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Review Article

Nanostructured Lipid Carrier:A Review

Shradha G. Kandalkar*[1], Kajal A. Choursiya[2], Saba Shaikh[3],Pradnya Gangurde[4], S. B. Gondkar[5], Rishikesh Bachhav[6]

[1-5] *Department of Pharmaceutics, KCTs R. G. Sapkal College of Pharmacy, Anjaneri, Nashik- 422212, Maharashtra, India.*
[6]*Department of Pharmacology, KCTs R. G. Sapkal College of Pharmacy, Anjaneri, Nashik-422212, Maharashtra, India.*

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ABSTRACT

Solid lipid nanoparticles were developed as an alternative carrier system to emulsion, liposomes and polymeric nanoparticles because they have advantages such as good release profile and objective drug delivery with excellent physical strength. They are binary systems which contain both solid and liquid lipids. It was found to have superior characteristics over other lipid formulations. As a novel type of lipid nanoparticles with solid matrix, the nanostructured lipid carriers (NLC) are presented. This paper reviews the types of NLCs, various excipients used in NLCs, method of preparation, characterization and applications of NLCs. Due to their biologically non-toxic, non-immunogenic and compatible nature, NLCs are going to be the widely used lipid nanocarrier systems.

INTRODUCTION

Research on a novel lipid nanoparticle drug delivery system began with the production of solid lipid nanoparticles (SLNs). Drug Encapsulation in various biocompatible lipids formulated in nanoregions has become a promising approach for drug delivery as lipid nanocarriers. This first-generation lipid nanocarrier was further developed to achieve drug delivery through multiple routes of administration in the treatment of physiological complications.1 In general, lipids can be defined as hydrophobic or amphipathic molecules that are insoluble in water and soluble in organic solvents. In the pharmaceutical industry, lipids can be used as a vehicle to transport poorly soluble active substances in water by various administration methods. 2 Conventional formulations applied to the skin are usually of a semi-solid consistency and contain aqueous gels (i.e. hydrogels), hydrophobic creams and gels (i.e. oleo gels), or a mixture of both aqueous and oil phases, such as water-in-oil (W /O) or oil-in-water (O /W) creams. In these

***Corresponding Author:** Shradha G Kandalkar
Address: *Department of Pharmaceutics, KCTs R G Sapkal College of Pharmacy, Anjaneri, Nashik- 422212 (M.S.) India.*
Email : shradhakandalkar123@gmail.com
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systems, the external phase of the formulation controls the release of the molecules. Thus, hydrogels and O/W creams provide rapid release, while hydrophobic formulations provide sustained release. In addition, aqueous formulations are easier to spread and are therefore preferred by consumers over high viscosity lipid formulations. due to their rheological properties (i.e., viscoelastic behavior), semi-solid emulsions remain at the point of use for a long time, thus prolonging the passage of molecules. In addition, these dosage forms are easy to dispense and can contain various substances.3 In the local treatment of respiratory diseases, lung administration is distinguished by the fact that it reaches directly the lung epithelium and thus the site of action, which means that the effect begins quickly, and the required dose is reduced compared to traditional administration methods. for example, orally. Furthermore, after local administration of poorly absorbed drugs, exposure of large doses to the systemic circulation and thus systemic side effects are minimized or avoided. 4 Nanostructured lipid carriers (NLCs), i.e., nanoparticles composed of a mixture of solid and liquid lipids with a lipid matrix solid at room and body temperature [3], are the second generation of solid lipid-based colloidal carriers with improved stability and drug content encapsulation ability. 5 NLCs consist of a mixture of solid and liquid lipids in a ratio of 70:30 to 99.9:0.1. By mixing solid and liquid lipids in different proportions, more space for the active component can be achieved by forming a less ordered lipid matrix. Therefore, NLCs are enriched with various advantages such as high percentage encapsulation efficiency (% EE), high storage stability, better biocompatibility, and better bioavailability compared to other nanocarrier systems. 6 The main advantage of this type of carrier/delivery system is its ability to incorporate large amounts of drugs due to the formation of a less ordered lipid matrix with many disadvantages. They have also been found to significantly increase skin hydration and exert occlusive properties due to reduced trans epidermal water loss. 7 As the main ingredients of a combination of natural lipids and surfactants, LBNs illuminate encapsulated drug delivery systems, especially to cross the GIT barriers. They probably have more advantages than other nanoparticles (NPs) due to the absence of organic solvents and their ability to withstand the degradation of matter. 9

Components and formulation Characteristics

Basically, and like emulsions, NLCs consist of a lipid phase, an aqueous phase, and surfactants. However, the choice of components and their ratio can influence the final behavior of a specially designed formulation. Various lipids have been used in the preparation of NLCs.8

Table 1. List of Excipients of NLCs

Ingredients	Examples	References
Solid Lipids	Stearic Acid	[2,4,6,9,11]
	Precirol*ATO 5	[2,4,6,11]
	Compritol	[2,6,9,11]
	Dynasan*	[2,6,11]
	Beeswax	[2,9,11]
Liquid Lipids	Oleic acid	[2,4,6,9,11]
	Miglyol 812	[2,4,6,9,11]
	Olive oil	[6]
Surfactant	Poloxamer 188	[2,4,6,11]
	Sodium lauryl sulphate	[2,11]
	Tween 80	[2,6,11]

	Soybean lecithin	[2,6,9,]

NLC Type

NLCs are divided into three categories based on lipid content and formulation parameters: imperfect, amorphous, and multiple structure. Imperfect NLCs are formed by combining lipids containing a variety of fatty acids, i.e., carbon chains of varying length and saturation, resulting in frequent crystal lattice flaws capable of accommodating lipid-soluble pharmacological molecules. As a result, increasing flaws allows for a larger medication payload. The amorphous type reduces drug ejection owing to lipid matrix crystallization by combining solid and liquid lipids that congeal to an amorphous state (e.g., hydroxyoctacosanyl hydroxystearate or iso-propyl myristate), resulting in a structureless, non-crystalline matrix. Numerous NLCs are oil-in-fat-in-water (O/F/W) carriers made up of a solid lipid matrix that houses numerous liquid oil nano-compartments. Lipophilic drug molecules are more soluble in liquid lipid than solid lipid, hence the existence of these oil nano-compartments boosts drug loading capacity. In addition, the solid matrix surrounding the nano-compartments functions as a barrier, preventing drug leakage and allowing for regulated drug release.15

NLC Type I:

It's an imperfect crystal core. There is more room for medication accommodation within the lipid core.1 As a result, increased drug loading is possible, with little or no drug ejection from the core. Spatially diverse lipids are combined, resulting in defects in the structural arrangement of lipid nanoparticles; demonstrate a high drug payload.17

NLC Type II:

This type is also known as the structureless type. Instead of converting into a crystalline structure, solid lipids put into this undergo amorphous transformation.1 Formed by combining solid lipids with specific lipids such as hydroxyoctacosenyl hydroxystearate, isopropyl myristate, or medium chain triglycerides such as miglyol 812, which prevents drug rejection and has a mild drug payload.17

NLC Type III:

This is a multi-model known as the O/F/W model. Drugs with a higher solubility in liquid lipids/oils than in solid lipids can be prepared in this way. It can be made using the phase separation method. The drug is dissolved in tiny oil droplets and distributed equally throughout the solid core.1The solubility of the medicine in the lipophilic phase diminishes during the cooling process following homogenization and crystallization during storage.17

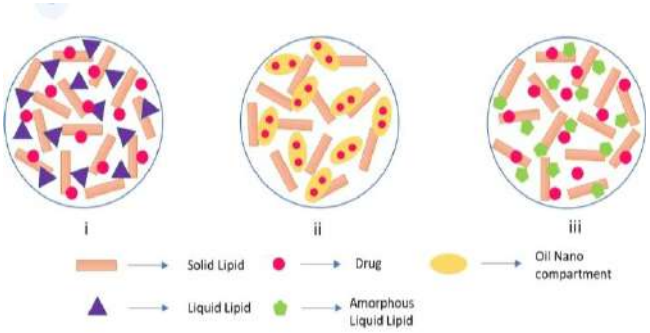

Fig. 1 Types of NLC: i) Imperfect type, ii) Amorphous type, iii) Multiple type

4. Method of preparation

The literature describes a number of methods for creating NLCs. These consist of phase inversion, solvent injection/solvent displacement, solvent diffusion, solvent emulsification evaporation, high pressure homogenization, microemulsion, and probe sonication.19

1.High pressure homogenization method[HPH]

A dependable and well-established technique for preparing lipid nanoparticles is high pressure homogenization. With HPH's assistance, lipid NPs preparation can be scaled up.1,20This approach comes in two varieties.

Hot HPH

To obtain drug dispersed lipid melt, the liquid and solid lipids are combined and heated above the melting temperature of the solid lipid before adding the medication. The aqueous phase is generated separately by adding sufficient surfactant to deionized water. This phase is heated to the same temperature as the lipid melt. To produce pre-emulsion, these two phases are mixed and exposed to high shear homogenization at elevated temperatures for a brief length of time. Immediately, the pre-emulsion is run through HPH at various pressures for 3-5 times. In general, the number of cycles is determined by the desired average droplet size of the nano-emulsion. The emulsion is then cooled to room temperature while stirring. The solidification of droplets occurs due to recrystallization of solid lipid.1,21

Cold HPH

In cold high-pressure homogenization, the lipids are first melted at 5-10 °C above their melting point before the medication is introduced to the lipid melt. The drug-lipid melt is then rapidly cooled with dry ice or liquid nitrogen before being pulverized to micron size. Following that, the solid lipid microparticles are mixed with the chilled surfactant solution and homogenized at or below room temperature. This approach is used for hydrophilic medicines and pharmaceuticals that degrade under heat pressure. However, this approach produces samples with larger particle sizes and a wider particle size distribution. The cold homogenization approach for encapsulating propranolol hydrochloride, a hydrophilic medication.14

2.Microemulsion

Melted lipids are mixed with a hydrophilic aqueous phase containing a surfactant and a co-surfactant to create an emulsion, which can be w/o or o/w depending on the quantities. The emulsion is then forcefully agitated to break down the particles to the micron size range. A transparent thermodynamically stable microemulsion is then generated and dispersed in a chilled hydrophilic phase to further reduce particle size and produce NLCs. This approach is straightforward, cost-effective, reproducible, suited for thermolabile pharmaceuticals, and does not require any specific equipment or energy to produce NLCs. However, the use of considerable amounts of surfactants is regarded the fundamental restriction of this approach.19

3.Solvent injection method

The solvent injection method is a simple, fast production approach that includes dissolving lipids in a water-miscible solvent and quickly injecting them into an aqueous solution containing surfactants using an injection needle.19,22This approach has the advantage of being simple to prepare while also avoiding excessive heat, shear stress, and complicated equipment. However, the primary drawbacks of this approach are the usage of organic solvents and the low particle concentration.19

4.Solvent diffusion method

The solvent diffusion method makes use of water-miscible organic solvents such as methanol, ethanol, and acetone. This approach involves adding the medication and lipids in a single or mixed organic phase. This is sonicated and kept at a high temperature to obtain a distinct lipid phase. The aqueous phase is created by adding a suitable stabilizer/surfactant and kept at the same temperature as the lipid phase. The organic-lipid phase is introduced to the aqueous phase while mechanically stirring at high temperature. To obtain NLCs, this dispersion is agitated at room temperature to cool and evaporate the organic solvent.1,23

5. Solvent emulsification evaporation method

To prepare lipid nanoparticles using the emulsification evaporation of the solvent method, the lipid mixture is first dissolved in a water-saturated organic solvent (the organic solvent used must be immiscible with water), and then the

active ingredient is added to this solution, allowing it to dissolve completely. The organic phase is then emulsified on an organic solvent-saturated aqueous solution of the stabilizing agent via mechanical stirring or ultrasonic. Finally, as the organic solvent evaporates, the nanoparticles precipitate in the aqueous phase [98]. This process is one of the most commonly utilized in the preparation of the SLN, along with the homogenization at high pressure.2

6.Phase inversion

This procedure involves heating and cooling the entire mixture of components three times. Following that, the heated mixture is shocked by dilution with cold water, and NLCs are generated via phase inversion.8

7.Doble Emulsion

This approach includes the created microemulsion to cold water (2-10°C) to accelerate consistently disseminated NLC particles.8

8.Sonication or ultra-sonication

This is a dispersion technique, similar to high shear homogenization. The procedure entails heating the lipid matrix (containing the medication) to 5-10°C above its melting point, then dispersing it in an aqueous phase containing surfactant at the same temperature while stirring at high speed to form an emulsion. This is then sonicated to minimize droplet size before gradually cooling to produce the nanoparticle dispersion. The utilization of extremely ordinary laboratory equipment is advantageous. However, obtaining lipid nanoparticles necessitates extended sonication durations, which increases the possibility of metal contamination from the probe. Furthermore, because the energy distribution in the sample is not uniform, the resultant particles are highly polydisperse.11

9.Membrane contactor technique

This approach was designed for large-scale synthesis of lipid nanoparticles. The melted lipid matrix containing the medication is pushed via a porous membrane (typically with a pore diameter of 0.05 μm) to the aqueous phase containing a surfactant, maintaining lipid melting temperature. When the lipid passes through the pores, it creates minute droplets that precipitate as lipid nanoparticles after the preparation cools to ambient temperature. The approach is scalable and easy, and the particle size can be adjusted by employing membranes with varying pore sizes.11

Characterization of NLC

1.Particle Size

PCS, also known as dynamic light scattering, is a fairly sensitive and precise technique. PCS can measure particle sizes under 3 μm, while bigger measurements require the LD technique. A combination of both is used to achieve more exact measurements. Practically, the instrument calculates average particle size (z-average) using the light scattering angle and intensity of scattered light. This measurement is based on the possibility of slightly irregular particle forms (a perfect sphere does not always exist). The average particle size determines whether the carrier may pass through biomembranes or not. Particles smaller than 400 μm are chosen for optimal penetration. Particle size is strongly influenced by the kind and concentration of surfactant(s). An increase in surfactant concentration induces a decrease in particle size. Particle size variations are also caused by differences in the quantity and percentage of various liquid and solid lipids.1

2.Polydispersity Index

Because colloidal particles are naturally polydisperse, the polydispersity index (PDI) must also be measured. PCS can also assess PDI. A PDI score between 0 and 0.5 is considered monodisperse and homogeneous, but a PDI value more than 0.5 indicates nonhomogeneity and polydispersity.10

3.Zeta potential

The zeta potential is a measure of a particle's potential difference that analyzes nanoparticle

aggregation. Ideal values for particle repellency are less than -30 mV and larger than +30 mV.14 It can be measured using photon correlation spectroscopy. Typically, lipid nanocarriers acquire a negative charge; however, when mucoadhesion or passage of complex barriers (BBB) is required, the carrier surface must be positively charged. Adsorption of surfactants and/or coating materials is also responsible for surface charge generation.1

4.Morphology

Transmission electron microscopy (TEM), scanning electron microscopy, and atomic force microscopy are common microscopic techniques used to determine the morphology of nanostructures. TEM is often used to investigate the morphology of NLCs. A small drop of the diluted NLCs suspension is dropped onto carbon-coated copper grids, stained (with uranyl acetate or phosphotungstic acid), and allowed to dry at room temperature before imaging. Several dark blotches emerged on the spherical shapes of the NLCs, which were attributed to liquid lipids adhering to the surfaces of the lipid nanoparticles.19,25

5.Entrapment efficiency

Entrapment efficiency assesses the carrier's ability to encapsulate the medication.14A specified amount of NLC dispersion is centrifuged, and the supernatant is analyzed for drug concentration in the dispersion media. Centrifugation will produce NLC sediment, while free dug will remain in the supernatant. The concentration of free drug is subtracted from the initial concentration of drug in dispersion to calculate the concentration of entrapped drug.1 Equation calculates entrapment efficiency by measuring the amount of drug in NLCs spectrophotometrically at the appropriate λmax after adding a sufficient volume of organic solvent (e.g., methanol) to break the NLCs and release the entrapped drug.19

$$\textbf{Entrapment efficiency (\%)} = \frac{\textbf{Amount of entrapped drug}}{\textbf{Total amount of initially added drug}} \times 100$$

6.Crystallanity and polymorphism

X-Ray Diffraction (XRD) and Differential Scanning Calorimetry (DSC) are useful methods for predicting drug/excipient crystallinity and potential polymorphic forms. The physical shape of the chemicals is significant for interpreting the formulation's stability and pharmacological action. The XRD pattern contains distinct peaks for each component. XRD patterns reveal the nature of the enclosed substance and the extent to which it is crystallized. The absence of a peak in DSC suggests a reduction in crystallinity of formulation components, which will be responsible for improved solubility.1

7. In-vitro release study

The analysis of drug compounds' in vitro release from NLCs is a valuable tool for predicting their performance in vivo. Dialysis is widely used to determine the cumulative amount of medication released from NLCs.15,26,27To dissolve drug-loaded NLCs, place them in a dialysis bag soaked in distilled water overnight, fasten it at both ends, immerse it in a dissolution medium, and shake it at 37°C. To maintain sink conditions, samples are withdrawn at regular intervals and replaced with an equal amount of new release medium. Drug concentrations can be measured spectrophotometrically at a certain λmax or using a validated high-performance liquid chromatography method using known concentration standards. Samples should be evaluated in triplicates, with the mean cumulative amount of drug release plotted against time. Importantly, free drug solution should be used as a control under identical experimental circumstances. The release data can then be examined to determine the kinetics of drug release from the NLC.19,28,29,30

8.Drug lipid interaction

Infrared Spectroscopy (FTIR) peaks reveal the wavenumbers at which specific functional groups in molecules transmit infrared radiation. The

transmission is measured between 4000 cm−1 and 400 cm−1. FTIR is commonly used to detect drug-excipient or lipid interactions. Interaction is demonstrated by changing or reducing the functional group peaks of the drug, as well as the appearance of previously unknown peaks in the physical combination. Peaks of lipid functional groups are typically detected in NLCs as the medication is embedded in the matrix.1

9.Stability study

Turbiscan® and LUMiSizer® are two new tools used to conduct expedited stability assessments on opaque mixtures. Turbiscan® technology employs gravity to accelerate particle separation. These technologies detect the transmission of near-infrared light through a sample. Sedimentation/creaming, defined as particle motion and aggregation, is identified by measuring the intensity of transmitted light in the form of an instability index (provided by software).1

10.Sutaible in vivo study

In vivo pharmacokinetic studies are conducted to evaluate the AUC, Cmax, and Tmax of drugs in order to determine their absorption, distribution, metabolism, and excretion (ADME) in formulations. In vivo pharmacodynamic investigations are conducted to determine the efficacy of drugs in diseased animal models. NLC drug formulations are examined, and their efficacy is compared to that of pure pharmaceuticals or conventional formulations of the same drugs.1

Application

1. Oral Delivery

Oral drug delivery systems account for the majority of the drug delivery market, but due to challenges such as low drug solubility, a narrow absorption window, rapid metabolism, high fluctuations in drug plasma levels, and variability due to food effects, oral drug delivery is constantly exploring newer options. These conditions may produce undesirable in vivo results, resulting in the failure of oral administration methods. Over the last few years, colloidal drug carriers such as micelles, liposomes, nanoemulsions, nanosuspensions, and polymeric nanoparticles have solved many of the issues mentioned above. However, these systems have various limitations, including limited physical stability, aggregation, drug leakage during storage, low yield, organic solvent residues in the final product, cytotoxicity, and so on. Many scientists were looking for lipid-based carrier systems that could improve the absorption of low water-soluble drugs such as ciclosporin and testosterone due to the absorption-promoting action of lipids in other routes of administration. There is a large body of in vivo research demonstrating an increase in absorption of weakly water soluble medications using lipids as a carrier, depending on the chemical composition of the lipid and the fineness of its dispersion in the gut.10

2. Nasal Delivery

Many scientists were looking for lipid-based carrier systems that could boost the absorption of low-water-soluble medicines like ciclosporin and testosterone since lipids promote absorption in other routes of administration. A substantial body of in vivo research has shown that employing lipids as a carrier increases the absorption of poorly water soluble drugs, depending on the chemical makeup of the lipid and the fineness of its dispersion in the gut.19

3. Topical Delivery

Some orally taken medicines are degraded due to stomach acid, hepatic first pass metabolism, and intestinal metabolism. These factors are responsible for medication loss and decreased bioavailability, resulting in repeated dosage form administration and the client experiencing a variety of side effects. Transdermal distribution of these medications is an alternate and appealing strategy, but it has certain drawbacks. The physicochemical features of the drug molecules influence transdermal delivery. In order to

permeate through subcutaneous tissue, the drug must have an appropriate partition coefficient, as well as a low molecular weight and melting point. Drug delivery by chemical mediators such as permeation enhancers and physical means such as iontophoresis and electroporation can have a deleterious impact on the integrity and function of skin tissue. Lipid nanocarriers have benefits over traditional transdermal medication delivery. Lipids are safe, biocompatible, non-irritating, and can be formulated in the nanosize range. The application of NLC formulation to the stratum corneum guarantees that the lipid structures of NLC are in intimate contact with the skin, resulting in excellent drug penetration. It also moisturizes the skin by creating an occlusive barrier that reduces transepithelial water loss. Some studies imply that negatively charged NLC aggregate at hair follicles and positively charged NLC interact electrostatically with the negative skin surface, both of which lead to medication penetration. Clobetasol propionate-loaded chitosan-coated NLC and terbinafine HCl-loaded NLC mixed into carbopol gel demonstrated greater drug penetration and cutaneous retention than commercial formulations.1

4. Ocular Delivery

Drug delivery through the eye is difficult due to the presence of different anatomical barriers such as layers of cornea, sclera, and retina, as well as lymphatic tear turnover, nasolacrimal drainage, and reflex blinking. NLCs' structure enhances corneal permeability and prolongs ocular residence duration, improving the bioavailability of integrated medicines and reducing systemic side effects. NLCs have been effectively employed for ocular administration of a variety of medicines, including ciprofloxacin, amphotericin B, and dasatinib.19Drugs often struggle to penetrate the ocular barrier and reach target tissues due to these factors. More effective topical formulations are needed to increase medication penetration and sustain therapeutic levels. To extend retention period, commonly used methods include increasing viscosity through the use of hydrogels or in situ gelling using Poloxamers. Increasing viscosity may lengthen retention duration, but it can also impede diffusion, resulting in a limited net benefit.10

5. Parenteral Delivery

Drugs are given into the lungs in appropriate formulations to treat local ailments or for systemic medication administration due to the increased surface area accessible for drug absorption. To achieve deep lung disposition in the alveolar area, systemic drug delivery via pulmonary route requires particles with a mean aerodynamic diameter of 1 to 3 μm. If local delivery is expected, particle characteristics must be tweaked or adjusted to ensure better medication disposal in the infected/targeted area.1,31 The potential of nanoparticle-based lipidic carriers, such as SLN and NLC, has thus been investigated in parenteral medication administration. The parenteral injection of SLN or NLC resulted in increased bioavailability, targeting, and cytotoxicity against multidrug resistant cancer cells.10

6. Drug delivery to brain

To prevent risks from infiltrating, the brain is heavily protected by a diffusion-restricting barrier known as the blood-brain barrier (BBB). The BBB can limit the passage of the majority of macromolecules (100%) and small molecules (98%). The protective roles of tight junctions and efflux transporters (most notably Pgps and MRPs) inhibit the chemicals' diffusion into the brain via paracellular and transcellular routes.8Brain targeting not only raises the drug's concentration in the cerebrospinal fluid, but it also minimizes the frequency of dose and associated side effects. The main advantages of this administration method are that it avoids first pass metabolism and has a faster onset of action than oral administration. Because of their quick uptake by the brain, bioacceptability,

and biodegradability, LNC (e.g., NLC) of this generation are regarded as one of the key drug delivery techniques that do not require any alteration to the drug molecules. Furthermore, their scalability and lack of burst impact make them more attractive carriers for drug delivery.17

7. Cosmetic

Recently, NLCs have been produced based on controlled nanostructuring of the particle matrix, which provides enormous advantages in terms of loading capacity and long-term stability. NLC dispersions can be delivered in several forms, including gel, cream, lotion, and ointment. The advantages of using NLCs in cosmetics are numerous, including increased skin bioavailability of active ingredients, film formation and controlled occlusion, UV protection, penetration enhancement and epidermal targeting, improved physical and chemical stability, and in vivo skin hydration17. Researchers created argan oil-based NLCs and put them into hydrogel for dermal treatment, resulting in increased skin hydration. Argan oil NLCs can be combined with other APIs to achieve synergistic effects in transdermal applications.1,32

8. Neutraceuticals

Nutraceuticals are bioactive chemicals that offer pharmaceutical or health advantages such as illness prevention and therapy. Carotenoids are one of the most important types of natural pigments due to their widespread distribution in plant tissues, structural variety, and multiple activities. Carotene-LNC with strong antioxidant and antibacterial activity was effectively synthesized using natural oils and a versatile high-shear homogenization process.17

9. Chemotherapy

Recent studies have demonstrated that NLCs not only improve the efficacy and stability of cytotoxic medicines, but also lessen their negative effects. Albumin-paclitaxel nanoparticles were approved in early 2005 as a chemotherapy for metastatic breast cancer; etoposide NLCs were discovered to be cytotoxic against human epithelial-like lung carcinoma cells; and topotecan NLCs were stabilized and released for the treatment of refractory ovarian and small-cell lung cancer. The advantages of putting anti-cancer medications into NLCs include high drug loading efficiency, a delayed release profile, enhanced chemical stability, and increased cytotoxicity. These NLCs kill a few of the issues related with SLN, such as medicate spillage amid capacity and decreased stacking capacity. They work by prolonging tumor cell exposure to anti-tumour drugs while also increasing permeability and retention, hence increasing the therapeutic effect.17

10. Food industry

The food and cosmetics business is currently replacing various synthetic excipients with natural ones. Menthol, an antimicrobial drug with low stability and insolubility, was synthesized as NLC and demonstrated increased antibacterial effectiveness against gram-positive bacteria.1,33 Because of their excellent stability and large loading capacity, NLCs are widely used in the pharmaceutical industry. It was rarely reported that NLC was used as a nutritional supplement carrier in the food industry for capsule and beverage formulations. However, because to issues with raw material supply, availability, and environmental constraints, the food industry continues to face significant risks in investing in this field. Coenzyme Q10-loaded NLCs for food applications were created to improve their physicochemical stability and bioavailability.17

CONCLUSION

Lipid nanoparticles such as NLC and so on were always potential carrier systems with strong therapeutic applications. The purpose of this work was to highlight the role that NLCs play as a novel drug delivery system for different drug categories. Consequently, they can be used for treatment and

control of various conditions in different applications. They reduced particle degradation and extended GIT residence times after oral administration. For cutaneous applications, NLCs provide a convenient carrier for dermal and transdermal drug delivery as they can hydrate skin and mix with skin lipid eventually. As the new generation, the smart NLC offers far more flexibility in drug loading, release modulation and improved performance in producing final dosage forms such as creams. Permeation via the gastrointestinal tract and BBB could be a trend of the future.

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