Poltava State Medical University

Lecture

Pharmacology of drugs that influence efferent innervation. Adrenergic drugs

AUTONOMIC NERVOUS SYSTEM

Autonomic nervous **system regulates the function of internal organs.**

It is divided into two sections:

- ***sympathetic system***
- ***parasympathetic system***

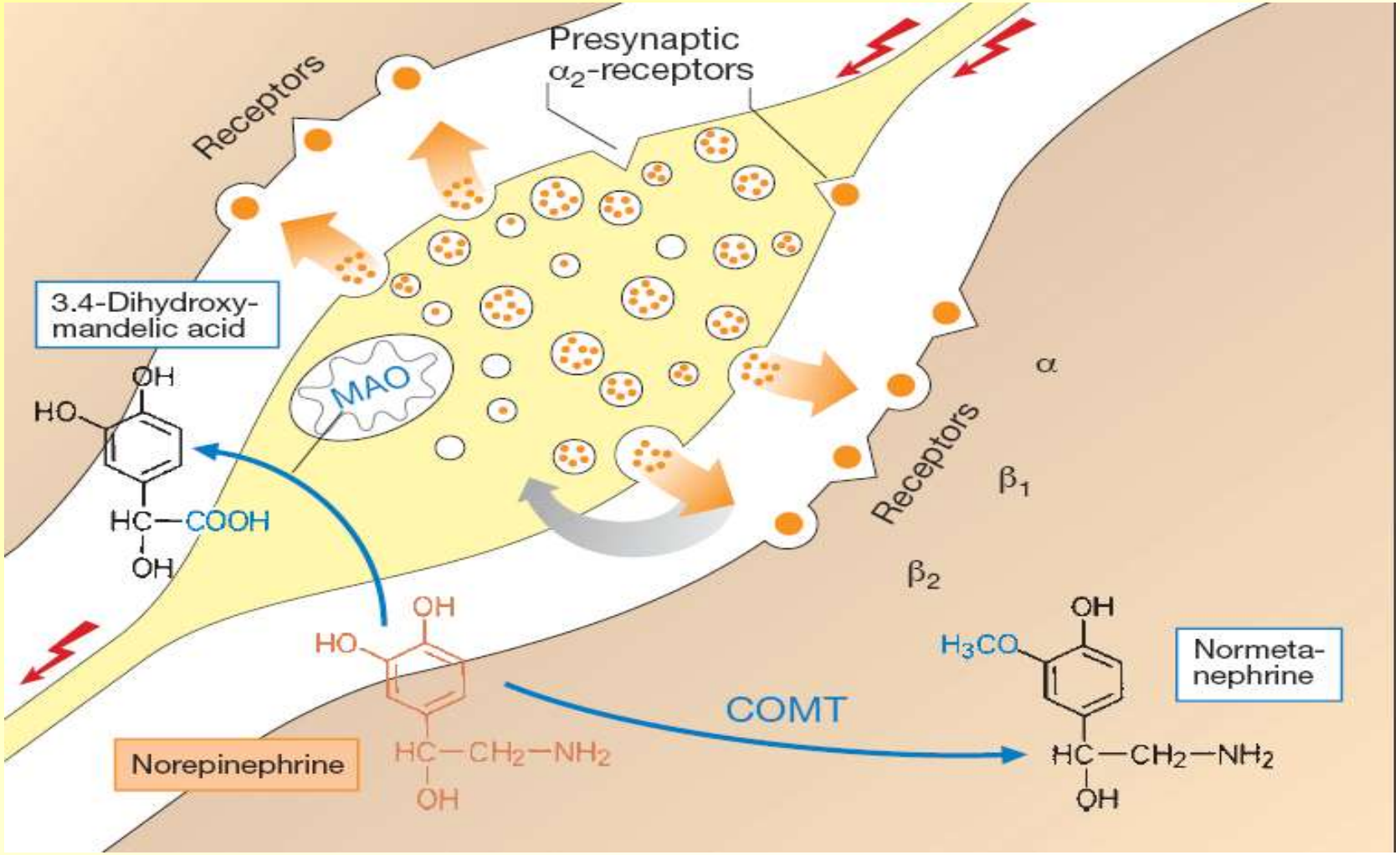
They exert opposite actions.

SYMPATHETIC SYSTEM (SANS)

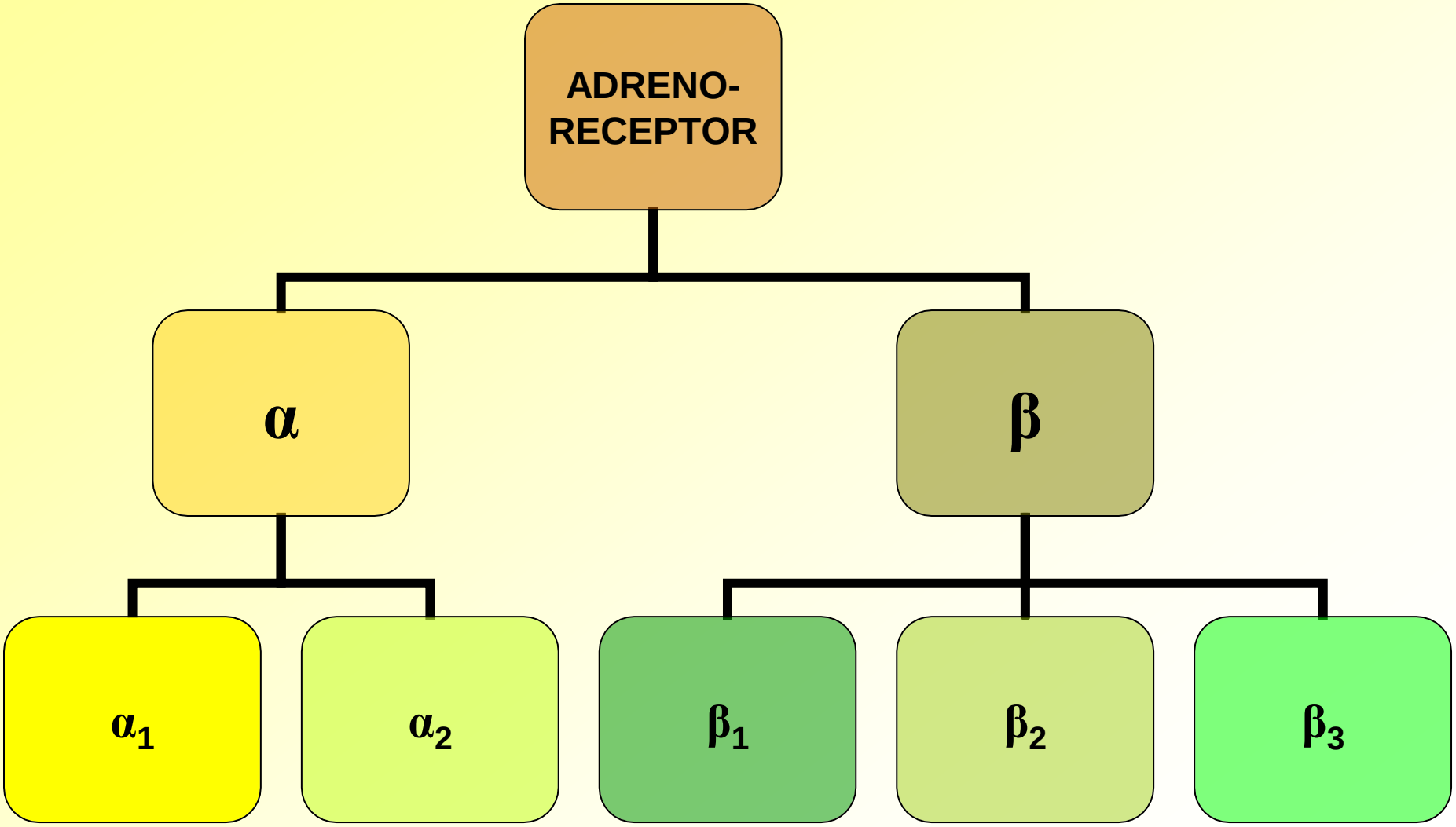
Centers **(the 1st neuron): thoraco-lumbal region of the spinal cord**

Ganglia **(the 2nd neuron): near the spinal cord (Thruncus sympaticus)**

ADRENERGIC SYNAPSE



TYPES OF ADRENOCEPTORS



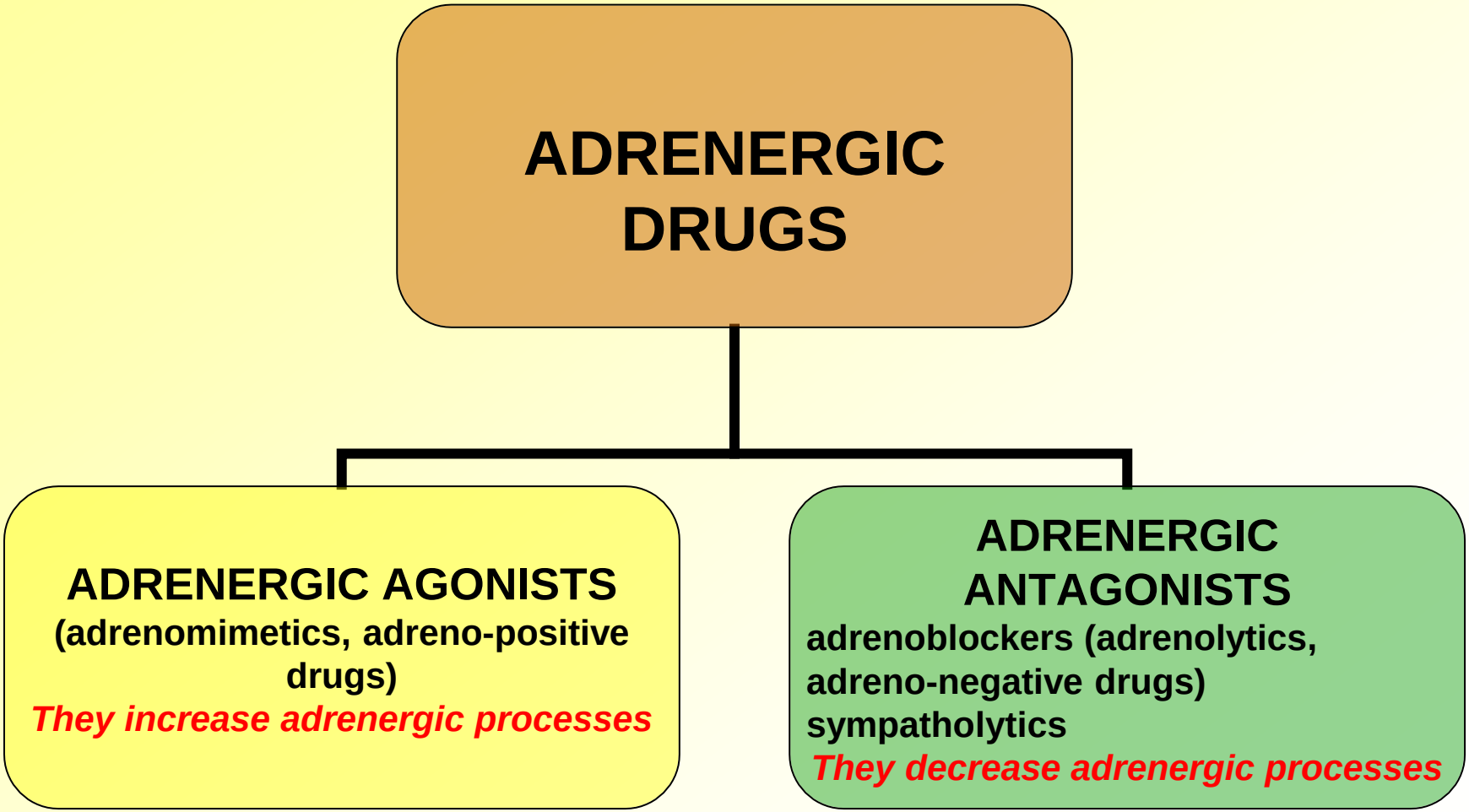
LOCATION AND EFFECTS OF α-ADRENOCEPTORS

Receptor	Location	Effect
α1	Blood vessels Spleen Eye Urinary bladder	Constriction, ↑of BP Constriction Mydriasis ↑ of sphincter closure
α2	Blood vessels Pancreas All adrenergic synapses	Constriction ↓ of insulin release ↓ of norepinephrine release

LOCATION AND EFFECTS OF β-ADRENOCEPTORS

Receptor	Location	Effect
β1	Heart Fat tissue	↑ of rate and contractility ↑ of lipolysis
β2	Blood vessels Bronchi Uterus Pancreas Liver Skeletal muscles	Vasodilation Dilation Relaxation ↑ of glucagon's release ↑ of glycogenolysis ↑ of glycogenolysis
β3	Pancreas Fat tissue Mast cells	↑ of insulin secretion ↑ of lipolysis ↓ of degranulation, ↓ of release of allergy mediators

DRUGS INFLUENCING ADRENERGIC SYNAPSES



ADRENERGIC AGONISTS

(ADRENOMIMETICS)

ADRENOMIMETICS
CLASSIFICATION

A. α-, β-adrenomimetics

1. Direct-acting

– Adrenaline hydrochloride (Epinephrine)

2. Indirect-acting (sympathomimetics)

– Ephedrine hydrochloride

B. α-adrenomimetics

1. Non-selective

– Noradrenaline hydrotartrate (α1, α2 > β)

2. Selective

– Phenylephrine (Mesatonum) (α1)

– Naphazoline (Naphthyzinum) (α2)

– Halazolin (Xylometazoline) (α2)

C. β- adrenomimetics

1. Non-selective

– Isoprenaline (Isadrinum) (β1, β2)

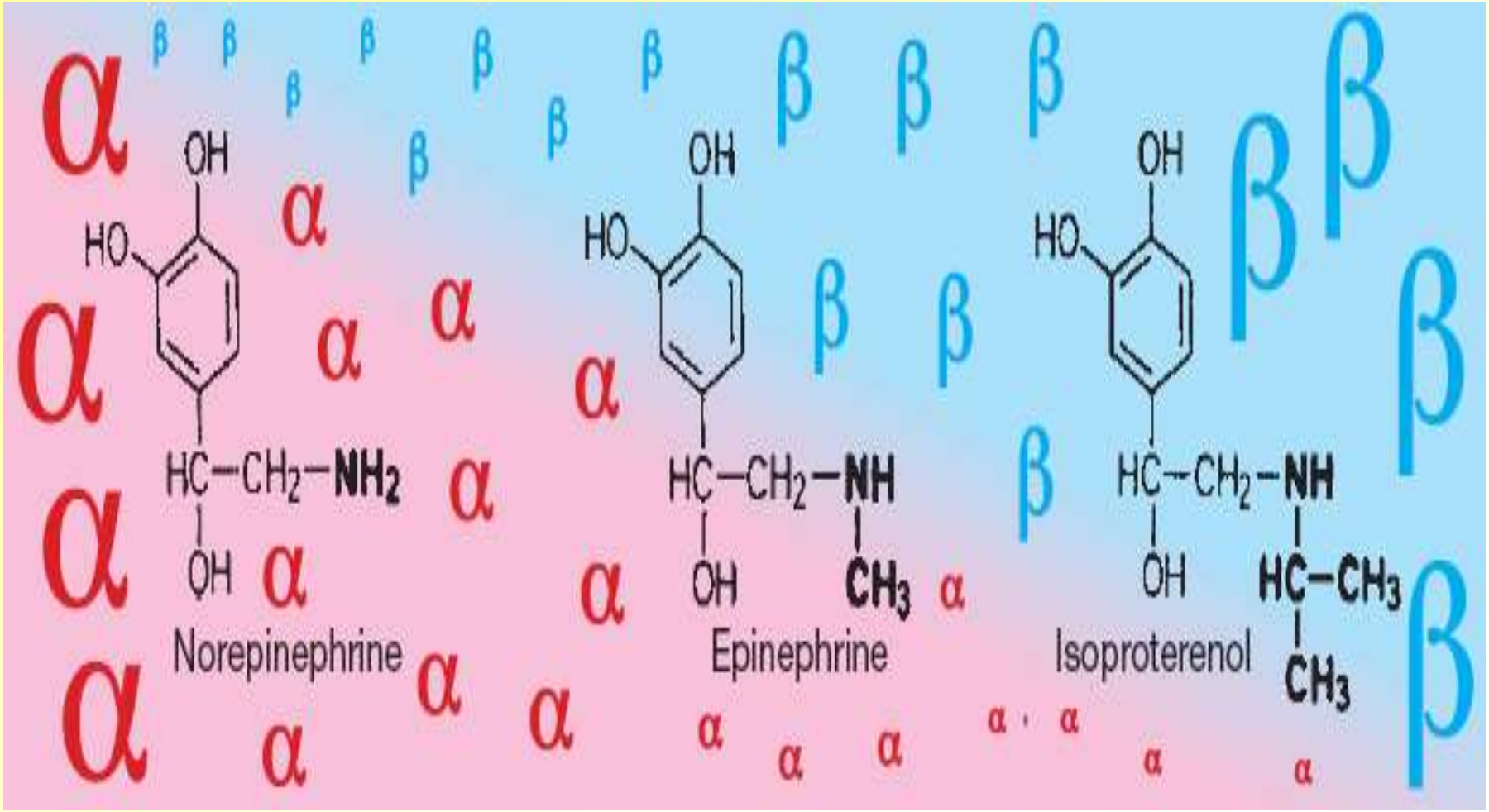
2. Selective

– Dobutamine (β1)

– Salbutamol (Albuterol) (β2)

– Fenoterol (β2)

COMPARISON OF ADRENOMIMETICS-CATECHOLAMINS



ADRENALINE
PHARMACOKINETICS

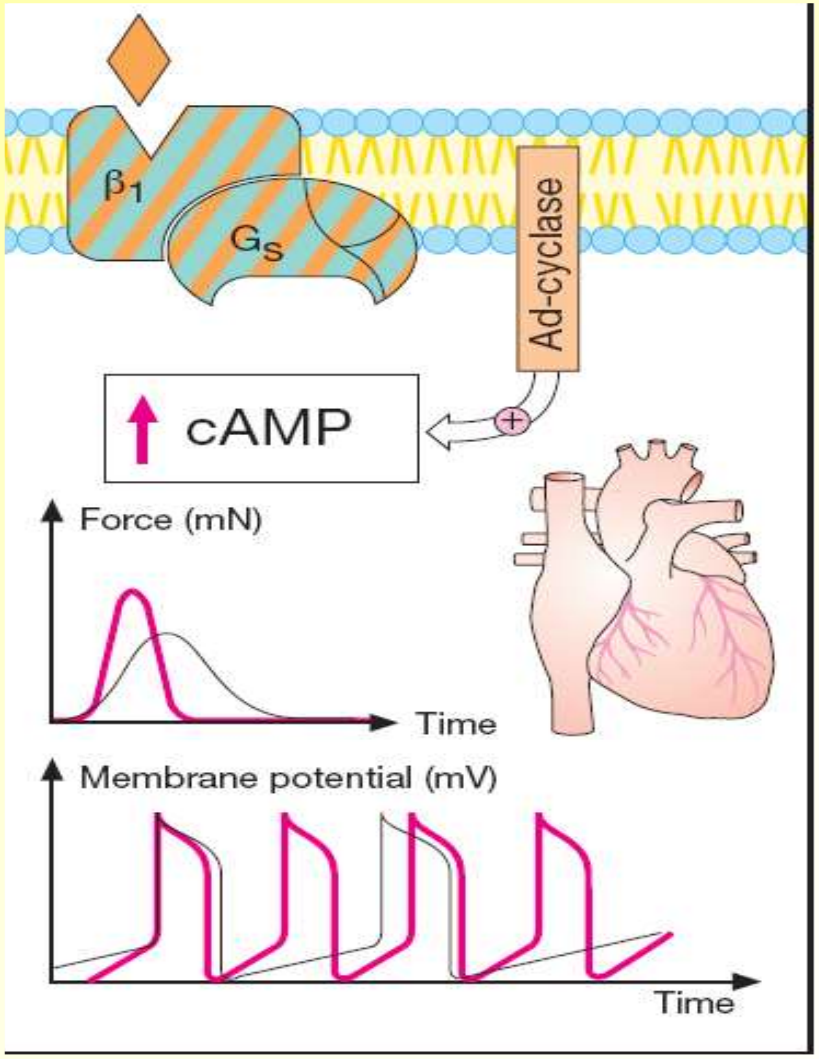
- is administered SC or topically
- is destroyed in the GI tract
- is not administered orally
- does not penetrate CNS
- is biotransformed by enzymes in blood
- acts during 15 min on the intern organs and during 30 min on metabolic processes

ADRENALINE

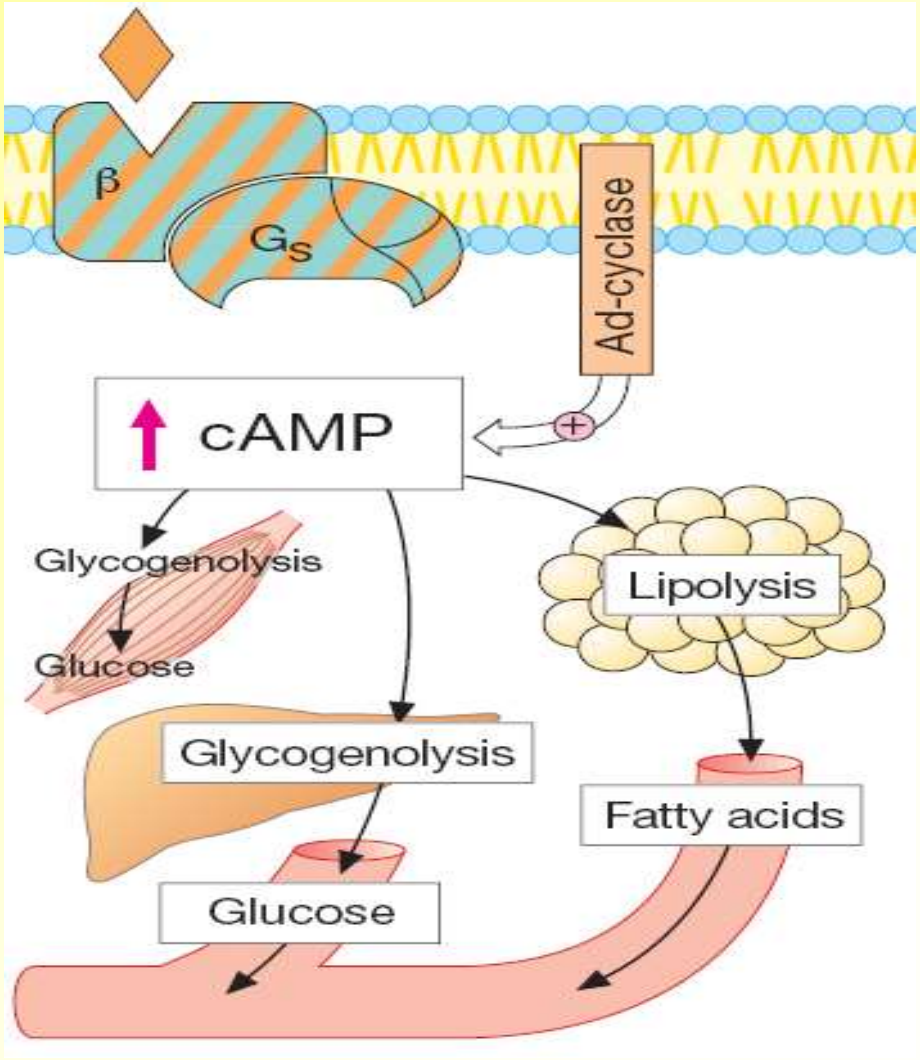
PHARMACODYNAMICS AND INDICATIONS

Pharmacodynamics	Indications
An increase in automaticity, conductivity, and contractility of the heart Constriction of blood vessels Elevation of BP Bronchodilation An increase in glucose concentration in the blood Inhibition of allergy Mydriasis A decrease in intra-eye pressure	Heart arrest Shock, collapse Bronchial asthma attack Hypoglycemic coma Anaphylactic shock Prolongation of local anethesia Capillary bleeding Acute inflammation of mucosa of the nose or eye Pupil dilation Open-angle glaucoma

ADRENALINE
CARDIAC EFFECTS



ADRENALINE
METABOLIC EFFECTS



ADRENALINE

SIDE-EFFECTS AND CONTRAINDICATIONS

Side-effects

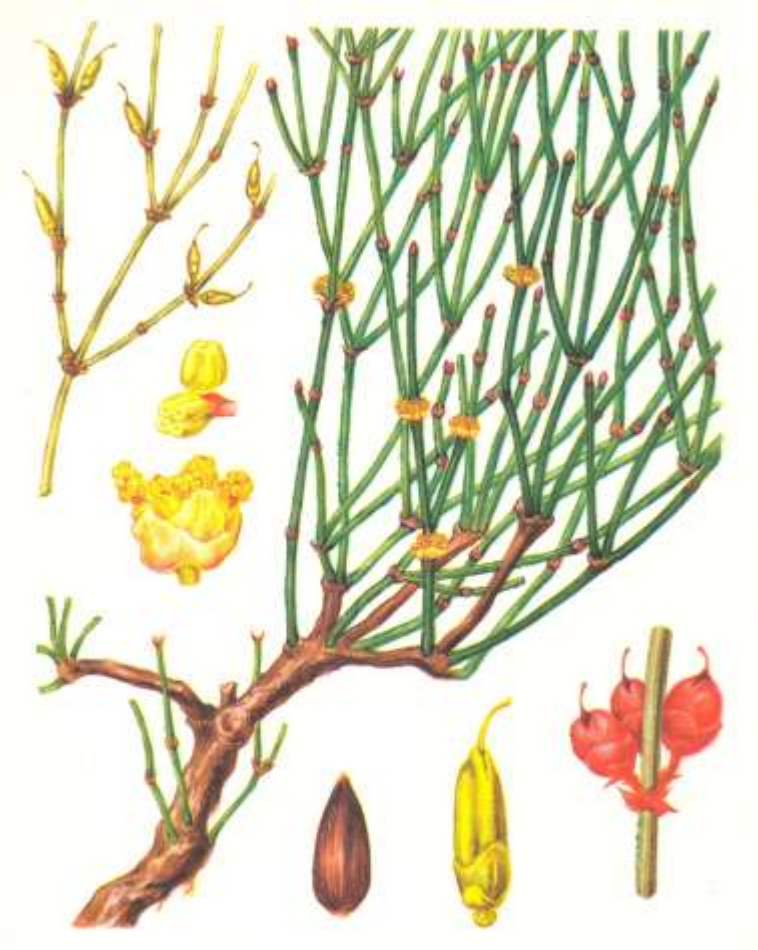
- Excitement, tremor
- Hypertension
- Arrhythmia
- Hyperglycemia

Contraindications

Hypertension, severe atherosclerosis, heart arrhythmia, diabetes mellitus, hyperthyroidism

EPHEDRINE

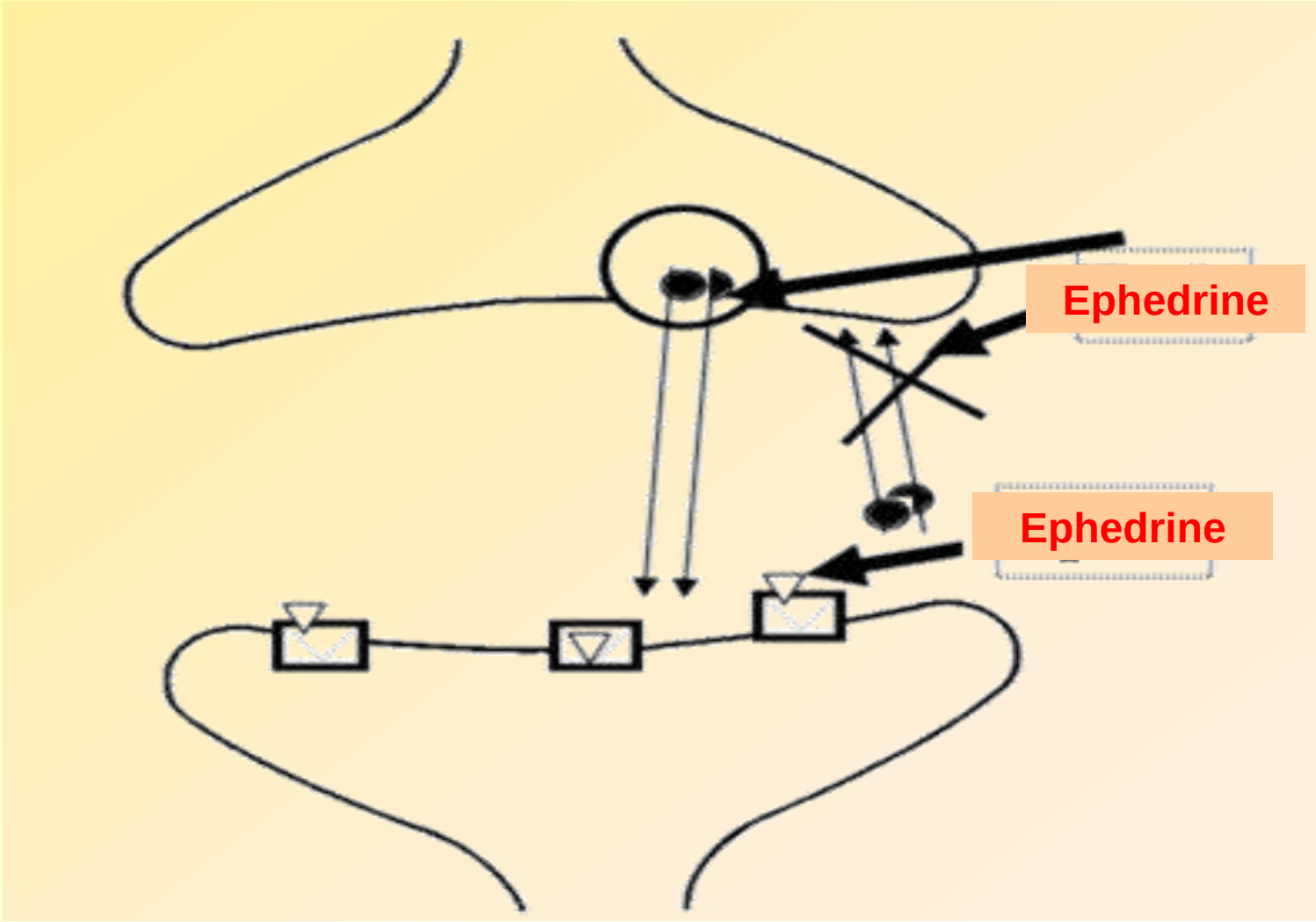
EPHEDRA EQUISETICA CONTAINING EPHEDRINE



EPHEDRINE
PHARMACOKINETICS

- is administered orally, SC, IM, IV, or topically
- is absorbed in the GI tract
- penetrates CNS
- is metabolized in the liver
- is excreted by kidney
- acts during 4-6 hrs

EPHEDRINE
MECHANISM OF ACTION



EPHEDRINE

PHARMACODYNAMICS AND INDICATIONS

Pharmacodynamics	Indications
Stimulation of CNS, an increase in ability to mental work, euphoria Stimulation of cardiovascular system Vasoconstriction Increase in BP Dilation of bronchi A decrease of GI tract motility Retention of urine Mydriasis	Shock, collapse Anaphylactic shock Bronchial asthma Bronchospasm Bradycardia, A-V block Acute rhinitis Acute conjunctivitis For pupil dilation Narcolepsia Myasthenia Enuresis

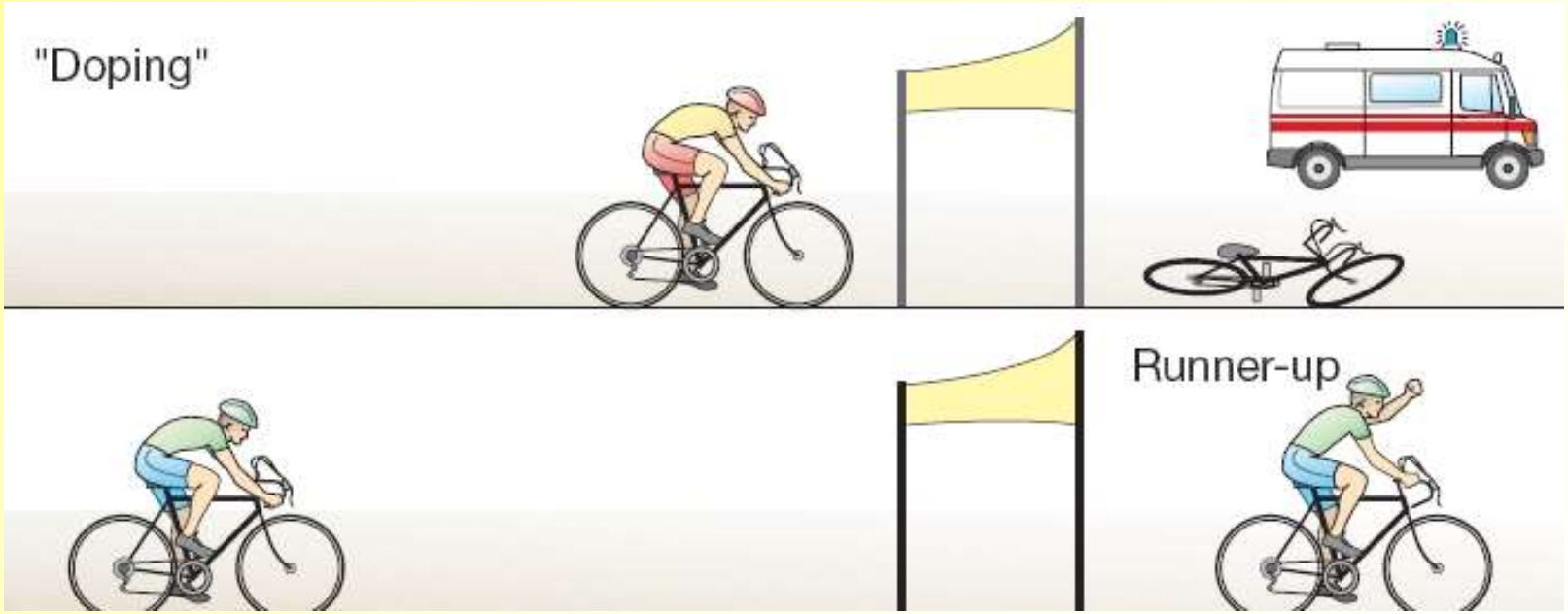
EPHEDRINE
SIDE-EFFECTS

- **Wakefulness**
- **Anxiety, restlessness, insomnia**
- **Tachycardia**
- **Palpitation**
- **Hypertension**
- **Rash on the skin**
- **Tolerance and tachyphylaxis**
- **Drug dependence**

✱ ***It should not be used in sportsmen (as doping)!***

EPHEDRINE

DOPING-EFFECT AND ABUSE POTENTIAL



α – ADRENOMIMETICS

Pharmacodynamics	Indications
Vasoconstriction An increase in BP Mydriasis (without cycloplegia)	Shock, collapse Prolongation of local anesthesia Capillary bleeding Rhinitis, conjunctivitis Glaucoma Diagnostics of eye diseases

α – ADRENOMIMETICS

PECULIARITIES OF PREPARATIONS

- ***Noradrenaline*** **is catecholamine; has non-selective action on adrenoceptors, especially on α-adrenoceptors; has short-durative action, is administered only by IV infusion for collapse and acute hypotension.**
- ***Phenylephrine (Mesatonum)*** **is non-catecholamine; has selective action on α1-adrenoceptors; may be taken orally, administered SC, IM, IV, or topically, duration of action is 4-6 hrs.**
- ***Naphazoline and halazolin*** **are non-catecholamines; have selective action on α2-adrenoceptors, are used as nasal drops for acute rhinitis, nasal bleeding, and rhinoscopia; cause tolerance and tachyphylaxis.**

β – ADRENOMIMETICS

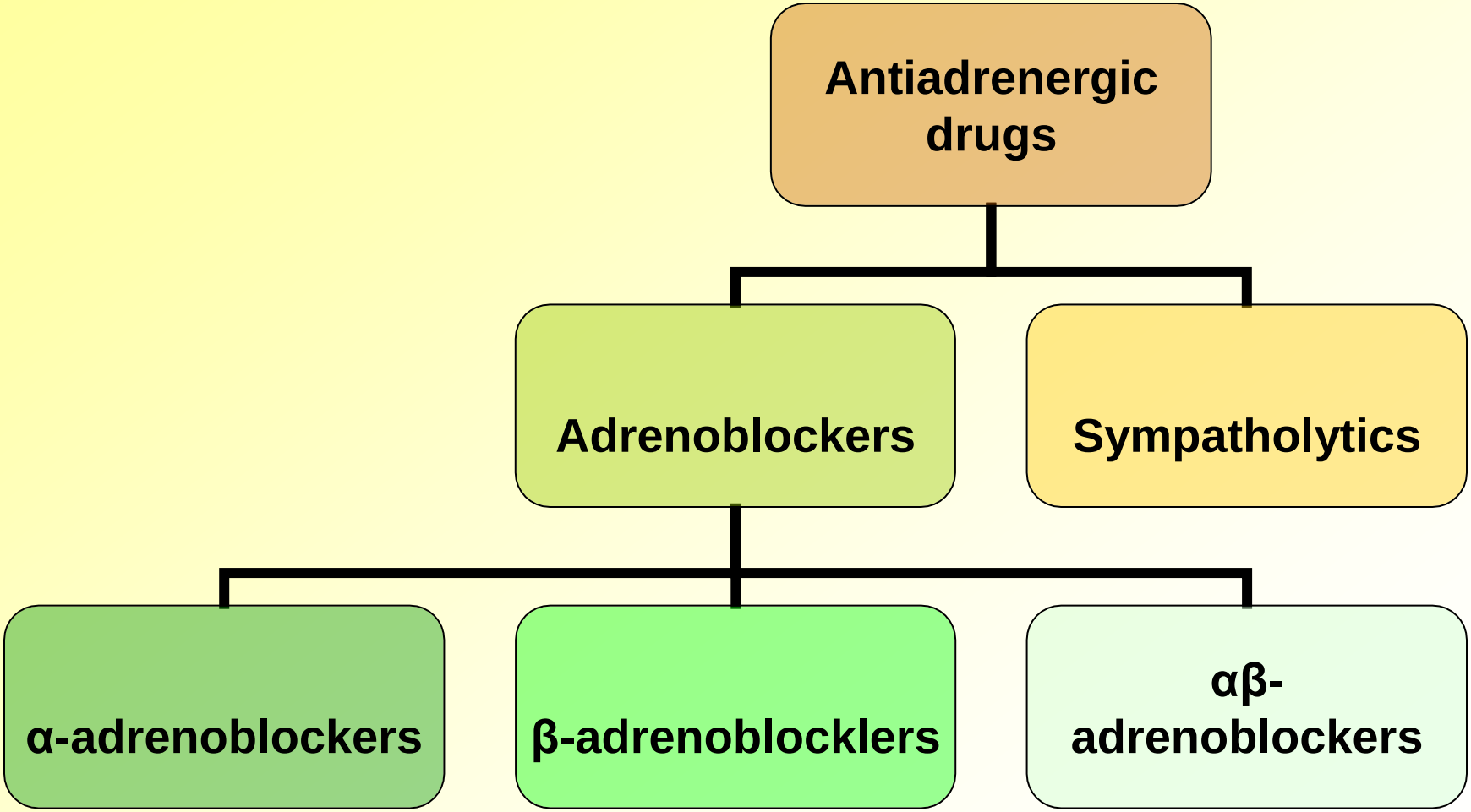
Pharmacodynamics	Indications
An increase in the heart contractions An increase in the heart rate Dilation of bronchi A decrease in myometrium tone	Acute heart failure *(Dobutamine)* Heart block, bradycardia *(Isoprenaline)* Bronchial asthma, spasm of bronchi *(Isoprenaline, salbutamol, fenoterol)* Danger of pregnancy interruption *(Fenoterol)*

β– ADRENOMIMETICS
PECULIARITIES OF PREPARATIONS

- ***Isoprenaline (Isadrinum)*** **is catecholamine; has non-selective action on β1- and β2-adrenoceptpors; is administered subligually, by inhalation, or IV; is used for bronchial asthma attack, heart block, some types of cardiogenous shock.**
- ***Salbutamol*** **is non-catecholamine; has selective action on β2-adrenoceptors, acts longer than isoprenaline; does not act on the heart; is used for bronchial asthma, bronchospasm and before bronchoscopia.**
- ***Fenoterol (Partusisten)*** **is non-catecholamine; has selective action on β2-adrenoceptors, acts during 4-6 hrs; does not act on the heart; is used for bronchial asthma and in danger of pregnancy interruption.**
- ***Dobutamine*** **has selective action on β1-adrenoceptors; increases cardiac output; is administered by IV infusion for emergency treatment of acute heart insufficiency and cardiogenous shock.**

ADREGERGIC ANTAGONISTS

GROUPS OF ADRENERGIC ANTAGONISTS



ADRENERGIC ANTAGONISTS
CLASSIFICATION

A. α-adrenoblockers:

1. Non-selective

– Phentolamine

– Tropaphenum

2. Selective

– Prazosin

– Doxazasin

B. β-adrenoblockers:

1. Non-selective

– Propranolol (Anaprilinum)

2. Selective

– Metoprolol

– Talinolol

– Atenolol

C. α-, β-adrenoblockers:

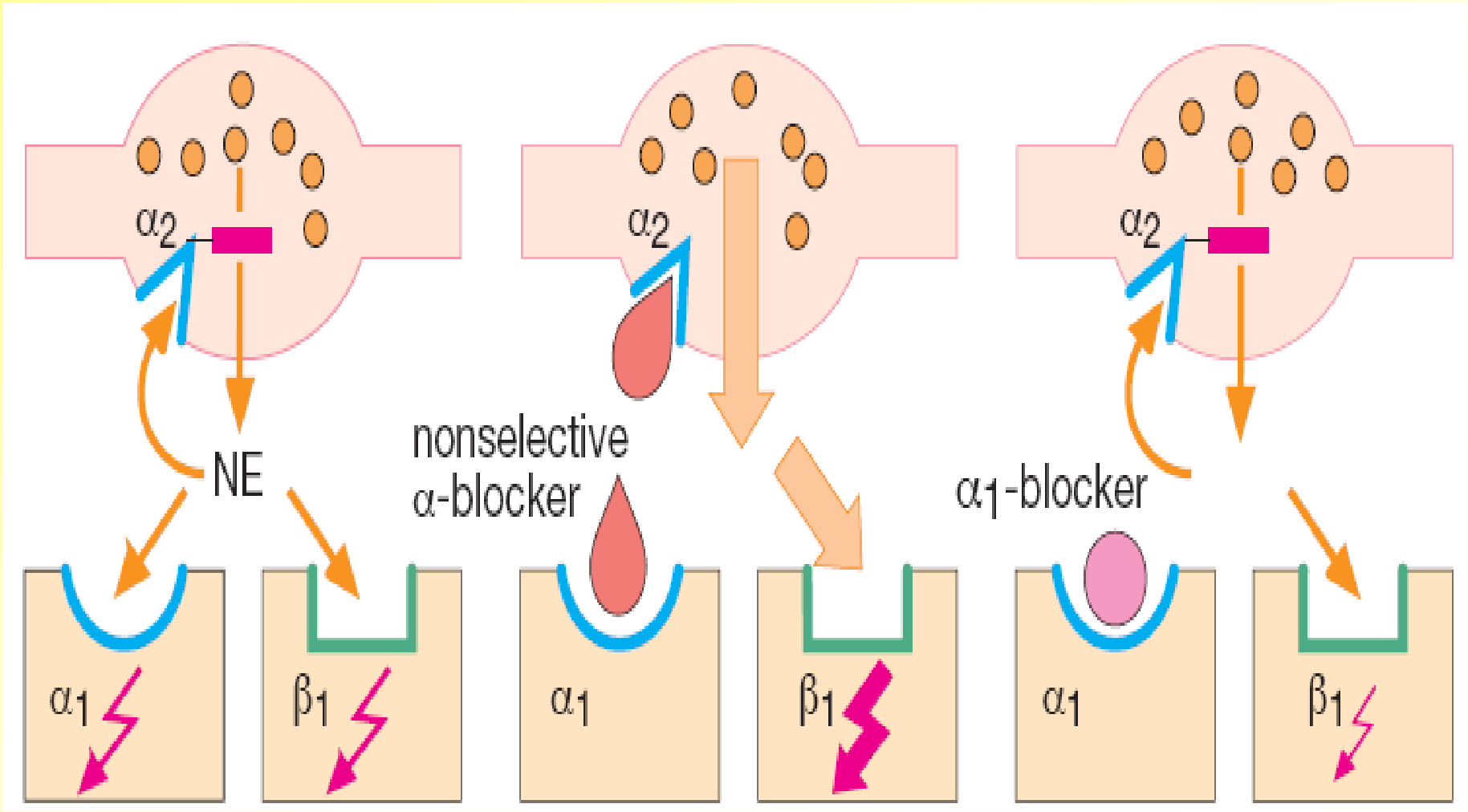
– Labetalol

D. Sympatholytics:

– Guanetidine (Octadinum)

– Reserpine

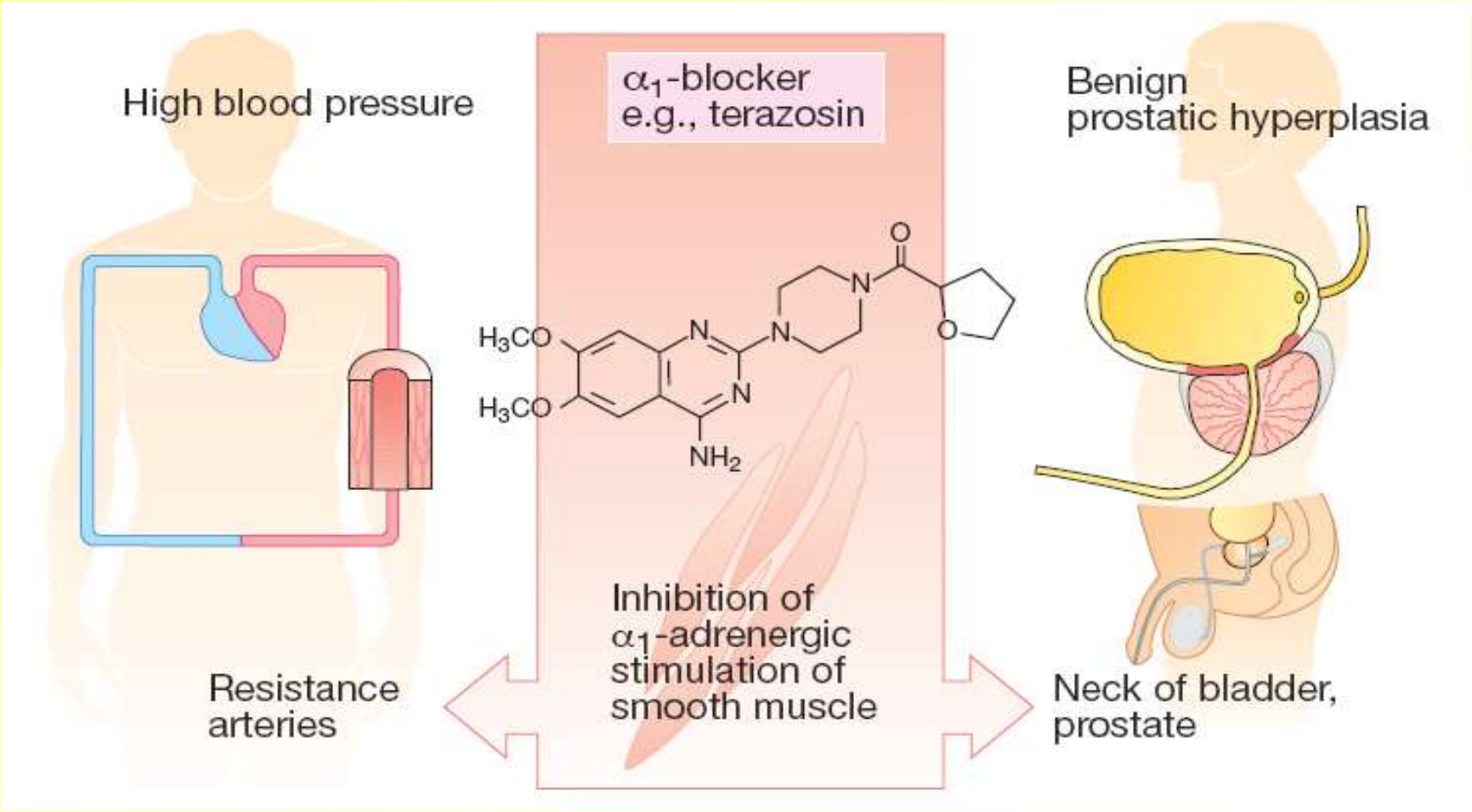
α-ADRENOBLOCKERS
MECHANISM OF ACTION



α- ADRENOBLOCKERS

Pharmacodynamics	Indications
Dilation of peripheral blood vessels A decrease in BP Improvement of trophy of peripheral tissues Stimulation of motility in the gut Stimulation of exocrinal secretion A decrease in retention of urine in patients with prostate hyperplasia.	Hypertension Spasms of peripheral blood vessels (Raynaud's disease) Frostbites, trophic ulcers Pheochromacitoma (diagnostics and treatment) Prostate hyperplasia

α- ADRENOBLOCKERS
MAIN CLINICAL USES



α- ADRENOBLOCKERS
SIDE-EFFECTS

- Headache, vertigo
- Hypotension
- Weakness
- Insomnia
- Orthostatic collapse
- Tachycardia (for non-selective drugs)
- Vomiting, nausea, diarrhea
- Rhinitis

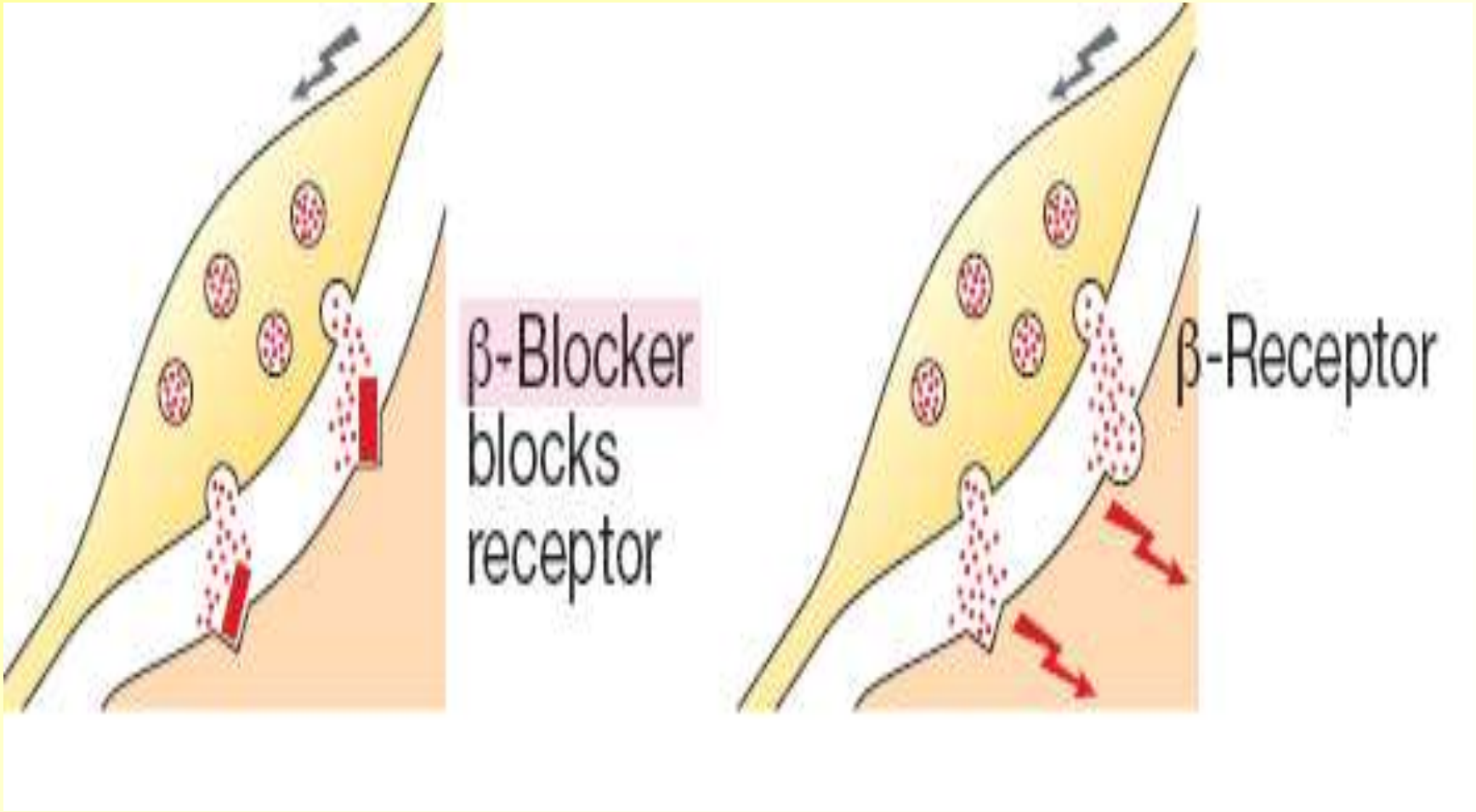
α- ADRENOBLOCKERS
PECULIARITIES OF PREPARATIONS

- ***Phentolamine hydrochloride*** has non-selective action (blocks α1 and α2-adrenoceptors); is administered orally or IV; has short duration of action; has many side-effects; causes tachycardia due to the blockage of α2-adrenoceptors and disorders in back-cross regulation of norepinephrine liberation in synapses.
- ***Prazosin*** has selective action (blocks α1-adrenoceptors); is taken orally; acts during 4-6 hrs; is used for treatment of hypertension; has less side-effects.
- ***Doxazosin*** has selective action (blocks α1-adrenoceptors); is taken orally; has more durative and strong action than prazosin; decreases urine retention in patients with adenoma of prostate; is used for treatment of hypertension and adenoma of prostate.

β- ADRENOBLOCKERS
PROPRANOLOL (ANAPRILINUM)
PHARMACOKINETICS

- is administered orally, IV, topically (eye drops)
- is absorbed in the GI tract
- is bound with proteins in blood serum
- penetrates CNS
- is metabolized in the liver
- is excreted by urine
- acts during 3-4 hrs

PROPRANOLOL
MECHANISM OF ACTION



PROPRANOLOL (ANAPRILINUM)
PHARMACODYNAMICS AND INDICATIONS

Pharmacodynamics	Indications
A decrease in automaticity, excitability, and conductivity of myocardium A decrease of the heart rate (*anti-arrhythmic* effect) A decrease in the heart contractility, striking and minute volume A decrease in consumption of oxygen by myocardium (*antianginal* effect) A decrease in renin secretion in the kidney A decrease in BP (*antihypertensive* effect) A decrease in intraocular pressure Sedative action	Hypertension Ischemic heart disease (angina pectoris, myocardial infarction) Tachyarrhythmia Hyperthyroidism Migraine Glaucoma

PROPRANOLOL (ANAPRILINUM)
SIDE-EFFECTS AND CONTRAINDICATIONS

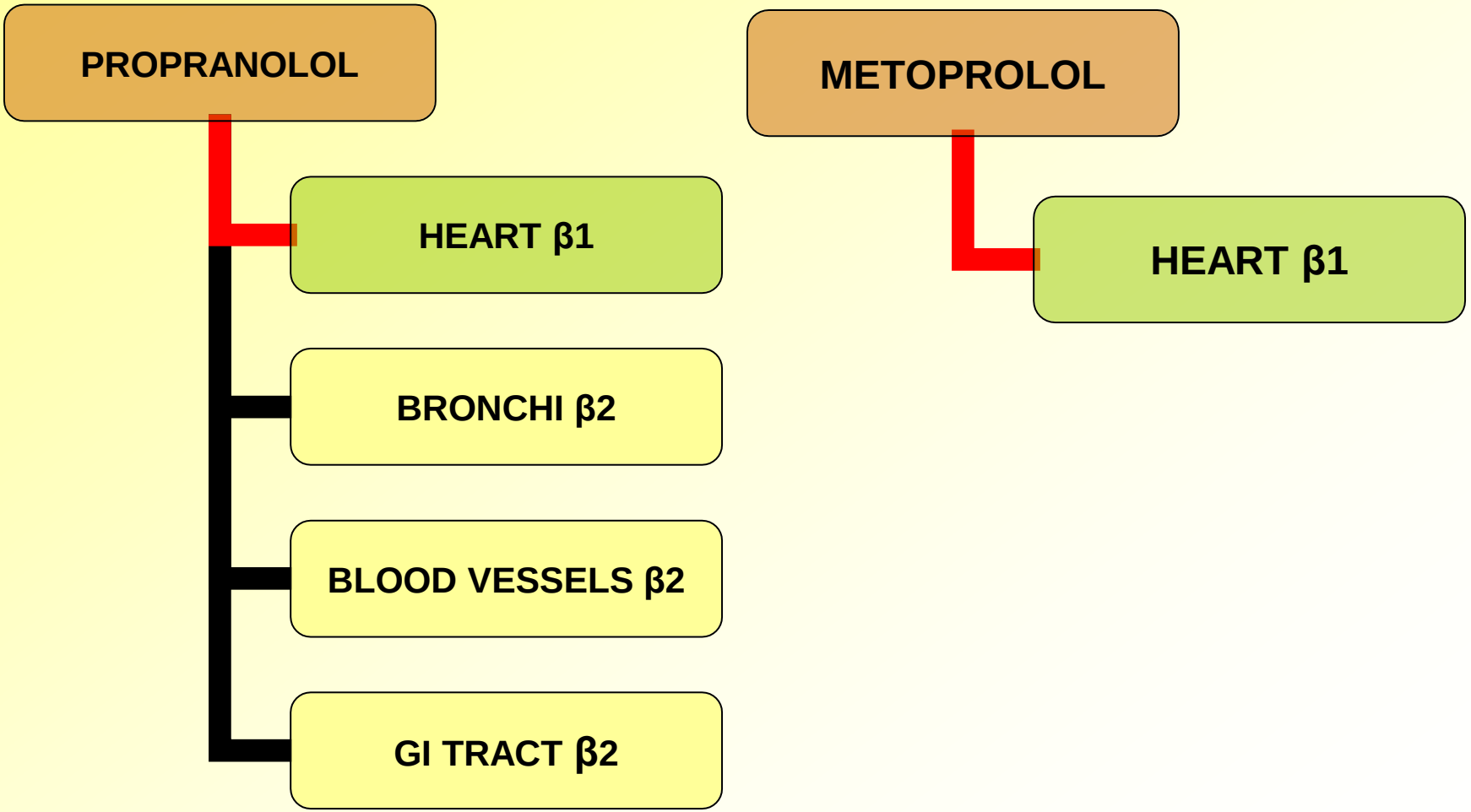
Side-effects

- Bradycardia
- Hypotension
- Increasing of heart incompetence
- Heart block
- Spasm of bronchi
- Hypoglycemia when insulin is given together
- Fatigue, drowsiness, vertigo, depression
- Disturbances of sexual function in men

Contraindications

Bradycardia, hypotension, severe heart failure, heart block, bronchial asthma, ulcerative disease, diabetes mellitus, disturbances of peripheral blood circulation, pregnancy

COMPARISON OF PROPRANOLOL AND CARDIOSELECTIVE β-ADRENOBLOCKERS



β-ADRENOBLOCKERS
PECULIARITIES OF PREPARATIONS

- ***Metoprolol*** **has cardioselective action (on β1-receptors); is taken orally for treatment of hypertension, angina pectoris and arrhythmia; less side-effects: does not cause spasm of bronchi and increase of gastric secretion; may be used in patients with bronchial asthma, ulcerative disease, and diabetes mellitus.**
- ***Talinolol*** **has cardioselective action (on β1-receptors); has *inner sympathomimetic activity* and membrane stabilizing effect (does not decrease heart contractility and conductivity); less side-effects; less contraindications connected with influence on β1-adrenoceptors.**
- ***Atenolol*** **has cardioselective action (on β1-receptors); is similar to metopolol.**

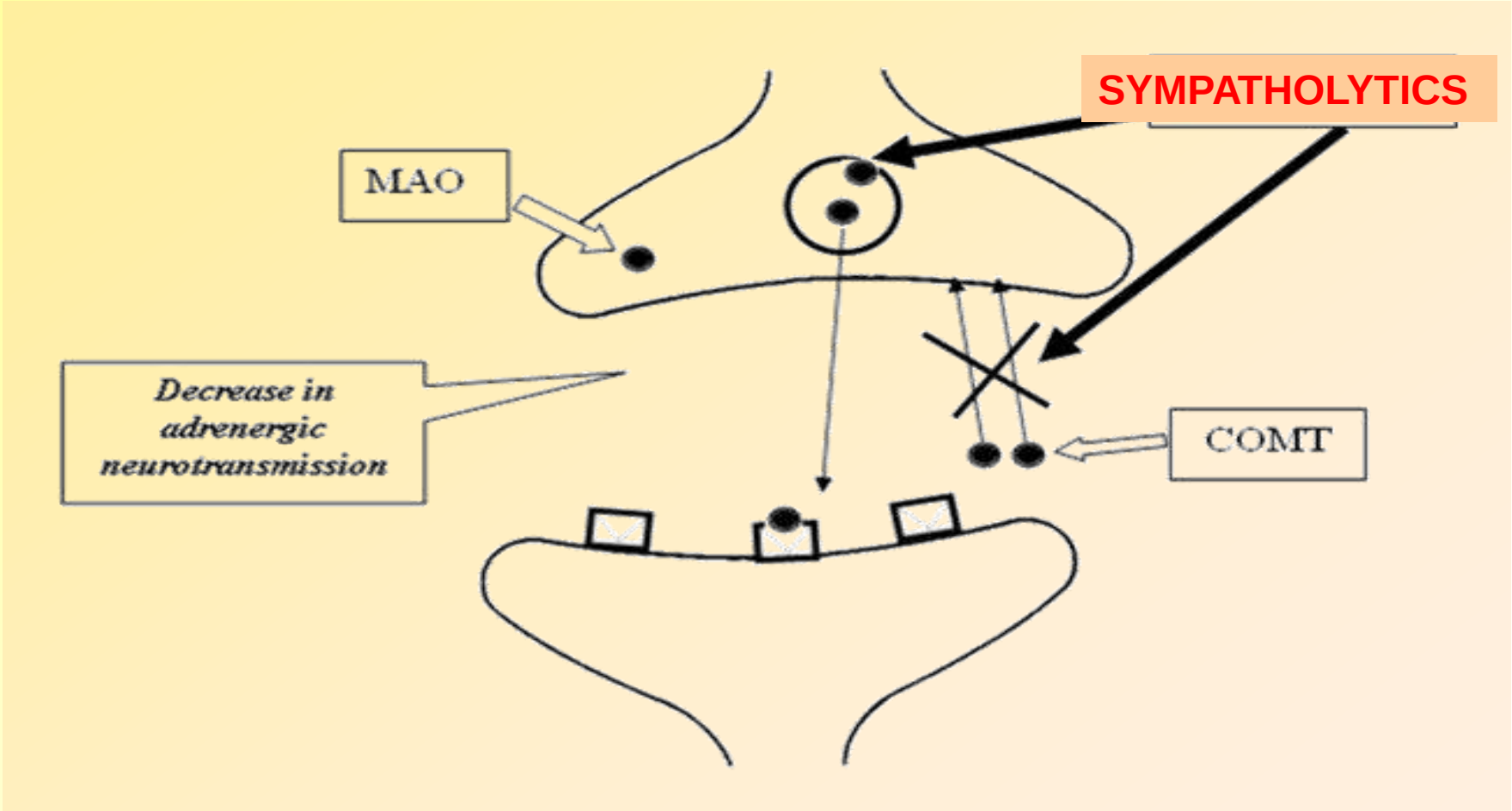
α-, β-ADRENOBLOCKERS LABETALOL

- blocks both α- and β-adrenoceptors
- action on β-receptors is 3 times more intensive than the action on α-receptors
- less active than propranolol
- less active than phentolamine
- is taken orally or IV
- is indicated for control of hypertension
- is contraindicated in heart block, spasm of bronchi, pregnancy

SYMPATHOLYTICS

Sympatholytics **are presynaptically acting anti-adrenergic drugs.**

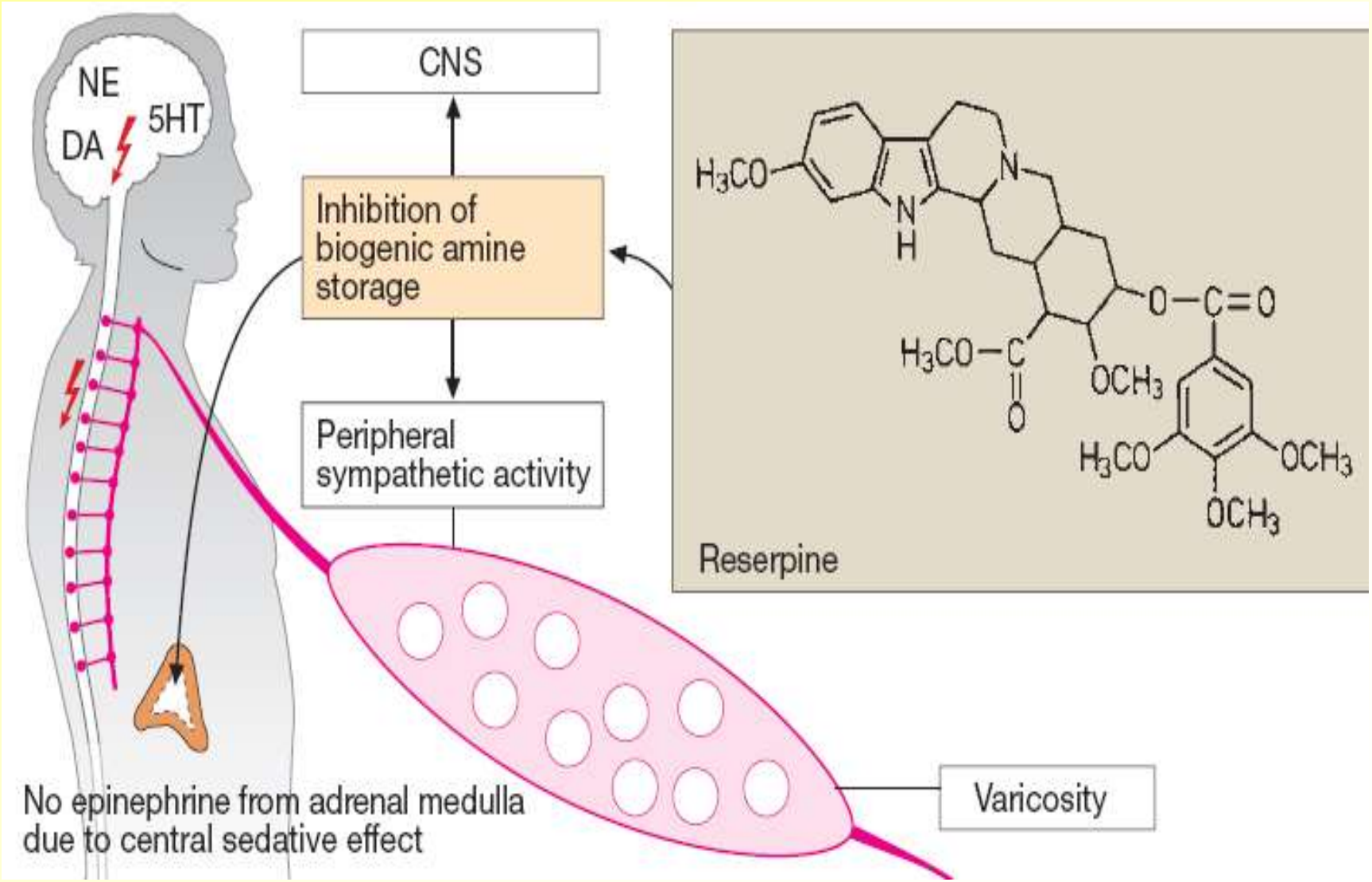
SYMPATHOLYTICS
MECHANISM OF ACTION



RESERPINE

- decreases the storage of norepinephrine
- penetrates CNS, has central and peripheral action
- has antihypertensive, sedative, and antipsychotic action
- is administered orally, IM or IV
- acts 8-12 hrs
- is indicated for hypertension
- may cause disturbances of sleep, depression, bradycardia, spasm of bronchi, stimulation of gastric secretion, diarrhea

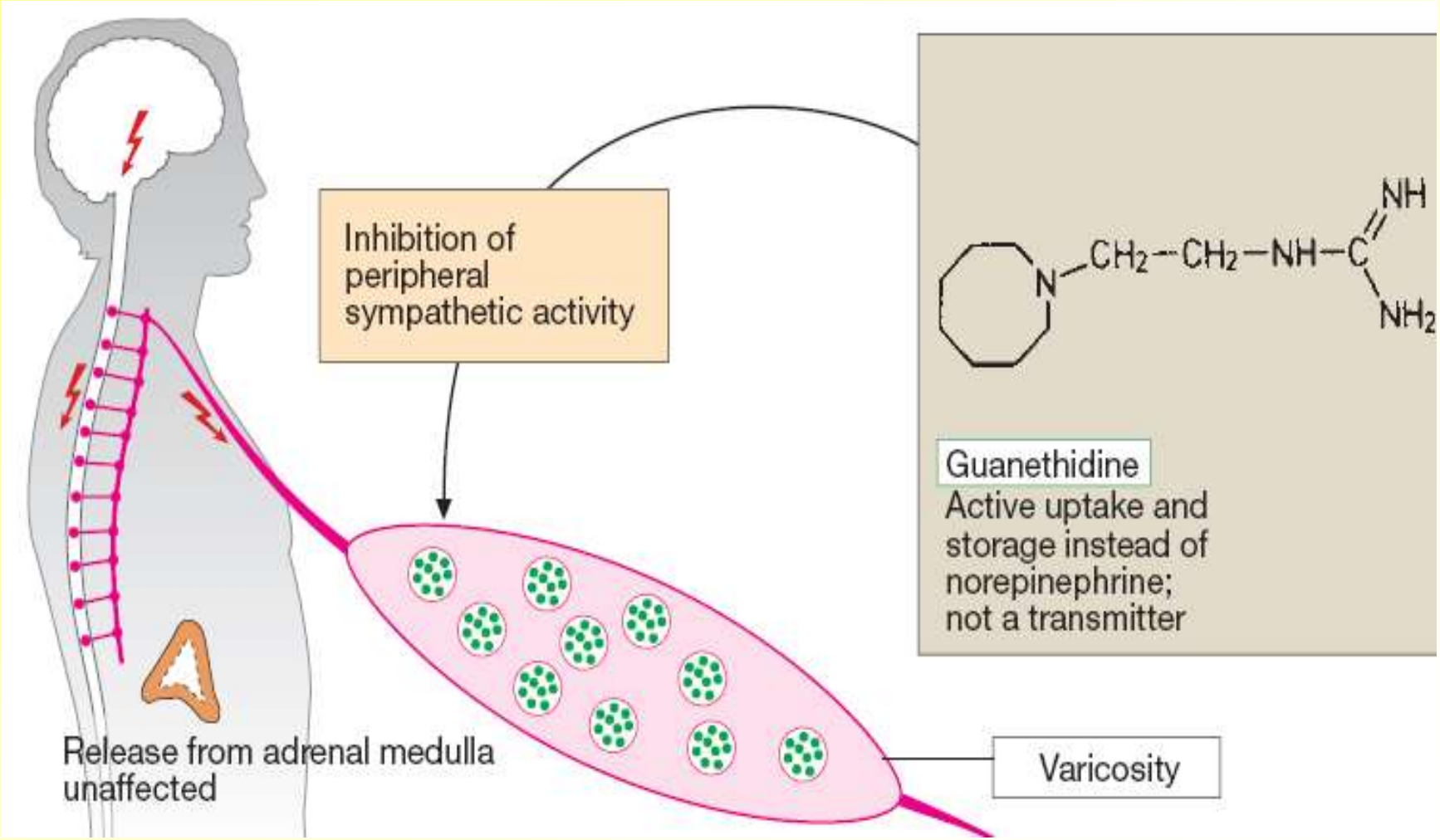
RESERPINE
CENTRAL AND PERIPHERAL ACTION



GUANETIDINE (OCTADINUM)

- decreases the storage of norepinephrine, decreases mediator release and re-uptake
- does not penetrate CNS, has only peripheral action
- has antihypertensive action, decreases intraocular pressure
- is taken orally or in the form of eye drops
- action is slow and long (it starts to act in 2-4 days after the beginning of treatment and continues to act during 10-14 days after the ending of treatment)
- is indicated for hypertension, glaucoma, some arrhythmias
- may cause orthostatic hypotension

GUANETIDIN
PERIPHERAL ACTION ONLY



THE END

Thank you for attention!