

Local hormones

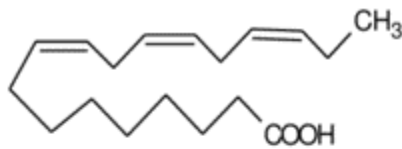
Eicosanoids

Histamine

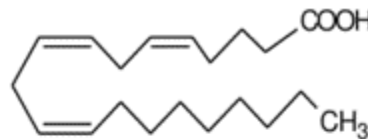
Serotonin

Eicosanoids

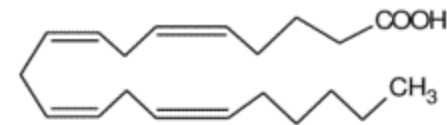
- derived from C₂₀ polyunsaturated fatty acids (PUFAs)
 - **arachidonic acid** (AA; 20: 4n-6)
 - eicosapentaenoic acid (EPA; 20: 5n-3)
 - dihomo- γ -linolenic acid (DGLA; 20: 3n-6)
- precursors in the cytoplasmic and nuclear membrane > released by **phospholipase A₂** > synthesis of eicosanoids by cyclooxygenases (COX), lipoxygenases (LOX) and other enzymes



Alpha-linolenic acid [ALA]



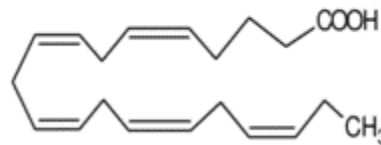
Eicosatrienoic Acid



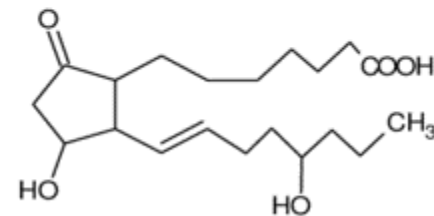
Arachidonic Acid [AA]



Docosahexaenoic acid [DHA]



Eicosapentaenoic Acid [EPA]



Prostaglandin [PGE]

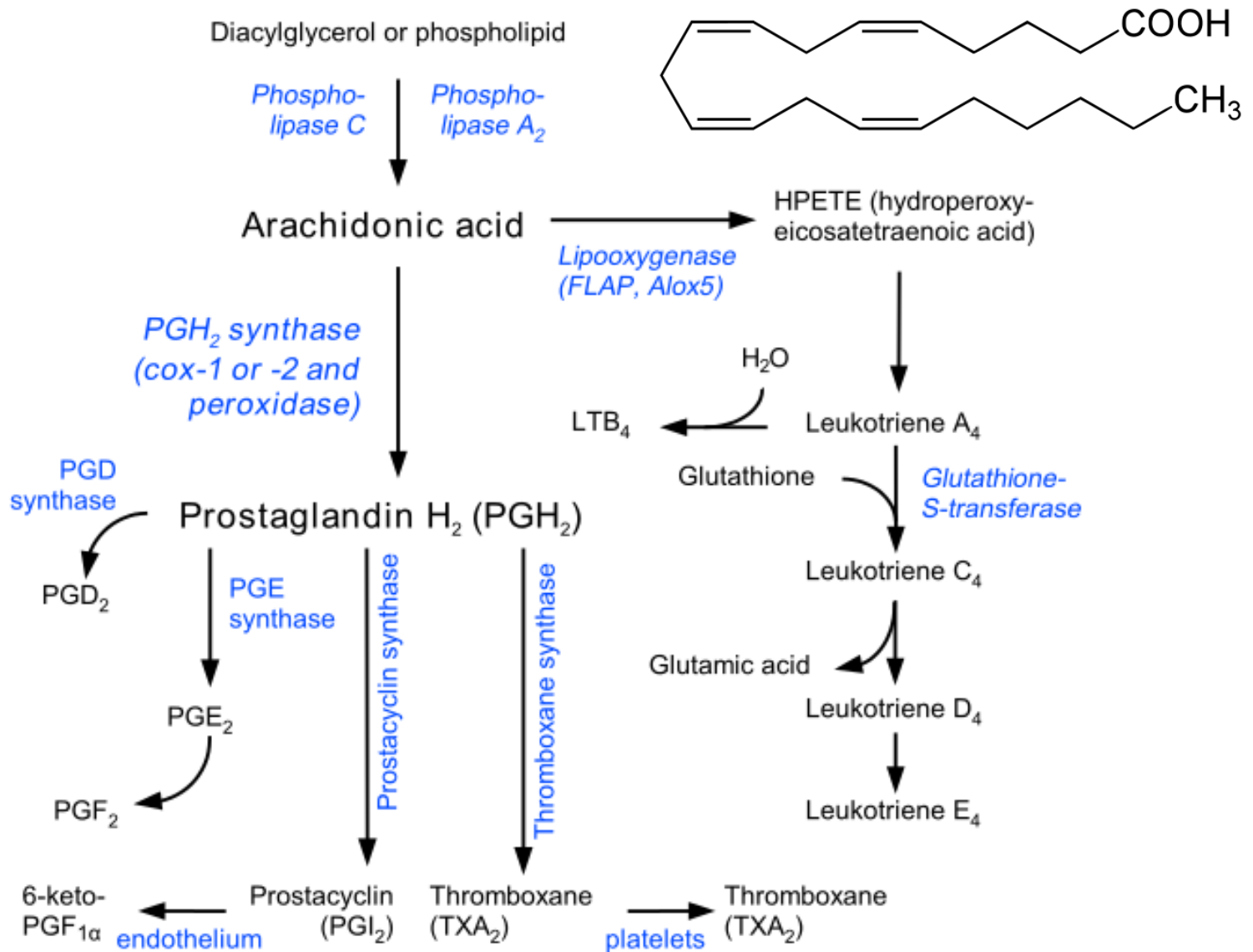
Eicosanoids - synthesis

- the synthesis takes place mainly in: endothelial cells
leukocytes
platelets
kidneys
- biosynthesis in all cell types except red blood cells
- eicosanoids are not stored in the cells
- four main groups:
 - leukotrienes (LOX)**
 - prostaglandins (COX)**
 - prostacyclins (COX)**
 - thromboxanes (COX)**

} **prostanoids**

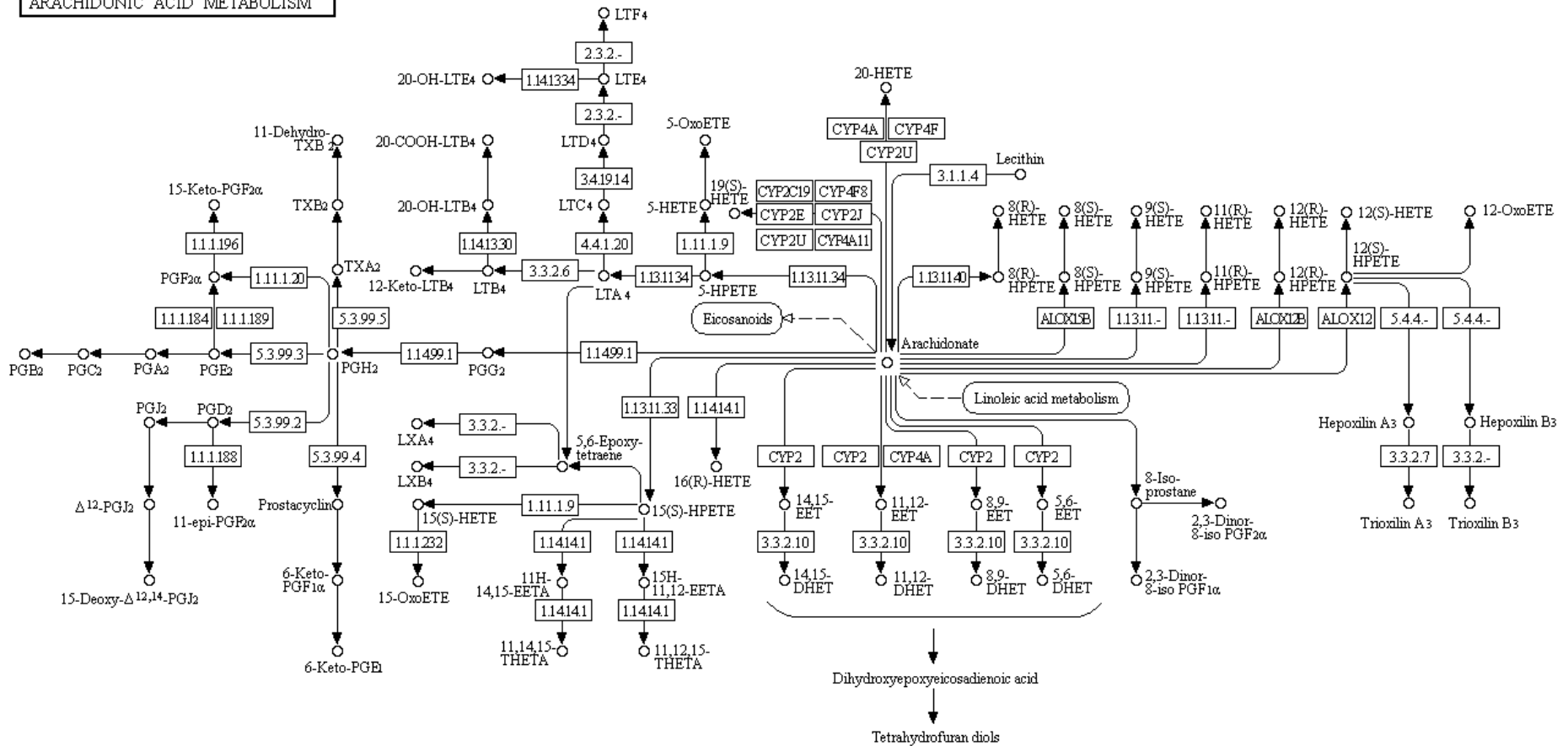
 - hepoxilins (LOX)
 - lipoxins (LOX)
 - epi-lipoxins (LOX)
 - epoxyeicosatrienoic acid (cytochrome P450 epoxygenase)
 - isoprostanes (cytochrome P450 epoxygenase)
- the basis of the COX pathway are prostaglandins G (PGG_2) and H (PGH_2)

Eicosanoids - synthesis



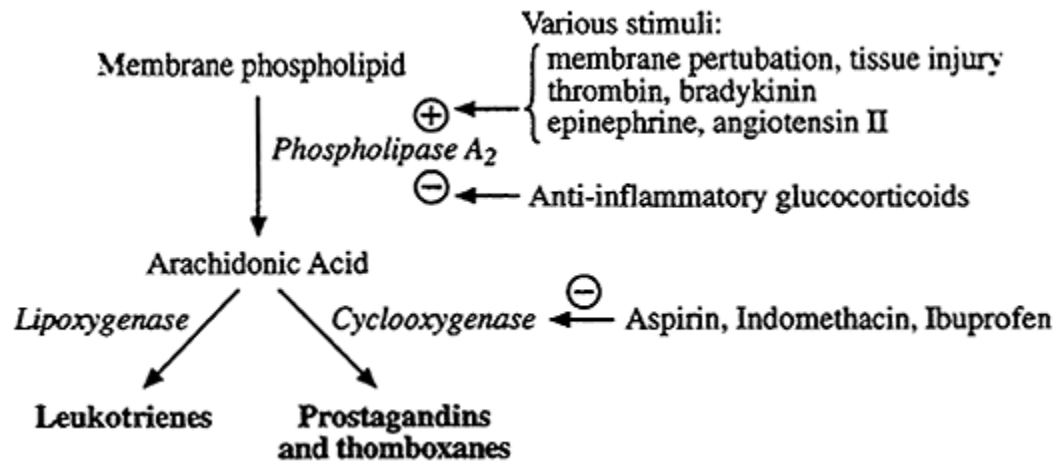
Eicosanoids - synthesis

ARACHIDONIC ACID METABOLISM



Eicosanoids – mode of action

- evolutionarily conserved
- production is neural- and hormonal-regulated (increase in Ca^{2+} levels, cell swelling, etc.)



- rapid degradation > transport to the long distances is limited
- specific effect on target cells near the site of their synthesis
- they can also act within intracellular signaling pathways
- bound to **G protein-coupled receptors** (stimulation or inhibition of cAMP synthesis; cleavage of phosphatidylinositol-4,5-bisphosphate and release of Ca^{2+}) or **nuclear receptors** (peroxisome proliferator-activated receptor, PPAR γ)

Eicosanoids – mode of action

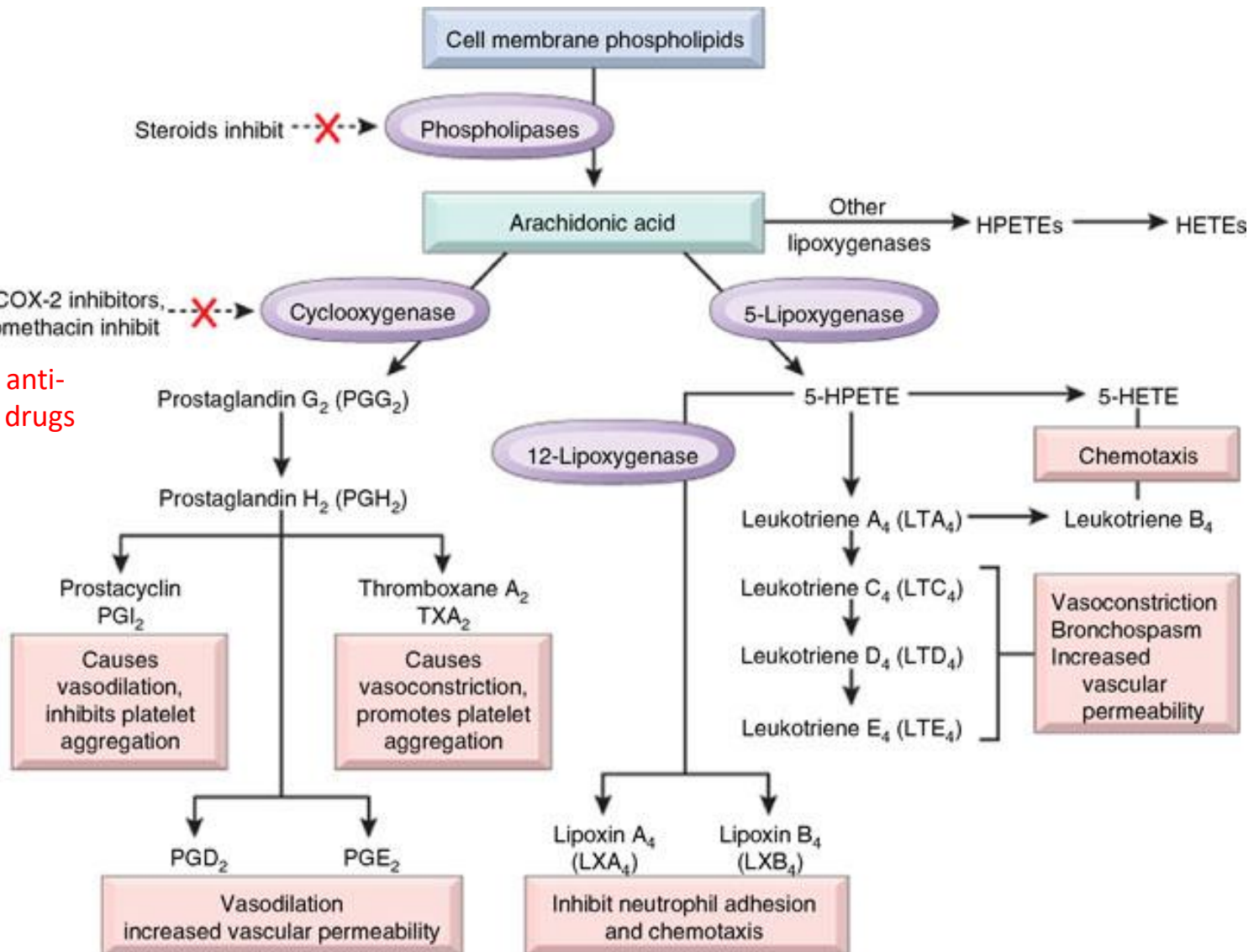
- eicosanoids act even in very low concentrations (like hormones)
- short half-life, therefore acting on autocrine and paracrine level (unlike classical hormones)
- effects in the body vary not only by species of eicosanoid, but also according to which receptors they can bind at a given tissue

Biological role of eicosanoids:

- mediate the inflammatory response, especially in the joints (rheumatoid arthritis), skin (psoriasis) and eyes
- mediating pain and fever
- participate in the regulation of blood pressure
- participate in the regulation of coagulation (e.g. platelet aggregation)
- mediate immune responses (chemotaxis, nodulation and more)
- affect kidney function (vasodilation and regulation of glomerular filtration)
- participates in the control of some processes in the reproductive system (e.g. childbirth)
- participate in sleep cycle regulation

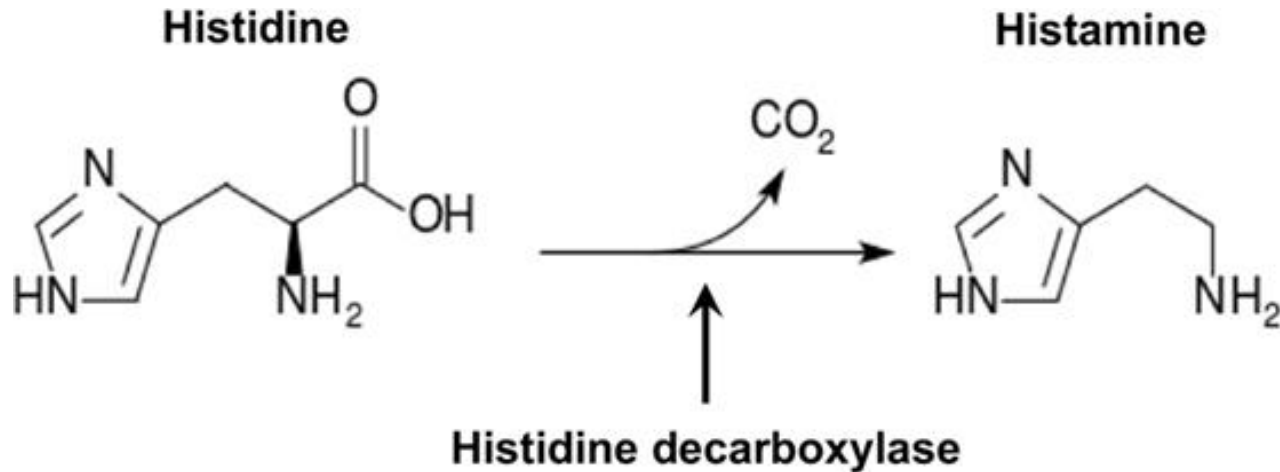
Eicosanoids – mode of action

Non-steroidal anti-inflammatory drugs (NSAID)



Histamine

- hormone and neurotransmitter
- derived from the amino acid histidine (histidine decarboxylase)



- produced mainly by nerves, tissue mast cells and basophilic granulocytes, enterochromaffin (ECL) cells in the stomach
- during the immune response, its synthesis is stimulated by antigen-antibody complexes (IgE) and activated complement
- its production is inhibited by adrenaline, PGE₂ and histamine itself
- primarily acts locally, but in response to the allergen may cause a whole-body reaction (anaphylactic shock)
- histamine receptors (H₁- H₄) coupled to G proteins

Histamine – mode of action

- **stimulates vasodilation and increases vascular permeability > edema > lower blood pressure** (despite being stimulated via H₂ receptors which strengthen heartbeat and increase heart rate)
- vasodilation induced directly or indirectly through the promotion of nitric oxide production in the endothelium
- affects smooth muscle (contractions of the uterus, bronchi and intestine)
- stimulates the parietal cells of the stomach to produce hydrochloric acid
- causes irritation of peripheral nerves > **itching**
- histamine causes the symptoms of allergic reaction type I (hives, hay fever)

Therapy

- antihistamines H₁ (allergic reactions), antihistamines H₂ (gastric ulcers)
- administration of sympathomimetics

Serotonin

- derived from the amino acid tryptophan (5-hydroxytryptamine)
- hormone and **neurotransmitter**
- **production in the CNS (10 %), enterochromaffin intestinal cells (90 %)**, platelets, proximal renal tubules and bronchi

Action:

- it is involved mainly in the transmission of nerve impulses
- mood control („hormone of happiness“)
- serotonergic neurons in the brain probably play an important role in alternating circadian rhythms and inducing sleep (part of melatonin synthesis)
- **stimulates smooth muscle contractions** (uterus, bronchi, intestine, blood vessels)
- promotes platelet aggregation and thus blood clotting
- in relation to the above mentioned, serotonin has a great impact on injuries
- can cause headaches by acting on blood vessels (migraine)