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A Comprehensive Review on Nanostructured Lipid Carriers

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ABSTRACT

Novel pharmaceutical formulations known as nanostructured lipid carriers (NLCs) are made of lipids that are physiological and biocompatible as well as surfactants and co-surfactants. In the past few years, the number of research describing formulations based on NLCs has significantly expanded. As a second-generation lipid nanocarrier (NLC) substitute for first-generation lipid nanocarriers, nanoparticles. NLCs can be produced using a variety of methods that are categorised based on the amount of energy they use. increased use Due to the technological challenges involved in creating lipid-based nanocarriers and the growing understanding of the fundamental principles governing their transport via multiple routes of administration and they can be applied in a variety of ways and through a variety of channels, including oral, cutaneous, ophthalmic, and pulmonary. This review article study provides an overview of the structure, composition, different methods of formulation, characterisation, benefits, drawbacks, and applications of lipid nanoparticles as carriers.

INTRODUCTION

DDS (Drug Delivery System) is a well-known, well-established, and commercially viable method of producing pharmaceuticals in various dose forms. Lipid formulations, such as (Nano Lipid Carriers) NLCs, necessitate the incorporation of a wide range of components. Bioavailability and solubility of insoluble medicines are two important parameters that can be improved with formulations such as NLCs(1).

As a second generation of lipid nanoparticles, nanostructured lipid carriers (NLCs) emerge to address the inadequacies of the first generation, SLNs. NLCs are made with biodegradable and suitable lipids (solid and liquid), as well as emulsifiers(2).

Lipid nano formulations can improve the sluggish and imperfect dissolution of somewhat water-soluble pharmaceuticals like Biopharmaceutics & classification on System (BCS) class II by making dispersions of fairly water-soluble drugs(3). The nanoparticulate drug delivery devices comprise two a drug and its carrier are its components. Several inorganic and organic carriers have been identified that are selected depending on the medication characteristics and desired therapeutic action. These Drug molecules can be shielded from hydrolytic degradation by nanocarriers. Extend the duration for circulation, and enzymatic breakdown, improve its therapeutic benefits(4).

History

Professor R.H. Müller (Germany) and Professor M. Gasco (Italy) began researching the possibility of a new nanoparticle-based formulation dubbed solid lipid nanoparticles in the early 1990s (SLNs)(5). Their lipid-based formulation has several advantages, including the ability to avoid using an organic solvent during the manufacturing process, as opposed to existing organic nanoparticles (e.g. PLGA nanoparticles), and a high level of stability in vivo, as they remained solid at body temperature(6).

Composition

NLCs are made up of a mixture of LL, SL, and surfactants dispersed in aqueous solutions in precise ratios. The chemicals employed in NLCs as carriers for chemotherapeutic drug molecules should be biocompatible, non-toxic, and acceptable for systemic administration(7). Examples of SL, LL, and surfactants utilised in the manufacture of NLCs for the delivery of anticancer medicines are included in Table 1.

Table No. 1. Ingredient used in formulation of NLCs.(8)

Some commonly used solid – liquid, liquid – liquid, Surfactants for preparation of NLCs.

component	Ingredient	Purpose and references
Solid – Liquid(9)	Stearic acid	• For topical delivery. • Controlled released and acidic protection to drug.
	Glyceryl monostearate	• Enhancement of orally bioavailability.
	Glyceryl Tripalmitate	• Moisturizing
	Cetyl palmitate	• Use as antifeedant. • Can helps hydration deeply into your skin, moisturizing.
	Precirol ATO 5	• Lubricant
Liquid – Liquid(10)	Oleic acid	• Used in the solution phase synthesis of nanoparticles. • It controls the size and morphology of nanoparticles.
	Capric triglycerides	• Emollient. • Helps to soften and smooth the skin's surface.
	Alpha – tocopherol / Vitamin E	• Antioxidant
	Squalene	• It maintains skin's moisture barrier and hydration.
	Sweet almond oil	• Emollient • Demulcent • Analgesic
	Capmul MCM C8	• emulsifier, emollient and solubilizer
Surfactant (11)	Soy bean oil	• Preventing coalescence by reducing interfacial tension or creating a physical repulsion between the droplets. • Improve their processability and to control the composite properties
	Tween 80	• Reducing agent and protecting agent to prepare stable water-soluble silver nanoparticles
	poloxamer 407	• Is used for its good solubilizing capacity
	Hydrogenated soybean phosphatidylcholine	• Improve the permeability and solubility of ranolazine

Structural types of NLC

Depending on the location of incorporated drug moieties in NLC, following three types of morphological models (Figure 1) has been proposed: (12)

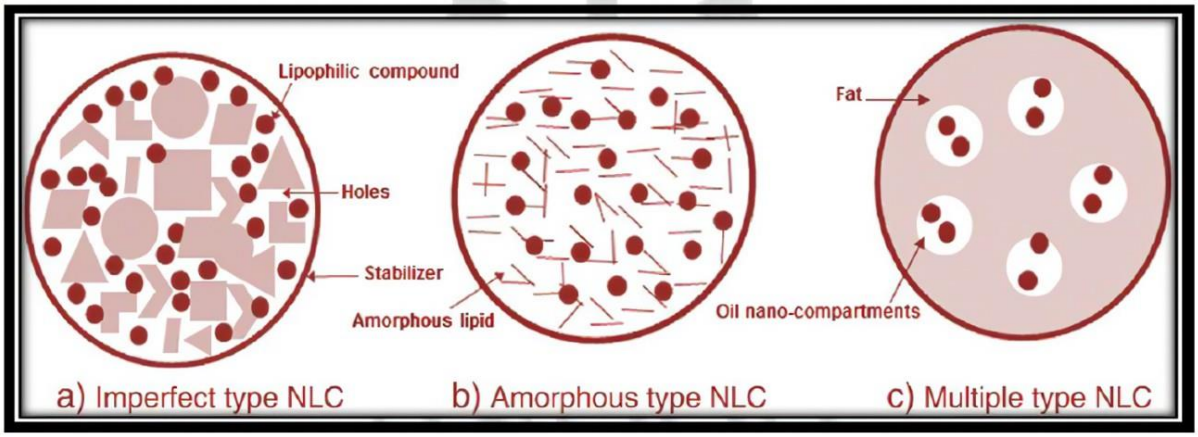

Figure No. 1: Types of NLCs

- NLC type I also called as imperfect crystal
- NLC type II also called as amorphous type
- NLC type III also called as multiple type.

a) **Imperfect crystal type-** NLC is made up of a highly disordered matrix with numerous voids and spaces that allow more drug molecules to fit into amorphous clusters. Solid lipids are mixed with an appropriate amount of liquid lipids to obtain these crystal order defects (oils). The matrix of NLC is unable to create a highly organised structure due to various chain lengths of fatty acids and a mixture of mono-, di-, and triacylglycerols. The capacity of the drug payload is increased by mixing geographically diverse lipids, although this model has a low entrapment efficiency(13)(14).

b) **Amorphous type**- Amorphous type NLC is made by carefully combining lipids in order to reduce drug leakage during the crystallisation process. Solid yet non-crystalline particles are formed by lipids such hydroxyl octacosanyl, hydroxyl stearate, isopropyl myristate, and dibutyl adipate. The lipid matrix is homogeneous and amorphous in nature(13).

c) **Multiple type -** The solubility of oil in type II NLCs is higher than the solubility of solid lipids. Due to the oil molecule's effortless diffusion into the lipid matrix at a low concentration of oil, a large amount of oil is mixed with solid lipids in type II NLCs. If more

oil is injected than is required for its solubility, it can result in the separation of various phases, resulting in microscopic oily nano compartments bordered by the solid lipid matrix. The HLs formulation allows for regulated drug release and drug leakage from the lipid matrix. Lipophilic medicines can be rendered soluble in oil first, and then the type II approach can be used with a hot homogenization process cooling operation(15).

Advantages of NLCs (16)(17)(18)

- NLCs have great biocompatibility and are simpler to validate and approve by regulatory agencies.
- Since the techniques are based on water, organic solvents can be avoided.
- When compared to polymeric/surfactant-based carriers, NLCs are less expensive, easier to scale up, and easier to sterilize.
- NLCs offer control and/or targeted medication release to enhance pharmaceutical stability.
- Compared to other carriers on the market, NLC's deliver excellent and higher medication content.
- The majority of lipids are biodegradable.
- NLCs have the ability to transport both lipophilic and hydrophilic medicines simultaneously.

METHOD OF PREPARATION OF NLC

In general, the nano emulsification of a lipophilic phase containing a mixture of LL and SL (e.g., tripalmitin and squalene, respectively) in an aqueous solution of water-soluble surfactants/emulsifiers is used to make NLCs. The methods used for the production of NLCs are based on the energy requirement, they are categorized into three types.

1. High Energy required methods

There are different methods used for the production of NLCs and require large amount of energy input such as High-pressure homogenization, High shear homogenization/sonication based. In this review these two methods are discussed as they are most widely used methods(19).

1.1. High pressure homogenization

The high-pressure homogenization method is considered as one of the most widely preferred method, because while preparation solvents are not added, as it produces highly stable particles and also required no organic solvent addition. It has been considered as powerful method for the large-scale production of NLCs. This method is further divided as hot homogenization and cold homogenization(20)(21).

a) Hot homogenization:

In this method using high-speed stirring, a hot aqueous solution of surfactant is mixed with a molten lipid mixture before the medication is added. The pre-emulsion is then thoroughly homogenized using a high-pressure homogenizer. Once the obtained nano emulsions recrystallize, NLCs are created at room temperature This method has some drawbacks, such as the heat-induced degradation of thermolabile actives, the reduction emulsification power of some surfactants at higher temperatures, and low drug encapsulation efficiencies due to the possibility of partitioning in both lipid and aqueous surfactant solution at high temperature, which encourages drug escape into aqueous phase(22)(23).

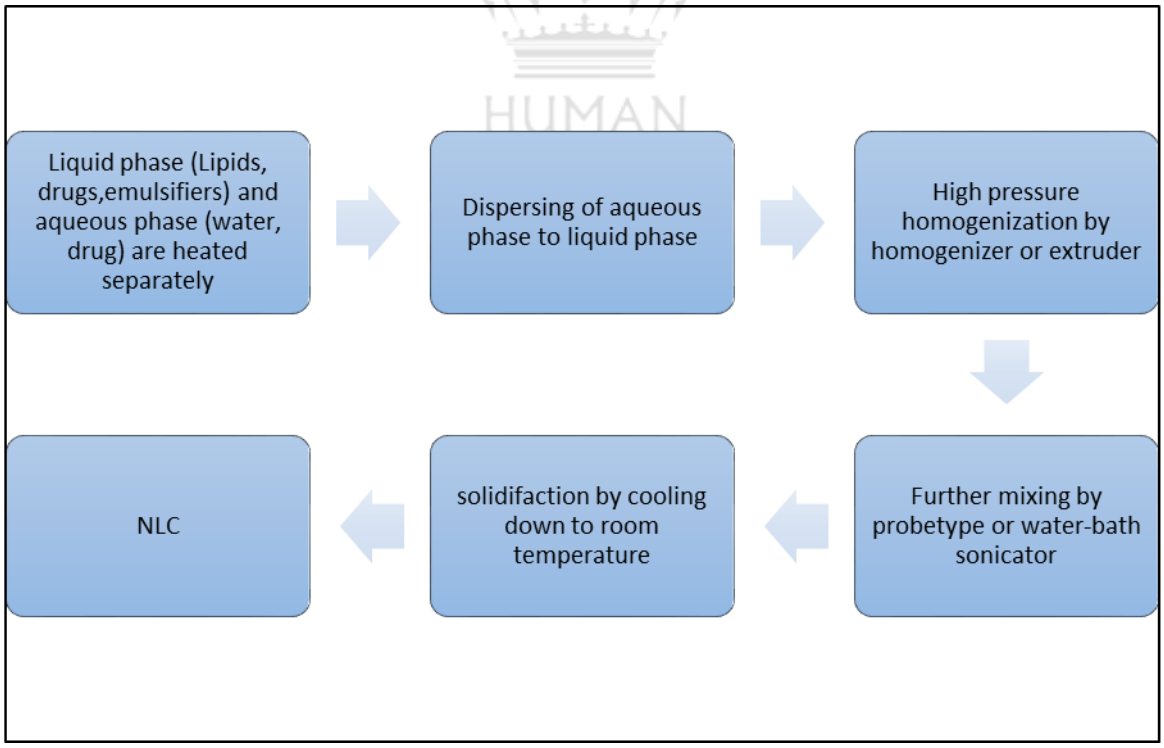

Figure No. 2: Hot homogenizer process

b) Cold homogenization:

In this procedure, the drug and molten lipid combination are rapidly cooled while being affected by liquid nitrogen or dry ice, solidifying the mixture. It is then micronized and dissolved in a cold aqueous surfactant solution. High pressure homogenizer is used to complete the final processing of the produced dispersion. The drawbacks of hot procedures, such as avoiding heating of medications and surfactants, can be somewhat resolved by this technique. Controlling the crystallization process is another way to get the desired crystal structure(24).

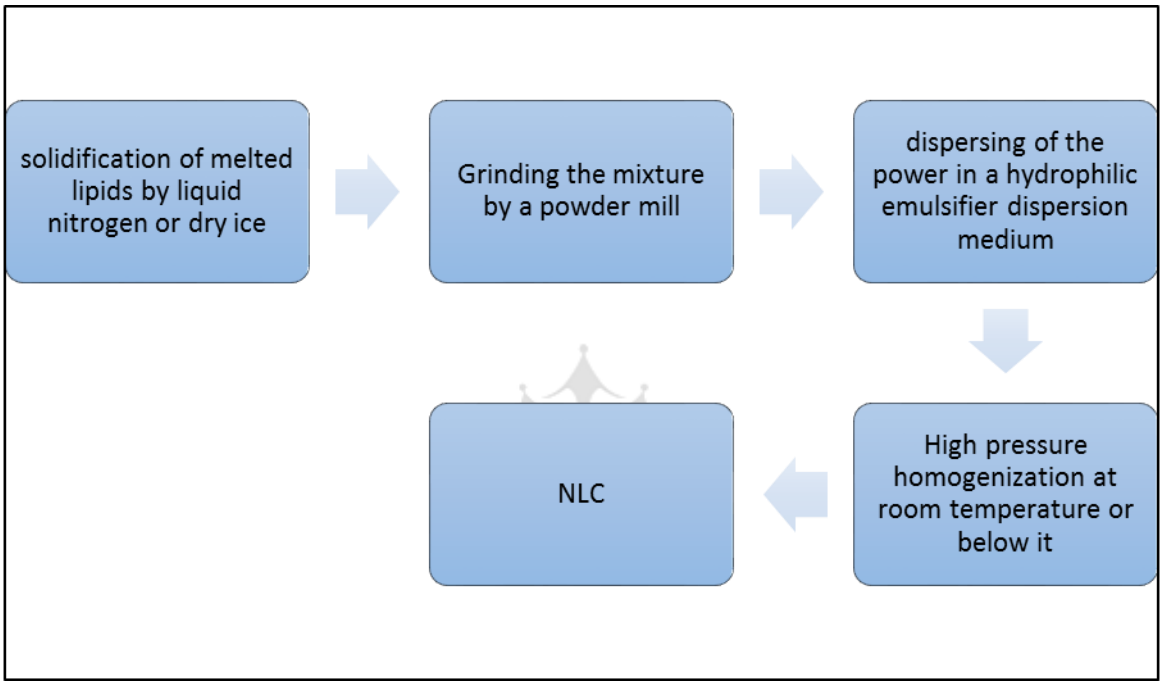

Figure No. 3: Cold homogenization

1.2. High shear homogenization / sonication

This technique involves dissolving or dispersing a lipophilic medication in a molten mixture of solid and liquid lipids. To make it difficult to recrystallize, the temperature utilized should be 10 C above the melting point of solid lipid. Pre-microemulsion is created by adding the aqueous surfactant solution to the lipid phase at the same temperature and stirring it vigorously. After being treated with a probe sonicator, the pre-emulsion is further homogenized using high shear homogenizers(25)(26).

2. Low energy required method:

2.1. Microemulsion:

Similar steps to the high shear homogenization/sonication process are used to create microemulsions. The hot microemulsion is then mixed with the cold water to create the nanoemulsion, which then recrystallizes to create the NLC(27).

2.2. Double emulsion

This procedure involves adding the produced microemulsion to cold water (2–10 C), which facilitates the precipitation of evenly distributed NLCs particles.

2.3. Phase inversion

This process involves three heating and cooling cycles for the combination of all the components. The hot mixture is then shocked by diluting it with cold water, and phase inversion causes NLCs to develop.

2.4. Membrane contractor

Using this technique, molten lipid is pressed against a porous membrane to create small lipid droplets. They are moved around inside the membrane module and swept out of the pore simultaneously. Cooling at normal temperature causes NLCs to develop.

3. Very low energy required method:

3.1. Emulsification solvent evaporation

In this method, the active ingredient and the lipids are both dissolved in a water-immiscible solvent. Aqueous surfactant solution is then used to emulsify the resulting solution. The solvent then evaporates while being continuously stirred, producing NLCs. This method is suitable for heat-sensitive actives because there is no heat involved. The main drawbacks of this technology are the toxicity of the solvent residue and the diluted NLC particles caused by the insufficient solubility of the lipids in the solvents utilized(28).

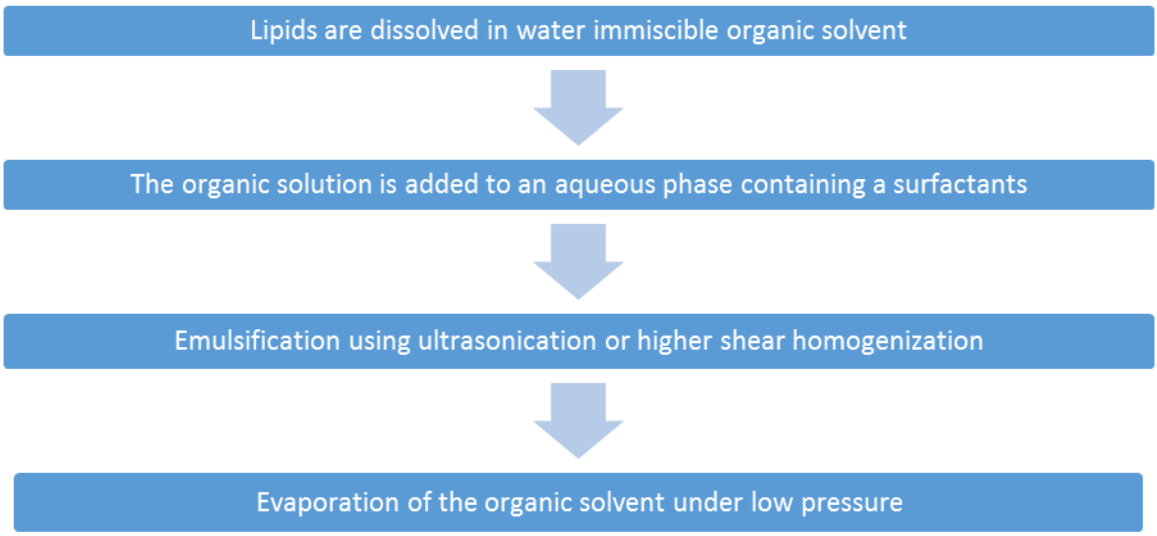

Figure No. 4: Preparation of NLCs by solvent emulsification/evaporation technique.

3.2. Emulsification Solvent diffusion

This method involves dissolving the active ingredient and the lipids in an organic solvent that has been saturated with water to achieve thermodynamic equilibrium. The resulting temporary o/w emulsion is poured into water and stirred until the dispersed phase solidifies(29).

3.3. Solvent injection

In the solvent injection method active substance are lipids are dissolved in organic solvent and injected it with aqueous surfactant solution(30).

CHARACTERIZATION OF NLCS

Nanocarriers must be characterised before they may be used in clinical settings. The characterisation of SLNs and NLCs is difficult due to their tiny size and the dynamic nature of the system when compared to other colloidal carriers. Nanoparticle stability and in vivo performance are directly influenced by characterization factors. Particle size, morphology, polydispersity index (PI), zeta potential, percentage drug entrapment efficiency, drug crystallinity, and stability are the primary characteristics of the SLN and NLC.

- **Size and Morphology**

The physicochemical features of lipid nanocarriers, particularly particle size distribution, influence their accumulation in the target tissue. As a result, preparing homogeneous (monodisperse) populations of nanocarriers of a specific size is required for the formulation

of safe, stable, and efficient nanocarriers(31). To estimate the size of lipid particles, laser diffraction (LD) and photon correlation spectroscopy [also known as dynamic light scattering (DLS)] are commonly utilised. The size distribution, which is represented by the polydispersity index, is assessed using both methodologies (PI). DLS provides a whole picture of solution homogeneity and particle size. A single sharp peak implies the presence of a single, uniform scatterer population(32).

- **Zeta Potential**

Zeta potential is defining the amount of charge on the particles' surfaces in aqueous dispersion, which is a crucial quantity in forecasting the formulations' long-term physical stability. Normally, the electrophoretic mobility of lipid nanoparticles predicts their zeta potential value, which is evaluated using photon correlation spectroscopy and LD methods. In absolute value, the zeta potential of the electrostatically stabilised nano dispersion is >30 mV. The chemical nature of the particle surface describes the zeta potential. It also depends on the nanoparticles' surroundings and the amount of sample used(33).

For exceptional and good physical stability in SLNs and NLCs, respectively, a minimum zeta potential of greater than 60.0 mV and higher than 30.0 mV is required. The zeta potential of formulations including non-ionic steric stabilisers such as polyhydroxy surfactants is predicted to be low. With increasing oil content in SLNs and NLCs, the zeta potential value has been reported to increase. Because of less electrostatic stabilisation and more steric stabilisation when SLNs are coated with a non-ionic surfactant like Tween R, they tend to stay stable at a lower zeta potential. The electrophoretic mobility of particles is reduced by SLN surface covering, which lowers the zeta potential.

- **Degree of Crystallinity**

The encapsulation efficiency and release rate of medicinal drugs from NLCs are influenced by the crystal lattice's structure and the state of its lipid components. More flaws in the crystal lattice benefit drug encapsulation in theory. Varying lipids have different melting enthalpies and melting points, hence differential scanning calorimetry can be used to assess the state of the lipid components. The amount of drug loaded, storage period, and viscosity of the formulation can all affect the crystallinity of lipid-based NPs. Because of improved entrapment and housing of the drug in the lipid matrix, employing SL with many crystal lattice defects can improve drug encapsulation as well as chemical stability in NLCs(34).

- **Entrapment Efficiency**

The amount of drug entrapped in the carrier as a percentage of the total amount of drug present in the dispersion is referred to as drug entrapment efficiency. The entrapment efficiency was determined using a combination of analytical [UV spectrophotometry or high-performance liquid chromatography (HPLC)] and separation procedures (ultrafiltration, centrifugation, and dialysis). The active component can be quantified using these procedures. The efficiency of entrapment can be judged in two ways: directly and indirectly(35).

The encapsulated drug is directly measured in the direct approach, whereas the amount of unencapsulated drug in the supernatant is assessed in the indirect method. The entrapment effectiveness of active compounds in lipid nanoparticles is generally greater than 70%. A mixture of liquid and solid lipids makes up NLCs. During the rigidization process, an incomplete core forms in NLCs because to the presence of liquid lipids. These defective cores provide enough room for drugs to be accommodated and enable for greater drug encapsulation(36).

- **Stability**

According to the ICH guidelines, the stability profile of SLNs and NLCs can be investigated by evaluating the mean particle size, size distribution, entrapment efficiency, and drug release profile throughout storage durations at various temperatures. At regular intervals, samples are taken and evaluated for these criteria. A UV spectrophotometer or HPLC are used to determine the % drug entrapment efficiency and drug release patterns(37).

- ***In vitro* Drug Release**

Biodegradation and diffusion mechanisms largely regulate the drug release profile from SLNs and NLCs. Side-by-side diffusion cells with a biological or artificial membrane-like reverse dialysis sac, ultra-centrifugation, dialysis bag, centrifugal ultra-filtration, and ultra-filtration are commonly used to estimate in vitro drug release from these nanocarriers. A UV spectrophotometer or HPLC are used to examine the medication release profile(38).

NLCs: ARISING APPLICATIONS BY DIFFERENT ROUTES OF ADMINISTRATION

- **Topical route of administration**

Skin infections are extremely frequent all around the world. Low therapeutic efficacy due to inadequate skin penetration or skin permeation of pharmaceuticals from the most traditional formulations is one of the key constraints for treating these disorders. The primary skin barrier, the stratum corneum, should be crossed by switching the penetration pathway from transcellular to paracellular or follicular. To promote skin penetration or permeation, lipid nanoparticles such as SLNs and NLCs have been produced. Mixing SLNs or NLCs with standard formulations produces these particulate formulations(39).

They could be made in a one-step procedure that produces drug-loaded SLNs or NLCs. Biocompatibility and biodegradability, regulated and extended drug release profiles, intimate contact and strong skin adhesion, skin hydration, and film formation to promote skin and dermal penetration are only a few of the benefits of lipid nanoparticles for topical drug administration(40).

Table 2: NLCs advantages and disadvantages as topical drug delivery systems

Advantages	Disadvantages
Increased skin penetration	Restricted transdermal drug delivery
Biocompatible and biodegradable nature	Loss of high amounts of drug
Easy and scalable production process	Lack of robust controlled drug release
Possibility of specific follicular targeting	
Good stability during storage period	

- **Oral route**

While enhancing the bioavailability of highly lipophilic medicines, NLCs have a longer residence period in the GIT than other lipid-based formulations and have a novel release mechanism that can be controlled by tuning the lipids in their solid lipid matrix. In general, lipid microemulsions (e.g., Self-Emulsifying Drug Delivery Systems (SEDDS)) disintegrate faster and to a greater extent than NLCs. Because of these characteristics, and based on the experimental data presented in this section, NLCs appear to be a potential delivery route for

lipophilic medicines with low bioavailability, which are particularly suited for gastrointestinal illnesses such as inflammatory bowel disease (IBDs)(41).

Because of the highest patient compliance, oral drug administration is the most prevalent route of drug delivery. The most major limits in oral medication administration that need be overcome are low oral bioavailability due to restricted drug solubility and/or a strong hepatic first pass effect. Nanoparticle-based medication delivery systems were thought to be a good option for increasing oral bioavailability(42).

Table 3: NLCs advantages and disadvantages as oral drug delivery systems.

Advantages	Disadvantages
Improving oral bioavailability	Drug expulsion during storage
Reducing hepatic first pass metabolism	Polymorphic transition
Low variation in oral absorption	Particle size growth during storage time
Preventing undesired plasma peak	Gelation of lipid dispersions
Increasing AUC and MRT values	Limited loading capacity for hydrophilic drugs
Modulated and controlled drug release	Lipid dispersions contain high amounts of water
Shorter onset of action and longer duration time	

- **Parenteral administration**

In order to improve parenteral drug delivery, nanomedicine and nanotechnology are crucial. Table 4 lists the benefits and drawbacks of lipid nanoparticles as parenteral medication delivery systems. The most important advantages of lipid nanoparticles for this purpose are their ease of scale-up, the biocompatibility and biodegradability of the formulation constituents, the controlled and modified drug release pattern, the prevention of drug degradation, and the ability to maintain more consistent drug serum levels. Intravenously, subcutaneously, intramuscularly, and directly into target organs, drug-loaded lipid nanoparticles can be injected(43).

Drug release from lipid nanoparticles can take place by erosion (such as enzymatic destruction) or diffusion, which can result in long-term drug release. Recent studies have proven the potential of lipid nanoparticles to incorporate peptides and proteins. In this case,

SLNs are not a good carrier because of their low drug loading capacity, but NLCs are a good alternative. Peptides and proteins can be protected against harsh environmental conditions using this technology(44)(45).

Table 4: NLCs advantages and disadvantages as parenteral drug delivery systems

Advantages	Disadvantages
Long physical stability	Lack of wide clinical studies
Controlled and sustained drug release	Drug burst release by erosion mechanism
Limited side effects	Drug expulsion
Good potential as vaccine adjuvants	Low drug payload for hydrophilic drugs
Longer drug circulation time	
Improving drug bioavailability	
Lower cytotoxicity	

- **Pulmonary delivery**

Inhaled drug delivery methods have improved in recent years, allowing for better treatment of local lung disorders such as lung cancer, cystic fibrosis, bronchiectasis, respiratory infections, and chronic obstructive disease(46). Rapid clearance makes medication distribution to the lungs difficult, hence a localised, long-acting release is preferred when targeting this organ. Nanotechnology has been a widely used technique for local pulmonary delivery, with a huge number of nanoparticles examined (e.g., polymeric nanoparticles, micelles, liposomes, solid lipid nanoparticles). Pulmonary medication administration is a relatively recent method with numerous benefits. It is a non-invasive medication delivery method that can be used for both local and systemic administration(47).

Drug dosage could be reduced and, as a result, drug side effects could be reduced with this direct delivery technology. Inhaling a medicine directly can potentially hasten the commencement of action. Another advantage of this administration route is the high drug accumulation at the target site. The pulmonary system's large surface area and thin alveolar epithelium may ensure significant drug permeability(48).

The delivery mechanism for lung targeting was lipid microparticles. In comparison to standard formulations, these particle systems demonstrated promising results, such as increased drug bioavailability. For pulmonary delivery, lipid nanoparticles such as SLNs and NLCs have been studied. In compared to previously proposed particle systems, they have the advantages of sustained drug release, biocompatibility and biodegradability, lower toxicity, and superior stability(49).

Table 5: NLCs advantages and disadvantages as pulmonary drug delivery systems.

Advantages	Disadvantages
Better biopharmaceutical properties	No human safety data available
Sustained drug release	Loss of loaded drug during nebulization
Prevention of adverse drug effects	Burst drug release from these nanocarriers may induce toxic effects
Good storage stability	Change in drug release profile because of lipase degradation in some lipid matrix compositions
Low toxicity	Agglomeration, clotting and fragmentation of lipid nanoparticles during nebulization
Bypassing hepatic first pass metabolism	
Prolong drug residence time in lung	

- **Ocular administration**

Because of distinct physiological and anatomical aspects of the eyes, ocular medication administration has significant limitations and remains hard. The eyes are a complicated and clever organ with a number of obstacles that must be overcome in order to reach specific ocular tissue(50). To circumvent these hurdles and improve ocular tissue bioavailability, novel drug delivery methods such as lipid nanoparticles were proposed. The most prevalent method of drug administration to the anterior portion of the eyes is topical application. This method of delivery has numerous advantages and is the preferred method for treating superficial ocular disorders. The corneal epithelium, blood ocular barrier, conjunctival blood flow, and tear drainage are all major obstacles in this system(51).

Lipid nanoparticles utilised as ocular drug delivery systems can cross the blood-ocular barrier, allowing for prolonged and regulated drug release, as well as protecting

pharmaceuticals from lacrimal enzymes and extending drug deposition and residence duration in the eyes. Ocular illnesses affecting the posterior region of the eyes are notoriously difficult to treat. The posterior portion of the eyes can be targeted in a variety of ways(52).

Table 6: NLCs advantages and disadvantages as ocular drug delivery systems.

Advantages	Disadvantages
High encapsulation efficiency	Initial burst release from SLNs
High ocular permeation	Low drug loading capacity
Enhancing drug corneal permeability	Lipid nanoparticles toxicity on retinal cells have not been studied completely yet
Good stability and biocompatibility	
Preventing ocular toxicity	
Appropriate pharmacokinetic properties	
Sustained and controlled release	

- **Brain delivery**

Because of the blood-brain barrier, drug distribution to the brain is one of the most difficult difficulties in pharmaceutical science (BBB)(53). Nanoparticles have been studied for selective targeting of brain tissues due to their small particle size and high drug encapsulation effectiveness. Nanoparticles are suitable as brain drug delivery devices because they can bypass the reticuloendothelial system (RES). Limited drug penetration across the BBB and efflux of delivered medicines from the brain to the blood circulation are two main roadblocks in brain medication delivery(54).

One of the colloidal drug delivery technologies that has been used to circumvent these obstacles is lipid nanoparticles such as SLNs and NLCs. Table 7 lists the benefits and drawbacks of lipid nanoparticles as brain medication delivery methods. Lipid nanoparticles have the advantage of increasing drug retention time in brain capillaries' blood and inducing a drug gradient from blood to brain tissues, as well as opening tight junctions to allow passage through the BBB and transcytosis of drug-loaded lipid nanoparticles through the endothelium

layer. Both lipophilic and hydrophilic medicines can be incorporated into lipid nanoparticles, which can be delivered via several ways(55).

Previous studies have shown the importance of surfactant compatibility for brain medication delivery. Suitable surfactants might be selected based on their HLB and packing characteristic. Polysorbates, particularly polysorbate 80, have demonstrated to be the most effective for site-specific brain medication delivery. Furthermore, positively charged lipid nanoparticles generate superior medication accumulation in the brain, according to the findings(56).

Table 7: Lipid nanoparticles advantages and disadvantages as brain drug delivery systems.

Advantages	Disadvantages
Opening tight junctions	The possibility of the detection of lipid nanoparticles by reticuloendothelial system (RES) cells.
Bypassing blood brain barrier	
Enhancing drug retention time in brain	
Long storage stability	
Non-invasive brain drug delivery	

FUTURE PERSPECTIVES

The development of medication delivery systems is a never-ending challenge that incorporates diverse research efforts in various fields. NLCs are lipid-based nanocarriers that include a mixture of solid and liquid lipids and allow lipophilic actives to be entrapped, protecting them from degradation and enhancing their stability.

The number of research organisations working with NLC, as well as the number of publications in this field, has expanded dramatically during the last five years. It reflects the fact that an increasing number of academic scientists have recognised the NLCs' potential and are working to develop it. Not just in Germany, Canada, and China, but also in Slovenia and Poland, research organisations have been established all over the world. If only academic research groups are working on a delivery system, there will be no breakthrough.

Success is feasible if the pharmaceutical business also invests in research and development to ensure that a carrier system is widely used. Contract research organisations engaged in the research and development of newer drug delivery systems develop pharmaceutical solutions tailored to the needs of a variety of pharmaceutical companies, implying that the technology will spread to a variety of companies rather than being restricted to just one or two.

Finally, greater research on NLC absorption, distribution, metabolism, and excretion, as well as techniques to scale up their manufacturing, and their use in clinical trials in the near future, could provide an alternative for a safer and more efficient delivery route for chemotherapeutic medicines.

CONCLUSION

The NLCs are carrier systems that have the potential to be very successful in the market. The NLCs are a new generation of formulations that offer much greater flexibility in drug loading, release regulation, and increased performance in the production of final dosage forms such as injectables, creams, tablets, and capsules, among other things. NLC dispersions can be employed in a variety of compositions due to their high uniformity.

NLCs are lipid-based nanoparticles with an unstructured solid lipid core that allow extremely lipophilic medicines to be encapsulated, preserving them from degradation and improving their stability. When compared to existing nanoparticulated drug delivery technologies, they offer a number of advantages.

NLCs have transformed the field of lipid-based NPs formation, offering a wide range of benefits over a variety of routinely used lipophilic preparations. NLCs as drug carriers provided a high-loading capacity platform for drug delivery via a variety of routes, including parenteral, oral, topical, ophthalmic, and pulmonary routes, while improving the physical and chemical stability of the drugs, providing flexible release control, protecting them from degradation, and improving their poor pharmacokinetic parameters.

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