UNIT–V: Pharmacology of Drugs acting on ANS (ADRENERGIC DRUGS)

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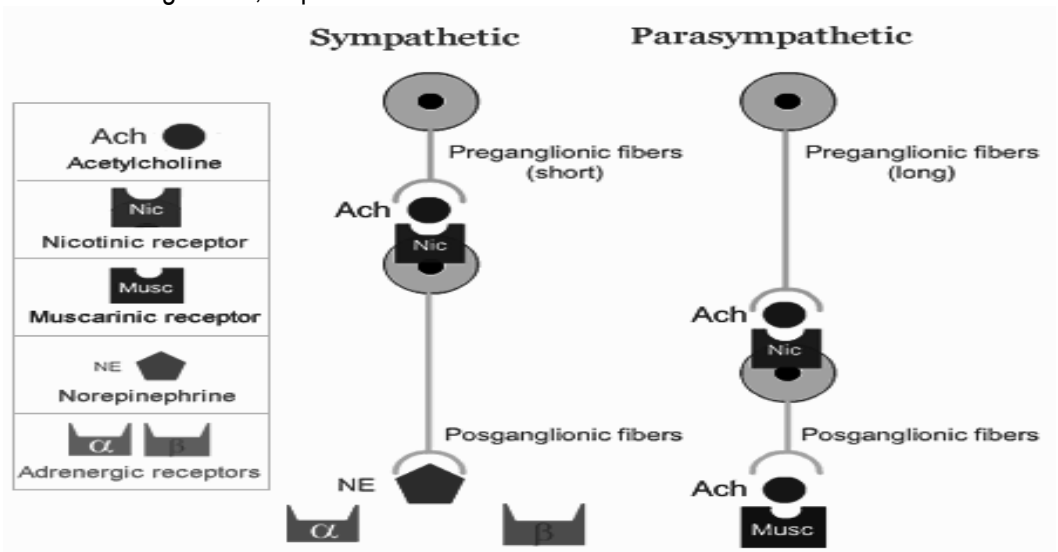
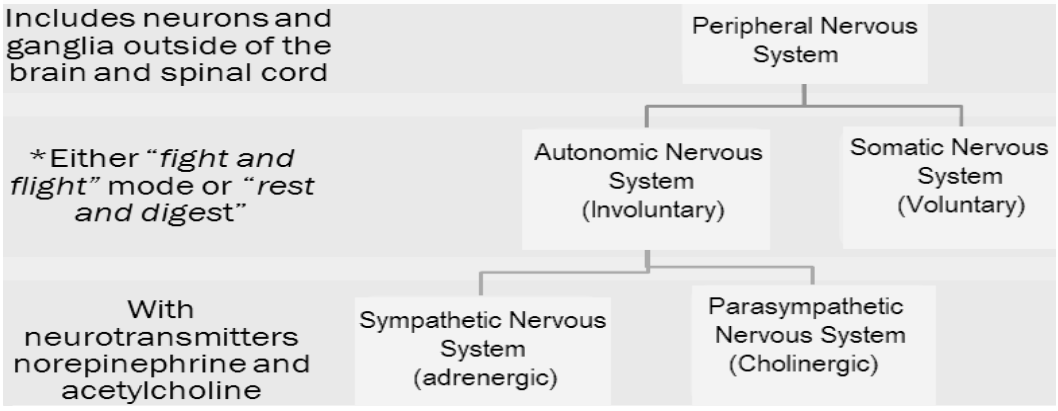
- Adrenergic is a term used to describe proteins and drugs that interact with adrenaline or noradrenaline, also known as epinephrine and norepinephrine, respectively.
- For example, adrenergic receptors are membrane proteins that are the target for epinephrine and norepinephrine, while adrenergic transporters are proteins that carry norepinephrine across the cell membrane of nerve cells.
- An adrenergic agonist is a drug that typically produces the same effect as epinephrine or norepinephrine.
- Where as an adrenergic antagonist is a drug that generally blocks the effects of epinephrine and norepinephrine.
- ***Epinephrine*** **and** ***norepinephrine*** act as hormones and neurotransmitters in numerous biological processes.
- When ***epinephrine*** is released, it contracts and relaxes smooth muscle and increased blood pressure.
- Epinephrine can also increase the level of glucose and fatty acids in the blood, generally leading to increased energy production within cells.
- In addition, ***epinephrine*** and ***norepinephrine*** initiate the ***flight-or-fight response.***
- ***Norepinephrine*** typically increases the heart rate and blood flow to muscles during stressful situations and affects the part of the brain that is responsible for attention and response. It also increases blood glucose levels, thus providing needed energy for cells. Norepinephrine also acts as an anti-inflammatory agent when it is released as a neurotransmitter between nerve cells of the brain.
- The **sympathetic nervous system** (SNS):
  - It is part of the autonomic nervous system.
  - The sympathetic nervous system activates in terms of Fight or flight response results in: Increased BP, Increased blood flow to brain, heart and skeletal muscles; Increased muscle glycogen for energy; Increased rate of coagulation; Pupil dilation

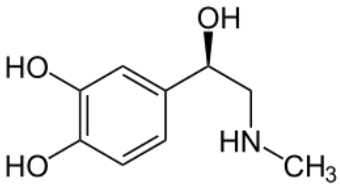




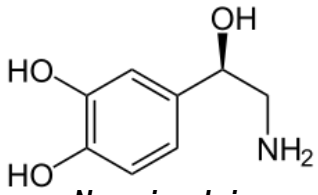
- **THE ADRENERGIC RECEPTORS (OR ADRENOCEPTORS)**

✓ It a class of G protein-coupled receptors that are targets of the catecholamines, especially norepinephrine (noradrenaline) and epinephrine (adrenaline).

✓ Many cells possess these receptors, and the binding of a catecholamine to the receptor will generally stimulate the sympathetic nervous system. The sympathetic nervous system is responsible for the fight-or-flight response, which includes widening the pupils of the eye, mobilizing energy, and diverting blood flow from non-essential organs to skeletal muscle.



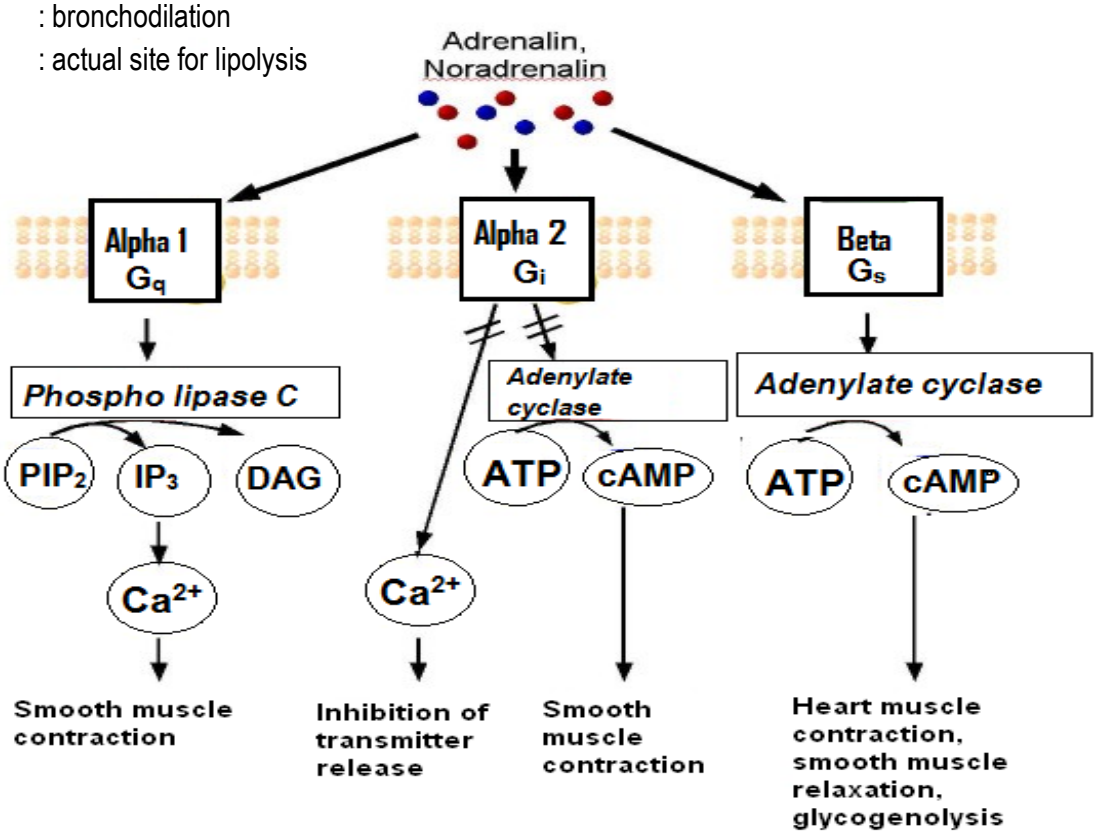
Epinephrine



Norepinephrine

✓ There are two main groups of adrenergic receptors, **α** and **β**, with several subtypes.

- **α** receptors have the subtypes α_1 (a G_q coupled receptor) and α_2 (a G_i coupled receptor). ***Phenylephrine*** is a selective agonist of the **α** receptor.
- **β** receptors have the subtypes β_1, β_2 and β_3. All three are linked to G_s proteins (although β_2 also couples to G_i), which in turn are linked to **adenylate cyclase**. Agonist binding thus causes a rise in the intracellular concentration of the second messenger **cAMP**.
- *Functions of sympathetic nervous system receptors*.
  - Alpha 1 : smooth muscle contraction
  - Alpha 2 : negative feedback causes less norepinephrine to be released so BP is reduced
  - Beta 1 : increased heart rate
  - Beta 2 : bronchodilation
  - Beta 3 : actual site for lipolysis



- ***The mechanism of adrenergic receptors.***

Receptor	Agonist potency order	Selected action of agonist	Mechanism	Agonists	Antagonists
α_1	Norepinephrine > epinephrine >> isoprenaline	Smooth muscle contraction, mydriasis, vasoconstriction in the skin, muscosa and abdominal viscera & sphincter contraction of the GI tract and urinary bladder	Gq: phospholipase C (PLC) activated, IP3,and DAG, rise in calcium	Noradrenaline Phenylephrine Methoxamine Cirazoline Xylometazoline Midodrine Metaraminol	Alfuzosin Doxazosin Phenoxybenzamine Phentolamine Prazosin Tamsulosin Terazosin Trazodone Amitriptyline
α_2	Epinephrine ≥ norepinephrine >> isoprenaline	Smooth muscle mixed effects, norepinephrine (noradrenaline) inhibition, Cardiac muscle relaxation and platelet activation	Gi: adenylate cyclase inactivated, cAMP down	Dexmedetomidine Medetomidine Romifidine Clonidine Brimonidine Xylazine Tizanidine Guanfacine	Phentolamine Yohimbine Idazoxan Atipamezole Trazodone
β_1	Isoprenaline > epinephrine = norepinephrine	Positive Chronotropic, Dromotropic and inotropic effects, increased amylase secretion	Gs: adenylate cyclase activated, cAMP up	Dobutamine Isoprenaline Noradrenaline	Metoprolol Atenolol Bisoprolol Propranolol Timolol Nebivolol
β_2	Isoprenaline > epinephrine >> norepinephrine	Smooth muscle relaxation (Ex. Bronchodilation)	Gs: adenylate cyclase activated, cAMP up (also Gi, see α2)	Salbutamol Bitolterol mesylate Isoprenaline Levalbuterol Salmeterol Terbutaline	Butoxamine Timolol Propranolol
β_3	Isoprenaline = norepinephrine > epinephrine	Enhance lipolysis, promotes relaxation of detrusor muscle in the bladder	Gs: adenylate cyclase activated, cAMP up	Amibegron Solabegron	

Note By:

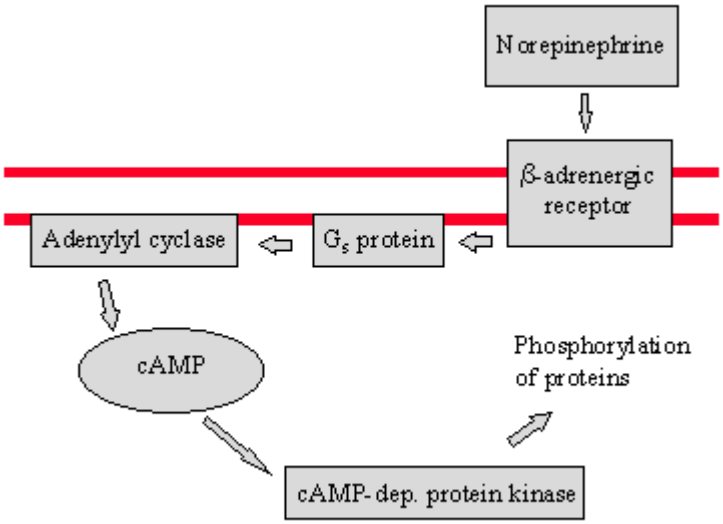
- **Epinephrine** (adrenaline) reacts with both α- and β-adrenoreceptors, causing vasoconstriction and vasodilation, respectively. Although α receptors are less sensitive to epinephrine, when activated, they override the vasodilation mediated by β-adrenoreceptors because there are more peripheral α1 receptors than β-adrenoreceptors. The result is that high levels of circulating epinephrine cause vasoconstriction. At lower levels of circulating epinephrine, β-adrenoreceptor stimulation dominates, producing vasodilation followed by decrease of peripheral vascular resistance.
- ***Increased cAMP*** *will promote relaxation in smooth muscle, while promoting increased contractility and pulse rate in cardiac muscle.*

❖ **The relative potencies of the various receptors are:**

α -adrenergic receptors:	EP > NE
β -adrenergic receptors:	EP = NE
β_1-adrenergic receptors (heart):	EP = NE
β_2-adrenergic receptors (most other tissues)	EP >> NE

α-receptor	**β-receptor**
vasocontriction	vasodilation (β_2)
iris dilation	cardioacceleration (β_1)
intestinal relaxation	intestinal relaxation (β_2)
intestinal sphincter contraction	uterus relaxation (β_2)
bladder sphincter contraction	bronchiodilation (β_2)

- The binding of the adrenergic receptor causes a series of reactions that eventually results in a characteristic response.



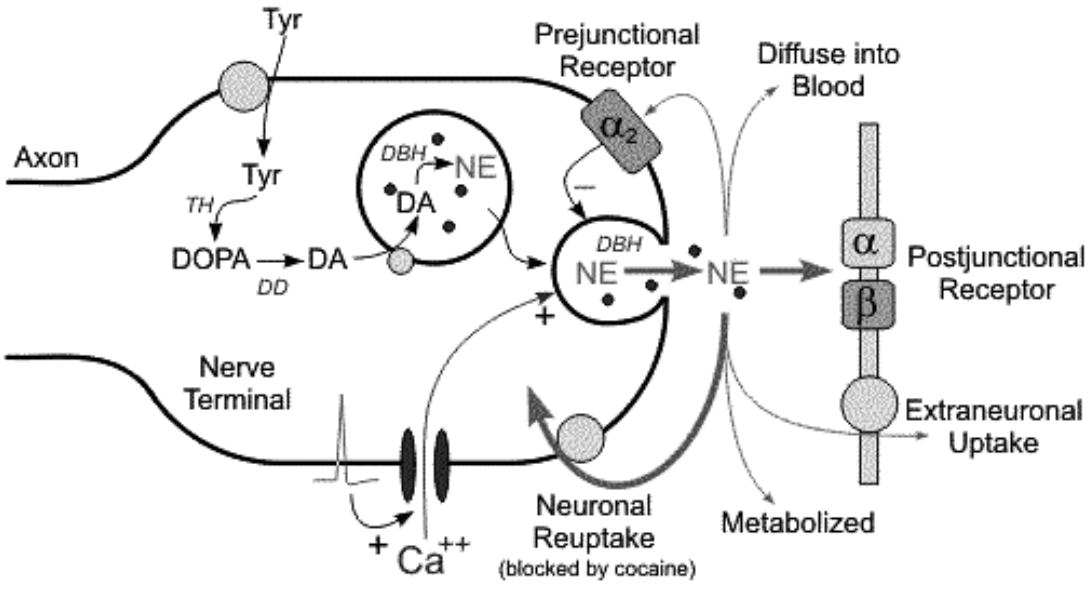
❖ Norepinephrine Synthesis and Release

Norepinephrine (NE) is the primary neurotransmitter for postganglionic sympathetic adrenergic nerves. It is synthesized inside the nerve axon, stored within vesicles, then released by the nerve when an action potential travels down the nerve. Below are the details for release and synthesis of NE:

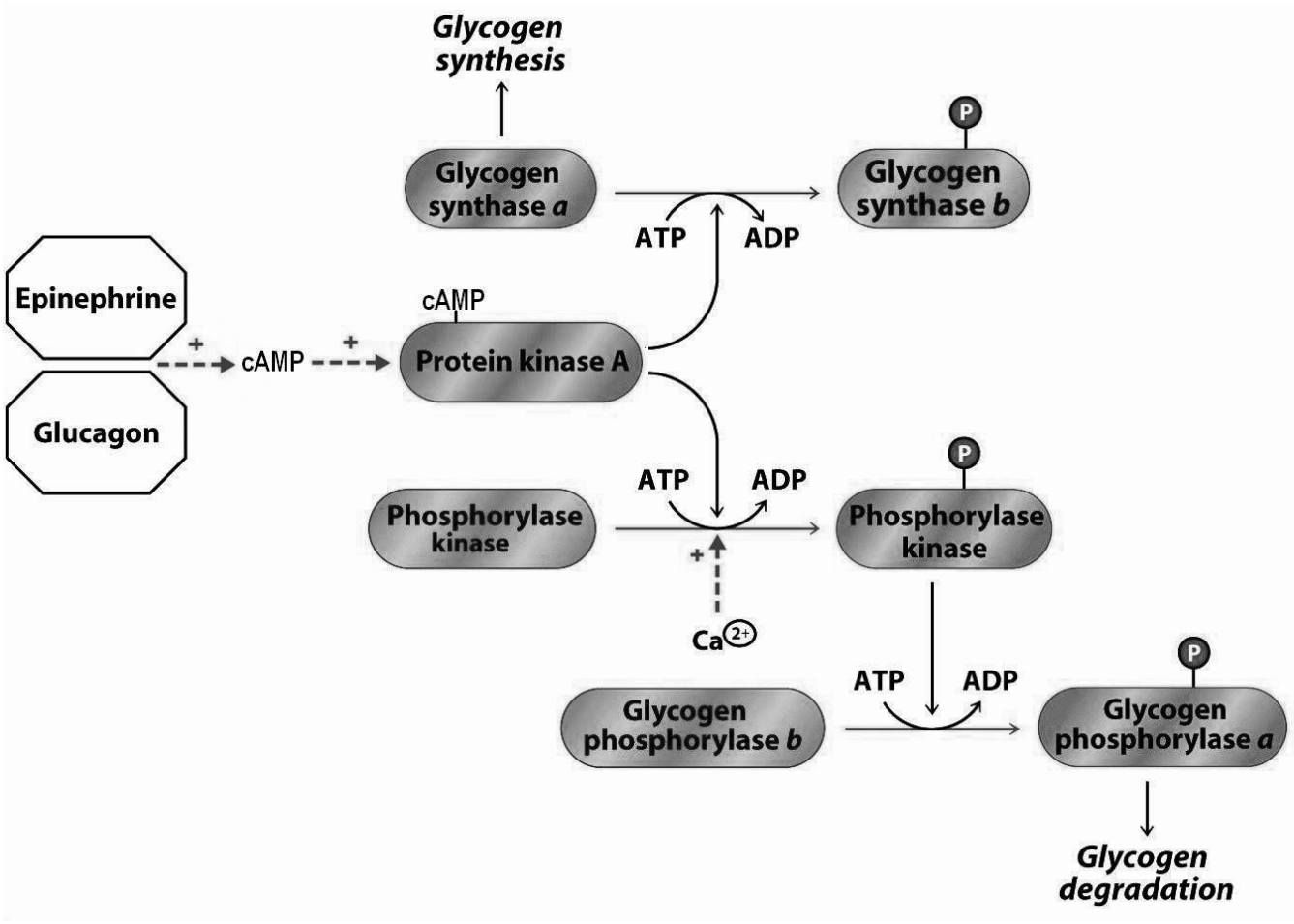
1. The amino acid **tyrosine** is transported into the sympathetic nerve axon.
2. Tyrosine (Tyr) is converted to **DOPA** by tyrosine hydroxylase (rate-limiting step for NE synthesis).
3. DOPA is converted to **dopamine** (DA) by DOPA decarboxylase.
4. Dopamine is transported into vesicles then converted to norepinephrine (NE) by dopamine β-hydroxylase (DBH); transport into the vesicle can by blocked by the drug **reserpine**.
5. An action potential traveling down the axon depolarizes the membrane and causes calcium to enter the axon.
6. Increased intracellular calcium causes the vesicles to migrate to the axonal membrane and fuse with the membrane, which permits the NE to diffuse out of the vesicle into the extracellular (junctional) space. DBH, and depending on the nerve other secondary neurotransmitters (e.g., ATP), is released along with the NE.
7. The NE binds to the postjunctional receptor and stimulates the effector organ response.

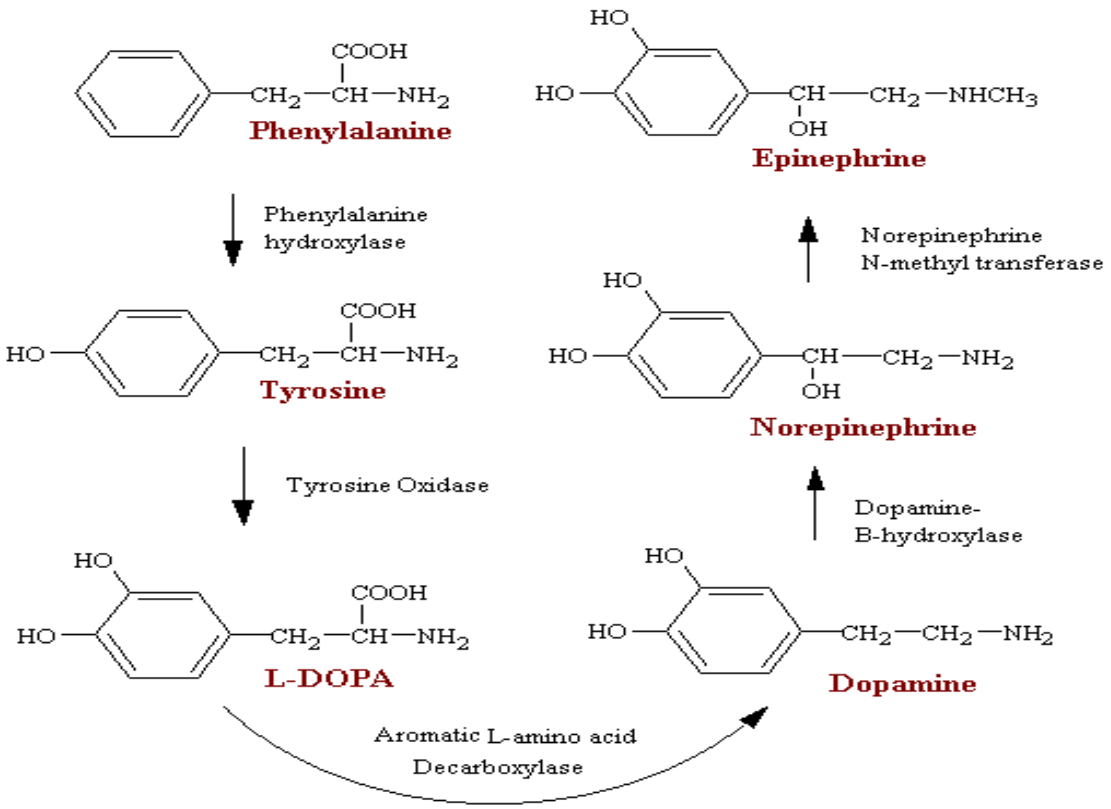
Epinephrine Synthesis and Release

Epinephrine is synthesized from norepinephrine within the adrenal medulla, which are small glands associated with the kidneys. Preganglionic fibers of the sympathetic nervous system synapse within the adrenals. Activation of these preganglionic fibers releases acetylcholine, which binds to postjunctional nicotinic receptors in the tissue. This leads to stimulation of NE synthesis within adenomedullary cells, but unlike sympathetic neurons, there is an additional enzyme (phenylethanolamine-N-methyltransferase) that adds a methyl group to the NE molecule to form epinephrine. The epinephrine is released into the blood perfusing the glands and carried throughout the body.



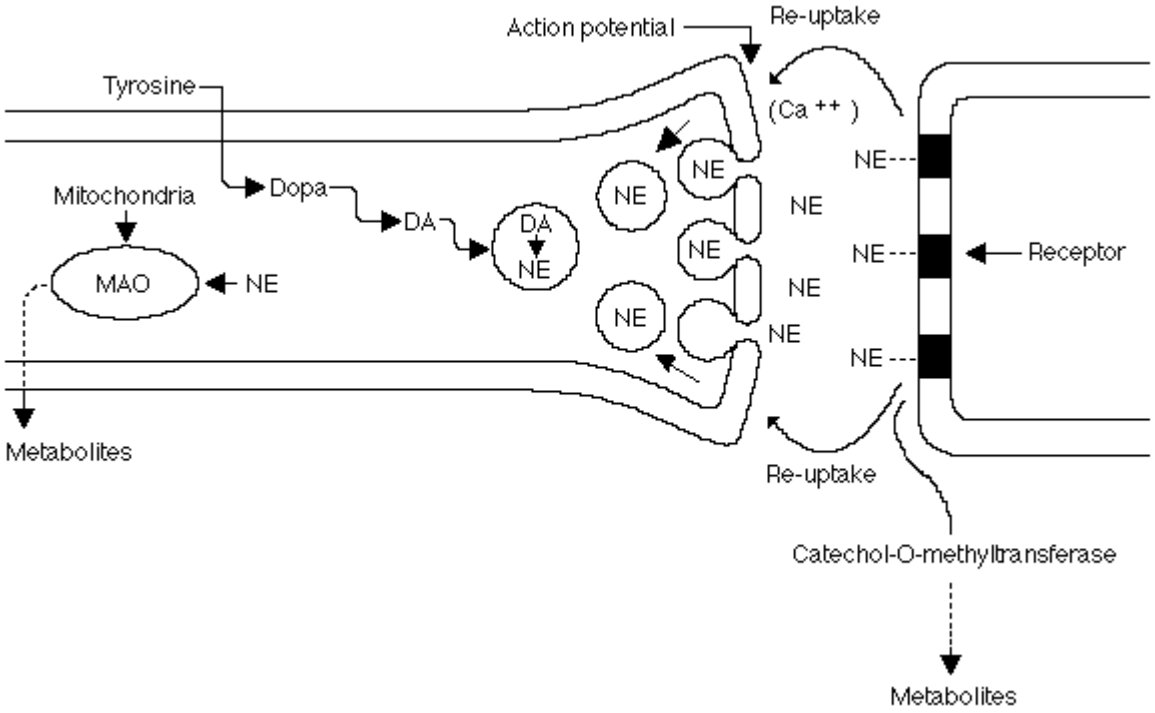
Tyr = tyrosine; TH = tyrosine hydroxylase; DD = DOPA decarboxylase;
DA = dopamine; DBH = dopamine β-hydroxylase; NE = norepinephrine


Glycogen synthesis
Glycogen synthase a
ATP
ADP
Glycogen synthase b
P
Epinephrine
Glucagon
cAMP
cAMP
Protein kinase A
Phosphorylase kinase
ATP
ADP
Phosphorylase kinase
Ca2+
Glycogen phosphorylase b
ATP
ADP
Glycogen phosphorylase a
Glycogen degradation

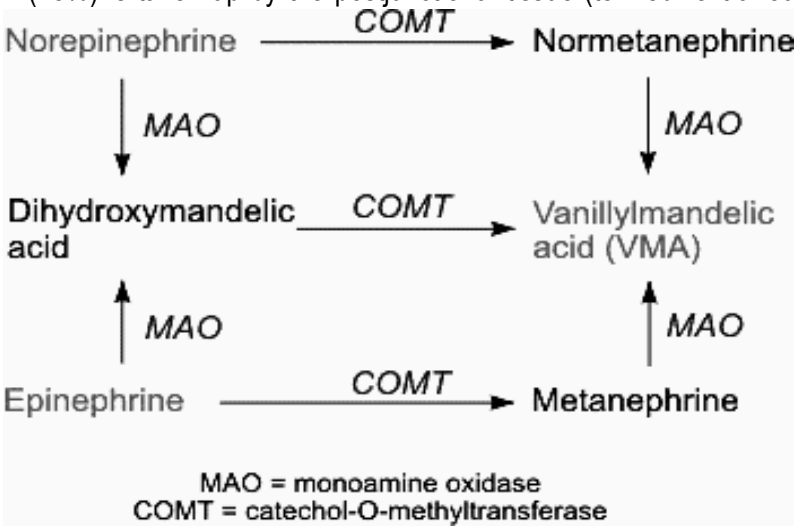

Phenylalanine
Epinephrine
Phenylalanine hydroxylase
Norepinephrine N-methyl transferase
Tyrosine
Norepinephrine
Tyrosine Oxidase
Dopamine-B-hydroxylase
L-DOPA
Dopamine
Aromatic L-amino acid Decarboxylase

❖ Catabolism of Catecolamines

- There are three main ways in which catacolamines are removed from a receptor - recycling back into the presynaptic neuron by an active transport reuptake mechanism, degredation to inactive compounds through the sequential actions of ***catecholamine-O-methyltransferase*** (COMT) and ***monoamine oxidase*** (MAO), and simple diffusion



- Norepinephrine and Epinephrine Removal and Metabolism
  - Most (~90%) of the NE is transported back into the nerve terminal by a neuronal reuptake transport system. This transporter is blocked by **cocaine**; therefore, cocaine increases junctional NE concentrations by blocking its reuptake and subsequent metabolism. (This is a major mechanism by which cocaine stimulates cardiac function and raises blood pressure.)
  - Some of the junctional NE diffuses into capillaries and is carried out of the tissue by the circulation. Therefore, high levels of sympathetic activation in the body increase the plasma concentration of NE and its metabolites.
  - Some of the junctional NE is metabolized within the extracellular space before reaching the capillaries.
  - A small amount of NE (~5%) is taken up by the postjunctional tissue (termed "extraneuronal uptake") and metabolized



❖ α_1 receptor or Alpha-1 adrenergic receptor

- ✓ α_1-adrenergic receptors are members of the G_q protein-coupled receptor superfamily.
- ✓ Activation of a heterotrimeric G protein, G_q, ***activates phospholipase*** C (PLC).
- ✓ This in turn causes an increase ***ininositol triphosphate*** (IP3) and **diacylglycerol** (DAG).
- ✓ The former interacts with **calcium channels** of **endoplasmic** and **sarcoplasmic reticulum**, thus changing the calcium content in a cell. This triggers all other effects.
- ✓ Specific actions of the α_1 receptor mainly involve smooth muscle contraction. It causes vasoconstriction in many blood vessels, including those of the skin, gastrointestinal system, kidney (renal artery) and brain.
- ✓ Other areas of smooth muscle contraction are:
  - ureter
  - vas deferens
  - hair (arrector pili muscles)
  - uterus (when pregnant)
  - urethral sphincter
  - blood vessels of ciliary body (stimulation causes mydriasis)

Further effects include glycogenolysis and gluconeogenesis from adipose tissue and liver, as well as secretion from sweat glands[11]and Na^+ reabsorption from kidney.

Antagonists may be used primarily in hypertension, anxiety disorder, and panic attacks.

Agonists

- Cirazoline
- Metaraminol
- Methoxamine
- Midodrine
- Naphazoline
- Oxymetazoline
- Phenylephrine (decongestant)
- Synephrine
- Tetrahydrozoline
- Xylometazoline

Antagonists

- Alfuzosin (used in benign prostatic hyperplasia)
- Arotinolol
- Carvedilol (used in congestive heart failure; it is a non-selective beta blocker)
- Doxazosin (used in hypertension and benign prostatic hyperplasia)
- Labetalol (used in hypertension; it is a mixed alpha/beta adrenergic antagonist)
- Phenoxybenzamine
- **Phentolamine (used in hypertensive emergencies; it is a nonselective alpha-antagonist)**
- Prazosin (used in hypertension)
- Tamsulosin (used in benign prostatic hyperplasia)
- Terazosin
- Tolazoline

❖ α_2 receptor or Alpha-2 adrenergic receptor

- ✓ The α_2 receptor is a presynaptic receptor, causing negative feedback on, for example, norepinephrine.
- ✓ When NA is released into the synapse, it feeds back on the α_2 receptor, causing less NA release from the presynaptic neuron. This decreases the effect of NA.
- ✓ There are 3 highly homologous subtypes of α_2 receptors: **α_{2A}**, **α_{2B}**, and **α_{2C}**.
- ✓ Specific actions of the α_2 receptor include:
  - Suppression of release of norepinephrine (noradrenaline) by negative feedback.
  - Transient hypertension (increase in blood pressure), followed by a sustained hypotension (decrease in blood pressure).
  - Vasoconstriction of certain arteries
  - Vasoconstriction of arteries to heart (coronary artery) however the extent of this effect may be limited and may be negated by the vasodilatory effect from β_2 receptors
  - Constriction of some vascular smooth muscle
  - Venoconstriction of veins
  - Decrease motility of smooth muscle in gastrointestinal tract
  - Contraction of male genitalia during ejaculation
  - Inhibition of lipolysis

- **Agonists**
  - Brimonidine
  - Clonidine
  - Detomidine
  - Dexmedetomidine
  - Guanfacine
  - Tolonidine
  - Xylazine
  - Oxymetazoline (partial α_2 agonist)

- **Antagonists**
  - Atipamezole
  - Efaroxan
  - Phenoxybenzamine
  - Phentolamine
  - Setiptiline
  - Tolazoline
  - Yohimbine

❖ β_1 or Beta-1 adrenergic receptor

- *Mechanism*: G_s renders *adenylate cyclase* activated, resulting in increase of cAMP.
- Actions of the β_1 receptor include:
  - stimulate viscous, amylase-filled secretions from salivary glands
  - Increase cardiac output
    - Increase heart rate in sinoatrial node (SA node) (chronotropic effect)
    - Increase atrial cardiac muscle contractility. (inotropic effect)
    - Increases contractility and automaticity of ventricular cardiac muscle.
    - Increases conduction and automaticity of atrioventricular node (AV node)
  - Renin release from juxtaglomerular cells.
  - Lipolysis in adipose tissue.
  - Receptor also present in cerebral cortex.
- **Agonists**
  - Isoprenaline has higher affinity for β_1 than adrenaline, which, in turn, binds with higher affinity than noradrenaline at physiologic concentrations. Selective agoniststo the beta-1 receptor are:
  - Denopamine
  - Dobutamine (in cardiogenic shock)
  - Xamoterol (cardiac stimulant)
- **Antagonists**
  - *(Beta blockers)* β1-selective ones are:
  - Acebutolol (in hypertension, angina pectoris and arrhythmias)
  - Atenolol (in hypertension, coronary heart disease, arrhythmias and myocardial infarction)
  - Betaxolol (in hypertension and glaucoma)
  - Bisoprolol (in hypertension, coronary heart disease, arrhythmias, myocardial infarction and ischemic heart diseases)
  - Esmolol (in arrhythmias)
  - Metoprolol (in hypertension, coronary heart disease, myocardial infarction and heart failure)
  - Nebivolol (in hypertension)

❖ B_2 or Beta-2 adrenergic receptor

- ***Mechanism:*** coupled to the Gs G protein, which activates *adenylyl cyclase*, catalysing the formation of cyclic adenosine monophosphate (cAMP) which then activates protein kinase A, and the counterbalancing phosphatase PP2A.
- **Circulatory system**
  - Heart muscle contraction
  - Increase cardiac output (minor degree compared to β_1).
    - Increase heart rate in sinoatrial node (SA node) (chronotropic effect).
    - Increase atrial cardiac muscle contractility. (Inotropic effect).
    - Increases contractility and automaticity of ventricular cardiac muscle.
  - Dilate hepatic artery.
  - Dilate arteries to skeletal muscle.
- **Eye**

In the normal eye, beta-2 stimulation by salbutamol increases intraocular pressure via net:

- Increase in production of aqueous humour by the ciliary process,
- Subsequent increased pressure, *despite* reduced drainage of humour via the Canal of Schlemm.

In glaucoma, drainage is reduced (open-angle glaucoma) or blocked completely (closed-angle glaucoma). In such cases, beta-2 stimulation with its consequent increase in humour production is highly contra-indicated, and conversely, a topical beta-2 antagonist such as timolol may be employed.

- **Digestive system**
  - Glycogenolysis and gluconeogenesis in liver.
  - Glycogenolysis and lactate release in skeletal muscle.
  - Contract sphincters of GI tract.
  - Thickened secretions from salivary glands.
  - Insulin secretion from pancreas
- **Other**
  - Inhibit histamine-release from mast cells.
  - Increase protein content of secretions from lacrimal glands.
  - Increase renin secretion from kidney.
  - Bronchiole dilation (targeted while treating asthma attacks)
- ***Agonists***: spasmolytics in asthma and COPD
  salbutamol (albuterol in USA)
  isoproterenol
  levosalbutamol (levalbuteral in USA)
  metaproterenol
  formoterol
  salmeterol
  terbutaline
- ***Antagonists:*** Butaxamine

A. NON-SELECTIVE ADRENERGIC AGONISTS

EPINEPHRINE

1. acts on both α and β receptors

2. *Effects*

a. Cardiovascular

(1) Potent elevator of blood pressure. Intravenous injection causes dose-dependent increases in blood pressure; systolic pressure is more affected than diastolic and so pulse pressure is increased. Effects are due to increased heart rate, increased contractions of the myocardium and vasoconstriction. Subcutaneous administration or intravenous infusion causes a lower increase in systolic blood pressure with decreased peripheral vascular resistance and diastolic blood pressure.

(2) Vasoconstriction of subcutaneous small vessels, increased blood flow to skeletal muscle

(3) Stimulation of myocardium – increased pulse, arrhythmias, increased work and oxygen consumption, increased cardiac output

b. Smooth muscle – increased blood flow, relaxation of GIT and bladder muscle, b2 selective agonists relax uterine smooth muscle

c. Respiratory system – relaxes bronchi

d. Metabolic effects – increased oxygen consumption, hyperglycemia, lactic acidosis, increased free fatty acids (β receptors); effects on insulin depend on receptor – α_2 inhibit secretion, β_2 stimulate it, the result is inhibition.

e. Other effects – eisonopenia (a decrease in the number of eosinophils in the blood), decreased intraocular pressure, **mydriasis** (Dilatation of the pupil), tears

3. *Uses*

a. Bronchodilatation in asthma and to relieve bronchospasm

b. To treat hypersensitivity reactions and anaphylactic shock

c. Used together with local anesthetics to prolong duration by causing vasoconstriction

d. Used in cardiac arrest

4. Toxic effects

a. May be transient – fear, anxiety, dizziness, pallor, tremors, headache and palpitations

b. More serious effects are arrhythmias and cerebral hemorrhage – due to rapid elevation of blood pressure

c. Worse in patients with psychiatric backgrounds, hypertension or hyperthyroidism

6. Contraindications – patients receiving nonselective beta blockers (a effects unopposed), patients with both emphysema and heart disease

NOREPINEPHRINE

1. More potent than epinephrine on a receptors, much less potent on b2 receptors and the same on b1 receptors

2. *Effects*

a. Cardiovascular

(1) Increases in systolic, diastolic and pulse pressures; increased peripheral vascular resistance, but no change in cardiac output

(2) Sinus bradycardia, arrhythmias

b. Other effects, as seen with epinephrine, are seen only at high doses of norepinephrine

3. Routes of administration as for epinephrine

4. Uses – used in shock

5. Toxic effects – as with epinephrine, but milder

a. Severe hypertension, headache, photophobia, pallor, sweating and vomiting

b. Increased risk of arrhythmias

6. Contraindication – pregnancy (will cause uterine contractions)

DOPAMINE

1. Precursor of both epinephrine and norepinephrine

2. *Effects*

a. CNS effects are minimal when given intravenously; does not cross blood-brain barrier

b. Cardiovascular effects are dose dependent.

(1) The first effects are vasodilatation, increased renal blood flow and glomerular filtration rate (GFR) – mediated through dopamine receptors.

(2) Increased dose has positive isotropic (Affecting the force or energy of muscular contractions) effects with increased systolic and pulse pressure (slight effect on diastolic pressure) and no change in total peripheral resistance. These are mediated through b1 receptors.

(3) With higher dose, vasoconstriction results, mediated through a1 receptors.

3. Not effective orally as it is rapidly broken down; used intravenously only

4. *Uses* – treatment of shock. Lowest dose is used to treat oliguria in hydrated patient.

5. *Side effects* – nausea, vomiting, tachycardia, chest pain, headache, hypertension, vasoconstriction and arrhythmias

6. Contraindications – (relative) patients receiving monoamine oxidase inhibitors

AMPHETAMINES

1. Other similar drugs are methylphenidate, ephedrine, pemoline and methamphetamine

2. *Effects*

a. Increased systolic and diastolic blood pressure

b. Contraction of bladder

c. CNS stimulation – alertness, lack of fatigue, euphoria, self-confidence, increased concentration, enhanced physical performance

d. Compensates for lack of sleep

e. Depresses appetite (but is tolerance)

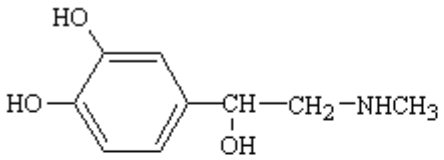
3. Uses – obesity, narcolepsy and attention deficit hyperactivity disorder (methylphenidate)

4. Can be given orally

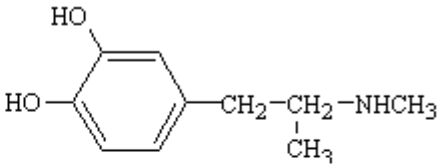
5. Side effects – increased errors in tasks performed, headache, palpitations, arrhythmias, depression, fatigue, dry mouth, increased sweating, nausea and vomiting, abdominal pain, confusion and psychomotor agitation.

6. Chronic use may cause psychotic reactions.

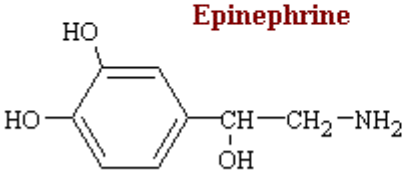
7. Toxic doses can cause convulsions, coma and death.



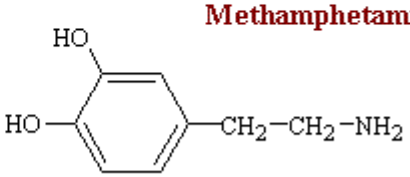
Epinephrine



Methamphetamine



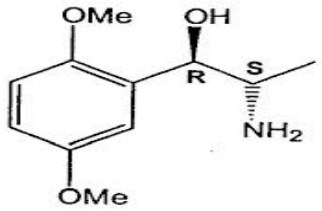
Norepinephrine



Amphetamine

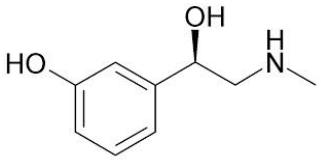
B. SELECTIVE ADRENERGIC AGONISTS

METHOXAMINE



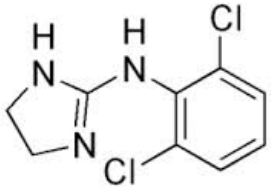
1. α_1 selective agonist
2. Effects – increased peripheral vascular resistance, elevated blood pressure, sinus bradycardia
3. Uses – in hypotension, shock and paroxysmal atrial tachycardia
4. Given intravenously

PHENYLEPHRINE



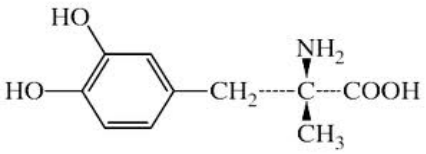
1. α_1 selective agonist
2. Effects – increased peripheral vascular resistance, elevated blood pressure, sinus bradycardia (Slow heart rate), vasoconstriction
3. Uses – as nasal decongestant and to dilate pupils
4. Given intravenously and topically to the nose and eyes
5. Side effects – strong vasoconstriction when given intravenously

CLONIDINE



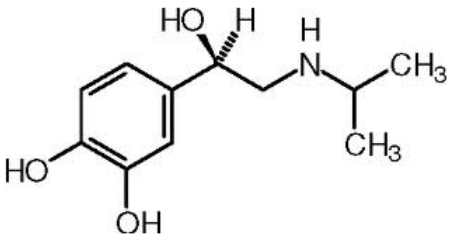
1. α_2 selective agonist
2. Effects – vasoconstriction, hypotension (intravenous administration causes transient hypertension with prolonged hypotension; oral causes hypotension only), bradycardia (Slow heart rate) and sedation
3. Uses – main use is as antihypertensive; other uses are in treatment of substance addiction, in the relief of vasomotor symptoms of the menopause and in anesthesia
4. Can be given orally or as transdermal patch
5. Side effects – dry mouth, sedation are very common; less so are sexual dysfunction and serious bradycardia. Patches can cause contact dermatitis.

METHYLDOPA



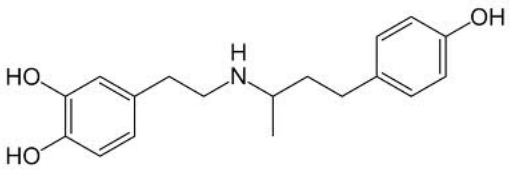
1. α_2 selective agonist
2. Centrally acting pro-drug
3. Effects – reduces peripheral resistance with normal renal blood flow
4. Given orally or intravenously
5. Uses – antihypertensive, can be used in pregnant women, especially useful in left ventricular hypertrophy
6. Side effects - mild and transient sedation, dry mouth, reduced libido, Parkinsonism, hyperprolactinemia
7. Toxic effects
a. hepatitis – usually transient, can be fatal
b. hemolytic anemia
c. rarer – leukopenia, thrombocytopenia, SLE, myocarditis, retroperitoneal fibrosis, pancreatitis

ISOPROTERENOL



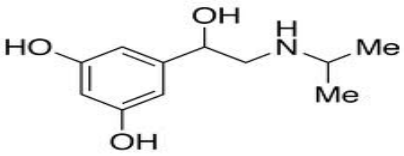
1. β selective agonist
2. Effects
a. Decreased peripheral vascular resistance and diastolic pressure (systolic pressure usually unchanged), increased cardiac output due to positive inotropic and positive chronotropic effects
b. Relaxes smooth muscle of respiratory and GI tracts
c. Mild hyperglycemia
3. Can be inhaled or given orally
4. Uses – to increase heart rate in bradycardia or heart blocks
5. Side effects – palpitations, sinus tachycardia, ischemia, arrhythmias, flushing, headache

DOBUTAMINE



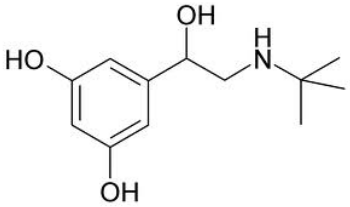
1. β selective agonist
2. Effects – more inotropic than chronotropic, increases stroke volume and cardiac output
3. Given intravenously
4. Used in congestive heart failure, acute myocardial infarction and before cardiac surgery
5. Side effects – hypertension, tachycardia

METAPROTERENOL



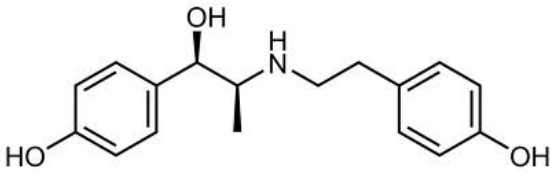
1. β2 selective agonist
2. Effects - bronchodilatation
3. Given orally and as inhalant (good absorption with minimal systemic side effects)
4. Uses – acute bronchospasm, asthma, Chronic Obstructive Pulmonary Disease (COPD)
5. Side effects – tremor (tolerance later develops), apprehension, anxiety,

TERBUTALINE



1. β_2 selective agonist
2. Effects - bronchodilatation
3. Given orally, subcutaneously and as inhalant
4. Uses - acute bronchospasm, asthma, COPD and for status asthmaticus; also used to treat uterine contractions

RITODRINE



1. β_2 selective agonist
2. Effects – relaxation of uterine muscle
3. Given orally and intravenously
4. Uses – to treat premature uterine contractions
5. Toxic effects – pulmonary edema, worsening of cardiac disease