



# PHARMACOLOGY

## Adrenergic antagonist

### OBJECTIVES:

- Describe the different classifications for drugs that can block sympathetic nervous system.
- Describe the kinetics, dynamics, uses and side effects of alpha adrenergic drugs.
- Identify Difference between selective and non selective alpha blockers.
- Know the difference between tamsulosin and other selective alpha receptor blockers.
  - Identify the different classifications for beta receptors blockers.
- Describe the kinetics, dynamics, uses and side effects of beta adrenergic drugs.
- Know the preferable drug for diseases as hypertension, glaucoma, arrhythmia, myocardial infarction, anxiety, migraine and ect....

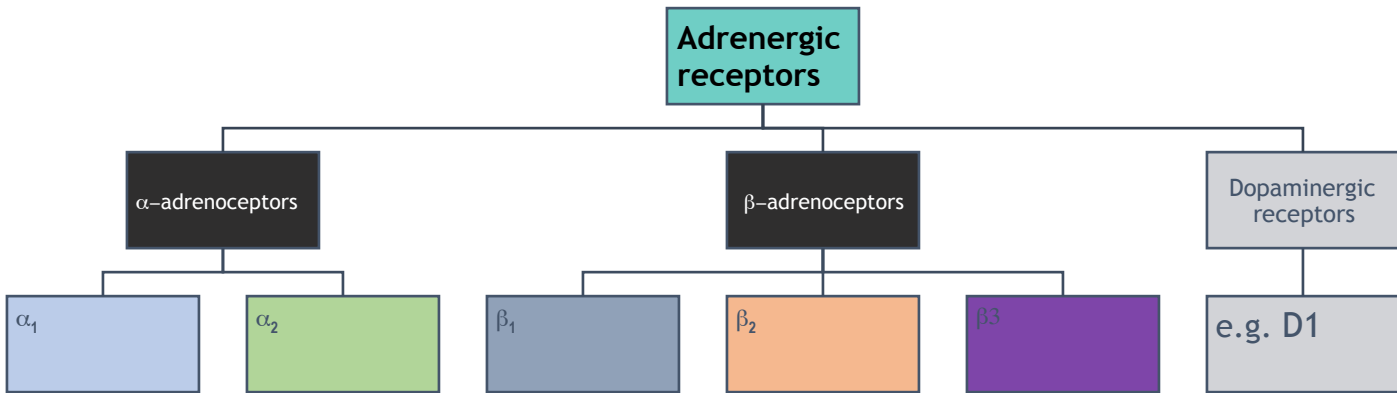


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**Important.**  
Extra notes

# Adrenergic receptors It's a recall, if you know it you can skip it!



## Post-synaptic

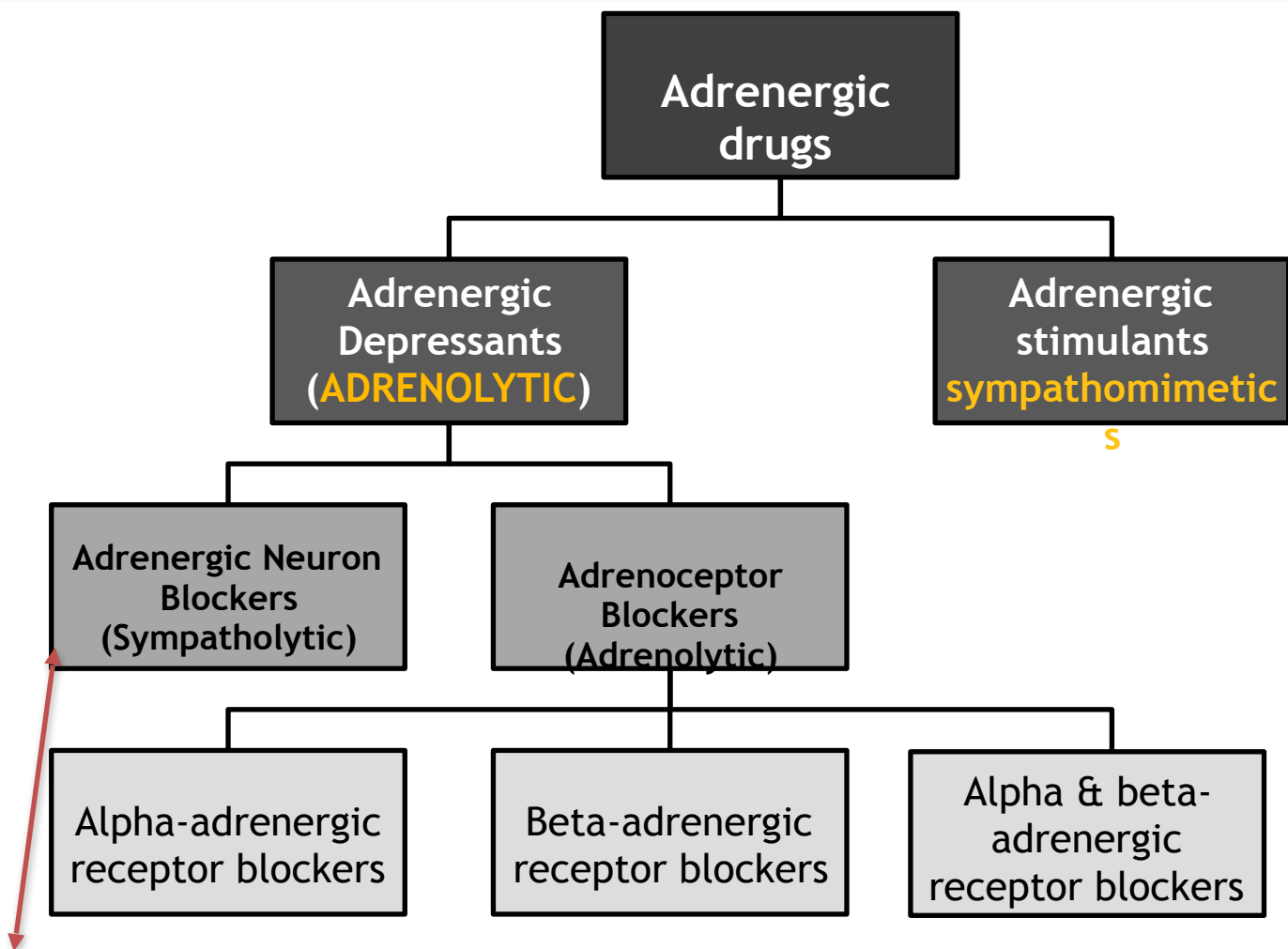
<p><b>α1</b></p> <p><b>excitatory</b> in function (cause contraction) except in GIT.</p> <p>Present mainly in smooth muscles.</p> <p>Contraction of pregnant uterus.</p> <p><b>Vasoconstriction</b> of <u>skin &amp; peripheral</u> blood vessels → increased peripheral resistance → hypertension.</p> <p>Relaxation of GIT muscles &amp; urinary bladder's muscles. Contraction of GIT sphincter (constipation) &amp; urinary bladder's sphincter (urinary retention).</p> <p>Contraction of radial muscle of eye causes active <b>mydriasis</b></p> <p>Increase blood glucose level (<b>hyperglycemia</b>), by:</p> <ul style="list-style-type: none"> <li>• ↓ insulin</li> <li>• ↑ <b>glycogenolysis</b></li> </ul>	<p><b>β2</b></p> <p><b>inhibitory</b> in function (cause relaxation)</p> <p>Relaxation of the uterus (Delay premature labor)</p> <p>Relaxation of <u>skeletal &amp; coronary</u> blood vessels (<b>vasodilatation</b>)</p> <ul style="list-style-type: none"> <li>• Relaxation of bronchial smooth muscles</li> <li>• <b>Tremor</b> of skeletal muscles</li> <li>• ↑ lipolysis</li> </ul> <p>↑ glucagon release from pancreas</p> <p>↑ liver &amp; muscle glycogenolysis</p>	<p><b>β1</b></p> <p>excitatory in function, present mainly in <b>heart</b></p> <p>↑ heart rate: + chronotropic effect, Tachycardia</p> <p>↑ force of contraction: + inotropic effect</p> <p>↑ conduction velocity: + dromotropic effect</p> <p>↑ blood pressure</p>	<p><b>β3</b></p> <p>In <b>adipose tissue</b></p> <p>↑ lipolysis</p> <p>↑ free fatty acids.</p> <p>↑ <b>renin</b> release</p> <p>Renin is an enzyme involved in the production of angiotensin II, a potent</p>
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## Pre-synaptic

<p>Inhibition of norepinephrine release (negative feed back mechanism).</p>	<p>Increase release of NE (Positive feed back mechanism).</p>
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# Classification of adrenergic drugs



## 1. Formation of False transmitters (alpha-2 agonist) :

### $\alpha$ -Methyldopa ( $\alpha$ -methyl tyrosine)

-False: Means released instead of NE (norepinephrine).

-Acts centrally as  $\alpha_2$  receptor agonist to inhibit NE release.

-**DRUG OF CHOICE in pregnancy hypertension (pre-eclampsia - gestational hypertension).**

## 2. Deplete storage:

-Reserpine (not used anymore).

## 3. Inhibition of release & enhance uptake:

-Guanethidine (not used anymore).

## 4. Stimulation of presynaptic $\alpha_2$ receptors:

-Clonidine &  $\alpha$ -Methyldopa

Note that Clonidine acts like  $\alpha$ -Methyldopa as antihypertensive drug in pregnancy, but it has a limited use due to its **rebound hypertension** (withdrawal symptoms after you stop or decrease the drug dose)

**Apraclonidine** (A derivative that doesn't affect blood pressure - used topically as eye drops in treating open angle glaucoma by decreasing aqueous humor formation (.

# α-receptor Antagonists

## 1. Non- selective antagonists (α1 & α2):

	Pharmacokinetics	Therapeutic use	ADRs
<b>Phenoxybenzamine</b>	<ul style="list-style-type: none"> <li>• Irreversible</li> <li>• Long-acting (24 hours)</li> </ul>	<ul style="list-style-type: none"> <li>• before removal of <b>Pheochromocytoma</b> to prevent Hypertensive crisis .</li> </ul>	<ul style="list-style-type: none"> <li>- <b>Postural hypotension</b> (form of low blood pressure that happens when you stand up from sitting or lying down).</li> <li>- <b>Reflex Tachycardia</b> (due to the fall in BP, mediated by baroreceptor* reflex and due to α2 block in heart).</li> </ul>
<b>Phentolamine</b>	<ul style="list-style-type: none"> <li>• Reversible</li> <li>• Short-acting (4 hours)</li> </ul>	<p>Before removal of <b>Pheochromocytoma</b> (tumor in the adrenal medulla that cause increase secretion of norepinephrine and epinephrine).</p>	<ul style="list-style-type: none"> <li>- Headache</li> <li>- Nasal stiffness or congestion</li> <li>- Vertigo &amp; drowsiness</li> <li>- Male sexual dysfunction</li> <li>- <b>inhibits ejaculation</b></li> <li>- Increase cardiac output (α2 block)</li> <li>- Decrease peripheral vascular resistance.</li> </ul>

**Note :** Both drugs can precipitate (cause) arrhythmias and angina.  
 Contra-indicated in: patients with decreased coronary perfusion\*.

\*baroreceptor reflex is one of the body's homeostatic mechanisms that helps to maintain blood pressure at nearly constant levels.

\*Coronary perfusion pressure (CPP): pressure gradient that drives coronary blood pressure, meaning the difference between the diastolic aortic pressure and the right atrial diastolic pressure.

# α-receptor Antagonists

## 2. α1- selective antagonists:

	Pharmacokinetics & Mechanism	Therapeutic use	ADRs
<b>Prazosin</b> (Short half-life)	<ul style="list-style-type: none"> <li>Vasodilation</li> <li>Fall in arterial pressure with <u>less tachycardia</u> than with non-selective</li> </ul> <p><b>Uroselective:</b> As α1 receptors present in prostate so when tamsulosin binds to the receptor, it produce <u>relaxation of bladder neck</u> and prostate resulting in increasing urine flow</p>	<p>-Used in <b>Raynaud's disease*</b>: induce peripheral vasodilatation.</p> <p>- Hypertension especially with prostate enlargement</p> <p><b>Selectively used in Benign prostatic hyperplasia with minimal effect on blood pressure</b></p>	<p>Like Non-selective but with a lesser degree</p>
<b>Doxazosin, Terazosin</b> (Long half-life)			
<b>Tamsulosin</b> (Uroselective)			

\*Raynaud's phenomenon is excessively reduced blood flow in response to cold or emotional stress, causing discoloration of the fingers, toes, and occasionally other areas (**vasospasm**)

## 3. α2- selective antagonists:

	Pharmacokinetics	Therapeutic use
<b>Yohimbine</b>	<ul style="list-style-type: none"> <li>Increase NO &amp; ADH released in the corpus cavernosum</li> <li>Vasodilatation</li> <li>Contributing to the erectile process</li> </ul>	Used as aphrodisiac* (the treatment of erectile dysfunction)

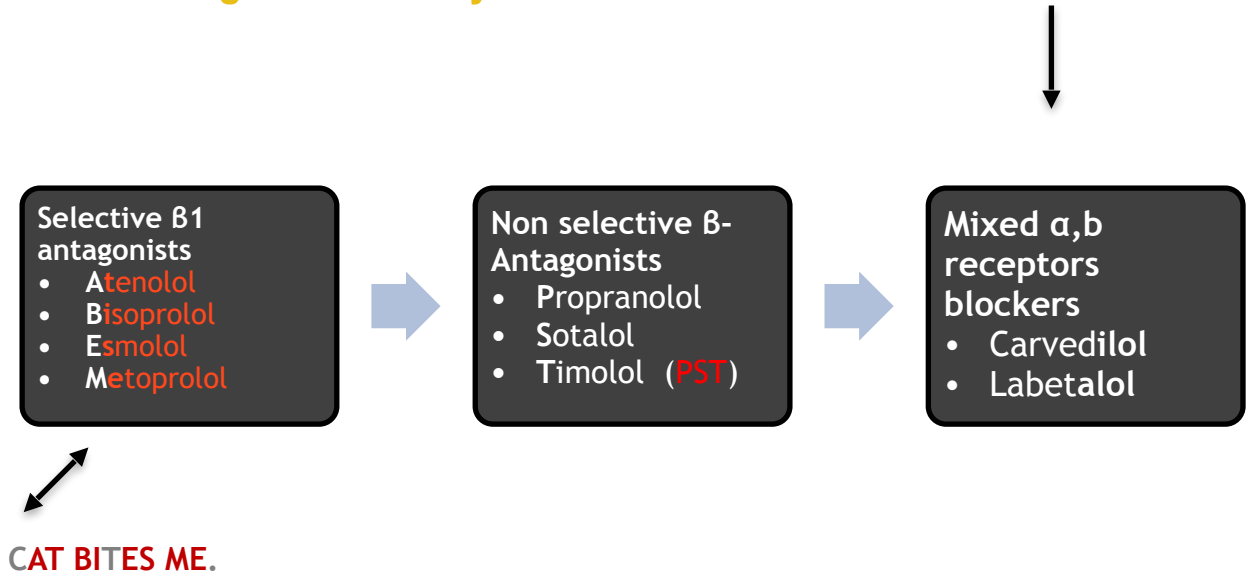
\*Aphrodisiac: a food, drink, or other thing that stimulates sexual desire.

# $\beta$ -Adrenoceptors blockers

## Classification of $\beta$ - Adrenoceptors Blockers:

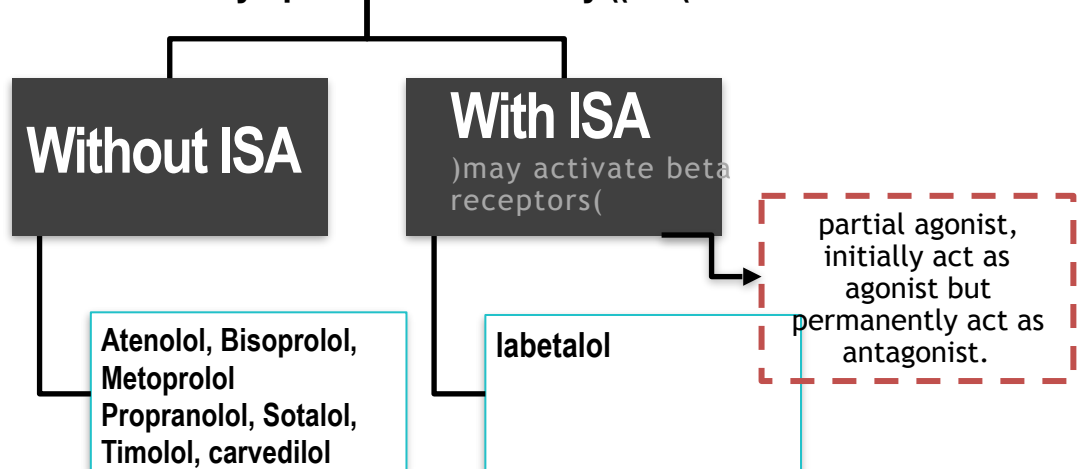
### 1. According to selectivity:

Suffix: lol (except the mixed)



### 2. According to presence of agonistic/antagonistic action;

Intrinsic Sympathomimetic Activity ((ISA(



# β -Adrenoceptors blockers

## 3. According to presence of membrane stabilizing effects:

Eg: Propranolol, labetalol

- Block Na Channels → Local anesthetic action.
- Quinidine-like action → Quinidine is antiarrhythmic drug , the action is decreasing propagation action potential.
- Antiarrhythmic action.

## 4 . According to lipid solubility:

	Lipophilic	Hydrophilic
Oral absorption	Complete	Irregular
Liver metabolism	Yes	No
$t_{1/2}$	Short [(mostly 3-10h)]	Long, except Esmolol (10min given IV)
CNS side effects	High (↓ Anxiety)	low
E.g.	Metoprolol Propranolol, Timolol Labetalol , Carvedilol	Atenolol, Bisoprolol, Esmolol , Sotalol ( <b>BASE</b> ) The <b>BASE</b> is hydrophilic

-Most of them are lipid soluble.

-Most of the lipid soluble metabolized in liver & excreted in urine.

# β Adrenoceptors blockers

## Pharmacological actions

<p><b>CVS</b> *important*</p>	<p>Negative inotropic, chronotropic, dromotropic . = <b>Decrease cardiac output</b></p>	<p><b>Antianginal* effects</b> (ischemic heart disease): 1-<b>Decrease heart rate</b> = (bradycardia) 2-<b>Decrease force of contraction</b> = ↓ <b>cardiac work</b> 3-<b>decrease oxygen consumption</b> due to <b>bradycardia</b></p>	<p><b>Anti-arrhythmic effects:</b> Decrease excitability Decrease automaticity Decrease conductivity (due to its sympathetic blocking).</p>
<p><b>BLOOD VESSELS</b></p>	<p>Increase peripheral resistance (PR) by <b>blocking</b> vasodilatory effect of <math>\beta_2</math></p>	<p><b>Decrease</b> blood flow to organs = cold extremities. <b>contraindicated</b> in peripheral diseases like <b>Reynaud's disease</b></p>	<p>In Reynaud's disease , better use selective beta 1 blockers , beta 2 blockers Exacerbating the disease.</p>
<p><b>BLOOD PRESSURE</b></p>	<p><b>Decrease</b> cardiac output <math>\beta_1</math></p>	<p><b>Decrease</b> renin, angiotensin 2 (vasoconstrictor( and aldosterone secretion <math>\beta_1</math> Beta receptors control renin system.</p>	<p><b>Presynaptic inhibition</b> of NE release from adrenergic nerves</p>
<p><b>RESPIRATORY TRACT</b></p>	<p><math>\beta_2 \rightarrow</math> Bronchoconstriction + <b>contraindicated</b> in asthmatic patients.</p>		
<p><b>EYE</b></p>	<p>In <b>glaucoma</b>, reduce intraocular pressure (IOP) + decrease aqueous humor production from ciliary body e.g. <b>Timolol</b> as eye drops</p>		
<p><b>INTESTINE</b></p>	<p>Increase intestinal motility</p>		
<p><b>METABOLIC EFFECT</b></p>	<p><b>Hypoglycemia:</b> ↓ glycogenolysis in liver , ↓ glucagon secretion in pancreas , ↓ lipolysis in adipocytes <b>Na<sup>+</sup> retention**</b> 2<sup>nd</sup>ry to decrease blood pressure + decrease renal perfusion All β-Adrenergic blockers <b>mask hypoglycemic</b> manifestations in diabetic patients type 1 ( <b>taking insulin</b>) The patient cant feel the reflex caused by hypoglycemia ( tachycardia + sweating) → <b>cause COMA</b> All beta blockers are <b>contraindicated</b> for diabetic patient type 1 ( <b>taking insulin</b>)</p>		

\*Angina = the amount of oxygen reaching the heart by coronary artery not enough , treatment either increase blood flow or

decrease heart work load .

\*\* This Na retention is due to the stimulation of aldosterone, but this stimulation is not strong enough to increase the hypertension (still b-blockers control the situation)



# Beta-Adrenoceptors blockers

## Clinical Uses of $\beta$ receptor blockers:

DISEASE	DRUG
CVS	<p><b>Hypertension</b></p> <p><b>Labetalol</b> INJECTION - Propranolol, atenolol, bisoprolol</p> <p><b>Labetalol</b> (<math>\alpha</math>, <math>\beta</math> blockers ) non selective used in treatment of hypertensive pregnant &amp; hypertensive crisis.</p>
	<p><b>Cardiac Arrhythmias</b></p> <p>Bisopoprolol and <b>Carvedilol</b> (antioxidant action*)</p> <p>Used In <b>supraventricular</b> &amp; <b>ventricular arrhythmias</b>. Beta blockers are <b>preferred</b> in ventricular arrhythmia more than atrial.</p>
	<p><b>Angina pectoris</b></p> <p>Beta blocker</p> <p>↓ heart rate, cardiac work &amp; oxygen demand. ↓ the frequency of angina episodes.</p>
	<p><b>Congestive Heart Failure</b></p> <p><b>Carvedilol</b> )antioxidant action(*)</p> <p>Carvedilol is non selective Decrease myocardial remodeling &amp; decrease risk of sudden death.</p>
	<p><b>Myocardial Infarction</b></p> <p>Beta blocker</p> <p>Have <b>cardio-protective effect</b>, decrease infarct size, decrease morbidity &amp; mortality, decrease myocardial O2 demand. <b>Anti-arrhythmic</b> action. Decrease the incidence of sudden death.</p>
<b>Glaucoma</b>	<p><b>Timolol</b></p> <p>Used as eye drop</p>
<b>Hyperthyroidism</b>	<p>Beta blocker</p> <p><b>Protect the heart against sympathetic over stimulation</b> Controls symptoms; tachycardia, tremors, sweating.</p>
<p><b>Anxiety</b> (Social and performance type)</p> <p><b>Migraine</b></p>	<p>Controls symptoms; tachycardia, tremors, sweating.</p> <p><b>Propranolol</b></p> <p><b>USED ONLY AS PROPHYLACTIC NOT EFFECTIVE IN ACUTE CONDITIONS</b> ↓reduce episodes of chronic migraine ↓catecholamine-induced vasodilatation in the brain vasculature Treatment : antagonize the sympathetic effect.</p>
<b>Pheochromocytoma</b>	<p>Combination Alpha &amp; Beta blockers</p> <p><math>\alpha</math>-blockers lower the elevated blood pressure. <math>\beta</math> -blockers protect the heart from NE.</p>

**Antioxidant:** A substance that reduces damage due to oxygen free radicals.

# Beta-Adrenoceptors blockers



	Drug	Pharmacological action	Admin	Indication
<p style="text-align: center;">Non-selective β-blockers</p>	<p style="text-align: center;">Propranolol</p>	<ul style="list-style-type: none"> <li>• Lipid soluble (CNS effect → sedative action + protection against anxiety)</li> <li>• Metabolized in liver, and excreted in urine</li> <li>• <b>NO ISA</b></li> <li>• Membrane stabilization (block Na channel → local anesthetic effect (antiarrhythmic effect)</li> <li>• <b>Heart: (B1)</b></li> <li>• ↓ cardiac output</li> <li>• Anti-ischemic: ↓ cardiac work + ↓ O2 consumption</li> <li>• Anti-arrhythmic (by membrane stabilization): ↓ excitability + ↓ automaticity + ↓ conductivity</li> <li>• <b>Blood Pressure: )B1, B2)</b></li> <li>• ↓ cardiac output</li> <li>• ↓ renin and RASS system</li> <li>• Inhibition of presynaptic NE release</li> <li>• Inhibition of sympathetic outflow in CNS</li> <li>• <b>Blood Vessels: (B2)</b></li> <li>• Vasoconstriction → ↓ blood flow to organs except brain → cold extremities</li> <li>• <b>Bronchi: (B2)</b></li> <li>• Bronchospasm</li> <li>• <b>Intestine: (B2)</b></li> <li>• ↑ intestinal motility</li> <li>• <b>Metabolism: (B2)</b></li> <li>• Liver: ↓ Glycogenolysis → Hypoglycemia</li> <li>• Pancreas: ↓ Glucagon secretion</li> <li>• Adipocytes: ↓ Lipolysis</li> <li>• Skeletal muscles: ↓ glycolysis</li> <li>• <b>PNS and CNS:</b></li> <li>• Local anesthetic effect: ↓ tremors, ↓ anxiety</li> </ul>	<p style="text-align: center;">Orally or IV</p>	<ul style="list-style-type: none"> <li>• Hypertension</li> <li>• Arrhythmias</li> <li>• Angina</li> <li>• Myocardial infarction</li> <li>• Migraine [Prophylaxis]</li> <li>• Pheochromocytoma; used with α-blockers )never alone(</li> <li>• Chronic glaucoma</li> <li>• Tremors</li> <li>• Anxiety; (specially social &amp; performance type(</li> <li>• Hyperthyroidism</li> </ul>
	<p style="text-align: center;">Timolol</p>	<ul style="list-style-type: none"> <li>• ↓ aqueous humor production from ciliary body</li> <li>• ↓ intraocular pressure (IOP)</li> </ul>		<p style="text-align: center;">Eye drops</p>

# Beta-Adrenoceptors blockers

	Drug	Pharmacological action	Admin	Indication	Adverse Effects
Mixed $\alpha/\beta$ -blockers	Labetalol	<ul style="list-style-type: none"> <li>Rapid acting with ISA and local anesthetic effect</li> <li>Does not alter serum lipids or blood glucose</li> <li>Membrane stabilization</li> </ul>	Orally or IV	<ul style="list-style-type: none"> <li>Severe hypertension in pheochromocytoma</li> <li>Hypertensive crisis (abrupt withdrawal of clonidine)</li> <li>Pregnancy-induced hypertension</li> </ul>	<ul style="list-style-type: none"> <li>Orthostatic hypotension</li> <li>Sedation and dizziness</li> </ul>
	Carvedilol	<ul style="list-style-type: none"> <li><b>NO</b> ISA</li> <li><b>NO</b> local anesthetic effect</li> <li>Has antioxidant action</li> </ul>		<ul style="list-style-type: none"> <li>Congestive heart failure (by reversing pathophysiological changes)</li> </ul>	Edema
Selective $\beta_1$ -blocker	<p>Mnemonic: <b>BEAM</b></p> <p>Bisoprolol</p> <p>Esmolol</p> <p>Atenolol</p> <p>Metroprolol</p>	<ul style="list-style-type: none"> <li>Selectively present in low doses</li> <li>Lost in high doses</li> <li><b>NO</b> change in lipid or glucose</li> <li><b>NO</b> bronchoconstriction</li> </ul>		<ul style="list-style-type: none"> <li>Asthma/COPD</li> <li>Raynaud's phenomenon and PVD recurrent vasospasm of the fingers and toes and usually occurs in response to stress or cold exposure</li> <li>Diabetics/Dyslipidemias</li> <li>Variant Angina (coronary spasm)</li> </ul>	

## $\beta$ -blocker Contraindications:

1) Heart Block (can precipitate heart block)

2) Bronchial Asthma (safer with selective  $\beta$ -blockers))

3) Peripheral vascular disease (safer with selective  $\beta$ -blockers)

4) Diabetes (Masking of hypoglycemia) Given Cautiously

5) Hypotension

6) Alone in pheochromocytoma (must be give with  $\alpha$ -blockers)

# Beta-Adrenoceptors blockers

## β-blockers Adverse Effects:

<b>β<sub>1</sub> blockage</b>	<ul style="list-style-type: none"> <li>••Bradycardia</li> <li>••Hypotension</li> <li>••Heart Failure</li> </ul>
<b>β<sub>2</sub> blockage</b>	<ul style="list-style-type: none"> <li>••Hypoglycemia</li> <li>••Bronchoconstriction</li> <li>••Vasoconstriction → cold extremities</li> <li>••Erectile dysfunction</li> <li>••↑TG (hyperglyceridemia) elevated levels of triglyceride</li> <li>••Coronary spasm (angina patient)</li> <li>••Masked hypoglycemic manifestations → Coma (when hypoglycemic manifestations are masked, the patient could fall into a hypoglycemic coma without any prior warning)</li> <li>••Depression + Hallucinations</li> <li>••GI disturbances</li> <li>••Sodium retention</li> </ul>

**Precaution:** Sudden stoppage will give rise to a withdrawal syndrome: Rebound angina, arrhythmia, myocardial infarction & Hypertension WHY? → **Up-regulation of β-receptors.**

To prevent withdrawal manifestations → drug withdrawn gradually.

Disease	Drug of choice
Hypertension	Atenolol, Bisoprolol > Metoprolol, Propranolol
Cardiac Arrhythmia	Esmolol (ultra-short acting), Atenolol, Propranolol
Congestive Heart Failure	Carvedilol, Bisoprolol, Metoprolol
Myocardial Infarction	Atenolol, Metoprolol, Propranolol
Glaucoma	Timolol
Migraine Prophylaxis	Propranolol
Relief of Anxiety (Social and performance)	Propranolol
Thyrotoxicosis	Propranolol

THANK YOU FOR CHECKING OUR WORK

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شادن العمران

لمى الزامل

كوثر الموسى

ديمه الراجحي

جواهر الحربى

دلال الحزيمي

رنيم الديبىخي

نورة الصومالى

منيرة السلولى

**QUIZ-1**  
**QUIZ-2**

For any correction, suggestion or any useful information do not  
hesitate to contact us: [Pharmacology.med435@gmail.com](mailto:Pharmacology.med435@gmail.com)



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