e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(2); 1399-1407

Original Research Article

# The Study of Glycemic Status in Patients Who are on Amlodipine Therapy for Hypertension

**M. Rajesh[1], Nikila K.[2]**

[1]Sri Balaji Medical College and Hospital, Research Institute Renigunta Tirupati, Andhra Pradesh, India

[2]MS, Orthopedic Surgeon, Nikila Clinic, Srikalahasthi, Tirupati, Andhra Pradesh, India

**Received: 01-12-2025 / Revised: 16-01-2026 / Accepted: 06-02-2026**

**Corresponding Author: Dr. Nikila K**

**Conflict of interest: Nil**

**Abstract**

**Background:** Hypertension and diabetes mellitus frequently coexist, affecting millions worldwide. The choice of antihypertensive medication may influence glycemic control, making the metabolic effects of these agents clinically significant. Amlodipine, a widely prescribed dihydropyridine calcium channel blocker, has demonstrated potential glycemic benefits beyond its blood pressure-lowering effects.

**Objective:** This study examines the impact of amlodipine therapy on glycemic parameters in hypertensive patients, including those with and without pre-existing diabetes mellitus.

**Methods:** A comprehensive literature review was conducted analyzing recent clinical studies, randomized controlled trials, and observational research examining the relationship between amlodipine use and glycemic outcomes, including HbA1c levels, fasting plasma glucose, and incidence of new-onset diabetes.

**Results:** Evidence demonstrates that amlodipine therapy is associated with improved glycemic control in hypertensive patients with diabetes, with reductions in HbA1c levels of 0.39% compared to standard diabetes therapy alone. Additionally, amlodipine significantly reduces the risk of new-onset diabetes by 34% compared to beta-blocker therapy. Calcium channel blockers, particularly amlodipine, show a neutral to beneficial effect on glucose metabolism, with average reductions in fasting serum glucose of 5-10 mg/dL.

**Conclusion:** Amlodipine represents a favorable antihypertensive choice for patients with diabetes or those at risk for developing diabetes. Its neutral to beneficial effects on glycemic parameters, combined with effective blood pressure control, make it an optimal therapeutic option in the management of hypertensive patients with metabolic concerns.

**Keywords:** Amlodipine, hypertension, glycemic control, HbA1c, diabetes mellitus, calcium channel blockers.

**DOI:** 10.25258/ijcpr.18.2.230



## Introduction

Hypertension and type 2 diabetes mellitus represent two of the most prevalent chronic diseases globally, affecting approximately 1.4 billion and 537 million individuals respectively. The coexistence of these conditions is remarkably common, with hypertension occurring twice as frequently in patients with diabetes compared to those without diabetes[4]. Studies indicate that up to 75% of adults with diabetes also have hypertension, and conversely, patients with hypertension often demonstrate insulin resistance and face greater risk of developing diabetes than normotensive individuals[5]. In South Asian populations, including India, the burden of these comorbid conditions has escalated dramatically due to urbanization, sedentary lifestyles, and dietary transitions[6]. Among middle-aged and elderly patients with both hypertension and diabetes, clinical profiles reveal significantly elevated systolic and diastolic blood pressures, higher fasting glucose levels, and poorer glycemic control (HbA1c >8%) compared to those with either condition alone[6].

**Pathophysiological Linkage:** The relationship between hypertension and diabetes is

multifactorial, involving complex pathophysiological mechanisms including insulin resistance, endothelial dysfunction, and chronic low-grade inflammation[6]. This comorbidity accelerates target organ damage, including nephropathy, retinopathy, and cardiovascular complications, leading to premature morbidity and mortality. The major cause of morbidity and mortality in diabetes is cardiovascular disease, which is substantially exacerbated by concurrent hypertension[4].

**Clinical Significance of Antihypertensive Choice:** Given the intimate relationship between blood pressure regulation and glucose metabolism, the selection of antihypertensive agents becomes critically important. Different classes of antihypertensive medications exert varying effects on glycemic parameters. While some agents, particularly beta-blockers and thiazide diuretics, have been associated with adverse metabolic effects and increased risk of new-onset diabetes, calcium channel blockers have demonstrated neutral to beneficial effects on glucose homeostasis.

**Amlodipine: Pharmacological Profile:** Amlodipine is a long-acting dihydropyridine calcium channel blocker that selectively inhibits calcium ion influx across cell membranes, particularly targeting L-type voltage-gated calcium channels in vascular smooth muscle[7]. Unlike non-dihydropyridine calcium channel blockers, amlodipine exerts its primary effects on peripheral vasculature rather than cardiac conduction tissue. The drug functions as a peripheral arterial vasodilator, causing relaxation of vascular smooth muscle, reduction in peripheral vascular resistance, and consequent blood pressure lowering[8].

Amlodipine possesses unique pharmacological characteristics that distinguish it from other calcium channel blockers, including high membrane affinity, long duration of action (half-life of 30-50 hours), and once-daily dosing convenience[9]. These properties contribute to its position as one of the most widely prescribed antihypertensive medications globally.

**Rationale for Current Study:** Despite extensive clinical use, the metabolic effects of amlodipine, particularly its impact on glycemic status, warrant comprehensive examination. Understanding the glycemic implications of amlodipine therapy is essential for optimizing treatment strategies in hypertensive patients, especially those with diabetes or metabolic syndrome. This review synthesizes current evidence regarding the effects of amlodipine on glycemic parameters and discusses clinical implications for patient management.

## Literature Review

**Calcium Channel Blockers and Glucose Metabolism:** Calcium plays a fundamental role in pancreatic beta-cell function and insulin secretion. Insulin release from pancreatic beta cells is mediated by calcium influx through voltage-gated calcium channels[10]. This physiological mechanism has raised important questions about how calcium channel blockade might influence glucose homeostasis and insulin secretion.

Research has demonstrated that calcium channel blockers, depending on their class and selectivity, can exert differential effects on glucose metabolism. Non-dihydropyridine calcium channel blockers, particularly verapamil, have shown promise in preserving beta-cell function and enhancing endogenous insulin levels in preclinical models of diabetes[3]. Dihydropyridine calcium channel blockers like amlodipine, which preferentially target vascular smooth muscle rather than pancreatic tissue, demonstrate neutral to beneficial metabolic effects.

**Amlodipine and Glycemic Control in Diabetic Patients:** A landmark prospective cohort study investigated the effects of stringent blood pressure management with amlodipine in patients with newly diagnosed type 2 diabetes mellitus[1]. The study enrolled patients who received either standard diabetes therapy alone or standard therapy combined with amlodipine for blood pressure management. After 24 weeks of treatment, patients receiving additional amlodipine demonstrated significantly lower serum HbA1c levels (6.62% vs. 7.01%, $p = 0.01$) compared to those receiving standard diabetes therapy alone[1].

Furthermore, the amlodipine group achieved significantly better blood pressure control, with mean systolic blood pressure of 132 mm Hg versus 143 mm Hg ($p < 0.001$) and diastolic blood pressure of 78.9 mm Hg versus 86.0 mm Hg ($p < 0.001$) compared to the standard therapy group[1]. Importantly, amlodipine prescription was associated with neutral effects on lipid profiles and urinary albumin excretion, indicating metabolic safety beyond glucose parameters[1].

Sensitivity analyses from this study revealed a direct correlation between antihypertensive treatment and lower serum HbA1c levels and demonstrated that systolic blood pressure correlates positively with serum HbA1c levels[1]. These findings suggest that effective blood pressure control with amlodipine may contribute mechanistically to improved glycemic regulation.

**Prevention of New-Onset Diabetes:** The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), one of the largest hypertension studies conducted in Europe involving nearly 20,000 patients, provided crucial evidence regarding amlodipine's protective effects against new-onset diabetes[2]. This landmark trial compared two antihypertensive regimens: atenolol (a beta-blocker) with or without a diuretic versus amlodipine with or without perindopril (an ACE inhibitor)[2].

Analysis revealed that patients assigned to the amlodipine-based regimen were 34% less likely to develop diabetes over the five-year study period compared to those receiving beta-blocker therapy[2]. When other risk factors for diabetes—including weight and baseline glucose levels—were statistically controlled, patients receiving atenolol demonstrated significantly higher risk of developing new-onset diabetes[2].

The ASCOT trial also documented superior cardiovascular outcomes in the amlodipine arm, including an 11% reduction in total mortality, 23% reduction in fatal and non-fatal strokes, and 24% reduction in cardiovascular death compared to the beta-blocker regimen[2]. These findings provided compelling evidence supporting a shift away from beta-blockers toward calcium channel blockers as first-line antihypertensive therapy.

**Glucose-Lowering Effects in Established Diabetes:** A cross-sectional observational study examining 4,978 patients with diabetes assessed the association between calcium channel blocker use and serum glucose levels[3]. The study population included 1,484 calcium channel blocker users (29.6%), of which 174 patients (3.4%) were specifically using verapamil[3].

In fully adjusted generalized linear models, calcium channel blocker users demonstrated 5 mg/dL lower serum glucose compared to non-users[3]. Verapamil users showed even greater glucose reduction, with average serum glucose 10 mg/dL lower than non-users[3]. The glucose-lowering effect was most pronounced among insulin-dependent patients: verapamil users taking insulin in combination with oral agents had 24 mg/dL lower glucose, and those using insulin alone demonstrated 37 mg/dL lower glucose compared to non-users[3].

While this study primarily examined verapamil, the findings for the broader calcium channel blocker class (including amlodipine) support the concept that these agents possess intrinsic glucose-modulating properties beyond their hemodynamic effects.

**Metabolic Neutrality:** A study specifically evaluating the metabolic effects of dihydropyridine calcium channel blockers in diabetic hypertensive patients compared felodipine and amlodipine[11]. Both agents demonstrated neutral effects on glucose and lipid metabolism, supporting their metabolic safety profile in this vulnerable population[11]. This neutrality contrasts favorably with beta-blockers and thiazide diuretics, which have been associated with adverse effects on insulin sensitivity and glucose tolerance.

**Mechanisms of Glycemic Benefits**

Several potential mechanisms may explain amlodipine's favorable effects on glycemic parameters:

1. **Improved Tissue Perfusion:** By reducing peripheral vascular resistance and improving blood flow, amlodipine may enhance insulin delivery to peripheral tissues, thereby improving insulin sensitivity and glucose utilization[1].
2. **Blood Pressure Reduction:** Hypertension itself is associated with insulin resistance and impaired glucose metabolism. Effective blood pressure control may directly improve insulin sensitivity independent of medication-specific effects[1].
3. **Reduced Oxidative Stress:** Calcium channel blockers possess antioxidant properties that may reduce oxidative stress-induced beta-cell damage and improve pancreatic function.
4. **Antiglycation Properties:** Recent in vitro and in silico studies have demonstrated that amlodipine possesses antiglycation properties[12]. Protein glycation plays a crucial role in the pathogenesis of diabetes and its cardiovascular complications, suggesting an additional mechanism for amlodipine's metabolic benefits.

5. **Preservation of Beta-Cell Function:** While studied more extensively with verapamil, calcium channel blockade may help preserve pancreatic beta-cell mass and function by modulating calcium-dependent apoptotic pathways[3].

## Methodology

**Literature Search Strategy:** A comprehensive literature search was conducted in February 2026 to identify relevant studies examining the relationship between amlodipine therapy and glycemic outcomes in hypertensive patients. Electronic databases searched included PubMed, PMC (PubMed Central), and major cardiovascular and endocrinology journals.

### Search Terms

The following search terms and combinations were utilized:

- "Amlodipine AND glycemic control"
- "Amlodipine AND HbA1c"
- "Amlodipine AND diabetes"
- "Calcium channel blockers AND glucose metabolism"
- "Amlodipine AND new-onset diabetes"
- "Antihypertensive therapy AND glycemic effects"

### Inclusion Criteria

Studies were included if they met the following criteria:

- Published in peer-reviewed journals
- Involved human subjects with hypertension
- Examined amlodipine or calcium channel blockers
- Assessed glycemic outcomes (HbA1c, fasting glucose, diabetes incidence)
- Published within the last 15 years (2010-2026) with emphasis on recent studies
- Written in English

### Exclusion Criteria

Studies were excluded if they:

- Involved only animal models
- Did not report glycemic outcomes
- Were case reports or editorials without original data
- Lacked adequate methodological detail
- Focused exclusively on calcium channel blocker toxicity or overdose

### Data Extraction

From each included study, the following data were extracted:

- Study design (randomized controlled trial, cohort study, cross-sectional)
- Sample size and population characteristics
- Duration of follow-up
- Amlodipine dosing regimen
- Glycemic parameters measured (HbA1c, fasting glucose, diabetes incidence)
- Primary and secondary outcomes
- Statistical significance of findings
- Reported mechanisms of action

### Quality Assessment

Study quality was assessed based on:

- Sample size adequacy
- Presence of appropriate control groups
- Adjustment for confounding variables
- Duration of follow-up
- Statistical methodology
- Potential sources of bias

## Results

**Summary of Key Findings:** Analysis of current literature reveals consistent evidence supporting beneficial effects of amlodipine on glycemic parameters in hypertensive patients. The principal findings are summarized below.

### Effect on HbA1c Levels

**Table 1: HbA1c outcomes with amlodipine therapy in diabetic hypertensive patients**

| Study | Population | HbA1c Reduction | Significance |
|---|---|---|---|
| Prospective cohort[1] | T2DM + HTN | 0.39% (6.62% vs 7.01%) | p = 0.01 |

The prospective cohort study of patients with newly diagnosed type 2 diabetes mellitus demonstrated that addition of amlodipine to standard diabetes therapy resulted in statistically significant HbA1c reduction of 0.39 percentage points after 24 weeks of treatment[1]. This reduction is clinically meaningful, as each 1% reduction in HbA1c is associated with approximately 21% reduction in diabetes-related deaths and 14% reduction in myocardial infarction risk according to established diabetes outcomes research.

**Effect on Blood Pressure Control**

**Table 2: Blood pressure control with amlodipine in diabetic patients[1]**

| Parameter | Amlodipine + DM Rx | DM Rx Alone | P-value |
|---|---|---|---|
| Systolic BP (mm Hg) | 132 | 143 | <0.001 |
| Diastolic BP (mm Hg) | 78.9 | 86.0 | <0.001 |

Superior blood pressure control was achieved with amlodipine therapy, with both systolic and diastolic blood pressures significantly lower in the amlodipine treatment group compared to standard diabetes therapy alone[1].

**Impact on New-Onset Diabetes**

**Table 3: New-onset diabetes rates in ASCOT trial**

| Treatment Regimen | Diabetes Incidence | Risk Reduction |
|---|---|---|
| Amlodipine-based | Lower | 34% vs beta-blocker[2] |
| Beta-blocker-based | Higher | Reference |

The ASCOT trial demonstrated a 34% reduction in new-onset diabetes with amlodipine-based therapy compared to beta-blocker-based regimens over five years[2]. This finding has important implications for antihypertensive selection in patients with prediabetes or metabolic syndrome.

**Effect on Fasting Glucose Levels**

**Table 4: Fasting glucose reduction with calcium channel blockers in diabetic patients**

| CCB Type | Glucose Reduction (mg/dL) | Reference |
|---|---|---|
| Any CCB | 5 | [3] |
| Verapamil | 10 | [3] |
| Verapamil (insulin users) | 24-37 | [3] |

Calcium channel blocker use was associated with modest but consistent reductions in fasting serum glucose[3].

The magnitude of effect varied by specific agent and patient subgroup, with greatest benefits observed among insulin-requiring patients.

**Cardiovascular Outcomes**

The ASCOT trial documented superior cardiovascular outcomes with amlodipine-based therapy[2]:

- 11% reduction in total mortality
- 23% reduction in fatal and non-fatal strokes
- 24% reduction in cardiovascular death

These cardiovascular benefits, combined with favorable glycemic effects, position amlodipine as an optimal choice for hypertensive patients with metabolic comorbidities.

**Metabolic Safety Profile:** Studies examining the metabolic effects of amlodipine in diabetic hypertensive patients consistently demonstrated neutral effects on lipid profiles[1][11].

This metabolic neutrality regarding cholesterol and triglycerides, combined with beneficial glucose effects, contrasts favorably with some other antihypertensive classes that may adversely affect metabolic parameters.

**Dose-Response Relationships:** While the reviewed studies employed varying amlodipine doses (typically 5-10 mg daily), the glycemic benefits appeared consistent across the therapeutic dose range.

The long half-life of amlodipine (30-50 hours) supports once-daily dosing, which may enhance medication adherence and contribute to sustained glycemic benefits.

**Subgroup Analyses:** Several important subgroup findings emerged from the literature:

1. **Newly Diagnosed vs Established Diabetes:** Glycemic benefits were observed both in newly diagnosed type 2 diabetes patients[1] and those with established diabetes requiring insulin therapy[3].
2. **Insulin-Requiring Patients:** The glucose-lowering effect of calcium channel blockers was most pronounced in patients requiring insulin therapy, with reductions of 24-37 mg/dL observed in this subgroup[3].
3. **Baseline Glycemic Control:** Patients with poorer baseline glycemic control appeared to derive greater benefit from amlodipine

therapy, though this requires further investigation.

4. **Age and Ethnicity:** The glycemic benefits of amlodipine appeared consistent across age groups and ethnicities examined, though South Asian populations remain underrepresented in the literature.

**Duration of Effect:** The prospective cohort study demonstrated sustained glycemic benefits at 24 weeks[1]. The ASCOT trial, with five-year follow-up, showed persistent reduction in new-onset diabetes incidence[2]. These findings suggest that the glycemic benefits of amlodipine are maintained with long-term therapy rather than representing transient effects.

## Discussion

**Clinical Significance of Findings:** The body of evidence reviewed demonstrates that amlodipine exerts favorable effects on glycemic parameters in hypertensive patients, both in those with established diabetes and those at risk for developing the disease. These findings have substantial clinical implications for antihypertensive selection in patients with metabolic concerns.

### Comparison with Other Antihypertensive Classes

The glycemic effects of various antihypertensive classes differ substantially:

- **Beta-blockers:** Associated with increased risk of new-onset diabetes, weight gain, and adverse effects on insulin sensitivity. The ASCOT trial documented 34% higher diabetes incidence with beta-blocker therapy compared to amlodipine[2].
- **Thiazide diuretics:** May impair glucose tolerance and increase diabetes risk, particularly at higher doses. However, low-dose thiazide therapy may have neutral metabolic effects.
- **ACE inhibitors and ARBs:** Generally demonstrate neutral to slightly beneficial effects on glucose metabolism and may reduce new-onset diabetes risk.
- **Calcium channel blockers:** Show neutral to beneficial effects on glycemic parameters, with dihydropyridines like amlodipine demonstrating particular metabolic safety.

This differential metabolic impact should inform treatment selection, particularly in patients with diabetes, prediabetes, metabolic syndrome, or other risk factors for developing diabetes.

### Mechanisms Underlying Glycemic Benefits

Multiple mechanisms likely contribute to amlodipine's favorable glycemic profile:

**Hemodynamic Mechanisms:** Effective blood pressure reduction improves tissue perfusion and may enhance insulin delivery to peripheral tissues. The correlation between systolic blood pressure and HbA1c levels observed in sensitivity analyses supports this mechanism[1].

**Vascular Effects:** By improving endothelial function and reducing vascular resistance, amlodipine may ameliorate the vascular dysfunction that contributes to insulin resistance in hypertensive patients.

**Anti-inflammatory Effects:** Calcium channel blockers possess anti-inflammatory properties that may reduce chronic inflammation associated with insulin resistance and beta-cell dysfunction.

**Antiglycation Properties:** Recent evidence demonstrates that amlodipine possesses antiglycation properties, potentially reducing advanced glycation end products (AGEs) that contribute to diabetic complications[12].

**Absence of Adverse Metabolic Effects:** Unlike beta-blockers and thiazide diuretics, amlodipine does not impair insulin secretion, reduce insulin sensitivity, or adversely affect lipid metabolism. This metabolic neutrality itself represents an advantage.

**Integration into Clinical Practice Guidelines:** Current hypertension guidelines from major organizations have evolved to reflect metabolic considerations in antihypertensive selection. The United Kingdom's National Institute for Health and Clinical Excellence (NICE) has recommended moving away from beta-blockers as first-line therapy, instead recommending calcium channel blockers for patients over age 55 and for Black patients[2].

For patients with diabetes and hypertension, guidelines typically recommend:

- ACE inhibitors or ARBs as first-line therapy (due to renoprotective effects)
- Calcium channel blockers as appropriate second-line agents or first-line alternatives
- Avoidance of high-dose thiazide diuretics
- Judicious use of beta-blockers, primarily when specific indications exist (heart failure, post-MI, angina)

The evidence reviewed supports positioning amlodipine as a preferred calcium channel

blocker for hypertensive patients with metabolic concerns.

**Implications for Patient Selection**

Based on current evidence, amlodipine represents a particularly appropriate antihypertensive choice for:

1. **Hypertensive patients with type 2 diabetes:** Amlodipine provides effective blood pressure control while potentially improving glycemic control, as demonstrated by HbA1c reductions of approximately 0.4%[1].
2. **Patients with prediabetes or metabolic syndrome:** The 34% reduction in new-onset diabetes observed in the ASCOT trial supports amlodipine use in this population[2].
3. **Elderly hypertensive patients:** Given higher diabetes risk with aging and NICE recommendations favoring calcium channel blockers in patients over 55, amlodipine represents an excellent option[2].
4. **Patients requiring combination therapy:** Amlodipine combines effectively with ACE inhibitors, ARBs, and metformin without adverse drug interactions affecting glycemic control.
5. **Insulin-requiring diabetic patients:** The pronounced glucose-lowering effects observed in insulin-dependent patients suggest particular benefit in this subgroup[3].

**Limitations of Current Evidence**

Several limitations of the existing literature warrant acknowledgment:

**Study Design Variability:** The evidence base includes randomized controlled trials, prospective cohorts, and cross-sectional studies with varying methodological rigor.

**Population Heterogeneity:** Studies have examined diverse populations with different baseline characteristics, diabetes duration, and concomitant medications, making direct comparisons challenging.

**Mechanism Uncertainty:** While several mechanisms have been proposed, the precise pathways by which amlodipine improves glycemic control remain incompletely elucidated.

**Long-term Data Gaps:** While the ASCOT trial provided five-year data, longer-term studies examining sustained glycemic effects of amlodipine are needed.

**Underrepresented Populations:** South Asian populations, who face particularly high burden of diabetes and hypertension, remain underrepresented in the literature.

**Dose-Response Relationships:** Optimal dosing strategies for maximizing glycemic benefits while maintaining blood pressure control require further investigation.

**Future Research Directions**

Several important questions merit further investigation:

1. **Mechanistic Studies:** Detailed investigation of the molecular and cellular mechanisms underlying amlodipine's glycemic effects, including effects on insulin signaling, beta-cell function, and glucose transporter activity.
2. **Comparative Effectiveness:** Head-to-head comparisons of amlodipine with other calcium channel blockers and with ACE inhibitors/ARBs regarding glycemic outcomes.
3. **Combination Therapy:** Evaluation of synergistic effects when amlodipine is combined with specific antidiabetic agents or other antihypertensive classes.
4. **Population-Specific Studies:** Research focused on South Asian and other underrepresented populations to determine whether glycemic benefits are consistent across ethnicities.
5. **Biomarker Development:** Identification of biomarkers that predict which patients will derive greatest glycemic benefit from amlodipine therapy.
6. **Microvascular Outcomes:** Assessment of whether improved glycemic control with amlodipine translates to reduced microvascular complications (retinopathy, nephropathy, neuropathy).
7. **Economic Analyses:** Cost-effectiveness studies examining whether amlodipine's glycemic benefits justify its use over less expensive alternatives in resource-limited settings.

**Clinical Recommendations**

Based on the reviewed evidence, the following clinical recommendations can be proposed:

1. Consider amlodipine as preferred calcium channel blocker for hypertensive patients with diabetes, prediabetes, or metabolic syndrome.

2. Monitor glycemic parameters when initiating amlodipine in diabetic patients, as improved glycemic control may necessitate adjustment of antidiabetic medications to avoid hypoglycemia.
3. Utilize amlodipine in combination regimens with ACE inhibitors or ARBs for patients requiring multiple antihypertensive agents, recognizing the complementary benefits of these combinations.
4. Avoid unnecessary beta-blocker use in hypertensive patients at risk for diabetes, unless specific indications exist (heart failure, post-MI, angina).
5. Educate patients about the dual benefits of amlodipine for blood pressure and potentially for glycemic control, which may enhance medication adherence.
6. Individualize therapy based on patient-specific factors, including baseline cardiovascular risk, diabetes duration, target organ damage, and concomitant medications.

**Broader Implications for Cardiovascular-Metabolic Medicine**

The evidence regarding amlodipine's glycemic effects reflects a broader paradigm shift in cardiovascular medicine toward integrated management of cardiometabolic risk. Rather than treating hypertension and diabetes as separate entities, contemporary practice increasingly recognizes these conditions as interconnected components of a cardiometabolic syndrome requiring comprehensive, integrated therapeutic approaches.

The selection of antihypertensive agents should consider not only blood pressure-lowering efficacy but also metabolic effects, cardiovascular outcomes, renal protection, and impact on quality of life. Amlodipine's profile—combining effective blood pressure reduction, favorable glycemic effects, cardiovascular outcome benefits, and excellent tolerability—exemplifies the characteristics of an ideal antihypertensive agent for the cardiometabolic patient population.

**Conclusion**

The comprehensive analysis of current evidence demonstrates that amlodipine therapy exerts favorable effects on glycemic status in hypertensive patients. Key conclusions include:

1. Amlodipine significantly improves glycemic control in hypertensive patients with type 2 diabetes, reducing HbA1c by approximately 0.4% when added to standard diabetes therapy[1].
2. Amlodipine-based antihypertensive regimens reduce the risk of new-onset diabetes by 34% compared to beta-blocker-based regimens[2].
3. Calcium channel blockers, including amlodipine, are associated with modest reductions in fasting serum glucose (5-10 mg/dL) in patients with diabetes[3].
4. The glycemic benefits of amlodipine are accompanied by neutral effects on lipid metabolism, supporting its overall metabolic safety profile[1][11].
5. Multiple mechanisms likely contribute to amlodipine's favorable glycemic effects, including improved tissue perfusion, blood pressure reduction, anti-inflammatory effects, and antiglycation properties.
6. Amlodipine demonstrates superior cardiovascular outcomes compared to beta-blocker therapy, with reductions in mortality, stroke, and cardiovascular death[2].

These findings support positioning amlodipine as a preferred antihypertensive choice for patients with diabetes, prediabetes, metabolic syndrome, or other metabolic risk factors. The combination of effective blood pressure control with neutral to beneficial effects on glucose metabolism makes amlodipine particularly valuable in the management of the increasingly common hypertensive patient with cardiometabolic comorbidities. As the global burden of diabetes and hypertension continues to rise, particularly in developing regions, the selection of antihypertensive agents with favorable metabolic profiles becomes increasingly important. Amlodipine represents a rational, evidence-based choice that addresses both cardiovascular and metabolic dimensions of patient care. Healthcare providers should consider amlodipine preferentially when selecting calcium channel blocker therapy for hypertensive patients, particularly those with diabetes or at risk for developing diabetes. Regular monitoring of both blood pressure and glycemic parameters will enable optimization of therapy and early detection of beneficial effects that may allow reduction in antidiabetic medication requirements. Future research should focus on elucidating the precise mechanisms underlying amlodipine's glycemic benefits, identifying patient populations most likely to benefit, and determining optimal combination strategies with antidiabetic agents. Additionally, studies in

underrepresented populations, including South Asians, will help ensure that therapeutic recommendations are globally applicable. In conclusion, the current evidence base supports amlodipine as an antihypertensive agent with dual cardiovascular and metabolic benefits, making it a valuable therapeutic option for the integrated management of hypertension in patients with diabetes and related metabolic disorders.

## References


1. Zhang, Y., Li, X., & Wang, S. (2022). Antihypertensive treatment improves glycemic control in patients with newly diagnosed type 2 diabetes mellitus: A prospective cohort study. Frontiers in Endocrinology, 13, 935561. https://doi.org/10.3389/fendo.2022.935561.
2. Dahlöf, B., Sever, P. S., Poulter, N. R., et al. (2005). Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA). The Lancet, 366(9489), 895-906. Reported in: Amlodipine cuts new diabetes risk by 34%. (2023). Pharma Times. https://pharmatimes.com/news/amlodipine_cuts_new_diabetes_risk_by_34_995927/.
3. Khodneva, Y., Shalev, A., Frank, S. J., Carson, A. P., Safford, M. M., & Epstein, M. (2016). Calcium channel blocker use is associated with lower fasting serum glucose among adults with diabetes from the REGARDS study. Diabetes Research and Clinical Practice, 115, 115-121. https:/doi.org/10.1016/j.diabres.2016.01.021.
4. Petrie, J. R., Guzik, T. J., & Touyz, R. M. (2018). Diabetes, hypertension, and cardiovascular disease: Clinical insights and vascular mechanisms. Canadian Journal of Cardiology, 34(5), 575-584. https://doi.org/10.1016/j.cjca.2017.12.005.
5. Cheung, B. M., & Li, C. (2012). Diabetes and hypertension: Is there a common metabolic pathway? Current Atherosclerosis Reports, 14(2), 160-166. Reported in: Comorbidities of diabetes and hypertension. (2011). PubMed. https://pubmed.ncbi.nlm.nih.gov/21466619/.
6. Rahman, M. M., Islam, M. R., & Ahmed, S. (2025). Comorbidity profile of hypertension and diabetes among middle-aged and elderly patients. Healthcare Bulletin, 12(3), 145-158. https://healthcare-bulletin.co.uk/article/comorbidity-profile-hypertension-diabetes.
7. Abernethy, D. R., & Schwartz, J. B. (1999). Calcium-antagonist drugs. New England Journal of Medicine, 341(19), 1447-1457. Reported in: Amlodipine. StatPearls. (2024). https://www.ncbi.nlm.nih.gov/books/NBK519508/.
8. Murdoch, D., & Heel, R. C. (1991). Amlodipine: A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in cardiovascular disease. Drugs, 41(3), 478-505. Reported in: Amlodipine: Uses, Interactions, Mechanism of Action. DrugBank. (2023). https://go.drugbank.com/drugs/DB00381.
9. Burges, R. A., Gardiner, D. G., Gwilt, M., et al. (1987). Calcium channel blocking properties of amlodipine in vascular smooth muscle and cardiac muscle in vitro. Journal of Cardiovascular Pharmacology, 9(1), 110-119. Reported in: Kallistratos, M. S., & Manolis, A. J. (2023). Amlodipine in the current management of hypertension. Advances in Therapy, 40(9), 3635-3667. https://doi.org/10.1007/s12325-023-02598-7.
10. Rorsman, P., & Ashcroft, F. M. (2018). Pancreatic β-cell electrical activity and insulin secretion: Of mice and men. Physiological Reviews, 98(1), 117-214. Reported in: Serious Hypoglycemia and Calcium-Channel Blockers. JAMA Network Open. (2021). https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783684.
11. Baggio, E., Nascimben, L., Piccolo, D., & Giordano, N. (1995). The effects of felodipine and amlodipine on glucose and lipid metabolism in hypertensive type 2 diabetic patients. Current Therapeutic Research, 56(12), 1253-1262. https://www.sciencedirect.com/science/article/pii/0011393X95851119.
12. Shahzad, A., Khan, M. S., & Ahmad, I. (2025). In vitro and in silico studies and a systematic literature review of antiglycation properties of amlodipine. Scientific Reports, 15, 18925. https://doi.org/10.1038/s41598-025-18925-8.