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DEVELOPMENT OF ROBUST NANOSTRUCTURED LIPID CARRIER SYSTEMS FOR ENHANCED THERAPEUTIC DELIVERY IN HYPERTENSION

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ABSTRACT

Hypertension is a major chronic cardiovascular disorder and an important risk factor for myocardial infarction, stroke, heart failure, renal dysfunction, and other cardiovascular complications. Although several antihypertensive drugs are clinically effective, conventional oral dosage forms may be associated with poor aqueous solubility, low and variable bioavailability, extensive first-pass metabolism, rapid elimination, and frequent dosing requirements. These limitations can affect therapeutic consistency and patient adherence, creating a need for advanced drug-delivery approaches. Nanostructured lipid carriers (NLCs), composed of a mixture of solid and liquid lipids stabilized by suitable surfactants, have emerged as promising lipid-based nanocarriers for improving the delivery of poorly soluble and bioavailability-limited therapeutic agents. The present research focuses on the development of robust NLC systems for enhanced therapeutic delivery in hypertension. A systematic formulation-development strategy can be employed to select suitable solid lipids, liquid lipids, surfactants, and process parameters. Quality by Design (QbD) principles may be integrated into development to identify critical material attributes and critical process parameters and to establish a robust design space. The developed NLC formulations can be

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characterized for particle size, polydispersity index, zeta potential, morphology, entrapment efficiency, drug loading, crystallinity, compatibility, in-vitro drug release, and physical stability. Differential scanning calorimetry (DSC), Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), and microscopic techniques can provide information regarding drug–excipient compatibility and the physicochemical characteristics of the nanocarriers. In-vitro release and pharmacokinetic investigations can subsequently be used to assess the ability of the optimized formulation to improve drug exposure and provide sustained therapeutic delivery. A robust NLC platform may enhance solubility, protect the incorporated drug from degradation, prolong drug release, and potentially improve oral bioavailability. Thus, NLC-based delivery represents a promising strategy for overcoming limitations associated with conventional antihypertensive therapy and developing more effective and patient-friendly treatment systems.

Keywords: **-** Hypertension, Nanostructured Lipid Carriers, lipid nanoparticles, antihypertensive drugs, drug delivery, bioavailability, sustained release, Quality by Design, pharmacokinetics.

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I. INTRODUCTION

Hypertension is one of the most prevalent chronic diseases worldwide and represents a major public-health challenge. Persistent elevation of arterial blood pressure increases the risk of cardiovascular, cerebrovascular, and renal complications. Effective management generally requires long-term pharmacotherapy, and several therapeutic classes, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium-channel blockers, β-blockers, and diuretics, are available for clinical use. Despite the effectiveness of these medicines, conventional drug-delivery systems do not always provide optimal therapeutic performance. Factors such as poor aqueous solubility, limited gastrointestinal absorption, extensive hepatic first-pass metabolism, short biological half-life, chemical instability, and variable pharmacokinetics can restrict the bioavailability of certain antihypertensive drugs.

Lipid-based nanocarrier systems have attracted considerable attention because they can modify the physicochemical and biopharmaceutical properties of incorporated drugs. Among these systems, nanostructured lipid carriers are particularly promising because they combine the advantages of solid lipid nanoparticles with those of liquid lipid-based systems. NLCs generally consist of a solid lipid matrix containing a controlled proportion of liquid lipid. The incorporation of liquid lipid produces imperfections within the lipid matrix, allowing greater drug accommodation than a highly ordered solid lipid matrix. Consequently, NLCs can provide improved drug loading, enhanced encapsulation, controlled drug release, and improved stability.

The development of NLCs for antihypertensive therapy is especially relevant for drugs with poor water solubility or absorption limitations. Encapsulation within a lipid matrix may improve drug solubilization in the gastrointestinal environment and facilitate absorption. Depending on the formulation and drug characteristics, lipid nanoparticles may also influence intestinal transport and reduce limitations associated with conventional drug dissolution. Furthermore, sustained drug release from NLCs may help maintain therapeutic drug concentrations for longer periods and potentially reduce fluctuations in plasma concentration.

A robust formulation-development approach is essential because the performance of NLCs depends on several interrelated formulation and process variables. The type and concentration of solid lipid, liquid lipid, surfactant, drug concentration, homogenization conditions, sonication conditions,

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temperature, and processing time can influence particle size, surface charge, entrapment efficiency, drug loading, and release characteristics. Therefore, empirical formulation development may be insufficient for systematically identifying the optimum combination of variables. Quality by Design provides a scientific and risk-based framework for understanding these relationships and establishing a formulation capable of consistently meeting predefined quality requirements.

The present research therefore focuses on the development of robust nanostructured lipid carrier systems for enhanced therapeutic delivery in hypertension. The study integrates formulation development, physicochemical characterization, optimization, in-vitro drug-release evaluation, stability assessment, and, where applicable, pharmacokinetic investigation to determine the potential of NLCs as an advanced delivery platform for antihypertensive therapy.

II. APPROPRIATE DOSAGE FORM AND ROUTE OF ADMINISTRATION

The selection of an appropriate dosage form and route of administration is a critical component in the development of nanostructured lipid carrier (NLC) systems for the treatment of hypertension. Hypertension is generally a chronic and long-term condition that requires continuous pharmacological management to maintain blood pressure within the desired therapeutic range and reduce the risk of cardiovascular and renal complications. Therefore, the dosage form should not only provide effective delivery of the antihypertensive drug but should also support patient compliance, reproducible drug absorption, adequate systemic exposure, and convenient long-term administration. For the proposed development of a robust NLC system, the oral route of administration is considered the most appropriate route because oral antihypertensive therapy is widely accepted, convenient, non-invasive, and suitable for chronic treatment. An optimized NLC formulation can be designed as an oral nanosuspension, dispersion, capsule, or other suitable oral dosage form depending on the physicochemical characteristics of the selected drug and the properties of the optimized lipid carrier.

The oral route offers several practical advantages for antihypertensive therapy. Patients with hypertension generally require medication for prolonged periods, and a non-invasive route can improve acceptability and adherence. Conventional oral tablets and capsules are commonly used because they are easy to administer, relatively inexpensive, convenient for self-administration, and suitable for large-scale manufacturing. However, many drug candidates used in pharmaceutical

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research may have limitations such as poor aqueous solubility, inadequate dissolution, variable gastrointestinal absorption, extensive first-pass metabolism, or short biological half-life. These characteristics can result in inconsistent systemic exposure and may necessitate frequent administration. Incorporation of such a drug into an NLC system can potentially address some of these biopharmaceutical limitations while retaining the convenience of oral administration.

The NLC system is particularly suitable for oral delivery because its lipid matrix can provide an environment in which poorly water-soluble drugs can be solubilized or molecularly dispersed. NLCs consist of a combination of solid and liquid lipids stabilized by appropriate surfactants. The presence of liquid lipid within the solid lipid matrix creates structural imperfections that may increase the capacity of the carrier to accommodate the drug. Following oral administration, the nanosized particles come into contact with gastrointestinal fluids, where their large surface area can facilitate interaction with the surrounding medium. Appropriate formulation design may consequently improve the apparent dissolution and dispersion of the incorporated drug and facilitate its availability for absorption.

The choice of the specific oral dosage form should depend on the characteristics of the optimized NLC formulation. An aqueous NLC dispersion or oral nanosuspension may be appropriate when the formulation demonstrates adequate physical stability and acceptable palatability. Such a system can provide the drug in a pre-dispersed nanoscale state and eliminate the need for the patient to disperse the formulation before administration. However, liquid formulations may present challenges related to microbial stability, sedimentation, aggregation, packaging, and storage. Therefore, a suitable preservative system, packaging system, and stability strategy may be required where applicable.

Alternatively, the optimized NLC dispersion may be converted into a dry form through techniques such as spray drying or lyophilization. The resulting dry NLC powder can potentially be filled into hard or soft capsules or incorporated into another suitable solid oral dosage form. Conversion into a solid dosage form can improve storage stability and simplify transportation and handling. However, the drying process must be carefully controlled because drying and subsequent reconstitution may influence particle size, aggregation, lipid crystallinity, drug distribution, and release characteristics. Cryoprotectants or other suitable stabilizing excipients may therefore be required during lyophilization to preserve the characteristics of the NLC system.

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For a chronic antihypertensive formulation, an oral capsule containing the optimized NLC formulation may represent a particularly practical final dosage form when the formulation can be successfully converted into a stable solid state. Capsules can provide accurate dosing, protect the formulation from environmental conditions, and offer patient convenience. The formulation can be designed to release the drug in the gastrointestinal tract, where the lipid components may undergo digestion and interact with endogenous bile salts and lipids. These processes can influence drug solubilization and absorption. The overall performance, however, depends strongly on the drug, lipid composition, surfactant system, particle characteristics, and physiological conditions.

The route of administration should also be selected according to the therapeutic objective. The primary objective of an antihypertensive formulation is usually to achieve sufficient systemic exposure and maintain effective drug concentrations over an appropriate period. Oral NLCs can potentially provide a controlled-release profile, thereby reducing rapid changes in plasma drug concentration. A formulation that produces sustained drug release may be useful for maintaining more consistent systemic exposure. This characteristic may be particularly valuable in hypertension because effective blood-pressure management requires prolonged pharmacological activity rather than short-lived drug exposure.

Another important consideration is the possibility of improving the oral bioavailability of drugs that undergo extensive first-pass metabolism. Lipid-based delivery systems can modify the gastrointestinal fate of incorporated drugs and, for selected compounds, may promote alternative absorption pathways. Nevertheless, the extent of this effect is drug-specific and should not be assumed solely on the basis of NLC formulation. Pharmacokinetic studies are therefore essential for demonstrating whether the optimized formulation actually improves systemic exposure compared with the conventional formulation.

The dose strength of the final formulation should be established according to the therapeutic dose of the selected antihypertensive drug and the drug-loading capacity of the NLC system. High entrapment efficiency alone does not guarantee a suitable dosage form. The formulation must contain a therapeutically appropriate amount of drug in a practical quantity of lipid and excipients. Dose uniformity, content uniformity, drug loading, and stability should therefore be evaluated during formulation development. The final dosage form should also demonstrate acceptable physical

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characteristics, ease of administration, and reproducibility between batches.

Patient acceptability is another important consideration in selecting the dosage form. Since hypertension frequently requires lifelong treatment, formulations that are difficult to administer may negatively affect adherence. An oral NLC dosage form should ideally be easy to swallow, stable during storage, convenient to transport, and capable of delivering a consistent dose. If a liquid NLC formulation is selected, taste, viscosity, dosing accuracy, and packaging must be considered. If a capsule or solid dosage form is selected, capsule size, powder flow, moisture sensitivity, and reconstitution behavior where relevant should be evaluated.

The development of the oral NLC dosage form should also incorporate Quality by Design (QbD) principles. The desired dosage form and route should be established within the Quality Target Product Profile. Critical quality attributes may include particle size, polydispersity index, zeta potential, entrapment efficiency, drug loading, drug content, release characteristics, and stability. Critical material attributes may include the type and concentration of solid lipid, liquid lipid, surfactant, and stabilizing excipients.

Critical process parameters may include homogenization speed, homogenization time, processing temperature, sonication conditions, cooling rate, and drying conditions where applicable. Design of Experiments can be used to determine how these factors affect the final product and to identify a robust formulation and process.

The oral route also provides flexibility in the design of modified-release systems. Depending on the drug and therapeutic requirement, NLCs can be formulated to provide immediate, sustained, or controlled drug release.

For hypertension, sustained delivery may be particularly attractive because prolonged therapeutic exposure can potentially reduce dosing frequency and improve convenience. Nevertheless, the release rate should be optimized carefully because excessive retardation of release could delay the onset of action, whereas excessively rapid release could eliminate the intended advantage of the nanocarrier.

Among potential oral dosage forms, an NLC nanosuspension, oral dispersion, or solid NLC-filled

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capsule may be selected according to formulation stability, manufacturing feasibility, dose requirements, and drug characteristics.

The optimized system should provide appropriate particle characteristics, high drug incorporation, reproducible drug content, controlled release, and adequate stability. Ultimately, selection of the dosage form should be based on systematic pharmaceutical development and experimental evidence demonstrating that the NLC formulation provides a meaningful improvement in drug delivery and therapeutic performance over the conventional dosage form.

III. PARTICLE SIZE AND POLYDISPERSITY INDEX

Particle size and polydispersity index (PDI) are two of the most important critical quality attributes for the development and characterization of nanostructured lipid carriers (NLCs). These parameters provide essential information about the nanoscale dimensions, homogeneity, physical stability, drug-release behavior, and biological performance of the developed lipid-based delivery system. In the present research, particle size and PDI are particularly important because the therapeutic performance of an NLC formulation intended for antihypertensive drug delivery is strongly influenced by the size and uniformity of the nanoparticles. A properly optimized NLC formulation should demonstrate a nanoscale particle size with a relatively narrow particle-size distribution to ensure reproducible formulation characteristics and consistent drug delivery.

Particle size refers to the average hydrodynamic diameter of the NLC particles dispersed in the formulation medium. NLCs are generally developed within the nanometer range, although the exact particle size depends on the composition of the lipid matrix, type and concentration of surfactant, drug characteristics, lipid-to-drug ratio, preparation method, homogenization conditions, sonication intensity, processing temperature, and other formulation and process variables. Particle size is commonly determined using dynamic light scattering (DLS) because this technique is rapid, non-destructive, and suitable for measuring particles dispersed in a liquid medium. In DLS analysis, the Brownian motion of particles is measured and converted into an estimate of their hydrodynamic diameter.

The particle size of an NLC system has a direct influence on its surface-area-to-volume ratio. Reduction in particle size increases the available surface area, which can improve the interaction

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between the lipid carrier and the surrounding aqueous medium. This characteristic can be particularly beneficial for poorly water-soluble antihypertensive drugs because a larger interfacial area may facilitate drug dissolution and transfer from the lipid carrier. Smaller particles may also interact more efficiently with gastrointestinal components following oral administration. However, particle size should not be minimized without considering formulation stability, because extremely small particles may require higher surfactant concentrations and may present challenges during processing and storage.

The selection of an appropriate particle-size range should therefore be based on the intended therapeutic application and formulation characteristics rather than on size alone. For orally administered NLCs, nanoscale particles with a uniform distribution are generally desirable because they can provide reproducible physical behavior and a high surface area. A formulation showing excessive particle growth during storage may indicate aggregation, lipid restructuring, or inadequate stabilization. Therefore, particle size should be evaluated not only immediately after preparation but also during stability studies.

The polydispersity index provides information about the width of the particle-size distribution. It indicates whether the particles in the formulation are relatively uniform or whether the formulation contains particles with widely different dimensions. PDI values are generally obtained simultaneously with particle-size measurements using DLS. A low PDI indicates a relatively narrow and homogeneous particle-size distribution, whereas a high PDI suggests greater variation in particle size. Consequently, PDI is an important indicator of formulation uniformity and can be used to assess the reproducibility of the NLC preparation process.

A PDI approaching zero represents a highly uniform particle population, whereas increasing PDI values indicate increasing heterogeneity. In practical formulation development, a PDI below approximately 0.3 is commonly considered indicative of a reasonably homogeneous nanosized dispersion, although the appropriate acceptance criterion should be defined according to the formulation, analytical method, and intended use. Extremely low PDI values are not always necessary, but a consistently high PDI may indicate inadequate control of the preparation process or the presence of aggregation and multiple particle populations.

The particle size and PDI of NLCs are strongly affected by the concentration and type of surfactant.

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Surfactants reduce interfacial tension between the lipid and aqueous phases and help prevent coalescence and aggregation during nanoparticle formation. Increasing surfactant concentration within an appropriate range can often reduce particle size and improve dispersion stability. However, excessive surfactant may adversely affect formulation properties and may influence drug release or biological compatibility. Therefore, surfactant concentration should be optimized rather than simply increased to obtain smaller particles.

The solid-to-liquid lipid ratio is another important factor influencing particle size and PDI. Changes in lipid composition can alter the viscosity of the lipid phase, melting behavior, interfacial characteristics, and solidification process. A suitable combination of solid and liquid lipids can produce stable nanoparticles with desirable particle-size characteristics. In NLCs, the incorporation of liquid lipid creates imperfections within the solid lipid matrix, which can improve drug incorporation; however, the amount of liquid lipid must be optimized because excessive liquid lipid may modify particle structure and physical stability.

Processing parameters also have a significant effect on particle size and PDI. High-shear homogenization and ultrasonication are commonly employed to reduce the size of lipid droplets or particles. Increasing homogenization intensity or processing time may reduce particle size by providing greater mechanical energy for particle disruption. However, excessive processing can result in unwanted temperature increases or other changes in formulation characteristics. Similarly, sonication conditions must be optimized to obtain the desired particle size without compromising the stability of the formulation.

Temperature is also important during NLC preparation. The lipid phase generally needs to be maintained above its melting point during formation of the primary emulsion. Inadequate temperature control can result in incomplete lipid melting and heterogeneous particle formation. During subsequent cooling, controlled solidification of the lipid matrix contributes to the final structure of the NLC. Consequently, variations in heating and cooling conditions may influence both particle size and PDI.

The measurement of particle size and PDI should be conducted under standardized analytical conditions. The NLC formulation should generally be appropriately diluted with a compatible dispersion medium to prevent multiple scattering effects during DLS analysis. The measurement

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temperature, dilution ratio, equilibration time, cuvette type, and number of measurement runs should be controlled. Multiple measurements should be performed to improve analytical reliability, and the results should be reported as mean ± standard deviation where appropriate.

Particle size and PDI can also provide useful information during formulation optimization. In a Quality by Design framework, particle size and PDI may be designated as critical quality attributes because they are influenced by several critical material attributes and critical process parameters. Design of Experiments can be employed to investigate the effects of variables such as lipid ratio, surfactant concentration, homogenization speed, sonication time, and processing temperature. Statistical analysis can then identify significant factors and interactions and help establish an optimized formulation within a suitable design space.

For the proposed antihypertensive NLC system, an optimized formulation should ideally demonstrate a suitable nanoscale particle size, low PDI, and minimal change in these parameters during storage. A formulation that initially has desirable particle size but exhibits substantial particle growth during storage cannot be considered robust. Therefore, monitoring particle size and PDI throughout the stability study is essential. An increase in particle size accompanied by an increase in PDI may indicate aggregation or instability of the nanoparticle dispersion.

Particle size may also influence drug-release characteristics. Smaller particles generally provide a greater surface area, which may facilitate faster interaction with the dissolution medium. Conversely, larger particles may provide a longer diffusion pathway and potentially slower drug release. However, drug-release behavior is not determined by particle size alone; lipid composition, drug location within the matrix, crystallinity, surfactant characteristics, and drug–lipid interactions also contribute substantially. Thus, particle-size optimization should be performed together with entrapment-efficiency and in-vitro drug-release studies.

In addition, PDI is an important indicator of batch-to-batch reproducibility. A robust manufacturing process should consistently produce NLCs with similar particle size and PDI. Significant variations between batches may indicate inadequate control of raw materials or processing conditions. Establishing appropriate specifications for particle size and PDI can therefore contribute to overall product quality and manufacturing consistency.

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IV. FOURIER-TRANSFORM INFRARED SPECTROSCOPY

Fourier-transform infrared spectroscopy (FTIR) is an important analytical technique used in the development and characterization of nanostructured lipid carrier (NLC) systems for enhanced therapeutic delivery in hypertension. FTIR spectroscopy provides valuable information regarding the chemical structure and functional groups of the drug, lipids, surfactants, and other formulation components. In the present research, FTIR analysis is particularly useful for assessing the compatibility between the selected antihypertensive drug and excipients and for determining whether significant chemical interactions occur during NLC formulation. Since the stability and therapeutic performance of a nanocarrier depend considerably on the compatibility of its individual components, FTIR serves as an important preliminary characterization tool during formulation development.

The fundamental principle of FTIR spectroscopy is based on the interaction of infrared radiation with molecules. When infrared radiation passes through a sample, specific frequencies of radiation are absorbed by chemical bonds present within the molecules. These absorptions correspond to molecular vibrations, including stretching, bending, rocking, and other vibrational modes. Because different functional groups absorb infrared radiation at characteristic frequencies, the resulting infrared spectrum provides a molecular fingerprint of the analyzed material. Fourier transformation is used to convert the raw interferogram generated by the instrument into a conventional infrared spectrum showing absorbance or transmittance as a function of wavenumber.

For the development of an antihypertensive NLC formulation, FTIR analysis can initially be performed on the pure drug, individual excipients, physical mixtures, and optimized NLC formulation. The spectrum of the pure drug serves as a reference and allows identification of its characteristic functional-group peaks. The spectra of the selected solid lipid, liquid lipid, surfactant, and other excipients are then examined individually. Subsequently, the physical mixture of the drug and excipients can be analyzed to determine whether any major changes occur in the characteristic absorption bands. Finally, the optimized NLC formulation can be subjected to FTIR analysis and compared with the spectra of the individual components.

One of the principal applications of FTIR in the present research is the evaluation of drug–excipient compatibility. Pharmaceutical excipients should ideally remain chemically compatible with the active pharmaceutical ingredient (API) throughout formulation and storage. Undesirable chemical

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interactions may result in degradation, loss of drug potency, altered drug release, or reduced stability. FTIR can provide preliminary evidence of such interactions by identifying changes in characteristic functional-group peaks. If the principal characteristic peaks of the drug remain identifiable in the physical mixture and optimized NLC formulation, without the appearance of substantial new peaks or disappearance of important bands, this may suggest that no major chemical incompatibility has occurred.

The FTIR spectrum of the pure antihypertensive drug is expected to show characteristic absorption bands corresponding to its specific functional groups. These may include O–H, N–H, C=O, C–O, C–N, aromatic C=C, aliphatic C–H, or other groups depending on the chemical structure of the selected drug. The exact peak positions must be identified experimentally because they vary according to the molecular structure and analytical conditions. The spectra of the selected lipids may predominantly show absorption bands associated with aliphatic C–H stretching, ester groups, carbonyl groups, and other lipid-related structural features. Surfactants may exhibit characteristic bands related to their hydrophilic and hydrophobic functional groups.

During interpretation, particular attention should be paid to changes in peak position, intensity, shape, and appearance or disappearance of absorption bands. A small shift in peak position does not necessarily indicate chemical incompatibility because changes may arise from hydrogen bonding, physical mixing, altered molecular environments, or differences in sample preparation. Therefore, FTIR findings should be interpreted together with other characterization techniques such as differential scanning calorimetry (DSC), X-ray diffraction (XRD), particle-size analysis, and drug-content studies.

FTIR can also provide information regarding the incorporation of the drug into the NLC matrix. When the drug is incorporated within the lipid system, its characteristic peaks may show reduced intensity, broadening, or minor shifts due to changes in the molecular environment. In some formulations, characteristic drug peaks may become less prominent because of dilution by the lipid matrix or because the drug is molecularly dispersed within the carrier. Such changes should not automatically be interpreted as evidence of chemical degradation. Instead, they should be correlated with drug assay, DSC, XRD, and stability results to determine whether the drug has remained chemically intact.

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The attenuated total reflectance (ATR) technique is particularly convenient for pharmaceutical FTIR analysis. ATR-FTIR requires minimal sample preparation and can be used for powders, liquids, semisolids, and lipid-based formulations. In this method, the sample is brought into contact with an ATR crystal, and infrared radiation interacts with the sample near the crystal surface. The resulting spectrum can be obtained rapidly and with relatively simple preparation. This makes ATR-FTIR suitable for screening the pure drug, excipients, physical mixtures, and optimized NLC formulations.

In a robust NLC-development program, FTIR should be performed using standardized analytical conditions. The instrument should be appropriately calibrated, and background spectra should be collected before sample analysis. Samples should be prepared consistently, and appropriate numbers of scans and spectral resolution should be selected. Spectral analysis should cover a suitable wavenumber range, commonly within the mid-infrared region. The same analytical conditions should preferably be maintained for comparative evaluation of all formulation components.

FTIR analysis is also useful in the Quality by Design (QbD) approach to NLC development. During the initial risk-assessment stage, compatibility between the API and formulation components can be considered an important material attribute. FTIR can help screen candidate excipients before they are incorporated into experimental formulations. This reduces the likelihood of selecting incompatible materials and supports rational formulation development. The information obtained from FTIR can subsequently be integrated with experimental-design studies and other characterization results to identify a robust formulation composition.

The relationship between FTIR findings and the physical characteristics of NLCs is also important. The lipid matrix is expected to maintain its characteristic chemical structure after nanoparticle formation, although changes in molecular organization may occur. If the drug interacts physically with the lipid matrix, changes in characteristic peaks may occur without the formation of a new chemical compound. Such interactions can influence drug crystallinity, drug loading, and release characteristics. Consequently, FTIR provides useful qualitative evidence that can support interpretation of the overall structure of the optimized formulation.

FTIR should not, however, be considered a standalone technique for confirming complete drug–excipient compatibility. It primarily provides information about molecular vibrations and functional groups and may not detect all types of interactions, particularly when changes are subtle. Therefore,

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FTIR results should be supported by complementary analytical techniques. DSC can provide information about thermal transitions, while XRD can evaluate changes in crystalline structure. Particle-size and PDI measurements provide information about physical characteristics, and chromatographic drug-assay methods can confirm chemical drug content and stability.

For the proposed antihypertensive NLC system, FTIR analysis can therefore be incorporated at several stages of formulation development. Initially, it can be used to characterize the pure drug and excipients. Subsequently, physical mixtures can be evaluated to identify possible incompatibilities. After preparation and optimization of the NLC, the formulation can again be analyzed to investigate changes in the drug's characteristic spectral features and to assess the overall chemical compatibility of the system. Stability samples may also be analyzed where necessary to investigate potential changes during storage.

The results can be presented by comparing the FTIR spectra of the pure drug, individual excipients, physical mixture, and optimized NLC formulation. Characteristic absorption bands can be tabulated along with their corresponding functional groups and observed changes. Interpretation should focus on whether the major characteristic peaks are retained, shifted, broadened, reduced, or replaced by new absorption bands. The absence of significant unexpected spectral changes would provide supportive evidence of acceptable drug–excipient compatibility.

In conclusion, Fourier-transform infrared spectroscopy is a valuable analytical technique for the development and characterization of nanostructured lipid carriers intended for antihypertensive drug delivery. It provides rapid and informative evaluation of functional groups and molecular characteristics and is particularly useful for preliminary drug–excipient compatibility studies. Comparison of FTIR spectra of the pure drug, excipients, physical mixtures, and optimized NLC formulation can help determine whether major chemical interactions occur during formulation. When combined with DSC, XRD, particle-size analysis, drug-release studies, and stability testing, FTIR contributes to a comprehensive understanding of the developed NLC system. Thus, FTIR represents an important component of the analytical characterization strategy for establishing the quality, compatibility, and robustness of NLC-based antihypertensive drug-delivery systems.

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V. CONCLUSION

The **development of robust nanostructured lipid carrier systems for enhanced therapeutic delivery in hypertension** represents a promising research strategy for addressing limitations associated with conventional antihypertensive drug delivery. NLCs provide a versatile lipid-based platform capable of incorporating therapeutic agents within a matrix composed of solid and liquid lipids. The structural imperfections generated by the combination of these lipids can improve drug loading and provide opportunities for controlled drug release.

A systematic QbD-based development strategy can strengthen the formulation-development process by identifying critical material attributes, critical process parameters, and critical quality attributes. Comprehensive characterization using particle-size analysis, zeta-potential measurement, FTIR, DSC, XRD, microscopy, entrapment-efficiency analysis, and in-vitro release testing can establish the physicochemical quality of the developed system. Subsequent stability and pharmacokinetic investigations can provide evidence regarding formulation robustness and potential improvement in drug exposure. a properly optimized NLC formulation may overcome important biopharmaceutical limitations of selected antihypertensive drugs by improving solubilization, dissolution, controlled release, and potentially oral bioavailability.

The integration of nanotechnology, pharmaceutical formulation science, analytical characterization, and QbD principles therefore provides a strong scientific framework for developing advanced antihypertensive drug-delivery systems.

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