

Targeted Delivery of Losartan Using a Biodegradable Polymeric Nanocarrier for the Management of Hypertension-Associated Vascular Remodeling

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Abstract

Background: Hypertension manifests through endothelial dysfunction, oxidative stress, and vascular remodeling. Angiotensin II–AT1 receptor signaling contributes to these processes, supporting the role of angiotensin-receptor blockade in vascular disease management. Losartan is an established AT1 receptor blocker, while biodegradable polymeric nanocarriers may allow for extended drug release and altered pharmacokinetics. [1,3,4]

Objective: The present study aims to characterize antihypertensive treatment patterns and record vascular or cardiovascular findings among 120 patients with hypertension who received care in selected tertiary-care hospitals in Punjab, Pakistan. This observational study will also establish the framework for subsequent evaluation of a losartan-loaded biodegradable polymeric nanocarrier.

Methods: The observational part of this study will involve retrospective extraction of demographical, blood-pressure, comorbidity, laboratory, prescription, treatment modification, adherence, and vascular or cardiovascular imaging data. A prospective experimental program will also be designed, which will entail formulation and characterization of a biodegradable losartan nanocarrier,

followed by in-vitro release trials, pharmacokinetic assessment, and safety and efficacy studies prior to clinical investigations.

Results: Please note that the results section cannot be generated without the actual data extracted from the 120 patient records. For this reason, the present manuscript provides the framework for observational analyses without presenting hypothetical findings. Similarly, the proposed biodegradable nanocarrier for losartan delivery is a

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concept that requires extensive preclinical and clinical investigations before safety and efficacy can be established.

Conclusion: Hospital records represent a valuable source of real-world evidence regarding treatment patterns and clinical outcomes associated with specific therapeutic approaches. The present study will generate practice-level insights and support the design of a future nanomedicine program for hypertension. Specifically, a biodegradable polymeric nanocarrier for losartan delivery will require extensive physicochemical, toxicological, pharmacokinetic, preclinical, and clinical evaluations before it can be considered a viable therapeutic option.

Introduction

Hypertension is a major cardiovascular risk factor associated with progressive vascular and target-organ changes. Persistent elevation of blood pressure can lead to endothelial dysfunction, altered vascular smooth-muscle behavior, oxidative stress and structural remodeling. The renin–angiotensin–aldosterone system plays an important role in this process, because angiotensin II signaling through the AT1 receptor promotes vasoconstriction and contributes to inflammatory, oxidative and remodeling responses. [1,2] Losartan is an established angiotensin II receptor blocker, which is used clinically in several cardiovascular and renal conditions. Experimental and clinical studies have also investigated effects of AT1-receptor blockade on endothelial function and vascular remodeling. However, these observations do not imply a clinical indication for losartan in a vascular-remodeling research programme, whereas the role of conventional losartan therapy remains distinct from any proposed experimental nanoparticle formulation. [1,3,4]

Hypertension guidelines now suggest the use of a range of evidence-based antihypertensive drug classes, including angiotensin-receptor blockers, angiotensin-converting enzyme inhibitors, calcium-channel blockers and thiazide or thiazide-like diuretics. Choice of treatment depends on blood pressure, comorbidities, kidney function, cardiovascular risk, tolerability and other patient-specific factors. Consequently, real-world hospital records can provide valuable insights into the therapies actually used, as well as the clinical characteristics of treated patients. [1,2] Nanomedicine provides the opportunity to modulate drug distribution, protect an active pharmaceutical ingredient, control release and modify pharmacokinetic exposure. Biodegradable polymers such as poly (lactic-co-glycolic acid), commonly abbreviated PLGA, have been extensively investigated for controlled drug delivery, and a losartan nanoparticle formulation has also been described experimentally using a natural polymeric material. However, these experimental findings do not establish clinical efficacy or safety in humans. [5,6] [6,8]

Research Gap and Rationale

Clinical management of hypertension is well established, but there remains a research opportunity to investigate whether controlled delivery of an established antihypertensive agent can produce pharmacokinetic or tissue-exposure advantages that are relevant to vascular remodeling. A locally generated hospital dataset can first describe the existing treatment landscape in the target population. These observations can then be used to define clinically meaningful endpoints for a future nanocarrier programme.

The rationale for the proposed programme is therefore sequential: first, document real-world treatment and clinical characteristics; second, develop and characterize a biodegradable losartan formulation; third, establish pharmacokinetic and safety behavior in preclinical models; and finally, if the preceding evidence supports progression, evaluate the formulation prospectively in an ethically approved clinical trial.

Objectives

The primary objective is to characterize antihypertensive treatment patterns and clinical characteristics among 120 adult patients with documented hypertension treated in selected tertiary-care hospitals in Punjab, Pakistan. Secondary objectives are to describe commonly used antihypertensive drugs, document blood-pressure control, characterize available renal and metabolic investigations, identify documented vascular or cardiovascular complications, and establish a research framework for future development of a losartan-loaded biodegradable polymeric nanocarrier.

Materials and Methods

Study design and setting

The clinical component will involve carrying out a retrospective observational hospital-record study among 120 adult patients diagnosed with hypertension. The research can be conducted in selected tertiary-care hospitals in Punjab, Pakistan, subject to obtaining the necessary permissions and consents from the relevant authorities to review the records. The specific hospitals, departments, and time frame for the study should be stated based on the research protocol and approvals from the participating institutions.

Participants

Eligible participants should be adults aged 18 years or older with a documented diagnosis of hypertension, at least one recorded blood-pressure measurement and an available prescription or treatment plan. Records may be excluded when the diagnosis cannot be verified, essential outcome information is unavailable, or the record falls outside the prespecified study period. Pregnancy and acute hypertensive emergencies may be excluded if they are outside the intended study population.

Data collection

Data has to be extracted using a case-record form standardized across the study. The form should capture age, sex, and body mass index of the participants. Clinical data includes the patients' hypertension duration, systolic and diastolic blood pressure, relevant comorbidities and cardiovascular history. Lab results should report serum creatinine, the estimated filtered glomerular rate, potassium, glucose or HbA1c, and lipid measurements if documented. The prescriptions should state the generic drug name, dose, frequency and duration if available, combination treatment, and documented changes in therapy.

Clinical variables

The data collection form should indicate whether a variable was measured or documented clinically. Blood pressure should be recorded verbatim and include the date and whether it was taken at admission, during follow-up, or after treatment modification. If several measurements are available, the protocol should prespecify whether the first valid measurement, the most recent measurement, or an averaged value will be used for a specific analysis. Hypertension-mediated organ damage should not be inferred based on the presence of hypertension alone; it should be coded only if supported by the medical record, laboratory result or imaging report. [1] For every antihypertensive prescription, the investigator should record the generic name, strength, dose, frequency, route where relevant, approximate duration if documented, and whether the drug was continued, discontinued or changed during follow-up. Combination therapy should be coded by its individual components so that the frequency of each pharmacological class can be calculated without double-counting patients. When adherence is discussed, the analysis should distinguish documented non-adherence from absence of adherence information; missing documentation should not automatically be classified as non-adherence.

Laboratory and imaging extraction

Laboratory variables should be copied from the relevant laboratory report with units preserved and reference ranges retained where clinically relevant. Renal function is particularly important when evaluating RAAS-blocking medicines because creatinine, estimated glomerular filtration rate and potassium may influence prescribing and monitoring. Vascular or cardiac imaging should be recorded only when an interpretable report

is available. The type of imaging, date, principal finding and whether the finding was considered clinically relevant should be captured in a structured format.

Quality control and data management

A standardized extraction sheet should be piloted on a small number of records before full data collection. Where feasible, a second reviewer should independently verify a sample of extracted records against the source files. Discrepancies should be resolved by returning to the original hospital record rather than by consensus based on memory. The final dataset should contain a data dictionary defining each variable, its permitted values and the coding of missing or unavailable information. These procedures are intended to improve reproducibility and reduce transcription error.

Retrospective use of patient records requires approval from the relevant institutional ethics or review committee and permission from the participating hospital. Only variables necessary for the research objectives should be extracted, and personal identifiers should be removed or replaced by study codes in the analytical dataset. If the future nanoparticle study proceeds to human research, it would require a separate prospective protocol, informed consent where applicable, independent ethical review and compliance with national regulatory requirements. The retrospective record review must therefore not be interpreted as authorization to administer the proposed nanocarrier.

Table 1. Variables to be collected from hospital records

Domain	Variables to extract	Preferred source
Demographics	Age, sex, weight/BMI	Admission record / clinical record
Hypertension	Duration, systolic BP, diastolic BP, documented hypertension stage	Vital signs
Comorbidities	Diabetes, CKD, dyslipidemia, cardiovascular disease, stroke and other documented conditions	Medical history
Renal function	Serum creatinine, eGFR, potassium	Laboratory record
Metabolic profile	Glucose/HbA1c and lipid profile	Laboratory record
Treatment	Drug name, dose, frequency, monotherapy or combination therapy, treatment changes	Prescription / treatment plan
Adherence	Documented adherence or non-adherence	Clinical notes / pharmacy record
Vascular findings	Imaging or documented vascular/cardiovascular complications	Radiology / clinical record

Outcomes	Follow-up BP, adverse effects and relevant hospitalization information	Follow-up record
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Antihypertensive treatment assessment

The treatment analysis should classify medicines according to pharmacological class and should preserve the actual prescription details recorded in the hospital file. The following table is a data-extraction framework rather than a statement that every listed medicine was prescribed to the 120 participants.

Table 2. Antihypertensive medicines to identify during retrospective record extraction [1]

Drug or class	Pharmacological role	Clinical information to record
Losartan	AT1-receptor blockade	Dose, frequency, duration and treatment changes
Telmisartan	AT1-receptor blockade	Dose, frequency, duration and treatment changes
Amlodipine	Dihydropyridine calcium-channel blockade	Dose, frequency and combination therapy
Enalapril	ACE inhibitor	Dose, frequency and treatment changes
Lisinopril	ACE inhibitor	Dose, frequency and treatment changes
Hydrochlorothiazide	Thiazide diuretic	Dose, frequency and combination therapy
Chlorthalidone	Thiazide-like diuretic	Dose, frequency and treatment changes
Bisoprolol	Beta-1 adrenergic blockade	Dose, frequency and indication
Carvedilol	Beta/alpha adrenergic blockade	Dose, frequency and indication
Spirolactone	Mineralocorticoid receptor antagonism	Dose, frequency and indication

Proposed losartan nanocarrier

The proposed formulation is a biodegradable polymeric nano-carrier of losartan. PLGA is an obvious choice of polymer to investigate, due to the polymer's biodegradability and considerable drug-delivery literature. The formulation should be optimized experimentally, rather than assign a predetermined set of performance characteristics. Candidate characteristics could include: particle size, polydispersity, zeta-potential, morphology, drug loading capacity, encapsulation efficiency, an in-vitro release-profile and storage stability. [5,7]

The proposed drug delivery concept should not be framed as direct implantation of nanoparticles into a patient's artery. For hypertension, a more plausible research trajectory would be to demonstrate systemic administration of the validated formulation and investigate biodistribution and vascular exposure. If active targeting is to be investigated, then the targeting-ligand and vascular molecular target must first be validated experimentally. A future formulation might then be investigated for whether controlled losartan-release, would change the pharmacokinetic exposure or tissue distribution to that of conventional losartan.

Table 3. Drug-delivery systems relevant to the proposed research programme.
[5,6,7]

Delivery system	Potential role for losartan	Potential advantage	Evidence/development status
Conventional oral tablet	Established systemic antihypertensive treatment	Established clinical use and simple administration	Clinical
PLGA polymeric nanoparticles	Proposed controlled-release losartan carrier	Biodegradability and tunable release	Preclinical/proposed
Natural-polymer nanoparticles	Experimental losartan delivery	Potential sustained release	Experimental
Targeted polymeric nanoparticles	Proposed vascular-targeting strategy	Potentially altered tissue exposure	Research stage
Liposomal systems	Alternative nanocarrier platform	Potentially altered distribution and release	Experimental
Stimuli-responsive nanoparticles	Potential environment-responsive release	Controlled release under selected conditions	Experimental
Implantable/local depot systems	Future local-release concept	Prolonged release	Experimental

Proposed preclinical development

Before any human administration, the formulation should undergo physicochemical characterization, including particle size distribution, polydispersity index, zeta potential, morphology, drug loading, encapsulation efficiency and stability. Fourier-transform infrared spectroscopy, differential scanning calorimetry and, where appropriate, X-ray diffraction can be used to investigate drug-polymer interactions and physical state. In-vitro release should compare the nanoparticle formulation with free losartan under a validated experimental protocol.

Pharmacokinetic assessment should determine parameters such as maximum concentration, time to maximum concentration, area under the concentration-time curve, elimination half-life, clearance and apparent volume of distribution. Safety studies should evaluate acute and repeated-dose toxicity, hematological and biochemical parameters, inflammatory responses and histopathology. These experiments are necessary because nanoparticle biodistribution and toxicity cannot be assumed from the safety profile of conventional losartan.

Proposed future clinical evaluation

If the formulation demonstrates acceptable physicochemical stability, pharmacokinetics, safety and efficacy in appropriate preclinical models, a prospective randomized clinical trial could be considered following institutional ethics approval and applicable regulatory requirements. A future study could compare a validated nanoparticle formulation with standard losartan therapy using blood-pressure control as a primary clinical outcome and selected vascular, biochemical, safety and adherence outcomes as secondary measures. The sample size should be calculated

from the expected treatment effect and variance rather than automatically using the retrospective sample of 120 participants.

Statistical Analysis

Continuous variables should be presented using mean and standard deviation if approximately normally distributed or median and interquartile range if skewed. Categorical variables should be reported as frequencies and percentages. Comparisons between groups may use independent-samples t-test or Mann-Whitney U test for continuous data and chi-square or Fisher's exact test for categorical data based on distribution and cell counts. Multivariable logistic regression may be employed to explore factors associated with uncontrolled blood pressure with clinically relevant covariates such as age, sex, body mass index, diabetes, chronic kidney disease and treatment regimen. A two-sided significance level of 0.05 may be pre-specified. Handling of missing data should be reported transparently and follow a predefined statistical analysis plan.

Results

The Results section must be populated from the authenticated records of the 120 participants. Because a patient-level dataset was not provided for this manuscript, numerical values have deliberately not been invented. The final manuscript should report participant characteristics, treatment patterns, blood-pressure measurements, laboratory findings, documented vascular findings and follow-up outcomes using the variables defined in Table 1.

For example, the final text should state the actual number and percentage of male and female participants, the actual mean or median age, the distribution of antihypertensive classes, and the proportion of patients with documented BP control. Any association between treatment and outcome should be reported only after statistical analysis of the real dataset, with the corresponding effect estimate, confidence interval and p-value.

Discussion

The proposed study links real-world clinical observation with a translational drug-delivery strategy. The retrospective component can describe how hypertension is managed in the selected hospitals and can identify clinically relevant patterns in medication use, BP control, comorbidities and available vascular findings. These findings may help determine which outcomes are practical for a future prospective study. [1,5,6]

Losartan provides a biologically plausible starting point for the nanocarrier programme because AT1-receptor blockade is established in hypertension and experimental work has examined effects of losartan on vascular remodeling and endothelial function. A biodegradable polymeric carrier could theoretically alter release kinetics and systemic exposure, but improved clinical outcomes cannot be assumed from the existence of a nanoparticle formulation. [3,4,6]

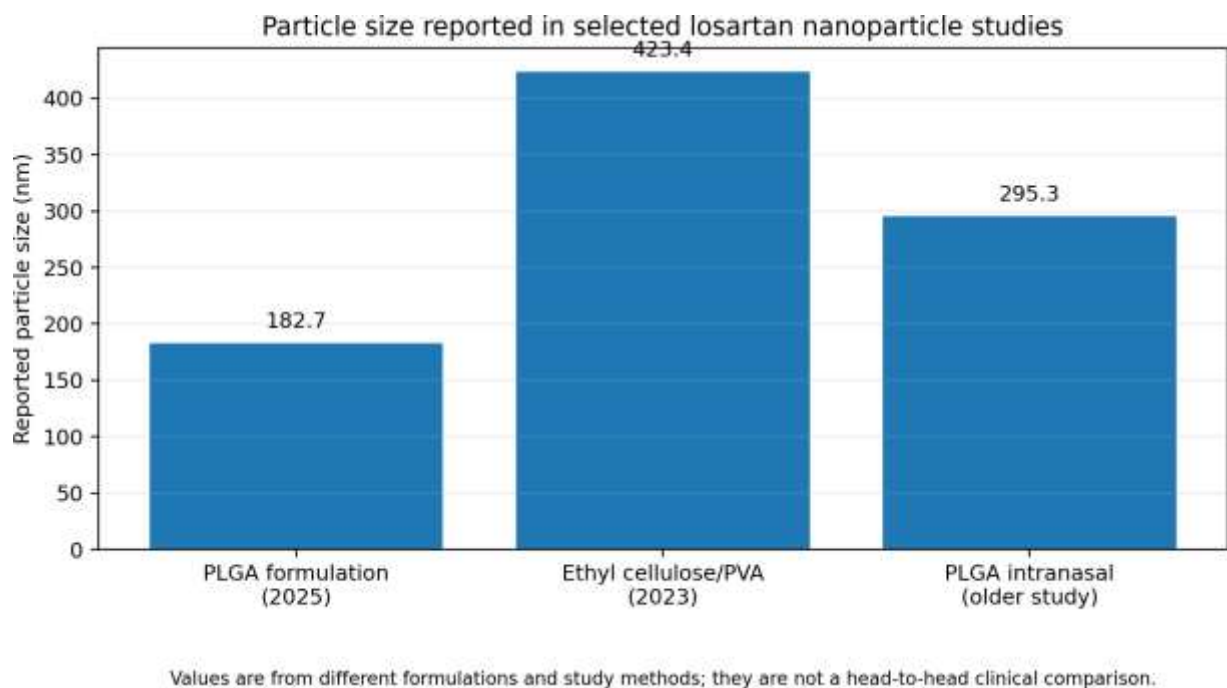


Figure 2. Reported particle sizes in selected losartan nanoparticle studies. Values are literature-derived and are not clinical patient data; differences in formulation and methods prevent direct head-to-head comparison. [6–8]

The literature demonstrates that losartan nanoparticle size is formulation-dependent rather than fixed. A 2025 PLGA-based formulation reported a mean particle size of 182.7 nm, while a 2023 ethyl-cellulose/PVA formulation reported 423.4 nm and an earlier PLGA intranasal study reported 295.3 nm. These values illustrate the range achievable through different formulation strategies, but they should not be interpreted as evidence that one formulation is clinically superior. For the proposed Punjab hospital research programme, particle size would be a formulation-development endpoint, whereas BP control and vascular outcomes would remain clinical endpoints. [6,8]

The major translational challenge is therefore not simply producing nanoparticles, but demonstrating reproducible manufacturing, physicochemical stability, appropriate biodistribution, acceptable toxicity, predictable pharmacokinetics and clinically meaningful benefit. The proposed research sequence is designed to address these questions progressively rather than moving directly from hospital records to human nanoparticle administration. [5,6,7]

Limitations

The retrospective design may be affected by missing documentation, inconsistent follow-up and selection bias. Patients treated in selected tertiary-care hospitals may not represent all hypertensive adults in Punjab or Pakistan. Vascular-remodeling measurements may also be unavailable in routine records. Medication adherence may be incompletely documented, and retrospective associations cannot establish causality. The proposed nanoparticle intervention is investigational; its safety, vascular targeting, pharmacokinetics and therapeutic efficacy require dedicated experimental validation.

Conclusion

A carefully conducted hospital-record study of 120 genuine patients can provide a useful description of antihypertensive treatment and clinical characteristics in the selected Punjab hospitals. Losartan and biodegradable polymeric nanocarriers provide a scientifically reasonable basis for a future translational programme, but

nanoparticle treatment should remain clearly separated from the retrospective clinical dataset. Progression toward human testing should occur only after formulation characterization, preclinical efficacy and safety assessment, appropriate ethical review and regulatory authorization.

Research Flow Diagram

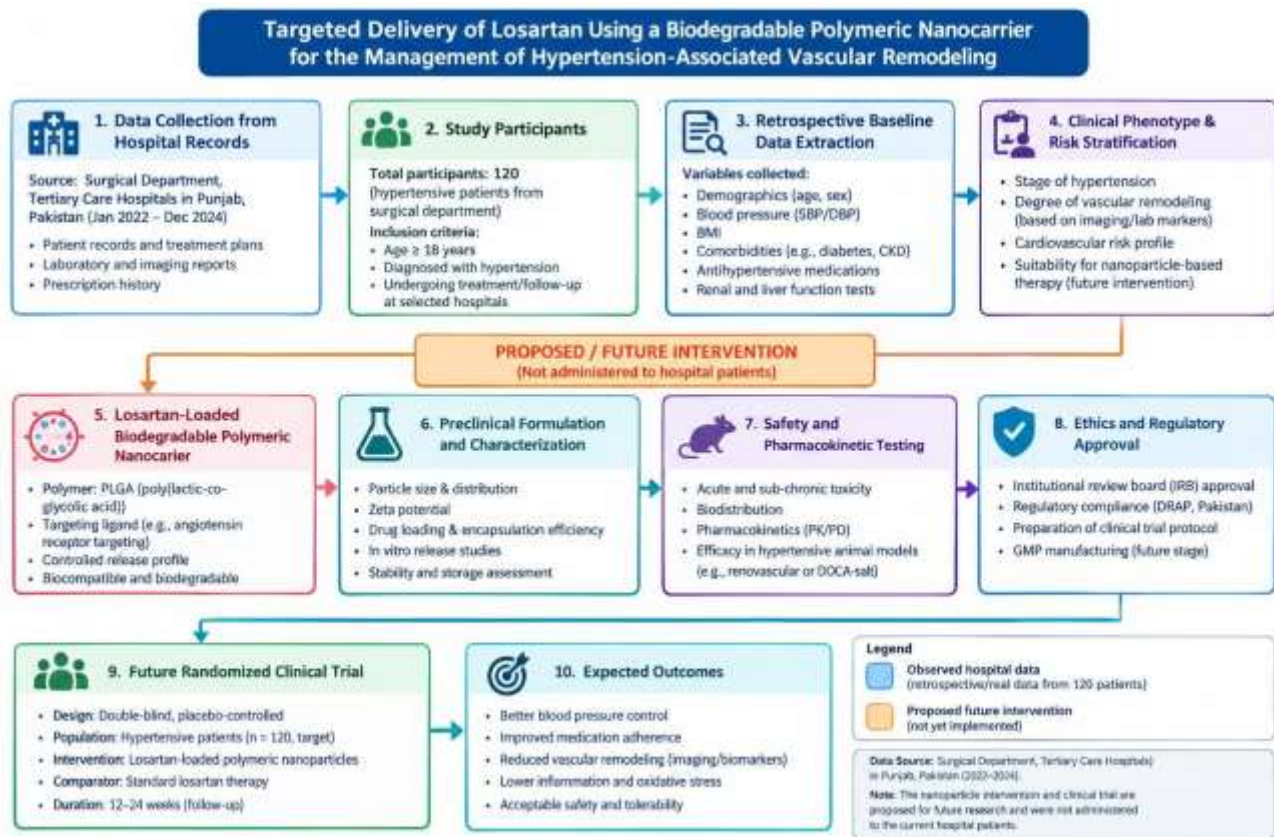


Figure 1. Proposed research pathway separating observed retrospective hospital data from the proposed future nanoparticle intervention.

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