



**Zaporizhzhia State Medical University  
Pharmacology Department**

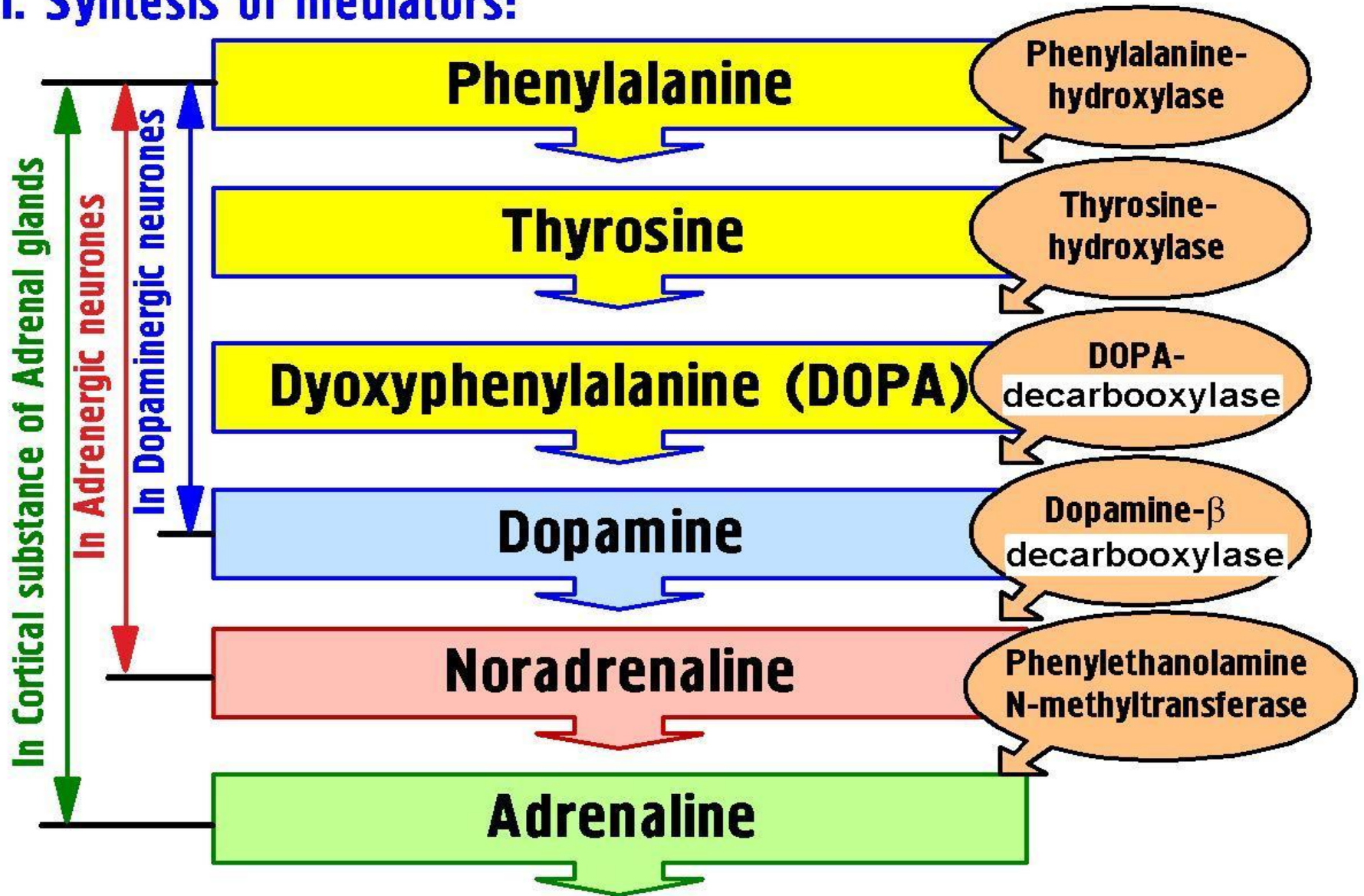
**Lecture №3**

**Adrenergic Drugs**

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

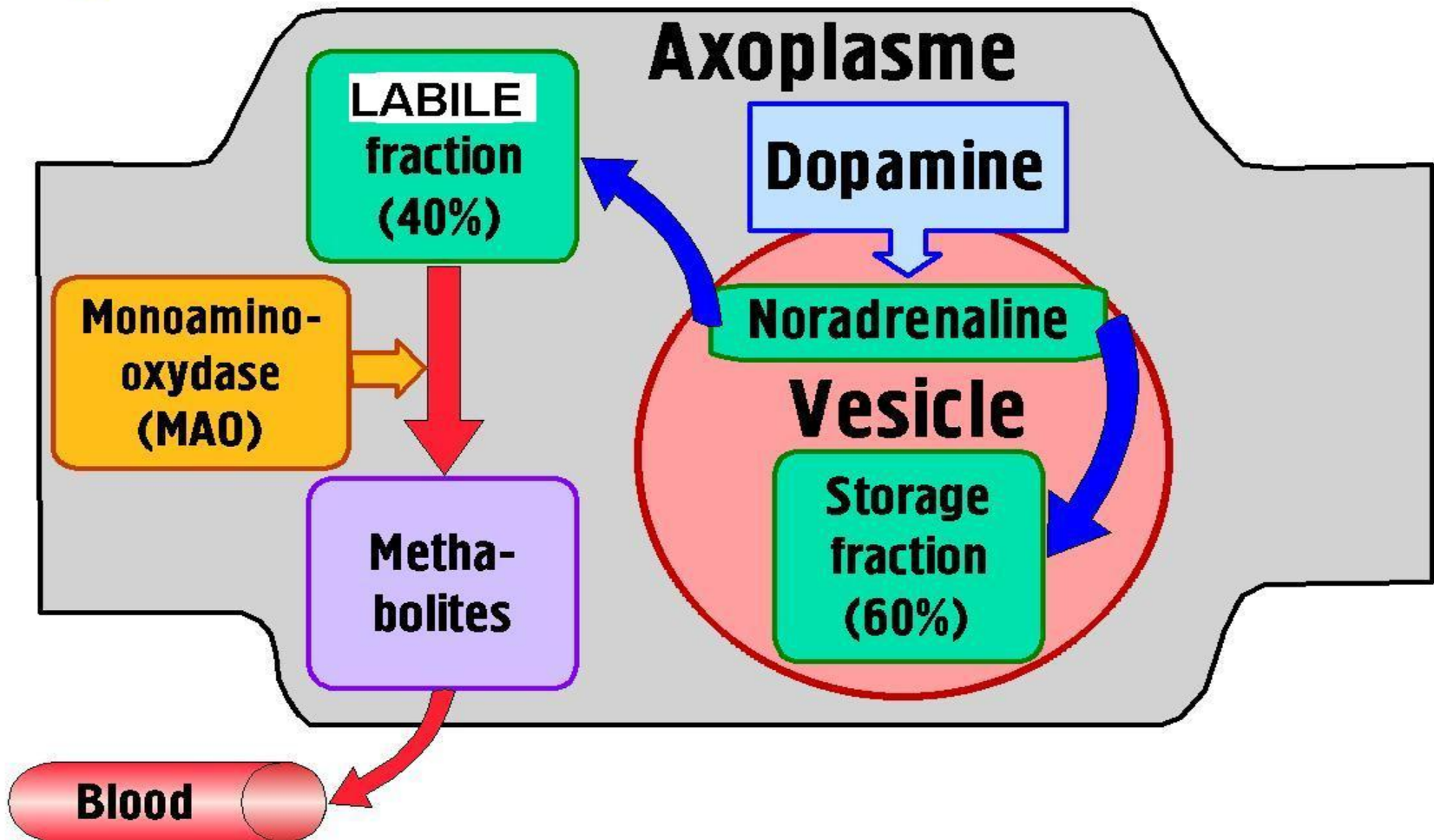
# Function of Adrenergic synapse

## 1. Syntesis of mediators:



# Function of Adrenergic synapse

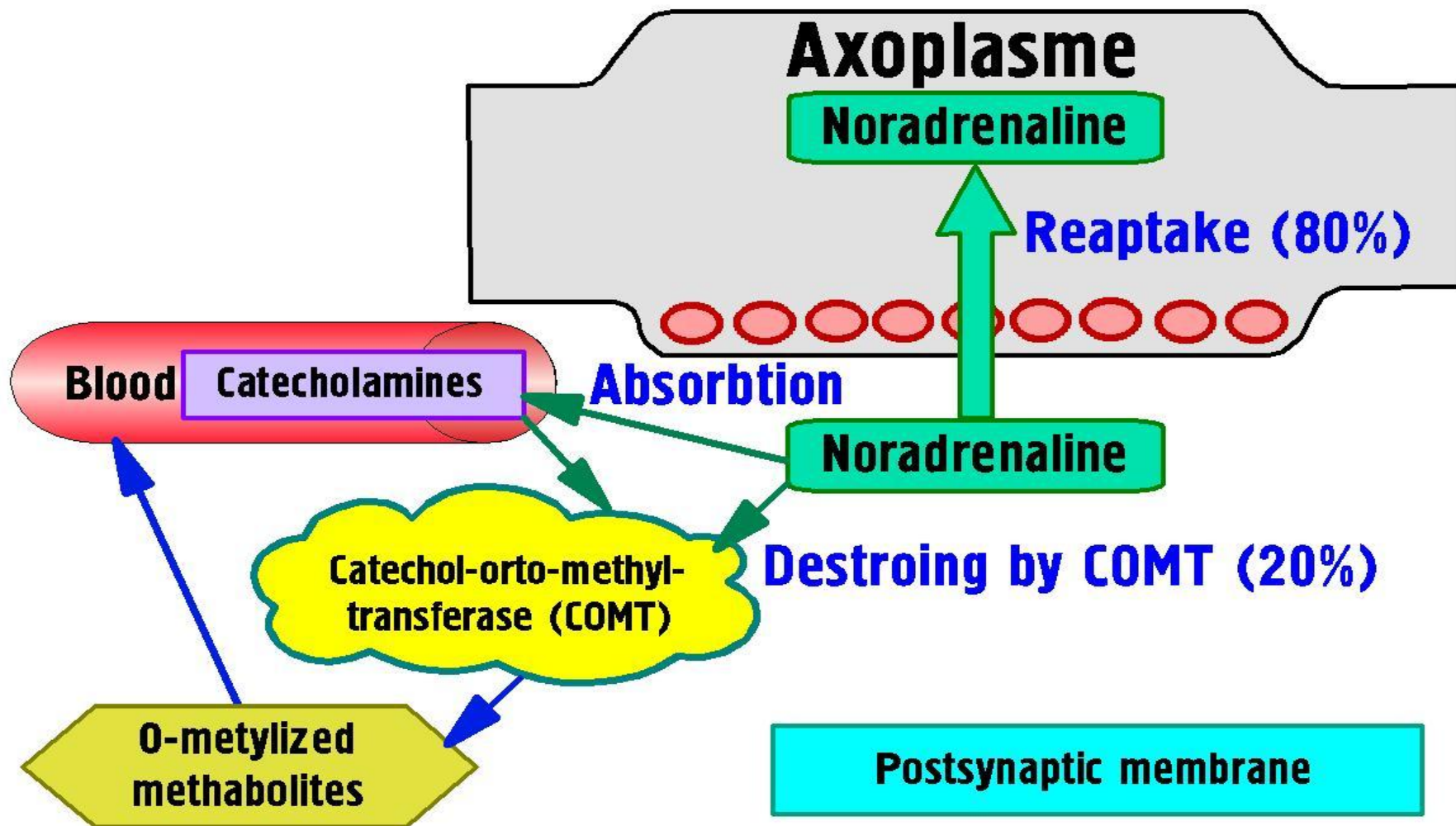
## 2. The fate of noradrenaline in varicose thickenings of nerve endings:





# 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**

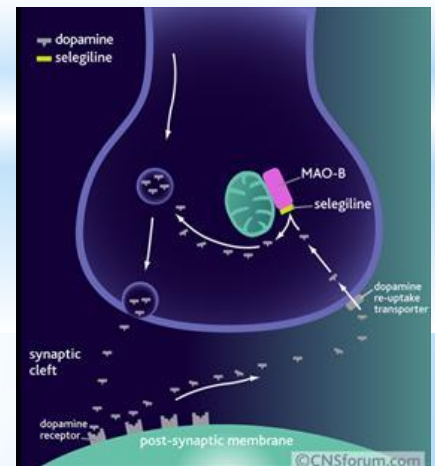
MAO inhibitors: **Nialamid, Transamine** and

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

**$\alpha_1$  Receptors:** on the Postsynaptic Membrane of the Effector organs – on smooth muscle and glands and are **excitatory**

**$\alpha_2$  Receptors:** on the Pre- and Postsynaptic Membrane of the Effector organs.

The stimulation of the **Presynaptic  $\alpha_2$ -Receptors** => **Feedback Inhibition** of **noradrenaline** release from the stimulated Adrenergic neuron –  
**Negative Feedback**



**$\beta_1$ -receptors:** HEART and are **Excitatory**

**$\beta_2$ -receptors:** on *Smooth Muscle* of –

Bronchi

Vasculature of Skeletal Muscle

Miometrium

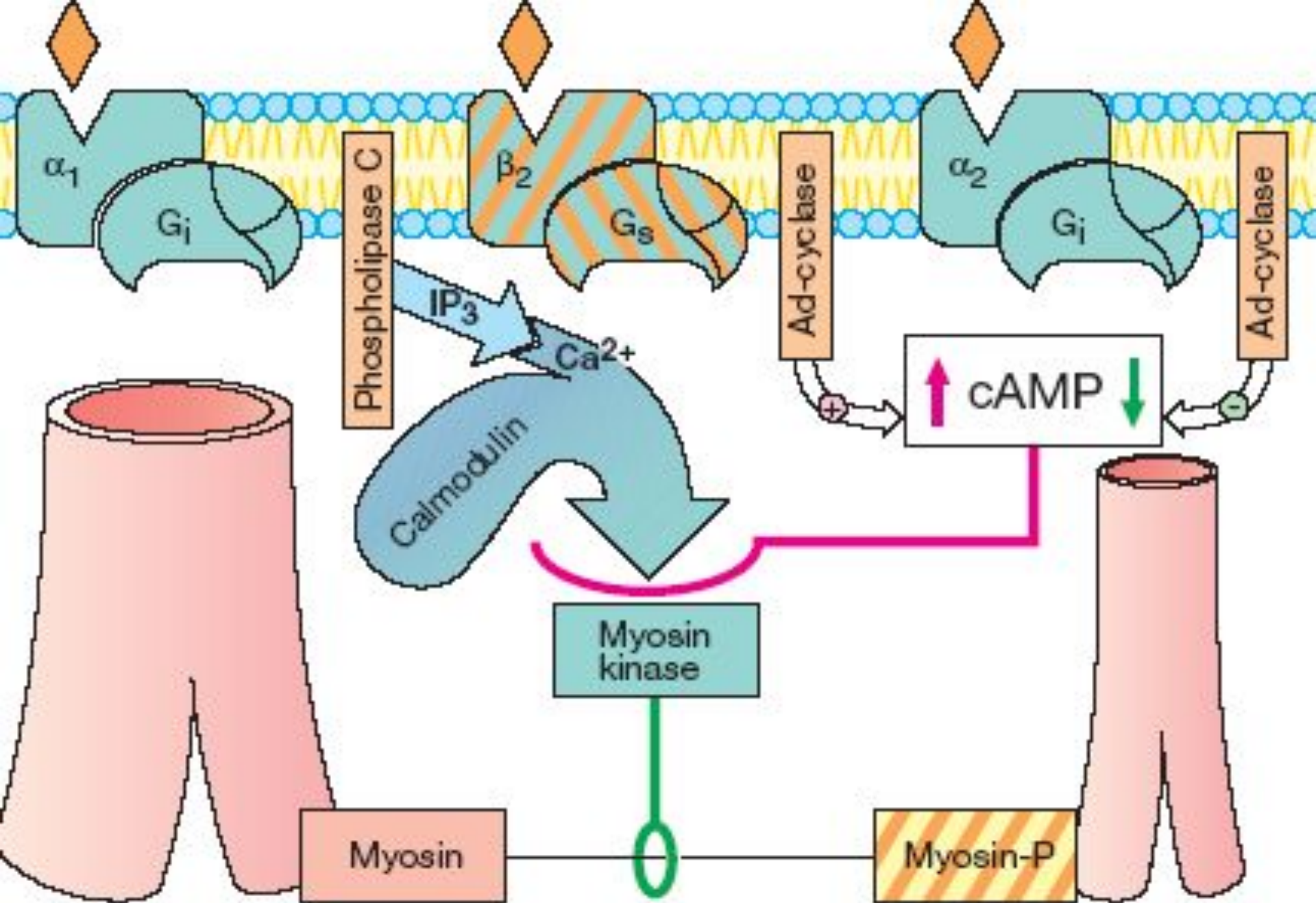
Glands

and are **Inhibitory**

**$\beta_3$ -receptors:** Adipose (Fat) cell =>  
stimulation of lipolysis







. Vasomotor effects of catecholamines



# Localisation of adrenoceptors and effects of their excitation

## 2. Effects upon the eye:

### → $\alpha_1$ -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 accommodation).
- ▶ Narrowing of Schlemm's 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 excitation

## 3. Effects upon another smooth muscles:

### → $\alpha_1$ -adrenoceptors:

- in the sphincters of gastrointestinal tract.

- ▶ Contraction of sphincters, decreasing of peristaltics.

### → $\beta_2$ -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.

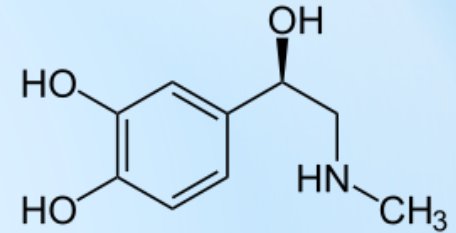


# I. Adrenomimetics of Direct Action

## 1). $\alpha$ -, $\beta$ - Adrenomimetics:

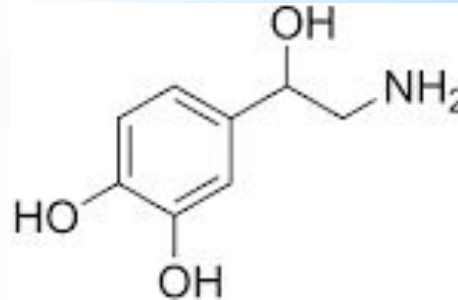
- **Adrenaline hydrochloride** -  $\alpha_1, \alpha_2, \beta_1, \beta_2, \beta_3$

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



- **Noradrenaline hydrotartrate** -  $\alpha_1, \alpha_2, \beta_1$

*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 ( **$\beta_2$  effect**)
  - ↓ **Release of Insulin** ( **$\alpha_2$  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*:  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$

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  $\alpha$ - $\beta$ -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 it's 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). $\alpha$ -Adrenomimetics:

**Mesatone** (*Phenylephrine*) ( $\alpha_1$ ) – amp. 1%-1 ml

**Naphthyzine** (*Naphtazoline*) ( $\alpha_2$ )

Vial 0.05% and 0.1% - 10 ml

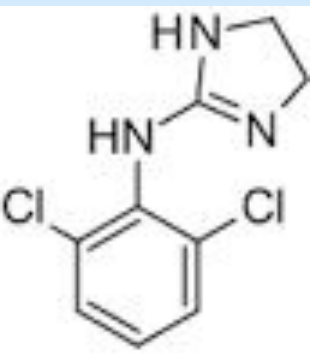
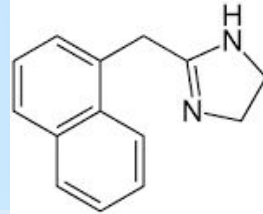
**Halazoline** (*Xylometazoline*) ( $\alpha_2$ )

Vial 0.05% and 0.1%-10 ml

**Clofeline** (*Clonidine*) ( $\alpha_2$ ) –

Tab. 0.000075 g and 0.00015 g,

amp. 0.01% - 1 ml





→  $\alpha_1$ -adrenomimetics: **MESATON** *[PHENYLEPHRINE]*,

- ▶ They are narrowing blood vessels containing  $\alpha$ -adrenoceptors, increase blood pressure and cause reflectory bradycardia.



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

→  $\alpha_2$ -adrenomimetics: **NAPHTHYZIN** *[NAPHAZOLINE]*,  
**HALAZOLIN** *[XYLOMETAZOLINE]*



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

**Clopheline** is an  $\alpha_2$ -agonist used

in Essential Hypertension to lower BP.

It acts mainly on **Central  $\alpha_2$ -Receptors** =>

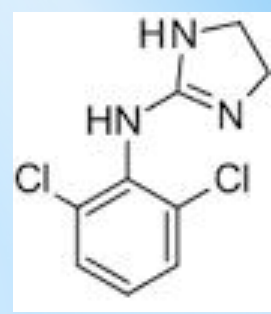
**Inhibition of Sympathetic Vasomotor centers -  
Negative Feedback.**

↓ **Peripheral Vascular Resistance** =>

=> ↓ **Cerebral Sympathetic Outflow.**

**Clopheline** may stimulate

Peripheral Postsynaptic  $\alpha_2$ -Receptors,  
producing **Transient Vasoconstriction.**



## Beta - Adrenomimetics

**Isadrin** (Isoprenaline) ( $\beta_1$ ,  $\beta_2$ )

Tab. 5 mg, vial 1%-25.0 ml

**Dopamine** ( $\beta_1$ )- amp 4%-5 ml; 0.5% - 5 ml

**Dobutamine** ( $\beta_1$ )- amp 5%-5 ml; 1.25%-20 ml

**Salbutamol** ( $\beta_2$ )- Tab 2 mg, aerez

**Terbutaline** ( $\beta_2$ ) - Tab 2.5 mg, aerez.

**Salmeterol** ( $\beta_2$ )- aerez

**Fenoterol** (Berotec, Partusisten) ( $\beta_2$ )

**Formoterol** ( $\beta_2$ ) (turbuhaler 4.5 and 9 mkg/dose)



**Dopamine** activates  $\beta_1$ -Receptors and  
is the metabolic precursor of **Norrenaline**

**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<sup>+</sup> Diuresis**

## Cardiovascular action:

Stimulation of  $\beta_1$ -Receptors =>

**inotropic** and **chronotropic** effects

## Renal and viscera :

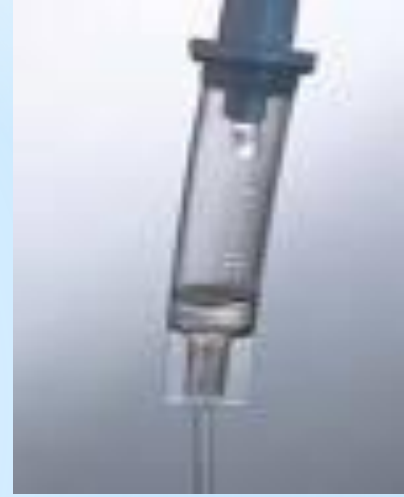
$D_1$ -receptors => Dilation of Renal Arterioles =>

↑ 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  $\beta_1$  AM -

the most commonly used

Inotropic Agent after **Cardiac Glycosides**.

$\uparrow$ cAMP  $\Rightarrow$  the Activation of Protein Kinase.

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

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

$\Rightarrow$  CONTRACTION  $\uparrow$



**Beta<sub>2</sub> agonists** Salbutamol, Terbutaline, Fenoterol,  
Salmeterol, Formoterol:

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

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

**Beta<sub>2</sub> agonists** are used as:

□ **Bronchodilators**

□ **Tocolytics** – to Relax the Uterus

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

All **β<sub>2</sub>-AMs** have some degree of β<sub>1</sub>-activity =>

Some degree of **Cardiostimulation** may occur



## I. $\alpha$ - Adrenoblockers:

### I. Non-Selective Adrenoblockers:

**PHENTOLAMINE** ( $\alpha_1, \alpha_2$ ) – Tab 25 mg

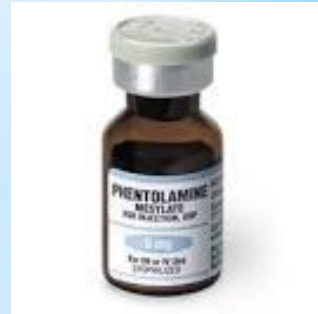
**TROPAPHENE** ( $\alpha_1, \alpha_2$ ) – Amp 20 mg

### II. Selective Adrenoblockers:

**PRAZOSINE** ( $\alpha_1$ ) – Tab 1, 3, 5 mg

**DOXAZOSINE** ( $\alpha_1$ ) – Tab 2 and 4 mg

**YOHIMBINE** ( $\alpha_2$ ) – Tab 5 mg



**Phentolamine** –  $\alpha_1$ -,  $\alpha_2$ - AB

The action lasts for **4 hours**.

**$\alpha$ -Receptors Blockade** =>

Prevention Peripheral Blood Vessels Vasoconstriction  
by CATECHOLAMINES.

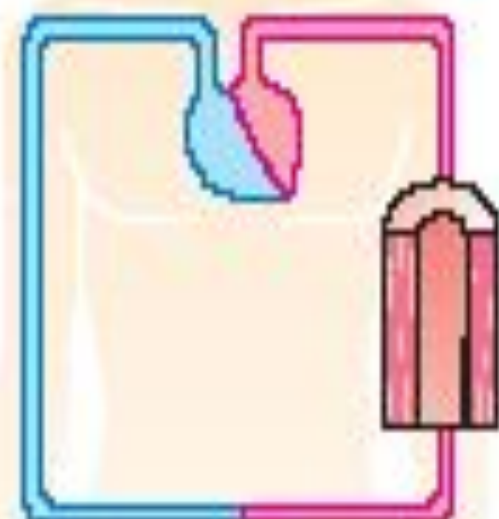
**Peripheral Resistance** => **Reflex Tachycardia**

**Postural Hypotension**

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

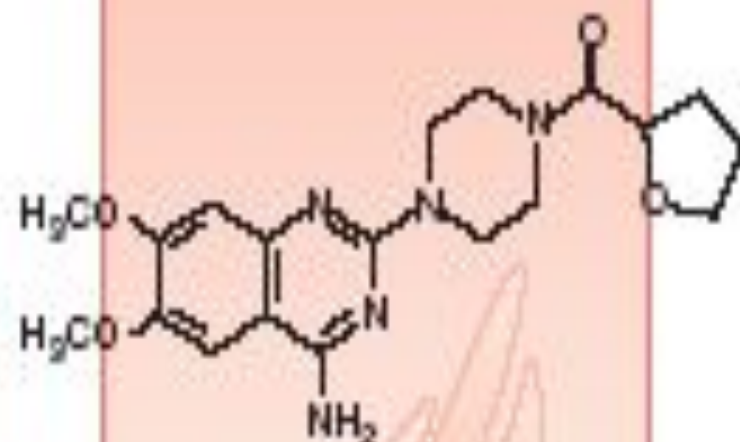


High blood pressure



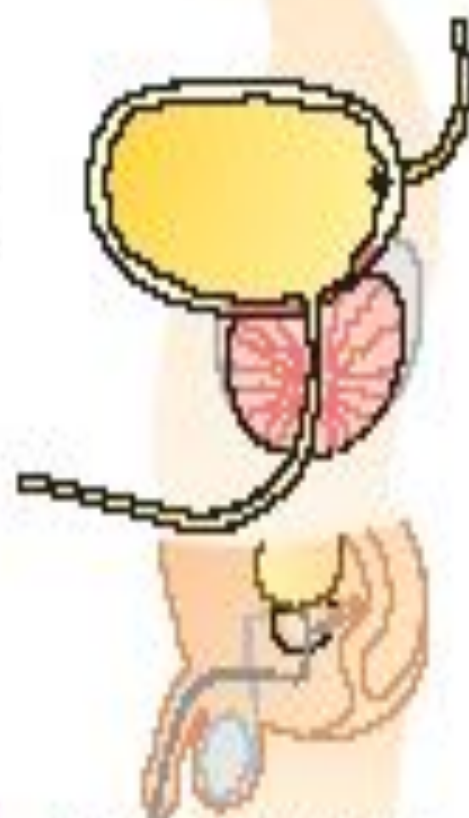
Resistance arteries

$\alpha_1$ -blocker  
e.g., terazosin



Inhibition of  
 $\alpha_1$ -adrenergic  
stimulation of  
smooth muscle

Benign  
prostatic hyperplasia



Neck of bladder,  
prostate

. Indications for  $\alpha_1$ -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

# $\beta$ -ADRENOBLOCKERS

## 1) NON-SELECTIVE:

Propranolol (Anaprilin) ( $\beta_1, \beta_2$ )

Nadolol (Corgard) ( $\beta_1, \beta_2$ )

Timolol ( $\beta_1, \beta_2$ )

## 2) SELECTIVE:

Atenolol ( $\beta_1$ )

Metoprolol ( $\beta_1$ )

## 3). $\beta_1$ -, $\alpha_1$ - Blockers:

Labetalol

Carvediol

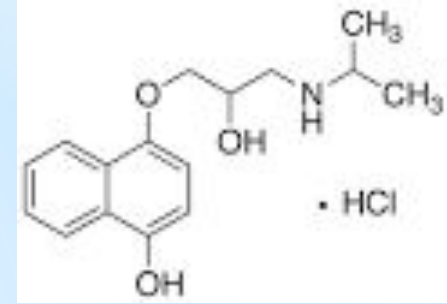




**Propranolol** (Anaprilin) –  $\beta_1$ - ,  $\beta_2$ - AB

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:** □AP, □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*** ,

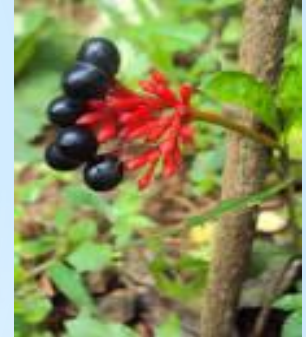
***EUPHYLLINE (AMINOPHYLLINE)***

## 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<sup>2+</sup>/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.





Thank You for Attention!



We make your life so easy