Oxide (NO): Highly diffusible stable gas

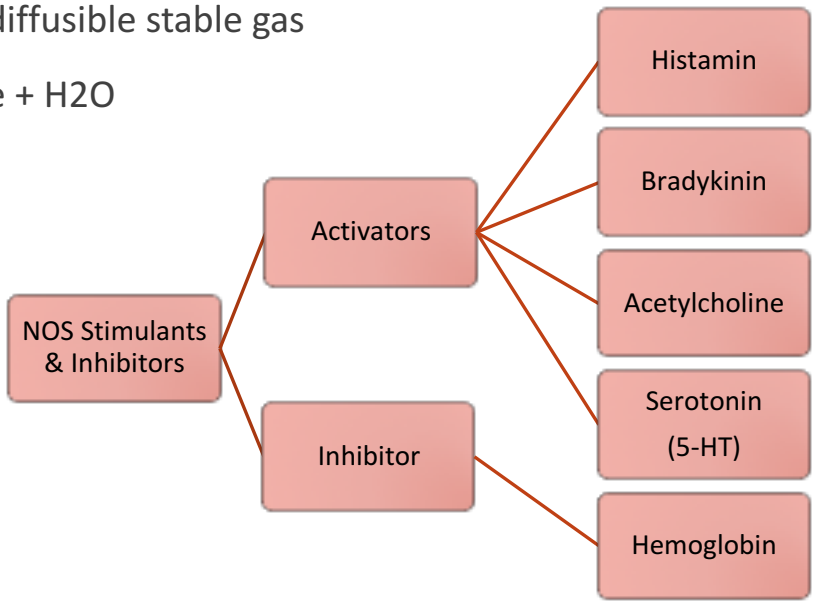
L-arginine + O2 NO + Citrulline + H2O

Synthesis:

Nitric Oxide Synthase (NOS).

Types of NOS:

1. n-NOS: Neuronal NOS
2. i-NOS: Inducible NOS
3. e-NOS: Endothelial NOS



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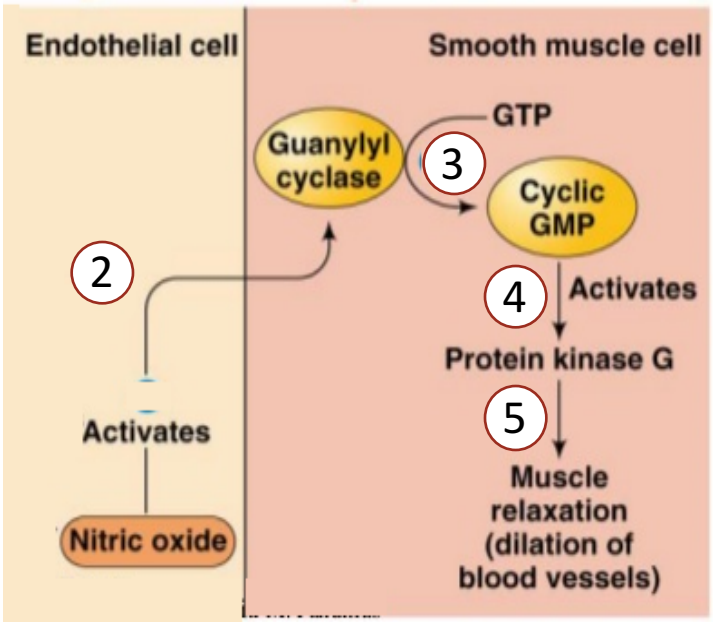
Neuronal NOS (nNOS)	Endothelial NOS (eNOS)	Inducible NOS (iNOS)
• Neurons • Skeletal muscle	• Endothelium • Cardiac myocytes • Osteoblasts • Osteoclasts	• Macrophages • Kupffer cells • Neutrophils • Fibroblasts • Vascular smooth • Muscle
Constitutive Forms (Physiological)		**Pathological**

Action of Nitric Oxide:

1. Vasodilation: (Paracrine)

1. Diffuse to Vascular smooth muscle cells
2. Binds soluble GC
3. Change GTP to cGMP
4. Activate PKG & inhibit Ca
5. Inactivate MLCK
6. Prevent actin myosin cross link
7. No contraction
8. RELAXATION



Actions of NO :

- Inhibition of platelet and monocyte adhesion and aggregation.*
- Inhibition of smooth muscle proliferation.*
  - Inhibition of angiogenesis
- Protection against atherogenesis.*
  - Atherogenesis: formation of fatty plaques in the arteries.
- Synaptic effect in the peripheral and central nervous system.
  - Potentiation of long-term memory.
- Host defense and cytotoxic effect on pathogens.
  - ↑ quantity of NO ⟶ act as free radical.
- Cytoprotection

Actions of NOS:

Classified according to the Isoenzyme producing the effect

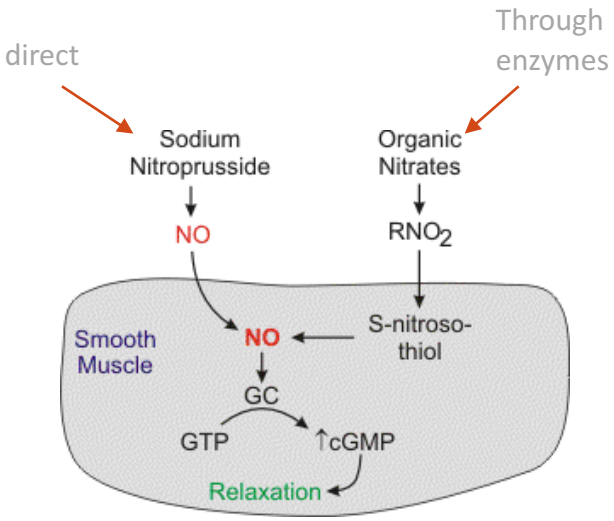
nNOS	eNOS	iNOS
• Long Term Potentiation • Cardiac function, Peristalsis, Sexual arousal	• Vascular tone, Insulin secretion, Airway tone, Regulation of cardiac function and angiogenesis • Embryonic heart development	• In response to attack by parasites, bacterial infection and tumor growth • Causes septic shock, autoimmune conditions

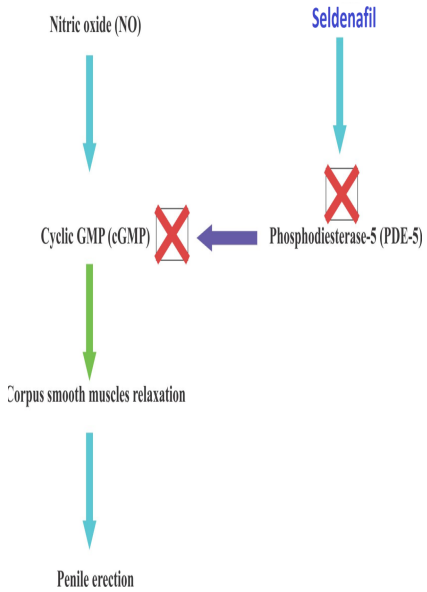
iNOS: Inflammatory and immune responses.

*Anti thrombotic mechanisms

NO in therapeutics:

- diabetes, hypertension & atherosclerosis causes reduction of Endothelial NO production.
- Overproduction of NO
  - Causing nerve damage in neurodegenerative diseases e.g. Parkinsonism.
  - in septic shock causing excessive vasodilatation.
- NO is used in critical care to treat pulmonary hypertension in neonates
- NO is used in patients with right ventricular failure secondary to pulmonary embolism
- NO donors* used e.g. in hypertension & angina pectoris
- ***Sildenafil*** potentiates the action of NO on corpora cavernosa smooth muscle. used to treat erectile dysfunction





* Drugs that produce NO

Pharmacology Team :

Boys	Girls
عبدالرحمن ذكري	اللولو الصليهم
عبدالعزيز رضوان	روان سعد القحطاني
---------	أميرة نيازي
فيصل العباد	جواهر أبانمي
فارس النفيسة	رانيا العيسى
خالد العيسى	غادة المزروع
معاذ الفرحان	لمى الفوزان
عبدالرحمن الجريان	نورة الشبيب
محمد خوجة	أسيل ناصر بادخن
عمر التركستاني	أنوار نجيب العجمي