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NANO STRUCTURED LIPID CARRIER SYSTEM- A NOVEL TARGETING CARRIER

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Keywords:

Nano-structured lipid carrier (NLCs), Solid-lipids, Liquid-lipids, High-pressure homogenization, Zeta-potential

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ABSTRACT: Oral administration of drugs is considered a convenient route; however, various drugs that are insoluble in water or cannot permeate across gastrointestinal tract membrane cannot be delivered by this route. To enhance the permeability through the physiological barriers, lipophilic drugs are introduced but, lipophilic drugs have low oral bioavailability. To enhance the bioavailability, a third-generation lipid matrix was introduced as nanostructured lipid carriers (NLCs), which are a mixture of solid lipids mixed with some incompatible liquid-lipids. NLCs have been reported to be an alternative system to emulsions, liposomes, microparticles, solid-lipid nanoparticles (SLNs). This article mainly focuses on the types and methods of preparation, advantages, the applicability of NLCs in the present and in the near future.

INTRODUCTION: Over the last 20 years, nanotechnology has practically made its influence in all technical fields, including pharmaceutics [1] [. Industry estimates suggest that approximately 40% of lipophilic drug candidates fail due to solubility and formulation stability issues, which have been solved by various novel and advanced lipophilic drug delivery technologies [2]. The most common problem is low solubility which leads to low bioavailability. For bioavailability enhancement, the researchers have attempted various approaches to overcome the challenges associated with oral delivery [3]. In order to overcome this problem, a lipid-based nanoparticle drug carrier was developed.

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Nano-structured lipid carriers (NLCs) were developed in 1999. Nanostructures are particles that range from 10 to 1000 nm, by which the drug molecules are absorbed or attached, which are dissolved, entrapped [4].

NLCs have efficient properties. NLCs are the second generation of lipid nanocarriers and are made up of a matrix that contains solid-lipid and liquid-lipid [5]. To overcome the disadvantages of SLN, NLCs have been developed in 2000 by Muller and developed nano repair Q10 cream [6].

1.1. Types of NLCs: NLC is a mixture of solid lipids mixed with some incompatible liquid lipids. It remains solid at room temperature. It has various advantages like the controlled release of drug from the carrier, biocompatible lipids, feasible to produce on a large scale using the existing machinery, avoids the first-pass metabolism, and protects the drug from biochemical degradation. In NLC, lipids can be used in the higher ratio (up to 95%).

NLCs are classified into Three Types:

1.1.1. The Imperfect Type: The imperfections are formed by blending solid and liquid lipids chemically, thereby increase drug loading. Liquid phase lipid (oil) is present in the minute amounts in the imperfect type of NLC. During the crystallization process of production, there will be expulsion of drugs in the imperfect NLC **Fig. 1** [7-10].

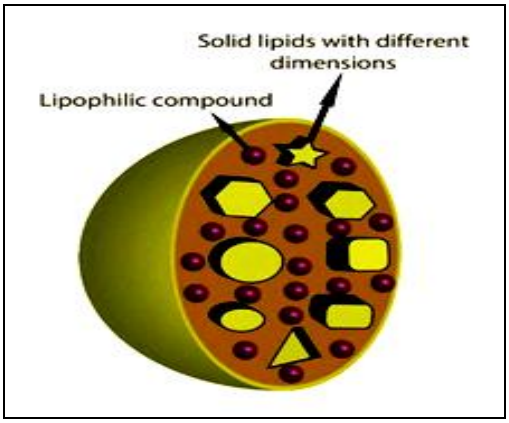

FIG. 1: IMPERFECT TYPE

1.1.2. The Amorphous Type: NLCs are obtained by blending special types of solid and liquid lipids in a controlled manner (*e.g.*, isopropyl myristate). This type of NLC forms solid lipid that lacks any crystalline structure **Fig. 2** [11-14].

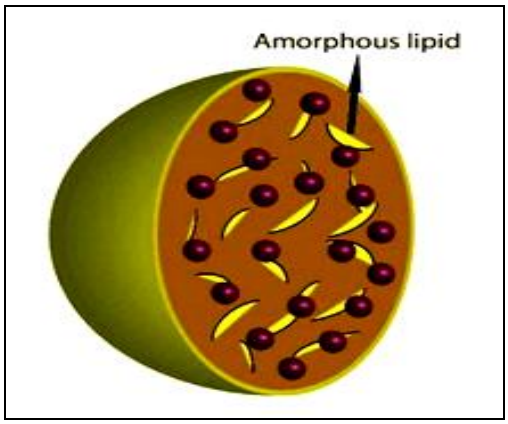

FIG. 2: AMORPHOUS TYPE

1.1.3. The Multiple Type: This contains solid lipid encapsulates oil nano compartments. In the oil compartments, the drug is loaded. Liqid-lipid precipitation method was used for the preparation.

In the lipid matrix, a high concentration of liquid lipids is mixed, and the drug expulsion can be avoided by the multiple types of NLC. Oil reaches its solubility limit and precipitates into nano compartments during the cooling effect **Fig. 3** [15-16].

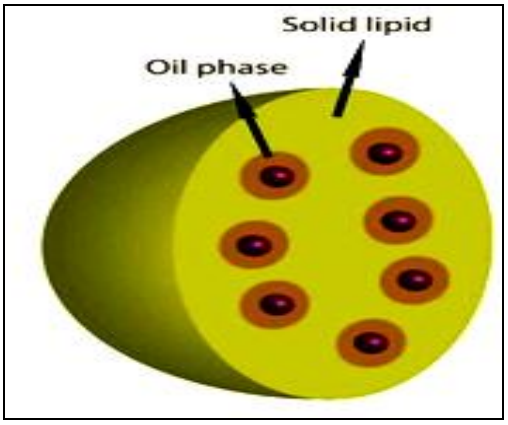

FIG. 3: MULTIPLE TYPE

Advantages of NLCs: [17]

• Better physical stability

• Increased dispersibility in an aqueous medium

• Ease of preparation and scale-up

• High entrapment of lipophilic drugs and hydrophilic drugs

• Extended release of the drug

• Controlled particle size

• Improve benefit/risk ratio

• Small size of the lipid particles ensures close contact to the stratum corneum, thus enhancing drug penetration into the mucosa or skin

• Increased skin hydration and elasticity

• These carriers are highly efficient systems due to their solid lipid matrices, which are also generally recognized as safe or have a regulatory accepted.

1.2. Limitations with Lipid Nanoparticles:

• Despite the great potential of NLCs in targeted delivery, they face certain limitations like:

• Cytotoxic effects related to the nature of matrix and concentration

• Irritative and sensitizing action of some surfactants

• Application and efficiency in case of protein and peptide exploited

• Lack of sufficient preclinical and clinical studies with these nanoparticles in case of bone repair.

1.4. Excipients used in NLCs: In the preparation of NLCs various components are used as follows:

1.4.1. Lipids: The inner cores consist of both solid and liquid lipids. Glyceryl behenate, glyceryl palmitostearate, fatty acids, triglycerides, steroids, and waxes were the solid lipids frequently used for NLCs. At room temperature, these lipids are in the solid-state. The lipids melt at high temperatures. Digestible oils from natural sources were used in NLC. Liquid lipids consist of Miglyol 812, which is a medium-chain triglyceride (MCT) that has similar structures to Compritol® used as a constituent. 2-octyl dodecanol, paraffin oil, isopropyl myristate, propylene glycol dicaprylocaprate, and squalene are also used. Oleic acid, linoleic acid, and decanoic acid, which are penetration enhancers, were also used for topical delivery. Tocopherol and other tocols were used for nanoemulsions. Due to their stability and good solubility in lipophilic drugs, tocols are very effective oils. The currently popular NLCs are produced by natural oils from plants [18].

1.4.1.1. Liquid-lipids: Digestible oils derived from natural sources are the most frequently used liquid lipids for NLCs. MCT and oleic acid are the famous liquid- lipids. To fabricate NLCs, liquid lipids such as edible oils such as soya bean oil and sunflower oil can be used. Among the natural edible oils, oleic acid is a common component. Using hydrolysis, oleic acid can be prepared from vegetable oils. In nutraceuticals formulation, oleic acid, which was used as an emulsifier, has a low viscosity. By esterification and fractionation methods, MCT with food grade was obtained. By the USFDA, MCT was recognized as safe and had high stability against oxidation and an emulsifying agent. The smell of the foods has been influenced by the free fatty acids which are obtained by the hydrolysis of MCT. These oils have been utilized as antioxidants that protect nourishment from oxidation; some oils incorporate γ- tocopherol, which generally appeared in corn oil. Likewise, they are economically contrasted with oleic acid and MCT. They have more level of un-saturation and consistency, so they are unacceptable to encapsulate some hydrophobic food additives. Low encapsulation effectiveness appeared by the soya bean oil contrasted with MCT and oleic acid, for example, paraffin oil [19-22].

1.4.1.2. Solid-lipids: The most ordinarily utilized for the manufacture of NLC are stearic acid, glyceryl monostearate (GMS), and glyceryl palmitostearate, and glyceryl behenate. They are especially surface-active and food-active compound carriers. The essential part of vegetable and animal lipids, as a noteworthy component of hydrogenated fats, is stearic acid, which is an endogenous long-chain saturated fatty acid. It has been accounted for that stearic acid is biocompatible with human tissues and body fluid. Contrasted with its synthesized counterparts, stearic acid has moderately lower toxicity and better biocompatibility. In the field of nutraceuticals, GMS, which is non-poisonous and non-irritating which has 40% of monoacylglycerol saturated fatty acids, is broadly utilized. GMS can use as a non-ionic emulsifying agent and plasticizer. Stearic unsaturated fats and mono, di, and triacylglycerols of palmitate are the constituents that are available in glyceryl palmitostearate, which has appeared promising sustained release profiles. Mono, di, and triacylglycerols of behenic acid are the segments that are available in glyceryl behenate. The high entrapment efficiency is shown by the glyceryl behenate solid-lipids and promising stability due to numerous defects in the crystalline cross-section [23-25].

1.4.2. Emulsifiers: To stabilize the lipid dispersions, emulsifiers have been widely used. Pluronic F68 (poloxamer 188) and polysorbates (Tween) were identified as the most widely used hydrophilic emulsifiers. For the fabrication of NLCs, lipophilic emulsifiers such as span 80 and lecithin are widely utilized. The particle aggregation can be prevented by the combination of emulsifiers which are used more efficiently. The nanoparticles shell has polyethylene glycol (PEG) prevents take-up by the reticuloendothelial framework, and to prolongs the circulation time of drugs. The physical stability of lipid dispersions can be impaired by the preservatives. Obeidat *et al.* demonstrated that Hydrolite® five for the preservation of coenzyme Q10-loaded NLCs [26-28]. Soya lecithin, phosphatidylcholine, egg lecithin are used as co-emulsifiers

1.4.3. Aqueous Surfactants: Surfactants are also called emulsifying agents, which lower the interfacial tension between two immiscible liquids or components. Hydrophilic surfactants are mostly used. Lipophilic amphiphilic emulsifiers are used for the fabrication of NLCs18, *e.g.*, tween-80 and pluroni F-68 [29].

2. Methods of Preparation: Lipid nanoparticles such as SLN and NLC do not vary much in their methods of preparation. The difference is just about the absence and presence of liquid lipids in the formulation. High-pressure homogenization, emulsification-ultrasonication, film ultrasonication and solvent emulsification are some of the commonly preferred methods for the preparation of NLCs and SLNs.

2.1. High-Pressure Homogenization Method (HPH): HPH has been used as a reliable and powerful technique for the large-scale production of NLCs, lipid drug conjugate, SLNs, and parenteral emulsions. The lipid is pushed with high pressure (100–2000 bars) through very high shear stress, resulting in the disruption of particles down to the submicrometer or nanometer range. Normally the lipid contents are in the range of 5-10%. In contrast to other preparation techniques, high-pressure homogenisation does not show a scaling-up problem. Homogenization may be performed either at elevated temperature (hot homogenization) or below room temperature (cold homogenization) [30].

2.2. Hot Homogenisation Technique: In this technique, the drug, along with melted lipid, is dispersed under constant stirring by a high shear device in the aqueous surfactant solution of the same temperature. The pre-emulsion obtained is homogenized by using a piston gap homogenizer, and the obtained nanoemulsion is cooled down to room temperature, where the lipid recrystallizes and leads to the formation of nanoparticles [31].

2.3. Cold homogenization Technique: Cold homogenization is carried out with the solid lipid-containing drug. Cold homogenization has been developed to overcome the problems of the hot homogenization technique such as temperature mediated accelerated degradation of the drug payload, partitioning, and hence loss of drug into the aqueous phase during homogenization. The first step of both the cold and hot homogenization methods is the same. In the subsequent step, the melt-containing drug is cooled rapidly using ice or liquid nitrogen for distribution of the drug in the lipid matrix, as shown in **Fig. 4** [32].

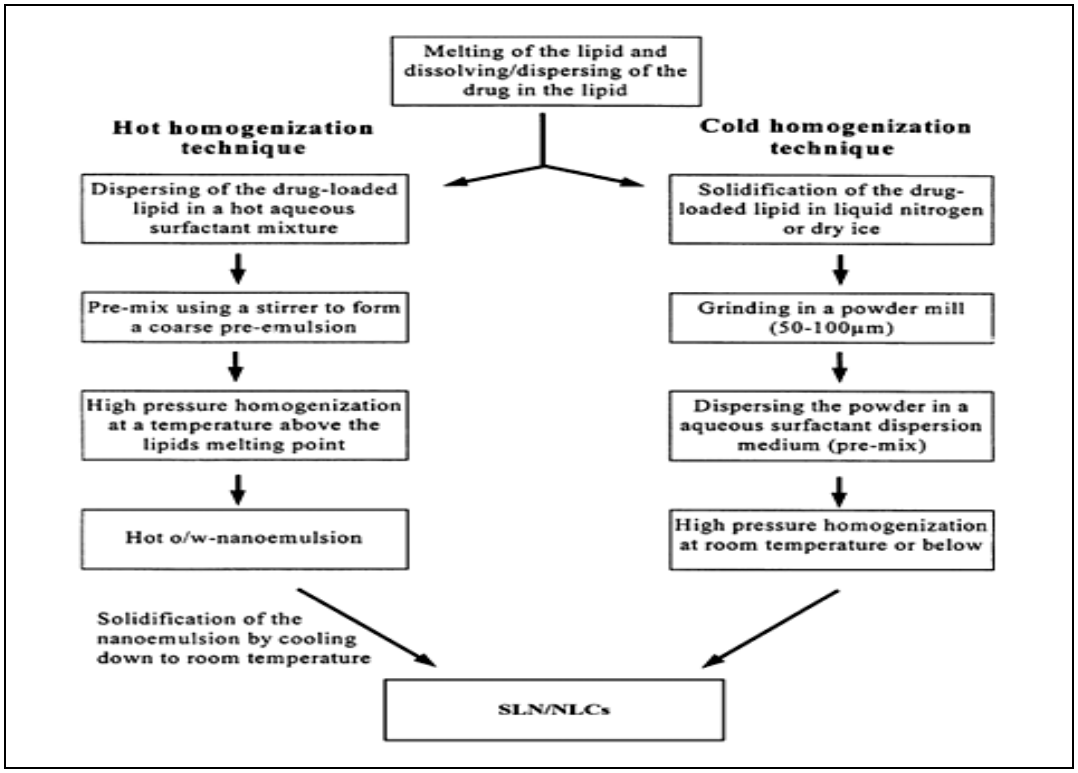

FIG. 4: METHOD OF PREPARATION OF SLN/NLCS

2.4. Microemulsion Technique: The lipids (fatty acids or glycosides e.g., lipid acid) are liquefied, and in this liquefied lipid, the drug is dissolved. A mixture of water, surfactant, and co-surfactant is heated at the same temperature and added to the lipid melt under mild stirring. A clean micro-emulsion was obtained when the components were mixed in the correct ratio.

The formed microemulsion is the basis for the nanoparticle formation of requisite size. This microemulsion is then dispersed in a cold aqueous medium under mild mechanical mixing of hot microemulsion with water during a quantitative relation in the range 1:25-1:50.

This dispersion in a cold aqueous medium leads to rapid recrystalization of the oil droplets. The micro-emulsion was prepared in a large temperature-controlled tank and then pumped from this tank into a cold water tank for precipitation [33-35].

2.5. Emulsification-ultrasonication Method: This method is somewhat similar to HPH. Drug, liquid and solid lipids are mixed and melted at 5-10 °C above the melting point of solid lipids. The surfactant is dissolved in distilled water and heated at the same temperature as lipid melt.

Aqueous phase is added in lipid phase, and this pre-emulsion is homogenized at high shear by applying required rpm for specific time. Then this emulsion is ultra-sonicated for specific time and then added to specified volume of distilled water. This is cooled at room temperature to solidify to obtain NLCs [36]. Contamination of formulation due to metal particles may occur during probe sonication.

2.6. Solvent Emulsification-evaporation Technique: In the solvent emulsification-evaporation method, the lipophilic material and hydrophobic drug are dissolved in a water-immiscible organic solvent and emulsified in an aqueous phase using a high-speed homogenizer.

The efficiency of fine emulsification is improved by immediately passing the coarse emulsion through a microfluidizer. Further, the organic solvent is evaporated by mechanical stirring at room temperature, and reduced pressure (e.g., rotary evaporator), leaving lipid precipitates nanoparticles as shown in **Fig. 5** [37].

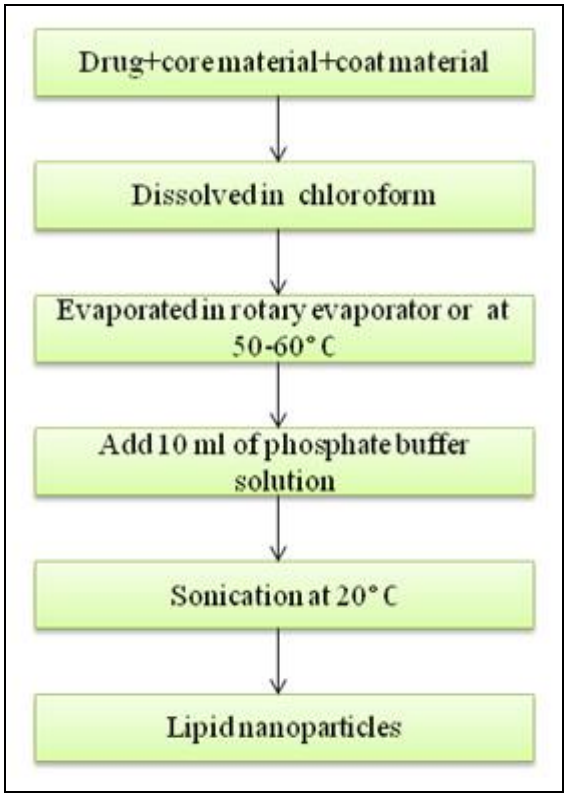

FIG. 5: SCHEMATIC PROCEDURE OF SOLVENT EMULSIFICATION EVAPORATION

2.7. Solvent Diffusion Method: The solvent diffusion method involves the use of water-miscible organic solvents such as methanol, ethanol, and acetone, *etc*. In this method, the drug and lipids are added in a single or a mixture of organic phases. This is sonicated and maintained at elevated temperatures to obtain a clear lipid phase. The aqueous phase is prepared by adding a suitable stabilizer/ surfactant and maintained at the same temperature as that of the lipid phase. The organic-lipid phase is added in the aqueous phase under mechanical stirring at elevated temperatures. This dispersion is stirred at room temperature for cooling and evaporation of organic solvent to obtain NLCs [38].

2.8. Solvent Injection: The basic principle of the solvent injection method is similar to the solvent diffusion method. In the solvent injection method, lipids are dissolved in a water-miscible solvent (e.g. acetone, isopropanol and methanol) or water-miscible solvent mixture and quickly injected into aqueous solution surfactants through an injection needle. The advantages of this method are the easy handling and fast production process without using technically sophisticated equipment (*e.g.,* high-

pressure homogenizer). However, the main disadvantage is the use of organic solvents [39].

Parameters considered in the successful formation of NLCs are shown in **Fig. 6**.

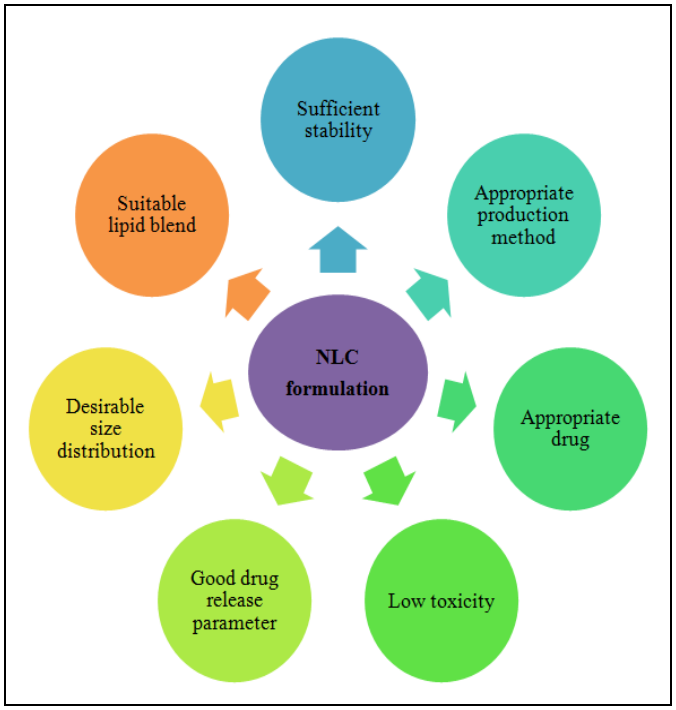

FIG. 6: PARAMETERS FOR NLC FORMULATION

3. Characterization of NLCs:

3.1. Particle Size and Zeta Potential: Photon correlation spectroscopy (PCS) is an established technique used for the measurement of the size and distribution of polydispersity index (PDI) of NLCs [40].

Average particle size indicates whether the carrier can permeate through biomembranes or not. Generally, particle size less than 400 µm is preferred as it shows desirable permeation. Particle size is highly affected by the type and concentration of surfactants. An increase in the concentration of surfactant causes a decrease in particle size. Also, the concentration and proportion of various liquid and solid lipids are responsible for variations in particle size.

3.2. Zeta Potential: It can be measured by photon correlation spectroscopy. Zeta potential is indicative of the stability of colloidal dispersion. Aggregation of the particles is avoided by inducing/acquiring surface charge on the particles (±30 mV). Most of the time, lipid nanocarriers acquire negative charge, but when mucoadhesion or crossing of complex barriers (BBB) is required, the carrier surface needs to be positively charged. Surfactant and/or coating material adsorption is also responsible [41].

3.3. Entrapment Efficiency (%) (Ee) and Drug Loading (DL): From the prepared NLCs formulation, 1ml of the dispersion was dissolved in (1:1) mixture of 10 ml of 7.4 phosphate buffer and ethanol. Then this mixture was centrifuged at high rpm (10000-20000) for 40 min at 25 °C [42]. The rpm was selected on the basis of particle size. The lesser the particle size higher will be the rpm.

3.4. Shape and Morphology: Scanning electron microscopy (SEM) produces images of components by scanning the surface with a focused beam of electrons. Transmission electron microscopy (TEM) gives images upon transmission of a beam of electrons through the specimen. SEM and TEM reveal the surface morphology and structure of particles from inside, respectively. SEM reveals the surface morphology, shape, porous nature, and size of the particle. TEM reveals the structure of particles from inside and gives an idea about particle diameter and matrix structure [43-44].

3.5. Drug-lipid (excipient) Interaction: Infrared spectroscopy (FTIR) peaks reveal the wavenumbers at which characteristic functional groups in molecules transmit IR radiations. The transmission is measured from 4000 cm^{-1} to 400 cm^{-1}. FTIR is generally used for the detection of interaction between drugs and excipients/lipids. Interaction is shown by shifting or diminishing the functional group peaks of drug or occurrence of peaks in the physical mixture that were not in the first place. Generally, peaks of functional groups of lipids are observed in NLCs as the drug is embedded in matrix [45].

3.6. *In-vitro* Drug Release Study: NLCs are evaluated for drug release pattern by using dialysis method, *in-vitro* lipolysis method (oral delivery), using cornea (*ex-vivo* permeation), in situ perfusion (intestinal drug absorption), and using suitable cell lines (cancer cell targeting) [45-46].

3.7. Suitable *In-vivo* Studies: *In-vivo* pharmaco-kinetic studies are carried out to investigate the AUC, C_{max}, and T_{max} of the drug to reveal the absorption, distribution, metabolism, and excretion

(ADME) of the drug in formulations. *In-vivo* pharmacodynamic studies are carried out to study the drug's efficacy in a suitable diseased animal model. NLC formulations of drugs are evaluated, and their efficacy is compared with the efficacy of a pure drug or conventional formulations of respective drugs [47].

4. Applications of NLCs: NLCs formulations are available currently in market under the therapeutic and non-therapeutic category as these formulations have well-established biocompatibility because of the presence of lipids in it. Here the applications of NLCs of different types of drugs are summarized in TABLE 1 along with their effect on targets.

4.1. NLCs for Cancer Therapy: Anticancer drugs can be incorporated into the NLCs. The improvement in chemical stability and cytotoxicity can be seen by incorporating anticancer drugs into the NLCs. In the melanoma and leukemia conditions, the NLCs containing drugs such as camptothecin and topotecan drugs incorporated in NLCs fight against the cell in that condition and exhibit greater cytotoxicity cell uptake. In lung cancer, ovarian cancer, breast cancer, the docetaxel drug show antitumor activity. A strong cytotoxicity effect was shown by Duopafei®, NLCs against cancer cells in the lungs. Compared to Duopafei, VEGFR- 2-antibody modified NLCs incorporated by docetaxel show high cytotoxicity and great tolerance in mice against melanoma. Cytotoxicity was exhibited by VEGFR-2-antibody modified NLC in melanoma. To overcome multidrug resistance, the NLCs-dextran sulfate has been developed. NLCs loaded with curcumin showed increased anticancer efficacy when tested in A172 cells and *in-vivo* in A172 xenograft-induced mice model with a reduction in dose [48]. Paclitaxel NLC conjugated with transferrin- formulation was responsible for selective targeting of brain tumor cells and showed superior efficacy and cellular uptake over non-targeted NLCs [49].

4.2. Pulmonary Drug Delivery: Drug delivery via inhalation is also a potential route for the treatment of several pulmonary disorders having advantages over conventional (parenteral and oral) dosage forms like a) noninvasive b) circumventing first-pass metabolism and systemic toxicity c) reduced frequent dosing d) site-specificity by directly reaching to the lung epithelium thereby enhancing local drug concentrations [50]. In pulmonary drug delivery systems, surfactants and co-solvents are also often used to prepare stable formulations of highly lipophilic active ingredients. Few attempts have been made to deliver anti-cancer agents using nanoparticles and liposomes *via* an inhalation route, but the major limitations being instability during nebulization, biodegradability, drug leakage and adverse side effects of the drug. The lipophilic COX-2 inhibitor, celecoxib, was successfully encapsulated in the NLC nanoparticles using a mixture of solid and liquid lipids where most of the nebulized nanoparticles were able to deposit in the alveolar region of the mice lungs and also enhanced the celecoxib lung residence time. Aerosolized itraconazole NLCs were developed and delivered for the treatment of pulmonary aspergillosis in falcons [51].

4.3. Intravenous Route: Oral drug delivery creates physiological complications while treating CNS diseases. Hence parenteral NLC therapy is developed to overcome the side effects and organ toxicity and selectively targets the brain. Artemether-lumefantrine combination intravenous NLC therapy selectively targeted CNS residing malarial parasites upon single injection per day for consecutive four days with 100% reversal of cerebral malaria (CM) symptoms with remarkable survival rates of animals causing no organ toxicity [52].

4.4. Ocular Delivery: Through the method meltultrasonic, the flurbiprofen-NLCs were prepared and then coated with chitosan oligosaccharides (COS) with a molecular weight of 3000–6000 kDa [53]. Thiolated NLC was prepared by the conjugate of cysteine-PEG monostearate and used as a nanocarrier for the topical ocular administration of cyclosporine A. Acyclovir used as NLC for the faster permeation through the cornea, which indicates the increased corneal penetration properties. For the effective treatment of inflammatory, edematous, and angiogenic ocular disease, the drug triamcinolone acetonide, which is a corticosteroid, was used. The drug which is incorporated in NLCs shows high bioavailability. By corneal and noncorneal pathways, the drug triamcinolone can be delivered effectively [54].

TABLE 1: APPLICATIONS OF NLCs

S. no.	Name of the drug	Route	Effect	Reference
1	Spironolactone	Oral	Formed mixed micelles enhance solubilization and bioavailability of drug from micelle	55
2	Silybum marianum	Oral	*In-vitro* lipolysis experiment has shown possible enhanced efficacy of drug in NLCs due to mixed micelle formation	56
3	Chitosan coated Amphotericin B	Oral	Mucoadhesion due to positive surface charge and delayed the gastric transit thereby improving oral bioavailability (BA)	57
4	Tacrolimu	Oral	Higher plasma drug concentration and increase in half life ofdrug was achieved by NLCs	58
5	Rosuvastatin calcium	Oral	Superior oral BA was achieved with greater antihyperlipidemic potential than conventional therapy	43
6	Docetaxel	Oral	Improvement in BA was observed due to mucoadhesion leading to longer residence time	59
7	Hydrogel of lansoprazole	Tansdermal	Accumulation of drug in skin was observed which lead to the release of drug for prolonged period of time	60
8	Flurbiprofen loaded NLC	Tansdermal	Greater diffusion of drug through skin, successful inhibition of edema and prolonged action of drug	61
9	Valdecoxib NLC gel	Tansdermal	Greater diffusion of drug through skin, successful inhibition of edema and prolonged action of drug	62
10	Voriconazole cationic NLC	Ocular	Increase in retention of carriers on corneal surface due to mucoadhesion and electrostatic binding,	63
11	Mangiferin	Ocular	Higher concentration of drug in aqueous humor than its solution	64
12	Genistein loaded NLC	Ocular	Enhanced cellular uptake	65
13	N-palmitoyl ethanolamide	Ocular	Higher concentration of drug in posterior segment of the eyes with desirable distribution upon topical instillation	66
14	Lamotrigine	Intranasal	Consistent drug release at zero order	46
15	Artemethe	Intranasal	No systemic exposure of drug	67
16	Efavirenz	Intranasal	No signs of toxicity	68
17	Artemether-lumefantrine	Intravenous	Remarkable survival rates of animals causing no organ toxicity	52
18	Itraconazole	Pulmonary	Disposition in deeper alveolar tissues	51
19	Mannose coated rifampicine loaded NLCs	Pulmonary	Shorten the tuberculosis treatment period and target drug selectively at the alveolar macrophages	69
16	Argan oil based NLCs	External (Cosmetic)	Improved skin hydration	70
17	N-acetyl glucosamine	External (Cosmetic)	Efficient skin lightning as compared to its solution due to high permeability offered by lipids	71
18	Coenzyme Q10 & retinaldehyde	External (Cosmetic)	Efficient penetration and distribution of NLC in skin followed by reduction in UV induced wrinkles with negligible signs of irritation	72
19	Lycopene	Food	Improved solubility and stability	73
20	Menthol	Food	Enhanced antimicrobial activity against gram positive bacteria	74

CONCLUSION: To overcome the problems of low solubility and bioavailability, numerous drug delivery systems are explored continuously on the laboratory and industrial levels. It has been found that a nano-based delivery system has a lot of potentials to increase the bioavailability of poorly soluble lipophilic drugs and also target the site of action. By combining a large portion of benefits of different novel colloidal delivery systems and by avoiding some of their limitations, NLCs are prepared, which are biodegradable, biocompatible transporter systems. NLCs seem to be suitable delivery systems intended for topical, oral, pulmonary, ocular, parenteral administration of drugs. The purpose of this work was to highlight the role of NLCs as a novel drug delivery system for various categories of drugs. They are the new generation, smart, flexible systems offering for enhanced drug loading, modulation of release, and improved performance in producing final dosage forms such as creams, tablets, capsules, and injectables. This versatile drug delivery system is

currently utilized in various cosmetics products and chemotherapeutic agent delivery. Considering its biological suitability, higher drug load, stability, and biocompatibility of NLCs will be the most appreciated topic of research in medicines. From all the information gathered from the recent literature, it can be concluded that NLC is an excellent drug carrier system for the treatment of disease.

FUTURE PROSPECTIVE: Future research groups are placed all over the world, not only in developed countries like Germany, Canada but also in developing countries such as India and Brazil. Success can be possible only if the pharmaceutical industry takes up developments as well to produce more drug products that will be formulated as NLC because of the obvious advantages for the pharmaceutical companies. Researchers have explored the capability of these lipid nanoparticles for accommodating great amounts of bio-actives, preventing their premature decomposition, and enhancing their oral bioavailability NLCs can serve as a promising tool for enhancing the therapeutic efficacy of drugs and also providing controlled release of encapsulated drugs. However, more pre-clinical and clinical studies need to be performed in the near future to establish these formulations in the market on the basis of low risk/high benefit ratio as compared to high risk/low benefit ratio in their present formulations.

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