IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Nanostructured Lipid Carrier : A Promising Tool

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ABSTRACT:
The novel drug delivery method known as nanostructures lipid carriers (NLCs) is a second-generation substitute for solid lipid nanoparticles (SLNs). They are made up of co-surfactants, surfactants, and biodegradable and biocompatible lipids that improve stability and drug loading. NLCs can be administered by topical, oral, ophthalmic, and parenteral routes because of their solid lipid matrix with liquid lipids integrated into it, which decreases crystallinity and stops drug leakage. Particle size (10 to 500 nm), drug entrapment efficiency, and release profiles are among the physicochemical characteristics of NLCs that are influenced by the careful selection of lipids and surfactants used in their formulation. Characterization techniques including dynamic light scattering (DLS), transmission electron microscopy (TEM), and differential scanning calorimetry (DSC) are used to assess these attributes. According to recent research, NLCs can efficiently encapsulate substances such as dihydrogen resveratrol (WHO) and resveratrol (OXR), improving their stability and skin penetration while preserving a high entrapment efficiency. By regulating monogenesis without having harmful effects on human keratinocyte cells, these formulations have demonstrated promise in lowering hyperpigmentation. Easy preparation, scalability, non-toxicity, and enhanced bioavailability are just a few benefits that NLCs provide. Their capacity to target particular tissues and improve skin hydration has raised attention in both medicinal and cosmetic uses.

KEYWORDS:
Nanostructure lipid carriers; preparation; characterization; applications.

A.INTRODUCTION:

Muller constructed the NLC carrier in 1999/2000, and it took five times for the first two products Nanorepair Q10 cream and Nanorepair Q10 serum to be introduced in Munich, Germany, in 2005. Within six months, Nanolipid CLR Restore was introduced as the third product. Among nanocarriers, NLC has one of the quickest reversal times from invention to launch. Over thirty goods are now commercially available after a twelve-year period. As of 16 January 2012 at 915 p.m. Indian time, the Google keyword NLC has formerly generated 207,000 hits. According to multitudinous exploration groups, the NLC is a promising delivery system. This is supported by 364 patents and 1038 published papers, which demonstrate the wide interest in this carrier system(16 January 2012 at 915 p.m. Indian time). Solid lipid nanoparticles(SLN) were the original form of lipid nanoparticles. SLN have been completely delved as medicine delivery systems for a variety of administration routes, including topical, cutaneous, parenteral, and peroral. The release characteristics

of the generated SLNs are told by the crystallinity of solid lipids. Lipids incompletely solidify in high-energy variations with multitudinous crystal clear chassis blights incontinently following the conflation of SLN. The integrated drug may be released from the lipid matrix if a polymorphic transition to low- energy revision occurs while the medicine is being stored. It's necessary to employ lipid composites that don't produce a largely structured crystalline arrangement in order to help drug expatriation during storehouse. The alternate generation of lipid nanocarriers, or NLCs, are made of liquid lipids combined with a solid lipid matrix. Compared to mixes, NLCs can effectively incapacitate specifics and stop the patches from cementing together because of their solid matrix. Furthermore, the fitted medicine motes' mobility is significantly lowered in the solid phase. Additionally, compared to SLNs, the medicine lading capacity is increased by the liquid oil painting driblets in the solid matrix. Low toxin, biodegradability, medicine protection, controlled release, and avoiding organic detergents during conflation are some of the other benefits that NLCs have over polymeric nanoparticles. NLCs have lately been the subject of expansive exploration as hydrophilic and hydrophobic medicine delivery vehicles. The NLCs were created with the intention of satisfying artificial demands in terms of low cost, simple technology, scale up, qualification and confirmation, etc [1].

B.NEED FOR NANOSTRUCTURE LIPID CARRIER:

Over half a century ago, Bangham identified "swollen phospholipids" as a representation of the cell membrane. These were subsequently dubbed liposomes. Since then, researchers have continuously investigated and developed the spontaneous rearrangement of lipids to create nano colloidal particles. With its exceptional ability to securely deliver medications while enhancing bioavailability and lowering toxicity, liposomes are set to become a popular drug delivery vehicle in the years to come. When liposomal doxorubicin received its initial FDA approval in 1995, a new era of lipid-based nanomedicine was launched. Liposomes offer a biodegradable, secure, and efficient medication delivery system. The physiological stability, complexity of nanomedicine, and expense of such medications caused the vesicle-based lipid nanosystem to fall short of expectations as a versatile drug carrier, prompting a search for other lipid systems. Although nanoemulsion is one of the less expensive alternatives to the vesicle-based technology, it is insufficiently stable and safe for medications. Owing to the drawbacks of the previous lipid-based nanosystem, a novel class of lipid-based particulate systems was created as a substitute by fusing the benefits of polymer nanoparticles, liposomes, and nanoemulsion. separately created first-generation lipid nanoparticles (SLNs) using several techniques in the early 1990s as an affordable and adaptable drug delivery strategy.The primary purpose of these lipid-based nanosystems is cosmetics. The medicine can be encapsulated in a solid lipid matrix core using SLN, which are solid lipid cores surrounded by lipidic and surfactant shells. Because of their many benefits, SLN are good drug carriers for lipophilic medications. They are made of biodegradable materials, have a scalable, quick, and efficient manufacturing process, and are physiologically more stable than other lipid-based nanosystems.They have a solid lipid core that allows them to be kept in water for extended periods of time, something liposomes cannot do. One of the main disadvantages of solid lipid nanoparticles for effective drug administration is their poor drug loading capacity, which results from their structured solid lipid core.Another drawback of SLN is its initial burst release and stability problems during long-term storage, including drug leakage and the polymeric transition to crystalline form. To address issues related to the SLN, a novel second-generation lipid nanoparticle surfaced in 1999. In addition to having a higher drug loading capacity and greater stability than SLN, NLC is a nanocarrier that possesses the benefits of earlier lipidic nanoparticles. Because of the qualities they provided, NLCs entered the cosmetics industry in 2005, and as of right now, there are about 40 cosmetics items available. Because of NLC's intrinsic properties and effective encapsulation ability, this drug delivery method has not yet been commercialized [2].

C.TYPES OF NLC PREPARATION

Type 1(Amiss)

The NLC type A solid matrix with shy structure is also appertained to as amiss crystalline forms. The total number of defects within the structure is responsible for, and profitable for, the scalability of an effective drug. The expression of type I NLCs entails mixing lipids that are spatially distinct, potentially leading to irregularities in the demitasse chassis [3].An amiss demitasse chassis or matrix is produced when liquid lipid or oil painting is incompletely substituted for solid lipid.This miracle suggests that there's lesser space for medicinals and that medicine lading is permitted [4].Amiss demitasse type NLC features a

significantly disordered matrix that contains multitudinous voids and gaps, able of casing fresh medicine motes within unformed clusters [5].

Type 2(Multiple)

The oil painting- in- lipid- in- water expression is known as type II NLC, frequently appertained to as the multiple type. In type II NLCs, the solubility of the oil painting is advanced compared to the solubility of solid lipids [3].When the medicine has a advanced solubility in oil painting, using this approach in the expression of NLCs can boost medicine lading capacity and stability. bitsy oil painting driblets are slightly distributed across a solid lipid matrix, which is dispersed throughout an waterless media [4].At low attention, oil painting factors are successfully distributed within the lipid matrix. The Type II model provides benefits similar as enhanced medicine ruse effectiveness, regulated medicine release, and reduced medicine leakage [5].

Type 3(unformed)

The III type of NLSs, known as the unformed type, involves a medication fashion for NLCs where the lipids are combined in a manner) that inhibits crystallization during the mixing process [3].An unformed core is constantly formed when liquid lipids are combined with solid lipids that maintain their αpolymorph during solidification and storage .This is preferable to class I NLCs because the medicine remains forcefully bedded in the unformed matrix and no crystallization occurs [4].Some lipids, similar as hydroxyoctacosanyl, hydroxystearic acid, isopropyl myristate, and dibutyl adipate, form solid patches but don't form liquid patches [5]..

D.COMPONENTS

The primary element of NLC that affects the phrasings stability, sustained release behavior, and drug loading capability is the lipid itself.Adipose acids, glycerides, and waxes are among the lipid factors that form the base of lipid nanoparticle dispersions. With the significant exception of cetyl palmitate, the ultimate of these lipids are physiologically well permitted and designated as generally recognized as safe(GRAS).Before using them to produce lipid nanoparticle dispersions, the right lipids must be chosen. Empirical parameters, analogous as the drugs solubility in the lipid, have been suggested as useful criteria for choosing the right lipid, indeed however there are no set rules.Lipids with longer adipose acid chains solidify further slowly than those with shorter chains.Despite being physically more stable, wax-predicated NLCs show notable drug ejection due to their farther liquid structure. Lipid nanoparticle dispersions, now known as nanostructured lipid carriers(NLC), were created by combining two spatially distinct solid lipid matrices a solid lipid and a liquid lipid(or oil painting oil) in a double amalgamation to help issues with lipid crystallinity and polymorphism [3]. Lipids, surfactants, and water in an arid media make up the NLC. Its size, loading capacity, drug release profile, and stability are all told by the fabrication process, matrix, and lipid content.The long and short chains of liquid and solid lipid make up the NLC amalgamation, which has a lipid attention that ranges from 5 to 40.At 0.5 to 5 w/ w attention, surfactants stabilize NLC phrasings in arid media [4].

D.1.Netting of liquid lipids(oils) and surfactants

The solubility of TH in a range of liquid lipids (castor oil) can be determined by mixing spare medication with 3 milliliters of oils in tiny vials. Surfactants (Tween 20, Tween 80, Span 80, Pluronic F 188, and Pluronic F 127) and oil painting oil (Oleic acid, Labrasol, Isopropyl myristate, and Cremophore EL) were evaluated. The vials were safely stopped and continuously spun in a mechanical shaker to reach equilibrium for seventy-two hours at 25 °C. A High Speed Centrifuge (3K30, SIGMA, Germany) set to 5000 rpm was also used to centrifuge the mixtures for 30 beats at 37°C.31 A UV Spectrophotometer was used to evaluate the supernatant's solubility at 223 nm after it had been extracted and dissolved in methanol [6].

D.2.Netting of solid lipids

The molten solid lipids were toasted at 5 °C above their melting point, and TH was added in supplements of 1 mg until it was unable to dissolve further in order to ascertain its solubility in a range of solid lipids, including Gellucire, Glyceryl Monostearate, Compritol 888 ATO, and Precirol ATO 5. The importance of solid lipids required to solubilize TH was ascertained. The trial was conducted three times [6].

D.3.Selection of a double lipid phase

The solid and liquid lipids with the same solubilizing potential for TH were mixed at different speeds, such as 955, 9010, 8515, 8020, 7030, and 6040, to ascertain the two lipids' miscibility. Lipid mixtures were agitated at 200 rpm for an hour at 85 °C using a glitzy stirrer (Remi Instruments Ltd., Mumbai, India). The miscibility between the two elements was investigated by applying a cooled sample of the solid amalgamation on a sludge paper and visually inspecting it to detect any liquid oil painting

droplets.A twofold combination with a melting point higher than 40 °C that prevented oil painting oil droplets from appearing on the sludge paper was selected for the production of TH laden NLCs [6].

D.4.Surfactants

The NLC drug method uses surfactants to maintain the structure of lipid nanoparticles in dispersion medium. They decrease the patches' inclination to assemble at the list interface through the reduction of the interfacial energy between the dry and lipid phases. This creates a layer around the patches, supporting the dispersion's physical stability throughout expression and storage. Two emulsifiers with hydrophilic and lipophilic rates can be used to improve results. Surfactants, which also stabilize the structure of lipid nanoparticles in dispersion media, stabilize the dispersive system. When drug delivery methods use a lot of surfactants, issues can occur.The HLB value of the surfactant and the molecular weight of the patch should be taken into consideration while concluding the right surfactant.

A. Ionic surfactants: Sodium Tauro deoxycholate, Sodium oleate, Sodium dodecyl sulphure, Polysorbate& 80. etc.
B. Non-Ionic surfactants: Polyoxyethylene, sorbitan monolaurate(Polysorbate 20, Tween 20), Polyoxyethylene, sorbitan monostearate(Polysorbate 60, Tween 60) Polyoxyethylene, sorbitan monooleate(Polysorbate 80), Poloxamer 188 Poloxamer 182 Ethoxylated p-tert- octylphenol formaldehyde polymer(Tyloxapol).
C. Amphoteric surfactants: Egg phospholipid (Lipoid E 80, Lipoid E 80 S) Soy, Hydrogenated soy phosphatidylcholine (Lipoid S PC- 3), Hydrogenated
D. Co-surfactants: Butanol, Butyric acid, Polyvinyl alcohol (PVA), Propylene glycol, Polyethylene glycol [4].

D.5.Emulsifying agent

Agents that reduce the interfacial pressure between two immiscible liquids or factors are known as emulsifying agents or surfactants.It increases colloidal exertion by braking the rate of aggregation when taken in modest amounts. The maturity of
surfactants are hydrophilic. By preventing the reticuloendothelial system(RES) from absorbing the cut, the expression lengthens the drug's gyration period.This product should benon-galling, biocompatible, provident, and sterile before use.NLCs are made using either lipophilic or ampiphillic emulsifiers.For case, tween 80, poloxamer, and miranol ultra [7].

D.6.UV blockers

added to reduce the trouble of skin cancer by preventing UV radiation damage. For case, avobenzone absorbs UV- A shafts[7].

D.7.Arid medium

Water that has been purified. The lipids that the medicine is most answerable in are chosen using liquid lipid netting tests in order to choose the right solid lipid.To make stable NLC, the chosen lipids must be combined in the right proportion.To do this, double lipid phase selection is also carried out, wherein various proportions of chosen liquid and solid lipids are combined, and the optimal rate is chosen for NLC drug [7].

E.METHOD OF PREPARATION OF NLC :

Nanostructured lipid carriers can be prepared using a variety of methods. High pressure homogenization, solvent emulsification, supercritical fluid extraction of emulsion, ultrasonication or high speed homogenization, and spray drying are the most often employed methods. The drug's solubility, stability, and administration route all influence the technique
choice [7].

E.1.The Method Of High-Pressure Homogenization This method is effective and dependable for producing NLCs on a commercial basis. The homogenization technique's high pressure allows for the environmentally friendly avoidance of organic solvents in preparations. Furthermore, high-pressure
homogenization is a desirable technology that is employed in the production of topical medications and cosmetics and is simple to scale up. Cold homogenization is carried out below room temperature, while hot homogenization is carried out at a higher temperature. Both methods include dispersing or dissolving the active component in the molten lipid prior to high pressure homogenization. High pressure (100–2000 bar) homogenizes the fluid by moving it through a small opening [5].There are two kinds of homogenizers on the market: piston-gap homogenizers and jet-stream homogenizers [3].

E.2.Hot Homogenization

The process of hot homogenization With this method, homogenization is carried out at a high temperature. At a temperature higher than 5–10°C over their melting point, the solid lipids melt. The medicine to be encapsulated and liquid lipid are

added to create a dispersion. A pre-emulsion is formed when the mixture is dispersed in an aqueous solution of surfactant (s) that has been heated to the same temperature using a high shear mixing equipment. At a regulated temperature, the pre-emulsion is added to a high pressure homogenizer. For homogenization, three to five cycles at 500– 1500 bar are usually adequate. With the slow cooling of the nanoemulsion, the lipid recrystallizes and forms nanoparticles. Using high temperatures throughout the procedure could cause heat-sensitive substances to degrade. Additionally, as surfactants have a cloud point below 85°C, high temperatures may cause them to lose some of their emulsifying power. This could make nanocarriers unstable [5].

E.3.Cold Homogenization

This method involves quickly cooling a lipid melt with an active ingredient using liquid nitrogen or dry ice, grinding it up, dispersing it in a cold surfactant phase, and finally homogenizing it at room temperature. The cold process uses a higher pressure, 5–10 cycles of 1500 bar. This method reduces the amount of heat that the medicine is exposed to and works well with thermolabile medications. Additional advantages of the technique include increased drug entrapment efficiency and consistent drug distribution within the lipid. However, it produces more variable-sized nanoparticles [5].

E.4.Microemulsion Technique

The temperature used to prepare the microemulsion is higher than the lipids' melting point. Water, one or more cosurfactants, and the surfactant are heated to the same temperature as the lipids and added to the lipid melt with gentle stirring after the lipids have been heated above their melting point. A cold aqueous medium made of water is then used to distribute the microemulsion while being gently stirred. In a coldaqueous media, this dispersion causes the oil droplets to quickly recrystallize [7].

E.5.Solvent-Emulsification Evaporation Method

This approach involves dissolving the medication and lipids (solid and liquid) in an organic solvent that is water insoluble (cyclohexane, chloroform). An o/w emulsion is created by dispersing the resulting mixture into an aqueous solution containing emulsifiers. The solvent is extracted from the emulsion by evaporation at lower pressure. Through lipid precipitation in the aqueous medium, evaporation causes nanoparticles to disperse in the aqueous phase. Although there is no heat stress with this approach, using an organic solvent has drawbacks. The solid lipid and surfactant can affect the particle size, which can range from 30 to 100 nm [7].

E.6.Solvent-Emulsification Diffusion Method

In this method, the initial thermodynamic equilibrium is maintained by mutually saturating the solvent and water. Following that, the medication and lipids are dissolved in the solvent that is saturated with water. Using a homogenizer, a solvent-containing medication and lipids are combined to create an o/w emulsion in a solvent-saturated aqueous emulsifier solution. Owing to the organic solvent diffusing from the emulsion droplets to the continuous phase, the lipid nanoparticles precipitate after being diluted with excess water (ratio: 1:5–1:10). Ultrafiltration andlyophilization are two methods for eliminating the solvent. Comparing solvent diffusion to volatile solvents, the majority of the solvents used exhibit a better safety profile and are more inventive [5].

E.7.High Shear Homogenization and Ultrasonication The drug is combined with the heated lipid phase, and the aqueous surfactant solution is heated to the same temperature at the same time.Next, a magnetic stirrer is used to pour the heated aqueous phase into the lipid mixture, creating a preemulsion. Using a probe sonicator and a water bath (at 0 °C), ultrasonication was given to the pre-emulsion. Impurities are eliminated by passing the product through 0.45 µm after ultrasonication. This process's excessive surfactant usage and stability problems brought on by the improper particle size distribution are its drawbacks. However, compared to hot and cold homogenization, this method can be considered the most accessible because the tools needed are comparatively more readily available in labs.In addition, research on invitro skin penetration revealed that methotrexate-loaded NLC had more skin penetration than free drug formulation [7].

E.8.Phase Inversion Technique

Phase inversion from o/w to w/o emulsion is a groundbreaking, economical, and solvent-free method for creating lipid nanocarriers. There are two steps involved.The first step entails combining the lipid, surfactant, and water in the ideal ratios. To

raise the temperature from room temperature to 85°C, the mixture is mixed and heated at a pace of 4°C. To approach the phase inversion zone, the system is subjected to three temperature cycles (85–60–85-60–85°C).Due to dilution with cold water (0oC), step 2 introduces an irreversible shock to

disrupt the system. Nanocapsules are created by the quick addition of cold water. Particle aggregation can be prevented by applying a slow magnetic stirring for five minutes.Many bioactive substances can be encapsulated in stable transparent dispersions (less than 25 nm) made possible by low energy involvement [5].

E.9.Microfluidization Method

The method makes use of a recently developed, patented mixing technology that uses a microfluidizer, a high shear fluid device. This procedure involves forcing the liquid through microchannels at high operating pressures at up to 400 m/s to an impingement location. The effective reduction of particle size in the "interaction chamber" is due to cavitation and the resulting shear and impact. The method can be applied at both the laboratory and production levels [5].

E.10.Melting Dispersion Method

The water phase is heated to the same temperature independently while the medication, solid lipid, and organic solvent are melted together in the melting process. The drug containing solid lipid melt is then introduced to the water phase and stirred rapidly for a few hours. To produce nanoparticles, the resultant mixture is cooled to room temperature [7].

E.11.Spray Drying

Compared to lyophilization, another process used for products with stability difficulties, spray drying is thought to be a more cost-effective procedure since it applies hot gas to liquid or viscous liquid to create dry powder. It is a preferred procedure for products that are sensitive to heat since they are exposed to high temperatures for brief periods of time. More than 70 °C is the ideal melting point for lipids; below that, they are inappropriate because of the high shear force and temperature, which causes them to agglomerate [7].

E.12.Membrane Contactor Technique

The term "membrane contactor" refers to membrane systems used to "keep in contact" two phases. The lipid phase is put in a pressured tank at a temperature higher than its melting point. When pressure is applied, it is permitted to enter the pores of the ceramic membrane and form tiny droplets. The aqueous phase flows tangentially inside the membrane module while being 4 continuously stirred, brushing away the droplets that develop at the pore exits. Lipid particles arise when the preparation is cooled to room temperature. The process variables influencing the size of lipid nanocarriers include the aqueous and lipid phase temperature, the aqueous phase tangential-flow velocity, the lipid phase pressure, and the membrane pore size.The advantages of this novel membrane emulsification method include control overparticle size through the use of optimal parameters and commercial scalability [5].

Table 1 : Process variables and their role in the preparation of NLCs. [3].

Process Variables	**Step involved**	**Process Responses**
Speed and Time	Mixing	Particle shape, Particle size
Temperature	Melting	Phase transition, Solubility
Speed and Time	Stirring	Particle shape, Particle size
Speed, Temperature, Pressure	Homogenisation	Particle shape, Particle size

F.DRUG ENCAPSULATION IN NLC;

Drugs can be encapsulated into lipid nanoparticles, or NLCs, using one of three techniques. They are made up of a drugenriched core, a drug-enriched shell, and a solid solution matrix. [8].

D.1.Homogenous solid matrix: The medication is continuously incorporated into the lipid matrix of the particles in this method, after which drug release occurs through diffusion.

D.2.Drug-enriched shell: In this encapsulation technique, the medication targets the outer layer or shell of the lipid nanoparticles. The drug is released in a burst from this type of nanoparticle due to the precipitation and solubilization processes.

D.3.Drug-enriched: This type of encapsulation results in prolonged release due to the medication's saturation solubility in the lipid.

G.AADVANTAGE OF NLC:

- Some medications have a higher loading capacity.
- The dispersion has less water.
- Reduce or stop drug ejection while being stored.
- It is possible to load both hydrophilic and lipophilic medications;
- Biodegradable and biocompatible lipids are used;
- Organic solvents are avoided; More reasonably priced (less costly than carriers based on polymers or surfactants);

- Simpler to qualify, validate, and obtain regulatory approval; Improved physical stability [9].
- Scale-up and preparation ease
- The ability of NLCs to simultaneously transport hydrophilic and lipophilic medications enhances pharmacological stability. [8].
- Close contact with the stratum corneum is ensured by small size. [5].
- Because their lipid components are approved or excipients used in commercially available topical cosmetic or pharmaceuticalformulations, they are one of the preferred transporters for medications used topically. [9].
- Greater drug solubility in liquid lipid within the matrix and a higher drug loading capacity due to the creation of an incomplete matrix.
- Throughout long-term storage, NLCs lessen drug expulsion. As is well known, drug ejection has happened while the lipid matrix is still crystallizing.
- The unique liquid oil is mixed into the formulation of NLCs to create an amorphous structure that inhibits the lipid matrix's crystallization and reduces drug ejection. Greater adaptability for controlling drug release by altering the kinds and concentrations of liquid lipids or surfactants. [10].

I.LIMITATIONS OFNLC's:

- Effects of cytotoxicity associated with matrix composition and concentration [9].
- Some surfactants have the potential to cause irritation and sensitization., the use of cationic surfactants in NLC formulation caused cell death and the release of inflammatory mediators [7].
- Cytotoxic consequences associated with matrix type and concentration [11].
- Some surfactants have an irritating and sensitizing effect, [11].
- More has to be done to improve the use and effectiveness of gene delivery systems and protein and peptide medications. [9].
- More has to be done to maximize the use and effectiveness of gene delivery systems and protein and peptide medications. [11]
- Inadequate preclinical and clinical research on these nanoparticles in relation to bone healing [11].

J.CHARACTERIZATION OF NLC :

The characterization of nanocarriers is essential for their clinical applications. For therapeutic uses, nanocarriers must be extensively characterised. NLCs are difficult to characterise because of their minuscule size and dynamic system in contrast to other colloidal carriers.Nanoparticle stability and in vivo performance are directly impacted by characterisation factors [12].

J.1.Size and Morphology

The physicochemical properties of lipid nanocarriers, such as their particle size distribution, determine how much of them accumulate in the target tissue. Therefore, homogenous (monodisperse) populations of nanocarriers of a specific size must be prepared in order to formulate safe, stable, and effective nanocarriers. The size of the lipi particles is typically ascertained by photon correlation spectroscopy, also known as dynamic light scattering (DLS), and laser diffraction (LD). The size distribution, represented by the polydispersity index (PI), is evaluatedusing both methods. DLS provides cumulative data on particle size and solution homogeneity.The presence of a single, homogeneous population of scatterers is indicated by a single, sharp peak. 400 µm is the ideal particle size for NLCs.A fully uniform sample in terms of particle size has a PI value of 0.00, while a highly polydisperse sample with numerous particle size distributions has a PI value of 1.00. Highly monodisperse standards are the primary source of PI values less than 0.05. A wide distribution of particle sizes is indicated by PI values greater than 0.7. The DLS technique is most likely not a good way to examine a sample with a wide range of particle sizes [12].

J.2.Zeta Potential

When assessing the stability of nano dispersion, zeta potential (ZP) is a crucial component. Particle electrophoretic mobility in an aqueous media serves as the basis for the ZP determination.Zeta Potential provides information on long-term stability and describes the surface charge.While dispersions with lower ZP tend to coagulate or flocculate, potentially resulting in reduced stability, higher ZP makes particle aggregation less likely due to electrostatic repulsion. For NLC to be electrostatically stabilized, the zeta potential of dispersion should typically be either greater than +30 mV or less than -30 mV. A Malvern ZetaSizer Nano ZS can be used for Laser Doppler electrophoresis to estimate zeta potential. By introducing an electric field across the sample, particles possessing a zeta potential will move toward the electrode of an opposing charge at a

speed that corresponds to the magnitude of the zeta potential. The speed is assessed using the method of Laser Doppler anemometry, which is also referred to as Laser Doppler velocimetry. The frequency shift of a laser beam that is incident, caused by these moving particles, is recorded as particle mobility, and this value is transformed into the zeta potential per the Henry equation. Zeta potential is affected by elements such as electrical conductivity, pH, and the
characteristics of the reagents [5].

J.3.Entrapment Efficiency

The amount of drug trapped in the carrier relative to the total amount of drug in the dispersion is known as the drug entrapment efficiency. Combining analytical methods (such as UV spectrophotometry or high-performance liquid chromatography, or HPLC) with separation methods (such as ultrafiltration, centrifugation, and dialysis) is how the entrapment efficiency is determined. These methods make it possible to measure the active component. There are two main approaches to measuring entrapment efficiency: direct and indirect methods. As opposed to the indirect approach, which
measures the amount of unencapsulated medicine in the supernatant, the direct method measures the encapsulated drug directly. The active components' entrapment efficiency in lipid nanoparticles is often greater than 70%. NLCs are formed of a combination of liquid and solid lipids. During the rigidization process, an incomplete core forms in NLCs because of the presence of liquid lipids. Higher drug encapsulation is made possible by these defective cores, which offer adequate area for drug accommodation. As a result, the medication is not released from the core during storage. However, the speed and duration of swirling, as well as the emulsifier and surfactant concentrations, determine how well an active molecule is entrapped into the lipid carriers. The type, concentration, and crystal structure of lipids have the biggest effects on entrapment efficiency. The entrapment efficiency of these nanocarriers is further impacted by drug partitioning between the melted lipid and the aqueous media. Determining the amount of drug combined with the lipid particles and the amount of drug dissolved in other structures within the formulation is crucial since the solubility of a drug in lipids diminishes when the molten lipids are cooled. Compared to liposomes, SLNs are more effective at entrapping hydrophobic compounds [12].

J.4.Crystallinity and Polymorphism

Characterizing the crystallinity of the NLC components is crucial because both the loaded medication and the lipid matrix may experience a polymorphic transitional change that could result in undesired drug leakage during storage.The efficiency
of encapsulation and release rates are also influenced by a particle's crystallinity. The following order shows a decrease in drug integration rate and an increase in thermodynamic stability and lipid packing density: Alpha modification > beta' modification > supercooled melt > beta modification.X-ray diffraction (XRD) and differential scanning calorimetry (DSC) tests are used to examine crystallinity and polymorphism status. By calculating the mean particle size, size distribution, entrapment efficiency, and drug release profile throughout storage periods at various temperatures in accordance with ICH criteria, the stability profile of SLNs and NLCs. Samples are taken out and analyzed for these parameters at pre-arranged intervals. Using an HPLC or UV spectrophotometer, the drug release patterns and percentage drug entrapment efficiency are examined [12].

K.EVALUATION OF NLC

K.1.Transmission Electron Microscopy

The purpose of the TEM investigations was to learn more about the morphology of the NLC systems. According to the study, the formulation's particle size grew after the medication was loaded into a placebo. This could be because the medication has enough room in the lipid matrix to accommodate it. The medication encapsulated in the lipid matrix is visible in the TEM images (Fig. 1(a). The TH-NLC TEM pictures display lipid nanoparticles with a roughly spherical shape and a homogeneous size distribution. Photon correlation spectroscopy yielded a minimal PDI (0.2), which correlates with the regularity of the particle size distribution. The TEM analysis revealed that the particle size was between 100 and 140 nm [70].

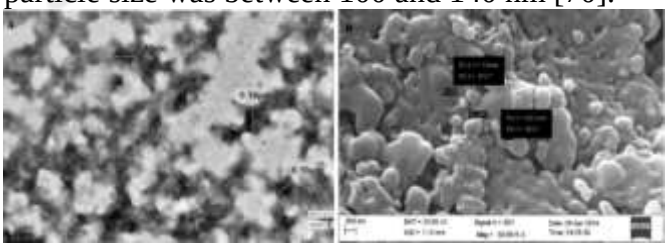

Figure 1: TEM image (A) of optimized formulation and (B) SEM image of drug loaded formulation.

K.2.X-Ray Diffraction Studies (XRD)

The X-ray scan showed prominent peaks at the 2θ value of TH, indicating that the powder was extremely crystalline (Fig.3 (b)). The freeze-dried TH loaded NLC's XRD patterns are displayed in Fig. 3(a). When combined into NLC, the separate components have partially lost their crystalline character, according to XRD of TH-NLC. The excipients of blank NLC that were accessible in the literature were compared based on their X-ray diffraction. Additionally, these results are consistent with those of previous researchers [70].

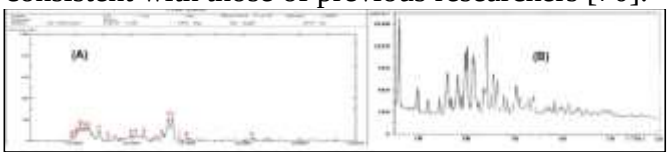

Figure 2: Xrd (A) drug loaded NLC; (B) XRD of pure drug.

K.3.Scanning Electron Microscopy

The SEM photomicrograph (Fig. 1(b)) showed that the NLCs had a smooth surface and were spherical in shape. There were also sporadic clumps in a few of the photos, which could be the result of issues with NLC shrinking after drying or dispersion medium concentration [70].

K.4.Differential Scanning Calorimetry (DSC)

The DSC thermogram of the pure drug and the freeze-dried TH- NLC patterns are displayed in Figure 2(a) and (b). Figure 2(b) showed a change in the peak, which might have resulted from the drug's interaction with the lipid matrix. The DSC thermogram shows that the drug peak in the formulation (NLC) vanishes, indicating that the drug is fully contained within the lyophilized drug-loaded NLC. The excipient's DSC curves were contrasted with those that had previously been published in the literature [70].

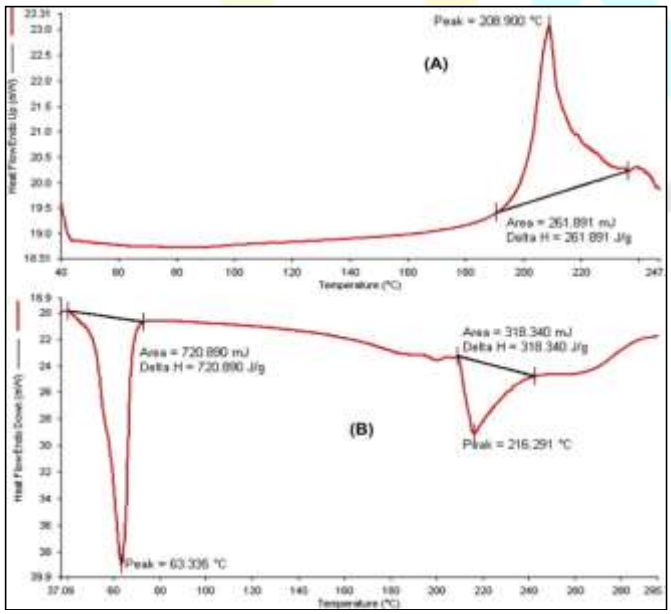

Figure 3: DSC Curve (A) Terbinafine Hydrochloride; (B) Optimized Formulation.

L.APPLICATIONS:

L.1.Application Of NLC

There are several different drug delivery methods that can use NLCs, including gene transfection, oral, transdermal, and injectable drug delivery systems. NLC as a vehicle for oral delivery. They made oral medications like antibiotics and enzymes that were insoluble or readily broken down by digestive enzymes. The lymphatic system has the ability to absorb the particles. By slowing down medication degradation and removal, the controlled-released particles can increase a medicine's bioavailability [13].

L.2.Oral bioavailability enhancement

The oral route has been one of the most extensively used administration methods for NLCs. Because of NLCs' higher drug loading capacity, the majority of these research have concentrated on how well NLCs can boost the oral bioavailability of medications that are weakly water soluble (designated as Biopharmaceutics Classification System (BSC)II or IV). A few instances of highly lipophilic medications whose oral bioavailability rises when they are made into NLCs. Encapsulation in Nanostructure Lipid Carrier (NLCs) has significantly improve the oral bioavailability of poorly bioavailable drugs:

- Etoposide (BCS IV): NLCs (<130 nm) improved oral bioavailability by 3.5-fold [14].
- Fenofibrate (BCS II): NLCs (<200 nm) increased Cmax and AUC by 4-fold [15].
- Iloperidone (BCS II): NLCs (~160 nm) enhanced bioavailability by 8.3-fold [16].
- Lovastatin (BCS II): NLCs (<300 nm) raised AUC by 6.4fold[17].
- Miconazole (BCS II): NLCs (~200 nm) achieved the same therapeutic effect with 17-fold lower doses [18].
- Montelukast (BCS II): NLCs (<200 nm) increased bioavailability by 143-fold [19].
- Silymarin (BCS III): NLCs (<100 nm) boosted bioavailability by 2.5- to 3-fold [20].
- Spironolactone (BCS II): NLCs (~150 nm) altered metabolic profiles [21].
- Vinpocetine (BCS II): NLCs (<200 nm) enhanced bioavailability by 322% [22].
- Saquinavir mesylate (BCS IV): NLCs (~250 nm) improved cellular transport by 3.5-fold [23, 24].

L.3.Carrier OfAnticancer

For anticancer therapy, the PNP drug delivery system is a very useful tool. PNPs can decrease harmful side effects, increase medication targeting to the tumor location (and hence efficacy), extend drug retention period in the body, and regulate drug release. Additionally, the elevated permeability of PNP improves the drug-loaded nanoparticles' ability to enter tumor cells. PNP transports across the cell membrane by a different method than the unbound drug. Since PNPs are integrated by endocytosis, the drug transporters in the cell membrane have little effect on their uptake.Therefore, the multi-drug resistance of tumor cells caused by drug transporters can be avoided by combining anticancer medications with PNPs [13].

L.4.Carriers for Antibiotic Drugs

In numerous infected bacterial cells, the effectiveness of penicillin, cephalosporin, and aminoglycosides can be restricted. The reduction in

In numerous infected bacterial cells, the effectiveness of penicillin, cephalosporin, and

Drug	Composition	Research Outcome	Ref.
Atorvastatin	Gelucire 43/01 (solid lipid), Capryol PGMC (propylene glycol monocaprylate type I; liquid lipid) and Pluronic F68 (surfactant).	In rats, bioavailability of atorvastatin loade NLCs revealed 3.6- and 2.1-fold increase in bioavailability when compared to atorvastatin suspension and commercial product (LipitorTM)	[25]
Fenofibrate	Precirol ATO 5 (solid lipid), Captex100 (liquid lipid) and tween-80 (surfactant).	In beagle dogs, bioavailability of Fenofibrate loaded NLCs suspension and solidified NLCs pellets revealed 3.6- and 3.5-fold respectively increase in bioavailability when compared to commercial product (LipanthylTM capsule)	[26]
In dogs, NLC optimized	Formulation was 3.75 fold enhancement in oral bioavailability when compared to raloxifene hydrochloride suspension		[27]
Ezetimibe	MonosteolTM (solid lipid), CapryolTM 90 (liquid lipid), KolliphorÒ EL (surfactant) and TranscutolÒ HP (Cosurfactant).	In rats, bioavailability of ezetimibe loaded NLCs revealed 2.5- and 1.6-fold increase in bioavailability when compared to atorvastatin suspension and commercial product LipitorTM)	[28]
Olmesartan medoxomil	Gelucire 44/14 (solid lipid, Capmul MCM EP (liquid lipid) and TPGS (surfactant).	In rats,bioavailability of olmesartan medoxomil loaded NLC was increased by about 5 fold compared to that of the pure drug suspension	[29]
Amisulpride	GelucireÒ43/01(solid lipid), Capryol TM90 (liquid lipid) and Tween-80 (surfactant)	The relative bioavailability of NLCs capsules was found to be 252.78% when compared to AmiprideÒ tablets	[30]
Raloxifene	Hydrochloride	The NLCs were composed of glyceryl monostearate (solid lipid) and Capmul MCM C8 (liquid lipid) and polyvinyl alcohol (surfactant)	[30]
Telmisartan	Glyceryl monostearate (solid lipid), oleic acid (liquid lipid) and Tween 20 (surfactant).	In rats, bioavailability of the telmisartan loaded NLC was increased by 2.17 and 3.46 fold compared to that of the marketed formulation and pure drug suspension, respectively	[31]

aminoglycosides can be restricted. The reduction in the intracellular concentrations (and effectiveness) of these antibiotics may be partially attributed to variations in cell permeability. Polymer nanoparticles (PNPs) can enhance targeting by encapsulating antibiotics within a polymeric carrier. By chemically altering the surface of the polymer nanoparticles, the PNPs can remain in the bloodstream for extended durations, ultimately increasing their availability to fight infections. Consequently, PNPs have the potential to amplify the effects of antimicrobial medications [13].

L.5.Parentral Delivery

Nano-drug delivery systems, including nanomicelles, nanoemulsions, and nanoparticles, have shown significant promise in enhancing the parenteral administration of hydrophobic agents over the past twenty years. Nanostructured lipid carriers (NLC) have emerged as a viable alternative to liposomes and emulsions due to their superior properties such as simplified manufacturing processes, high drug loading capacity, increased flexibility in modifying drug release profiles, and their aqueous nature. Additionally, the biocompatibility of the excipients facilitates intravenous drug delivery with passive targeting capabilities and straightforward elimination [11]. Nanostructured lipid carriers (NLCs) and solid lipid nanoparticles (SLNs) have been incorporated to enhance the therapeutic efficacy, bioavailability, and targeted delivery of various drugs:

- Nabumetone: Used for anti-inflammatory purposes, SLN/NLCs prolonged the drug's action through topical administration [32].
- Ciprofloxacin: Incorporated to reduce dose and adverse effects, administered orally [33].
- Pyrazinamide, Isoniazid, and Rifampicin: Tuberculosis drug with improved bioavailability delivered via nasal route [34].
- Mitoxantrone: Used in breast cancer treatment, NLCs enhanced bioavailability and reduced toxicity when administered intraperitoneally (i.p.). [35].
- Tamoxifen: For breast cancer therapy, NLCs provided prolonged drug release via intravenous (i.v.) route [36].
- Methotrexate: Anti-cancer drug targeted specifically to tumorsites via i.v. administration. [17].
- Lovastatin: Anti-hyperlipidemic drug with low bioavailability improved through oral administration [37].

Table 2 : Highly lipophilic drugs encapsulated within NLCs for oral bioavailability enhancement.

- Domperidone: For gastro-esophageal reflux, bioavailability increased by reducing first-pass metabolism via oral route [38].
- Naringenin: An antioxidant with increased bioavailability delivered via pulmonary route [38].
- Sesamol and Ficus benjamin: Both hepatoprotective agents showed enhanced bioavailability through oral delivery [39], [40].
- Tripterine: Anti-cancer drug with improved bioavailability via oral administration [41].
- Hydroxycitric Acid and Epigallocatechin Gallate: Cardioprotective and anti-obesity agents, respectively, with enhanced bioavailability via oral administration [38].
- Genistein: Anti-cancer drug with improved bioavailability via oral route [42].
- Breviscapine: Anti-hypertensive drug with sustained release and protection against liver enzyme degradation in vivo through oral administration [43].
- β-Elemene: Anti-cancer agent with reduced irritation, toxicity, and enhanced bioavailability via oral route [44].
- Silymarin: Anti-cancer drug with increased absorption and oral bioavailability in vivo [20].
- Tetrandrine: Calcium channel blocker delivered via ocular route to reduce eye mucous membrane irritation in vivo [79].
- Resveratrol: Anti-obesity agent with improved absorption and oral bioavailability [45].
- Puerarin: Anti-hypertensive drug with enhanced absorption and bioavailability via oral delivery [[46], [47].
- Triptolide: Anti-cancer agent with reduced gastric irritation and improved absorption and bioavailability via oral route. [48].
- Curcumin: Anti-cancer agent with enhanced antitumor activity and brain targeting via nasal delivery [49].
- Quercetin: Anti-obesity agent with improved bioavailability via oral administration [38].

L.6.Drug delivery to brain

Brain targeting lowers the frequency of dosage and adverse effects while simultaneously raising the drug's concentration in the cerebrospinal fluid. When opposed to oral administration, the main benefits of this mode of administration are the avoidance of first pass metabolism and the quick

beginning of effect. Because of their quick absorption by the brain,
bioacceptability, and biodegradability, LNCs (like NLC) of this generation are regarded as one of the main methods for drug delivery without modifying the drug molecule. They are also more promising drug delivery vehicles due to their scalability and lack of burst effect. Furthermore, NLC improved duloxetine's intranasal medication delivery in the brain to treat major depressive disorder.For Parkinson's disease treatment, bromocriptine (BC), a dopamine receptor agonist, has also been added to NLCs for regulated drug delivery that may prolong BC half-life in vivo and produce long-lasting therapeutic effects [11].

L.7.Anti-Mycotics

An imidazole-type lipophilic antifungal medication, clotrimazole (CZ) is used to treat a variety of skin and mucous conditions, including tinea pedis and tinea crusis.79 Due to its low oral bioavailability and poor water solubility, CZ is an ideal model medication for SLN and NLC development. CZ served as a prototype medication for the first used by Suoto et al. in 2008 to illustrate NLCs' occlusive and drug-release capabilities. By using hot high-pressure homogenization, the lipidic carriers made of Dynasan116 as the solid matrix and Miglyol812 as the liquid lipid were created. NLCs maintained their colloidal state even after three months of storage at various temperatures, according to the stability investigations. 20 Likewise, Das et al created CZ-loaded NLCs using the emulsification–ultrasonification approach in 2012 and shown that NLCs are superior to SLNs for the delivery of lipophilic medications [11].

L.8.Anti Inflammatory Drug

By examining the in vitro penetration of indomethacin from NLCs including gel and gel without NLC through the SC and epidermis, Ricci et al. (2005) demonstrated that lipidic carriers can prolong the duration of anti-inflammatory effect. NLCs were made up of xanthan gum, Lutrol F68, Miglyol ATO, and Compritol 888 ATO. The UV-B-induced erythema paradigm was used to test the indomethacin-loaded NLC gel's in vivo anti-inflammatory properties. When compared to the indomethacin- loaded NLC gel, the study found that the topical administration of indomethacin had a longer-lasting antiinflammatory effect [15]. Nanostructured Lipid Carriers (NLCs) have shown significant potential for topical drug delivery:

- Alpha Lipoic Acid (ALA): HPH-produced NLCs (103 ±9nm, −34.8 ±0.5 mV) were effective carriers for water insoluble ALA, enhancing its physiochemical and biological properties [50].
- Calcipotriol-Methotrexate: Solvent evaporation-based NLCs (267.3 ±12.3 nm, −44.6 ±1.4 mV) improved skin permeation and compatibility, making them promising for anti-psoriatic therapy [51].
- Camptothecin: HPH-generated NLCs (192.3 ±10.2 nm,−36.8 ±2.8 mV) showed sustained drug release, superior to other carriers [52].
- Coenzyme Q10: HPH NLCs (195.9 ±3.6 nm, −45.7 ±0.8 mV) provided high stability, biphasic release, and effective skin concentration maintenance [53].
- Benzocaine-Lidocaine: Ultrasonication-created NLCs (386.1 ±65.6 nm for benzocaine, 342.0 ±23.9 nm for lidocaine) prolonged anesthetic effects and demonstrated high encapsulation efficiency [54], [55].
- Flurbiprofen: HPH NLCs (179.7 ±3.1 nm, 23.0 ±0.6 mV) enhanced drug permeation and reduced oral NSAID-related side effects [56].
- Fluticasone Propionate: Microemulsion-based NLCs (316– 408 nm) achieved high encapsulation efficiency and remained stable for 60 days [57].
- Itraconazole: HPH-formulated NLCs (106 nm, −32.7 mV) were stable during nebulization, making them suitable for pulmonary antifungal delivery [58].
- Lidocaine: Ultrasound dispersion NLCs (72.1 nm) in gel form provided prolonged local anesthesia with slow drug permeation [59].
- Tacrolimus: Hot sonication-based NLCs (123.4 nm, −24.3 mV) showed better skin penetration than Protopic® [60].
- Ketoprofen: Ultrasonication NLCs (494 nm) improved dissolution and skin permeation, leveraging benefits of cyclodextrins and NLCs [61].
- Oxybenzone: Solvent diffusion NLCs (327–797 nm, −10.6 to−29.7 mV) overcame solubility issues, enhanced sunscreen efficacy sixfold, and reduced side effects [62].
- Lutein: Ultrasonic emulsification NLCs (134 nm) provided gastric protection and slow intestinal release [63].
- Flurbiprofen: NLCs prepared via probe ultrasonication (55.4 nm, −0.446 mV) coated with chitosan oligosaccharides

showed longer retention time and improved corneal permeability [64].

- Silybin: Emulsion evaporation technique produced NLCs (232.1 ±8.3 nm, −20.7 ± 1.5 mV) with a biphasic release pattern, demonstrating sustained drug release and prolonged residence time [65].
- Tocotrienol: Ultrasonication NLCs (139.8 ± 2.2 to 407.2 ± 0.7 nm) effectively entrapped tocotrienol in oily nano compartments, enhancing drug stability [66].
- β-Carotene and Tocols: HPH-created NLCs (150–200 nm) enhanced the chemical stability of heat-sensitive bioactives and improved the physical stability of the system [67].
- Nevirapine: Microemulsion-based NLCs (159.6 nm, 25.7 mV) coated with human serum albumin (HSA) reduced thermal resistance and enhanced the release of nevirapine, making them promising for viral therapy [68].
- Topotecan: Microemulsion NLCs (108–168 nm, −45.31 ± 1.29 mV) exhibited high entrapment efficiency, small particle size, and satisfactory drug loading [17].

L.9.Cancer Chemotherapy

In the addition, the role of NLC in cancer treatment is discussed, and research hotspots are highlighted. In the near future, it is anticipated that the development of nanostructured lipid carriers will enable the more precise, safe, and effective delivery of cytotoxic anticancer drugs. ZER's anti-proliferative action was unaffected by its penetration into NLC. Through the intrinsic route, ZER and ZER-NLC both markedly and time-dependently increased apoptosis. The activation of caspase-9 and caspase-3, suppression of anti-apoptotic protein, and stimulation of proapoptotic protein expressions are the suggested mechanisms by which ZER and ZER-NLC trigger apoptosis in cancer cells. The bioavailability of the insoluble ZER in the treatment of malignancies will be increased by loading it into NLC. L-arginine lauryl ester (AL) was incorporated into nanostructured lipid carriers (NLCs), and subsequently, these carriers were coated with bovine serum albumin (BSA). This led to the creation of pH-sensitive, membranolytic, and lysosomolytic nanocarriers (BSA-ALNLCs) designed to enhance anti-cancer efficacy. The goal was to endow the nanocarriers with a greater lysosomolytic potential while minimizing cytotoxicity, thus improving the therapeutic index of the active agents loaded within [9].

L.10.NLCs of natural and synthetic bioactive components administered by different routes.

- Nabumetone: Used for anti-inflammatory purposes, SLNs NLCs prolong the action when administered topically [32].
- Ciprofloxacin: An antimicrobial agent, its incorporation reduces dose and adverse effects, and it is administered orally [33].
- Pyrazinamide, Isoniazid, and Rifampicin: Used for tuberculosis treatment, SLNs/NLCs improve their bioavailability via nasal administration [34].
- Mitoxantrone: An anti-cancer drug for breast cancer, SLNs/ NLCs increase bioavailability and reduce toxicity when administered intraperitoneally [35].
- Tamoxifen: Prolonged release is achieved via intravenous administration for breast cancer treatment [36].
- Methotrexate: Incorporation into SLNs/NLCs enables sitespecific targeting, administered intravenously [17].
- Lovastatin: A drug for hyperlipidemia with low bioavailability, its oral administration in SLNs/NLCs improves efficacy [37].
- Domperidone: For gastro-esophageal reflux, SLNs/NLCs enhance bioavailability by reducing first-pass metabolism, administered orally [38].
- Sesamol: A hepatoprotective agent with reduced irritation, administered orally [39].
- Ficusbenjamin: This hepatoprotective drug demonstrates enhanced bioavailability when administered orally [40].
- Tripterine: An anticancer agent, its bioavailability is enhanced through oral administration [41].
- Genistein: This anticancer agent exhibits enhanced bioavailability via oral administration [42].
- Breviscapine: An antihypertensive agent, it achieves sustained release and protection against liver enzyme degradation in vivo when administered orally [43].
- β-Elemene: An anticancer agent, SLNs/NLCs reduce irritation, toxicity, and enhance bioavailability when administered orally [44].
- Silymarin: Used for anticancer purposes, SLNs/NLCs increase absorption and oral bioavailability in vivo [20].

- Tetrandrine: A calcium channel blocker, SLNs/NLCs reduce eye mucous membrane irritation when administered ocularly [45].
- Resveratrol: For anti-obesity effects, it improves absorption and oral bioavailability via oral administration [69].
- Puerarin: An antihypertensive agent, it shows improved absorption and oral bioavailability when taken orally [46], [47].
- Triptolide: An anticancer agent, SLNs/NLCs improve absorption, oral bioavailability, and reduce gastric irritation when administered orally [48].
- Curcumin: SLNs/NLCs improve its antitumor activity and brain targeting in vitro, administered nasally [49].

M.FUTURE PERSPECTIVE:

The creation of a delivery system that is adaptable enough to be used for many administration routes is of importance to the pharmaceutical business. NLCs appear to be appropriate drug delivery methods for parenteral, topical, oral, pulmonary, and ocular administration. The excipients utilized have been approved by regulatory bodies, are GRAS, or have previously been utilized in food or pharmaceutical goods. Nonetheless, the excipients must be utilized at the recognized concentrations. A toxicity study should be conducted to demonstrate the safety of the excipients at that specific concentration if larger concentrations are needed for NLC manufacture. Another appealing aspect of NLC formulation is the simplicity with which the formulation procedure may be scaled up.. To meet the precise requirements of particle size, encapsulation efficiency, and release profile, the physiochemical characteristics of the drug and lipid matrix components might be tuned. Because of the system's intricacy and the particles' colloidal size, characterization of the NLC is also a crucial necessity. However, to regulate the product's quality, stability, and release kinetics, the formulations must be properly characterized. NLCs are regarded as a more intelligent generation of nanoparticles with enhanced drug loading capabilities, delivery profile adjustment capabilities, and stable drug incorporation over the course of storage. NLCs are thought to be particularly helpful for the delivery of lipophilic medicines because of the lipophilic character of the matrix they form.Furthermore, NLCs are non-irritating, non-sensitizing, biocompatible, and biodegradable.NLCs can be created based on the targeted locations, the administration route, and the physicochemical characteristics of the active medicinal components. Given that about 40% of the novel pharmacological molecules are lipophilic, NLCs have a very bright future.Both the number of publications in this field and the number of research groups collaborating with NLC have significantly expanded during the past five years. It shows that an increasing number of academic scientists have begun to create NLCs after realizing their potential. Worldwide, research teams are stationed in nations including Slovenia and Poland in addition to Germany, Canada, and China.If a delivery system is exclusively being developed by university research groups, there is no breakthrough. If the pharmaceutical sector adopts innovations to ensure a wideranging use of a carrier system, success may be achievable. Contract research organizations that work on the development of newer drug delivery systems create pharmaceutical solutions tailored to the requirements of numerous pharmaceutical companies. This means that the technology will be used by many businesses rather than just one company that uses it for its own medications. Given the clear benefits for pharmaceutical businesses, it seems likely that more medical formulations will soon be created as NLC.To put these formulations on the market based on a low risk/high benefit ratio rather than a high risk/low benefit ratio in their current forms, more pre-clinical and clinical research must be conducted soon [1].

N.CONCLUSION:

The NLCs are the carrier systems that have the right viewpoints for effective marketing. The latest generation of formulations known as NLCs provide enhanced performance in creating final dosage forms such injectables, creams, tablets, capsules, and more, as well as considerably greater flexibility in drug loading and release modulation. NLC dispersions are very consistent, which allows for a wide range of compositions. The unique nanostructure of this kind of NLC also aids in improving the drug's bioavailability, drug loading, and solubility in various settings. These carriers can also improve the drug's distribution to the intended organ, alter the pharmacokinetic properties of drug carriers to improve the therapeutic effect, and lessen unfavorable side effects [3].

REFERENCE :

[1]M. A. Iqbal, S. Md, J. K. Sahni, S. Baboota, S. Dang, and J. Ali, "Nanostructured lipid carriers system: Recent advances in drug delivery," Journal of Drug Targeting, vol. 20, no. 10, pp. 813–830, Aug. 2012, doi: https://doi.org/10.3109/1061186x.2012.716845.

[2]S. Khan, A. Sharma, and V. Jain, "An Overview of Nanostructured Lipid Carriers and Its Application in Drug Delivery through Different Routes," Advanced Pharmaceutical Bulletin, vol. 13, no. 3, Sep. 2022, doi: https://doi.org/10.34172/apb.2023.056.

[3]A. Sharma and A. Baldi, "Nanostructured Lipid Carriers: A Review," ResearchGate, vol. 7, no. 1, p. 1000191, Dec. 2018, doi: https://doi.org/10.4172/2329-6631.1000191.

[4]E. Gopinath, A. Nesalin, and V. Chandy, "Nanostructured Lipid Carrier for Hyperpigmentation Treatment: A Dermal Prospective," IJFMR240114029, vol. 6, no. 1, 2024, Available: https://www.ijfmr.com/papers/2024/1/14029.

[5]I. Chauhan, M. Yasir, M. Verma, and A. P. Singh, "Nanostructured Lipid Carriers: A Groundbreaking Approach for Transdermal Drug Delivery," Advanced Pharmaceutical Bulletin, vol. 10, no. 2, pp. 150–165, Jun. 2020, doi: https://doi.org/10.34172/apb.2020.021

[6]B. Gaba, M. Fazil, S. Khan, A. Ali, S. Baboota, and J. Ali, "Nanostructured lipid carrier system for topical delivery of terbinafine hydrochloride," Bulletin of Faculty of Pharmacy, Cairo University, vol. 53, no. 2, pp. 147–159, Dec. 2015, doi: https://doi.org/10.1016/j.bfopcu.2015.10.001

[7]M. Zaky, M. Megahed, T. Hammady, S. Gad, and M. Ghorab, "RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES Nanostructured Lipid Carriers as Novel Drug Delivery System: A Review." Available: https://rpbs.journals.ekb.eg/article_302640_84eaea6f7a9f624c7da261e8af101fb3

[8]N. S. S., P. P. P., W. A. B., and K. Kayande, "NANOSTRUCTURED LIPID CARRIERS: A PROMISING APPROACH FOR TOPICAL DRUG DELIVERY SYSTEM," International Journal of Pharmaceutical Sciences and Medicine, vol. 6, no. 7, pp. 81–101, Jul. 2021, doi: https://doi.org/10.47760/ijpsm.2021.v06i07.007

[9]S. kaur, U. Nautyal, R. Singh, S. Singh, and A. Devi, "Nanostructure Lipid Carrier (NLC): the new generation of lipid nanoparticles," Asian Pacific Journal of Health Sciences, vol. 2, no. 2, pp. 76–93, Apr. 2015, doi: https://doi.org/10.21276/apjhs.2015.2.2.14

[10]"Fischbach's A Manual of Laboratory and Diagnostic Tests," Google Books, 2021. https://books.google.co.in/books/about/Fischbach_s_A_Manual_of_Laboratory_and_D.html?id=xnJAEAAAQBAJ&redir_esc=y

[11]G. Sharma, K. Thakur, K. Raza, B. Singh, and O. P. Katare, "Nanostructured Lipid Carriers: A New Paradigm in Topical Delivery for Dermal and Transdermal Applications," Critical Reviews in Therapeutic Drug Carrier Systems, vol. 34, no. 4, pp. 355–386, 2017, doi: https://doi.org/10.1615/critrevtherdrugcarriersyst.2017019047

[12]N. Dhiman, R. Awasthi, B. Sharma, H. Kharkwal, and G. T. Kulkarni, "Lipid Nanoparticles as Carriers for Bioactive Delivery," Frontiers in Chemistry, vol. 9, Apr. 2021, doi: https://doi.org/10.3389/fchem.2021.580118

[13]Q. Li, T. Cai, Y. Huang, X. Xia, S. P. C. Cole, and Y. Cai, "A Review of the Structure, Preparation, and Application of NLCs, PNPs, and PLNs," Nanomaterials, vol. 7, no. 6, May 2017, doi: https://doi.org/10.3390/nano7060122

[14]T. Zhang, J. Chen, Y. Zhang, Q. Shen, and W. Pan, "Characterization and evaluation of nanostructured lipid carrier as a vehicle for oral delivery of etoposide," European Journal of Pharmaceutical Sciences, vol. 43, no. 3, pp. 174–179, Jun. 2011, doi: https://doi.org/10.1016/j.ejps.2011.04.005

[15]T. H. Tran, T. Ramasamy, D. H. Truong, H.-G. Choi, C. S. Yong, and J. O. Kim, "Preparation and Characterization of Fenofibrate-Loaded Nanostructured Lipid Carriers for Oral Bioavailability Enhancement," AAPS PharmSciTech, vol. 15, no. 6, pp. 1509–1515, Jul. 2014, doi: https://doi.org/10.1208/s12249-014-0175-y

[16]L. Mandpe and V. Pokharkar, "Quality by design approach to understand the process of

optimization of iloperidone nanostructured lipid carriers for oral bioavailability enhancement," Pharmaceutical Development and Technology, vol. 20, no. 3, pp. 320–329, Dec. 2013, doi: https://doi.org/10.3109/10837450.2013.867445

[17]C.-C. Chen, T.-H. Tsai, Z.-R. Huang, and J.-Y. Fang, "Effects of lipophilic emulsifiers on the oral administration of lovastatin from nanostructured lipid carriers: Physicochemical characterization and pharmacokinetics," European Journal of Pharmaceutics and Biopharmaceutics, vol. 74, no. 3, pp. 474–482, Mar. 2010, doi: https://doi.org/10.1016/j.ejpb.2009.12.008

[18]A. Mendes, Ana Maria Silva, José A. M. Catita, F. Cerqueira, C. Gabriel, and C. Lopes, "Miconazole-loaded nanostructured lipid carriers (NLC) for local delivery to the oral mucosa: Improving antifungal activity," vol. 111, pp. 755–763, Nov. 2013, doi: https://doi.org/10.1016/j.colsurfb.2013.05.041

[19]A. Patil-Gadhe and V. Pokharkar, "Montelukast-loaded nanostructured lipid carriers: Part I Oral bioavailability improvement," European Journal of Pharmaceutics and Biopharmaceutics, vol. 88, no. 1, pp. 160–168, Sep. 2014, doi: https://doi.org/10.1016/j.ejpb.2014.05.019

[20]M. Shangguan et al., "Binary lipids-based nanostructured lipid carriers for improved oral bioavailability of silymarin," Journal of Biomaterials Applications, vol. 28, no. 6, pp. 887–896, Sep. 2013, doi: https://doi.org/10.1177/0885328213485141

[21]A. Beloqui, Maria Ángelés Solinís, A. Delgado, C. Évora, A. Isla, and A. Rodríguez-Gascón, "Fate of nanostructured lipid carriers (NLCs) following the oral route: design, pharmacokinetics and biodistribution," Journal of Microencapsulation, vol. 31, no. 1, pp. 1–8, Apr. 2013, doi: https://doi.org/10.3109/02652048.2013.788090.

[22]C.-Y. Zhuang et al., "Preparation and characterization of vinpocetine loaded nanostructured lipid carriers (NLC) for improved oral bioavailability," International Journal of Pharmaceutics, vol. 394, no. 1–2, pp. 179–185, Jul. 2010, doi: https://doi.org/10.1016/j.ijpharm.2010.05.005

[23]A. Beloqui, M. ngeles Solins, A. R. Gascn, A. del Pozo-Rodrguez, A. des Rieux, and V. Prat, "Mechanism of transport of saquinavir-loaded nanostructured lipid carriers across the intestinal barrier," Journal of Controlled Release, vol. 166, no. 2, pp. 115–123, Mar. 2013, doi: https://doi.org/10.1016/j.jconrel.2012.12.021

[24]K. Park, "Transport of nanostructured lipid carriers across the intestinal barrier," Journal of Controlled Release, vol. 166, no. 2, pp. 195–195, Mar. 2013, doi: https://doi.org/10.1016/j.jconrel.2013.01.024

[25]M. Elmowafy, H. M. Ibrahim, M. A. Ahmed, K. Shalaby, A. Salama, and H. Hefesha, "Atorvastatin-loaded nanostructured lipid carriers (NLCs): strategy to overcome oral delivery drawbacks," Drug Delivery, vol. 24, no. 1, pp. 932–941, Jan. 2017, doi: https://doi.org/10.1080/10717544.2017.1337823

[26]Z. Tian et al., "Solidification of nanostructured lipid carriers (NLCs) onto pellets by fluid-bed coating: Preparation, in vitro characterization and bioavailability in dogs," vol. 247, pp. 120–127, Oct. 2013, doi: https://doi.org/10.1016/j.powtec.2013.07.010

[27]N. V. Shah, A. K. Seth, R. Balaraman, C. J. Aundhia, R. A. Maheshwari, and G. R. Parmar, "Nanostructured lipid carriers for oral bioavailability enhancement of raloxifene: Design and in vivo study," Journal of Advanced Research, vol. 7, no. 3, pp. 423–434, May 2016, doi: https://doi.org/10.1016/j.jare.2016.03.002

[28]G. Shevalkar and P. Vavia, "Solidified nanostructured lipid carrier (S-NLC) for enhancing the oral bioavailability of ezetimibe," Journal of Drug Delivery Science and Technology, vol. 53, p. 101211, Oct. 2019, doi: https://doi.org/10.1016/j.jddst.2019.101211

[29]V. Kaithwas, C. P. Dora, V. Kushwah, and S. Jain, "Nanostructured lipid carriers of olmesartan medoxomil with enhanced oral bioavailability," Colloids and Surfaces B: Biointerfaces, vol. 154, pp. 10–20, Jun. 2017, doi: https://doi.org/10.1016/j.colsurfb.2017.03.006

[30]I. El, N. F. Younes, and Amal, "Enhanced Oral Absorption of Amisulpride Via a Nanostructured Lipid Carrier-Based Capsules: Development, Optimization Applying the Desirability Function Approach and In Vivo Pharmacokinetic Study," AAPS PharmSciTech, vol. 20, no. 2, Jan. 2019, doi: https://doi.org/10.1208/s12249-018-1283-x

[31]C. Thapa, A. Ahad, Mohd. Aqil, S. S. Imam, and Y. Sultana, "Formulation and optimization of nanostructured lipid carriers to enhance oral bioavailability of telmisartan using Box–Behnken design," Journal of Drug Delivery Science and Technology, vol. 44, pp. 431–439, Apr. 2018, doi: https://doi.org/10.1016/j.jddst.2018.02.003

[32]R. ALAND, GANESAN M, and RAJESWARA RAO P, "DEVELOPMENT AND OPTIMIZATION OF TAZAROTENE LOADED SOLID LIPID NANOPARTICLES FOR TOPICAL DELIVERY," Asian Journal of Pharmaceutical and Clinical Research, pp. 63–77, Jul. 2019, doi: https://doi.org/10.22159/ajpcr.2019.v12i10.31755

[33]S. Alarifi, S. Massadeh, M. Al-Agamy, M. A. l. Aamery, A. Al Bekairy, and A. E. Yassin, "Enhancement of ciprofloxacin activity by incorporating it in solid lipid nanoparticles," Tropical Journal of Pharmaceutical Research, vol. 19, no. 5, pp. 909–918, Jun. 2020, doi: https://doi.org/10.4314/tjpr.v19i5.1

[34]A. Vila, H. Gill, O. McCallion, and AlonsoM. J., "Transport of PLA-PEG particles across the nasal mucosa: effect of particle size and PEG coating density," Journal of Controlled Release, vol. 98, no. 2, pp. 231–244, Aug. 2004, doi: https://doi.org/10.1016/j.jconrel.2004.04.026

[35]Y.-C. Kuo and J.-F. Chung, "Physicochemical properties of nevirapine-loaded solid lipid nanoparticles and nanostructured lipid carriers," Colloids and Surfaces B: Biointerfaces, vol. 83, no. 2, pp. 299–306, Apr. 2011, doi: https://doi.org/10.1016/j.colsurfb.2010.11.037

[36]G. Fontana, L. Maniscalco, D. Schillaci, G. Cavallaro, and G. Giammona, "Solid Lipid Nanoparticles Containing Tamoxifen Characterization andIn VitroAntitumoral Activity," Drug Delivery, vol. 12, no. 6, pp. 385–392, Jan. 2005, doi: https://doi.org/10.1080/10717540590968855

[37]R. Thatipamula, C. Palem, R. Gannu, S. Mudragada, and M. Yamsani, "Formulation and in vitro characterization of domperidone loaded solid lipid nanoparticles and nanostructured lipid carriers," Daru : journal of Faculty of Pharmacy, Tehran University of Medical Sciences, vol. 19, no. 1, pp. 23–32, 2011, Available: https://pubmed.ncbi.nlm.nih.gov/22615636

[38]P. Ganesan, P. Ramalingam, G. Karthivashan, Y. T. Ko, and D.-K. Choi, "Recent developments in solid lipid nanoparticle and surface-modified solid lipid nanoparticle delivery systems for oral delivery of phyto-bioactive compounds in various chronic diseases," International Journal of Nanomedicine, vol. Volume 13, pp. 1569–1583, Mar. 2018, doi: https://doi.org/10.2147/ijn.s155593

[39]P. Sharma, B. Dube, and K. Sawant, "Development and Evaluation of Nanostructured Lipid Carriers of Cytarabine for Treatment of Meningeal Leukemia," Journal of Nanoscience and Nanotechnology, vol. 11, no. 8, pp. 6676–6682, Aug. 2011, doi: https://doi.org/10.1166/jnn.2011.4235

[40]A. K. Sharma et al., "Preparation and therapeutic evolution of Ficus benjamina solid lipid nanoparticles against alcohol abuse/antabuse induced hepatotoxicity and cardio-renal injury," RSC Advances, vol. 7, no. 57, pp. 35938–35949, 2017, doi: https://doi.org/10.1039/c7ra04866a

[41]Y. Chen, L. Yuan, Liu Congyan, Z. Zhang, L. Zhou, and D. Qu, "Antitumor activity of tripterine via cell-penetrating peptide-coated nanostructured lipid carriers in a prostate cancer model," International Journal of Nanomedicine, pp. 4339–4339, Nov. 2013, doi: https://doi.org/10.2147/ijn.s51621

[42]Jeong Tae Kim et al., "Absorption Study of Genistein Using Solid Lipid Microparticles and Nanoparticles: Control of Oral Bioavailability by Particle Sizes," Biomolecules & Therapeutics, vol. 25, no. 4, pp. 452–459, Jul. 2017, doi: https://doi.org/10.4062/biomolther.2017.095

[43]M. Li, Y. Zheng, F. Shan, J. Zhou, T. Gong, and Z. Zhang, "Development of ionic-complex-based nanostructured lipid carriers to improve the pharmacokinetic profiles of breviscapine," Acta Pharmacologica Sinica, vol. 34, no. 8, pp. 1108–1115, Jun. 2013, doi: https://doi.org/10.1038/aps.2013.43

[44]F. Shi, Yang, Juan Ren, Guo, Du, and N. Feng, "Formulation design, preparation, and in vitro and in vivo characterizations of β-Elemene- loaded nanostructured lipid carriers," International Journal of Nanomedicine, p. 2533, Jul. 2013, doi: https://doi.org/10.2147/ijn.s46578

[45]J. Li et al., "Preparation and evaluation of charged solid lipid nanoparticles of tetrandrine for ocular drug delivery system: pharmacokinetics, cytotoxicity and cellular uptake studies," Drug Development and Industrial Pharmacy, vol. 40, no. 7, pp. 980–987, May 2013, doi: https://doi.org/10.3109/03639045.2013.795582

[46]C.-F. Luo et al., "Pharmacokinetics, tissue distribution and relative bioavailability of puerarin solid lipid nanoparticles following oral administration," International Journal of Pharmaceutics, vol. 410, no. 1–2, pp. 138–144, May 2011, doi: https://doi.org/10.1016/j.ijpharm.2011.02.064

[47]C. Luo et al., "Metabolic profile of puerarin in rats after intragastric administration of puerarin solid lipid nanoparticles," International Journal of Nanomedicine, pp. 933–933, Mar. 2013, doi: https://doi.org/10.2147/ijn.s39349

[48]C. Zhang et al., "Preparation and Optimization of Triptolide-Loaded Solid Lipid Nanoparticles for Oral Delivery with Reduced Gastric Irritation," Molecules, vol. 18, no. 11, pp. 13340–13356, Oct. 2013, doi: https://doi.org/10.3390/molecules181113340

[49]R. G. Madane and H. S. Mahajan, "Curcumin-loaded nanostructured lipid carriers (NLCs) for nasal administration: design, characterization, andin vivostudy," Drug Delivery, pp. 1–9, Nov. 2014, doi: https://doi.org/10.3109/10717544.2014.975382

[50]U. Ruktanonchai et al., "Physicochemical Characteristics, Cytotoxicity, and Antioxidant Activity of Three Lipid Nanoparticulate Formulations of Alpha-lipoic Acid," AAPS PharmSciTech, vol. 10, no. 1, Mar. 2009, doi: https://doi.org/10.1208/s12249-009-9193-6

[51]J.-Y. Fang, "Combination of calcipotriol and methotrexate in nanostructured lipid carriers for topical delivery," International Journal of Nanomedicine, p. 117, Feb. 2010, doi: https://doi.org/10.2147/ijn.s9155

[52]W. M. Obeidat, K. Schwabe, R. H. Müller, and C. M. Keck, "Preservation of nanostructured lipid carriers (NLC)," European Journal of Pharmaceutics and Biopharmaceutics, vol. 76, no. 1, pp. 56–67, Sep. 2010, doi: https://doi.org/10.1016/j.ejpb.2010.05.001

[53]Z. HUANG, S. HUA, Y. YANG, and J. FANG, "Development and evaluation of lipid nanoparticles for camptothecin delivery: a comparison of solid lipid nanoparticles, nanostructured lipid carriers, and lipid emulsion," Acta Pharmacologica Sinica, vol. 29, no. 9, pp. 1094–1102, Sep. 2008, doi: https://doi.org/10.1111/j.1745-7254.2008.00829.x

[54]C. Puglia, M. G. Sarpietro, F. Bonina, F. Castelli, M. Zammataro, and S. Chiechio, "Development, Characterization, and In Vitro and In Vivo Evaluation of Benzocaine- and Lidocaine-Loaded Nanostructrured Lipid Carriers," Journal of Pharmaceutical Sciences, vol. 100, no. 5, pp. 1892–1899, May 2011, doi: https://doi.org/10.1002/jps.22416

[55]E. Gonzalez-Mira, M. A. Egea, M. L. Garcia, and E. B. Souto, "Design and ocular tolerance of flurbiprofen loaded ultrasound-engineered NLC," Colloids and Surfaces B: Biointerfaces, vol. 81, no. 2, pp. 412–421, Dec. 2010, doi: https://doi.org/10.1016/j.colsurfb.2010.07.029

[56]S. Doktorovová, J. Araújo, M. L. Garcia, E. Rakovský, and E. B. Souto, "Formulating fluticasone propionate in novel PEG-containing nanostructured lipid carriers (PEG-NLC)," Colloids and Surfaces B: Biointerfaces, vol. 75, no. 2, pp. 538–542, Feb. 2010, doi: https://doi.org/10.1016/j.colsurfb.2009.09.033

[57]P. Pathak and M. Nagarsenker, "Formulation and Evaluation of Lidocaine Lipid Nanosystems for Dermal Delivery," AAPS PharmSciTech, vol. 10, no. 3, Jul. 2009, doi: https://doi.org/10.1208/s12249-009-9287-1

[58]J. Pardeike et al., "Development of an Itraconazole-loaded nanostructured lipid carrier (NLC) formulation for pulmonary application," International Journal of Pharmaceutics, vol. 419, no. 1–2, pp. 329–338, Oct. 2011, doi: https://doi.org/10.1016/j.ijpharm.2011.07.040

[59]R. A. Sanad, N. S. AbdelMalak, T. S. elBayoomy, and A. A. Badawi, "Formulation of a Novel Oxybenzone-Loaded Nanostructured Lipid Carriers (NLCs)," AAPS PharmSciTech, vol. 11, no. 4, pp. 1684–1694, Nov. 2010, doi: https://doi.org/10.1208/s12249-010-9553-2

[60]M. Cirri, M. Bragagni, N. Mennini, and P. Mura, "Development of a new delivery system consisting in 'drug – in cyclodextrin – in

nanostructured lipid carriers ’for ketoprofen topical delivery,” European Journal of Pharmaceutics and Biopharmaceutics, vol. 80, no. 1, pp. 46–53, Jan. 2012, doi: https://doi.org/10.1016/j.ejpb.2011.07.015

[61]Y. NAKAI, K. YAMAMOTO, K. TERADA, and K. AKIMOTO, “The dispersed states of medicinal molecules in ground mixtures with .ALPHA.- or .BETA.-cyclodextrin.,” Chemical and Pharmaceutical Bulletin, vol. 32, no. 2, pp. 685–691, 1984, doi: https://doi.org/10.1248/cpb.32.685

[62]C.-H. Liu and C.-T. Wu, “Optimization of nanostructured lipid carriers for lutein delivery,” Colloids and Surfaces A: Physicochemical and Engineering Aspects, vol. 353, no. 2–3, pp. 149–156, Jan. 2010, doi: https://doi.org/10.1016/j.colsurfa.2009.11.006

[63]L. Jia et al., “Nanostructured lipid carriers for parenteral delivery of silybin: Biodistribution and pharmacokinetic studies,” Colloids and Surfaces B: Biointerfaces, vol. 80, no. 2, pp. 213–218, Oct. 2010, doi: https://doi.org/10.1016/j.colsurfb.2010.06.008

[64]D. Liu, Z. Liu, L. Wang, C. Zhang, and N. Zhang, “Nanostructured lipid carriers as novel carrier for parenteral delivery of docetaxel,” Colloids and Surfaces B: Biointerfaces, vol. 85, no. 2, pp. 262–269, Jul. 2011, doi: https://doi.org/10.1016/j.colsurfb.2011.02.038

[65]P. M. Chaudhari and Mahananda. V. Ghodake, “Development and Optimization of Solid Lipid Nanoparticle for Topical Delivery,” Journal of Drug Delivery and Therapeutics, vol. 9, no. 5-s, pp. 105–121, Oct. 2019, doi: https://doi.org/10.22270/jddt.v9i5-s.3648

[66]N. Anton, J.-P. Benoit, and P. Saulnier, “Design and production of nanoparticles formulated from nano-emulsion templates—A review,” Journal of Controlled Release, vol. 128, no. 3, pp. 185–199, Jun. 2008, doi: https://doi.org/10.1016/j.jconrel.2008.02.007

[67]L. C. Hung et al., “An improved method for the preparations of nanostructured lipid carriers containing heat-sensitive bioactives,” Colloids and Surfaces B: Biointerfaces, vol. 87, no. 1, pp. 180–186, Oct. 2011, doi: https://doi.org/10.1016/j.colsurfb.2011.05.019

[68]V. Kakkar, S. Singh, D. Singla, and I. P. Kaur, “Exploring solid lipid nanoparticles to enhance the oral bioavailability of curcumin,” Molecular Nutrition & Food Research, vol. 55, no. 3, pp. 495–503, Oct. 2010, doi: https://doi.org/10.1002/mnfr.201000310

[69]N. AR, Lúcio M, Martins S, Lima JL, and Reis S, “Novel resveratrol nanodelivery systems based on lipid nanoparticles to enhance its oral bioavailability,” International Journal of Nanomedicine, vol. 2013, no. default, pp. 177–187, 2013, Accessed: Mar. 08, 2025. [Online]. Available: https://doaj.org/article/57fee4ca1e2d429fa1fce518f011c7a8

[70]“A Manual of Laboratory and Diagnostic Tests,” Google Books, 2015. https://books.google.co.in/books/about/A_Manual_of_Laboratory_and_Diagnostic_Te.html?id=8avfXndX3BMC&redir_esc=y