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ANTIHYPERTENSIVE DRUGS: AN ADVANCED COMPREHENSIVE REVIEW OF MECHANISMS, THERAPIES, AND CLINICAL INNOVATIONS

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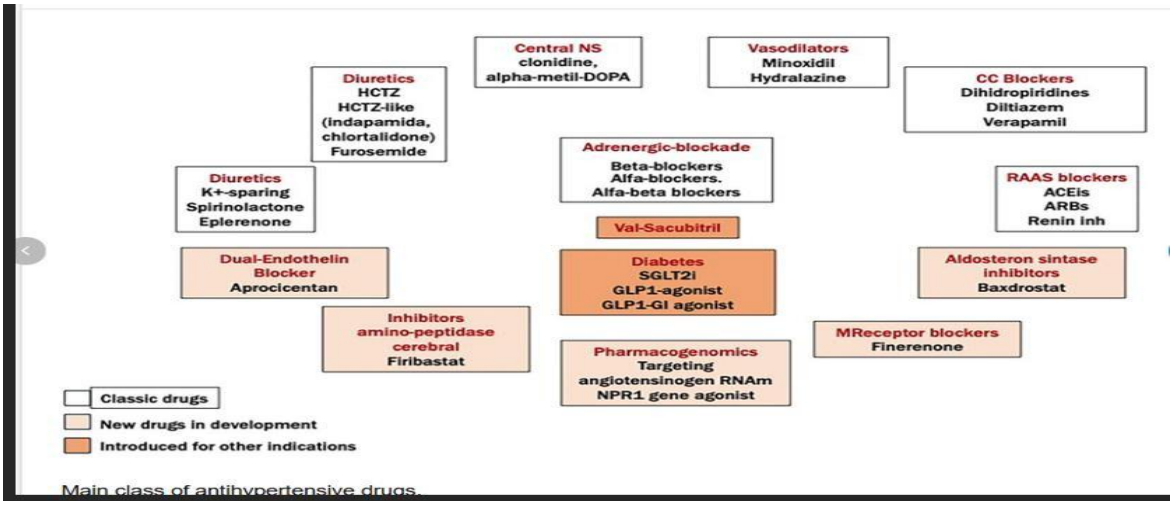
ABSTRACT

Hypertension is a leading global cause of morbidity and mortality.[4–6], contributing to cardiovascular, renal, and cerebrovascular disease. Antihypertensive pharmacotherapy continues to evolve, with new agents, combination strategies, and device-basedinterventions.[18–23] Precision medicine, pharmacogenomics.[26–28] and digital health technologies.[24–25] are reshaping individualized care. Overview of Major Antihypertensive Drug Classes (Section supported by Goodman & Gilman.[1], Katzung[2], Rang & Dale.[3]



KEYWORDS: Antihypertensive therapy, renin–angiotensin–aldosterone system, SGLT2 inhibitors, fixed dose combinations, resistant hypertension, renal denervation, pharmacogenomics.

1. INTRODUCTION

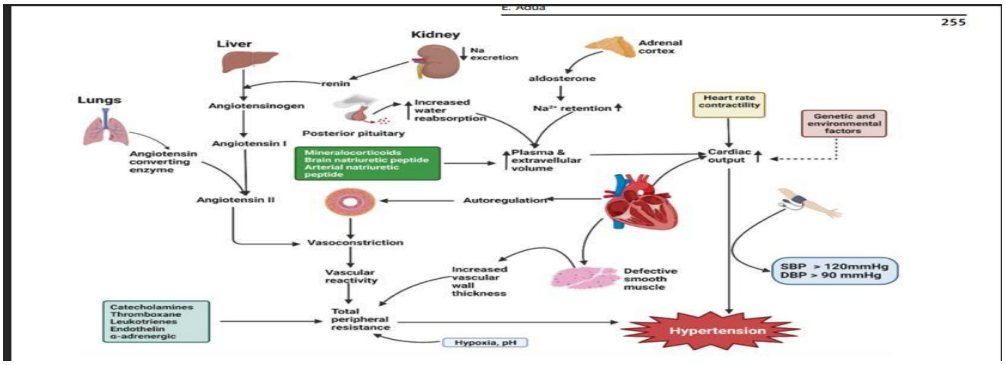
Hypertension affects more than **1.2 billion people** globally.[4–6] and is a major modifiable risk factor for stroke, myocardial infarction, heart failure, and CKD. Recent guidelines emphasize early combination therapy and risk-based treatment.[5,29,30]

Modern antihypertensive care incorporates.

- Physiologic pathway targeting (RAAS, sympathetic system, vascular tone).[1–3,7–12]
- Personalized medicine using genetic markers.[26–28]
- Digital BP monitoring & wearable devices.[24–25]
- Long-acting formulations.[20]
- Device-based therapies, including renal denervation (RDN).[21–22]

2. Pathophysiology of Hypertension & Key Drug Targets

(Supported by pharmacology textbooks [1–3] and epidemiological data.[4–6])



2. Classification of Antihypertensive Drugs

2.1 Diuretics

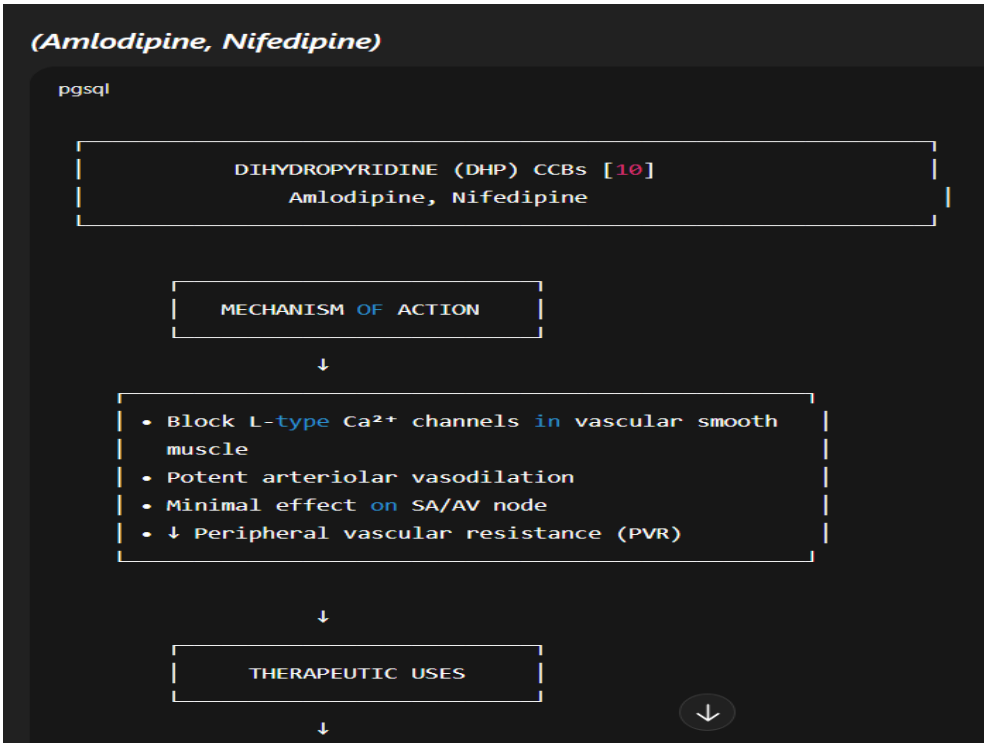
- Thiazides (HCTZ, Chlorthalidone — superior BP lowering.[7])
- Loops: Furosemide, Torsemide (preferred in CKD).[7]
- K^+-sparing: Spironolactone, Eplerenone (effective in resistant HTN).[19]

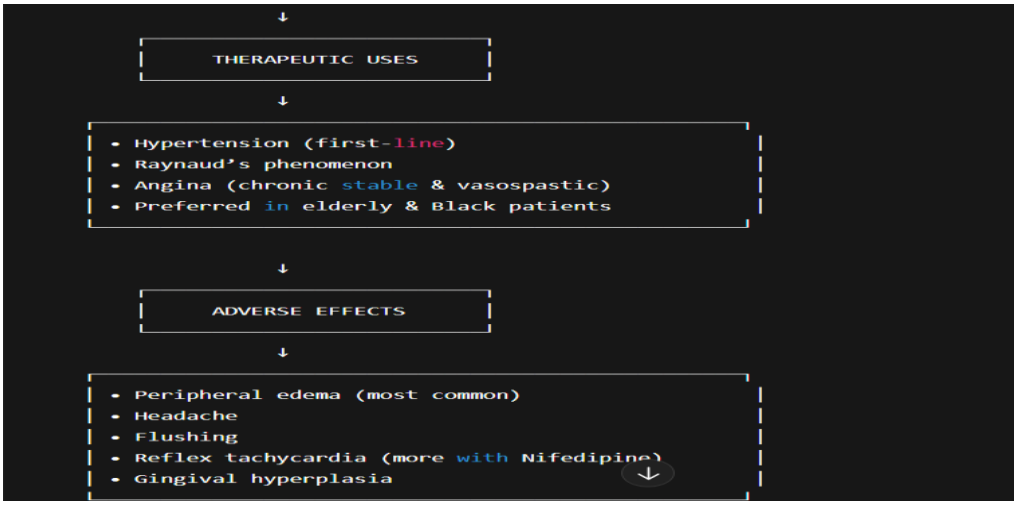
2.2 Sympatholytic Agents

- Beta-blockers: Metoprolol, Nebivolol (↑NO release).[8–9]
- Alpha-blockers: Prazosin, Doxazosin (mainly BPH).[1]
- Central: Clonidine, Methyldopa (pregnancy).[1–3]

2.3 Calcium Channel Blockers

Potent vasodilators (Amlodipine, Nifedipine).[10] Non-DHPs: Verapamil, Diltiazem.[10]





2.4 RAAS Inhibitors

ACEIs, ARBs—renal protection and CV benefits.[11]

2.5 Vasodilators

- Hydralazine: NO-mediated action.[12]
- Minoxidil: K^+ channel opener.[12]

2.6 Emerging Agents

- SGLT2 inhibitors (BP ↓ 4–6 mmHg)[13,23]
- Endothelin antagonists (experimental)[14]
- Finerenone—novel MRA.[14]

3. Mechanisms of Action (Advanced Overview)

Supported by major pharmacology sources.[1–3] beta-blocker and CCB studies.[8–10]

- Diuretics reduce plasma volume & chronic PVR.[7]
- Beta-blockers ↓ HR, ↓ renin secretion.[8]
- CCBs block L-type Ca^{2+} channels.[10]
- ACEIs/ARBs inhibit Ang-II effects & slow CKD.[11]
- Vasodilators enhance NO or open K^{+} channels.[12]

4. Therapeutic Uses

- Diabetes + HTN: ACEIs/ARBs first-line.[11]
- Black patients respond better to thiazides/CCBs.[15]
- HF: ACEIs, ARBs, β-blockers, MRAs.[15]
- Pregnancy-safe: Methyldopa, Labetalol, Nifedipine.[15]
- Resistant HTN: Spironolactone proven superior (PATHWAY-2).[19]

5. Adverse Effects

(General mechanisms supported by Pacher & Kecskemeti.[17])

6. Recent Clinical Advances

6.1 Fixed-Dose Combination Therapy

Improves adherence 30–40%.[18]

Supported by TRIUMPH & PATHWAY trials.[18–19]

6.2 Long-Acting Antihypertensives

Ultra-long-acting ARBs, weekly clonidine patches.[20]

6.3 Renal Denervation (RDN)

SYMPLICITY HTN-3 & 2023 follow-ups confirm BP reduction.[21–22]

6.4 SGLT2 Inhibitors

BP reduction & strong renal/CV outcomes.[13,23]

6.5 AI & Digital Monitoring

Wearables + machine learning predict hypertensive crises.[24–25]

6.6 Pharmacogenomics

- β1-receptor polymorphisms influence metoprolol response.[27]
- ACE I/D polymorphism affects ACEI response.[28]

7. Current Guidelines (2024–2025)

Based on AHA/ACC 2024 and ESC 2024 recommendations.[29–30]

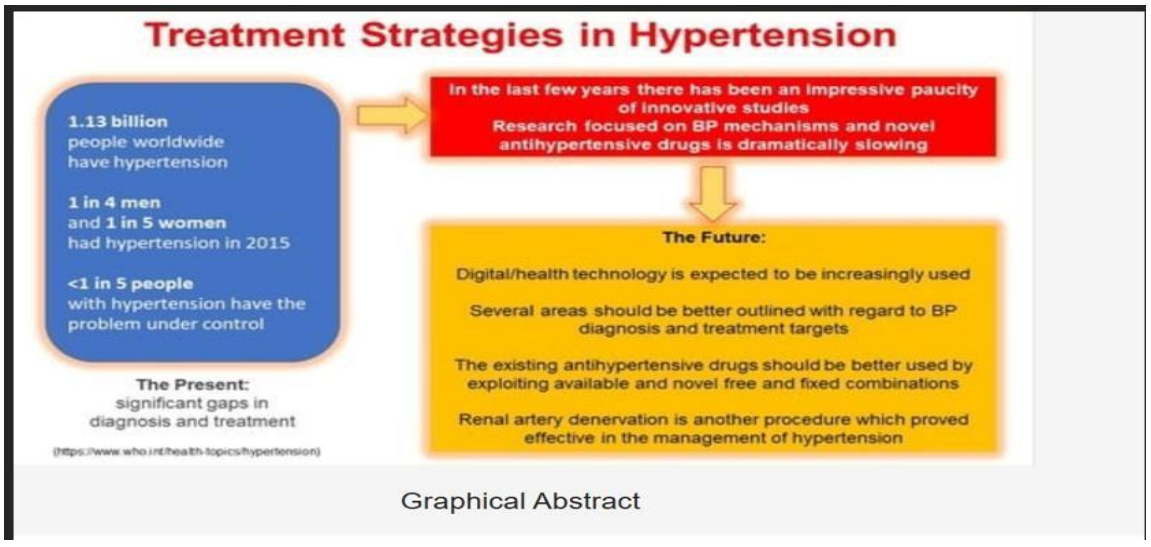
- First-line: ACEI/ARB, CCB, Thiazide
- Avoid ACEI + ARB combination
- Target <130/80 mmHg in high-risk patients
- Encourage home BP monitoring and telemedicine.[24]

8. DISCUSSION

Recent advances emphasize precision therapy, long-acting formulations, and emergent device-based methods.[18–23] AI monitoring and pharmacogenomics offer the next evolution in personalized hypertension care.[24–28]

9. CONCLUSION

Hypertension management is evolving through improved mechanisms, combination approaches, novel drugs, and digital innovations. Continued research into genetics, biomarkers, and interventional treatments will define future therapeutic standards.[13,18– 30]



Graphical Abstract

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