



Zaporizhzhia State Medical University Pharmacology Department

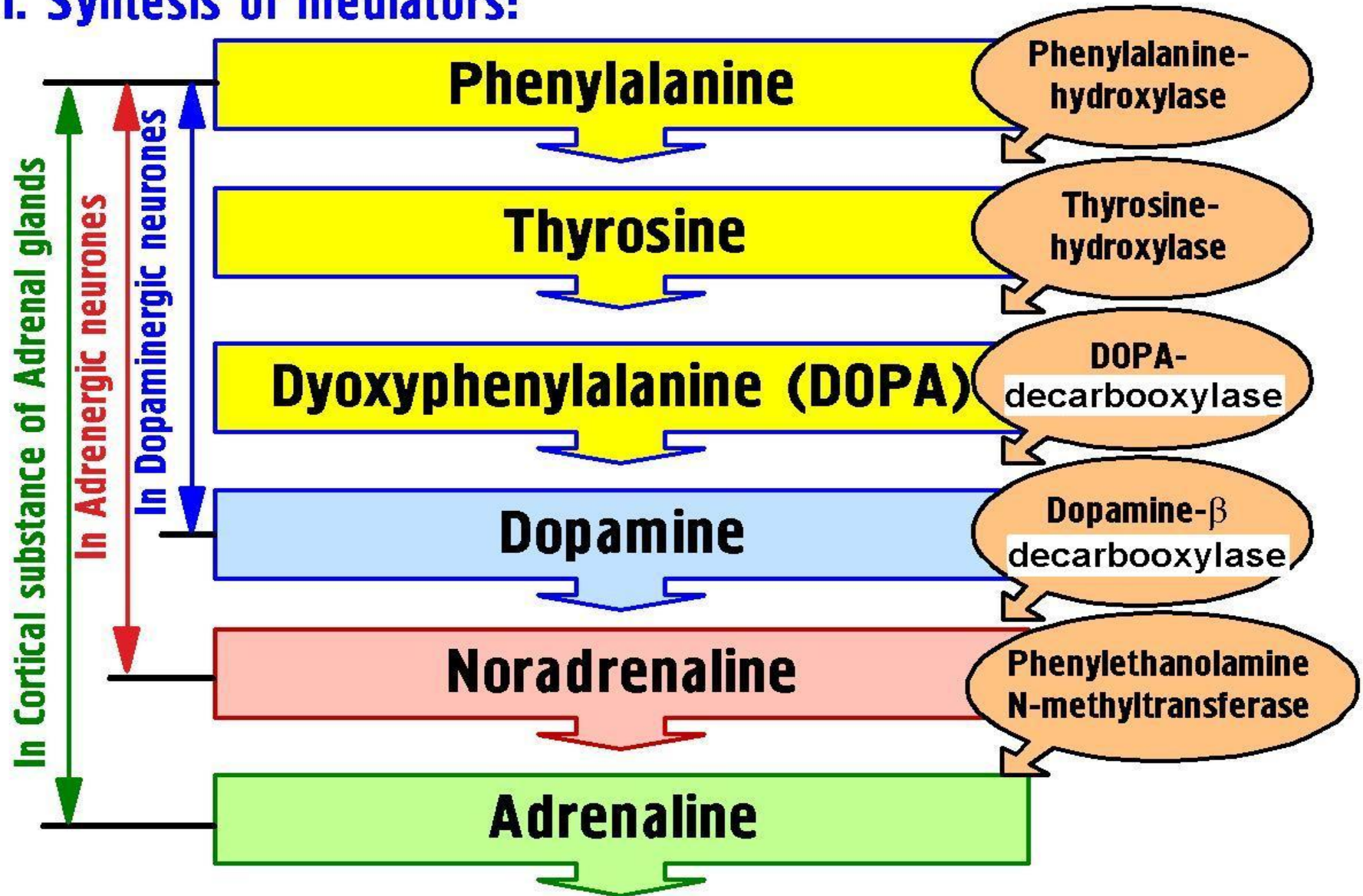
Lecture №3

Adrenergic Drugs

Lecturer: Assoc.Prof. **Irina Borisovna Samura**

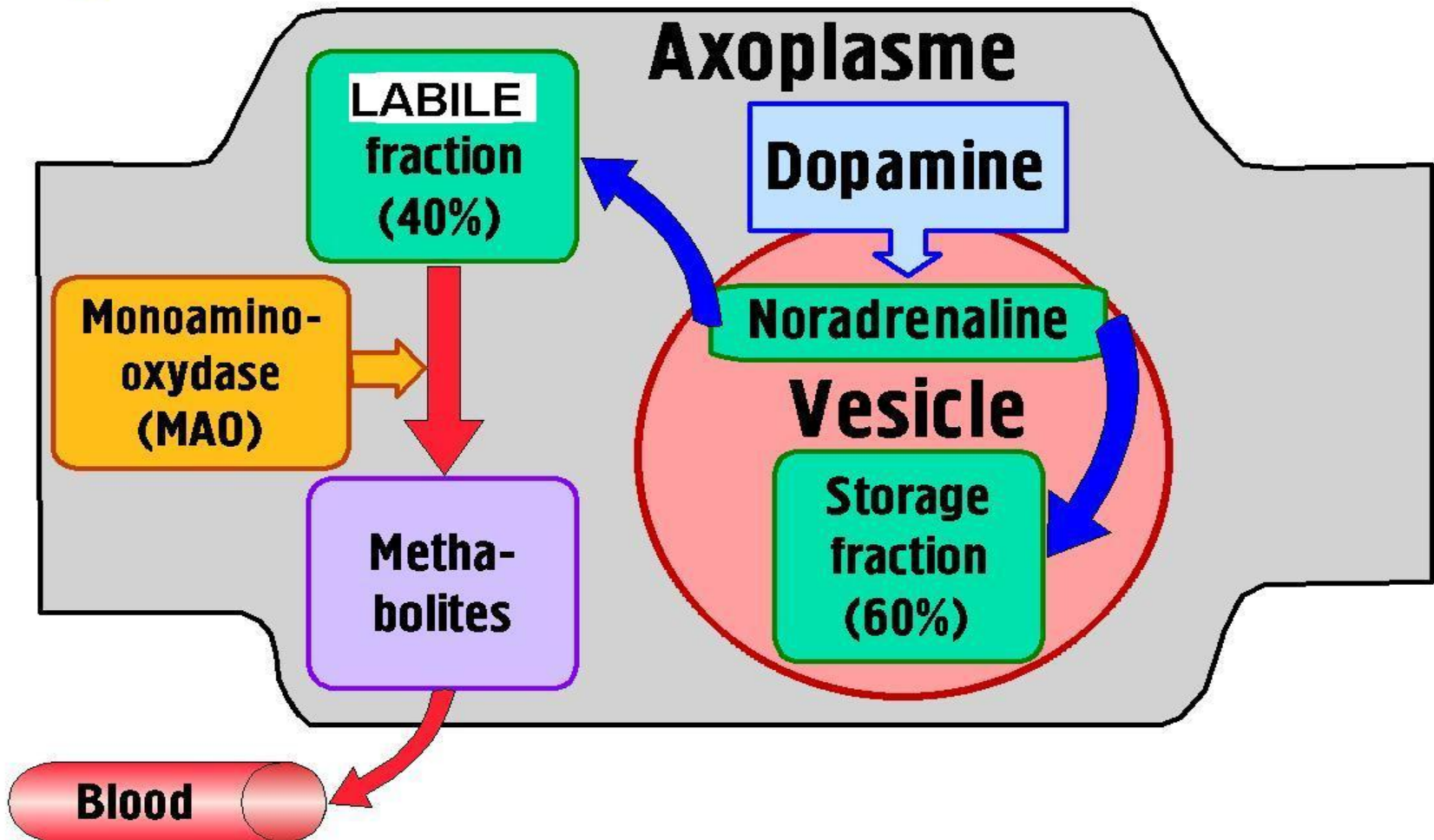
Function of Adrenergic synapse

1. Syntesis of mediators:



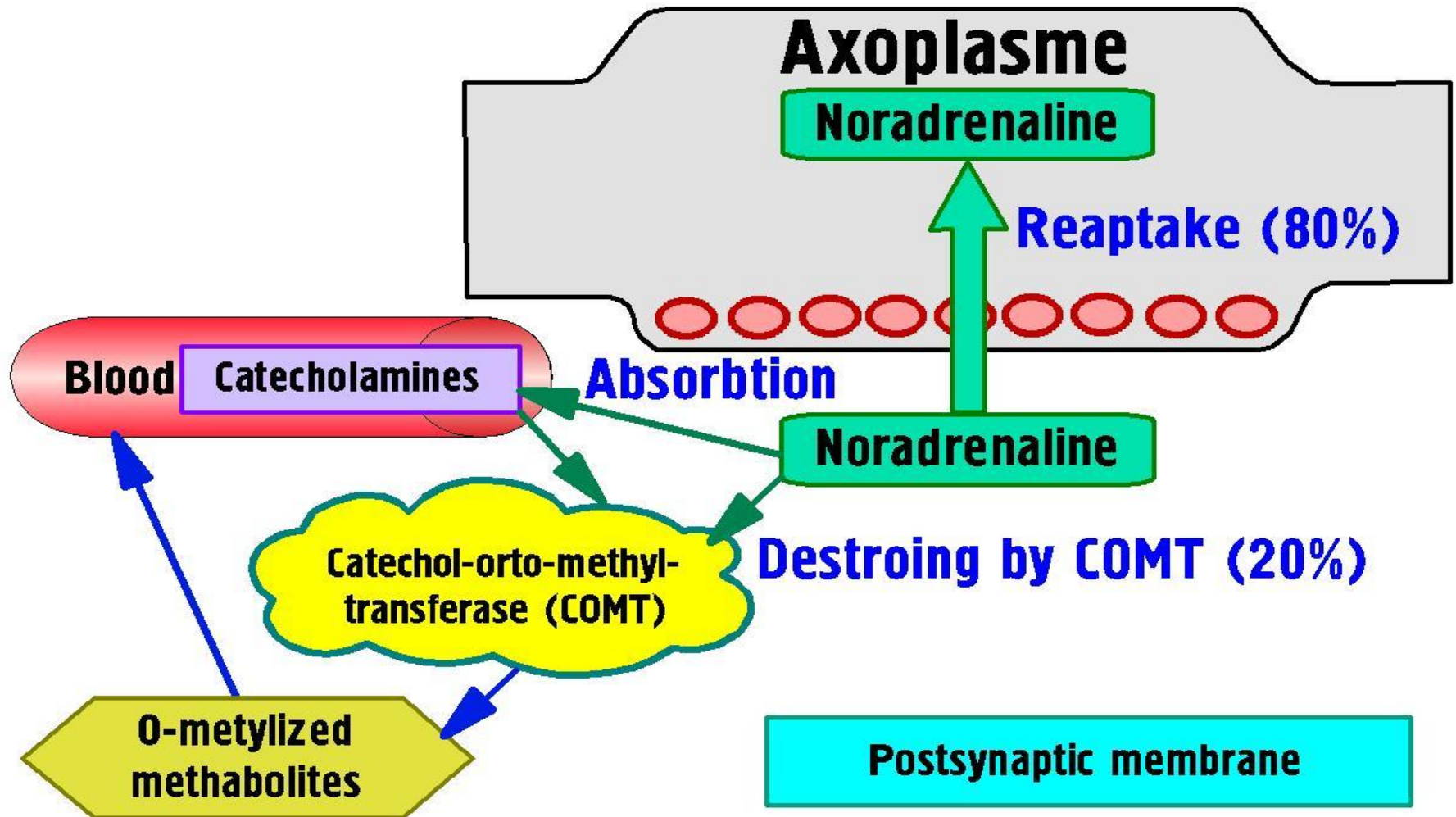
Function of Adrenergic synapse

2. The fate of noradrenaline in varicose thickenings of nerve endings:



Function of Adrenergic synapse

4. The fate of noradrenaline in synaptic slit:



MAO-A - metabolizes **Noradrenaline** and **Serotonin**,
MAO-B - **Dopamine**, **Phenylethylamine** and **Tyramine**

Tyramine is a product of **tyrosine** metabolism and
is found in fermented foods:

Cheese - 130 mg/100 g

Beans - also contain *Dopamine*

Chicken Liver

Chocolate - also contains *Phenylethylamine*

Fermented Sausage, Beer,

Smoked or Pickled Fish

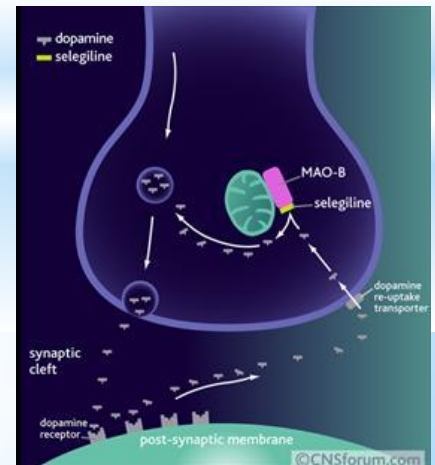
MAO inhibitors: Nialamid, Transamine and

MAO-A inhibitors: Moklobemid, Pirazidol - □□BP

α_1 Receptors: on the Postsynaptic Membrane of the Effector organs – on smooth muscle and glands and are **excitatory**

α_2 Receptors: on the Pre- and Postsynaptic Membrane of the Effector organs.

The stimulation of the **Presynaptic α_2 -Receptors** => **Feedback Inhibition** of **noradrenaline** release from the stimulated Adrenergic neuron –
Negative Feedback



β_1 -receptors: HEART and are **Excitatory**

β_2 -receptors: on *Smooth Muscle* of –

Bronchi

Vasculature of Skeletal Muscle

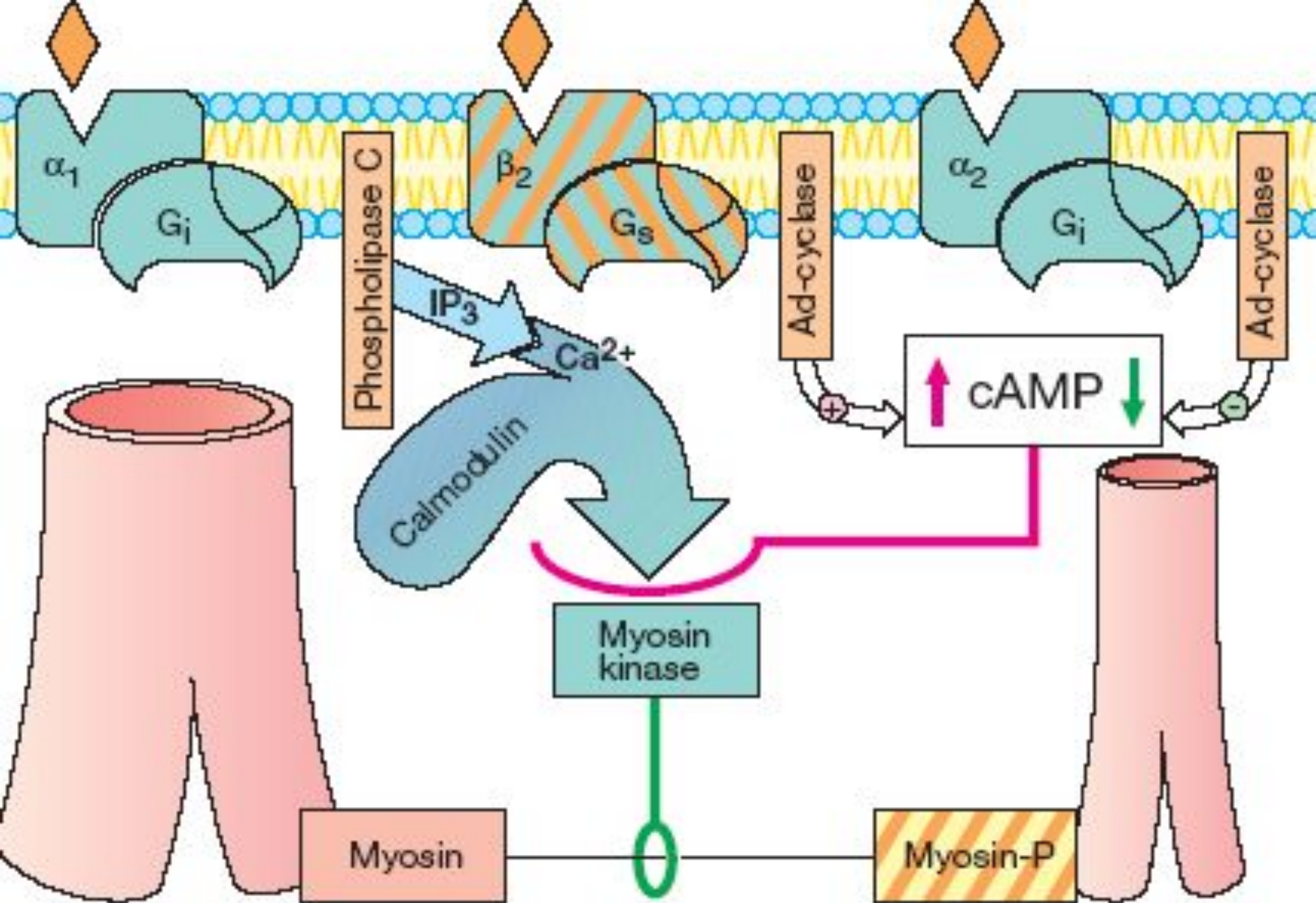
Miometrium

Glands

and are **Inhibitory**

β_3 -receptors: Adipose (Fat) cell =>
stimulation of lipolysis





. Vasomotor effects of catecholamines

Localisation of adrenoceptors and effects of their exitation

2. Effects upon the eye:

→ α_1 -adrenoceptors:

■ in the smooth muscle - dilatator of pupil.

- ▶ Contraction of radial muscle of the iris, dilation of pupil (mydriasis) and photophobia.
- ▶ Tightening of Zinn's ligament, decrease of curvature of lens: eye sets for distant point of vision (paralysis of accomodation).
- ▶ Narrowing of Schlemms' channel and Fontana's spaces which cause decreasing of the aqueous humor outflow from the anterior chamber of the eye. It contribute to increasing of intraocular pressure.

■ in the blood vessels of eye fundus.

- ▶ Decreasing of the aqueous humor production. It contribute to decreasing of intraocular pressure.

 Result effect - decreasing of intraocular pressure.

Localisation of adrenoceptors and effects of their exitation

3. Effects upon another smooth muscles:

→ α_1 -adrenoceptors:

- in the sphincters of gastrointestinal tract.

▶ Contraction of sphincters, decreasing of peristaltics.

→ β_2 -adrenoceptors:

- in the smooth muscles of bronchi.

▶ Dilatation of bronchi (broncholytic effect).

- in the smooth muscles of uterus.

▶ Decreasing of rhythmic contractions of uterus on labors (tocolytic effect).

- in the skeletal muscles.

▶ Increasing of contractive activity.

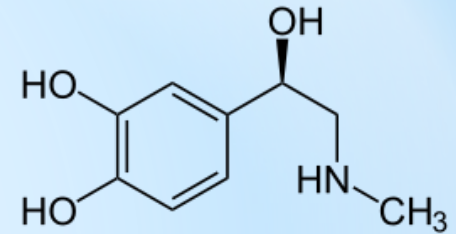


I. Adrenomimetics of Direct Action

1). α -, β - Adrenomimetics:

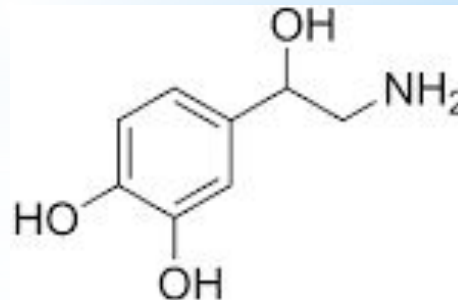
- **Adrenaline hydrochloride** - α_1 , α_2 , β_1 , β_2 , β_3

amp. 0.1%-1ml; vial 0.1%-10 ml



- **Noradrenaline hydrotartrate** - α_1 , α_2 , β_1

amp. 0.2% -1 ml (IV infusion)



THE MAIN EFFECTS of *ADREANALINE* :

- ▶ **Cardiac Stimulation**
- ▶ Relaxation of **Bronchial Muscle**
- ▶ **Dilation of Skeletal Muscle Vasculature**
- ▶ Significant **Hyperglycemia**:
 - ↑ **Glycogenolysis** in the Liver (**β_2 effect**)
 - ↓ **Release of Insulin** (**α_2 effect**).

Adrenaline is metabolized by 2 enzymatic pathways:

COMT and **MAO**

Clinical uses:

- ☐ Bronchospasm
- ☐ Anaphylactic shock: is the drug of choice
- ☐ Cardiac arrest and acute ☐ AP
- ☐ Hypoglycemic coma (overdose with ***Insulin***)
- ☐ Glaucoma

Noradrenaline hydrotartrate: α_1 , α_2 , β_1

the strongest **Peripheral Vasoconstrictor**

↑↑ **Total Peripheral Resistance** => ↓ **HR**

↑ **Systolic and Diastolic AP**

- ↓ Blood Flow to Vital Organs, Skin, and Skeletal Muscle
- Constriction of Renal Blood Vessels
- ↑ Heart Contraction

Clinical Uses: Acute Hypotensive States,
GI Bleeding.

Adrenomimetics

Indirect α - β -adrenomimetics (sympatomimetics):

→ **EPHEDRINE, DEPHEDRINUM**
[PSEUDOEPHEDRINE],
PHENYLPROPANOLAMINE

→ **Mechanism of action: stimulation of noradrenaline release from the synaptic nerve endings and slight direct excitation of adrenoceptors.**

► **Effects of ephedrine similar to adrenaline, but its activity less by 50-100 times and lasts longer.**



Ephedra distachya

As ADRENALINE, **EPHEDRINE** is used for Arterial Hypotension, Bronchial Asthma, Bronchospasm



→ **Effects of ephedrine which are different to adrenalline:**

- ▶ **Effectiveness on peroral taking.**
- ▶ **Significant stimulation of CNS - may cause psychomotor excitement, insomnia, drug dependence.**



The ephedrine is used for treatment of narcolepsy (pathological sleepiness).



When ephedrine introduction repeated after small interval (10-30 min), weakeing of effect (tachyphylaxis) appears. it's associated with decrease of noradrenalline amount in vesicles.

2). α -Adrenomimetics:

Mesatone (*Phenylephrine*) (α_1) – amp. 1%-1 ml

Naphthyzine (*Naphtazoline*) (α_2)

Vial 0.05% and 0.1% - 10 ml

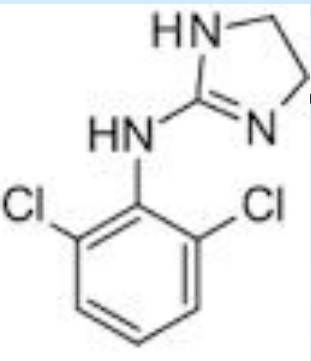
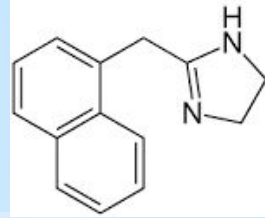
Halazoline (*Xylometazoline*) (α_2)

Vial 0.05% and 0.1%-10 ml

Clofeline (*Clonidine*) (α_2) –

Tab. 0.000075 g and 0.00015 g,

amp. 0.01% - 1 ml



→ α_1 -adrenomimetics: MESATON *[PHENYLEPHRINE]*,

- They are narrowing blood vessels containing α -adrenoceptors, increase blood pressure and cause reflexory bradycardia.



They are used for treatment of the acute arterial hypotension intravenously, for rhinitis (intranasally) for glaucoma.

→ α_2 -adrenomimetics: NAPHTHYZIN *[NAPHAZOLINE]*,
HALAZOLIN *[XYLOMETAZOLINE]*



They are used for treatment of the rhinitis (intranasally only) because they are toxic agents.

Clopheline is an α_2 -agonist used

in Essential Hypertension to lower BP.

It acts mainly on **Central α_2 -Receptors** =>

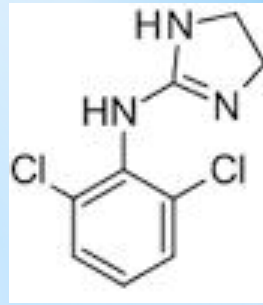
**Inhibition of Sympathetic Vasomotor centers -
Negative Feedback.**

↓ **Peripheral Vascular Resistance** =>

=> ↓ **Cerebral Sympathetic Outflow.**

Clopheline may stimulate

Peripheral Postsynaptic α_2 -Receptors,
producing **Transient Vasoconstriction.**



Beta - Adrenomimetics

Isadrin (Isoprenaline) (β_1 , β_2)

Tab. 5 mg, vial 1%-25.0 ml

Dopamine (β_1)- amp 4%-5 ml; 0.5% - 5 ml

Dobutamine (β_1)- amp 5%-5 ml; 1.25%-20 ml

Salbutamol (β_2)- Tab 2 mg, aerox

Terbutaline (β_2) - Tab 2.5 mg, aerox.

Salmeterol (β_2)- aerox

Fenoterol (Berotec, Partusisten) (β_2)

Formoterol (β_2) (turbuhaler 4.5 and 9 mkg/dose)

Dopamine activates β_1 -Receptors and
is the metabolic precursor of **Norarenaline**

D-receptors are prominent in the periphery
(*splanchnic* and *renal vasculature*),

where they mediate **Vasodilation** => *useful* in SHOCK
and Acute Heart Failure.

↑ Blood Flow to the Kidney =>

↑ the Glomerular Filtration Rate =>

Na⁺ Diuresis

Cardiovascular action:

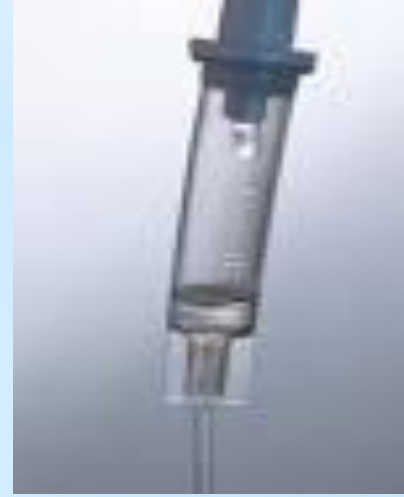
Stimulation of β_1 -Receptors =>

inotropic and chronotropic effects

Renal and viscera :

D₁-receptors => Dilation of Renal Arterioles =>
↑ Blood Flow to the Kidneys and other Viscera.

Dopamine is far Superior to *Noradrenline*, which
↓ the Blood Supply to the **Kidney** and
may cause **Kidney Shutdown**.



Dobutamine (amp. 5%-5 ml)

selective β_1 AM -

the most commonly used

Inotropic Agent after **Cardiac Glycosides**.

\uparrow cAMP \Rightarrow the Activation of Protein Kinase.

Slow Ca^{2+} channels are one important site of
Phosphorylation by Protein Kinase.

When phosphorylated, the Entry of Ca^{2+}
into the Myocardial Cells $\uparrow \Rightarrow$

\Rightarrow CONTRACTION \uparrow

Beta₂ agonists Salbutamol, Terbutaline, Fenoterol,
Salmeterol, Formoterol:

☐ **Relax** smooth muscle of the **Bronchial tree**,
Vasculature, Uterus and Intestines

☐ Hepatic and Muscle **glycogenolysis** =>
=> HYPERGLYCEMIA



Beta₂ agonists are used as:

☐ **Bronchodilators**

☐ **Tocolytics** – to Relax the Uterus

and **delay delivery** in *premature labor*

All **β₂-AMs** have some degree of β₁-activity =>

Some degree of Cardiostimulation may occur

I. α - Adrenoblockers:

I. Non-Selective Adrenoblockers:

PHENTOLAMINE (α_1, α_2) – Tab 25 mg

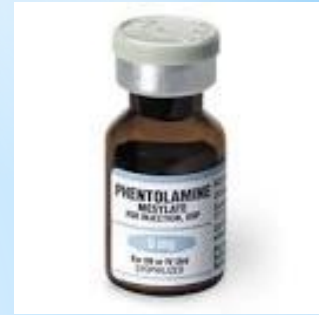
TROPAPHENE (α_1, α_2) – Amp 20 mg

II. Selective Adrenoblockers:

PRAZOSINE (α_1) – Tab 1, 3, 5 mg

DOXAZOSINE (α_1) – Tab 2 and 4 mg

YOHIMBINE (α_2) – Tab 5 mg



Phentolamine – α_1 -, α_2 - AB

The action lasts for **4 hours**.

α -Receptors Blockade =>

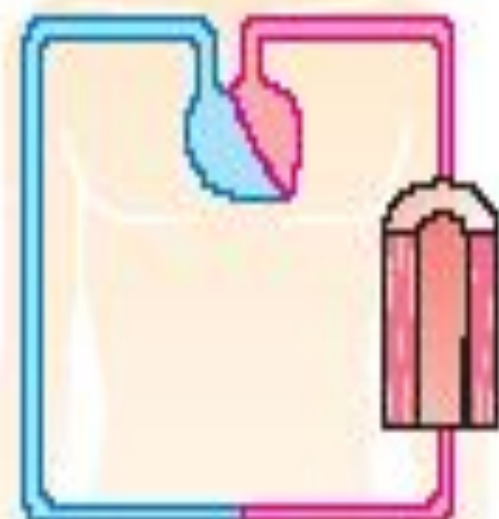
Prevention Peripheral Blood Vessels Vasoconstriction
by CATECHOLAMINES.

☐ **Peripheral Resistance** => Reflex Tachycardia

☐ **Postural Hypotension**

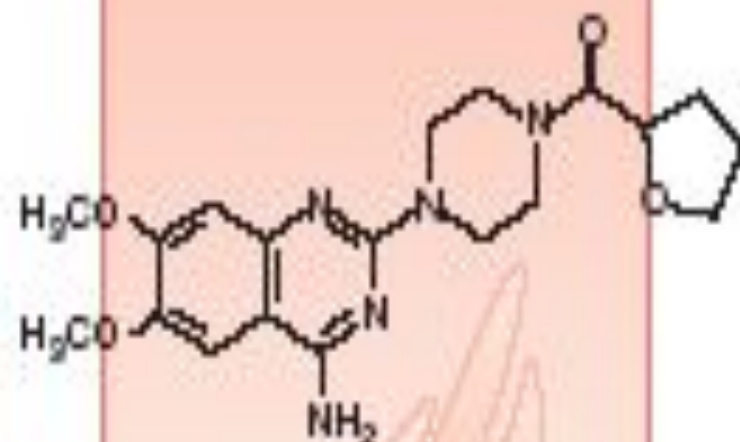
Phentolamine had been used in the diagnosis of **pheochromocytoma** and in other situations associated with excess release of **catecholamines**.

High blood pressure



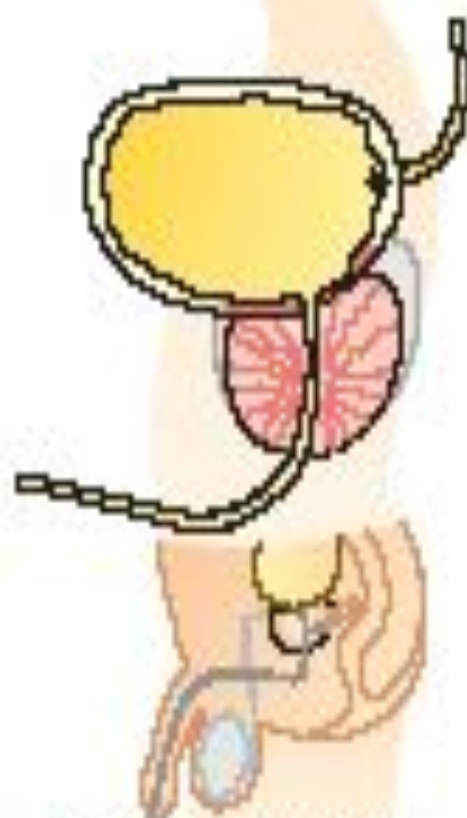
Resistance arteries

α_1 -blocker
e.g., terazosin



Inhibition of
 α_1 -adrenergic
stimulation of
smooth muscle

Benign
prostatic hyperplasia



Neck of bladder,
prostate

Indications for α_1 -sympatholytics

PRAZOSIN

TERAZOSINE

DOXAZOSINE (*Cardura*)



- ☐ Relaxation of Arterial and Venous Smooth Muscle
- ☐ ↓ Peripheral Vascular Resistance
- ☐ ↓ AP
- ☐ ↓ Tone in the smooth muscle of the Bladder Neck and Prostate
- ☐ Improve Urine Flow

Clinical use: Hypertension,
Benign Prostatic Hypertrophy

β -ADRENOBLOCKERS

1) NON-SELECTIVE:

Propranolol (Anaprilin) (β_1 , β_2)

Nadolol (Corgard) (β_1 , β_2)

Timolol (β_1 , β_2)

2) SELECTIVE:

Atenolol (β_1)

Metoprolol (β_1)

3). β_1 -, α_1 - Blockers:

Labetalol

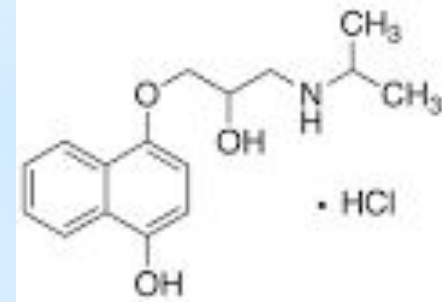
Carvediol



Propranolol (Anaprilin) – β_1 - , β_2 - AB

Tab. 10 and 40 mg;

amp. 0.25%-1 ml



Cardiovascular Effects:

- ☐ Negative Inotropic - ☐ Cardiac Output
 - ☐ Negative Chronotropic effects - ☐ HR
 - ☐ Depresses Sino-Auricular and AV activity
- => ☐ Cardiac Work and O_2 consumption



CLINICAL uses of Propranolol (Anapriline):

- ☐ Hypertension
- ☐ Angina Pectoris, Myocardial Infarction,
- ☐ Arrhythmias
- ☐ Glaucoma, Migraine ,
- ☐ Hyperthyroidism

Adverse effects:

- Bronchoconstriction
- Peripheral Vasoconstriction
- Arrhythmias, Sexual impairment
- Disturbances in Metabolism:
- ↓Glycogenolysis and ↓Glucagon Secretion

Overdose with Propranolol: \square AP, \square HR,
heart failure, bronchospasm.

Treatment: Gastric lavage, *Activated charcoal*,
Symptomatic and Supportive care:

Treat **Bradycardia** with ***ATROPINE***, ***ISADRINE***

Treat Cardiac Failure with

Cardiac Glycosides: ***Strophanthine***
and **Diuretics:** ***Furosemide***

Treat **Hypotension** with **vasopressors:**
ADRENALINE is preferred.

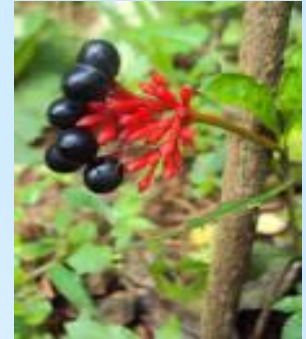
Treat **Bronchospasm** with ***ISADRINE*** ,
EUPHYLLINE (***AMINOPHYLLINE***)

SYMPATHOLYTICS:

Reserpine – Tab. 0.1 mg and 0.25 mg

Octadin – Tab. 0.025 g

Ornid – amp, 5% - 1 ml



Reserpine - a Plant Alkaloid from the roots of an Indian plant *Rauwolfia Serpentina*. It **blocks Mg^{2+} /ATP-dependent transport** of **biogenic amines** => □ the ability of Aminergic Vesicles to take up and store biogenic amines :

Noradrenaline

Dopamine

Serotonine

from the cytoplasm into storage vesicles in the Adrenergic Nerves of ALL BODY TISSUES.

An abstract, vibrant background featuring a mix of colors including red, yellow, blue, and green, with some darker, textured areas.

Thank You for Attention!

