

Drugs Acting on Cardiovascular System

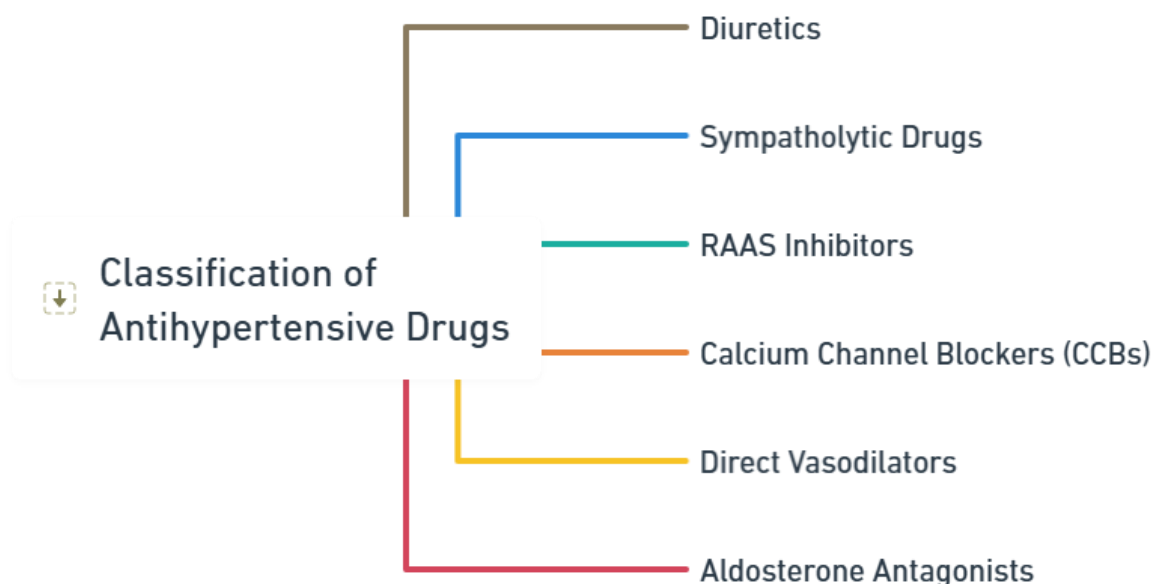
Anti-Hypertensive Drugs

Introduction

- **Hypertension** is defined as a sustained increase in arterial blood pressure. Persistent hypertension can lead to serious complications such as stroke, myocardial infarction, renal failure, and heart failure.
- Antihypertensive therapy aims to reduce morbidity and mortality by lowering blood pressure and preventing target organ damage.
- Blood pressure is determined by:
 - **Cardiac output (CO)**
 - **Peripheral vascular resistance (PVR)**
- Thus, drugs that reduce CO and/or PVR can lower blood pressure. Antihypertensives work by:
 - Decreasing blood volume
 - Suppressing sympathetic nervous system activity
 - Causing vasodilation
 - Inhibiting the renin-angiotensin-aldosterone system (RAAS)

Classification

Antihypertensives are classified based on their mechanism of action:



A. Diuretics

- **Thiazide diuretics:** Hydrochlorothiazide, Chlorthalidone
- **Loop diuretics:** Furosemide, Bumetanide
- **Potassium-sparing diuretics:** Spironolactone, Amiloride, Eplerenone

B. Sympatholytic Drugs

- **Centrally acting alpha-2 agonists:** Clonidine, Methyldopa
- **Beta-blockers:** Atenolol, Metoprolol, Propranolol
- **Alpha-1 blockers:** Prazosin, Terazosin
- **Combined alpha and beta-blockers:** Labetalol, Carvedilol

C. RAAS Inhibitors

- **ACE inhibitors:** Enalapril, Lisinopril, Ramipril
- **Angiotensin II receptor blockers (ARBs):** Losartan, Valsartan
- **Direct renin inhibitors:** Aliskiren

D. Calcium Channel Blockers (CCBs)

- **Dihydropyridines:** Amlodipine, Nifedipine
- **Non-dihydropyridines:** Verapamil, Diltiazem

E. Direct Vasodilators

- Hydralazine
- Minoxidil
- Sodium nitroprusside (for emergencies)
- Diazoxide

F. Aldosterone Antagonists

- Spironolactone
- Eplerenone

Mechanism of Action

Each class acts at a different site:

1. Diuretics

- Promote sodium and water excretion → decrease blood volume → decrease CO → reduce BP.
- Long-term: reduce PVR.

2. Beta-blockers

- Block β_1 receptors in the heart → decrease heart rate and contractility → ↓ CO.
- Inhibit renin release from juxtaglomerular cells → ↓ RAAS activation.

3. Alpha-blockers

- Block α_1 receptors in vascular smooth muscle → vasodilation → ↓ PVR.

4. Centrally acting drugs

- Stimulate central α_2 receptors → decrease sympathetic outflow → reduced HR and vasodilation.

5. ACE inhibitors

- Inhibit conversion of Angiotensin I to II → vasodilation + ↓ aldosterone → ↓ PVR and blood volume.

6. ARBs

- Block angiotensin II receptors → prevent vasoconstriction and aldosterone secretion.

7. Direct Renin Inhibitors

- Inhibit renin → ↓ Ang I and Ang II → vasodilation + reduced aldosterone effect.

8. Calcium Channel Blockers

- Block L-type calcium channels in heart and smooth muscle:
 - Dihydropyridines: mainly vasodilation
 - Non-dihydropyridines: reduce HR and contractility (verapamil, diltiazem)

9. Vasodilators

- Direct relaxation of arteriolar smooth muscle → reduce PVR.
- Sodium nitroprusside releases nitric oxide → vasodilation (used in emergencies).

Pharmacokinetics

- Varies by class and drug; examples:
 - **Thiazides:** Oral, onset in hours, duration 12–24 hours, renal excretion.
 - **Beta-blockers:** Oral, hepatic metabolism (e.g., propranolol), renal (atenolol).
 - **ACE inhibitors:** Oral, converted to active forms (except lisinopril), excreted by kidneys.
 - **CCBs:** High oral bioavailability, hepatic metabolism, long half-life (e.g., amlodipine).

Pharmacodynamics

- Reduction in systolic and diastolic BP
- **Onset:** Immediate (IV drugs), days to weeks (oral)
- **Effect plateau:** Often seen after 4–6 weeks of therapy
- **Tolerability:** Most classes are well tolerated; side effects vary.

Adverse Effects

Class	Common Adverse Effects
Diuretics	Hypokalemia, hyperuricemia, hyponatremia

β-blockers	Bradycardia, fatigue, erectile dysfunction, bronchospasm
ACE inhibitors	Dry cough, hyperkalemia, angioedema
ARBs	Hyperkalemia, less cough
CCBs	Peripheral edema, headache, flushing, bradycardia (verapamil)
Vasodilators	Reflex tachycardia, lupus-like syndrome (hydralazine), hypertrichosis (minoxidil)
Central agents	Sedation, dry mouth, rebound hypertension (clonidine)

Contraindications

- **Beta-blockers:** Asthma, bradycardia, AV block
- **ACE inhibitors & ARBs:** Pregnancy, bilateral renal artery stenosis, hyperkalemia
- **Thiazides:** Gout, severe renal failure
- **Non-dihydropyridine CCBs:** Heart block, bradycardia
- **Alpha-blockers:** Elderly (risk of falls)
- **Centrally acting agents:** Depression, mental status changes

Therapeutic Uses

- Primary hypertension
- Hypertensive emergencies (e.g., nitroprusside, labetalol)
- Heart failure (ACEIs, ARBs, beta-blockers, diuretics)
- Post-myocardial infarction (beta-blockers, ACEIs)
- Chronic kidney disease (ACEIs, ARBs)
- Diabetes with proteinuria (ACEIs, ARBs)
- Benign prostatic hyperplasia (alpha-blockers)

Drug Interactions

- **ACEIs/ARBs + potassium-sparing diuretics** → Hyperkalemia
- **NSAIDs + ACEIs/ARBs/Diuretics** → Reduced antihypertensive effect, risk of renal dysfunction
- **Beta-blockers + non-dihydropyridine CCBs** → Bradycardia, AV block
- **Diuretics + digoxin** → Risk of digoxin toxicity due to hypokalemia
- **Alpha-blockers + other vasodilators** → Severe hypotension

Dose and Route of Administration

Doses vary by drug and patient characteristics. Some examples:

A. Hydrochlorothiazide

- Dose: 12.5–25 mg/day orally
- Route: Oral

B. Amlodipine

- Dose: 5–10 mg/day orally
- Route: Oral

C. Lisinopril

- Dose: 10–40 mg/day orally
- Route: Oral

D. Losartan

- Dose: 50–100 mg/day orally
- Route: Oral

E. Metoprolol

- Dose: 50–200 mg/day (divided)
- Route: Oral

F. Sodium Nitroprusside

- Dose: IV infusion, 0.3–10 mcg/kg/min
- Route: Intravenous (used in hypertensive emergencies)

- Dosing must be individualized based on blood pressure response, renal function, and comorbidities.

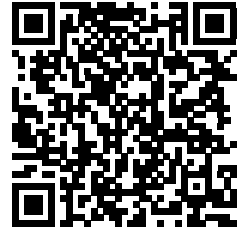


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