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SYMPATHOTROPIC DRUGS

SYMPATHOLYTICS

Department of Pharmacology

Sympatholycs (direct and indirect)

Indications:

- hypertension (mild and moderate)
- antimigraine drugs
- disorders of peripheral vascularity
- benign prostatic hyperplasia
- urinary obstruction – postoperative atonia
- pheochromocytoma

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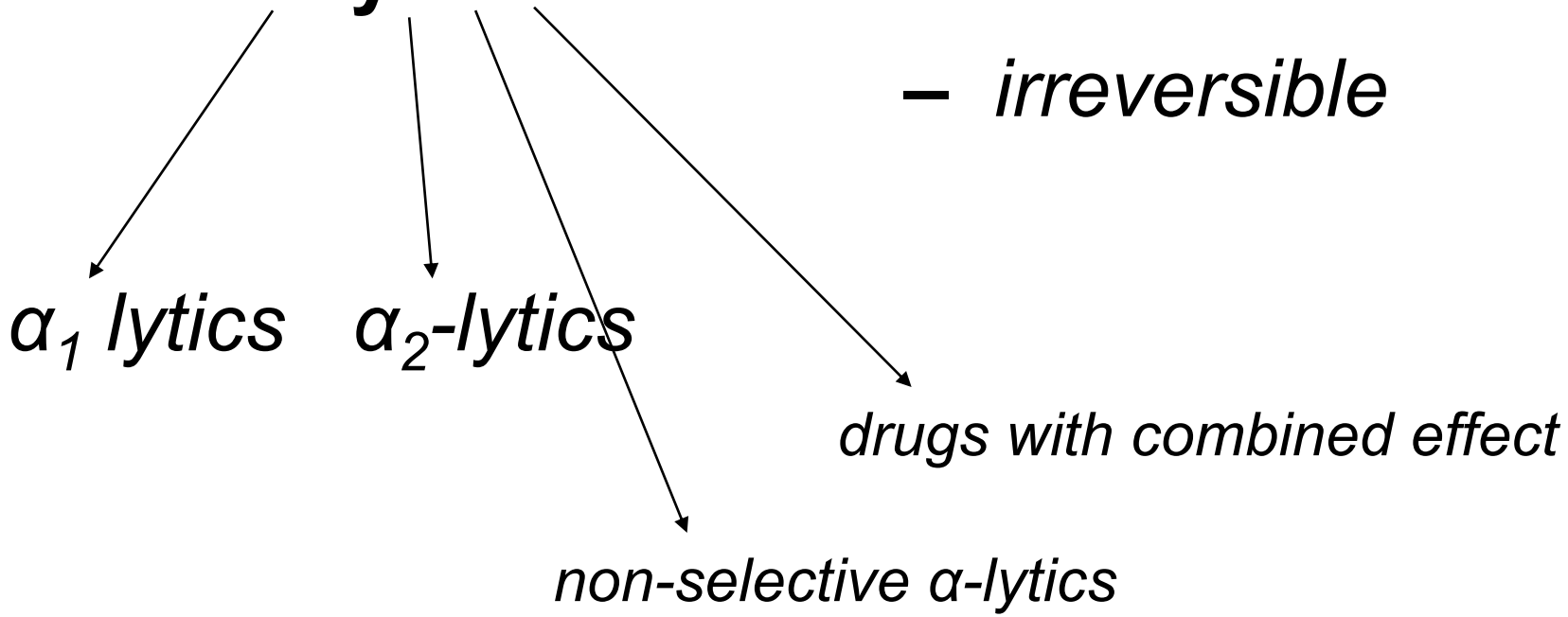
Direct sympatholytics

α

α-lytics

- *reversible*
- *irreversible*



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Direct sympatholytics
α non-selective

- **ergot alkaloids** (ergotamine, ergometrine, ergotoxine, methylergometrine, dihydroergotamine, dihydroergotoxine, dihydroergocristine)

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Direct sympatholytics
α non-selective

Ergot alkaloids and their derivatives ➔ reversible α-lytics

- in *Secale cornutum*, product of *Claviceps purpurea*, fungus that infects cereal crops
- derivatives of lysergic acid
- effects:

- CNS (halucinations, ↓ prolactine secretion)
- smooth muscle of blood vessel (effects mimetic or **lytic**)
- uterine muscle → contractions

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Direct sympatholytics
α non-selective
Ergot alkaloids

- **ergotamine, ergometrine**

  - parcial α-agonistic effects

  - uterotonic effect, amplified by methylation of derivatives (methylergometrine)

- **ergotoxine**

  - mixture of alkaloids, mainly **ergocristine, ergocriptine** and **ergocornine** - especially α-lytic effects

- **<u>α-lytic effects are increased in dihydro-derivatives</u>** ***(dihydroergotamine, dihydroergotoxine, dihydroergocristine)*** !

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Direct sympatholytics
α non-selective
Ergot alkaloids

- **methylergometrine**

uterotonic effect

• therapy and prevention of uterine bleeding after childbirth (in hypotony and atony of myometrium)

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Direct sympatholytics
α_1 selective

$\alpha_1$sympatholytics

Overview of drugs, use

- **terazosin, doxazosin, alfuzosin, tamsulosin…**
- **prazosin (in Czech Rep. non registered)**

- **Use:**

  - hypertension (relaxation of arterial and venous smooth muscle)

  - benign prostatic hyperplasia

  - urinary obstruction

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Direct sympatholytics with combined effect

- **urapidil**

- combined central and peripheral action, blocks α_1 receptors, in CNS blocks H_1 receptors, activates 5-HT_{1A} receptors

- **Use:**
  - hypertension (hypertension crisis, severe, respectively, very severe forms of hypertension and hypertension resistant to standard therapy)

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Direct sympatholytics
α_2 selective

α_2 sympatholytics

- **yohimbine** (in Czech Rep. non registered)
- vasodilation in the pelvic area, afrodisiac effect
- it is contained in some dietary supplements

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Direct sympatholytics
β-blockers, β-sympatholytics

- **competitive antagonists** (intrinsic aktivity = 0) or **partial agonists**

  (ISA - *intrinsic sympathomimetic activity*) = dualists

- **nonselective** or **cardioselective** (selectively block í β_1 receptors)

- sufficient solubility in fats → penetration across HEB

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Direct sympatholytics
β-blockers, β-sympatholytics

Organ effects

cardiovascular system: negatively chronotropic and inotropic effect →

↓ **BP** and **HR**

- inhibition of vasodilation by β_2-receptor blockade → **peripheral vascular resistence increase**

- renine secretion reduction

bronchi: bronchoconstriction

eye: intraocular pressure decrease

metabolic effects: glycogenolysis reduction, lipolysis inhibition

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Direct sympatholytics
β-blockers, β-sympatholytics

NONSELECTIVE (β_1 + β_2)	**propranolol, metipranolol**
(CARDIO)SELECTIVE (β_1)	**atenolol, metoprolol**
NONSELECTIVE (β_1 + β_2) WITH ISA	**pindolol, bopindolol (in Czech Rep. non registered)**
(CARDIO)SELECTIVE (β_1) WITH ISA	**acebutolol**
WITH COMBINED EFFECTS α + β	**labetalol carvedilol**

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Direct sympatholytics
β-blockers, β-sympatholytics

Use, indications:

- hypertension
- Ischemic heart disease, non-stabil *angina pectoris*, status after acute myocardial infarction
- arrhytmia
- glaucoma
- hyperthyreosis
- anxiety (moderate effect)

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Direct sympatholytics
β-blockers, β-sympatholytics

Side effects:

- *asthma bronchiale*, dyspnoea
- heart insufficiency
- bradycardia, blockade of heart impuls conduction
- masking of hypoglycemia symptoms
- disorders of peripheral blood circulation
- sleep disorders, depression (lipophilic drugs)
- rash, fever and other allergic symptoms (rarely)
- abrupt discontinuation of therapy – „**rebound phenomena“**

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Nondirect sympatholytics

decreases catecholamine concentration in the synaptic cleft by:

- inhibition of NT synthesis
- inhibition of NT storage
- inhibicí of NT release
- false precursors

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