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NANOSTRUCTURED LIPID CARRIERS V/S SOLID LIPID NANOPARTICLES: COMPARATIVE REVIEW ON ENHANCING DRUG DELIVERY AND THERAPEUTIC EFFICIENCY

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ABSTRACT

Oral drug administration is widely preferred for its convenience and patient compliance. However, BCS Class III drugs, with high solubility but low permeability, often face absorption challenges and low bioavailability due to hepatic first-pass metabolism. Nanostructured Lipid Carriers (NLCs) offer a promising solution by enhancing permeability, promoting lymphatic absorption and bypassing first-pass metabolism, thereby improving drug bioavailability. NLCs, an advanced lipid-based drug delivery system, overcome the limitations of Solid Lipid Nanoparticles (SLNs) by incorporating both solid and liquid lipids, enhancing drug loading, stability and controlled release. They improve drug absorption via various mechanisms, including M-cell uptake, adherence to mucosal membranes and surfactant-mediated permeability enhancement. Formulation techniques such as high-pressure homogenization ensure optimal particle size and encapsulation efficiency. Research demonstrates that NLCs outperform SLNs in drug retention and bioavailability, making them a valuable platform for pharmaceuticals, cosmetics and nutraceuticals, thereby revolutionizing modern drug delivery systems.

KEYWORDS

Nanostructured Lipid Carriers (NLCs), Solid Lipid Nanoparticles (SLNs), Bioavailability, permeability, Drug delivery and Lymphatic absorption.

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INTRODUCTION

The greatest advantages and benefits for patients and pharmaceutical companies are provided by the oral route of drug delivery. One major obstacle that many hydrophilic medications, which are categorised as BCS Class III with high solubility and poor permeability, must overcome is the restricted gastrointestinal tract penetration that prevents them from being absorbed into the body.

Therefore, rather than their solubility[1], the rate of absorption of these medications becomes the limiting determinant in their delivery[1]. Low bioavailability of medications that have hepatic first pass effect can be enhanced by encapsulating them in nanostructured lipid carriers, which increase permeability and consequently, oral bioavailability[2].

NANO- FORMULATION[3-7]

"Nano" comes from the Greek word for "dwarf" and nanotechnology is the manipulation of materials at the nanometre (10^{-9}m) scale[3]. Environmental science, health, cosmetics and nutraceutical research are just a few of the sectors that use nanotechnology[4]. It is an effective tool for creativity and problem-solving in these domains due to its adaptability[5]. Nanotechnology has emerged as a useful instrument in recent years for getting around the drawbacks of conventional medicine delivery systems. Despite the fact that nanotechnology may seem like a relatively new area, nanoparticles (NPs) were initially created more than 40 years ago as a way to deliver drugs. Since then, significant advancements have been made in the creation of nanoscale materials and the assessment of their potential to improve human health[3]. Nanocarriers' surface, composition, and form are among their physical and chemical characteristics that can be altered to increase their efficacy and lessen their adverse effects[6]. Medication can be efficiently delivered to the desired place via nanocarriers, including silicon, polymers, magnetic nanoparticles, dendrimers, carbon materials, lipid-based systems, and silicon[7].

NANASTRUCTURED LIPID CARRIER[8-15]

NLCs, the second generation of lipid nanocarriers, were developed in the late 1990s to overcome the limitations of SLNs[8,9]. They are composed of an aqueous phase that contains a surfactant [10,11] and a mixture of liquid and solid lipids in a ratio of up to 70:30[10,11]. Because of their biological compatibility, the lipids utilised in these formulations reduce the possibility of toxicity[12]. The NLC structure becomes more disordered when solid and liquid lipids are combined, which improves drug loading and integration efficiency[13]. The use of NLCs as drug delivery vehicles for hydrophilic and hydrophobic substances has been thoroughly investigated. By avoiding first-pass metabolism and facilitating lymphatic absorption, they improve therapeutic efficacy by enabling more medication to reach the intended location. Furthermore, by lowering dosage frequency, enhancing patient compliance and delaying medication release, drug encapsulation in the lipid matrix promotes sustained release[14]. In addition to serving as a vital delivery system for food, cosmetics, and medications, NLCs have lately been used to gene therapy, cancer treatment, and brain targeting[2]. Drugs are dissolved or integrated into a mixture of solid and liquid lipids in NLCs (Figure No.1), which typically have a size range of 10 to 500nm[15].

COMPARSION OF NANOSTRUCTURED LIPID CARRIER AND SOLID LIPID NANOPARTICLES[16-25]

Lipid nanoparticles, particularly solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), have garnered increasing attention in recent years[16]. Because SLNs are made entirely of solid lipids, they have a crystal lattice structure that leaves little room for therapeutic agents[17]. Innovative lipid-based drug delivery methods called Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) are designed to improve the stability and bioavailability of lipophilic medications. Despite having comparable functions, their structural makeups are different. Solid lipids make up SLNs, which encapsulate medications in a stable matrix for regulated release and degradation prevention. On the other hand, a second-generation lipid nanoparticle called Nanostructured Lipid Carriers (NLCs) blends liquid and solid lipids. Compared to SLNs, this special structure enhances stability and boosts drug loading capacity[18]. Like oil-in-water emulsions, solid lipid nanoparticles (SLNs) are lipid-based drug delivery vehicles that may be manufactured on an industrial scale. However, they could run into problems

including restricted medication loading capacity and drug leakage[19]. Solid lipids at room temperature are substituted for liquid lipids in the formulation of SLNs. Solid lipids were the only substance used in the initial generation of SLNs. Solid and liquid lipids are combined to create the second generation of lipid carriers, or nanostructured lipid carriers (NLCs). The stability and drug-loading capabilities of the nanoparticles are improved by this combination[15].

NLCs improve drug loading and stop drug leakage during storage by substituting oil for some of the solid lipid, resulting in an unevenly ordered lipid matrix[20]. Likewise, NLCs provide increased stability by keeping solid lipids from recrystallising, guaranteeing that the particle size stays mostly constant throughout storage[21]. Reduced toxicity, biodegradability, enhanced medication safety, controlled release and the removal of organic solvents during production are all benefits that NLCs and SLNs have in common[22]. NLC formulations have been shown to be more effective lipid carriers than SLNs, with benefits in skin penetration, entrapment efficiency, and drug loading capacity[23].

Structural Characteristics of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers

Lipid-based nanoparticles exhibit distinct physical, mechanical, chemical and biological properties at the nanoscale, which can significantly differ from their core components in SLNs and NLCs (Figure No.2). These nanostructures primarily consist of lipids and surfactants and serve as carriers for therapeutic agents through encapsulation, incorporation, or surface attachment, facilitating targeted delivery to specific tissues[24,25]. The following sections highlight the key structural differences between SLNs and NLCs. In (Table No.1) their classification by properties is shown, which highlights the comparison between SLNs and NLCs.

TYPES OF NLC's /SLN's[26,27]

Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) are advanced lipid-based drug delivery systems, each with distinct structural types that influence drug localization and release profiles. Different types of SLNs and NLCs are depicted in Figure No.2 (a, b).

Types of SLNs

Homogeneous Matrix Model (Type I)

In this configuration, the drug is uniformly dispersed within a solid lipid matrix, forming a solid solution. This structure is typically achieved through the cold homogenization technique and is suitable for controlled drug release applications.

Drug-Enriched Shell Model (Type II)

Here, a drug-free lipid core is surrounded by an external solid shell containing both the drug and lipid. This arrangement is often produced using the hot homogenization method, where the lipid core forms at the lipid's recrystallization temperature, resulting in a drug-enriched outer layer.

Drug-Enriched Core Model (Type III)

This model is formed when the drug concentration approaches its saturation solubility in the lipid, leading to drug precipitation within the core during cooling. The resulting structure comprises a drug-enriched core with a lipid coating, facilitating extended drug release profiles[26].

Types of NLCs

Imperfect Crystal Type (Type I)

A partial substitution of liquid lipid or oil for solid lipid results in an incomplete crystal lattice or matrix. This occurrence indicates that there is more room for drugs to be accommodated and permits increased drug loading. A highly structured or ordered matrix would have forced the drug out of the core, whereas the development of an imperfect crystal core allows for additional space for drug integration.

Amorphous Type (Type II)

Combining liquid lipids with solid lipids that retain their α polymorph after solidification and storage often results in the formation of an amorphous core. Compared to type I NLCs, this is better since the medication stays entrenched in the amorphous

matrix and no crystallization happens. Solid lipids with the β polymorph form a matrix with a crystalline structure.

Multiple Type (Type III)

It is essentially NLC of the oil-in-solid or fat-in-water kind, which can only be produced via the phase separation method. Using this method in the formulation of NLCs can increase drug loading capacity and stability when the medication exhibits higher solubility in oil. A solid lipid matrix contains evenly distributed tiny oil droplets, and this system is distributed in an aqueous medium[27].

It's important to note that slight variations in formulation parameters can significantly impact the structure and applicability of SLNs and NLCs. For instance, the homogeneous matrix model (SLN Type I) is suitable for controlled release, while the drug-enriched core model (SLN Type III) is ideal for extended-release profiles. Similarly, the choice between different NLC types depends on the desired drug loading capacity, release kinetics, and stability requirements[26].

COMPOSITION OF NLCs /SLNs[28-33]

NLCs are composed of lipids, surfactants, and water in an aqueous medium. Several factors influence their size, drug loading capacity, release profile, and stability, including lipid content, matrix composition, and the production process. The NLC structure typically consists of a combination of long- and short-chain liquid and solid lipids, with lipid content ranging from 5% to 40%. Surfactants, at concentrations of 0.5% to 5% w/w, stabilize the NLC formulation within the aqueous medium[28].

The main components of NLC includes as follows;

LIPIDS

Lipids play a vital role in Nanostructured Lipid Carriers (NLCs), influencing drug loading capacity, action duration, and formulation stability. The inner core is composed of both solid and liquid lipids, with the most effective lipids being those that are physiologically acceptable, biodegradable, non-toxic and classified as generally recognized as safe (GRAS).

Solid lipids

NLC is a blend of chemical substances with a melting point over 40°C, biodegradable *in vivo*, and a GRAS rating. Lipids used in NLC are chosen based on their high solubility, determined by dissolving the component in liquified solid lipids in increasing amounts to achieve the maximum amount of activity[29].

Ex: Glyceryl tristearate/tristearin, Stearic acid, Glyceryl monostearate, Propylene glycol monostearate, Cetyl palmitate, Cholesterol, Beeswax, Carnauba wax, Preciface, Emulcire.

Liquid lipids

Natural sources of digestible oils are the most often utilized liquid lipids for NLCs. These liquid lipids have a GRAS (Generally Recognized as Safe) rating and are well tolerated. The lipophilic excipients utilized to integrate the solid lipid core and lessen its crystallinity are called liquid lipids, or oils[30]. Ex: Soyabean oil, vitamin-E/tocopherol, Castor oil, Corn oil, Oleic acid, Palm oil, Olive oil, Squalene, caprylic/capric triglyceride, Propylene glycol dicaprylate/caprate, Miglyol.

Surfactants

Surfactants are essential in the preparation of NLCs, as they stabilize the lipid nanoparticles within the dispersion medium. By reducing the interfacial tension between the lipid and aqueous phases, surfactants minimize the tendency of particles to aggregate at the interface. This forms a protective layer around the particles, maintaining the physical stability of the dispersion during storage and formulation. Using two emulsifiers with complementary lipophilic and hydrophilic properties can further enhance stability. However, high surfactant concentrations in drug delivery systems can pose challenges. Selecting the appropriate surfactant depends on its hydrophilic-lipophilic balance (HLB) value and molecular weight[31].

Ionic surfactants

Sodium Tauro deoxycholate, Sodium oleate, Sodium dodecylsulphure, Polysorbate 60 and 80.etc.

Non-Ionic surfactants

Polyoxyethylene, sorbitan monolaurate (Polysorbate 20, Tween 20), Polyoxyethylene, sorbitan monostearate (Polysorbate 60, Tween 60) Polyoxyethylene, sorbitan monooleate (Polysorbate 80), Poloxamer 188 Poloxamer 182 Ethoxylated p-tert-octylphenol formaldehyde polymer (Tyloxapol).

Amphoteric surfactants

Egg phospholipid (Lipoid E 80, Lipoid E 80 S) Soy, Hydrogenated soy phosphatidylcholine (Lipoid S PC-3), Hydrogenated

Co-surfactants

Butanol, Butyric acid, Polyvinyl alcohol (PVA), Propylene glycol, Polyethylene glycol.

Other excipients

In the development of nanostructured lipid carriers (NLCs), organic salts and ionic polymers can be used as counterions to address the challenge of encapsulating water-soluble drug molecules. Surface modifiers are another class of excipients employed in NLCs formulations to reduce phagocytic uptake by macrophages in the reticuloendothelial system (RES). To extend the systemic circulation time of therapeutic compounds, lipophilic particles are coated with hydrophilic polymers such as PEG, poloxamines, or poloxamers. Surface modification also offers additional potential benefits, including improved drug targeting, enhanced physical stability, better epithelial transport and increased biocompatibility[32].

SLNs are composed of three primary components: solid lipids, surfactants (emulsifiers) and water or solvent.

Solid lipid

The solid lipid core, which remains solid at both room and body temperatures, serves as the matrix for drug incorporation. Commonly used solid lipids include triglycerides (e.g., tristearin), partial glycerides (e.g., glyceryl behenate), fatty acids (e.g.)

Surfactants

The Surfactants are employed to stabilize the lipid core and prevent particle agglomeration. Various emulsifiers, such as Pluronic F68 and F127, have been used for this purpose. The combination of emulsifiers might prevent particle agglomeration more efficiently.

Aqueous phase

The aqueous phase, typically water or a suitable solvent, acts as the dispersion medium for the lipid and surfactant mixture, facilitating the formation of a stable colloidal system[33].

MECHANISM NLCs / SLNs[18,34]

NLCs promote the medication's oral bioavailability by augmenting the uptake of drugs by microfold cells (M-cells) in the intestinal membrane and also, can bypass first-pass hepatic metabolism. Lipid nanocarriers can be transported across the intestinal wall via several pathways such as transcellular absorption, paracellular transport, P-glycoprotein and cytochrome 450 inhibition. In addition, lipidic compounds instigate the production of chylomicrons, which help in their transfer across the membranes.

The various mechanisms by which NLCs augment the bioavailability of poorly soluble drugs are as follows:

Direct uptake

Nanostructured lipid carriers (NLCs) enhance the bioavailability of lipophilic drugs by leveraging intestinal lymphatic transport. Utilizing triglycerides, NLCs promote chylomicron formation, enabling transcellular absorption and directing lipophilic drugs through the intestinal lymphatic system, thereby bypassing the first-pass metabolism. Triglyceride hydrolysis begins in the gastrointestinal tract (GIT) with the aid of lingual and gastric lipases, leading to the formation of a triglyceride emulsion. This emulsion stimulates the secretion of bile salts, pancreatic enzymes and biliary lipids. Biliary lipids adsorb onto the emulsion surface, stabilizing it, while pancreatic lipase converts triglyceride droplets into monoglycerides and fatty acids. These products are absorbed by enterocytes, where they are reassembled to form the lipid core of chylomicrons. Phospholipids and apolipoproteins further stabilize

the chylomicrons, which are then secreted into the lamina propria and mesenteric lymph nodes, eventually entering lymphatic circulation.

Adherence to the mucosal membrane

Nanostructured lipid carriers (NLCs) adhere to the mucus layer, prolonging their residence time and enhancing drug release. The tight epithelial cells of the gastrointestinal tract (GIT) are covered by a hydrophilic, negatively charged mucus layer that acts as a protective barrier, restricting the passage of foreign particles. However, researchers have leveraged this mucus barrier as a strategy to improve drug plasma concentrations and therapeutic efficacy. By engineering nanoparticles capable of binding to mucus, their retention time in the GIT is extended, facilitating passive drug transport and improving absorption.

Upsurged permeability

Nanostructured lipid carriers (NLCs) contain surfactants that modify intestinal permeability through various mechanisms. For example, the surfactant poloxamer induces structural alterations in cell membranes, leading to the opening of tight junctions in intestinal epithelial cells and promoting paracellular transport. Additionally, it inhibits P-glycoprotein efflux, further enhancing NLC transport.

Formation of mixed micelles

The lipid content in NLCs stimulates bile secretion in the small intestine. As enzymes degrade the lipid, it combines with bile to form mixed micelles. NLCs promote the release of bile, bile salts, phospholipids and cholesterol from the gallbladder, facilitating micelle formation, preventing lipid precipitation and enhancing the solubilization of NLCs lipids and drugs. Additionally, these micelles assist in the transfer of carriers across the stationary layer between the intestinal bulk fluid and the brush-border membrane of enterocytes, further improving drug absorption.

Bypassing First-Pass Metabolism

Well-engineered NLCs act as a delivery system, protecting drugs from early degradation as they pass through the gastrointestinal tract, thus avoiding first-pass metabolism. Within the GIT, NLCs interact with bile salts, leading to the formation of mixed micelles. These micelles are selectively absorbed by the lymphatic system, circumventing the liver. Additionally, the mixed micelles aid in the solubilization of lipid digestion products in the gut lumen, creating a concentration gradient that facilitates absorption. This ability of NLCs to bypass hepatic metabolism improves the therapeutic effectiveness of drugs that are extensively metabolized by the liver, while also reducing dosing frequency and minimizing dose-related side effects.

(Figure No.3) illustrates the various mechanisms by which NLCs are absorbed in the GIT, their ability to bypass first-pass metabolism and their stability in withstanding both acidic conditions and enzymatic degradation[18].

SLNs enhance the oral bioavailability of poorly water-soluble drugs through several mechanisms:

Improved Solubilization

SLNs increase the solubility of hydrophobic drugs in the gastrointestinal tract, facilitating better absorption.

Protection from Degradation

Encapsulating drugs within the solid lipid matrix shields them from enzymatic degradation and acidic conditions in the gastrointestinal environment, preserving their integrity.

Enhanced Lymphatic Uptake

SLNs can be absorbed via the intestinal lymphatic system, bypassing the hepatic first-pass metabolism. This pathway involves the uptake of SLNs by M cells in the Peyer's patches, leading to entry into the lymphatic circulation.

Prolonged Gastrointestinal Residence Time

The small size and lipid composition of SLNs allow them to adhere to the mucosal surface, extending their residence time in the gastrointestinal tract and increasing the window for drug absorption.

Facilitated Cellular Uptake

SLNs can be internalized by intestinal epithelial cells through endocytosis, enhancing drug transport across the intestinal barrier[34].

CHARACTERIZATION OF NLCs /SLNs[16]

Characterizing Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) is essential to ensure their efficacy, stability and suitability for drug delivery applications. Table No.2 and Table No.3 describes several examples of studies about the development, applications and as well nanoparticle characterization of NLCs and SLNs

In addition to the advantages, SLNs also have relevant disadvantages such as possible aggregation, instability during storage and low drug loading for some drugs. For these reasons and to overcome them, NLCs have been developed[16].

IN VITRO PERFORMANCE OF SOLID LIPID NANOPARTICLES AND NANOSTRUCTURED LIPID CARRIER

These lipid-based nanoparticles have potential as novel delivery system. Therefore, numerous studies have been carried out to evaluate the stability of these drug-loaded nanoparticles, their size, zeta potential and entrapment efficiency, as well as *in vitro* studies to analyse their release profiles and bioavailability.

Yuan *et al*, investigated the impact of folic acid (FA) modification on paclitaxel-loaded solid lipid nanoparticles (SLNs). Their study demonstrated that FA-modified SLNs exhibited increased uptake via folate receptor-mediated endocytosis in A549 cell lines. Consequently, the cytotoxicity of paclitaxel was significantly enhanced compared to the free drug solution[36].

In another study, Das *et al*, compared SLNs and nanostructured lipid carriers (NLCs) as delivery systems for clotrimazole. They found statistical differences between the two in terms of particle size, zeta potential, polydispersity index (PdI) and encapsulation efficiency. For the same drug concentration, NLCs had a slightly smaller particle size. Drug release at 80 hours was 56.6% for NLCs and 42.5% for SLNs; however, these differences were not statistically significant. Regarding stability, NLCs showed slightly better results than SLNs, especially at high drug loading[37].

Similarly, Dudhipala *et al*, evaluated SLN and NLC delivery systems for nisoldipine. They concluded that an NLC composed of oleic acid and dynasan-114 exhibited superior characteristics in terms of particle size, PdI, zeta potential, entrapment efficiency, and in vitro controlled release compared to the optimal SLN formulation. The formulated NLCs remained stable for three months at room temperature after lyophilization, supporting the advantages of NLCs over SLNs[38].

APPLICATIONS OF NLCS / SLNS[39-43]

SLN and NLC have a remarkably wide range of applications and have demonstrated significant efficacy in controlling the skin penetration of various active compounds, as well as in the delivery of food, drugs, cosmetics and other substances.

Oral drug delivery applications

Oral drug administration is a widely used and preferred route due to its non-invasiveness, high patient compliance, and therapeutic effectiveness. However, the poor water solubility of many drugs poses a significant challenge to their absorption. To overcome this limitation and enhance bioavailability, lipid-based drug delivery systems have gained significant attention in recent decades. These systems encompass various formulations, including self-nanoemulsifying drug delivery systems (SNEDDS), self-microemulsifying drug delivery systems (SMEDDS), nanoemulsions, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). By dissolving the drug in lipids, these systems effectively improve the bioavailability of poorly water-soluble, particularly lipophilic, drugs. They enhance drug dissolution, prolong residence time, and facilitate lymphatic uptake. Notably, in most cases, these systems have demonstrated a favorable safety profile without observed toxicity[39,40].

Pulmonary drug delivery applications

Lipid nanoparticles (LNPs) can be easily incorporated into carriers for inhalation, allowing for deep lung deposition, strong adhesion and prolonged retention in the lungs. Due to their enhanced and sustained therapeutic effects, solid

lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) offer extended dosing intervals, improving patient compliance. As particulate systems, they are widely used for various drug delivery applications. The advantages of lipid-based drug release in the lungs include controlled release profiles, prolonged drug action, faster *in vivo* degradation, and better tolerability compared to polymeric materials such as polylactic acid (PLA) or poly(lactic-co-glycolic acid) (PLGA). While pulmonary delivery of SLNs has not been widely accepted due to toxicity concerns, the use of physiological lipids is expected to enhance safety compared to polymer-based systems. For pulmonary drug delivery, SLNs can be formulated as dry powders or aqueous suspensions. Numerous studies have explored SLNs as carriers for both local and systemic drug delivery, including small molecules and macromolecules, via pulmonary administration[41,42].

Gene transfer applications

Lipid nanoparticles (LNPs) efficiently penetrate biological membranes through receptor-mediated pathways, as lipids are essential components of cell membranes. This property enhances the cellular uptake of genetic materials. The targeted delivery of bioactive compounds and their release behavior are closely linked to particle size. The success of gene therapy, which involves the transfer of DNA and RNA, relies on innovative bioactive delivery techniques. Since the 1980s, over 400 clinical studies on gene therapy have been reported. Due to the limited ability of naked DNA to enter cells and its susceptibility to enzymatic degradation, delivery vectors are essential for effective gene transfer. Cationic solid lipid nanoparticles (SLNs) have emerged as promising nonviral gene delivery vectors for systemic applications. These SLNs can directly bind with DNA and facilitate gene transfection. Genospheres, such as cationic SLNs, hold great potential for targeted gene delivery, typically carrying materials like plasmid DNA and other nucleic acids. Three key factors influence their effectiveness: the composition of cationic SLNs, their ability to condense DNA and their efficiency in transferring nucleic acids into cells. Additionally, nanostructured lipid carriers (NLCs) are considered a novel and effective nonviral gene transfer vector, offering a promising strategy for gene therapy.

Cosmetic applications

Lipid nanoparticles (LNPs), including solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), serve as excellent vehicles for cosmetic and dermatological applications. Their unique properties make them highly effective carriers in cosmetics, such as protecting sensitive compounds from chemical degradation and enhancing skin hydration. LNPs have been explored as delivery systems for sunscreens, anti-acne treatments and anti-aging actives.

Due to their ability to regulate the penetration of active substances into the skin, LNPs provide UV protection and improve skin moisture retention. In cosmetic formulations, minimizing itching and preventing skin damage are crucial factors. Because these lipid-based formulations closely mimic the skin's natural structure, they ensure compatibility, reducing the risk of irritation or toxicity when applied topical[43].

Table No.1: Comparison between SLN and NLC. Advantages and disadvantages[16]

S.No		SLN and NLC	
1	Lipids	Use of physiological lipids; however, there is a lower stability comparatively with other materials	
2	Solvents	Absence of organic Solvents	
3	Application	Application in different industries (food, cosmetic, pharmaceutical)	
4	Bioavailability	Improved bioavailability of drugs	
5	Drugs loaded	Loads both lipophilic and hydrophilic drugs; however, has difficulty in loading therapeutic proteins	
6	Drug delivery	Targeted drug delivery and enhanced drug permeation	
7	Scale-up	Cheaper and easier to scale-up then polymeric nanoparticles	
8	Protection	Protection of drug molecules from enzymatic activity, harsh pH and moisture	
9	Cytotoxicity	Cytotoxicity concerns due to the nature and concentration of matrix lipids	
10	Drug loading capacity	Limited drug loading capacity	Improved drug loading capacity
11	Controlled drug release profile	Difficulty in adjusting the drug release profile	Better controlled drug release profile
12	Polymorpic transitions	Prone to polymorpic transitions	No polymorpic transitions takes place
13	Release during storage	Unwanted drug release during storage	Minimal drug release during storage
14	Physical stability	Possible particle aggregation or fusion during storage	Better physical stability during storage
15	Water content	High water content	Low water content

Table No.2: Examples of studies performed using SLN. The nanoparticles components and features, loaded drug, production method and therapeutic purpose are debriefed

S.No	Solid-Lipid	Surfactant	Drug	Production Method	Therapeutic Purpose	Delivery Route	Charactertistics
1	Gelucire ^{o}50/13	Tween ^{o}85	Grapeseed-derived proanthocyanidins	Melt Emulsification Technique	Chronic Respiratory Diseases	Spray Instillation	Size: 243±24nm Pdl: 0.41 Zeta: -14.5±1.0mV EE: NA
2	Palmitic Acid/ Cholesteryl Myristate (68, 5/31, 5%) (w/w)	Sodium Lauryl Sulfate (SLS)	Rifampicin	Melt Emulsification Technique	Tuberculosis	NA	Size: 400±20nm Pdl: 0.43±0.09 Zeta: -35.3± 0.29mV EE: 56.48% (w/w)
3	Compritol 888 ATO, cholesterol and Tf-PEG-OA	1% Poly Vinyl Alcohol (PVA)	Paclitaxel (PTX)	Solvent Evaporation Method	Leukemia	NA	Size: 176nm Pdl: NA Zeta: -22.5±1.56mV EE: 92.5±1.35%
4	Tripalmitin/ Hydrogenated Soybean Phosphatidyl Choline (HSPC)	Polyethylene Glycol Monostearate (PGM)	Apomorphine	NA	Parkinson's Disease	Oral	Size: 63.20±0.98nm Pdl: 0 31±0.02 Zeta: -7.3±0.25mV EE: NA

	(80/20%) (w/w)						
5	Compritol °888 ATO	Tween °80	Quercetin	NA	Alzheimer's Disease	Oral	Size: 0.42 to 4.62µm Pdl: NA Zeta: -23.6 to -5.13mV EE: 85.7%
6	Beeswax	Tween °80 Poloxamer 407	NA	Hot melt microemulsion	Skin Hydration	Topical	Size: 95.72 ±9.63nm Pdl: 0.323±0.03 Zeta: -98.5±0.57mV EE: NA

Table No.3: Examples of studies performed with NLC. The nanoparticles' components and features, drug loading, production method and therapeutic purpose are debriefed

S.No	Solid Lipid	Liquid Lipid	Surfactant	Drug	Production Method	Therapeutic Purpose	Delivery Route	Charactertistics
1	Stearic acid	Oleic acid	Soya Lecithin Glyceryl Monostearate	Doce Ta-Xel (DTX)	Modified Film ultra-sonication-dispersion method	Murine Malignant Melanoma	Parenteral	Size: 203.67± 4.15nm Pdl: NA Zeta: -31.17±2.20mV EE: 89.39±0.99%
2	Precirol °ATO-5	Squalene	Myverol	Lovastatin	Hot melt homogenization	Cholesterol	Oral	Size: 278.8± 0.6nm Pdl: ≤0.25 Zeta: -32.4±0.4mV EE: 83.8±2.5
3	Comprito °888 ATO	Miglyol 812 N	Lecithin	Vinpocetin (VIN)	High-pressure homogenization	Brain Disorders	Oral	Size: 177± 5.4nm Pdl: NA Zeta: -24.7± 1.4mV EE: 95.3±1.4
4	Precirol ° ATO-5	Oleic Acid	Tween °80	1-carbaldehyde-3, 4 dimethoxyxanthone (LEM2)	Ultrasonication	Melanoma	Topical	Size: 219.67± 5.26nm Pdl: ≤0.3 Zeta: -24.88± 1.78mV EE: 72%
5	Cetyl Palmitate	Miglyol 812 N	Tween °60	Curcumin	Modified hot homogenization	Brain Disorders	Oral/ Intravenous	Size: 183± 12nm Pdl: 0.13±0.01 Zeta: -21.2 mV EE: 82±15%
6	Glyceryl Tribehenate	Oleic acid	P407	Raloxifene hydrochloride (RLX)	Hot homogenization	Osteoporosis	Oral	Size: 120± 3nm Pdl: 0.293 Zeta: 14.4±0.5mV EE: 91.71

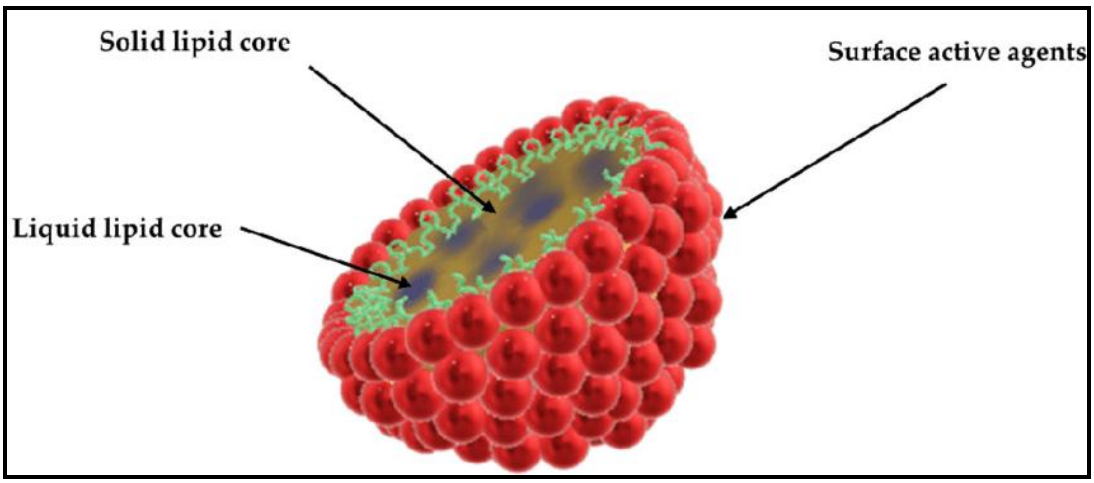

Figure No.1: Nanostructured Lipid Carrier

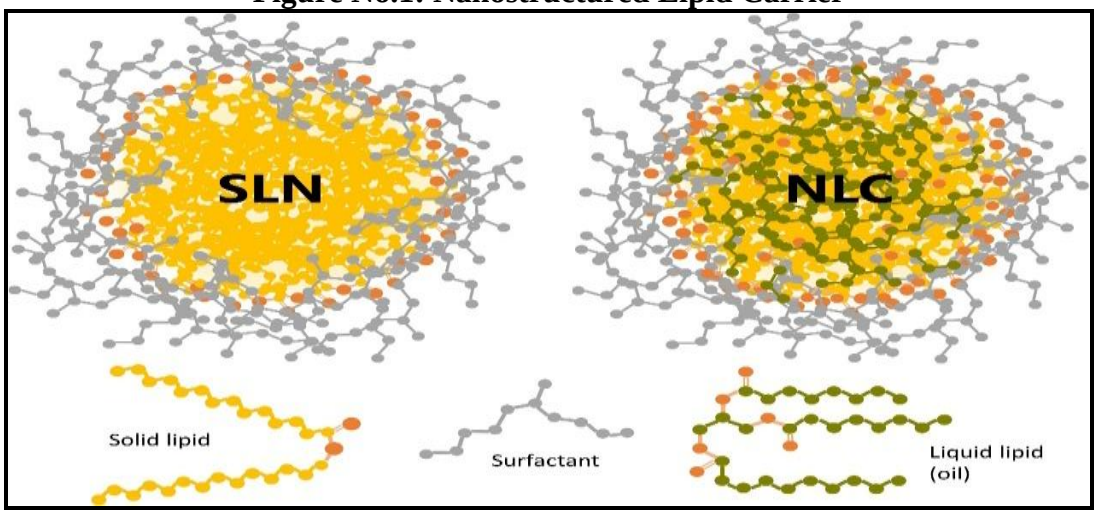

Figure No.2: Structural matrix of SLN and NLC

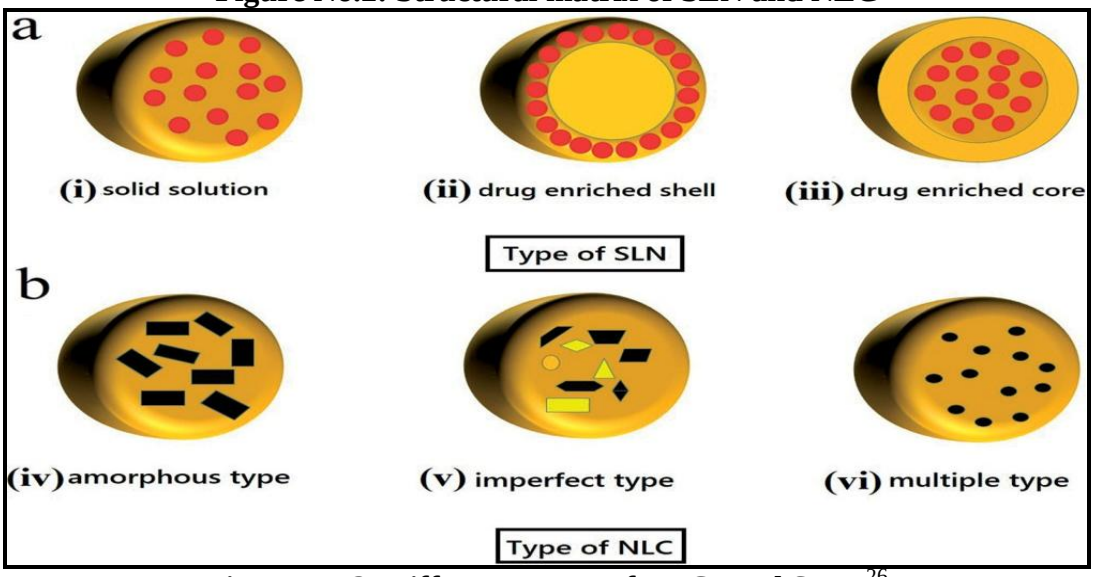

Figure No.2: Different Types of NLCs and SLNs[26]

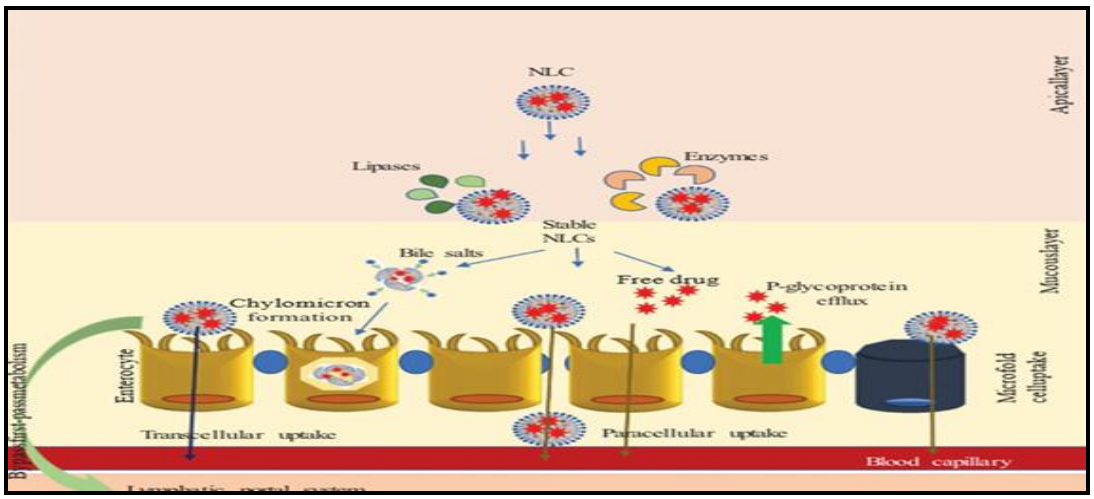

Figure No.3: The drug-loaded NLC absorption pathway via the intestinal wall

METHODS INVOLVED IN FORMULATION OF NLCs /SLNs

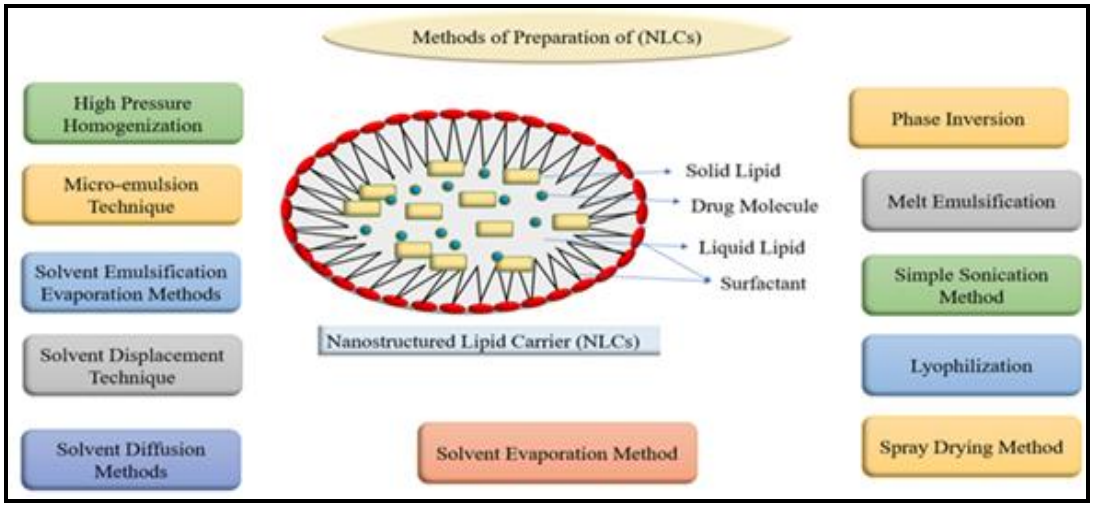

Figure No.4: Method of Preparation of Nanostructured Lipid Carrier (NLCs)

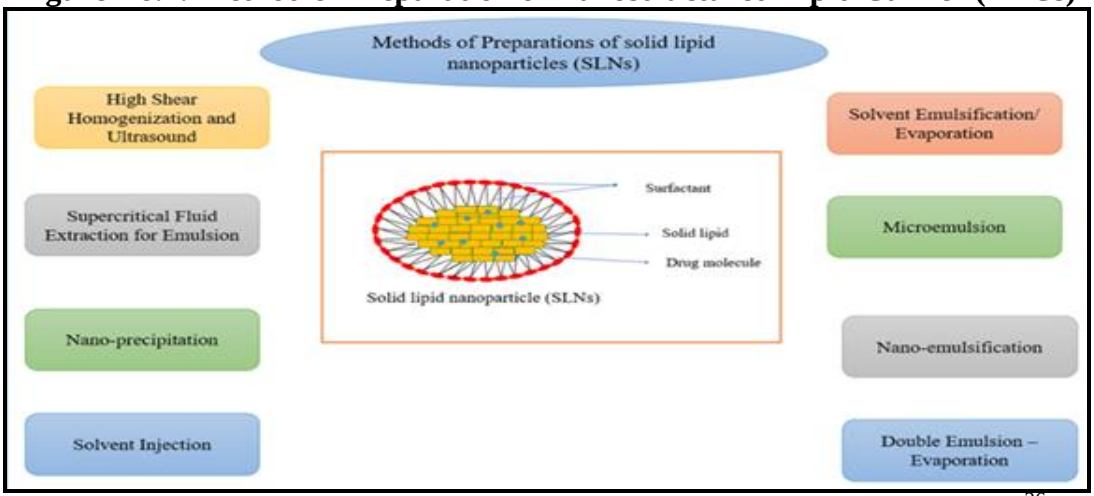

Figure No.5: Method of Preparation of Solid Lipid nanopartical (SLNs)[36]

CONCLUSION

Nanostructured Lipid Carriers (NLCs) and Solid Lipid Nanoparticles (SLNs) are innovative lipid-based drug delivery systems that improve bioavailability, stability and controlled drug release. NLCs, with their unique combination of solid and liquid lipids, offer superior drug loading capacity, enhanced permeability, and prolonged therapeutic effects, making them highly valuable in pharmaceuticals, nutraceuticals and cosmetics compare to SLN's. Their ability to bypass first-pass metabolism and cross biological barriers, such as the blood–brain barrier, makes them particularly promising for applications in cancer therapy, neurological disorders and gene delivery.

Beyond pharmaceutical applications, SLNs and NLCs are widely explored for oral and pulmonary drug delivery, gene therapy and skincare formulations. Their potential to enhance drug solubility, protect bioactive compounds and provide targeted delivery has revolutionized modern medicine. Despite challenges like cytotoxicity and scalability, continuous research and technological advancements are optimizing their formulations, paving the way for safer, more efficient and patient-friendly therapeutic solutions across various fields.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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