# Nanostructured Lipid Carriers in Drug Delivery: A Review

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**Abstracts:** Over the past 20 years, lipid-based colloidal systems have gained attention as a means of delivering medications that are not readily soluble in water. The research that has been done has centred on creating various formulations with a broad range of active molecules and excipients. On the particle structure of these colloidal systems, there is disagreement, though. This is partially because there haven't been many studies focused on understanding the drug's preferred location within the particle as well as the arrangement of lipids and stabilising agents during particle formation. This review presents the most widely used materials and preparation techniques for obtaining lipid particles as a contribution in this regard. Additionally, scientometrics tools are used in the synthesis and analysis of the particle characteristics, such as shape, size and distribution, zeta potential, drug loading capacity, and drug entrapment efficiency. A simulation of particle framework based on the creation of the various polymorphic forms of the solid lipid due to the initial ingredients and processing circumstances is proposed in along with the existing evidence. In general, the significance of gaining a thorough understanding of the lipid nanoparticles' structure is emphasised, as this is helpful for the logical design of these nanocarriers.

**Keywords:** Colloidal Systems, Active Molecules, Solid Lipid, Zeta Potential, Lipid Nanoparticles, Nanocarriers

## 1. INTRODUCTION

Drug therapy has a potential platform in nanoparticulate systems that can overcome its limitations and perform better. Lipid nanoparticles are one of the many nano systems under investigation that show the most promise for drug delivery. In order to avoid using organic solvents in the process of preparing polymeric nanoparticles, Müller and Gasco initially developed and recommended solid lipid nanoparticles (SLN) in the 1990s.(1) Many of these nanostructures have also been employed as diagnostic instruments, including inorganic nanoparticles and various polymeric/lipid nanoparticles. The synthesis of "theragnostic" nanoparticles was made possible by the combination of therapy and diagnosis; sadly, the majority of these devices only employ synthetic polymers and do not utilise lipid-based nanostructures, such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs).(2) According to Chinese Pharmacopoeia, Pueraria radix (also known as Gegen) is a major active ingredient in traditional Chinese medicine. It is derived from dried roots of Pueraria lobata (Willd.) Ohwi. In China, patients with cardiocerebrovascular diseases are frequently prescribed pue. It has been reported that pue demonstrates promising pharmacological activities, such as effects on arteriosclerosis, diabetes mellitus, cerebral ischemia, myocardial infarction, and hypertension. Significant attention has been paid to its anti-cancer activities in recent decades.(3) In fact, a significant issue that must be addressed in order to provide effective treatment is the inadequate bioavailability of many medications and functional foods. Thus, the need to create a drug delivery system that eliminates these problems exists. These days, a number of nanocarriers have been progressively investigated to improve drug release characteristics and therapeutic efficacy while addressing problems such as inadequate solubility and inadequate bioavailability.(4) Because cardiovascular drugs can be used to treat a variety of clinical conditions, including heart failure, hypertension, hypovolemic shock, and oedema, they are frequently used in hospital pharmacies for galenic paediatric preparations. Diuretic medications, like hydrochlorothiazide (HCT), are among them and are frequently used to treat hypertension. HCT is classified as a BCS class IV medication due to its inadequate solubility and permeability, which also causes issues with its poor and inconsistent bioavailability. Furthermore, reports of HCT stability issues in aqueous solutions have been made.(5)

## TYPES OF LIPID CARRIERS

Lipid-based carriers can be classified into a number of groups based on their physicochemical characteristics and the manufacturing process. Among the primary lipid-based carriers are:

1) Niosomes, which are cholesterol and non-ionic surfactants arranged in a lamellar self-assembled structure. 2) Transferosomes: these are lipid bilayers made by a lipid matrix stabilised by a range of surfactants. They resemble

both liposomes and niosome. 3) liposomes in which are sphere-shaped vesicles made of phospholipid lipid bilayers 4) solid lipid nanoparticles, which have a solid lipid core that is both body temperature and room temperature. 5) The nanostructured lipid carriers, which are made up of a liquid lipid phase within a solid lipid phase at their core.(2)

**TYPES OF NANO-STRUCTURED LIPID CARRIER**

Based on the lipid mixture's composition and its manufacturing technique, three distinct types of NLCs can be identified based on the lipidic framework of the prepared NLCs -:

1. Imperfect Type NLC

Imperfect NLCs are made by combining lipids with different structural properties, like glycerides and fatty acids, which leads to crystal order imperfections.(6)

2. Amorphous Type NLC

Another name for this type is structureless type. When liquid lipids are combined with solid lipids that retain their α polymorph after its solidification and storage, an amorphous core is typically formed. Compared to type I NLCs, this is better because the drug stays embedded in the amorphous matrix and there is no crystallisation. Solid lipids with the β polymorph form a matrix with a crystalline structure.(7)

3. Multiple Type NLC

In this kind, the medication is highly dissolved in a number of nanosized liquid oils that are part of the solid lipid matrix. Consequently, there is an increase in drug encapsulation. Additionally, because the solid lipid matrix surrounds the tiny oil droplets, the drug is released with controlled release behaviour and drug leakage is less noticeable (stability factor).(1)

**ADVANTAGES**

1. The stratum corneum is kept in close contact by the small dimensions of the lipid particles, which improves drug penetration into the skin or mucosa.(8)
2. Boost the benefit-to-risk ratio.(8)
3. Enhanced skin hydration and suppleness.(8)
4. Because of their lipid-based solid matrices that which are also widely acknowledged as safe or to have a regulatory-accepted status, these carriers are very effective systems.(8)
5. High loading capacity and encapsulation efficiency.(2)
6. Sensitive to biological (enzymes, pH, ROS) and/or physical stimuli (electric current, light, magnetic fields, ultrasounds).(2)
7. Manageable dimensions and form.(2)

**DISADVANTAGES**

1. Restricted drug loading capacity because of the solid lipid's crystalline structure.(9)
2. Modifications to the drug release profile.(9)
3. Particle expansion.(9)
4. Innately harmful.(2)
5. Low hydrophilic therapeutics encapsulation efficiency.(2)

6. Certain polymers, like PLGA, have low solubility in water and when they break down, produce acidic byproducts.(2)

7. Challenges in increasing in size.(2)

**MATERIALS AND METHODS-:**

**1. COMPONENTS OF NLC'S**

Lipid (s), both liquid and solid, surfactant(s), organic solvents, and additional agents like surface modifiers and counter-ions make up NLCs in general.(10)

1. Solid Lipids

Solid lipids serve to be matrix-forming lipids and make up the solid lipid essential of NLCs. Various solid lipids utilised in the NLC formulations, together with information on their melting points and compositions.13 Kerry Specialty Fats Co. Ltd. produced a variety of food-grade commercial goods, including fully modified sunflower oil (HSF or sunflower oil), fully modified rapeseed oil (HRO or rapeseed oil), and a combination of palm oil and palm stearin (PO + ST or palm mixture).(11)

2. Liquid Lipids

The lipophilic additives used for integrating the solid lipid vital and lessen its ability to crystallise are called liquid lipids, or oils.(6)

3. Emulsifying agents - Surfactants

The substances that are retained at connections and lower the interfacial tension are known as surfactants. Small quantities of a surfactant increase stability by lowering the rates of surfactants, also known as surface-active agents. Surfactants adsorb onto a system or interface's surface at low concentrations. Surfactants reduce the tension or surface or interfacial pressure between the two phases as well as their outermost or interfacial free energy.(12)

4. Other Ingredients

One possible solution to the problem of encasing water-soluble drug molecules in nanostructure carriers is to use ionic polymers and organic salts as counter-ions. Another class of excipients used in NLC formulations is surface-modifiers, which reduce the excipients' phagocytes uptake by the macrophages in the reticuloendothelial system (RES).(10)

**2. METHOD OF PREPARATIONS OF NLC'S**

1. HPH Technique

Due to its ease of scale-up, lack of chemicals, and shorter manufacturing period when compared to other approaches, the HPH methodology is still among the most popular ones. There are two types of HPH protocols: Hot HPH and Cold HPH.

Melting solid lipids first, then combining them into liquid lipids and medications, is the hot HPH technique. After combining this dispersion with a hot surfactant fluid in water, a pre-emulsion is created. This homogenization process can be repeated up to three times at 500 bar and a high temperature, producing the final product that is wanted: SLNs/NLCs. High temperatures typically lower PS by lowering lipid viscosity, but they also raise the risk of substance or carrier mechanism degradation.(6)

The solid lipid is crushed into lipid microparticles using the cold homogenization technique, which involves cooling the lipid melt. To create a pre-suspension, the microparticles are scattered in a cold emulsifying solution. The suspension is then homogenised at room temperature or lower. The microparticles can break straight through to NLCs due to the high enough cavitation force. By preventing the lipids from melting, this procedure can reduce the

amount of hydrophilic medication lost to the aqueous phase. It should be noted, though, that in the absence of hot treatment, the particle size might not reach the nanosized range.(13)

2. Microemulsion

By combining melted lipids with a hydrophilic liquid phase that contains a co-surfactant and a surfactant, this method creates an emulsion that can be either w/o or o/w depending on the ratios utilised. To break the fragments down to the microns size range, the emulsion is then thoroughly mixed. Next, a clear, thermodynamically resistant microemulsion is created, and to further reduce particle size and produce NLCs, it is further scattered in a cooled hydrophilic phase. The synthesis of NLCs using this method is easy, affordable, repeatable, appropriate for drugs that are thermolabile, and requires no additional energy or special equipment. However, the primary drawback of this method is thought to be the substantial surfactant incorporation.(14)

3. Solvent Emulsification-Diffusion Technique

This method can be used in both the aqueous and oily phases, provided that the solvent used is at least somewhat miscible with water. In the beginning, the solvent and water are mutually soaked to maintain the two liquids' initial thermodynamic equilibrium. Saturation is carried out at identical temperature as heating in order to solubilize the lipid. Next, the drug and lipid were dissolved in a solvent that was saturated with water, and a mechanical stirrer was used to agitate the organic phase. Water is introduced into the system in an average ratio of 1:5 to 1:10 after the o/w emulsion has been formulated. This allows the diffusion of solvent into the steady state, which causes the lipids in the nanoparticles to agglomerate. Although this diffusion step is carried out at room temperature, both phases must be kept at the same high temperature.(8)

4. Multiple Emulsion Technique

Based on a w/o/w double emulsion, this is a modified solvent emulsification-evaporation method. The medication is emulsified inside the molten lipid after being dispersed in an aqueous solution. This primary emulsion is stabilised by the stabilising agents.
By using the double emulsion method, the need to melt the lipid in order to create peptide-loaded lipid nanoparticles is avoided. Therefore, by altering the surface of the nanoparticles, lipid-PEG derivatives may be used to stabilise them.(15)

5. Phase Inversion Temperature (PIT) Method

It has been possible to create SLNs, NLCs, and nanoemulsions using the PIT method. The method relies on the inversions of w/o to o/w formulations and vice versa caused by temperature.Non-ionized polyoxyethylated surfactants with dependent on temperature properties are needed for this method. These surfactants have a high hydrophilic-lipophilic balance (HLB) value at low temperatures due to the high hydration of their hydrophilic groups. The ethoxy group dehydrates at higher temperatures, increasing the lipophilicity of the surfactants and lowering their HLB values. The temperature that determines the surfactants' affinities for the lipid and aqueous phases are equal is known as PIT. The surfactants prefer the formation of w/o emulsions at temperatures >PIT, but they also form o/w emulsions at temperatures < PIT. Oil, water, and a surfactant are initially elevated at a temperature > PIT while stirring to form w/o emulsions before being used to make SLNs and NLCs. They are then rapidly cooled while being stirred continuously, which encourages the decomposition of w/o micro-emulsion and causes o/w nanoemulsions to form. Low temperature precipitation of lipids results in the formation of SLNs and NLCs. Metronidazole-loaded NLCs were created using this technique using monostearin and Capmul a MCM (glyceryl monocaprylate).
NLCs had an EE of about 40% and a PS of less than 300 nm. Carbopol 974 P-containing NLCs gel improved the drug's antibacterial activity, skin retention, and sustained release. This approach has been reported to produce SLNs and NLCs with small PSs, reduce size distributions, and excellent stabilities. For instance, NLCs containing tocopherol and beta-carotene possess a PS of 35 nm. This process doesn't need organic solvents and only needs a small amount of energy. Nevertheless, it results in low nanoemulsion stability and occasionally calls for multiple temperature cycles (three cycles, for example, between 60 and 90 C).(16)

## CHARACTERIZATION OF NLC'S

1. Particle Size

Using a Malvern Zetasizer (ZS90, Malvern Instruments, UK), dynamic light scattering (DLS), also referred to as photon correlation spectroscopy (PCS), was used to analyse the nanoparticle size and the polydispersity index (PDI). Before the measurements, ultrapure water was used to dilute each sample 200 times, resulting in a weak opalescence. The average of three measurements made at 25°C with a scattering angle of 90° was used to determine the mean particle size (z-ave) and PDI values of the studied samples. Using a Malvern Mastersizer (MS2000, Malvern Instruments, UK) with a measuring range of up to 2000 m, static light scattering (SLS), also known as laser diffractometry (LD), was used as an additional characterization method to identify possible larger particles and oil droplets. The real refractive index (1.456) and imaginary refractive index (0.01) were the optical parameters used in the analysis of the LD data using the Mie theory. The obtained LD data were assessed using the volume distribution and the diameter values of D10, D50 and D90. The diameter values show what proportion of particles have a diameter that is the same as or less than the specified size.(17)

2. Zeta Potential

Zeta potential, also known as the shear plane or slipping potential, is the electrical potential of an element that is not on its surface but rather far from it in a disperse layer. This movement of particles in the fluid is related to ZP. It's closely associated with the stability of the suspension and the shape of the particle surface. In contrast to the size of the particle or molecular weights, ZP depends not only on the particles themselves but also on the conditions surrounding them, including pH, ionic strength, and the kinds of ions that are present. ZP provides valuable insights into the agglomeration tendency and long-term stability of nanoparticles. ZP of ±60mV generally denotes exceptional stability. Nonetheless, in cases where stability is the outcome of both steric and electrostatic stabilisation, a minimum ZP of ±20mV is preferred, and a minimum of ±30mV is required for adequate stability of electrostatically stabilised nanodispersion. Particle repulsion will reduce the tendency for aggregation when there is a high positive or negative potential on every particle. Based on the electrophoretic/electroacoustic mobility principle, ZP is readily measured with analytical tools. To measure particle charge and particle size with the same instrument in commercial instruments, a ZP unit is incorporated with a DLS instrument.(18)

3. TEM Analysis

A transmission electron microscopy (TEM, HITACHI H-7650, Japan) was used to analyse the physical characteristics of drug-loaded lipid nanoparticles. Samples were made by covering a 200-mesh copper grid with a carbon coating, adding a drop of the drug-loaded lipid nanoparticle diluent solution, and then negative staining the grid with 0.2% w/v sodium phosphotungstate solution.(19)

4. Entrapment Efficiency

The effectiveness of the carrier in encasing the medication is measured by entrapment efficiency. It is computed by taking the total quantity of drug added throughout formulation (WI) and dividing it by the proportion of drug integrated into the carrier (WT). The following is the formula used to calculate entrapment efficiency (EE):

$$EE = (WT/WI) \times 100\%$$

Generally speaking, the solubility of the drug in a solid or liquid lipid determines how much of it is added. However, physical stressors such as homogenization and ultrasonication, as well as the presence of organic solvents, can influence entrapment during the formulation process. This section will address parameters that have a significant impact on entrapment efficiency, including drug concentration, surfactant concentration, and different kinds of lipids and surfactants.(20)

5. Corneal penetration study

Using a perfusion apparatus, the penetration-enhancing effect of COS-coated NLCs was evaluated on isolated rabbit corneal tissue (available areas 0.70cm2). Male, 2.5–3.0 kg albino rabbits from New Zealand were utilised. Resuming, the epithelial (donor) and endothelial (receptor) sides of the cornea were treated with 1 mL of sample and 7.8 mL of glutathione is bicarbonate Ringer (GBR) buffer, respectively. The apparatus was kept at 35°C.A 1.0 mL sample was taken out of the receiving compartment at 40-min intervals, and it was quickly replaced with an equivalent volume of heated GBR buffer. Every experiment was run in triplicate for four hours. Using glycerol, the osmolality of each perfusion solution was brought down to 292–298 mOsm/kg. This was determined by measuring the freeze-256 drying point using a Fiske osmometer.(21)

6. DSC (Differential Scanning Calorimetry) Analysis

The dispersions were left in tiny Petri dishes with hoover overnight to dry the lipid nanoparticles. Utilising a DSCQ200 V24.8 Design120 (United States, TA), the thermograms were captured. Standard aluminium pans were hermetically sealed with about 5 mg of samples. As a guide, a vacant sealed pan was employed. Every sample was heated at a rate of 10°C per minute, within a range of 15 to 100°C. An atmosphere of inert gas was created using a nitrogen purge at an intensity of 20 mL/min.(22)

7. XRD (X-ray Diffraction)

Wide angle X-ray emission was used for the analysis using XRD (Bruker D8 Advance, Bruker, Germany), with a scan rate of 2 ◦/min and an interval of 2θ = 3.00–40.00◦. A 2.2 kW Cu anode (40 kV, 40 mA, Cu-K radiation, λ = 0.15406 nm) served as the X-ray origin.
The NLC specimens were lyophilized in order to remove any water before evaluation. Analysis of the bulk lipid was conducted without any prior therapy.(11)

8. Crystallinity and Lipid Modification

Since these characteristics have a strong correlation with drug integration and release profiles, crystallinity and lipid alteration are also essential for the characterization of SLBNs. The following is the order in which drug encapsulation efficiencies decline, lipid packing density and thermodynamic stability rise: supercooled melt with a modification of α, β andβ’. However, emulsifiers and small particle sizes may cause lipid modification and crystallization to be delayed.(23)

9. Statistical Analysis

The information is presented as means ± a standard deviation derived from multiple independent experiments. Student's T-test was used for statistical analysis, and an outcome of $P < 0.05$ was regarded as statistically significant.(24)

10. Drug Release

In order to investigate the transfer of a fluorescent marker from nanoparticles to liposomes using an abridged lipid bilayer model, three distinct experimental procedures were carried out to release RhB in vitro. The first step involved adding nanoparticles, which were packaged in a dialysis sack (MWCO: 12,000), to 10 millilitres of heated PBS. Secondly, positioned as an indirect interaction with liposomes in the liposomal dispersion. Finally, using a direct contact method, nanoparticles and liposomes were sealed in a dialysis sack (MWCO: 12,000) and then added to 10 millilitres of heated PBS. After that, each sample vial was shaken at 34°C in a thermostat shaker and the samples were taken at the appropriate intervals. The fluorescence of RhB was measured using a fluorometer (Spectramax, Molecular Devices) with λex = 530 nm and λem = 590 nm to determine the release quantity. The intensity of the fluorescence was compared to a standard curve of fluorescence intensity as a function of RhB concentration in order to quantify the RhB in solution. Every measurement was made three times over.
The percentage of RhB that was transferred into liposomes in this study was determined as follows, respectively: $Q_{lip\text{-}direct}$, which was direct contact with liposomes; $Q_{lip\text{-}indirect}$, which was indirect contact with liposomes.

$$Q_{lip\text{-}direct}\% = (C_{PBS} - C_{direct})\ V / W \times 100$$

$$Q_{lip\text{-}indirect}\% = (C_{indirect} - C_{PBS})\ V / W \times 100$$

where W is the mass of RhB in NLC for the release test (μg); V is the overall volume of the testing quantity (mL); $C_{PBS}$ is the mean concentration of RhB in PBS (g/mL); $C_{direct}$ is the amount of RhB in PBS that NLC contacts with liposomes directly (μg/mL); and $C_{indirect}$ is the amount of RhB in PBS that NLC contacts with liposomes indirectly (μg/mL).(25)

## THERAPEUTIC APPLICATIONS OF NLC’S

Many NLC formulations are now available for use in medicine and cosmetics, most likely as a result of their well-established biocompatibility owing to the use of lipids. The process of creating and characterising NLCs that investigate potential therapies for diverse illnesses and ailments is continuous. Teixeira et al. provided an overview

of the therapeutic uses of nanoparticles of lipids in the management of different illnesses. According to the paper's summary, lipid nanoparticles can be used to incorporate medications.(26)

## LINKS TO GREEN AND SUSTAINABLE CHEMISTRY

These days, poorly water-soluble compounds present difficulties for formulation, as well as for pharmacological, toxicological, and pharmacokinetic research in biological settings and during the drug development phase. Furthermore, it bears primary responsibility for toxicity issues related to drug design, development, and optimisation as well as the drug's biological fate within the body. However, all of these issues can be resolved by preparing them as lipid nanoparticles, which not only makes it easier to absorb into the bloodstream via the intestinal lymphatic route and prevents the first-pass effect but also makes it easier to achieve the benefits associated with green chemistry that are listed below.

- The excipients used in these lipid nanoparticles are made of physiological or physiologically associated lipids, as opposed to synthetic or semisynthetic excipients used in the formulation of pharmaceutical formulations. Therefore, the body has pathways for absorption, metabolism, and transportation, all of which may have a significant impact on the biodestination of lipidic carriers.

- Moreover, the lipid, surfactant, and cosolvent excipients that of lipid nanoparticles play significant roles in the body's physiology, including energy storage (lipids), biomembrane function (phospholipids), and metabolism (bile acids). For these reasons, they are generally regarded as safe and fall into the FDA-approved, widely accepted safe category.

- Furthermore, lipid nanoparticles are far simpler to make than biopolymeric nanoparticles from a formulation standpoint. Also, it has a lot of benefits, including-:

  - No special solvent needed.

  - Good manufacturing scalability (sustainability).

  - Prevention of chemical solvents in the manufacturing process.

  - Standard emulsion production techniques are appropriate. Easily expandable and sterilisable.

  - Suitable for industrial use.

- Furthermore, lipid nanoparticles can enhance the bioavailability of APIs, or active pharmaceutical ingredients, by combining the qualities of lipid carriers and nanosized particles.(27)

## FOOD APPLICATIONS OF NLCS

Not only are NLCs a useful delivery system in the food industry, but they are also used in the beauty and medicinal products sectors. Consumers are becoming more wary of the connection between their eating habits and overall health these days. Foods that offer additional health benefits beyond their basic nutritional value are referred to as functional foods. Conversely, reducing the amount of fatty foods in a consumer's diet may result in a deficiency of nutrients that are fat-soluble like vitamins, carotenoids, vital fatty acids, antioxidants, some flavonoids, or as well as nutraceuticals. Foods must therefore be fortified with these health-promoting substances. However, bioactive compounds have certain drawbacks, such as their low absorption by cells in the gut because of their lipophilic nature, their poor stability during processing and storage, and being susceptible to degradation by external factors like pH, light, oxygen, and so forth. Therefore, bioactives may be protected from unwanted factors and their bioavailability, penetration, absorption, and release may be optimised by using nanodelivery systems like NLCs. Being a liposoluble vitamin that is necessary, vitamin D3 is oxidation-prone and can't be strengthened in goods with an aqueous base. Encapsulation can increase their dispersibility in aqueous media for these reasons. As dietary supplement substances, carotenoids are unstable chemically, poorly soluble in water, and easily oxidised. Carotenoids must therefore be included in an appropriate nanodelivery system. The oxidative deterioration of omega-3 fatty acids can cause an unwanted odour in foods that have been fortified. It has been demonstrated that encasing omega-3 fatty acids can shield them from oxidative deterioration and, as a result, cover up their unpleasant smells. Valuable plant sterols known as phytosterols have a very high melting point, are unable to dissolve in water, and are easily oxidised. These properties can be avoided by employing encapsulation

techniques. A sizable class of naturally occurring polyphenols known as flavonoids are poorly bioavailable and taste bad. These factors make incorporation in an appropriate nano delivery system potentially beneficial. Numerous studies on the encapsulation of vital nutrients within NLCs have been conducted up to this point.(28)

## ROUTE OF ADMINISTRATION OF NLC'S

Numerous articles that discuss the different delivery methods—topical, parenteral, nasal, oral, and brain—that are currently used to produce lipid nanoparticles.

1. Topical Drug Delivery

It is better to apply topical treatments for skin conditions. Topical administration decreased systemic side effects when compared with alternative administration routes like oral and parenteral. Furthermore, it keeps the drug's concentration at the point where it acts for extended periods of time and avoids the first pass metabolism. The stratum corneum, which functions as an obstacle for both toxic and therapeutic molecules, is the reason for the low drug uptake in this delivery system. Lipid nanoparticles have drawn interest lately as novel colloidal agents for topical administration. NLCs offer a number of benefits and special qualities, including reduced skin irritation, improved permeability into the skin, protection of the active ingredient, and controlled release.(15)

2. Brain Drug Delivery

One of the major problems caused by the BBB is the delivery of drugs to the brain. Because nanoparticles can subsequently cross the reticuloendothelial system (RES), they are suitable as candidates for brain drug delivery agents. Two major obstacles to brain drug delivery are insufficient drug penetration through the blood-brain barrier and drug transporters' efflux via the cerebral cortex into the bloodstream. SLNs and NLCs have been used as colloidal systems for drug delivery to allay these worries. Novel levofloxacin/doxycycline (LEVO/DOX)-loaded solid-liquid nanoparticles (SLNs) were created using an emulsification technique that involved high-speed homogenization and ultrasonication. Comparing the brain maximal amount and the AUC0–360min of the optimised SLN-HPMC gel to the inhalation LEVO/DOX free solution, the pharmacokinetic study's results in plasma and the brain revealed a significant increase.(29)

3. Parentral Drug Delivery

Parenteral drug delivery can be made better with the help of nanomedicine and nanotechnology. The benefits and drawbacks of lipid nanoparticles as parenteral drug delivery systems are enumerated. For this purpose, the main benefits of lipid nanoparticles are their easy scalability up production, their biocompatible and biodegradable composition, their controlled and altered drug release structure, their ability to prevent drug breakdown, and their ability to maintain steady drug blood levels. Lipid nanoparticles that are loaded with drugs can be injected intravenously, subcutaneously, intramuscularly, or straight into the intended organs. Lipid nanoparticles can release drugs either by diffusion or erosion, which may allow for a prolonged release of the drug. Recent studies have validated the ability of nanoparticles of lipids to incorporate proteins and peptides. Because of their restricted ability to load drugs, SLNs are not a good carrier in this situation; however, NLCs are a suitable substitute. This technique protects proteins and peptides from adverse environmental conditions.(30)

4. Nasal Drug Delivery

An intriguing method of drug delivery that improves drug permeation, boosts efficacy, and permits brain targeting is through the intranasal delivery of medications loaded into NLCs. A variety of medications, including ketoconazole, temazepam, and ondansetron hydrochloride, have been effectively delivered using NLCs. It's interesting to note that drug-loaded NLCs can improve nasal retention and make drug transportation across the barrier easier when added to in situ gels.(14)

## CONCLUSION

Two research groups simultaneously developed and filed patent applications for nanoparticles of lipids (SLN) with solid particles matrix in 1991. The scientific community cast its votes with their hands and brains, not with its feet: a large number of research groups from around the world began experimenting with this system after determining that it held great promise for controlled drug delivery via oral, dermal, full name (i.v.), and parenteral routes in general. The published articles provide clear documentation of the number of investigation groups. When

one searches for "solid lipid nanoparticles" on Google, 1.49 million results come up (May 13, 2013). There are 4.32 million results for "polymeric nanoparticles," but pharmaceutical nanoparticles made from polymers are 40 years old, having been developed by P.P. Speiser in 1973, while the lipid nanoparticle system is only 21 years old. The nanoparticles of lipids in the kind of NLC have made their way into the cosmetics industry, much like liposomes. Assuming accuracy - the first year of SLN filings for patents, it took them less than 15 years, faster than liposomes, to reach the global cosmetic market. Large-scale industrial production is validated, and the product's make-ability is demonstrated. In light of this, lipid nanoparticles (SLN, NLC) ought to have a good chance of entering the pharmaceutical industry and enhancing oral and/or dermal delivery, hopefully within the next ten years.

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