International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 20-05-2022, Accepted: 05-06-2022, Published: 21-06-2022
Volume 7, Issue 2, 2022, Page No. 61-72

A review on nanostructured lipid carrier

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Abstract
NLCs (nanostructured lipid carriers) are novel medicinal formulations that combine physiological and biocompatible lipids with surfactants and co-surfactants. Over time, NLC has evolved into a second-generation lipid nanocarrier and a potential alternative to first-generation nanoparticles. According to this review research, the structure, content, numerous formulation techniques, and description of NLCs are all factors for establishing a reliable drug delivery system. NLCs have a lot of promise in the pharmaceutical and cosmetics sectors because of their multiple advantages such skin hydration, occlusion, improved bioavailability, and skin targeting. This essay aims to arouse interest in the most cutting-edge NLC by demonstrating how they can aid existing drug delivery methods. The simplicity of production, biocompatibility, scale-up practicality, non-toxicity, improved drug loading, and stability of NLC make it a potential drug delivery technology.

Keywords: nanostructure lipid carrier, lipid, topical, skin, drug delivery system

Introduction

The DDS (Drug Delivery System) is a well-known, well-established, and economically successful way of generating pharmaceuticals in a variety of dosage forms. The integration of a wide range of components is required in lipid formulations such as (Nano Lipid Carriers) NLCs. Insoluble drug bioavailability and solubility are two critical factors that may be enhanced using formulations like NLCs. Many pharmaceutical companies have developed a well-established industrial process for producing large-scale batches of nanostructured lipid carriers, but all major parameters such as lipid choice, surfactants, other essential excipients, and preparation methods vary, resulting in differences in particle shape and size, phase transition, solubility, and drug bioavailability, among others.

Unique properties of lipid nanoparticles are necessary and crucial for their medicinal efficacy. Nanoparticles (NP) have unique properties such as a high surface to mass ratio, additional colloidal particles, and the capacity to bind and transport substances, making them more intelligent therapeutic products. Lipid Nano formulations make it easier to make solubilized phases from which drugs may be absorbed quickly, and they can lessen the slow and incomplete dissolution of somewhat water-soluble medicines like Biopharmaceutics &classification System (BCS) class II. The degree and manner of drug release from any other vehicle-mediated delivery system, such as an emulsion or a liposome, is important for the delivery system's mobility *in vivo*.

A lipid matrix is found within newly manufactured NLCs with a very unique nanostructure devised by Muller. Furthermore, in a number of contexts and conditions, HL's unique kind of NLC nanostructure assists in enhancing medication bioavailability, drug loading, and solubility. This sort of NLC can be prepared or formulated in a variety of methods, including by high-pressure homogenization. According to the literature, by adjusting the different variables and surroundings, these ways can create between 30 and 80 percent of the output yield.

NLCs are a new type of DDS and formulation that improves stability and loading while permitting the production of concentrated dispersions. Many pharmaceutical companies have developed well-established industrial processes for producing large-scale batches of nanostructured lipid carriers, but all major parameters such as lipid choice, surfactants, other essential excipients, and preparation methods vary, resulting in differences in particle shape, size, phase transition, solubility, and drug bioavailability, among others.

NLCs were initially introduced as a novel carrier system in the 1990s. Liposomes have been offered as an alternative for solid lipid carrier systems, such as solid lipid nanoparticles (SLN), which are accessible in the nanometre range. However, SLN has several flaws, including insufficient drug loading and drug ejection during storage. Newer solid lipids DDS, like as NLCs, can alleviate or remove all of these disadvantages. A new and improved form of NLC with a precise nanostructure is now available. These precise nanostructures are responsible for boosting bioavailability and drug loading while also improving formulation stability.

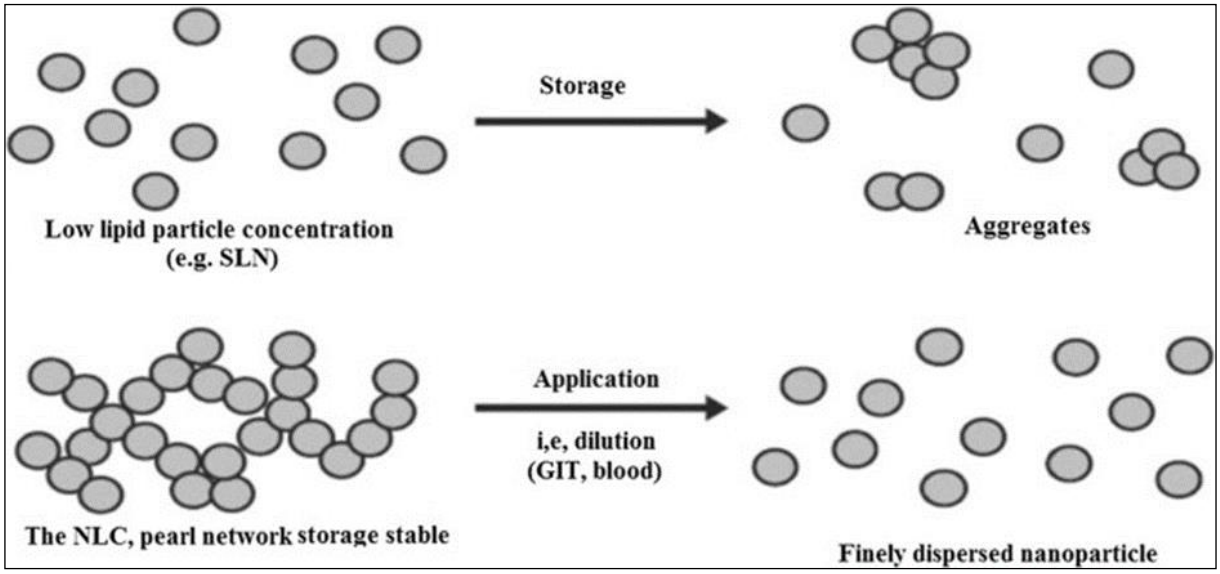

Fig 1: A potential drug carrier for cancer chemotherapy

NLCs dramatically decreased the amount of difficulties that many drugs encounter when utilising SLN, including poor payload, drug ejection during storage, and SLN dispersions owing to its high-water content.

Types of NLC'S

NLSs have a structure that is similar to that of SLNs, but they differ in three ways. Three different processes were employed to create and produce nanostructure NLCs, depending on the place where the drug would be administered.

- Type I NLC is also known as imperfect crystal.
- Type II NLC is also known as many types.
- Type III NLC is also known as amorphous NLC.

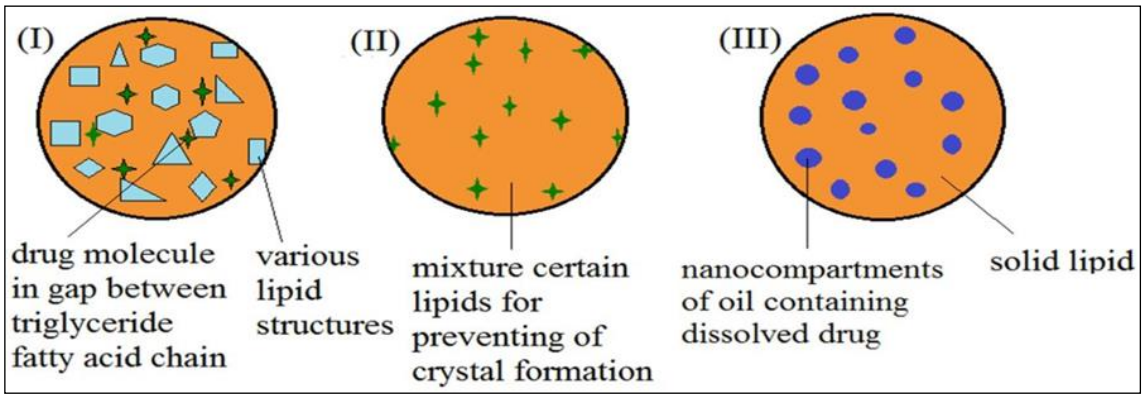

Fig 2: Drug molecule, oily compartment and drug molecule in oily compartment model of NLC's

Type I NLC

NLC type I solid matrix, often called as defective crystal types, is disorganised. To enhance and change the structure, glycerides and other fatty acids can be used. The total amount of defects in the construction is both accountable for and useful to a good medicine's property, which can readily be improved. NLCs of type I are created by mixing spatially different lipids, which might result in crystal lattice defects. In their chemical state, the drug molecules form amorphous clusters and additional disordered crystals. To avoid this, a tiny amount of liquid lipid is supplemented with additional leans to maximise drug loading. To get around this obstacle, take advantage of the glycerides' poor quality. When the structure of lipids changes, issues such as clustering of drugs occur, resulting in a chaotic, faulty lipid matrix, which is all due to the crystallisation procedure.

Type II NLC

The numerous type of NLC is defined as an oil-in-lipid-in-water mixture. Oil has a better solubility in type II NLCs than solid lipids. Oil molecules can easily enter the lipid matrix even at low concentrations because type II NLC has a substantial quantity of oil coupled with solid lipids. If more oil is provided than is necessary for solubility, this might result in the separation of the components. Various phases combine to form small oily nano compartments surrounded by a solid lipid matrix. This formulation provides for controlled medication release

and lipid matrix drug leakage. Lipophilic pharmaceuticals can be rendered soluble in oil first, and then the type II approach with the cooling operation of a hot homogenization process can be used.

Type III NLC

The III kind of NLS is also known as the amorphous form. The lipids are combined in this technique for generating NLCs in such a way that the mixing prevents crystallisation. In the type III technique, the lipid matrix remains solid yet amorphous. The crystallisation process and strategy are commonly responsible for drug ejection. To decrease this, solid lipids can be properly mixed with particular lipids such as hydroxy octacosanyl hydroxyl stearate, isopropyl palmitate, or MCT. NLC is a solid yet non-crystalline material.

NCLs Have the Following Advantages

- They are easy to validate and obtain approval from regularity agencies.
- NLC is extremely biocompatible.
- Organic solvents may be avoided because the processes are water-based.
- Compared to polymeric/surfactant-based carriers, NLCs are simple to scale-up and sterilise.
- NLCs help improve pharmaceutical stability by controlling and/or targeting drug release.
- When compared to other carriers on the market, NLCs give better and greater medication content.
- NLCs may transport both lipophilic and hydrophilic medicines at the same time, and the majority of lipids are biodegradable.

Disadvantages of NCL's

- Cytotoxic effects related to the type of the lipid matrix and concentration of NCLs.
- Surfactants cause irritation and sensitization.

Preparation and Formulation

For the preparation of NLSs, numerous approaches have been established. The following are the most common command methods:

- Solvent Emulsification evaporation method
- Solvent Emulsification diffusion solvent method
- Double emulsion technique
- Solvent injection technique
- High-pressure homogenization
- Ultrasonication and high shear homogenization
- Phase inversion
- Membrane contractor method
- High-pressure homogenization: This process divides particles into nano-sized particles, resulting in a stable emulsion. On the market, there are two types of homogenizers: jet-stream and piston-gap homogenizers. As shown in Figure 4, high-pressure homogenization is typically used to manufacture NLCs.

1. **High-temperature homogenization:** This procedure entails homogenization at a high temperature. Solid lipids are melted at a temperature 5-10 degrees Celsius over their melting point. A dispersion is generated by mixing liquid lipid with the drug to be encapsulated. A high shear mixing device disperses the mixture in an aqueous surfactant (s) solution heated to the same temperature, resulting in the formation of a pre-emulsion. The pre-emulsion is injected at a controlled temperature into a high-pressure homogenizer. At 500-1500 bar, homogenization may normally be accomplished in 3 to 5 cycles.

2. **Cold homogenization:** A lipid melt containing an active component is quickly solidified with liquid nitrogen or dry ice, then milled and powdered before being dispersed in a cold surfactant phase and homogenised at room temperature. The pressure is higher in the cold process, with 5-10 cycles of 1500 bar. This approach decreases the temperature exposure of the medication and is especially useful for thermolabile drugs. Improved drug entrapment efficiency and constant drug distribution inside the lipid are further advantages of the approach.

3. **Microemulsion:** These are transparent dispersions of water, oil, and surfactant that are stable.

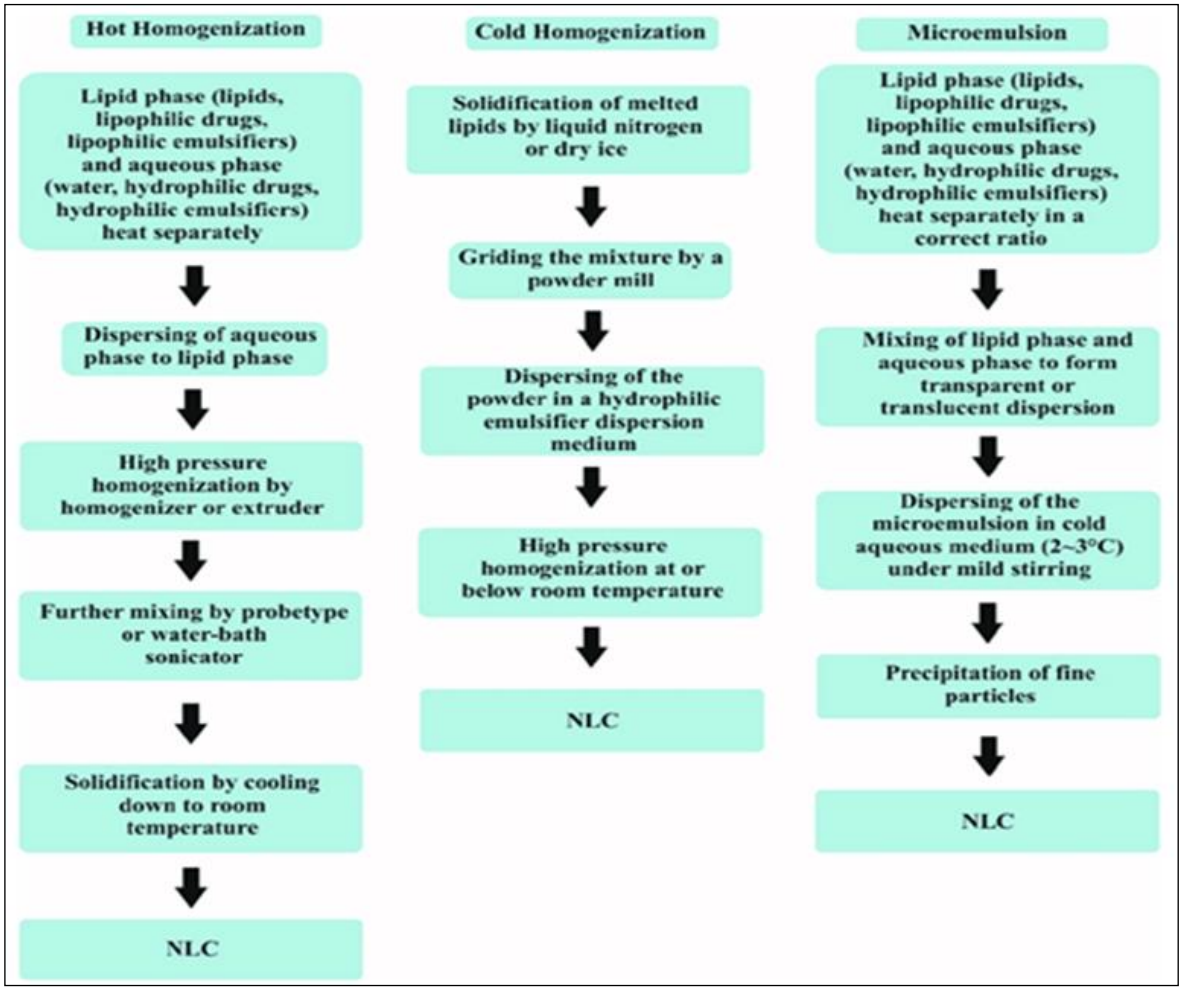

Fig 3: Preparation procedures of NLCs: by various homogenization technique

- **Solvent-Emulsification Evaporation Technique**: The lipids (solid lipid + liquid lipid) and medicine are dissolved in a water insoluble organic solvent in this approach (cyclohexane, chloroform). The resulting mixture is dispersed in an aqueous emulsifier solution to produce an o/w emulsion. To remove the solvent from the emulsion, evaporation at lower pressure is used. Evaporation causes nanoparticles to disperse in the aqueous phase (by lipid precipitation in the aqueous medium). This approach eliminates thermal stress, but it has the drawback of using an organic solvent. Depending on the solid lipid and surfactant, particle size can range from 30-100 nm.

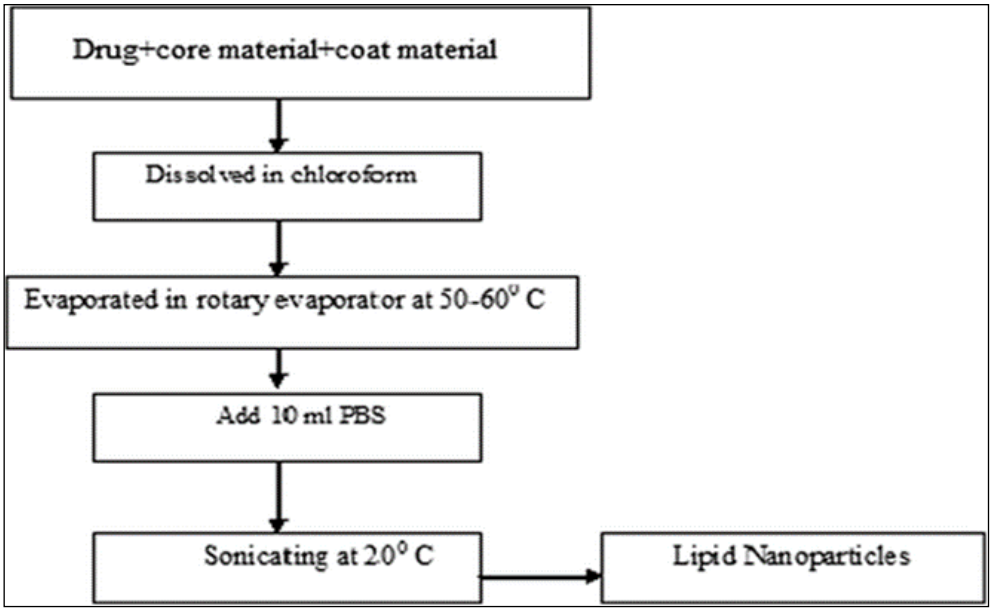

Fig 4: Schematic procedure of solvent emulsification evaporation

- **Solvent-Emulsification Diffusion Method:** This approach maintains initial thermodynamic equilibrium by saturating the solvent and the water. Following that, in a water-saturated solvent, the lipids and medication are dissolved. To make an o/w emulsion, a homogenizer emulsifies a solvent-containing medicine and lipids in a solvent-saturated aqueous emulsifier solution. After dilution with excess water (ratio: 1:5–1:10), the organic solvent diffuses from the emulsion droplets to the continuous phase, causing the lipid nanoparticles to precipitate. To remove the solvent, ultrafiltration or lyophilization might be utilised. Solvent diffusion is more innovative than volatile solvents, and the majority of the solvents employed have a greater safety profile.

- **Double Emulsion Technique:** This approach is generally utilised to make hydrophilic drug-loaded lipid nanoparticles. This methodology overcomes the drawback of water-soluble moiety separating in the aqueous phase from the oily phase, as demonstrated by the microemulsion method. The medication is first dissolved in an aqueous solvent (inner aqueous phase) and then distributed in a lipid phase (molten solid lipid + liquid lipid+ lipophilic surfactant+ lipophilic active moiety) to create a primary emulsion (w/o). The temperature of both the lipid and aqueous phases is kept constant. The stabiliser prevents medication loss to the outer phase during solvent evaporation. The main emulsion is then sonicated and dispersed into a large quantity of surfactant aqueous solution to generate a double emulsion (w/o/w). The lipid nanoparticles are purified by ultrafiltration or solvent evaporation.

- **Solvent Injection Technique:** This might be a novel way to make lipid nanoparticles. Lipids are dissolved in a water-miscible solvent (e.g., acetone, methanol, ethanol, isopropyl alcohol) or a water-soluble solvent combination, then injected rapidly into an aqueous surfactant solution while being constantly agitated. Any excess lipid is filtered out of the resultant dispersion. Rapid solvent diffusion over the solvent–lipid interface with the aqueous phase is used in this approach. The particle size of nanocarriers is determined by the pace at which the organic solvent diffuses across the lipid-solvent interface. This approach offers the advantages of being easy to use, efficient, and adaptable, as well as needing no specialised equipment (such as a high-pressure homogenizer) and only employing approved organic solvents.

- **Ultrasonication and High Shear Homogenization:** Ultrasonication or high shear homogenization is one of the methods for producing NLCs. Nanocarriers are created using devices in these dispersion procedures. Solid and liquid lipids are melted and distributed in an aqueous surfactant solution under high shear homogenization or ultrasonication, resulting in nano dispersion. The strong shear forces necessary for nano-emulsification are generated by ultrasonic cavitation, which creates violently and asymmetrically bursting vacuum bubbles and breaks apart particles down to the nanometre scale. Probe-type ultrasonication is used to accomplish homogenization, emulsification, dispersion, deagglomeration, milling There are several aspects to consider, including the kind and concentration of lipid and surfactant, their ratio, and sonication or agitation. In order to construct a repeatable process that creates microscopic size nanocarriers, time and speed are some of the parameters that must be regulated. Ultrasonication and high shear homogenization have the drawback of low dispersion quality. When microparticles are present in the lipid nanoparticles created by these techniques, their dispersion quality suffers, resulting in physical instability when stored. Metal contamination from the device is another serious hazard with ultrasonication.

- **Phase inversion approach:** For the formulation of lipid nanocarriers, phase inversion from o/w to w/o emulsion is a novel, cost-effective, and solvent-free process. It consists of two stages.
  The first stage involves properly mixing all of the materials (lipid, surfactant, and water). The temperature of the mixture is progressively increased to 85°C from room temperature at a rate of 4°C. The system is exposed to three temperature cycles (85–60–85-60–85°C) to approach the phase inversion zone.
  Step 2's dilution with cold water provides an irreversible shock that breaks the system (0oC). The fast addition of cold water results in the formation of nano capsules. The use of a gentle magnetic stirring for 5 minutes prevents particle agglomeration. Low energy is required to create stable transparent dispersions (less than 25 nm) that may be utilised to encapsulate a variety of bioactive compounds.

- **Membrane Contactor Technique:** Membrane contactors are membrane systems that are used to maintain two phases in contact. The lipid phase is kept at a temperature above its melting point in a pressurised tank. It is allowed to seep via ceramic membrane perforations under pressure and create minute droplets. The aqueous phase travels tangentially within the membrane module under continual stirring, brushing away the droplets that form at the pore outputs. When the preparation is cooled to room temperature, lipid particles are formed. Aqueous and lipid phase temperature, aqueous phase tangential-flow velocity, lipid phase pressure, and membrane pore size are all process variables that impact the size of lipid nanocarriers.

Mechanism of Skin Penetration and Drug Release in NLC'S

The rate of drug release is influenced by a number of parameters, including drug solubility, surface bound/adsorbed drug desorption, drug diffusion through the nanoparticles matrix, nanoparticles matrix erosion/degradation, and a combination of erosion/diffusion processes. The release process is thus governed by

the matrix components' solubility, diffusion, and biodegradation. When the particles are delivered, an impulse can also cause this sort of release (as shown in figure 6). The extremely disordered lipid structures present in NLCs are the cause of greater drug loading. This can activate NLCs in certain structures. For a suitably high drug-load, the creation of a less organised solid lipid matrix is desired. In general, the drug can be found between the fatty acids or lipid layers, as well as in defects (e.g. amorphous). When using mono acid highly pure glycerides like tristearin that are spatially extremely comparable to the more or less highly organised matrix molecules, drug load is quite restricted, and drug expulsion occurs within hours or days.

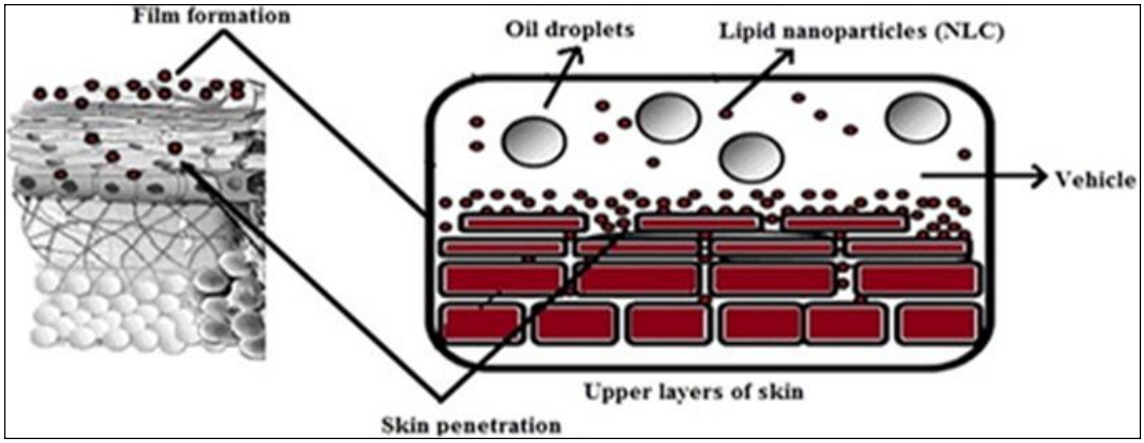

Fig 5: Mechanism of penetration into skin.

The smaller size of NLCs promotes close contact with SC and can help the active chemical penetrate deeper into the skin. The paths of nanoparticle penetration via the skin have been agreed upon by researchers. The following are proposed processes for enhanced particle penetration into the stratum corneum followed by drug diffusion:

1. Unblemished medication-loaded vesicles enter the skin's various layers.
2. Through their skin lipid-fluidizing and altering properties, lipid vesicles operate as penetration enhancers.
3. Mingling of carrier lipids with cellular skin lipids induces nanostructure lipid carrier and cutaneous drug exchange.
4. Hair follicles (HF), pilosebaceous, and sweat gland pores are all part of the appendageal pathway.

Skin penetration of NLCs is determined by their composition as well as physicochemical properties such as size, aggregation, charge on particle surface, hydrophobicity, solubility in the skin, solubilizing properties of particles towards skin lipids, and whether or not the particle has the ability to form films.

NLC encapsulation of drugs

Drugs can be included or encapsulated in lipid nanoparticles or NLCs in three ways. They consist of a solid solution matrix, a drug-enriched shell, and a drug-enriched core.

a. Homogeneous solid solution matrix: In this technique of encapsulation, the drug is homogeneously disseminated within the lipid matrix of the particles, and the drug is released by diffusion.
b. Drug-enriched shell; in this procedure, the drug is focused on the lipid nanoparticles' outermost layer or shell. Because of the precipitation and solubilization mechanisms, these nanoparticles deliver the medication in bursts.
c. Drug-enriched core: The saturation solubility of the drug in the lipid causes extended release in this approach.

Materials Employed in Formulation of NLC'S

Glycerol behenate (Compritol® 888 ATO), Glycerol palmitostearate (Precirol® ATO 5), and Cetyl palmitate are among the lipids used in the nano lipid carriers for topical application to skin (wax).

In the case of NLCs, liquid lipids such as medium chain triglycerides (Miglyol® 812) are typically employed at room temperature. Alternatively, oleic acid, one of the most often used penetration enhancers in semisolid skin carriers, may improve drug absorption even more. Nano dispersions comprise 5-40 percent lipid and have a mean particle size ranging from 50 to 1000 nm. Higher concentration preparations have a semisolid appearance and are visually acceptable. Surfactants ranging from 0.5 to 5% are used to physically stabilise the particles, depending on the kind and concentration of the lipid. Tables I and II show the various lipids and surfactants employed in the synthesis of lipid nano carriers, respectively.

Table 1

Sr No.	Types of Lipids	Examples
1.	Triacylglycerols	Tricaprin, trilaurin, trimyristin
2.	Acyl glycerol	Glycerol monostearate, glycerol behenate
3.	Fatty acids	Stearic acid, palmitic acid, decanoic acid

4.	Waxes	Cetyl palmitate
5.	Cyclic complexes	Cyclodextrin and para-acyl-calix-arenes

Table 2: List of surfactants used for preparation of lipid nanocarrier

Sr No	Types of Surfactants	Examples
1.	Phospholipids	Soya lecithin, egg lecithin
2.	Ethylene oxide propylene oxide copolymer	Poloxamer 188, poloxamer 182, poloxamer 407
3.	Sorbitan ethylene oxide/ propylene oxide copolymer	Polysorbate 20, polysorbate 60, polysorbate 80
4.	Alkaryl polyether alcohol polymer	Tyloxapol
5.	Bile salts	Sodium cholate, sodium glycol cholate, sodium taurocholate
6.	Alcohol	Ethanol and butanol

Surfactant and Lipid Functions in Formulation Development

The quality and efficacy of nano lipid carriers and lipid nanoparticles are highly influenced by the characteristics and concentrations of surfactant. Because of their amphiphilic character, these surface-active agents preferentially accumulate at interfacial areas, where they reduce the interfacial tension between the lipid and aqueous phases. The ionic surfactant sodium deoxycholate, which has a low emulsification efficiency, can be used to raise the nanoparticle charge, which is linked to increased electrostatic repulsion and improved colloidal system physical stability. Non-ionic emulsifiers, particularly Poloxamer 188, provide further steric stabilisation, preventing fine particle aggregation in colloidal systems.

Stability of Nanostructured Lipid Dispersions

Micelles, mixed micelles, liposomes, and nano emulsions are examples of other colloidal structures that contribute to the stability of NLCs. During storage, there are also some substantial stability concerns, such as particle size increase, dispersion gelation, and drug ejection from the lipid matrix. The creation of the network and lipid bridges between the particles causes gelation. Particle size (Photon correlation spectroscopy, PCS; Laser diffraction, LD), zeta potential (ZP), and thermal analysis are commonly used to assess the physical stability of these dispersions (Differential scanning calorimetry, DSC). SLN dispersion was shown to be physically stable for more than a year in several experiments. As reported in the case of SLNs, long-term storage of lipid dispersions causes aggregation and shell formation. The particles in highly concentrated NLC dispersions form a 'pearl-like network,' resulting in collision and peri kinetic flocculation. The network is disrupted once NLCs are administered and diluted with gastrointestinal fluid, releasing single, non-aggregated particles. Lipid particle dispersions with low lipid content (below 30%, outside patent coverage) and 35 percent lipid were made at the same surfactant concentration. The low particle dispersion aggregated after time, whereas the gel-like NLC dispersion remained stable, and single particles were produced following dilution with no size growth. In low concentration dispersions, freely diffusible nanoparticles can collide and aggregate (upper), but in highly concentrated dispersions, the particles are trapped in a network, and additional water dilution releases non-aggregated definite nanoparticles (as shown in figure 7).

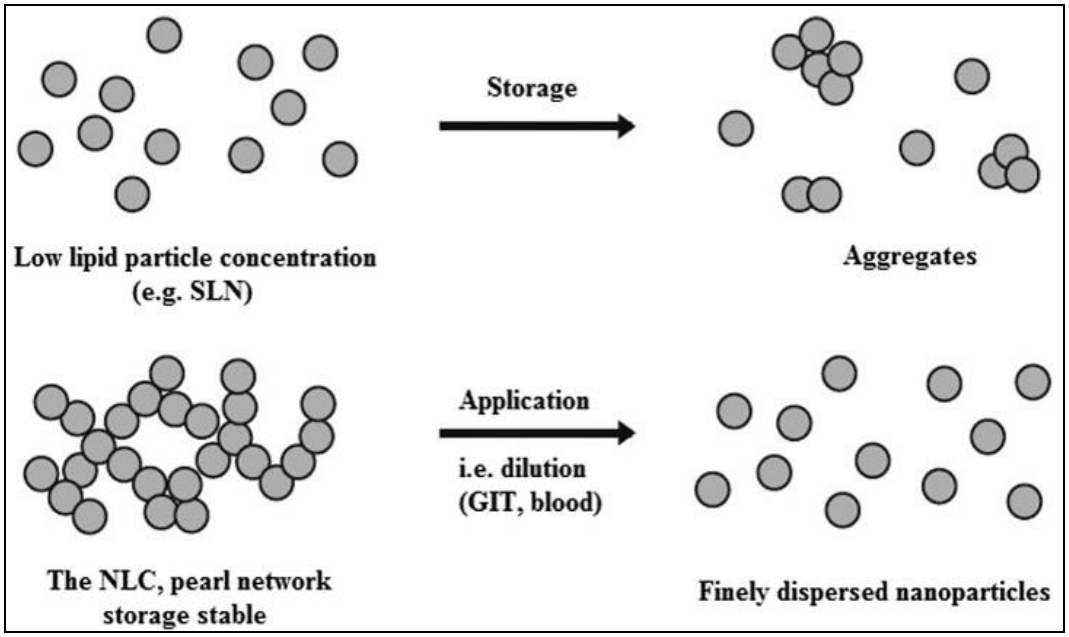

Fig 6: Stabilisation effect in highly concentrated lipid particle dispersions

Strategies Used to Overcome Issues Related to NLC Stability

1. **Polyethylene glycol (PEG):** Surface modification of colloidal particles with a hydrophilic material such as polyethylene glycol (PEG) has been shown to have the following benefits:
- Improving the presence of colloids in blood circulation for systemic use,
- Increasing the stability of colloids in body fluids such as gastrointestinal (GI) fluids,
- Accelerating colloid transport across the epithelium,
- Modulation of collloid interaction with mucosa for specific delivery requirements and drug targeting,
- Increasing biocompatibility and decreasing thrombogenicity of drug carriers, and

2. **Spray drying:** SLNs/NLCs dispersions can be spray dried to boost their stability in addition to the optimal storage conditions. For spray drying, the lipid matrix's melting point must be greater than 70°C.

3. **Lyophilisation:** Lyophilisation is another effective approach to boost stability. When SLN is lyophilized without a cryoprotectant, the final product frequently results in particle aggregation. Trehalose, sorbitol, glucose, sucrose, mannose, and maltose are some of the most often utilised cryoprotectants. Trehalose was shown to be the most effective cryoprotectant in inhibiting particle development by Schwarz and Mehnert.

Table III lists a number of medications that have been evaluated and integrated into these adaptable nano delivery systems for diverse biomedical uses.

Table 3: List of drugs incorporated in NLC's

Sr no	Drug (class)	Method of preparation	Outcome of work
1.	Fluconazole (anti-fungal)	Solvent diffusion method	NLCs had an excellent skin targeting effect, as well as a long-lasting release and a localised impact.
2.	Oridonin (anti-cancer)	Low temperature solidification	For PEG coated oridonin NLCs, the mean residence duration in blood was shown to be longer.
3.	Flurbiprofen (anti-inflammatory)	High-pressure homogenisation	When compared to oral administration, the drug-loaded NLC gel demonstrated higher penetration characteristics for topical distribution, with less adverse effects.
4.	Quercetin (antioxidant, anti-inflammatory)	Emulsion evaporation solidification	NLCs were found to improve drug retention in the epidermis in both in vitro and *in vivo* skin penetration experiments, improving the therapeutic efficacy.
5.	Triamcinolone acetonide (corticosteroid)	High pressure homogenisation	*In vivo* tests on mice revealed that the drug was more stable and delivered to the posterior segment of the eye.
6.	Resveratrol (antioxidant)	High shear homogenisation	In comparison to SLNs, drug loaded NLCs with smaller particle size and higher drug loading demonstrated higher antioxidant activity.
7.	Docetaxel (anti-cancer)	Modified film ultrasonication dispersion method	*In vivo* trials indicated higher effectiveness and fewer negative effects in the treatment of malignant melanoma.
8.	Itraconazole (anti-fungal)	Hot high-pressure homogenisation	NLCs that were stable and kept their characteristics after nebulization for pulmonary distribution were created.
9.	Topotecan (anti-cancer)	Micro-emulsification technique	Topotecan's chemical stability and cytotoxicity were enhanced thanks to nanoencapsulation.
10.	Amphotericin B (anti-fungal)	Solvent diffusion method	Electrostatic repulsion was shown to be more critical than stearic hindrance in providing stability to the NLC.

Applications

NLCs as nano lipid carriers have applications in a variety of industries. The applications are separated into two categories: therapeutic applications, which include the numerous routes of administration in drug delivery, and applications in other disciplines, such as cosmetics, nutraceuticals, food, chemotherapy, and gene delivery. The following are some of them:

Applications in Medicine

- **Topical Delivery**: Using lipid-based nanoparticles, the topical route has been extensively utilised for drug delivery to cutaneous regions. Many investigations and trials on the topical use of NLCs for their unique features have been conducted in recent years. NLCs can increase the perceived solubility of entrapped pharmaceuticals, allowing a high concentration gradient to develop on the skin, allowing for easier drug penetration. Nanoparticles cling to the skin surface firmly and release medications in a more regulated manner. As a result, NLCs are utilised to increase the penetration and sustained release of a variety of medications when applied topically. Another advantage of NLCs for topical administration of active chemicals is the speed with which these products may be brought to market. Figure 8A shows the spherical form of the manufactured NLCs, and the release research revealed a biphasic drug release pattern, with an initial sustained release phase lasting up to 10 hours followed by a continuous drug release phase. The release profile of acitretin suspension and acitretin NLC in phosphate buffer pH 7.4 containing 3% w/v sodium lauryl sulphate is shown in Figure 8B.

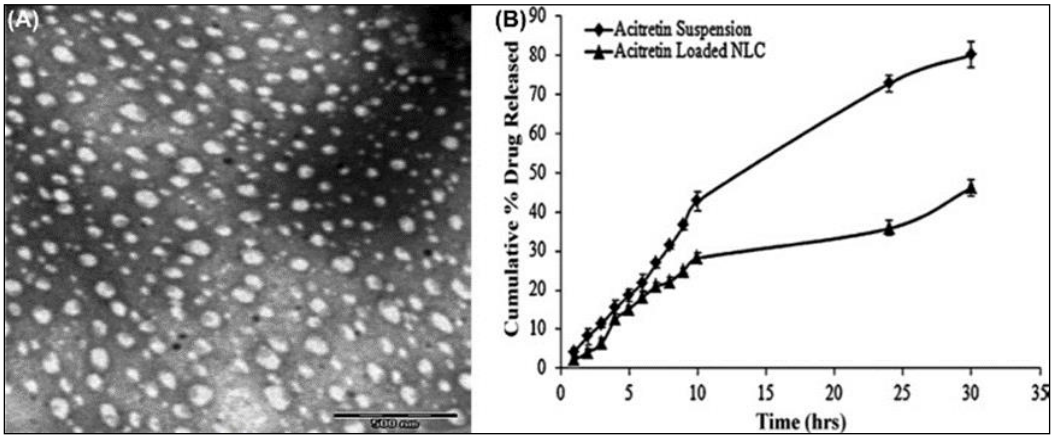

Fig 7: (A) TEM image of acitretin loaded NLC; adapted from; (B) Cumulative percentage drug release from act suspension and Acitretin-NLC in phosphate buffer pH 7.4

- **Oral administration**: NLCs have been shown to be one of the most effective techniques for administering poorly water-soluble medicines with limited bioavailability. Another distinguishing property of NLCs is their great dispersion, which results in a large specific surface area for enzymatic assault by intestinal lipases. Increased drug loading, enhanced drug inclusion, patient compliance, high particle concentration, and a cream-like consistency of the carrier are all advantages of delivering NLC in oral forms.

- **Parenteral Delivery:** Nano-drug delivery technologies including nano micelles, nano emulsions, and nanoparticles have showed significant promise in enhancing parenteral administration of hydrophobic medicines during the last two decades. Nano lipid carriers have been suggested as an alternative to liposomes and emulsions due to superior qualities such as simplicity of manufacture, high drug loading, more flexibility in altering drug release profile, and their aqueous nature and biocompatibility of the excipients. These, together with the excipients' biocompatibility and watery nature, have allowed for i.v. drug administration with passive targeting and easy elimination.

- **Medication delivery to the brain:** Targeting the brain increases drug concentration in the cerebrospinal fluid while reducing dosage frequency and adverse effects. The primary advantages of this route of administration over oral administration are the avoidance of first pass metabolism and the early onset of action. Because of their bioacceptability and biodegradability, they are quickly absorbed by the brain. LNC (e.g., NLC) are one of the most important techniques for drug delivery without creating any modifications to the drug molecule in this generation. Furthermore, because of the simplicity with which they may be ramped up and the lack of a burst effect, they are more viable drug delivery vehicles. Furthermore, NLC enhanced the brain delivery of duloxetine intranasal medicine for the treatment of major depressive disorder. Bromocriptine (BC), a dopamine receptor agonist, has also been incorporated into NLCs for controlled drug administration, possibly extending BC 12 *in vivo* for Parkinson's disease therapy.

Conclusion and Future Perspective

NLC has a big effect on the large bars that are necessary for constructing a successful drug delivery system. The use of nanocarriers in transdermal drug delivery has opened up a whole new world of possibilities. NLCs are chemically and physically stable structures that improve medication incorporation and bioavailability. In recent years, the industry's increased interest in lipid carrier systems has resulted in major achievements. There are already around 30 commercial NLC formulations on the market, including pharmaceutical and cosmetics constituents. Skin targeting, occlusive action, and long-term release are all possible with NLC, a new type of

lipid nanoparticles. Lipid nanocarriers are garnering industry attention due to approved and validated scale-up of technologies, GRAS status of excipients, and simplicity of large-scale production. Future NLC formulations may offer greater success to the lipid carrier system because to its significant benefits over first-generation systems. The investigation of nanostructure toxicity and health hazards is also a future issue. More preclinical and clinical research will pave the way for the development of nano-lipid structures. It is feasible to succeed in this sector if the pharmaceutical industry invests in academic research to develop a carrier system for a variety of medicinal and aesthetic compounds.

Abbreviations

NLC's: Nanostructured Lipid Carriers
DDS: Drug Delivery System
NP: Nano Particles
BCS: Biopharmaceutics & classification System
SLN: Solid Lipid Nanoparticles
MCT: Medium Chain Triglycerides
HF: Hair Follicles
PCS: Photon Correlation Spectroscopy
LD: Laser Diffraction
ZP: Zeta Potential
DSC: Differential Scanning Calorimetry
PEG: Polyethylene Glycol
GI: Gastrointestinal
BC: Bromocriptine

Acknowledgement

I would like to extend my special thanks to Sandip Institute of Pharmaceutical Sciences. The assistance provided by Swati talele, Dr. Laxmikant Borse, Dr. Atul Bendale and Dr. Anil Jadhav is really appreciated.

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