

SYMPATHOTROPIC DRUGS

SYMPATHOLYTICS

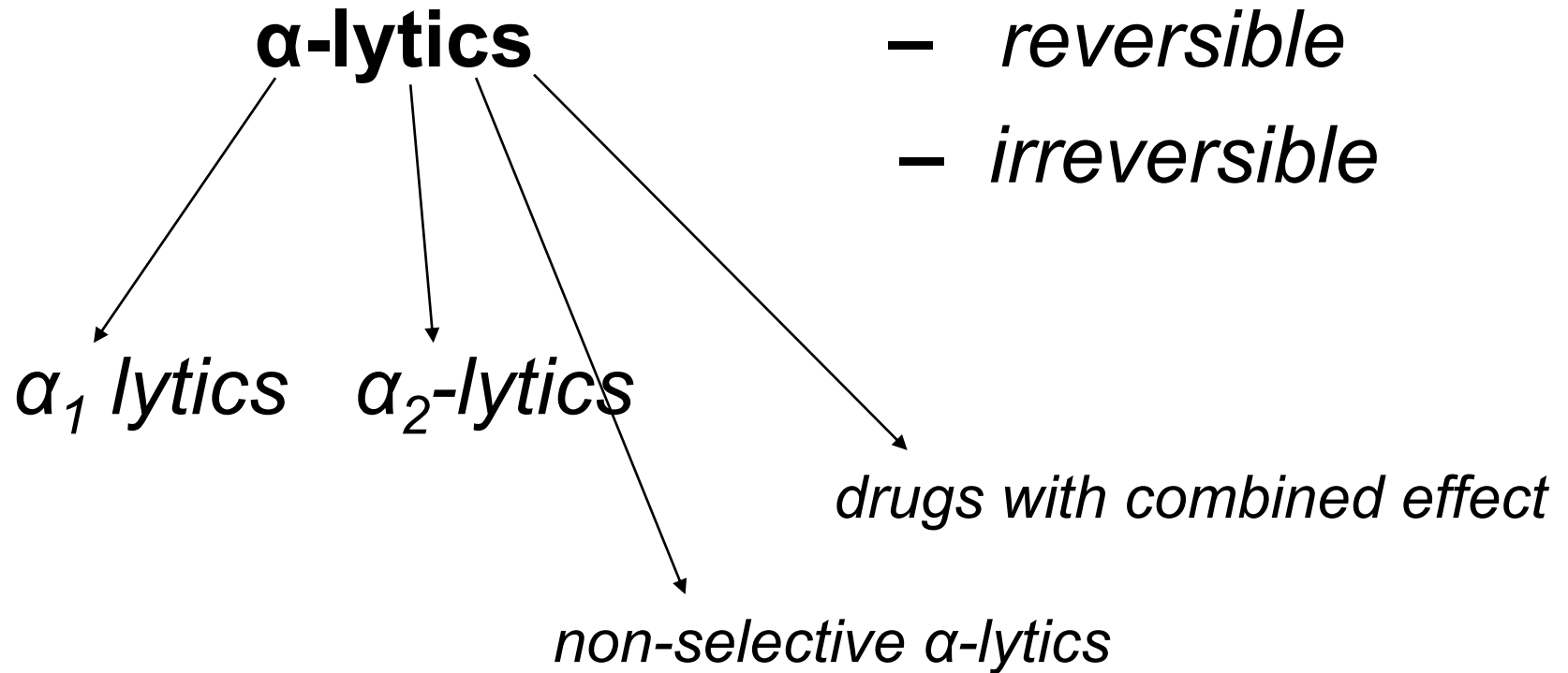
Sympatholytics (direct and indirect)

Indications:

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

Direct sympatholytics

α



Direct sympatholytics α non-selective

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

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 (hallucinations, ↓ prolactin secretion)
 - smooth muscle of blood vessel (effects mimetic or **lytic**)
 - uterine muscle → contractions

Direct sympatholytics

α non-selective

Ergot alkaloids

- **ergotamine, ergometrine**
 - partial α -agonistic effects
 - uterotonic effect, amplified by methylation of derivatives (methylergometrine)
- **ergotoxine**
 - mixture of alkaloids, mainly **ergocristine, ergocriptine** and **ergocornine** - especially α -lytic effects
- **α -lytic effects are increased in dihydro-derivatives**
(*dihydroergotamine, dihydroergotoxine, dihydroergocristine*)

!

Direct sympatholytics

α non-selective

Ergot alkaloids

- **methylergometrine**

uterotonic effect

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

Direct sympatholytics

α_1 selective

α_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

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)

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

Direct sympatholytics β -blockers, β -sympatholytics

- **competitive antagonists** (intrinsic activity = 0) or **partial agonists**
(ISA - *intrinsic sympathomimetic activity*) = dualists
- **nonselective** or **cardioselective** (selectively block β_1 receptors)
- sufficient solubility in fats \rightarrow penetration across HEB

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 resistance increase**

- renine secretion reduction

bronchi: bronchoconstriction

eye: intraocular pressure decrease

metabolic effects: glycogenolysis reduction, lipolysis inhibition

Direct sympatholytics β -blockers, β -sympatholytics

NONSELECTIVE ($\beta_1 + \beta_2$) propranolol, metipranolol

(CARDIO)SELECTIVE (β_1) atenolol, metoprolol

NONSELECTIVE ($\beta_1 + \beta_2$) WITH ISA pindolol,
bopindolol (in
Czech Rep. non
registered)

(CARDIO)SELECTIVE (β_1) WITH ISA acebutolol

WITH COMBINED EFFECTS $\alpha + \beta$ labetalol
carvedilol

Direct sympatholytics β -blockers, β -sympatholytics

Use, indications:

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

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**“

Nondirect sympatholytics

decreases catecholamine concentration in the synaptic cleft by:

- inhibition of NT synthesis
- inhibition of NT storage
- inhibic  of NT release
- false precursors