Effects of drugs on Blood Pressure

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➢ **Arterial blood pressure** is the product of the **cardiac output** (CO) and the **peripheral vascular resistance (PVR).**

- BP=CO×PVR
- CO=HR×SV

➢ This means:

- If either CO or PVR increases, BP rises.
- Conversely, if they decrease, BP falls.

➢ When blood pressure (BP) **drops**, it triggers a response in the body to bring it back to normal. Pressure-sensitive sensors called **baroreceptors** (found in the aortic arch and carotid sinuses) detect this change and send signals to the brain.

- The brain responds by **activating the sympathetic nervous system** and **reducing signals from the parasympathetic system** (vagus nerve). This leads to:

- ✓ **Vasoconstriction (narrowing of blood vessels).**

- ✓ **Increased heart rate and cardiac output.**

- Together, these changes raise the blood pressure to compensate for the drop.

- On the flip side, when blood pressure gets too high, the baroreceptors send more signals to the brain. This reduces sympathetic activity and increases parasympathetic signals, causing:

- ✓ **Vasodilation (widening of blood vessels).**
- ✓ **Slower heart rate (bradycardia).**
- ➢ These adjustments lower the blood pressure back to normal.
- ➢ This process helps maintain stable blood pressure in the body.

Effect of Ach

❖ Heart rate: ⇩

- Ach hyperpolarizes the SA node cells($\mathbf{M_2}$).
- It increases the refractory period of the AV node and Purkinje fibers.

❖ Blood pressure: ⇩

- Ach dilates blood vessels by acting on $\mathbf{M_3}$ receptors present on vascular endothelial cells, leading to the release of **nitric oxide**.

Effect of Atropine

❖ Heart rate:

- Atropine blocks muscarinic receptors(**M_2**) on the SA node, reducing vagal tone and increasing heart rate.
- A brief initial bradycardia may occur after i.m./s.c. injection due to increased ACh release from blocked muscarinic autoreceptors (M_1).

❖ Blood pressure:

- Atropine has minimal direct effects on BP as cholinergic impulses do not regulate vascular tone.
- **Factors influencing BP:**

✓ Tachycardia increases cardiac output, potentially raising BP.

✓ High doses may cause vasodilation, possibly lowering BP.

Effect of Adrenaline($\alpha_1 \alpha_2 \beta_1 \beta_2$)

❖ Heart rate:

- Adrenaline increases heart rate by enhancing pacemaker activity in the SA node.
- When BP rises significantly, **reflex bradycardia** occurs:
- The rise in BP stimulates baroreceptors, which activate the vagus nerve to slow the heart.

❖ Blood pressure:

- Causes a temporary rise in both systolic and diastolic BP (α-effects predominate at high doses, causing widespread vasoconstriction).
- BP normalizes quickly due to rapid uptake of adrenaline, followed by a secondary BP drop as β_2 effects (vasodilation) dominate at lower concentrations.

Effect of Noradrenaline($\alpha_1\alpha_2\beta_1$)

❖ Heart rate: ⇧

- Direct action of noradrenaline on the heart is to increase the heart rate by stimulating **β_1** receptors.
- However, the indirect action of noradrenaline on the heart is to decrease the heart rate due to **reflex bradycardia** caused by a rise in blood pressure.

❖ Blood pressure: ⇧

- Causes **vasoconstriction** via α-receptors, with no β_2-mediated vasodilation.
- Increases **systolic, diastolic, and mean BP.**
- Peripheral resistance consistently increases.

Effect of Isoprenaline($\beta_1\beta_2$)

❖ Heart rate:

- Isoprenaline strongly stimulates beta-1 adrenergic receptors in the heart.
- The result is enhanced calcium ion availability, which increases the rate and force of cardiac contractions.

❖ Blood pressure:

- **Systolic Blood Pressure**: Due to the increased cardiac output from beta-1 stimulation, **systolic pressure may rise slightly** or remain stable.
- **Diastolic Blood Pressure**: Beta-2 receptor activation causes vasodilation in peripheral blood vessels, leading to a **reduction in diastolic blood pressure**.

Effect of Phentolamine($\alpha_1\alpha_2$#)

❖ Heart rate:

- The decrease in blood pressure triggers a reflex tachycardia via the baroreceptor reflex.
- Additionally, blocking alpha-2 receptors on presynaptic nerve terminals leads to increased release of norepinephrine, further stimulating beta-1 adrenergic receptors in the heart.

❖ Blood pressure:

- Phentolamine blocks alpha-1 receptors on vascular smooth muscle, causing vasodilation.
- This reduces peripheral vascular resistance, leading to a decrease in blood pressure

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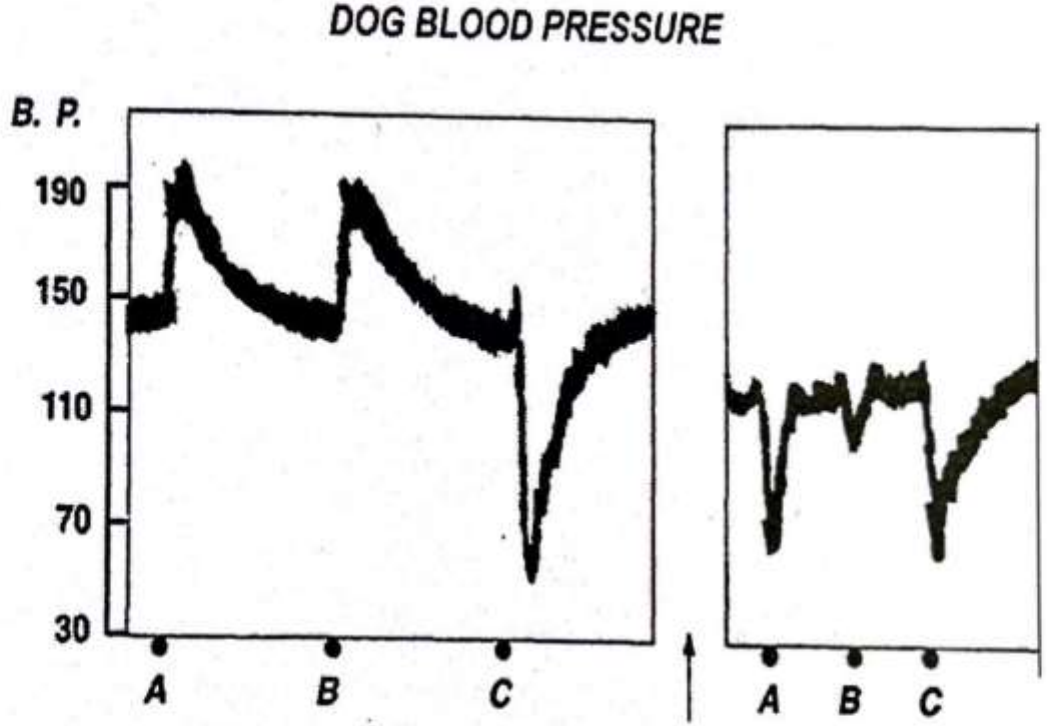
Spot exercise

Following graph shows the effects of drugs A, B and C on dog mean blood pressure. The responses of these drugs are recorded after administration of prazosin.



A :
B :
C : Isoprenaline (2.0 µg/kg)

Identify the probable nature of drugs A and B with reasons.

A: Adrenaline
B: Nor adrenaline

Vasomotor reversal of Dale

- Normally, **adrenaline** primarily acts on two types of adrenergic receptors in blood vessels:

✓ **Alpha-adrenergic receptors**, which cause **vasoconstriction**.

✓ **Beta-adrenergic receptors**, which cause **vasodilation**.

- In most blood vessels, alpha receptors dominate, so adrenaline typically causes vasoconstriction.

❖ Mechanism of Vasomotor Reversal

- When an **alpha-adrenergic receptor blocker** (such as **phentolamine** or **ergot alkaloids**) is administered, the alpha receptors are inhibited, preventing adrenaline from causing vasoconstriction. As a result:

- The **beta-adrenergic receptors**, which mediate vasodilation, become unopposed.

- Subsequent administration of adrenaline leads to **vasodilation** instead of vasoconstriction.

- This "reversal" of vascular response from constriction to dilation is the **vasomotor reversal of Dale**.

Effect of Ephedrine

❖ Heart rate:

- Directly stimulates beta-1 adrenergic receptors in the heart, increasing the rate and force of cardiac contractions.
- Indirectly causes the release of norepinephrine, which further stimulates beta-1 receptors.
- **Outcome**: **Increases heart rate.**

❖ Blood pressure:

- **Systolic Blood Pressure**:Increases due to enhanced cardiac output (beta-1 stimulation) and vasoconstriction (alpha-adrenergic receptor stimulation).
- **Diastolic Blood Pressure**:May increase or remain stable due to vasoconstriction from alpha-adrenergic receptor activation.

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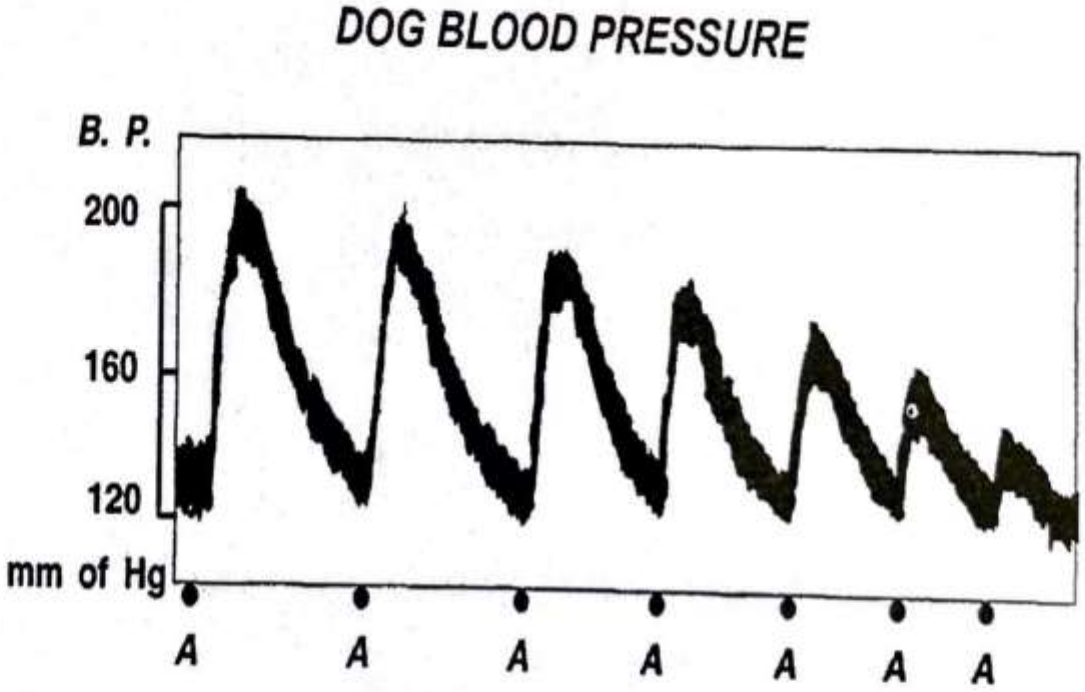
Spot exercise

Following graph shows the effect of repeated administration of same doses of drug A on mean blood pressure of dog.



Identify the probable nature of drug. Explain the effect.

Tachyphylaxis

Effect of Propranolol($\beta_1\beta_2$#)

❖ Heart rate:

- Propranolol blocks beta-1 receptors in the heart, which decreases the effects of sympathetic nervous system stimulation.
- Propranolol causes a **reduction in heart rate,** especially under conditions of increased sympathetic activity (e.g., stress or exercise).

❖ Blood pressure:

- Propranolol has no direct effect on blood vessels.
- Propranolol decreases blood pressure primarily by reducing cardiac output (due to lower heart rate and contractility).
- It also inhibit the renin release from the kidneys (via beta-1 receptor blockade).

Sp Exp Pharm1.1

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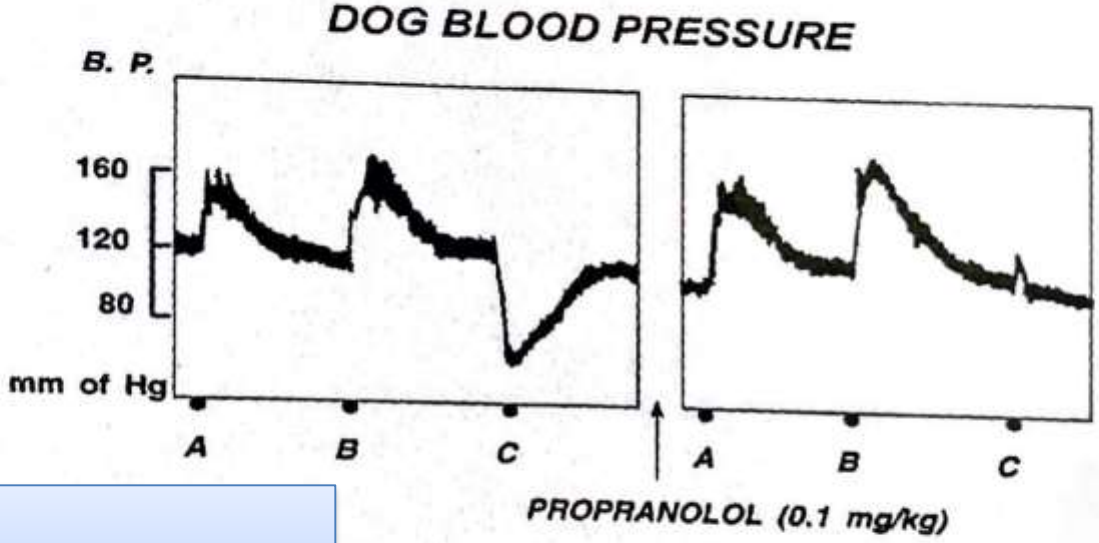
Spot exercise

The Following graph shows effects of drugs A, B and C on dog mean blood pressure. The responses of drugs A, B and C are obtained after administration of propranolol.



C : Isoprenaline

Identify the probable nature of drug C with reasons

Effect of Histamine

❖ Heart rate:

- Histamine acts on **H2 receptors** in the heart, which increase cyclic AMP (cAMP). This enhances calcium influx into cardiac cells, increasing the rate and force of contraction.
- Additionally, reflex tachycardia may occur as a compensatory response to histamine-induced hypotension.

❖ Blood pressure:

- **H1 receptors** in endothelial cells promote the release of nitric oxide, leading to vasodilation.
- **H2 receptors** in vascular smooth muscle cells directly induce relaxation.
- The combined effect is **systemic vasodilation**, particularly in the skin, which decreases peripheral resistance.

Sp Exp Pharm1.5

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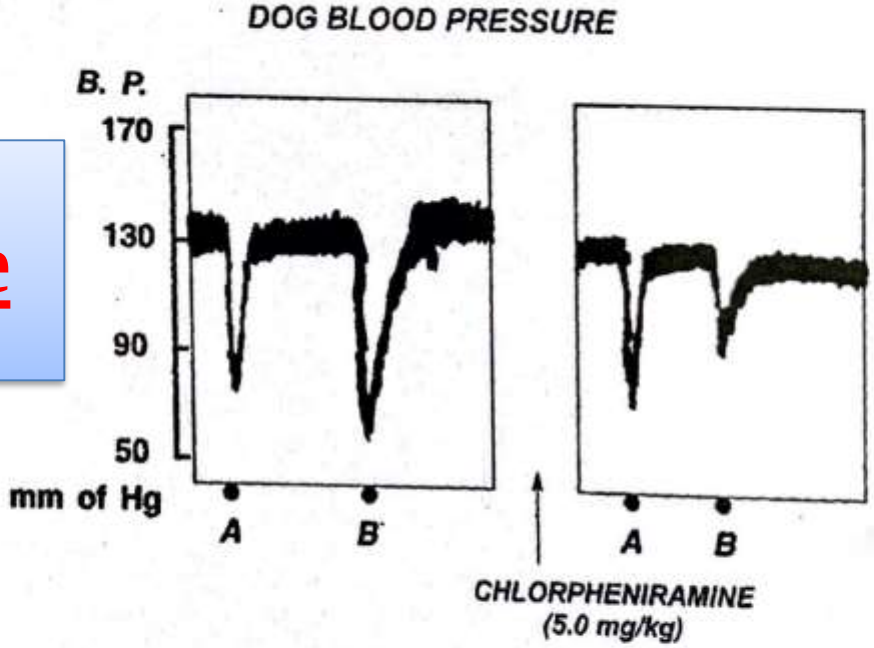
Spot exercise

Following graph shows the effects of drugs A and B on dog mean blood pressure. The responses of drugs A and B are obtained again after administration of chlorpheniramine.



B : Histamine

A : Acetylcholine (3 µg/kg)

Identify the probable nature of drug B with reasons.

Effect of Mepyramine

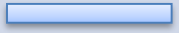
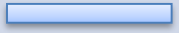
❖ Heart rate:

- Mepyramine does not directly act on the heart but may influence heart rate indirectly.
- At therapeutic doses, it typically has minimal direct impact on heart rate.

❖ Blood pressure:

- By antagonizing H1 receptors, mepyramine blocks histamine-induced vasodilation in peripheral blood vessels, preventing the associated drop in blood pressure.
- However, in individuals without elevated histamine levels, the blood pressure effect is usually mild or negligible.

No.	Drug	Blood pressure	Heart rate
1.	Acetylcholine	↓	↓
2.	Atropine	—	↑
3.	Adrenaline	↑ ↓	↑
4.	Noradrenaline	↑	↑
5.	Isoprenaline	↓	↑
6.	Histamine	↓	↑
7.	Propranolol	↓	↓

No.	Drug	Blood pressure	Heart rate
8.	Phentolamine		
9.	Ephedrine		
10.	Mepyramine		

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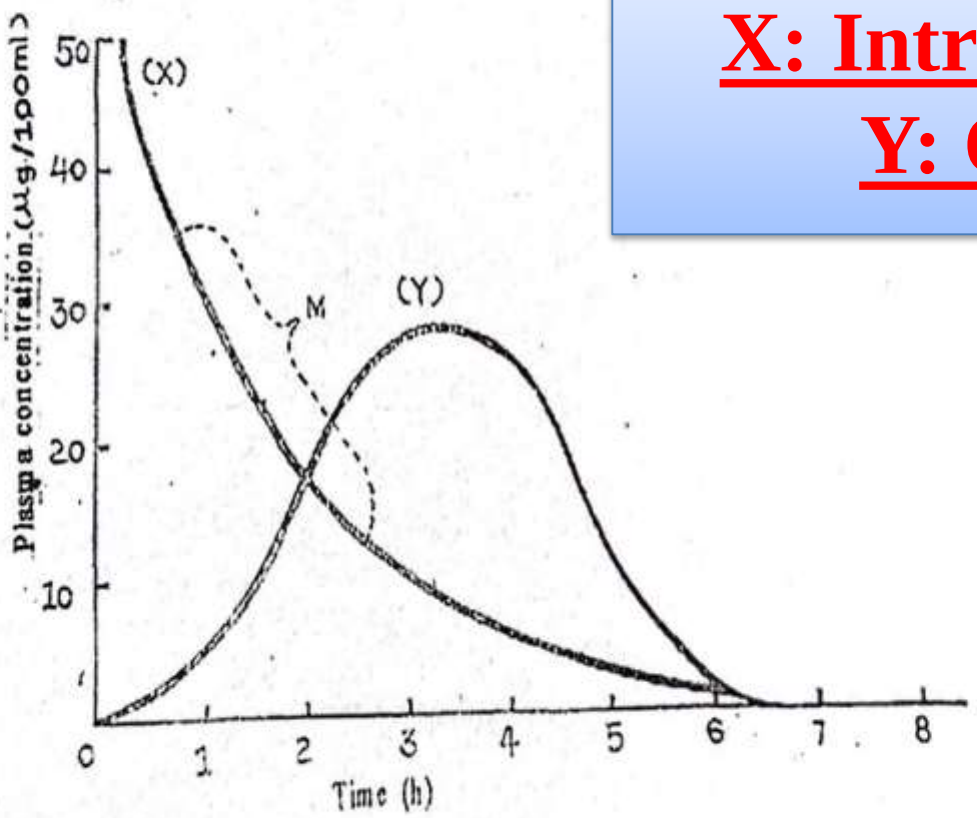
Spot exercise

The given graph shows plasma concentration of a drug given by two different routes of administration verses time.



X: Intravenous
Y: Oral

Identify the route of administration of graph X and Y. Give reasons.

Sp Exp Pharm1.17

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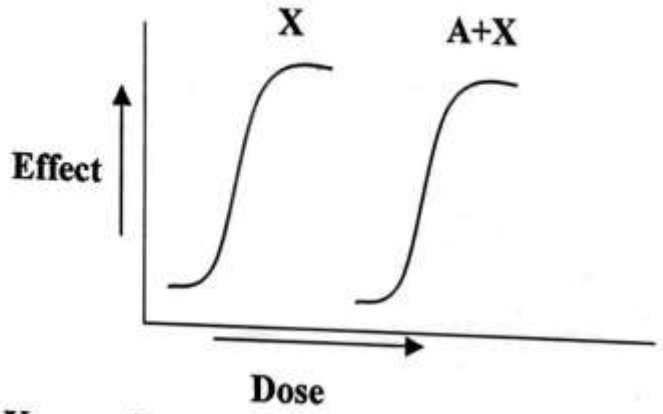
Spot exercise

Following graph shows Dose response curves of drug X and drug X in presence of drug A.



Competitive antagonist

X : - Dose Response Curve of Drug X.
A+X: - Dose Response Curve of Drug X in presence of Drug A

Answer the following questions-

1. What is the type of drug antagonism observed in the graph?
2. Mention the reasons to support your answer.

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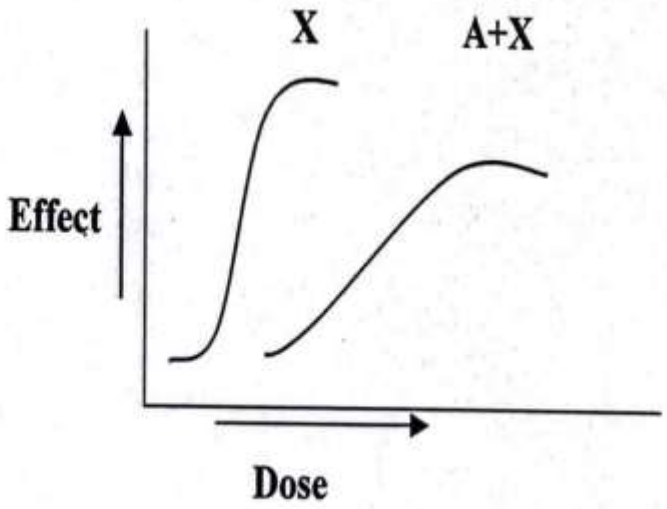
Spot exercise

Following graph shows Dose response curves of drug X and drug X in presence of drug A.



Non competitive antagonism

X : - Dose Response Curve of Drug X.

A+X: - Dose Response Curve of Drug X in presence of Drug A

Answer the following questions-

1. What is the type of drug antagonism observed in the graph?
2. Mention the reasons to support your answer.