ANTIHYPERTENSIVE AGENTS

(Unit Objective - Student should able to understand the Chemistry of various classes of antihypertensive agents.)

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**HYPERTENSION**

It is defined as a physiologic condition where there is an increase in the arterial blood pressure above normal.

- Normal B.P is **120/80** mm Hg.
- An individual is hypertensive when B.P is **>140/90** mm Hg.
Hypotension may be defined as a physiologic state where there is a lower blood pressure (B.P) than the normal. An individual is said to be hypotensive when the B.P is less than 90/60 mm of hg.

HYPERTENSION IS DIVIDED INTO 2 TYPES:

1. PRIMARY HYPERTENSION OR ESSENTIAL HYPERTENSION

1. SECONDARY HYPERTENSION OR MALIGNANT HYPERTENSION.
In PRIMARY OR ESSENTIAL HYPERTENSION in majority of cases where etiology is unknown cause and is known as primary hypertension. The following factors may contribute to elevate of B.P:

- Dietary intake of more sodium and less potassium.
- In some cases primary hypertension may be hereditary.
- Advancement of age.
- Decreased vascular synthesis of Nitric oxide (No) (is useful in vasodilatation)

In SECONDARY HYPERTENSION where etiology can be identified. Secondary hypertension is due to:

- Renal disease (kidney disorders (Chronic glomerular nephritis.))
- Adrenal disease (endocrine disorders)
  - Pheochromocytoma (tumour on adrenal medulla) which secretes excessive catechol amines like adrenaline and nor adrenaline)
  - Hyper aldosteronism.
- Muscular disorders:
  - Contraction (narrowing) of aorta.
  - Renal artery stenosis (narrowing of artery)
  - Toxemia of pregnancy (presence of toxins in the blood stream)
  - Encephalitis (inflammation of the brain)
  - Increased intra cranial pressure.
  - Thyrotoxicosis (toxic condition caused by over activity of thyroid gland)
  - Oral contraceptives.
CAUSES OF HYPERTENSION

- Age
- Renal diseases
- Genetic factors
- Drugs, alcohol, liquorice
- Arterial diseases (from aorta essentially)
- Over-synthesis of hormone (adrenaline, angiotensine)
- Unknown (95%)
<table>
<thead>
<tr>
<th>Classification (category of Hypertension)</th>
<th>Systolic Blood Pressure (mmHg)</th>
<th>Diastolic Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (B.P)</td>
<td>120 and</td>
<td>80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>121-139 or</td>
<td>81-89</td>
</tr>
<tr>
<td>Stage 1 (mild) hypertension</td>
<td>140-159 or</td>
<td>90-99</td>
</tr>
<tr>
<td>Stage 2 hypertension (moderate)</td>
<td>160-179 or</td>
<td>100-109</td>
</tr>
<tr>
<td>Stage III (severe)</td>
<td>180-209</td>
<td>110-119.</td>
</tr>
<tr>
<td>Stage IV (very severe)</td>
<td>&gt;210</td>
<td>&gt;120.</td>
</tr>
</tbody>
</table>

On etiological basis hypertension is divided into two types

1. Primary hypertension
A definite cause is not known in primary hypertension.

Following factors may contribute to elevation of B.P.
- Dietary intake of more sodium and less potassium.
- Decrease in vascular synthesis of nitric oxide responsible for vasodilation.
- In some cases it may be hereditary.
2. Secondary Hypertension

In some cases Hypertension may be secondary to other diseases like

a. Endocrine disorders
   • Pheochromocytoma
   • Hyperaldosteronism
b. Chronic glomerular nephritis
c. Muscular disorders
   • Contraction of aorta
   • Renal artery stenosis
Classification of antihypertensive agents

Hypertension = Disease of the blood vessels

Vascular biology altered

Treat the vasculature

Therapeutic options

Beta Blockers  ACE  ARB  Diuretics  CCB  Others

Adapted from Vascular Biology Working Group, University of Florida College of Medicine, Carl Pepine, MD, Director
Sites of action of the major classes of antihypertensive drugs

Sympathetic nerve terminals
- Guanethidine
- Guanadrel
- Reserpine

β-Receptors of heart
- Propranolol and other β-blockers

Angiotensin receptors of vessels
- Losartan and other angiotensin receptor blockers

α-Receptors of vessels
- Prazosin and other α₁ blockers

Vasomotor center
- Methyldopa
- Clonidine
- Guanabenz
- Guanfacine

Sympathetic ganglia
- Trimethaphan

Vascular smooth muscle
- Hydralazine
- Minoxidil
- Nitroprusside
- Diazoxide
- Fenoldopam

Kidney tubules
- Thiazides, etc.

β-Receptors of juxtaglomerular cells that release renin
- Propranolol and other β blockers

Angiotensin-converting enzyme

Angiotensin II
- Angiotensin I
- Angiotensinogen

Renin

Captopril and other ACE inhibitors

Aliskiren
The Renin-Angiotensin Cascade and the 3 Available Approaches to Pharmacologic Inhibition of Production or Action of Angiotensin II. Direct renin inhibitors (DRI), angiotensin-converting enzyme inhibitors (ACEI), and angiotensin (AT) type 1 receptor blockers (ARB).
Renin-angiotensin-aldosterone system

- Angiotensinogen → Angiotensin I → Angiotensin II
- Decrease in renal perfusion (juxtaglomerular apparatus)
- Renin
- Surface of pulmonary and renal endothelium: ACE
- Lungs, Kidney
- Tubular Na⁺ Cl⁻ reabsorption and K⁻ excretion, H₂O retention
- Adrenal gland: cortex
- Aldosterone secretion
- Arteriolar vasoconstriction, increase in blood pressure
- ADH secretion
- Pituitary gland: posterior lobe
- Collecting duct: H₂O absorption

Legend:
- Blue: secretion from an organ
- Green: stimulatory signal
- Red: inhibitory signal
- Black: reaction
- Dashed: active transport
- Dotted: passive transport

Water and salt retention. Effective circulating volume increases. Perfusion of the juxtaglomerular apparatus increases.
Depending on chemical classification

ACE inhibitors

- Sulphhydril
  E.g: Captopril

- Dicarboxylate
  E.g: Enalapril, Lisinopril

- Phosphate
  E.g: Fosinopril
<table>
<thead>
<tr>
<th>S.No.</th>
<th>Compound Name</th>
<th>( R_1 )</th>
<th>( R_2 )</th>
<th>Ring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Enalapril</td>
<td>(-\text{CH}_3)</td>
<td>(-\text{C}_2\text{H}_5)</td>
<td><img src="image" alt="Ring" /></td>
</tr>
<tr>
<td>2.</td>
<td>Enalaprilate</td>
<td>(-\text{CH}_3)</td>
<td>(-\text{H})</td>
<td><img src="image" alt="Ring" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>---</td>
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<td>---</td>
<td>---</td>
</tr>
<tr>
<td>3.</td>
<td>Lisinopril</td>
<td>$-(\text{CH}_2)_4\text{NH}_2$</td>
<td>-H</td>
<td><img src="image" alt="Lisinopril structure" /></td>
</tr>
<tr>
<td>4.</td>
<td>Ramipril</td>
<td>-CH$_3$</td>
<td>-C$_2$H$_5$</td>
<td><img src="image" alt="Ramipril structure" /></td>
</tr>
<tr>
<td>5.</td>
<td>Quinapril</td>
<td>-CH$_3$</td>
<td>-C$_2$H$_5$</td>
<td><img src="image" alt="Quinapril structure" /></td>
</tr>
<tr>
<td>6.</td>
<td>Trandolapril</td>
<td>-CH$_3$</td>
<td>-CH$_2$CH$_3$</td>
<td><img src="image" alt="Trandolapril structure" /></td>
</tr>
<tr>
<td>7.</td>
<td>Sprapril</td>
<td>-CH$_3$</td>
<td>-CH$_2$CH$_3$</td>
<td><img src="image" alt="Sprapril structure" /></td>
</tr>
<tr>
<td>8.</td>
<td>Moexipril</td>
<td>-CH$_3$</td>
<td>-CH$_2$CH$_3$</td>
<td><img src="image" alt="Moexipril structure" /></td>
</tr>
</tbody>
</table>
**Structure activity relationship [SAR]**

- **Sulfhydryl group** leads to shorter duration of action.
- **Methyl group** resembles side chain of alanine.
- **Groups that bind to Zn\(^{+2}\) ion**
  - **Essential for stabilisation**
  - **Enhances the potency of the compound**
  - **n-butylamine in dicarboxylate containing compounds orally active.**
Synthesis

2-Methyl-2-propenoic acid + HCl → Cl.CH₂.CH - CH₃
2-Methyl-3-chloropropanoic acid + SOCl₂ → Cl.CH₂.CH - CH₃ + Pyrrolidine-2-carboxylic acid

CH₃

HSCH₂ - CH - CO

N

COOH

Captopril

CH₃

NH₄SH / CH₃OH → CO CH - CH₂ Cl

N

COOH
Mechanism of action

They inhibit ACE which is involved in the conversion of AngI to Ang II.
• Which is a potent vasoconstrictor.

Adverse effects

• Dry cough
• Dysgysia
• Skin rashes
• Foetal toxicity
Uses

- First choice in treatment of Hypertension.
- In left ventricular failure
- In diabetic nephropathy
- In myocardial infarction
ACE Inhibitors
CAPTOPRIL:

**Mechanism of Action:**
It decreases angiotensin II and increase bradykinin levels. Vasodilation is a result of decreased vasoconstriction from diminished levels of angiotensin II and enhanced vasodilation from increased bradykinin. By reducing circulating angiotensin II levels, ACE inhibitors also decrease the secretion of aldosterone, resulting in decreased sodium and water retention.

Captopril, 1-[(2S)-3-mercapto-2-methyl-1-oxopropionyl]proline (Capoten), blocks the conversion of angiotensin I to angiotensin II by inhibiting the converting enzyme. The rational development of captopril as an inhibitor of ACE was based on the hypothesis that ACE and carboxypeptidase A functioned by similar mechanisms. It was noted that $d$-2-benzylsucciinic acid 7 was a potent inhibitor of carboxypeptidase A, but not ACE. By use of this small
ACE inhibitors

- Benazepril (Lotensin®)
- Captopril (Capoten®)
- Fosinopril (Monopril®)
- Lisinopril (Prinivil®, Zestril®)
- Enalapril (Vasotec®)
- Quinapril (Accupril®)
- Ramipril (Altace®)
- Trandolapril (Mavik®)
Angiotensin receptor Antagonists

B. Irbesartan

Use: It is a angiotensin II type I receptor antagonist.

C. Candesartan

Use: It is a angiotensin II type I receptor antagonist, used as antihypertensive agent.
A. Losartan

2-Butyl-4-chloro-5-hydroxy methyl-1-[[2'(1H-tetrazol-5-yi)-biphenyl-4-yi]methyl]imidazole
LOSARTAN:-

It is a competitive antagonist and inverse agonist, it is more selective for AT1 than for AT2 receptor. It does not block any other receptor or ion channel except thromoxane A2 receptor.

Other action of ARBs blocker are vasoconstriction, central and peripheral sympathetic stimulation, release of aldosterone and Adr from adrenals, renal action promoting salt and water reabsorption, central action like thirst, vasopressin release and growth promoting action on heart and blood vessels.
**STRUCTURE ACTIVITY RELATIONSHIP [SAR]**

Required to mimic the His side chain of Angiotensin-II.

Acidic group

Substituted with ketones, cooH forms Ionic, dipole-dipole helps drug to interact with AT1.

Essential for activity to mimic Asp1 carboxylate of Ang-II.
Mechanism of action

They act by blocking the Angiotensin I which regulates the effects of angiotensin on B.P, heart and sodium and water balance.

Adverse effects

- Hyperkalaemia
- Angioedema
- Foetal toxicity
- Gidisturbances
Uses

In treatment of hypertension as an alternative to ACE Inhibitors.
Angiotensin receptor blockers

- Valsartan (Diovan®)
- Telmisartan (Micardis®)
- Candesartan (Atacand®)
- Losartan (Cozaar®)
- Irbesartan (Avapro®)
Diuretics

- Diuretics ("water pills") increase the kidneys' excretion of salt (sodium) and water, decreasing the volume of fluid in the bloodstream and the pressure in the arteries. Diuretics are the oldest and most studied antihypertensive agents.
Thiazide
  chlorthalidone, hydrochlorothiazide (HCTZ),
  indapamide, metolazone
Loop
  bumetanide, furosemide, torsemide
Potassium-sparing
  amiloride, triamterene
Aldosterone antagonists
  eplerenone, spironolactone
Thiazide Diuretics

- **Dose** in morning to avoid nocturnal diuresis
- **More effective** antihypertensives than loop diuretics
  - **Chlorthalidone** 1.5 to 2 times as potent as HCTZ

**Adverse effects**
- hypokalemia
- hypomagnesemia
- hypercalcemia
- sexual dysfunction
- lithium toxicity with Concurrent administration.
Loop Diuretics

- **Dose**: in AM or afternoon to avoid nocturnal diuresis

- **Higher doses** may be needed for patients with severely decreased glomerular filtration rate or heart failure

**Adverse effects:**
- hypokalemia,
- hypomagnesemia,
- hypocalcemia

![Furosemide](image)
2, 4-Dichloro-benzoic acid

(i)  \( \text{ClSO}_2\text{OH} \); \( \Delta \);
(ii) Amidation

2, 4-Dichloro-5-sulphamoyl-benzoic acid

\( + \text{H}_2\text{NCH}_2\text{-} \)

Furfurylamine ;
\( (\text{NaHCO}_3) \)

Furosemide
Mechanism of Action

- inhibit Na+ and Cl- transporter in distal convoluted tubules

- increased Na+ and Cl- excretion

- weak inhibitors of carbonic anhydrase, increased HCO3- excretion

- increased K+/Mg2+ excretion

- decrease Ca2+ excretion
Potassium-sparing Diuretics

- Dose in AM or afternoon to avoid nocturnal diuresis
- Generally reserved for diuretic-induced hypokalemia patients
- Weak diuretics, generally used in combination with thiazide diuretics to minimize hypokalemia

**Adverse effects:**

- May cause hyperkalemia especially in combination with an ACE inhibitor, angiotensin-receptor blocker or potassium supplements
- Avoid in patients with diabetes
Aldosterone antagonists

- Dose in AM or afternoon to avoid nocturnal diuresis

- Adverse effects:
  - May cause hyperkalemia especially in combination with ACE inhibitor, angiotensin-receptor blocker or potassium supplements
  - Gynecomastia: up to 10% of patients taking spironolactone
Calcium channel blockers

Depending upon their chemical structure

- Diphenylalkylamines
  - Eg: Verapamil

- Benzothiazepines
  - Eg: Diltiazem

- 1,4-dihydropyridines
  - Eg: Nifedipine

- Diaminopropanol ether
  - Eg: Bepridil
Verapamil

Diltiazem

Nifedipine
<table>
<thead>
<tr>
<th>DRUGS</th>
<th>Mode of action</th>
<th>Adverse Drug reactions</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diltiazem</td>
<td>Acts by inhibiting Voltage sensitive Calcium channels in myocardium and vascular smooth muscles.</td>
<td>o Constipation ♫ Dizziness ♫ Oedema</td>
<td>♫ In arrhythmias ♫ In Angina</td>
</tr>
<tr>
<td>Verapamil</td>
<td></td>
<td>o Flushing ♫ Oedema</td>
<td>♪ In Angina ♫ In Arrhythmias</td>
</tr>
<tr>
<td>Nifedipine</td>
<td></td>
<td>o Tachycardia</td>
<td>In Angina</td>
</tr>
</tbody>
</table>
Calcium channel blockers

- Idradipine (DynaCirc®)
- Nicardipine (Cardene®)
- Nisoldipine (Sular®)
- Felodipine (Plendil®)
- Amlodipine (Norvasc®)
Methyldopa is an α2 adrenergic receptor agonist acts centrally by decreasing the sympathetic outflow which in turn lowers B.P.
4-hydroxy 3-methoxy phenyl acetone

L-isomer of Methyldopa
Adverse effects

- Sedation and drowsyness
- Constipation
- Gynacomastia
- Sexual impotence

Uses

Treat of Hypertension in combination With diuretics.
clonidine

Mode of action:
Its acts by stimulating α2-adrenergic receptros and thereby reducing sympathetic outflow and noradrenaline release
**Clonidine Hydrochloride.**

2-[(2,6-dichlorophenyl)imino]imidazolidine monohydrochloride (Catapres), was synthesized in 1962 as a derivative of the known -sympathomimetic drugs naphazoline and tolazoline, potential nasal vasoconstrictors, but instead it proved to be effective in the treatment of mild-to-severe hypertension. Clonidine hydrochloride acts by both peripheral and central mechanisms in the body to affect blood pressure. It stimulates the peripheral -adrenergic receptors to produce vasoconstriction, resulting in a brief period of hypertension. Clonidine hydrochloride acts centrally to inhibit the sympathetic tone and cause hypotension that is of much longer duration than the initial hypertensive effect. Administration of clonidine hydrochloride thus produces a biphasic change in blood pressure, beginning with a brief hypertensive effect and followed by a hypotensive effect that persists for about 4 hours. This biphasic response is altered by dose only. Larger doses produce a greater hypertensive effect and delay the onset of the hypotensive properties of the drug.
<table>
<thead>
<tr>
<th>Adverse drug reaction</th>
<th>uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation and drowsiness</td>
<td>In moderate to severe hypertension</td>
</tr>
<tr>
<td>Dryness of mouth and nose</td>
<td>For withdrawal therapy of alcohol opioids</td>
</tr>
<tr>
<td>Constipation</td>
<td>To diagnose pheochromocytoma</td>
</tr>
<tr>
<td>Bradycardia</td>
<td></td>
</tr>
</tbody>
</table>


Adrenergic receptor antagonist

Prazosin

phentolamine
**Clonidine Hydrochloride.**

2-[(2,6-dichlorophenyl)imino]imidazolidine monohydrochloride (Catapres), was synthesized in 1962 as a derivative of the known -sympathomimetic drugs naphazoline and tolazoline, potential nasal vasoconstrictors, but instead it proved to be effective in the treatment of mild-to-severe hypertension. Clonidine hydrochloride acts by both peripheral and central mechanisms in the body to affect blood pressure. It stimulates the peripheral -adrenergic receptors to produce vasoconstriction, resulting in a brief period of hypertension. Clonidine hydrochloride acts centrally to inhibit the sympathetic tone and cause hypotension that is of much longer duration than the initial hypertensive effect. Administration of clonidine hydrochloride thus produces a biphasic change in blood pressure, beginning with a brief hypertensive effect and followed by a hypotensive effect that persists for about 4 hours. This biphasic response is altered by dose only. Larger doses produce a greater hypertensive effect and delay the onset of the hypotensive properties of the drug.
### Adrenergic receptor antagonists

#### α-blockers

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mode of action</th>
<th>Adverse drug reaction</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>prazosin</td>
<td>It acts by selective blocking of α-1 receptors in the peripheral blood vessels leading to vasodilation</td>
<td>First dose effect:</td>
<td>In the treatment of moderate to severe hypertension in combination with a β-blocker and a diuretic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postural hypotension and syncope</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drowsiness</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nasal congestion</td>
<td></td>
</tr>
<tr>
<td><strong>Drugs</strong></td>
<td><strong>Mode of action</strong></td>
<td><strong>Adverse drug reaction</strong></td>
<td><strong>Uses</strong></td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>It blocks both $\alpha_1$ and $\alpha_2$-receptors leading to vasodilation and increase in noradrenaline release</td>
<td>ᵃ Hypotension ᵃ Tachycardia ᵃ Increase in gastric acid secretion</td>
<td>ᵃ Pheochromocytoma</td>
</tr>
</tbody>
</table>
β-adrenergic Blockers

- PROPANOLOL
- ATENOLOL
- LABETOLOL
Epichlorhydrin + \[\text{Cl} \quad \rightarrow \quad \text{H}_2\text{NCH}(\text{CH}_3)_2\]

Isopropylamine

PROPRANOLOL
### β-adrenergic Blockers

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mode of action</th>
<th>Adverse drug effects</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propanolol</td>
<td>Inhibits sympathetic activity by blocking β1 and β2 receptors</td>
<td>• Fatigue</td>
<td>• In angina</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bradycardia</td>
<td>• In myocardial infarction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypoglycemia</td>
<td>• In arrhythmias</td>
</tr>
</tbody>
</table>
DL-4-hydroxy phenyl glycine

NaCN/NaOH
DMF, heat

4-hydroxy phenyl acetonitrile

H₂O

OCH₂CH(OH)CH₂NH
(CH₃)₂CH

Atenolol
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mode of action</th>
<th>Adverse drug reactions</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>Inhibit Sympathetic activity by selective blockage of β1 receptors.</td>
<td>• Fatigue</td>
<td>In angina</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bradycardia</td>
<td>In arrhythmias</td>
</tr>
<tr>
<td>Drug</td>
<td>Mode of action</td>
<td>Adverse effects</td>
<td>Uses</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>They block β and α₁ receptor thereby inhibit sympathetic activity.</td>
<td>Dry mouth</td>
<td>Cavedilol-CHF</td>
</tr>
<tr>
<td>Labetalol</td>
<td></td>
<td>Gidisturbances</td>
<td>Labetalol-Emergencies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sexual dysfunction</td>
<td></td>
</tr>
</tbody>
</table>
Direct vasodilators

MINOXIDIL

HYDRALAZINE
Synthesis

Ethyl cyano acetate + Guanidine \[ \xrightarrow{\text{C}_2\text{H}_5\text{ONa}} \]
\[ \xrightarrow{\text{POCl}_3} \]
2,4-Diamino-6-hydroxy pyrimidine

\[ \xrightarrow{(\text{O})} \]
m-Chloro benzoic acid

Minoxidil
# Direct Vasodilators

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mode of action</th>
<th>Adverse effects</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minoxidil</td>
<td>It opens the potassium channels and causes hyperpolarization.</td>
<td>• Tachycardia</td>
<td>• In treatment of Baldness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fluid retention</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypertrichosis</td>
<td></td>
</tr>
</tbody>
</table>
Synthesis

2-Formyl benzoic acid + NH₂ - NH₂ \[\rightarrow\] Hydrazine

\[\text{Hydralazine}\]
<table>
<thead>
<tr>
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<th>Mode of action</th>
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<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
<td>Direct relaxation of vascular smooth muscles by stimulating cGMP</td>
<td>• Flushing</td>
<td>Emergencies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Tachycardia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fluid retension</td>
<td></td>
</tr>
</tbody>
</table>
"Saunders said. "Doctors are using ACE inhibitors, Calcium channel blockers, Beta-blockers, Angiotensin-receptor blockers (ARBs), Alpha-blockers and low-dose diuretics in ways that don't cause the sexual complications and other side effects of older therapies. Also, these new drugs only need to be taken once a day, instead of two or three times a day. This is a lot easier for patients."

We need to make sure that we eat eight servings of fruits and vegetables a day, and get more exercise. We need to get ourselves and our children away from the television sets and the computers, and start them exercising early in their lives."
I would like to express my special thanks of gratitude to Power point presentation by PROF. RAVISANKAR, Vigyan Pharmacy college, Valdlamudi, Guntur Dist. A.P.
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