

The mechanisms of sympathomimetic drugs can be:

Drug	Receptor	Effects	Used for	Notes
A. Direct Acting Sympathomimetics Drugs (direct interaction between drug and receptor)				
Phenylephrine	α-1 Receptors Agonists	- Mydriatic. - Decongestant.	- Hypotension.	- Noncatecholamine. - Not inactivated by COMT → Longer duration than CA
Methoxamine		- Vasoconstriction. - Vagal Bradycardia. → Prolonged raise in BP	- Limited for Hypotension	- Rarely used
Midodrine		- Diminished fall in BP - Hypertension when supine.	- Orthostatic Hypotension	- Prodrug, hydrolyzed into desglymidodrine
Clonidine	α-2 Receptors Agonists	- Decrease in BP and Cardiac output. - High dose: Suppression of NE release → lowers HR (<i>vagomimetic</i>). - Over dose: vasoconstriction leading to hypertension. - Side effects: Sedation, Dry mouth, dizziness and constipation.	- Sedative, analgesic and antishivering actions. - ADHD in children. - Opioids/alcohol withdrawal, hypertension, restless legs. - Low dose for: Migraine prophylaxis, menopausal flushing and chorea.	- Stimulates Alpha2-A in the vasomotor center brainstem. - Sedation site of action: locus ceruleus. - Analgesic site of action: in the spinal cord.
Guanfacine		-	- Hypertension	-
Dexmedetomidine		- Reduces requirements of opioids in pain control.	- Sedation of intubated and mechanically ventilated patients.	-
Methyldopa		- Similar to clonidine. - Reduces sympathetic outflow lowering BP. - Reduction of plasma rennin activity.	- Hypertension during pregnancy.	- Metabolized to alpha-methyl norepinephrine - Used instead of ACE Inhibitors and angiotensin II receptors blockers whom are more effective but they are strongly contraindicated in pregnancy.
Oxymetazoline		- Constriction of nasal mucosa. - Large doses: Hypotension	- Topical decongestant.	- Direct affinity for α2-A receptors.



Drug	Receptor	Effects	Used for	Notes
Isoproterenol	Very potent β -receptor agonist, with little effect on α -receptors	<ul style="list-style-type: none"> - Positive chronotropic and inotropic actions - Potent vasodilator(beta2) - leads to: <ul style="list-style-type: none"> → Increased cardiac output. Fall in diastolic and MAP. Decrease/increase in systolic pressure. 	<ul style="list-style-type: none"> - Heart block - Cardiac Arrest 	-
Dobutamine	β -1 Receptors agonists	<ul style="list-style-type: none"> - Positive inotropic effect - It has relatively greater inotropic than chronotropic effect compared with isoproterenol. 	<ul style="list-style-type: none"> - Acute heart failure and cardiogenic shock due to massive myocardial infarction. 	<ul style="list-style-type: none"> - Racemic mixture of (-) and (+) isomers. - The (+) isomer is a potent β 1 agonist and an α 1 receptor antagonist. - The (-) isomer is a potent α 1 agonist. - The resultant effects of dobutamine is β 1 stimulation.
Salbutamol	β -2 Receptors agonists	- Bronchodilation	- Asthma	-
Terbutaline				- Can also be used for uterine relaxation in premature labor
Ritodrine				- Uterine relaxation

Drug	Mechanism	Used for	Notes
B. Indirect Acting Sympathomimetics (interaction not between drug and receptor)			
1. Amphetamine Like “Displacers” (displace stored catecholamine transmitter)			
Amphetamine	- Actions are mediated through the release of NE and dopamine.	- Readily enters the CNS, where it stimulates mood and alertness, and a depressant effect on appetite.	- A racemic mixture where D-isomer is more potent than the L-isomer.
Methylamphetamine	-	-	- Very similar to amphetamine with a higher ratio of central to peripheral actions.
Methylphenidate	-	- ADHD in children	- Its major pharmacologic effects and abuse potential are similar to those of amphetamine.
Modafinil	- Inhibits both NE & DA transporters. - Increases interstitial concentrations of NE, DA, serotonin and glutamate - Decreases GABA levels.	- Psychostimulant. - Improve wakefulness in narcolepsy. It is often associated with mild increases in BP & HR.	-
Tyramine	- If administered parenterally, it releases stored catecholamines	-	- Found in ↑ conc. in some fermented foods such as cheese. Metabolized by MAO in GIT & the liver so it is inactive orally. - In patients treated with MAO inhibitors, tyramine may cause marked increases in blood pressure (Cheese reaction).
2. Catecholamine Reuptake Inhibitors (interfering with the action of the NE transporter “NET” or inhibit NE & serotonin reuptake)			
Atomoxetine	- Selective inhibitor of the NE reuptake transporter.	- Attention deficit disorders (ADHD)	-
Sibutramine	- Serotonin and NE reuptake inhibitor	- Appetite suppressant for long-term treatment of obesity.	-
Cocaine	- <u>Peripherally</u> : Inhibition of NE reuptake (<i>amphetamine-like psychological effect</i>) - <u>In the CNS</u> : (Pleasure centers): Inhibits dopamine reuptake into neurons in the.	-	- Local anesthetic with a sympathomimetic. - A shorter lasting and more intense effect than amphetamine. - It can be smoked, snorted into the nose, or injected. It is a heavily abused drug.

Drug	Receptor	Effects	Used for	Notes
C. Mixed Acting Sympathomimetics (they show both direct and indirect actions)				
Ephedrine ¹	β- receptors Agonists	- It releases NE & a mild stimulant of β ₂	- Asthma, hay fever & the common cold	- high bioavailability & a relatively long duration. - <u>Source</u> : The plant, Ephedra Sinica
Pseudoephedrine		-	- Component of many decongestant mixtures	- One of four ephedrine enantiomers. - Available over the counter
Phenylpropanolamine		-	- Appetite suppressants	- Removed from the market because its use was associated with hemorrhagic strokes in young women.

1) Ephedrine is also used as a bronchodilator, decongestant and a pressor agent (constricts arterioles) during spinal anesthesia.

Drug	Effect	Used for
D. Dopaminergic Agonists (Stimulation of the D1 receptor)		
Levodopa	- Converted to dopamine in the body.	- Valuable in the treatment of Parkinson's disease.
Fenoldopam	- A D1-receptor agonist that selectively leads to peripheral vasodilation in some vascular beds.	- The primary indication for fenoldopam is in the IV treatment of severe hypertension.

Therapeutic uses of sympathomimetics

Used for	Drug	Notes
Acute Hypotension	NE, phenylephrine and methoxamine (giving desired vasoconstriction)	Treatment is of short duration to preserve cerebral and coronary blood flow.
Cardiogenic shock and acute heart failure (Usually due to myocardial infarction)	Dopamine and dobutamine (Positive inotropic agents)	In low to moderate conc., these drugs increase cardiac output and cause relatively little peripheral vasoconstriction.
Chronic orthostatic hypotension	Midodrine (orally active) Ephedrine and phenylephrine	Impairment of autonomic reflexes that regulate BP due to either diabetes, medications or other diseases.
Heart block and cardiac arrest	Isoproterenol and epinephrine	Used in the temporary emergency management of complete heart block and cardiac arrest
Local vasoconstriction (Local anesthetics)	Epinephrine (for epistaxis or gingivectomy) Cocaine (for nasopharyngeal surgery)	Combining α -agonist such as epinephrine with LA greatly prolongs the duration of the LA and reduces its toxicity.
Decongestants	Phenylephrine (nasal decongestant) Ephedrine or pseudoephedrine (longer duration but higher effect on cardia and CNS) Xylometazoline or oxymetazoline (long acting topical decongestants)	Rebound congestion may follow their use. Most of them are available over the counter. Phenylephrine is used for minor allergic hyperemia
Asthma	Salbutamol, metaproterenol and terbutaline (β -2 selective agents)	Using other drugs than β -2 selective agonist are rarely used because they have more adverse effects.
Anaphylaxis	Parental administration of epinephrine. Glucocorticoids and antihistamines.	Epinephrine is useful because it increase cardiac output (β -1), relaxes bronchioles (β -2) and constricts capillaries (α -1).
Glaucoma	β - blocking agents Apraclonidine	Apraclonidine (α -2 selective agonist) lowers intraocular pressure.
Mydriatic	Phenylephrine	-
Suppress premature labor	Ritodrine and terbutaline	They relax the pregnant uterus.
Stress incontinence	Ephedrine and pseudoephedrine (They tighten the urethral sphincter)	Stress incontinence is the loss of small amount of urine with coughing, laughing, etc.
Narcolepsy	Modafinil	-
ADHD	Methylphenidate and clonidine Modafinil can be used too	-