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Lacidipine: Beyond Hypertension-Cardiovascular, Neuroprotective, and Renoprotective Effects

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ABSTRACT

Background: Hypertension remains a leading contributor to cardiovascular, cerebrovascular, and renal disease worldwide. While calcium channel blockers are well established for blood pressure management, growing attention is being given to agents that provide organ protection beyond hemodynamic control. Lacidipine, a highly lipophilic dihydropyridine calcium channel blocker, shows strong membrane affinity and antioxidant properties, suggesting potential benefits that extend beyond its antihypertensive role.

Purpose: This review critically examines lacidipine's therapeutic profile by integrating evidence of its vascular, cardiovascular, neurovascular, and renal protective effects alongside its established clinical use.

Methods: A comprehensive analysis of preclinical studies, clinical trials, and mechanistic reports was conducted to examine lacidipine's pharmacological properties, antioxidant activity, and vasoprotective roles beyond blood pressure control.

Results: Lacidipine exhibits pronounced vascular selectivity and sustained activity with good tolerability in clinical use. Experimental studies demonstrate antioxidant and anti-inflammatory effects that mitigate endothelial dysfunction, vascular remodeling, and oxidative injury. Clinical evidence supports its efficacy is comparable to other major antihypertensive classes. Emerging data further indicate neuroprotective effects in models of stroke and neurodegeneration, renoprotective actions through improved microvascular and glomerular function, and cardioprotective benefits including attenuation of left ventricular hypertrophy and atherosclerotic progression.

Conclusions: Beyond effective blood pressure management, lacidipine shows multi organ protective properties that may enhance long term outcomes in hypertension associated disorders. Further studies are warranted to validate these benefits in clinical settings and to explore repositioning strategies that leverage its pleiotropic therapeutic potential.

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1. Introduction

Hypertension remains among the leading global health burdens, propelling cardiovascular disease, stroke, renal damage, and early death. Although calcium channel blockers (CCBs) are well proven cornerstones of antihypertensive therapy, there is increasing appreciation that drugs providing multi target protection in addition to blood pressure control are an urgent necessity (Chaudhari *et al.*, 2024).

Lacidipine, a lipophilic 1,4 dihydropyridine calcium channel antagonist, is used for hypertension (2 to 4 mg per day). By binding L type Ca^{2-} channels, it reduces calcium influx. Its high membrane affinity forms a reservoir, producing slow onset, sustained vasodilation, and hypotensive effects comparable to other calcium antagonists (Grewal *et al.*, 2023). Since calcium ions act as intracellular messengers involved in muscle contraction and depolarization, their inhibition results in the relaxation of vascular smooth muscle and lower blood pressure (Bravo Sagua *et al.*, 2020). Some studies suggest that lacidipine's interaction with its receptor occurs in two steps. First, the drug binds and accumulates within the lipid bilayer, and then it diffuses to reach the calcium channel receptor, facilitated by its high membrane affinity. Oxidative stress contributes to triggering numerous diseases, including chronic and degenerative conditions, inducing acute pathological changes (such as stroke), and accelerating the aging process, which is well established (Leyane *et al.*, 2022).

LCD is reported to occupy the pioneer position in terms of possessing antioxidant activity amongst calcium channel antagonists, thus implicating its potential in combating oxidative stress (McCarty *et al.*, 2021). In the last decade, new mechanistic findings have emphasized lacidipine's antioxidant, anti-inflammatory, and vasoprotective effects, positioning it as a drug of value beyond its role as a blood pressure lowering agent (Yang *et al.*, 2021).

Lacidipine is a very fascinating drug, as it does much more than just lowering blood pressure levels. Being a calcium channel blocker used for hypertension, researchers are now finding that it is highly lipophilic in nature, which allows it to act like a slow-release reservoir for its long-lasting effects (Lee, 2023). Preclinical laboratory reports have shown strong potential in helping protect the brain after a stroke, preventing unhealthy cardiac remodeling, and protecting the kidney and liver from damage (Al Naimi *et al.*, 2019; Hajdys *et al.*, 2023). It also strengthens bones and helps fight infections such as Leishmania (Abdel Ghany *et al.*, 2020).

The drug lacidipine is highly effective as a once daily treatment of hypertension in human clinical trials, with blood pressure lowering potency comparable to commonly used agents such as ACE inhibitors (enalapril), beta blockers (atenolol), and diuretics (chlorthalidone) (Lee, 2023; Zhang *et al.*, 2022). Its features in real world patients are notable, as it is also metabolically friendly. In addition to lowering blood pressure, it improves insulin sensitivity and lowers levels of HbA1c in individuals suffering from both hypertension and type 2 diabetes (Błaszczyk *et al.*, 2024). Major studies, including the European Lacidipine Study on Atherosclerosis (ELSA), highlight its long-term benefits and its potential to significantly slow arterial wall thickening and plaque formation, which are key processes in preventing strokes and heart attacks (Tsinari *et al.*, 2025; Zhao *et al.*, 2025). Another strong feature of this drug is its pharmacokinetics. Because of its anchoring into the cell membrane, it provides steady 24-hour effects without sudden heart rate increases often seen with other antihypertensive medications (Lee, 2023).

2. Mechanism of Action

Lacidipine is a constantly orally administered lipophilic 1,4 dihydropyridine, a pharmacodynamic calcium antagonist with a slow onset and long duration of action. The drug's lipophilic nature causes it to accumulate in membrane lipid bilayers, where it is slowly and continuously released. Lacidipine inhibits voltage dependent L type calcium channels, causing vasodilation and, as a result, lowering total peripheral vascular resistance and blood pressure (BP). Furthermore, lacidipine has antioxidant activity, which is thought to play a role in reducing endothelial dysfunction caused by oxidative stress (Liu *et al.*, 2021).

The antihypertensive impact initiates 0.5 to 1.0 hours after dosing and persists for 24 hours when multiple doses are administered. Lacidipine administration once daily in the morning provides a 24-hour hypotensive effect established by ambulatory blood pressure monitoring; however, night-time blood pressure is reduced to a lesser degree than daytime blood pressure (Minh *et al.*, 2021; Wang & Tang, 2020). Plasma trough to peak ratios that reach or exceed 65 percent are also commonly observed, and the pharmacokinetic profile justifies once daily use. Due to the gradual onset of action, lacidipine may cause only mild and slow reflex tachycardia or sympathetic activation with chronic administration.

In addition to its calcium channel blocking properties, lacidipine has marked antioxidant activity, which may be due to scavenging of reactive oxygen species and limiting oxidative stress upon the endothelium, which is one of the major factors underlying vascular dysfunction in hypertension (Cardoso & Salles, 2021). This antioxidative potential also provides a protective effect of its hypotensive action by maintaining endothelial integrity. Lacidipine possesses natriuretic and diuretic properties while being metabolically neutral without adverse effects on glucose or lipid metabolism. Lacidipine exerts certain effects on renal protection in animal experiments, but these are not as potent as RAAS inhibitors. In vitro and animal studies have demonstrated pharmacodynamic evidence that lacidipine could have anti atherosclerotic effects at least partly independent of blood pressure reduction (Wu *et al.*, 2021; Zhao *et al.*, 2022).

3. Pharmacokinetics and Pharmacodynamics

The key pharmacokinetic and pharmacodynamic properties of lacidipine, including absorption, distribution, metabolism, excretion, dosing regimen, and clinical relevance, are summarized in Table 1.

Table 1: Pharmacokinetic and Pharmacodynamic Properties of Lacidipine

Parameter	Findings	Clinical Relevance	Reference
	• Lacidipine has a high lipoid-water partition coefficient and is quickly absorbed from the gastrointestinal tract after oral administration, with peak plasma concentrations being reached 30–150 min after administration.		(Aremu *et al.*, 2025; Story *et al.*, 2023)

Absorption	• Oral administration of 4 mg in young volunteers produced peak levels in plasma of 1.6-5.7 g/L. • Bioavailability of oral administration is low (<10%) and is mainly a result of the extensive first-pass metabolism in the liver. The average dose response to oral lacidipine that exerts arterial tension is within the therapeutic ranges of the report in patients with mild-to moderate essential hypertension, a major class of antihypertensive drugs.	Explains variability of systemic exposure; requires daily consistent dosing.	
Distribution	• The highly lipophilic nature of lacidipine facilitates its extensive accumulation within the lipid bilayers of biological membranes, particularly in vascular smooth muscle cell membranes. • Radiotracer and biophysical investigations demonstrate a high membrane partition coefficient, with lacidipine penetrating deeply into the phospholipid hydrocarbon core. • This leads to delayed release, extended action, and prolonged blood pressure reduction. • It is tightly (>95%) bound to plasma proteins, predominantly albumin and, to a lesser extent, α1-acid glycoprotein, which decreases the concentration of free drug in the plasma and affects its tissue distribution. • Lacidipine's volume of distribution is relatively large, estimated to be around 4.8 L/kg in animal models, reflecting its extensive tissue affinity. • The half-life of elimination is 13 to 19 hours and indicates that the intake of the nitrofurantoin involves once-daily use and that for a relatively stable therapeutic effect	Emphasize extended action, vascular selectivity, and limited reflex tachycardia.	(Hajdys *et al.*, 2023; Shriya *et al.*, 2025; Zakaraya *et al.*, 2024)
Metabolism	• Lacidipine is extensively metabolized in the liver, principally via the cytochrome P450 enzyme CYP3A4, to a series of inactive metabolites. • This hepatic metabolism by CYP3A4 suggests that lacidipine plasma concentrations can be altered by agents that inhibit or induce this enzyme, thus resulting in clinically significant drug-drug interactions.	Potential drug–drug interactions with CYP3A4 inhibitors/inducers.	(Zhao *et al.*, 2021)
Excretion	• Approximately 70% of the administered dose is excreted as metabolites either into the feces via the biliary system following metabolic degradation or in urine. • Significantly, the unmetabolized drug is not excreted in urine or feces indicating a complete metabolic conversion of lacidipine.	Assures complete metabolic conversion before elimination.	(Chebrolu *et al.*, 2021)
	• The recommended and effective oral dose of lacidipine in fair-degree clinical trials has been 4 mg per day. The recommended UK starting dose (and that is adopted by many continental European countries where the drug is not manfactured) is 2 mg once daily for the first three to four weeks, increasing thereafter to a maintenance regimen of 4 mg/day.		

Dose & Administration	• In France, for example, the first dose is 4 mg once daily, increasing to 6 mg if blood pressure was less than 147/98 to 6 mg after 6 weeks if blood pressure remains uncontrolled, Preferred practice dictates that lacidipine should be administered once daily at a fixed time, preferably in morning. • Calcium channel inhibitors are major in the treatment of essential hypertension and are frequently combined with diuretics and/or β-adrenoceptor antagonists. There are also modified-release forms such as SR verapamil and nifedipine GITS for once-daily dosing.	Enhances compliance and stable BP control.	(Liu *et al.*, 2021; Wang & Tang, 2020)
Mechanism of Action	• Very lipophilic 1,4-dihydropyridine calcium channel blocker; selectively inhibits L-type calcium influx in vascular smooth muscle, leading to vasodilation with little effect on the heart.	Produces vasodilation with little adverse inotropic or chronotropic effects.	(Leyane *et al.*, 2022)
Contraindication	• Acute myocardial infarction (AMI)-In cases of Q-wave myocardial infarction, calcium channel blockers are generally less effective compared to beta-blockers for both immediate treatment and long-term management. Moreover, these drugs are typically not recommended for patients who have experienced a heart attack and also present with left ventricular dysfunction. • Conditions such as aortic stenosis and lacidipine should be avoided in patients with a known hypersensitivity to any component of lacidipine. Lacidipine and other dihydropyridine calcium channel blockers are not recommended in severe aortic stenosis. Literature indicates lacidipine does not have a deleterious effect on sinoatrial (SA) node activity and does not significantly prolong atrioventricular (AV) node conduction. • High Blood Pressure –Beta-blocker therapy should be avoided during acute decompensated heart failure (ADHF) with cardiogenic shock, as it can rapidly decrease the heart's pumping ability. Angiotensin-II receptor blockers; (ARBs) are a relatively new group of antihypertensive agents used as first-line therapy, their use steadily increasing, in particular, among patients who are intolerant of ACE inhibitors. • Unstable angina: Lacidipine may introduce complications when administered in hypertensive emergencies, having previously raised the risk of coronary events in unstable angina or following a recent myocardial infarction.	Avoid acute coronary syndromes or impaired LV function and other contraindicated situations.	(Joo, 2023)
Precautions	• Heart failure with congestive edema, cardiovascular disease, High blood pressure, Obstruction of the left ventricular outflow, abnormalities in conduction, Impairment of the liver. Withdraw the medication gradually and with caution. Use with caution when combined with other antihypertensive medications. If ischemic chest pain or cardiogenic shock occurs after starting therapy, the drug is stopped.	Prevents rebound hypertension and adverse cardiovascular outcomes.	(Zhang *et al.*, 2025)

Interaction	• Combination with potent CYP3A4 inhibitors such as ketoconazole, itraconazole, and erythromycin should be avoided, if possible, due to the risk of an excessive increase in plasma concentrations of lacidipine, which may increase the antihypertensive effect and enhance adverse reactions such as hypotension or dizziness. • Conversely, CYP3A4 inducers like rifampicin and carbamazepine may decrease the levels of lacidipine, thereby reducing its ability to control blood pressure. • Lacidipine with other antihypertensive agents, for instance beta-blockers or ACE inhibitors, can produce additive hypotensive effects, which, while therapeutically beneficial, require careful dose titration to prevent excessive blood pressure reduction. • Co-administration with grapefruit juice, a known CYP3A4 inhibitor, may elevate lacidipine plasma concentrations unpredictably, warranting dietary counseling for patients. • Lacidipine may interact with drugs affecting P-glycoprotein transport, potentially altering its absorption and elimination, though this mechanism remains less fully characterized. • Pharmacodynamic interactions with nitrates or phosphodiesterase inhibitors may result in excessive vasodilation and hypotension when lacidipine is used concurrently.	Requires monitoring for hypotension or therapeutic failure; patient counseling is indicated.	(Rudic *et al.*, 2024)

4. Preclinical Pharmacological Insights

4.1. L-type Calcium Channel Blockade

Lacidipine, a dihydropyridine calcium channel–blocking agent, relaxes vascular smooth muscle by inhibiting the influx of extracellular calcium into vascular smooth muscle cells. This effect is mediated through its interaction with dihydropyridine receptors, resulting in blockade of voltage-dependent L-type calcium channels. Specifically, lacidipine binds to the dihydropyridine-sensitive α1c subunit of these channels at their transmembrane region.

Due to its high lipophilicity, lacidipine exhibits a slow onset of action but a prolonged duration of effect. The drug rapidly accumulates within lipid bilayers of plasma membranes and other mucosal tissue compartments, forming a depot around calcium channel receptors (Jones *et al.*, 2024). The gradual and sustained release of lacidipine from these lipid reservoirs contributes to its long-lasting vasodilatory action and delayed pharmacological response.

One notable clinical advantage of lacidipine is its reduced tendency to induce reflex tachycardia. This characteristic is attributed to the slower rate of vasodilation, as reflex tachycardia is more strongly influenced by the speed rather than the magnitude of vascular relaxation. Among calcium channel blockers, dihydropyridine derivatives are considered vascular-selective, primarily targeting vascular smooth muscle with minimal effects on myocardial contractility or cardiac conduction (Zakaraya *et al.*, 2024). Lacidipine demonstrates greater vascular selectivity than many other dihydropyridines. Studies using rabbit aortic rings and ventricular muscle strips have shown that lacidipine possesses a high vascular-to-cardiac activity ratio, indicating preferential activity in vascular tissues (Liu *et al.*, 2021).

4.2. Antioxidant and Anti-inflammatory Pleiotropic Effects

Oxidative stress plays a significant role in endothelial injury, contributing to impaired endothelium-dependent vasorelaxation commonly observed in essential hypertension. Similar to other dihydropyridine-type calcium antagonists, lacidipine exhibits antioxidant properties; however, its antioxidant potency is greater than that of many agents within the same class.

Electrochemical studies have demonstrated that lacidipine undergoes a reversible two-electron oxidation process, producing two one-electron intermediates. Importantly, the second electron release occurs at a less positive potential than the first, supporting its classification as an efficient antioxidant. Clinical studies indicate that administration of lacidipine at doses of 4–6 mg/day for 2–6 months significantly improves endothelium-dependent vasodilation in hypertensive patients, as assessed using acetylcholine- or bradykinin-induced vasodilatory responses.

The observed improvement in ischemic responses among patients treated with lacidipine appears to be associated with enhanced nitric oxide (NO) bioavailability. These effects are presumed to be largely independent of direct calcium channel modulation in endothelial cells, as these cells lack voltage-operated calcium channels. Several studies have shown that restoration of endothelial function may occur independently of, or in addition to, blood pressure reduction (Liu *et al.*, 2021).

4.3. Preclinical Evidence Supporting Organ-Protective Effects of Lacidipine

Preclinical studies provide strong mechanistic evidence supporting the organ-protective effects of lacidipine beyond its blood pressure–lowering action. In spontaneously hypertensive rat models, lacidipine has been shown to restore endothelial senescence and reduce inflammatory injury via modulation of the CXCR7/P38/C/EBP-β signaling pathway, leading to improved endothelial cell viability under oxidative stress conditions (Liu *et al.*, 2021). Its high lipophilicity facilitates sustained membrane localization, enabling prolonged antioxidant activity and stabilization of endothelial function (Nawrot *et al.*, 2022).

In cardiovascular models, lacidipine reduces left ventricular hypertrophy and myocardial fibrosis by limiting calcium overload, suppressing oxidative injury, and modulating pro-inflammatory signaling pathways (Ramachandra *et al.*, 2021). Animal studies have also demonstrated inhibition of vascular smooth muscle cell proliferation and attenuation of atherosclerotic lesion development, associated with reduced oxidized low-density lipoprotein (LDL) accumulation and macrophage foam cell formation. Notably, these effects occur even at sub-antihypertensive doses, highlighting direct vasculoprotective mechanisms (Park *et al.*, 2024).

Additional research has demonstrated neurovascular and renal protective effects of calcium channel blockers, particularly third-generation agents. Lacidipine exerts endothelial protection through the CXCR7/P38/C/EBP-β signaling pathway (Liu *et al.*, 2021). In stroke models, peroxisome proliferator-activated receptor-α (PPAR-α) activation has shown promise in improving neurovascular outcomes by reducing oxidative stress, blood–brain barrier dysfunction, and neuroinflammation (Boese *et al.*, 2020). Similarly, glucagon-like peptide-1 (GLP-1) receptor agonists have demonstrated cerebral protective effects in animal stroke models, including reduced infarct volume, oxidative stress, neuroinflammation, and blood–brain barrier permeability, while enhancing neurogenesis and cerebral perfusion (Vergès *et al.*, 2022).

Collectively, these findings establish a strong mechanistic foundation for lacidipine's pleiotropic effects and support further clinical evaluation of its organ-protective potential.

5. Clinical Applications and Therapeutic Efficacy

Building upon robust preclinical evidence, multiple clinical investigations have explored whether the antioxidant, vasoprotective, and organ-preserving effects of lacidipine translate into measurable benefits in human populations. Clinical trials and long-term observational studies have evaluated lacidipine not only for effective blood pressure control but also for its impact on endothelial function, arterial remodelling, metabolic neutrality, and target-organ protection. This section summarizes the clinical evidence supporting lacidipine's translational relevance across cardiovascular, neurovascular, and renal domains.

5.1. Neuroprotection in Stroke and Alzheimer's Disease

Lacidipine's neuroprotective effects represent a compelling extension of its therapeutic versatility, positioning it as a candidate for managing neurovascular disorders beyond its established role in hypertension. Preclinical studies have demonstrated that lacidipine enhances cerebral blood flow and mitigates ischemic injury in stroke models, notably reducing infarct size following middle cerebral artery occlusion. Its ability to attenuate vascular damage and endothelial dysfunction within the cerebral microvasculature is partly independent of its systemic blood pressure–lowering effects, underscoring a direct protective impact on neurovascular integrity (Kim *et al.*, 2020). This is largely attributed to lacidipine's potent antioxidant properties, which counteract oxidative stress, a key driver of neuronal injury and neurodegeneration, by scavenging reactive oxygen species and inhibiting pro-inflammatory cascades. Additionally, lacidipine has been shown to modulate calcium influx in neuronal and glial cells, helping preserve cellular homeostasis and prevent excitotoxicity under pathological conditions (Ashok *et al.*, 2022). Emerging evidence also points to its capacity to reduce microvascular remodeling

and endothelial inflammation, thereby preserving cerebral microcirculation and potentially delaying cognitive decline linked to small vessel disease. Together, these multifactorial mechanisms suggest that lacidipine holds promise not only for acute cerebrovascular protection but also as a therapeutic agent against chronic neurodegenerative processes, warranting further clinical investigation into its role in neuroprotection and cognitive health. Alzheimer's disease (AD) is consistently associated with cholinergic deficits and oxidative stress (AD) (Mustapha *et al.*, 2019). Acetylcholine is known to inhibit the Ca^{2-} current in the brain as per various research findings. Cholinergic antagonists (such as scopolamine) provoke a Ca^{2-}-mediated oxidative imbalance, inflammation, and neuronal death mechanisms, which ultimately can generate Alzheimer's disease–pattern memory loss. Earlier, some Ca^{2-}-channel blockers (CCB, such as the dihydropyridine type) and cholinergic enhancers have shown beneficial effects in animal disease.

Lacidipine has shown promising effects related to Alzheimer's disease (AD) in preclinical research, mainly through its antioxidant and neuroprotective properties (Chen *et al.*, 2022). In mouse models mimicking AD-like memory impairment induced by scopolamine, lacidipine administration prevented memory loss and improved learning performance. This protective effect is linked to lacidipine's ability to reduce oxidative stress and inhibit acetylcholinesterase (AChE) activity in the brain, helping to maintain cholinergic function, which is often compromised in AD. By modulating calcium influx through L-type calcium channels, lacidipine helps restore cellular calcium homeostasis, which otherwise can be disrupted by amyloid-beta pathology and contribute to neuronal damage. These actions collectively mitigate pathways involved in oxidative damage, inflammation, and cell death that underlie AD-related neurodegeneration (Khurana *et al.*, 2021) (Figure 1). Figure 1 highlights calcium channel blockade and antioxidant mechanisms that enhance cerebral blood flow, reduce oxidative stress and inflammation, limit amyloid-β deposition, and preserve cognitive function.

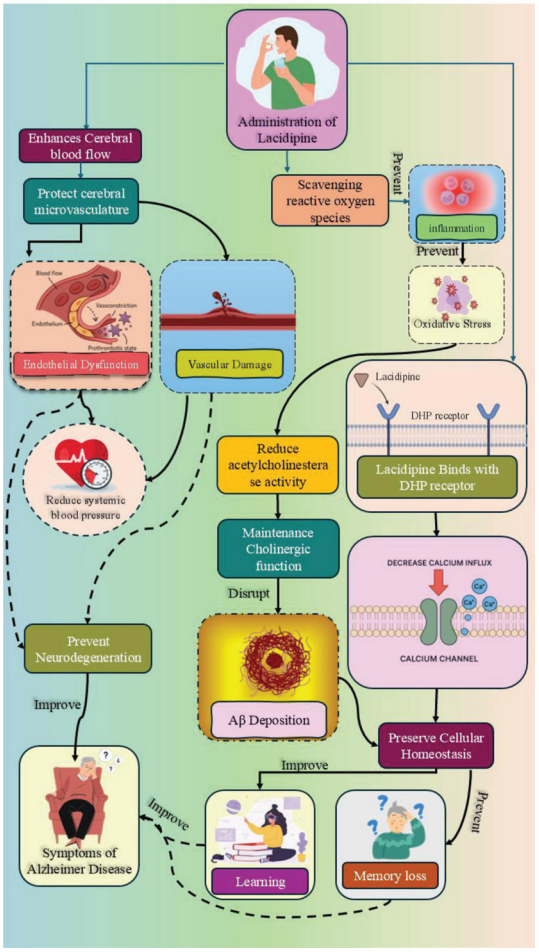

Figure 1: Neuroprotective mechanisms of lacidipine in Alzheimer's disease

5.2. Cardiovascular Protective Mechanisms

5.2.1. Effects on Heart Rate

Because lacidipine acts gradually, its antihypertensive effect is not associated with the reflex tachycardia often triggered by short-acting calcium channel blockers such as nifedipine or felodipine. Clinical studies, involving both single and repeated doses in patients with hypertension, indicate that treatment with 2–6 mg of lacidipine may cause a slight rise in heart rate. In animal models, lacidipine showed minimal direct chronotropic effects (i.e., effects that alter heart rate). Any observed increases were minor, transient, and not associated with adverse clinical outcomes (Jones *et al.*, 2024). This is further supported by lacidipine's weak activity at cardiac L-type calcium channels compared to its vascular effects, explaining the lack of pronounced chronotropic activity. Lacidipine does not appear to provoke bradycardia. Studies involving long-term administration report that heart rate remains stable throughout treatment courses, without compensatory decreases that might be associated with negative chronotropic drugs. There is no significant increase in heart rate during lacidipine treatment with 2–6 mg/day for 1–60 months in randomised comparative trials in patients with essential or isolated systolic hypertension (Liu *et al.*, 2021) (Figure 2).

5.2.2. Effects on Sympathetic Activity

Plasma levels of catecholamines as a marker for sympathetic activity found that, in the context of prolonged treatment, lacidipine does not induce compensatory sympathetic nervous activation. In a double-blind, randomized study of lacidipine and manidipine (which are both highly lipophilic dihydropyridine calcium channel blockers), there was no significant increase in plasma norepinephrine from baseline values after 24 weeks of treatment in patients with mild to moderate essential hypertension (Fogari *et al.*, 2003). In contrast, patients receiving felodipine and amlodipine demonstrated a marked elevation in plasma norepinephrine levels (approximately 35–39%; $p < 0.01$), despite all four drugs achieving similar reductions in blood pressure (Lee, 2024) (Figure 2).

5.2.3. Vasoprotective Effects

Lacidipine exhibits significant vasoprotective effects that extend beyond its antihypertensive actions. One of the pivotal mechanisms underlying its vasoprotective role is the preservation and improvement of endothelial function. Lacidipine has been shown to effectively prevent endothelial cell aging, oxidative stress, and inflammatory injury, largely through the modulation of the CXCR7/P38/C/EBP-β signaling pathway. Treatment with lacidipine elevates CXCR7 expression in endothelial cells, which leads to the suppression of P38 MAPK expression and phosphorylation, a pathway known to mediate oxidative stress, inflammation, and cell aging. This, in turn, results in the downregulation of the transcription factor C/EBP-β, further reducing inflammation and apoptosis within endothelial cells. Collectively, these molecular changes decrease oxidative stress and inflammatory injury by lowering levels of reactive oxygen species (ROS) and pro-inflammatory cytokines, ultimately improving endothelial cell viability and migration and reducing cellular senescence (Liu *et al.*, 2021). These processes ameliorate hypertension-induced endothelial dysfunction and vascular injury. This enhancement lowers the risk of plaque formation within the blood vessels. By averting the deposition of atherosclerotic plaque, the development of atherosclerosis is significantly retarded. Finally, these processes are integrated, offering holistic control of the cardiovascular system, thus blocking the process from vascular injury to atherosclerosis and its sequelae. Vasoprotective effects of lacidipine in rat models (cardiovascular and cerebrovascular circulation) may not be attributable to the reduction of blood pressure, since vasoprotective effects could be obtained using a dose of lacidipine that does not lower blood pressure. In the absence of BP reduction, the vasoremodeling-inhibitory action of calcium channel blockade with lacidipine may protect against vascular remodeling, possibly through the inhibition of pathogenic processes that depend on calcium overload (Yang *et al.*, 2025) (Figure 2).

5.2.4. Effect on Vasoactive Hormone

Lacidipine influences several vasoactive hormones primarily through its vasodilatory actions and interaction with vascular smooth muscle tone. By inducing peripheral vasodilation, lacidipine can indirectly modulate the release and activity of hormones involved in vascular regulation, such as nitric oxide (NO) and endothelin-1. It enhances the endothelial role, promoting increased NO bioavailability, which contributes to vasodilation and vascular homeostasis (Ahmed *et al.*, 2023; Kumar *et al.*, 2020). Additionally, lacidipine may reduce the expression or activity of endothelin-1, a potent vasoconstrictor implicated in hypertension and vascular remodeling. Through these effects, lacidipine helps restore the balance between vasodilatory and vasoconstrictive forces at the vascular level, contributing to improved arterial compliance and BP management. Lacidipine has been demonstrated to inhibit the rise of plasma aldosterone produced by increased PRA associated with intravenous furosemide infusion in hypertensive subjects. Nevertheless, treatment for up to 4 weeks does not appear to affect baseline levels of atrial natriuretic factor, BNP, or aldosterone, nor the overall renin–angiotensin–aldosterone system (Gaydarski *et al.*, 2025) (Figure 2).

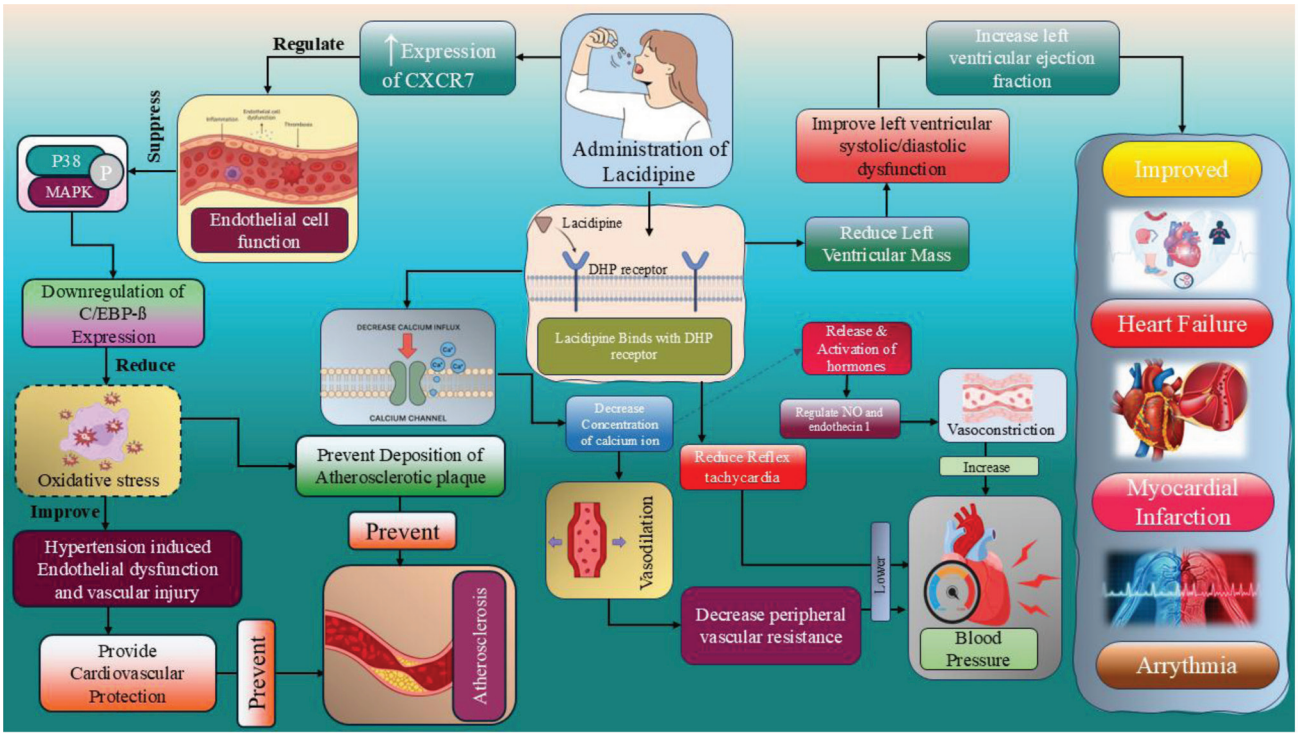

Figure 2: Illustration of the Cardiovascular Protective Mechanisms of Lacidipine

5.3. Anti-Atherosclerotic and Antihypertensive Benefits

5.3.1. Anti-hypertensive Effects

Lacidipine is a dihydropyridine calcium channel blocker with the most significant action on arteriolar (resistance) rather than venous blood vessels. It therefore reduces total peripheral vascular resistance, which is the most characteristic hemodynamic abnormality of essential hypertension and leads to a reduction in blood pressure. Clinical studies have shown that lacidipine is highly effective at lowering both systolic as well as diastolic blood pressures in patients with mild to moderate and isolated systolic hypertension (Sheng *et al.*, 2025; Wang *et al.*, 2021a). Additionally, its long duration of action and minimal impact on heart rate make lacidipine a favorable option for long-term management of hypertension, with a low risk of reflex tachycardia and related adverse cardiovascular events. There is vasodilation in several vascular beds, including the coronary arteries, which enhances arterial compliance. Antihypertensive effects of lacidipine are observed 0.5–1.0 h post administration, achieving a maximum between 1 and 3 hours, and persist during and after exercise. The duration of BP lowering after a single dose in the range of 2–4 mg is approximately 4–8 hours, extending to 12 hours with the higher dose of 5 mg, whereas most blood pressures are controlled for a 24-hour period with multiple dosing (Godfraind, 2017) (Figure 2).

5.3.2. Twenty-Four Hour Blood Pressure Control

Lacidipine therapy with a dose of 2–8 mg in the morning provides consistent 24-hour control of blood pressure and significantly lowers BP over 24 hours compared to placebo, according to 24-hour ambulatory BP monitoring, with no effect on circadian rhythms. Whereas the decline in nighttime BP was less pronounced, lacidipine effectively controlled the initial morning rapid increase in BP. In a 16-week randomized, double-blind equivalent comparison between morning and evening administration, it was found that morning dosing is very effective in controlling the circadian blood pressure curve, particularly the morning BP surge, while an evening dose can be added for patients who have a limited or absent nocturnal example of considerable discomfort on urination (Nair *et al.*, 2022). At once-daily lacidipine doses of 2–6 mg, positive placebo-corrected trough-to-peak ratios for both systolic blood pressure and diastolic blood pressure over 65 percent have been reported in many studies; the duration of action is thus suitable for once-daily administration. With lacidipine 4 mg taken once daily for 4 weeks, the mean daytime and nighttime systolic blood pressure and diastolic blood pressure decreased, as well as the average over 24 hours in patients with mild-to-moderate essential hypertension and type 2 diabetes, whereas a reduction of 24-hour systolic blood pressure variability characterizes these diabetic hypertensive subjects exchanged to antihypertensive treatment by long-

acting dihydropyridines during their reproducibility phase (Findeisen *et al.*, 2010). At least one volunteer study, though, has raised doubt about the 24-hour pharmacological activity of the medication. When administered to healthy volunteers as lacidipine 4 mg once daily for 14 days, the maximum pharmacological activity occurred about 2 h after administration; the effect at 6 and 24 h was less pronounced and was not maintained over time (Collier *et al.*, 2024) (Figure 2).

5.3.3. Impacts on Left Ventricular Hypertrophy and Cardiac Function

Left ventricular hypertrophy is a major risk factor for cardiovascular events. Hyperpiesis is associated with changes in left ventricular geometry and performance accompanying hypertrophy. Angiotensin-converting enzyme inhibitors and calcium channel blockers seem to be the major effective antihypertensive drugs that reduce left ventricular hypertrophy (Kim *et al.*, 2022). Several studies have demonstrated that lacidipine either effectively decreases left ventricular mass or improves left ventricular diastolic and systolic function, both at rest and during exercise in hypertensive patients. Accordingly, lacidipine induces a decrease in left ventricular afterload, enhanced flow rate, and higher left ventricular ejection fraction (Oh & Cho, 2020) (Figure 2).

5.3.4. Anti-Atherosclerotic Activity

Platelets play an important role in the process of atherosclerosis. Adhesion and aggregation of thrombocytes are also involved in early endothelial damage, as well as atherosclerotic plaque formation. These functions are mediated or regulated by eicosanoids. It has been demonstrated that calcium antagonists, particularly dihydropyridines, may slow the development of atherosclerotic lesion progression (Wang & Tang, 2020b). Atherosclerosis is a chronic and progressive vascular disease induced by endothelial dysfunction, clinically presenting as coronary artery disease. High levels of plasma cholesterol and hypertension are identified as the major risk factors for atherosclerosis. The progression of this condition involves a series of events, starting with the infiltration of monocytes and macrophages into the injured vascular wall, followed by their transformation into cholesterol-laden foam cells—a process largely driven by oxidized low-density lipoproteins (LDL) (Patial *et al.*, 2024). Evidence suggests that the antioxidant properties and calcium channel-blocking effects of lacidipine may play a protective role by disrupting early mechanisms within this cascade that ultimately lead to atherosclerotic plaque formation. Findings from both in vitro and animal studies indicate that lacidipine decreases levels of pro-inflammatory oxidized LDL, suppresses the upregulation of adhesion molecules, and inhibits cholesterol esterification in macrophages (Hatamian *et al.*, 2025) (Figure 2).

5.4. Renoprotective Potential and Clinical Outcomes

Collectively, calcium channel inhibitors seem to have favourable impacts on renal function, as they lower blood pressure rapidly and effectively and dilate the preglomerular arterioles in animal models, causing increases in renal plasma flow and leading to an overall increase in renal blood flow through reduction of renal vascular resistance, which has direct natriuretic and diuretic effects, with maximal impact seen for any class of drug among the dihydropyridines. Renal hemodynamics may be influenced by calcium antagonists through the blockade of renal vasoconstrictors, thereby reducing total peripheral resistance and improving systemic as well as intrarenal circulation. The renal response, in terms of GFR and renal plasma flow, seems to be dependent both on the nature of the vasoconstrictor present as well as the basal tone of the renal vasculature (Scholtes *et al.*, 2021). A potential drawback is that most calcium antagonists selectively dilate afferent renal arterioles rather than efferent renal arterioles. If pressure was inadequately lowered, it potentially would lead to an increase in glomerular pressure, promoting proteinuria as well as disease progression rather than nephroprotection. Mild-to-moderate hypertensive patients showed an increase in blood pressure over time. However, appropriate blood pressure control with calcium antagonists may contribute to reduction of glomerular hyperfiltration, thereby limiting pressure-mediated renal injury. The beneficial renal protective role of calcium antagonists is supported by evidence that chronic treatment with these drugs in patients afflicted with nephropathy is associated with preserved renal function (Lin *et al.*, 2022). Amlodipine is less effective than the ACE inhibitor ramipril for slowing the rate of progression of hypertensive kidney disease in African Americans and less effective than the angiotensin II receptor antagonist irbesartan for slowing the progression of nephropathy in type 2 diabetic hypertensive patients. Lacidipine has been demonstrated to significantly enhance renal plasma flow, both following a single oral dose and during chronic treatment, when compared with placebo in hypertensive patients with normal renal function and without the fluid retention observed after administration of conventional vasodilators such as hydralazine. In a study of 41 hypertensive patients with chronic renal failure not on antihypertensive treatment, the addition of lacidipine 4 mg/day for six months to established therapy increased GFR. GFR increased after 6 months from 43 mL/min to 48.4 mL/min (Pugh *et al.*, 2019) (Figure 3).

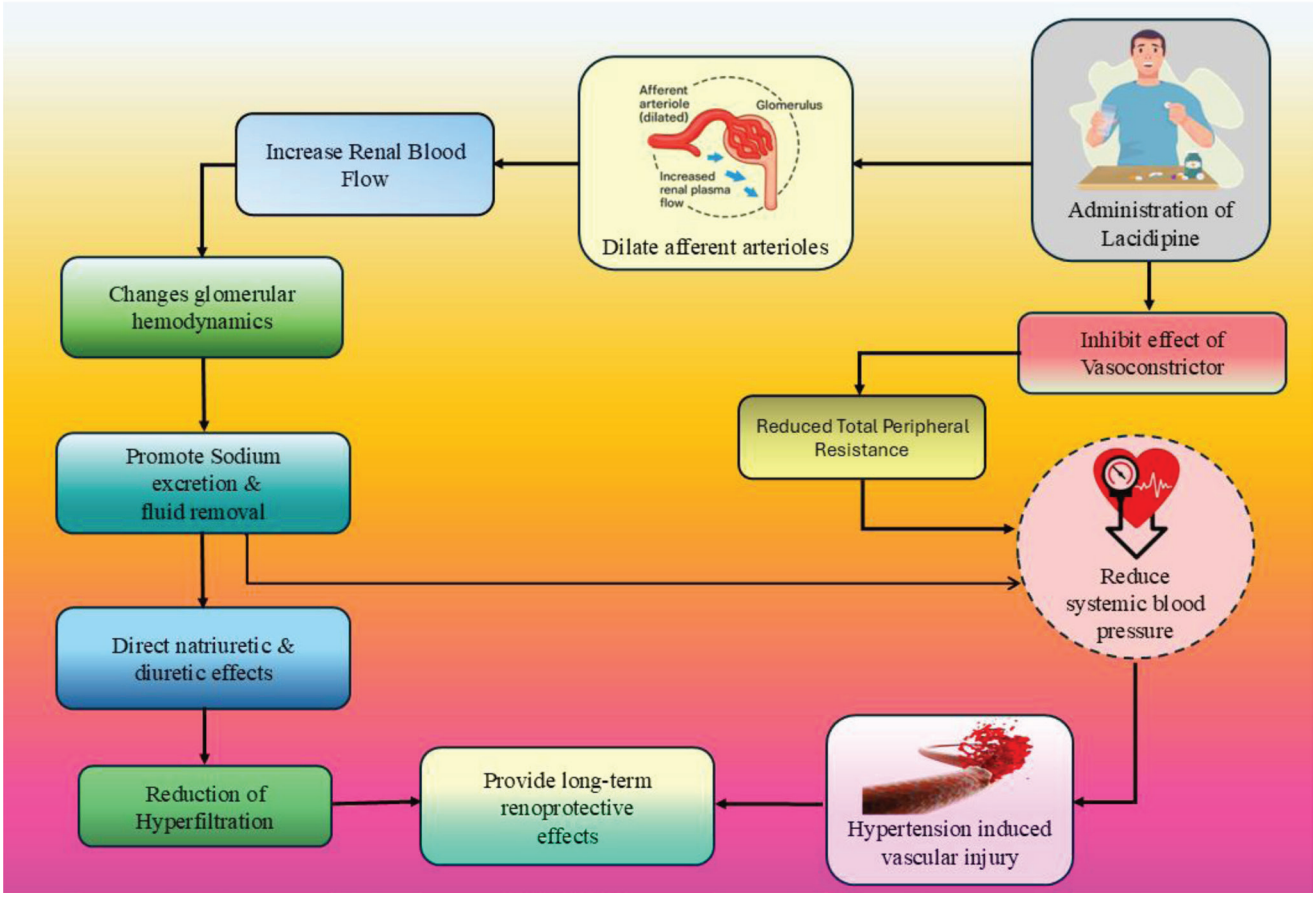

Figure 3: Illustration of Lacidipine-Mediated Renoprotective Mechanisms Regulating Renal Hemodynamics, Sodium Excretion, and Blood Pressure under Hypertensive Conditions

6. Clinical Trials and Patent Profile

Lacidipine has been extensively evaluated in clinical trials across diverse hypertensive populations, including patients with isolated systolic hypertension, diabetes-associated hypertension, stable angina, and elderly individuals. In addition, several patents highlight its therapeutic potential in cardiovascular and vascular remodeling disorders. An overview of completed and ongoing clinical trials, as well as key patents related to lacidipine, is presented in Table 2 and Table 3.

Table 2: Detailed Clinical Trials of Lacidipine

S. No.	Clinical Trials / Patent	Disease Name	Treatment	Study Design	Phase	Outcome Measure	NCT No
1	The efficacy and safety of lacidipine and amlodipine in hypertensive adult patients	Hypertension	Lacidipine 4 mg or 6 mg	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Parallel assignment	IV	Primary: Efficacy of lacidipine on blood pressure profiles; Secondary: Compare overall safety of amlodipine and lacidipine in reported adverse events	NCT00338338

2	Lacidipine in mild to moderate essential hypertension patients with type 2 diabetes in Korea	Type 2 Diabetes Mellitus	Lacidipine 2, 4, 6 mg	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Single group assignment	IV	Primary: Clinical effectiveness on elevated SBP; Secondary: Effect on elevated DBP and endothelial function	NCT00328965
3	Efficacy and safety of lacidipine in chronic stable angina	Angina Pectoris	Lacidipine low, medium, and high doses	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Parallel assignment	II	Primary: Change in total treadmill exercise duration; Secondary: Change in time to ST segment and frequency of anginal attacks	NCT02232607
4	Tolerability and pharmacokinetics of lacidipine with and without co-administration of telmisartan in healthy subjects	Healthy Subjects	Lacidipine 6 mg	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Crossover assignment	I	Primary: Changes in vital signs and laboratory parameters	NCT02203500
5	Influence of Telmisartan and Lacidipine, Combined or Alone, on QT Interval in Healthy Volunteers	Healthy Subjects	Lacidipine high and low dose	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Parallel assignment	I	Primary: Change in QT interval; Secondary: Change in PQ, QRS, and RR interval	NCT02264158
6	Efficacy and safety of lacidipine and amlodipine on blood pressure in Korean ISH patients aged 60–80 years (ELDER)	Hypertension	Lacidipine	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Parallel assignment	IV	Primary: Change from baseline in mean SBP; Secondary: Change in mean DBP and CRP	NCT00460915
7	Lacidipine in medical practice in patients with mild to moderate essential hypertension	Hypertension	Lacidipine	Primary Purpose: Treatment; Allocation: N/A; Interventional Model: Single group assignment	III	Primary: Number of patients with adverse drug reactions; Secondary: Change in serum glutamic oxaloacetic transaminase and SBP	NCT02177331
8	Observation of the efficacy and tolerance of Motens (Lacidipine) in patients with essential hypertension	Hypertension	Lacidipine	Not Specified	Not Specified	Primary: Investigator assessment of efficacy on a 4-point verbal rating scale based on BP change	NCT02235415

9	Tolerability and pharmacokinetics of telmisartan in combination with lacidipine in healthy male subjects	N/A	Lacidipine	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Parallel assignment	I	Primary: Number of subjects with adverse events; Secondary: Complete investigation of AUC, tmax, CL/F and MRT	NCT02218684
10	A Randomized, Parallel-Group, Double-Blind, Double-Dummy Study to Compare the Effects of Lacidipine Versus Bendrofluazide on Markers of Platelet Activation and Hemorheological Factors in Hypertensive Patients	N/A	Lacidipine and Bendrofluazide	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Parallel assignment	IV	Primary: Changes in β-TG; Secondary: Changes in p-selectin, rheological factors, and lipid levels	NCT02235402
11	Bioavailability of Lacidipine and Telmisartan Fixed-Dose Combination Tablets Relative to Separate Tablets in Healthy Subjects	N/A	Lacidipine and Telmisartan	Primary Purpose: Treatment; Allocation: Randomized; Interventional Model: Crossover assignment	I	Primary: Number of patients with adverse events, abnormal findings in physical examination, and clinically relevant ECG changes	NCT02209649
12	IMI PROTECT (Work package 2): Calcium channel blockers and cancer	Hypertension	Calcium Channel Blockers	Time Perspective: Retrospective	Not Specified	Primary: Changes in incidence of primary cancer cases; Secondary: Changes in incidence of breast, prostate, and colon cancer cases	NCT01587742

Table 3: Detailed Patent Profile of Lacidipine

S. No.	Patent	Disease Name	Treatment	Objective	Status	Key Findings	Patent Number
1	Lacidipine for the treatment of arteriosclerosis	Arteriosclerosis	Lacidipine	Establish the use of lacidipine, a calcium channel blocker, for the treatment and prevention of arteriosclerosis in mammals, particularly humans.	Granted	Lacidipine reduces vascular smooth muscle calcium influx and shows anti-arteriosclerotic activity, demonstrated by reduced cholesterol esterification in macrophages and decreased plaque formation in cholesterol-fed rabbits, suggesting therapeutic potential for atherosclerosis and related cardiovascular disorders.	US5455257A

2	Lacidipine Particles	Hypertension	Lacidipine	Develop novel compounds and pharmaceutical compositions designed to modulate cannabinoid receptor activity, for treating neurological, psychiatric, metabolic, and inflammatory conditions.	Granted	Identifies new chemical entities that act as cannabinoid receptor ligands, demonstrating potential therapeutic value in managing obesity, diabetes, anxiety, depression, neurodegeneration, and inflammatory disorders.	WO2006113309A1
3	Pharmaceutical composition comprising lacidipine and process of preparation	–	Lacidipine	Describe a pharmaceutical composition containing lacidipine and its preparation process, aimed at improving oral bioavailability and consistent pharmacokinetic performance in hypertension treatment.	Granted	By optimizing the lacidipine:polyvinylpyrrolidone ratio (~1:9), the invention controls drug absorption (Cmax) without altering dissolution, yielding tablets that meet bioequivalence with reference drugs, ensuring therapeutic effectiveness and reduced variability.	EP2705839B1
4	Medicaments for the treatment of hypertension	Hypertension	Lacidipine & Telmisartan	Disclose a pharmaceutical composition comprising lacidipine (calcium antagonist) and telmisartan (angiotensin-II antagonist) or derivatives, for synergistic antihypertensive treatment.	Granted	In spontaneously hypertensive rats, the lacidipine-telmisartan combination (0.2 mg/kg + 0.3–1 mg/kg) achieved synergistic reductions in mean BP (-30.5%) and diastolic BP over 24 hours, exceeding individual drug effects, without significant heart rate increase, and prolonged action up to 24 hours.	US6071939A

7. Side Effects

Like other medications, this drug may cause adverse effects; however, they do not occur in everyone. Angina is commonly associated with chest pain. This is uncommon in people using lacidipine and probably occurs when starting this medicine. The side effects of lacidipine are divided based on their frequency, such as very common, which may affect more than 1 in 10 individuals; common side effects, which may include dizziness, headache, palpitations, flushing, swelling (particularly of the ankles), stomach upset, nausea, rash, redness of skin, itching, increased urination, asthenia, and changes in results of blood test parameters (changes mostly seen in liver function tests), may affect up to 1 in 10 people, and the side effects usually resolve as treatment continues. Compared to other dihydropyridine calcium channel blockers, such as amlodipine and nifedipine, lacidipine is similarly well tolerated. However, studies suggest an important difference in safety with lacidipine, namely that some studies have reported the incidence of pedal edema is significantly less with lacidipine (with a SUCRA ranking of 12.8%) when compared to nifedipine,

which is ranked most likely to cause peripheral edema (SUCRA 81.8%) (Wang *et al.*, 2021). Moreover, lacidipine shows a lower overall incidence of side effects than the beta-blocker atenolol but produces more vasodilatory effects than the diuretic hydrochlorothiazide (Zanchetti *et al.*, 2002). Uncommon side effects, including worsened anginal symptoms, low blood pressure associated with fainting, and swelling of gums, are seen in up to 1 in 100 people. Rare side effects are associated with rapid swelling of the face, mouth, and throat, which also causes difficulty in breathing, urticaria, and muscle cramps, and may impact up to 1 in 1000 people. Very rare side effects may be associated with tremor and depression and affect up to 1 in 10000 people (Finlay *et al.*, 2022; Kotruchin *et al.*, 2021).

8. Toxicity and Tolerability

There have been no reports of people overdosing on lacidipine tablets. Excessive use can result in symptoms such as prolonged peripheral vasodilation, hypotension, and tachycardia. Theoretical possibilities include bradycardia or prolonged AV conduction. Because there is no known antidote for lacidipine, standard general cardiac function monitoring, as well as appropriate supportive and therapeutic measures, is advised. The oral LD50 in mice, rabbits, and rats is 300 mg/kg, 3200 mg/kg, and 980 mg/kg, respectively, according to the MSDS (Baid *et al.*, 2023; Isbister *et al.*, 2025). Lacidipine usually has a similar tolerability profile to other dihydropyridine calcium blockers, but in some studies, the frequency of pedal edema was found to be lower with lacidipine than with other dihydropyridine calcium antagonists. The most common side effects are headache, flushing, pedal edema, dizziness, and palpitations, all of which result from the vasodilatory action of the drug. About 32% of patients, roughly, in controlled therapeutic trials reported adverse events. These adverse events are more frequent during the first six months of therapy and less frequent thereafter. Lacidipine has certain safety advantages compared to other major classes of antihypertensives. It does not produce the persistent dry cough seen with ACE inhibitors such as enalapril and ramipril, which occurs in up to 20% of patients (Liang *et al.*, 2022). Moreover, in contrast to atenolol or other beta-blockers, lacidipine does not substantially lower heart rate, making it a preferred drug in patients with bradycardia (United Kingdom Lacidipine Study Group, 1991). The ELSA study examined serious adverse events and demonstrated that lacidipine has a safety profile similar to atenolol over 4 years. The Northern Italian Study Group confirmed that lacidipine has a tolerability similar to that of slow release nifedipine but with a lower incidence of tachycardia and ankle swelling in diabetics (Liang *et al.*, 2022; Zanchetti *et al.*, 2002).

9. Future Directions and Challenges

Although lacidipine is clearly established as an effective antihypertensive drug with added vascular and metabolic effects, its extensive therapeutic role is yet to be fully explored. Future studies should aim to extend evidence beyond blood pressure management and assess lacidipine in areas such as neuroprotection, renal protection, and metabolic control (Felkle *et al.*, 2022). Preclinical evidence already points to protective functions against oxidative stress, endothelial dysfunction, and atherosclerotic remodeling, but large-scale randomized clinical trials are required to confirm these advantages in heterogeneous patient populations. Another potential future direction is to investigate the role of lacidipine in conditions not related to cardiovascular disease (Li *et al.*, 2025). Recent data suggest possible applications in neurodegenerative disorders, such as Alzheimer's disease, and in metabolic disorders, such as insulin resistance and diabetes. Similarly, its documented anti-inflammatory and anti-infective properties present opportunities for investigating new therapeutic uses. The incorporation of lacidipine into multimodal therapy regimes combining standard antihypertensive treatment with disease-modifying advantages may increase its clinical applicability (Torres-Rico *et al.*, 2024). On the drug development side, progress in drug delivery and formulation can further improve lacidipine's performance. Due to its strong lipophilicity and membrane affinity, novel delivery platforms such as nanocarriers or sustained-release systems could enhance bioavailability, reduce adverse effects, and expand therapeutic windows (Ezike *et al.*, 2023). Some challenges also need to be overcome. First, long-term safety experience in special populations such as patients with chronic kidney disease or heart failure is still limited. Second, the variability of drug metabolism via CYP3A4 and P-glycoprotein mechanisms carries the risk of drug-drug and food-drug interactions that must be carefully controlled. Third, although it has promising pleiotropic effects, lacidipine is not yet approved universally across all markets, including the United States, which limits wide access and comparative studies (Zhang *et al.*, 2024). Lastly, head-to-head comparisons with newer antihypertensives and combination therapy are needed to place lacidipine appropriately in contemporary treatment protocols. Overall, the way forward for lacidipine research will be to bring mechanistic understanding together with translation and clinical application. Filling these gaps will establish whether lacidipine's pleiotropic effects can be leveraged to transcend hypertension treatment toward more widespread cardiovascular, renal, and neuroprotective uses (Rossi *et al.*, 2002).

10. Conclusion

Lacidipine is more than a well-proven antihypertensive agent. Its pharmacological profile includes vascular selectivity, prolonged blood pressure control, and effective antioxidant activity, and its benefits extend to cardiovascular, cerebrovascular, renal, and even metabolic areas. Preclinical and clinical data identify its potency in the prevention of endothelial dysfunction, vascular remodeling, and oxidative stress-induced damage, and thus indicate therapeutic efficacy in stroke, Alzheimer's disease, diabetic neuropathies and retinopathies, and renal failure. In spite of these promising results, the manifestation of lacidipine's pleiotropic effects in durable clinical practice is yet to be achieved. Large-scale, well-controlled trials are expected to elucidate its long-term effects on neurovascular outcomes, renal protection, and metabolic status. Additionally, knowledge of its role relative to newer generation antihypertensives and its use within combination therapy will be critical to establish its position in contemporary management protocols. Collectively, lacidipine appears to be a multifaceted therapeutic prospect superior to traditional blood pressure reduction. By crossing mechanistic grounds with clinical proof, subsequent studies can ascertain the possibility of repositioning lacidipine as a multi-target agent with the capability of treating the complex burden of cardiovascular, renal, and neurodegenerative disease.

Abbreviations

LCD: Lacidipine; **DHP**: Dihydropyridine; **Ca^{2-}**: Calcium ion; **ROS**: Reactive Oxygen Species; **BP**: Blood Pressure; **DBP**: Diastolic Blood Pressure; **SBP**: Systolic Blood Pressure; **ACE**: Angiotensin-Converting Enzyme; **ARB**: Angiotensin II Receptor Blocker; **ADHF**: Acute Decompensated Heart Failure; **AMI**: Acute Myocardial Infarction; **AV**: Atrioventricular; **SA**: Sinoatrial; **C/EBP-β**: CCAAT/ Enhancer Binding Protein Beta; **MAPK**: Mitogen-Activated Protein Kinase; **CXCR7**: C-X-C Chemokine Receptor Type 7; **GFR**: Glomerular Filtration Rate; **RPF**: Renal Plasma Flow; **LDL**: Low-Density Lipoprotein; **NO**: Nitric Oxide; **AChE**: Acetylcholinesterase; **AD**: Alzheimer's Disease; **CCB**: Calcium Channel Blocker; **Syst-Eur**: Systolic Hypertension in Europe Study; **INSIGHT**: Intervention as a Goal in Hypertension Treatment Study; **LD_{50}**: Median Lethal Dose.

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Authorship Contribution

Prabir Maity and Soumarshi Das conceived and designed the manuscript, conducted the literature review, performed data compilation and interpretation, prepared figures, and drafted the manuscript. Anjali Sharma assisted with data extraction, reference organization, and initial manuscript editing. Sarita Jangra provided overall supervision and expert guidance, critically reviewed the manuscript, and approved the final version for submission.

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise, related to this work.

Data Availability Statement

The authors declare that data sharing is not relevant to this article as no new data were generated or analyzed in this study.

Declarations

The authors declare that this manuscript is original, has not been published previously, and is not under consideration for publication elsewhere. All authors have contributed significantly and consent to publication in the present journal.

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