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NANOSTRUCTURED LIPID CARRIERS IN ENHANCING BIOAVAILABILITY OF HERBAL EXTRACTS: A PHARMACOGNOSTIC PERSPECTIVE

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ABSTRACT

Nanostructured lipid carriers (NLCs) are advanced drug delivery systems designed to enhance the bioavailability and efficacy of herbal extracts, overcoming inherent challenges such as poor solubility and stability. By encapsulating bioactive herbal constituents within lipid matrices, NLCs not only improve solubility and stability but also enable targeted delivery to specific body sites. This review comprehensively explores NLCs, covering their composition, properties, preparation methods, and characterization techniques. Mechanistically, NLCs enhance pharmacokinetic parameters through improved solubility, degradation protection, enhanced gastrointestinal absorption, and sustained release. Case studies highlight their potential in augmenting therapeutic outcomes across various medicinal properties. Integration of NLC technology with traditional medicine promises to revolutionize healthcare by merging ancient herbal knowledge with modern pharmaceutical advancements, facilitating personalized medicine through tailored NLC formulations. Overall, this review will discuss NLCs encorporating a transformative strategy in pharmacognostic research, offering opportunities to enhance the therapeutic potential and sustainability of herbal medicines in contemporary healthcare. Interdisciplinary collaboration and ongoing innovation are essential to fully harnessing NLCs' potential in addressing global health challenges and integrating herbal medicine into mainstream healthcare practices.

KEYWORDS: Nanostructured lipid carriers (NLCs), herbal extracts, drug delivery, pharmacognosy, bioavailability enhancement, traditional medicine.

INTRODUCTION

Overview of Herbal Extracts: Herbal extracts have been a cornerstone of traditional medicine systems for millennia, offering a rich source of bioactive compounds with diverse therapeutic properties. From ancient civilizations to modern times, plants have been utilized to treat a wide array of ailments, ranging from common colds to chronic diseases. The World Health Organization estimates that approximately 80% of the global population relies on herbal medicines for some aspect of primary healthcare. This enduring popularity stems from the perception of herbal remedies as natural, accessible, and often having fewer side effects compared to synthetic drugs.

In recent decades, there has been a resurgence of interest in herbal extracts within the scientific community. This renewed focus is driven by the potential of plants to provide novel drug leads, the growing consumer preference for natural products, and the recognition of traditional knowledge as a valuable resource in drug discovery. Herbal extracts are complex mixtures containing numerous phytochemicals, including alkaloids, flavonoids, terpenoids, and phenolic compounds. These bioactive constituents often work synergistically, contributing to the holistic therapeutic effects observed in traditional medicine practices.

Challenges with Herbal Extracts

Despite their potential, the widespread adoption of herbal extracts in modern medicine faces several significant challenges. Chief among these is the issue of bioavailability – the proportion of an administered dose that reaches systemic circulation and exerts a therapeutic effect. Many herbal extracts contain compounds with poor aqueous solubility, leading to limited dissolution in the gastrointestinal tract and, consequently, reduced absorption. This poor solubility is often attributed to the lipophilic nature of many phytochemicals.

Furthermore, the stability of herbal extracts poses another hurdle. Phytochemicals can be sensitive to environmental factors such as light, heat, and pH, potentially degrading during storage or processing. This instability not only affects the potency of the herbal preparation but also complicates the standardization and quality control processes crucial for pharmaceutical development.

Another significant challenge is the first-pass metabolism effect. Many herbal compounds undergo extensive metabolism in the liver before reaching systemic circulation, drastically reducing their bioavailability. This metabolic process can also lead to the formation of metabolites with altered or diminished therapeutic activity.

These challenges collectively contribute to the variable and often suboptimal efficacy of herbal extracts in clinical settings, highlighting the need for innovative strategies to enhance their bioavailability and therapeutic potential.[1]

Introduction to Nanostructured Lipid Carriers (NLCs)

Nanostructured lipid carriers (NLCs) are an advanced form of lipid-based nanocarriers designed to overcome the limitations of traditional drug delivery systems. NLCs are composed of a mixture of solid lipids and liquid lipids, forming a nanostructured matrix that can encapsulate both hydrophilic and lipophilic compounds.[2]

Advantages of NLCs in Drug Delivery

Enhanced Solubility: NLCs improve the solubility of poorly water-soluble compounds by incorporating them into the lipid matrix.

Improved Stability: The encapsulation of herbal extracts within NLCs protects them from environmental degradation, enhancing their stability.

Increased Bioavailability: By improving solubility and stability, NLCs significantly enhance the bioavailability of herbal compounds. The nanoscale size of NLCs also promotes better absorption and penetration of bioactive compounds.

Controlled Release: NLCs can be engineered to provide controlled and sustained release of encapsulated compounds, maintaining therapeutic levels over extended periods.

Biocompatibility and Safety: Composed of physiological lipids, NLCs are biocompatible and exhibit low toxicity, making them suitable for a wide range of therapeutic applications.

The integration of NLCs into the formulation of herbal extracts represents a promising strategy to harness their full therapeutic potential, paving the way for more effective and reliable natural health treatments. This review aims to explore the role of NLCs in enhancing the bioavailability of herbal extracts, examining the underlying mechanisms, preparation methods, and specific applications in pharmacognosy.

NLCs can be tailored to improve the bioavailability, stability, and therapeutic efficacy of herbal extracts, offering a promising solution for modern pharmacognosy.[3]

MECHANISMS OF ENHANCED BIOAVAILABILITY

Nanostructured lipid carriers (NLCs) significantly enhance the bioavailability and therapeutic efficacy of herbal extracts by addressing key challenges such as poor solubility, degradation, absorption, and controlled release. The lipid matrix of NLCs improves the solubility of hydrophobic phytochemicals by mimicking biological membranes and incorporating surfactants for efficient distribution in the body. NLCs protect sensitive bioactive compounds from environmental degradation by encapsulating them in a lipid matrix and incorporating antioxidants. They enhance intestinal absorption through mechanisms such as increased permeability, mucus penetration, inhibition of P-glycoprotein efflux, and lymphatic transport, bypassing first-pass metabolism. Additionally, NLCs provide controlled and sustained release of encapsulated herbal extracts through matrix degradation, diffusion-controlled release, erosion-controlled release, or a combination of these mechanisms. This leads to prolonged therapeutic effects, reduced dosing frequency, and improved patient compliance, ultimately enhancing the efficacy and therapeutic potential of herbal extracts in pharmacognosy.[4]

METHODS OF PREPARATION OF NANOSTRUCTURED LIPID CARRIERS (NLCS)

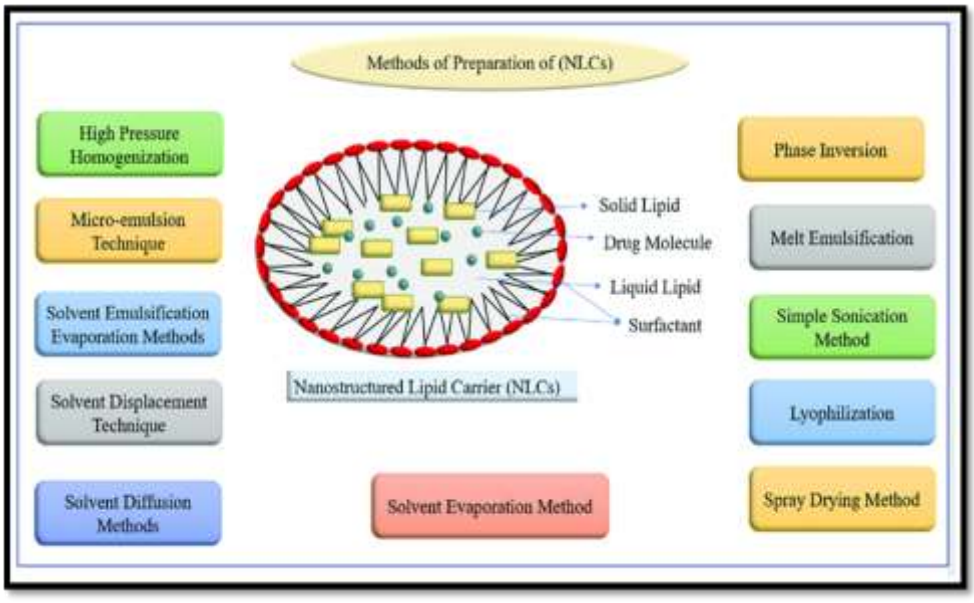

Figure No. 1.

High-Pressure Homogenization

High-pressure homogenization is a widely used method for preparing NLCs. It involves the following steps:

1. Melting of solid lipids: Solid lipids are melted to form a homogenous lipid phase.

2. Mixing with liquid lipids and drugs: Liquid lipids and drugs are added to the melted solid lipids.

3. Formation of emulsion: The mixture is stirred to form an emulsion.

4. High-speed impact and decompression: The emulsion is subjected to high-speed impact and decompression under an extremely high shear force to break the fluid droplets into nanoparticles.

This method is suitable for insoluble and lipophilic drugs but not entirely suitable for hydrophilic drugs. It avoids the use of organic solvents and can be used for large-scale production.

Solvent Emulsification-Evaporation

The solvent emulsification-evaporation method involves the following steps.

1. Dissolving solid lipids, liquid lipids, and drugs in a water miscible organic solvent: The mixture is dissolved in a solvent such as chloroform.

2. Emulsification: The organic solution is slowly added to an aqueous phase containing surfactants.

3. Evaporation of solvent: The solvent is evaporated, leaving behind the NLCs.

4. Sonication: The pre-emulsion is sonicated to reduce the particle size.

This method is associated with a rapid and non-sophisticated production process but involves the use of organic solvents and requires further evaporation or ultra-filtration.

Microemulsion Template

Microemulsion is another method used for preparing NLCs. It involves the following steps:

1. Mixing melted lipids with a hydrophilic aqueous phase: Melted lipids are mixed with a hydrophilic aqueous phase containing surfactants and co-surfactants.

2. Formation of microemulsion: The mixture is stirred to form a microemulsion.

3. Cooling and solidification: The microemulsion is cooled and solidified to form NLCs.

Other Novel Methods

Several emerging techniques have been developed for preparing NLCs, including.

1. Solvent Diffusion: This method involves the diffusion of a solvent through a lipid film to form NLCs.

2. Solvent Injection/Solvent Displacement: This method involves the injection of a solvent into a lipid film to displace the solvent and form NLCs.

3. Phase Inversion: This method involves the inversion of a phase to form NLCs.

These novel methods offer advantages such as improved scalability, reduced solvent usage, and enhanced control over particle size and morphology.[5, 6, 7, 8]

CHARACTERIZATION OF NLCS

Particle Size and Distribution

The particle size and size distribution of nanostructured lipid carriers (NLCs) are critical parameters that influence their stability, drug release profile, and bioavailability. Dynamic Light Scattering (DLS) is one of the most widely used techniques for measuring these parameters.

Dynamic Light Scattering (DLS)

Principle: Dynamic Light Scattering (DLS): This technique measures the particle size and distribution of NLCs by analysing the scattering of light by particles in a solution. DLS measures the Brownian motion of particles in suspension, which causes fluctuations in the intensity of scattered light. The particle size is determined based on these fluctuations.

Procedure: A sample of NLCs is dispersed in an appropriate solvent and placed in the DLS instrument. The instrument measures the intensity of scattered light and calculates the hydrodynamic diameter and polydispersity index (PDI), indicating the size distribution.

Advantages: DLS is quick, non-destructive, and provides information on particle size distribution and stability.

Surface Morphology

Understanding the surface morphology of NLCs helps in assessing their structural integrity and interactions with biological systems. Techniques like Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are commonly employed.

Scanning Electron Microscopy (SEM)

Principle: Scanning Electron Microscopy (SEM): SEM is used to visualize the surface morphology of NLCs, providing information on particle shape, size, and distribution.

SEM uses a focused beam of electrons to create an image of the sample surface. The sample's atoms and electrons interact to produce signals that provide details on the composition and shape of the surface.

Procedure: A sample of NLCs is dried and coated with a thin layer of conductive material (e.g., gold). The sample is then scanned with an electron beam, and the emitted signals are captured to form an image.

Advantages: SEM provides high-resolution images of the NLC surface, revealing details about particle shape, size, and surface texture.

- **Transmission Electron Microscopy (TEM)**

Principle: Transmission Electron Microscopy (TEM): TEM is employed to observe the morphology of NLCs at higher resolution, providing detailed information on particle size, shape, and distribution. TEM passes an electron beam through a thin sample, creating an image based on the transmitted electrons. This technique provides detailed information about the internal structure and morphology of the particles.

Procedure: A drop of NLC suspension is placed on a TEM grid, dried, and examined under the electron microscope. The resulting images show the internal structure and particle size at a high resolution.

Advantages: TEM offers extremely high resolution, allowing for the visualization of the internal structure of NLCs and their crystallinity.

- **Zeta Potential Measurement**

Zeta potential is a measure of the surface charge of NLCs and is crucial for predicting their stability in suspension.

Principle: Zeta potential measurement: This technique is used to determine the surface charge of NLCs, which is crucial for their stability and interaction with biological systems. Zeta potential is determined by measuring the electrophoretic mobility of particles in an electric field. It reflects the degree of electrostatic repulsion or attraction between particles, indicating stability.

Procedure: A sample of NLCs is dispersed in a suitable medium, and the zeta potential is measured using a zeta potential analyser. The analyser applies an electric field and measures the velocity of particle movement.

Advantages: A high zeta potential value (positive or negative) typically indicates good stability, as particles repel each other, preventing aggregation.

- **Drug Loading and Encapsulation Efficiency**

Assessing the drug loading and encapsulation efficiency of NLCs is essential for determining their capacity to carry and release the bioactive compounds.

Drug Loading (DL)

Definition: The percentage of drug loaded into the NLCs is calculated to evaluate their capacity to load the drug. Drug loading is the amount of drug incorporated in the NLCs relative to the total weight of the NLCs.

Calculation: DL (%) = (Weight of the drug in NLCs / Weight of the NLCs) × 100

Encapsulation Efficiency (EE):

Definition: Entrapment efficiency (EE%): The percentage of drug encapsulated within the NLCs is calculated to evaluate their efficiency in encapsulating the drug. Encapsulation efficiency is the percentage of the initial drug that is successfully encapsulated within the NLCs.

Calculation: EE (%) = (Weight of the encapsulated drug / Weight of the initial drug) × 100

Procedure

1. Preparation: NLCs are separated from the free drug using centrifugation or filtration.
2. Quantification: The amount of drug in the NLCs and the free drug in the supernatant is quantified using techniques like High-Performance Liquid Chromatography (HPLC) or UV-Visible spectroscopy.

Advantages: High drug loading and encapsulation efficiency are desirable for reducing the dose and frequency of administration.

- **In vitro Release Studies**

In vitro release studies provide information on the release kinetics and mechanisms of the encapsulated drug from NLCs.

- **In vitro Release Studies**

Principle: In vitro release studies: These studies are conducted to evaluate the release profile of the encapsulated drug from NLCs under various conditions, such as different pH levels and temperatures. These studies simulate the release of the drug from NLCs under physiological conditions, providing insights into the release rate and pattern.

Procedure

1. Preparation: NLCs are placed in a dialysis bag or release medium.
2. Incubation: The system is incubated at 37°C with continuous stirring to simulate body conditions.

3. Sampling: At predetermined intervals, samples are withdrawn and replaced with fresh medium to maintain sink conditions.
4. Quantification: The amount of drug released is quantified using HPLC or UV-Visible spectroscopy.

Data Analysis: The release data are analysed using kinetic models (e.g., zero-order, first-order, Higuchi, Korsmeyer-Peppas) to determine the release mechanism.

Advantages: In vitro release studies provide valuable information on the controlled and sustained release properties of NLCs, helping to predict their in vivo behaviour.

By thoroughly characterizing NLCs using these techniques, researchers can optimize their formulation, ensuring improved bioavailability and therapeutic efficacy of herbal extracts.[9, 10, 11]

CASE STUDIES AND APPLICATIONS

Specific Herbal Extracts Encapsulated in NLCs

Numerous studies have demonstrated the successful encapsulation of herbal extracts in nanostructured lipid carriers (NLCs), highlighting their potential in enhancing the bioavailability and therapeutic efficacy of these natural compounds. Some notable examples include.[12, 13]

Table No. 1

Sr. No.	Drug Name	Background	Study	Outcome
1.	**Curcumin**	Curcumin, derived from turmeric, has potent anti-inflammatory and antioxidant properties but suffers from poor solubility and bioavailability.	NLCs encapsulating curcumin were developed using glyceryl monostearate as the solid lipid and oleic acid as the liquid lipid.	The curcumin-loaded NLCs showed significantly improved solubility, stability, and bioavailability compared to free curcumin.
2.	**Quercetin**	Quercetin is a flavonoid with strong antioxidant and anti-inflammatory effects, limited by low water solubility and poor absorption.	Quercetin was encapsulated in NLCs prepared with Compritol 888 ATO and Capryol 90.	The NLCs enhanced the solubility, protected quercetin from degradation, and increased its bioavailability in animal models.
3.	**Berberine**	Background: Berberine, an alkaloid found in several plants, has antidiabetic and antimicrobial properties but has low oral bioavailability.	Berberine-loaded NLCs were formulated using stearic acid and oleic acid.	The NLCs improved the bioavailability and therapeutic efficacy of berberine, leading to better pharmacological effects.

Improvement in Pharmacokinetic Parameters

The encapsulation of herbal extracts in NLCs has been shown to improve pharmacokinetic parameters, leading to enhanced absorption, distribution, metabolism, and excretion (ADME) profiles. Some examples include:[14, 15]

Table No. 2.

Sr. No.	Drug Name	Study	Outcome
1.	**Curcumin NLCs**	Oral administration of curcumin-loaded NLCs to rats resulted in a significant increase in curcumin plasma concentration compared to free curcumin.	The bioavailability of curcumin was enhanced by over 50-fold, demonstrating improved absorption and prolonged circulation time.
2.	**Quercetin NLCs**	Pharmacokinetic studies in rats showed that quercetin-loaded NLCs achieved higher plasma levels and a longer half-life than free quercetin.	The bioavailability of quercetin was increased by approximately 20-fold, indicating enhanced intestinal absorption and reduced metabolism.
3.	**Berberine NLCs**	Berberine-loaded NLCs administered orally to mice exhibited higher plasma concentrations and improved pharmacokinetic parameters compared to free berberine.	The bioavailability of berberine was significantly increased, leading to better therapeutic outcomes.

- **Therapeutic Applications**

The improved bioavailability and stability of herbal extracts encapsulated in NLCs have translated into enhanced therapeutic effects in various disease models. Some notable applications include.

1. Anti-inflammatory.

Curcumin NLCs: Studies have shown that curcumin-loaded NLCs exhibit stronger anti-inflammatory effects in animal models of inflammation compared to free curcumin. This is attributed to the enhanced bioavailability and targeted delivery of curcumin.

Quercetin NLCs: Quercetin-loaded NLCs demonstrated superior anti-inflammatory activity in models of acute and chronic inflammation, reducing cytokine levels and oxidative stress markers more effectively than free quercetin.

2. Antioxidant

Resveratrol NLCs: Resveratrol, known for its antioxidant properties, was encapsulated in NLCs to improve its stability and bioavailability. The resveratrol-loaded NLCs showed enhanced antioxidant activity in vitro and in vivo, protecting cells from oxidative damage.

EGCG NLCs: Epigallocatechin gallate (EGCG), a major component of green tea, was encapsulated in NLCs to enhance its stability and antioxidant efficacy. The EGCG-loaded NLCs exhibited improved antioxidant activity in various oxidative stress models.

3. Anticancer

Berberine NLCs: Berberine-loaded NLCs have shown promising anticancer activity in various cancer cell lines and animal models. The enhanced bioavailability and targeted delivery of berberine resulted in increased cytotoxicity and apoptosis in cancer cells.

Paclitaxel NLCs: Although not a herbal extract, paclitaxel is a plant-derived anticancer drug. Encapsulating paclitaxel in NLCs has been demonstrated to improve its solubility, reduce systemic toxicity, and enhance anticancer efficacy in tumour models.

The encapsulation of herbal extracts in NLCs offers significant advantages in terms of improved pharmacokinetic parameters and therapeutic efficacy. These advancements highlight the potential of NLCs as a versatile and effective delivery system for herbal medicines, paving the way for their application in various therapeutic areas.[16, 17]

PHARMACOGNOSTIC PERSPECTIVE

Synergy with Traditional Medicine

Nanostructured lipid carriers (NLCs) offer a modern technological approach to enhancing traditional medicinal practices. By improving the bioavailability, stability, and efficacy of herbal extracts, NLCs can integrate seamlessly with traditional medicine, providing a bridge between ancient knowledge and contemporary science.[18 19, 20]

Integration with Traditional Practices

Enhanced Formulations: Traditional herbal formulations often face challenges related to solubility and stability. NLCs can encapsulate these herbal extracts, enhancing their therapeutic potential without altering their fundamental properties.

Dose Reduction: By improving bioavailability, NLCs allow for lower doses of herbal extracts to achieve the desired therapeutic effect, minimizing potential side effects and making treatments more efficient.

Targeted Delivery: NLCs can provide targeted delivery of herbal compounds, aligning with traditional practices that focus on specific health issues. This ensures that the active components reach the desired site of action more effectively.

Examples

Ayurvedic Medicine: Incorporating curcumin-loaded NLCs into Ayurvedic formulations can enhance the anti-inflammatory and antioxidant effects traditionally sought in turmeric.

Traditional Chinese Medicine (TCM): NLCs can be used to improve the delivery and efficacy of TCM herbs like ginseng and ginkgo biloba, ensuring consistent therapeutic outcomes.[18]

Sustainability and Natural Sources

The use of natural and sustainable materials in the formulation of NLCs aligns with the principles of pharmacognosy, which emphasizes the importance of natural products in medicine.

1. Sustainability Considerations

Natural Lipids: Using natural lipids such as stearic acid, glyceryl monostearate, and beeswax in NLC formulations ensures biocompatibility and minimizes environmental impact.

Renewable Sources: Selecting lipids and surfactants derived from renewable sources supports sustainability and reduces dependency on synthetic materials.

Biodegradability: Natural materials used in NLCs are typically biodegradable, reducing the environmental footprint of the drug delivery system.[18, 19]

Importance in Pharmacognosy

Conservation of Medicinal Plants: By enhancing the efficacy of herbal extracts through NLCs, the pressure on harvesting large quantities of medicinal plants is reduced, aiding in the conservation of these species.

Ethical Sourcing: Emphasizing the use of ethically sourced and sustainably harvested natural materials ensures that traditional medicine practices are respected and preserved.[18, 20]

Ethnopharmacological Relevance

NLCs can play a significant role in enhancing the efficacy of ethnomedicine, where traditional knowledge of medicinal plants is utilized for therapeutic purposes.

Ethnopharmacological Case Studies

Neem (Azadirachta indica): Neem has been used in various cultures for its antibacterial and antifungal properties. Encapsulating neem extracts in NLCs can enhance its bioactivity, making it more effective in treating skin infections and other ailments.

Artemisia annua: Traditionally used for its antimalarial properties, the bioavailability of artemisinin (the active compound) can be significantly improved using NLCs. This enhances its efficacy in treating malaria and potentially reduces the incidence of resistance.

Milk Thistle (Silybum marianum): Known for its hepatoprotective effects, silymarin from milk thistle shows poor bioavailability. NLCs can encapsulate silymarin, improving its solubility and absorption, thereby enhancing its liver-protective effects.[20]

Regulatory and Safety Aspects

Regulatory Guidelines for NLCs

Nanostructured lipid carriers (NLCs) containing herbal extracts are subject to regulatory guidelines that ensure their safety, efficacy, and quality. Understanding these regulations is crucial for the development, approval, and commercialization of NLC-based products.

- **Overview of Current Regulations and Standards**

1. FDA (Food and Drug Administration): In the United States, NLC-based products fall under the FDA's regulatory framework for drug products. Depending on the intended use (e.g., as a pharmaceutical or cosmetic), different regulations apply. NLC formulations must comply with regulations regarding drug stability, efficacy, manufacturing practices (cGMP), and labeling requirements.

2. EMA (European Medicines Agency): In Europe, NLCs are regulated as medicinal products under the EMA. They must undergo rigorous evaluation for quality, safety, and efficacy through centralized or national regulatory procedures. Guidelines such as ICH (International Council for Harmonisation) provide harmonized standards for pharmaceutical development, including NLC-based formulations.

3. WHO (World Health Organization): The WHO provides guidelines on quality assurance and safety for pharmaceutical products, including those using novel drug delivery systems like NLCs. These guidelines emphasize the need for comprehensive preclinical and clinical studies to demonstrate safety and efficacy.

4. Compliance Requirements: Quality Control: NLC formulations must adhere to stringent quality control measures to ensure batch-to-batch consistency, stability, and purity.

Safety: Toxicological studies are essential to assess the safety profile of NLCs, including potential interactions with herbal extracts and other components.

Efficacy: Clinical trials are required to demonstrate the therapeutic efficacy of NLC-based products, particularly those containing herbal extracts.[21, 22]

FUTURE DIRECTIONS AND CHALLENGES

Key Highlights include-

Personalized Medicine: Tailoring NLC formulations to individual patient needs based on genetic and pharmacogenomic data.

Combination Therapies: Exploring synergistic effects of NLCs encapsulating multiple herbal extracts or combining with conventional therapies.

Global Collaboration: Collaborative efforts among researchers, regulators, and industry stakeholders to streamline the approval process and promote global acceptance of NLC-based products.

Technological Advancements

Nanostructured lipid carriers (NLCs) are continuously evolving with advancements in formulation techniques and characterization methods, driving innovation in drug delivery systems.

Emerging Technologies in NLC Formulation.

Advanced Lipid Matrices: Incorporation of novel lipids and lipid combinations to enhance drug loading capacity, stability, and targeted delivery.

Hybrid Nanocarriers: Development of hybrid systems combining NLCs with polymers or other nanoparticles to optimize drug release profiles and bioavailability.

Precision Nanomedicine: Integration of nanotechnology with personalized medicine approaches, tailoring NLC formulations to individual patient needs based on genetic and pharmacogenomic data.

Responsive Delivery Systems: Design of stimuli-responsive NLCs that release drugs in response to specific physiological cues, such as pH, temperature, or enzymatic activity.

Characterization Advancements

Multi-modal Imaging Techniques: Integration of techniques such as cryo-TEM (Transmission Electron Microscopy), AFM (Atomic Force Microscopy), and advanced spectroscopic methods for comprehensive characterization of NLC structure, morphology, and drug distribution.

In situ Monitoring: Real-time monitoring technologies to assess NLC behaviour and drug release kinetics in biological environments, enhancing understanding of their pharmacokinetics and pharmacodynamics.

Computational Modelling: Utilization of computational modelling and simulation tools to optimize NLC formulation parameters and predict their performance in vivo, reducing experimental time and costs.[23, 24, 25, 26]

CONCLUSION

In conclusion, nanostructured lipid carriers (NLCs) represent a pivotal advancement in drug delivery, particularly in enhancing the bioavailability and efficacy of herbal extracts within pharmacognostic contexts. By overcoming challenges such as poor solubility and stability of herbal compounds, NLCs offer a promising avenue to integrate traditional medicinal practices with modern pharmaceutical technology. The ability of NLCs to protect sensitive phytochemicals, improve absorption rates, and provide controlled release profiles underscores their potential to revolutionize treatment strategies. Looking forward, continued research and development in NLC formulation, coupled with rigorous regulatory oversight and expanded clinical validation, will be crucial in realizing their broader impact on healthcare, sustainability, and the preservation of traditional medicine knowledge.

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REFERENCES

1. Zhang J, Wider B, Shang H, Li X, Ernst E. Quality of herbal medicines: challenges and solutions. Complementary therapies in medicine, 2012 Feb 1; 20(1-2): 100-6.
2. Patel DK, Tripathy S, Nair SK, Kesharwani R. Nanostructured lipid carrier (Nlc) a modern approach for topical delivery: a review. World J. Pharm. Pharm. Sci, 2013 Mar 17; 2(3): 921-38.
3. Üner M. Preparation, characterization and physico-chemical properties of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC): their benefits as colloidal drug carrier systems. Die pharmazie-an international journal of pharmaceutical sciences, 2006 May 1; 61(5): 375-86.

4. Gaba B, Fazil M, Ali A, Baboota S, Sahni JK, Ali J. Nanostructured lipid (NLCs) carriers as a bioavailability enhancement tool for oral administration. Drug delivery, 2015 Aug 18; 22(6): 691-700.
5. Gomaa E, Fathi HA, Eissa NG, Elsabahy M. Methods for preparation of nanostructured lipid carriers. Methods, 2022 Mar 1; 199: 3-8.
6. Patel D, Dasgupta S, Dey S, Roja Ramani Y, Ray S, Mazumder B. Nanostructured lipid carriers (NLC)-based gel for the topical delivery of aceclofenac: preparation, characterization, and in vivo evaluation. Scientia pharmaceutica, 2012 Sep; 80(3): 749-64.
7. Üner M. Preparation, characterization and physico-chemical properties of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC): their benefits as colloidal drug carrier systems. Die pharmazie-an international journal of pharmaceutical sciences, 2006 May 1; 61(5): 375-86.
8. Zhuang CY, Li N, Wang M, Zhang XN, Pan WS, Peng JJ, Pan YS, Tang X. Preparation and characterization of vinpocetine loaded nanostructured lipid carriers (NLC) for improved oral bioavailability. International journal of pharmaceutics, 2010 Jul 15; 394(1-2): 179-85.
9. Cirri M, Maestrini L, Maestrelli F, Mennini N, Mura P, Ghelardini C, Di Cesare Mannelli L. Design, characterization and in vivo evaluation of nanostructured lipid carriers (NLC) as a new drug delivery system for hydrochlorothiazide oral administration in pediatric therapy. Drug delivery, 2018 Jan 1; 25(1): 1910-21.
10. Andonova V, Peneva P. Characterization methods for solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC). Current pharmaceutical design, 2017 Dec 1; 23(43): 6630-42.
11. Han F, Yin R, Che X, Yuan J, Cui Y, Yin H, Li S. Nanostructured lipid carriers (NLC) based topical gel of flurbiprofen: design, characterization and in vivo evaluation. International journal of pharmaceutics, 2012 Dec 15; 439(1-2): 349-57.
12. Chaudhari VS, Murty US, Banerjee S. Nanostructured lipid carriers as a strategy for encapsulation of active plant constituents: Formulation and in vitro physicochemical characterizations. Chemistry and Physics of Lipids, 2021 Mar 1; 235: 105037.
13. Lacatusu I, Istrati D, Bordei N, Popescu M, Seciu AM, Panteli LM, Badea N. Synergism of plant extract and vegetable oils-based lipid nanocarriers: Emerging trends in development of advanced cosmetic prototype products. Materials Science and Engineering: C., 2020 Mar 1; 108: 110412.

14. Tirumalesh C, Suram D, Dudhipala N, Banala N. Enhanced pharmacokinetic activity of Zotepine via nanostructured lipid carrier system in Wistar rats for oral application. Pharmaceutical nanotechnology, 2020 Apr 1; 8(2): 148-60.
15. Rizwanullah M, Amin S, Ahmad J. Improved pharmacokinetics and antihyperlipidemic efficacy of rosuvastatin-loaded nanostructured lipid carriers. Journal of drug targeting, 2017 Jan 2; 25(1): 58-74.
16. Rizwanullah M, Ahmad MZ, Garg A, Ahmad J. Advancement in design of nanostructured lipid carriers for cancer targeting and theranostic application. Biochimica et Biophysica Acta (BBA)-General Subjects, 2021 Sep 1; 1865(9): 129936.
17. Nnamani PO, Hansen S, Windbergs M, Lehr CM. Development of artemether-loaded nanostructured lipid carrier (NLC) formulation for topical application. International journal of pharmaceutics, 2014 Dec 30; 477(1-2): 208-17.
18. Javed MN, Dahiya ES, Ibrahim AM, Alam MS, Khan FA, Pottoo FH. Recent advancement in clinical application of nanotechnological approached targeted delivery of herbal drugs. Nanophytomedicine: Concept to Clinic, 2020: 151-72.
19. Bansal K, Bhati H, Bajpai M. Recent Insights into Therapeutic Potential and Nanostructured carrier systems of Centella asiatica: An Evidence-Based Review. Pharmacological Research-Modern Chinese Medicine, 2024 Feb 23: 100403.
20. Ng PQ, Ling LS, Chellian J, Madheswaran T, Panneerselvam J, Kunnath AP, Gupta G, Satija S, Mehta M, Hansbro PM, Collet T. Applications of nanocarriers as drug delivery vehicles for active phytoconstituents. Current pharmaceutical design, 2020 Oct 1; 26(36): 4580-90.
21. Doktorovová S, Kovačević AB, Garcia ML, Souto EB. Preclinical safety of solid lipid nanoparticles and nanostructured lipid carriers: Current evidence from in vitro and in vivo evaluation. European Journal of Pharmaceutics and Biopharmaceutics, 2016 Nov 1; 108: 235-52.
22. Gonzalez-Mira E, Nikolić S, Calpena AC, Egea MA, Souto EB, García ML. Improved and safe transcorneal delivery of flurbiprofen by NLC and NLC-based hydrogels. Journal of pharmaceutical sciences, 2012 Feb 1; 101(2): 707-25.
23. Beloqui A, Solinís MÁ, Rodríguez-Gascón A, Almeida AJ, Préat V. Nanostructured lipid carriers: Promising drug delivery systems for future clinics. Nanomedicine: Nanotechnology, biology and medicine, 2016 Jan 1; 12(1): 143-61.
24. Livney YD. Nanostructured delivery systems in food: Latest developments and potential future directions. Current Opinion in Food Science, 2015 Jun 1; 3: 125-35.

25. Priscilla P, Malik P, Kumar A, Castagna R, Singh G. Recent advances and future perspectives on nanoparticles-controlled alignment of liquid crystals for displays and other photonic devices. Crit Rev Solid State Mater Sci, 2023 Jan 2; 48: 57-92.
26. Sutarkar AP, Bahe VG, Khan SA. ADVANCES IN NANOSTRUCTURED LIPID CARRIERS: FORMULATION STRATEGIES, APPLICATIONS, AND FUTURE PERSPECTIVES.