Advanced Nanocarriers for Drug Solubilization: A Focus on Lipid-Based Systems

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Abstract-Nanotechnology has revolutionized medicine, particularly through the advancement of nanomedicine, which has introduced innovative solutions in drug delivery systems. Among these, lipid-based Nano carriers have emerged as promising tools to enhance the solubility, stability, and bioavailability of poorly water-soluble drugs, such as those in the Biopharmaceutical Classification System Class II. These drugs, characterized by low solubility and high permeability, face significant challenges in formulation, primarily due to their poor aqueous solubility, which results in low oral bioavailability. Various strategies have been developed to Prevent these challenges, including solid dispersion and lipid-based systems like liposomes, solid lipid nanoparticles, and self-nanoemulsifying drug delivery systems. Liposomes, for example, are spherical vesicles that can encapsulate both hydrophilic and lipophilic drugs, offering a versatile platform for drug delivery. Furthermore, self-nanoemulsifying systems Enhance the solubility and bioavailability of lipophilic drugs by enhancing their dissolution rate and facilitating lymphatic transport. Another advancement is the use of nanostructured lipid carriers, which combine both solid and liquid lipids to improve drug loading and release properties. The development of these advanced Nano carriers, which include Solid Lipid Nano carriers, sphingolipid-based systems, has demonstrated significant potential in targeted therapy, including applications in cancer treatment and topical drug delivery. By improving drug stability, controlled release, and minimizing side effects, lipid-based Nano carriers represent a transformative approach to precision medicine, with broad implications for enhancing the effectiveness of existing and emerging therapies.

Index Terms—Nontechnology, Lipid Based Nanocarrier, Solubility Enhancement, Sphingolipid-based Nano carrier, Ionisable Lipid Nanoparticle

I. INTRODUCTION

Nanotechnology has revolutionized numerous industries, with its most notable impact in the fields of food, agriculture, and particularly medicine. In medicine, the introduction of nanotechnology has led to the development of Nano medicine, a cutting-edge field that encompasses a wide range of applications, from Nano-diagnostics and Nano-robotics to the design of advanced drug delivery systems based on nanoparticles [1, 2]. These innovations have the potential to significantly improve the precision and effectiveness of medical treatments, paving the way for more targeted and personalized healthcare solutions. Among the different types of Nano carriers being explored for drug delivery, lipid-based Nano carriers have gained substantial interest due to their excellent biocompatibility and functional versatility. This category includes liposomes, lipid micelles, solid lipid nanoparticles (SLNs), Nano emulsions, and Nano suspensions, all of which have unique structural and functional properties that make them suitable for a wide variety of therapeutic applications.

Liposomes, for instance, are one of the most well-established lipid-based carriers. These vesicular structures consist of phospholipid bilayers that encapsulate an aqueous core, which allows them to carry both hydrophilic and lipophilic compounds. This feature makes liposomes particularly effective in the delivery of a wide range of drug types, increasing the solubility, stability, and bioavailability of poorly soluble drugs [3].

Lipid nanoparticles (LNPs), another widely studied class of lipid-based carriers, typically range in size from 1 to 100 nm. These nanoparticles are particularly effective for delivering payloads such as small interfering RNA (siRNA) and other biologically active molecules. By protecting these fragile molecules from degradation in the bloodstream, LNPs enhance the stability and transfection efficiency of siRNA, enabling successful systemic administration and precise delivery to targeted areas, such as tumor sites. Furthermore, LNPs are capable of facilitating intracellular trafficking and promoting endosomal escape, which Promote the therapeutic potential of the encapsulated drug or genetic material [4]. As research in Nano medicine continues to revolve, lipid-based nanoparticles are expected to play an increasingly important role in the development of next-generation therapeutic strategies, offering novel solutions to previously challenging medical conditions.

II. APPLICATIONS OF LIPID-BASED DRUG DELIVERY SYSTEMS IN CANCER THERAPY

Lipid-based drug delivery systems, including liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), Nano emulsions, Nano suspensions, and Niosomes, have emerged as highly promising carriers in the field of oncology. While they all belong to the lipid-based category, each of these systems exhibits distinct structural and physicochemical properties that influence their performance, efficacy, and specific applications in cancer treatment [5]. Among the various lipid-based carriers, liposomes have been the most extensively studied and

widely utilized due to their unique ability to encapsulate a wide range of therapeutic agents. These spherical vesicles are typically composed of one or more layers of phospholipids, which form a bilayer structure that can enclose an aqueous core. Liposomes are characterized by their size and lamellarity, with small unilamellar vesicles (SUVs) typically measuring under 100 nm in diameter and large unilamellar vesicles (LUVs) exceeding 100 nm. These structural features are critical in determining their pharmacokinetic properties and impact their ability to interact with biological membranes, influence circulation time, and facilitate drug release [6,7]. One of the key advantages of liposomes in oncology is their ability to encapsulate both hydrophilic and lipophilic drugs, allowing for the delivery of a diverse range of therapeutic agents. Moreover, liposomes can be engineered for targeted drug delivery, enhancing the precision of treatment and minimizing off-target effects. The biodegradability, low toxicity, and capacity for functionalization of liposomes further enhance their appeal, as these features contribute to their safety and versatility in clinical settings. Additionally, liposomes can provide sustained drug release, which is particularly beneficial in cancer therapy, where prolonged exposure to drugs may improve therapeutic outcomes [8]. Given these attributes, liposomes and other lipid-based carriers represent a transformative approach in cancer treatment, offering potential solutions for improving drug delivery, enhancing bioavailability, and optimizing therapeutic efficacy. As research progresses, the development of these lipid-based systems will likely play a key role in advancing targeted and personalized cancer therapies.

III. LIPID-BASED DRUG DELIVERY IN TOPICAL THERAPY

In recent years, lipid-based colloidal carriers have gained significant attention for their role in transdermal drug delivery applications. These systems have shown remarkable efficacy in enhancing drug permeation through the skin, enabling the transport of both hydrophilic and lipophilic drugs across the stratum corneum. This feature allows for either localized or systemic drug delivery, depending on the specific therapeutic requirements [9]. The skin's epidermal layer, which is inherently rich in lipids, provides an ideal environment for lipid-based carriers, offering high compatibility and penetration efficiency. This synergy between the lipid composition of the skin and the lipid-based carriers significantly enhances their ability to deliver bioactive compounds effectively. These carriers' adaptability and capacity to incorporate a broad spectrum of bioactive molecules make them an excellent choice for topical drug delivery, facilitating both cosmetic and therapeutic applications.

Lipid-based Nano carriers have also made significant strides in cancer therapy, particularly in targeted delivery systems for lung, colon, and breast cancer. The last decade has seen an exponential rise in the use of liposomes for anticancer drug delivery, with their excellent biocompatibility and versatile properties driving the development of more advanced formulations. These include cationic liposomes, temperature-sensitive liposomes, virosomes, and archaeosomes, each designed to address specific challenges in drug delivery, such as targeting, controlled release, and minimizing side effects [10].

Liposomes, first introduced by Alec D. Bangham in 1965, were among the pioneering Nano systems used for drug delivery. These vesicles are classified based on their size and bilayer structure, which can range from small unilamellar vesicles (300–500 Å) to large unilamellar vesicles (500–1000 Å), and multilamellar vesicles (1–5 μm) with multiple concentric phospholipid bilayers [11]. Their ability to encapsulate both hydrophilic and lipophilic drugs, combined with their biocompatibility and ability to be functionalized for targeted delivery, has made liposomes a cornerstone of advanced drug delivery strategies. Over time, innovations in liposome technology have allowed for the precise delivery of therapeutic agents to specific tissues, thereby improving the efficacy and reducing the toxicity of cancer treatments. These developments underscore the growing potential of lipid-based Nano carriers in revolutionizing cancer treatment and other areas of medicine.

Revent studies have investigated surface types of nanoparticles for both stealth and active coating purposes, as summarized in Table 1 modifications of various

Table No.1 surface types of nanoparticles for both stealth and active coating

Types of Nanoparticles	Types of Surface Modification	Nanoparticle	Surface Modifier	Outcome	Reference
Polymeric Nanoparticle	Stealth Coating	Polubutylcynoacrylate Nanoparticle	Chitosan	Enhance Nanoparticle Stability	Lin.et.al. (2021) (12)
	Active Coating	Chitosan Nanoparticle	PEG	Enhance Nanoparticle Stability and Prolonged blood Circulation	Deng.et.al (2021) (13)
		PLGA Nanoparticle	Folic Acid	Improve Cellular uptake into Tumour Cells	Barnaud et.al (2024) (14)
		Polymeric Micelle	Cyclic Arginine-glycine aspartic acid	Improve Cellular uptake into Tumour Cells	De. Lorengi et.al (2023) (15)
Lipid Nanoparticle	Stealth Coating	Liposome	Chitosan Grafted Poluhydroxy Polymers	improved Circulation time in vivo	Miao at .al (16)

		Lipid Nanoparticle	Albumin	Enhance solubility in serum and reducer nonospecific cell Interaction	Notabi et al. (17)
	Active Coating	Solid Lipid Nanoparticle	Polyoxyethylene steryl ether grafted PEG	Improved Cellular uptake	Balenzano et al. (18)
		Liposome	Cholesteryl acetyl carnitine	Improved Cellular Uptake	Zahednezhad et al. (19)
		Cubosome	Hyaluronic acid	increase cytotoxic activity on cancer cell	Nisha et al. (20)

IV. TYPES OF LIPIDS BASED NANO CARRIERS

The term lipid-based Nano carriers encompass several nanostructured systems including liposomes, Nano emulsions, Nano capsules, and self-Nano emulsifying drug delivery systems (SNEDDS) [21]. These systems have proven advantageous in improving the solubility, stability, and bioavailability of drugs with challenging properties.

1. Liposomes

Liposomes are spherical Nano carriers formed by lipid bilayers surrounding an aqueous core. Typically made from phospholipids and cholesterol, these structures offer membrane-stabilizing effects and support both lipophilic and hydrophilic drug loading [22]. Their high biocompatibility enhances cellular uptake, and they are capable of carrying amphotericin B, silymarin, fenofibrate, dapsone, budesonide, and artemisinin [23, 24]. Drug encapsulation in liposomes can occur in three compartments: the aqueous core (for water-soluble drugs), the lipid bilayer (for lipid-soluble drugs), and the lipid-aqueous interface (for peptides and small proteins) [25]. An example of a highly lipophilic drug effectively delivered using lipid-based systems is Efavirenz (EFA), a non-nucleoside reverse transcriptase inhibitor (NNRTI) with a, indicating strong lipophilicity [26]. Liposomes are mostly made up of phospholipids, which are amphiphilic molecules with a hydrophilic head and two polar hydrophobic chains. Because of their amphipathic character, phospholipids have a strong inclination to form membranes when distributed in aqueous solutions. They can entrap both lipophilic and hydrophilic substances in the lipid membrane and the watery core, respectively [27]. Despite massive research and development efforts on liposomes, only a few liposomal products have been authorized for human use thus far. This might be due to a variety of factors, including the toxicity of some liposomal formulations, poor entrapment of molecules

and chemicals into liposomes, the instability of the liposomal carriers, and the high expense of liposome manufacture, particularly on large quantities [28].

2. Self-Nano emulsifying Drug Delivery Systems (SNEDDS)

SNEDDS are isotropic mixtures of oils, surfactants, and co-surfactants that spontaneously form oil-in-water Nano emulsions upon dilution in the gastrointestinal fluids under mild agitation. They improve the solubility of lipophilic drugs by:

- Maintaining drugs in a solubilized state,
- Enhancing surface area through Nano-droplet formation,
- Facilitating lymphatic transport.

SNEDDS has significantly enhanced the bioavailability of BCS Class II drugs such as ritonavir and celecoxib [29] the oral delivery of BCS Class II drugs, which are typically characterized by poor aqueous solubility and high permeability, presents a persistent challenge in pharmaceutical formulation. To address this, Self-Nano emulsifying Drug Delivery Systems (SNEDDS) have emerged as a highly effective lipid-based strategy to enhance the solubility and absorption of these drugs. The mechanism behind SNEDDS is rooted in their ability to keep the poorly soluble drug in a solubilized state throughout its passage in the gastrointestinal tract. This not only enhances the drug's dissolution profile but also helps prevent precipitation. Moreover, SNEDDS facilitate lymphatic transport of lipophilic drugs, thereby bypassing hepatic first-pass metabolism and further improving systemic bioavailability [30].

3. Solid Lipid Nanoparticles (SLNs):

Solid lipid nanoparticles (SLNs) are an innovative drug delivery system designed to enhance the solubility and bioavailability of poorly water-soluble drugs. These nanoparticles are composed of biocompatible lipids and surfactants, which stabilize the drug and enhance its therapeutic efficacy. SLNs have been shown to increase drug solubility, cellular uptake, and stability, while reducing enzyme degradation and prolonging circulation time, making them a promising approach for drug delivery across various administration routes. The following sections detail the mechanisms and benefits of SLNs in enhancing drug solubility.

Mechanisms of Solubility Enhancement

- Lipid Matrix Composition: SLNs utilize a solid lipid matrix that can encapsulate both hydrophilic and lipophilic drugs, enhancing their solubility and stability [31]

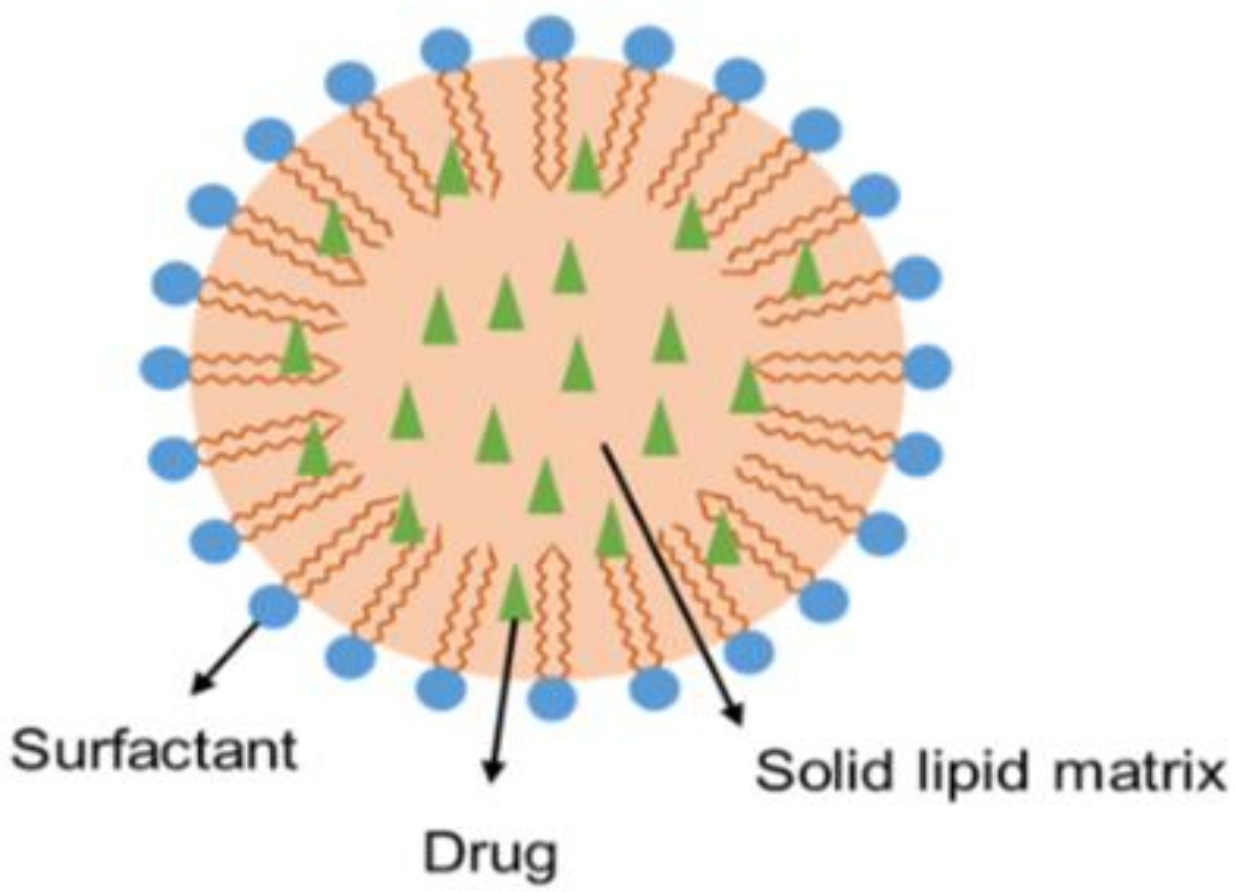

Figure. No 1. Solid Lipid Nanoparticle

SLN can be prepared by a variety of technologies including heat or cold homogenization, which is easy to scale up production, has good preparation repeatability and does not require toxic organic solvents in the preparation process [32]. SLNs can be orally administered as aqueous dispersions or in the dosage forms of capsules, tablets, and pellets [33]. SLN have many advantages like easy manufacturing, the stability of pharmaceuticals, increased drug content, effective release of drug and high long-term stability. Additionally In terms of drug delivery, SLN system can efficiently encapsulate antitumor drugs and other substances with poor water-solubility due to its high lipid content [34]. Solid lipid nanoparticles enable the delivery of both hydrophobic and hydrophilic molecules, so they have shown great potential to enhance the oral bioavailability of a wide variety of molecules, including anti-tumour drugs, e.g., paclitaxel or docetaxel [35]. Solid lipid nanoparticles enabled to improve both pharmacokinetic and pharmacodynamics profiles of cilnidipine after oral administration to rats, compared with free drug. Concretely, oral area under the curve (AUC) was 2.4-fold increased and a 38% decrease in systolic blood pressure was achieved, maintaining more than a 20% decrease for 64 h, compared with free cilnidipine [36]

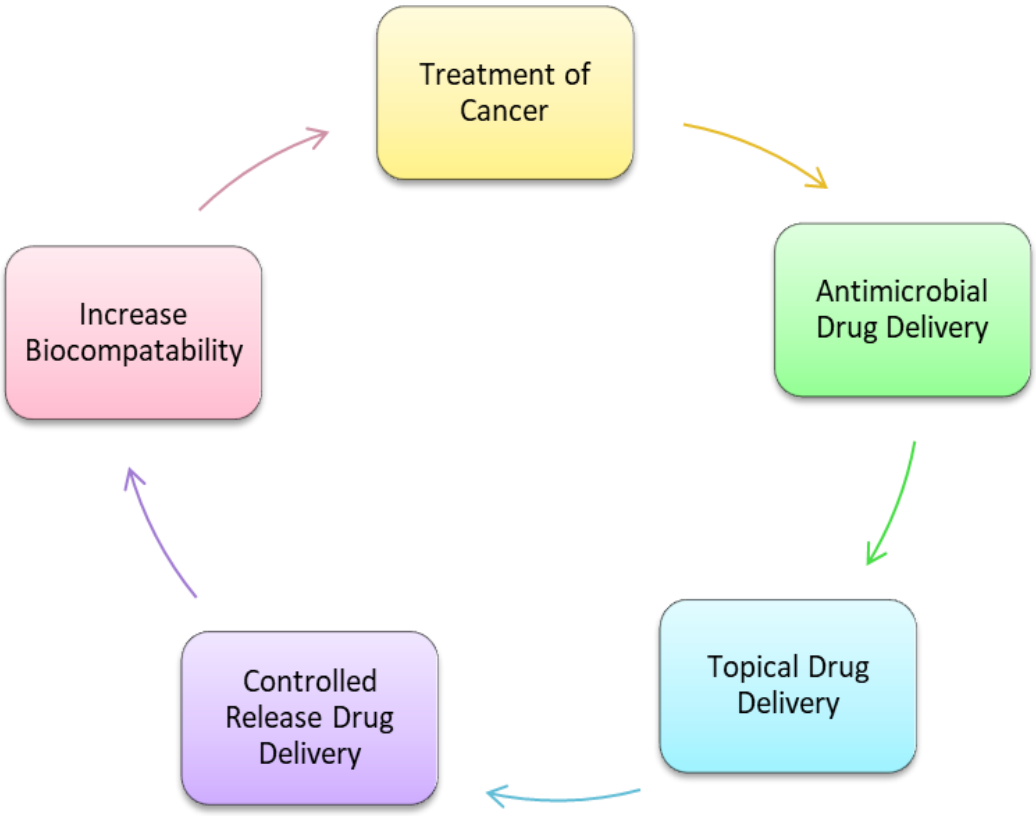

Figure. No 2. Application of Solid Lipid Nanoparticle [36]

4. Nanocarriers:

Based on Polymers Branches: In general, polymers are made up of multiple linear and branched co-polymers or cross-linked polymer networks. The physical and chemical changes in the polymer in response to external factors like pH and temperature provide them with distinctive features [37] Polymer-based Nano carriers have tree-like structures and consist of hyper branched polymers, dendrigrafts, Dendron's and dendrimers. Each of these four classes reflects the structural features of these complex macromolecular architectures [38]

5. Nano emulsion:

Nano emulsions, referred to as dispersed systems with ≤100 nm droplets, are gaining importance in healthcare and cosmetics sectors as a result of the unique properties of Nano sized droplets, such as high surface area [39]. The small-sized droplet with a high surface area makes Nano emulsions important in many industries [40] Nano emulsions are dispersions of an oily and an aqueous phase stabilised by an appropriate surfactant or combination of surfactants with size values over 100 nm [41] The different preparation methods to obtain Nano emulsions can be classified into high-energy or low-energy approaches. High-energy methods, such as ultrasonic homogenisation or micro fluidisation, usually entail high formulation temperatures, what may limit their use of thermo labile molecules like peptides [42] SNEDDS, in particular, form fine emulsions upon contact with gastrointestinal fluids, significantly enhancing the solubilisation and absorption of lipophilic drugs

[43]. The small particle size of lipid-based Nano emulsions increases the surface area available for drug dissolution, which is crucial for enhancing solubility [44] the research indicates that these formulations effectively improve the delivery of drugs like Fucoxanthin and Ramipril, which are used for obesity and hypertension. By utilizing emulsification and ultra-sonication methods, the study demonstrated that lipid nanoparticles can overcome challenges related to low drug solubility and enzymatic stability, thereby facilitating better therapeutic outcomes.[45]

6. Nanostructured Lipid Carriers (NLCs):

The purpose of NLCs, also known as the second generation of LBNPs, is to get around the drawbacks of SLNs. They are classified as colloidal drug delivery systems because their core matrix contains both liquid and solid lipids [46]. NLCs as the name suggest are Nano sized multiarticulate system in the size range of 50 nm to 500 nm. The particle size distribution of NLC depends on nanoparticles manufacturing process and composition [47]. It was once thought that these second-generation lipid nanoparticle systems could only load lipophilic medications, making it difficult to load water-soluble ones. To solve this issue, lipid-drug conjugates were later developed, and NLCs are still the ideal method for loading hydrophilic pharmaceuticals [48]. SLN has gained a lot of popularity amongst researchers due to their applicability for various routes, site specificity and controlled drug delivery with less side effects. Some challenges with these include low drug loading, drug expulsion during storage. These limitations can be overcome with NLC which are the second-generation lipid carriers offering advantages of improved drug loading capacity and better release properties of poorly soluble drugs mainly due to their imperfect structure, the stability of bioactive compounds, enhanced shelf-life, functionality, costumer acceptability and controlled release of encapsulated materials. SLNs use only one form of lipid which is a solid lipid that orients the drug between the fatty acid chains of glycerides [49]. The lipid Nano carrier-filled hydrogel delivery system, an emerging innovation derived from conventional hydrogel delivery systems, has garnered increasing attention in recent years. This system effectively addresses the stability of lipid Nano carriers and enables hydrogels to serve as a delivery system for hydrophobic active ingredients. Lipid Nano carriers, such as emulsions and lipid nanoparticles, suffer from flocculation and coalescence during storage due to Brownian motion.

Immobilizing these carriers within the hydrophilic polymer network of hydrogels effectively restricts their mobility, thereby enhancing system stability [50] SLNs and NLCs have emerged as novel systems composed of physiological lipid materials suitable for topical, dermal and transdermal administration. These carrier systems exhibit many features of lipid nanoparticles attracting major attention as novel colloidal drug carriers for topical use. SLN has gained a lot of popularity amongst researchers due to their applicability for various routes, site specificity and controlled drug delivery with Fewer side effects. Some challenges with these include low drug loading, drug expulsion during storage. These limitations can be overcome with NLC which are the second-generation lipid carriers offering advantages of improved drug loading capacity and better release properties of poorly soluble drugs mainly due to their imperfect structure, the

stability of bioactive compounds, enhanced shelf-life, functionality, consumer acceptability and controlled release of encapsulated materials. SLNs use only one form of lipid which is a solid lipid that orients the drug between the fatty acid chains of glycerides [51]

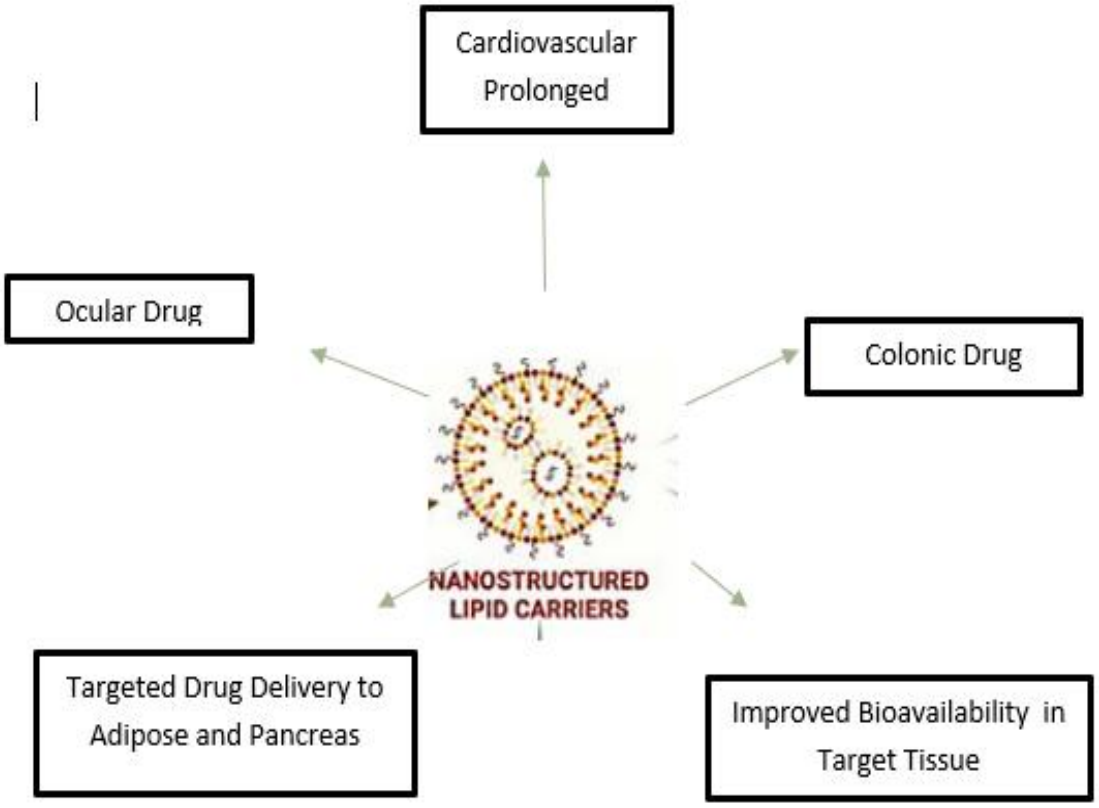

Figure. No 3. Application of Nanostructured Lipid Carrier [51]

7. Sphingolipid-based Nano carrier:

Sphingolipids (SL) are well recognized for their cell signalling through extracellular and intracellular pathways. Based on chemistry different types of SL are biosynthesized in mammalian cells and have specific function in cellular activity. SL has an amphiphilic structure with have hydrophobic body attached to the polar head enables their use as a drug delivery agent in the form of Nano carriers. SL-based liposomes can improve the solubility of lipophilic drugs through host and drug complexes and are more stable than conventional liposomal formulations. Preclinical studies of SL Nano carriers are reported on topical delivery, oral delivery, ocular delivery, chemotherapeutic delivery, cardiovascular delivery and Alzheimer's disease. The commercial challenges and patents related to SL Nano formulations are highlighted in this article.[52].

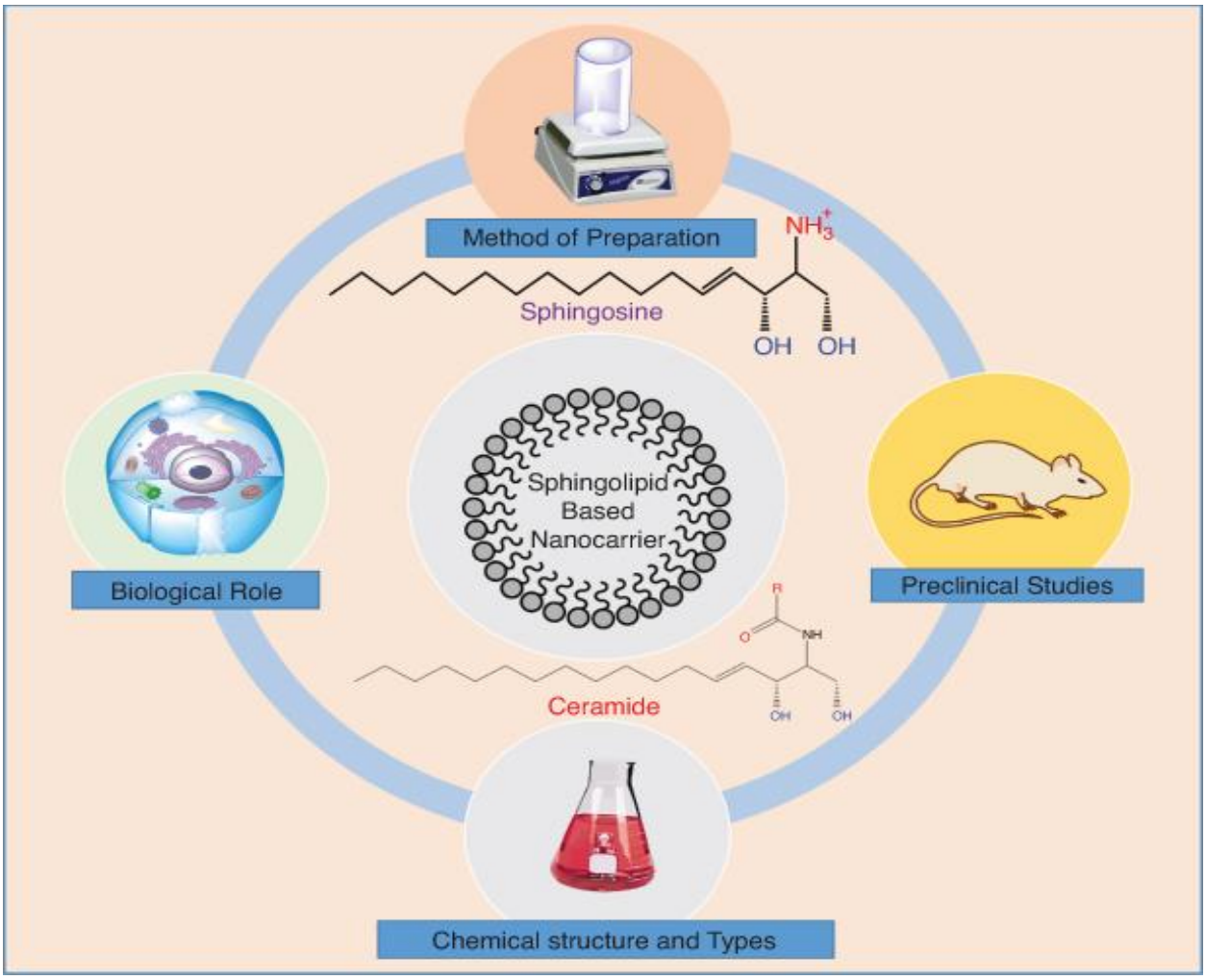

Figure.No4. Chemical structure and type of Nano carrier [53]

SL-based liposomes can improve the solubility of lipophilic drugs through host and drug complexes and are more stable than conventional liposomal formulations. Preclinical studies of SL Nano carriers are reported on topical delivery, oral delivery, ocular delivery, chemotherapeutic delivery, cardiovascular delivery and Alzheimer's disease [51]. Short-chain sphingolipids are known to enhance cellular uptake of amphiphilic drugs. We hypothesized that short-chain sphingolipids could be utilized to further improve intracellular drug delivery from a thermos responsive formulation by enhancing the cell membrane passage of released drug.

The following two strategies were investigated:

(1) Co-delivery of C8-glucosylceramide and doxorubicin within the thermosensitive liposomes and

(2) Pre-treatment with glucosylceramide-enriched drug-free liposomes and subsequent treatment with doxorubicin loaded thermosensitive liposomes.

Liposomes were prepared and extensively characterized. Drug uptake, cell cytotoxicity and live cell imaging were performed under normothermic and hyperthermic conditions in melanoma cells. In these studies, hyperthermia improved drug delivery from doxorubicin loaded thermosensitive formulations. [52]. Sphingolipid-based Nano carriers are biocompatible and biodegradable, making them safe for use in drug delivery systems. Their biocompatibility reduces the risk of adverse effects, while their biodegradability ensures that they can be metabolized by the body without causing long-term toxicity [53]. The ability to modify the surface of sphingolipid-based Nano carriers with targeting ligands allows for site-specific drug delivery. This targeted approach can enhance the efficacy of drugs by ensuring that they are delivered directly to the site of action, reducing systemic side effects [54].

8. Niosomes:

Niosomes, or NSVs, are non-ionic surfactant-prepared vesicles. In terms of structure and physical features, niosomes are comparable to liposomes. They are created as unilamellar or multilamellar vesicles using the same techniques and under the same circumstances.[55] Niosomes are made up of two sorts of components: non-ionic surfactants and additions. The vesicular layer is formed by non-ionic surfactants, and the additions utilized in niosome production include cholesterol and charged molecules.[56] The hydrophobic portions of the molecule are orientated away from the aqueous solvent in this closed bilayer form, whilst the hydrophilic head is in contact with the aqueous solvent. It is similar to phospholipid vesicles in liposomes and hence allows for the trapping of hydrophilic medicines. Non-ionic surfactants have been exploited as alternatives to phospholipids due to their low cost, stability, and simplicity of storage.[57] Various procedures are used to manufacture niosomes for medication administration and gene therapy vectors. Furthermore, for specialized purposes, they might be coated with various types of agents such as polyethylene glycol (PEG), hyaluronic acid (HA), antibodies, and so on to improve targeting, increase circulation, and target obtaining time [58]. Niosomes have been intensively explored in recent years for their potential to function as a carrier for the transport of medicines, antigens, hormones, and other bioactive molecules. Aside from that, niosomes have been employed to tackle medication insolubility, instability, and fast degradation [59].

9. Ionisable Lipid Nanoparticles:

In recent years, nucleic acid-based gene therapy has been widely concerned and applied in the treatment of cancer, genetic diseases, and other diseases [60]. Ionisable lipid nanoparticles (LNPs) are the most clinically advanced Nano-delivery system to maintain the stability of therapeutic nucleic acids [61]. And achieve effective delivery into cells for gene regulation [62]. LNP is positively charged at acidic pH, where it binds well with negatively charged nucleic acids. It is neutral in blood (physiological pH environment) and can reduce the toxic effects of cationic lipids. LNP can be internalized by cells through endocytosis, and then release the drugs into the cytoplasm through endosomal escape, which plays an in role in the intracellular function of mRNA, not only protecting mRNA from degradation, but also allowing nucleic acid to enter cells. Early nucleic

acid delivery systems relied on permanently cationic-charged lipids, but their use was limited by cytotoxicity concerns, mainly as they activate several cellular pathways, such as pro-apoptotic and pro-inflammatory cascades [63]. This led to the development of ionisable lipids, which switch from a positive charge in acidic pH (favouring their interaction with negatively charged mRNA) to neutral in physiological pH. Therefore, LNPs are formed at an acidic pH and then subjected to buffer exchange to achieve a pH of 7.4. Upon administration, LNPs are endocytosed, and the tertiary amine of the ionisable lipids is protonated to form a quaternary ammonium ion in the acidic environment of the endosome (pH ~4). Protonated ionizable lipids interact with anionic lipids of the endosome membrane, and this electrostatic interaction disrupts the endosomal membrane, releasing mRNA into the cytosol. The effectiveness of ionizable lipids is often linked to their pKa and 3D structural properties. The pKa of LNPs should be sufficiently high to achieve protonation in acidic environments and sufficiently low to carry a smaller positive surface charge at physiological pH, minimizing toxicity [64]. The optimal pKa range of ionizable lipids to elicit an adaptive immune response *via* the intramuscular route [65]. Inclusion of PEGylated lipids within the LNP formulations offers steric stability to LNPs, which is crucial for particle integrity. Typically, 1.5 mol% of PEG lipid is used in clinically approved LNPs [66]. The PEG lipid content can affect LNP characteristics, such as the number of mRNA copies per LNP [67]. The length of the lipid tail of the PEG lipid also dictates the expression profile by affecting the desorption rate of the PEG chain [68]. After LNPs enter the body, it is proposed that the PEG chain needs to be released (*via* desorption) from the LNPs so that the LNPs can be internalized into the cells. The number and length of hydrophobic chains.

Table No.2.Drug Solubility &Their Challenges Overcome by Nanocarrier Type

Drug Example	Category	Solubility Challenges	Nanocarrier Type	Mechanism of Solubility Enhancement	Key outcome	Reference
Paclitaxel (PTX)	Anticancer (various)		Albumin-bound nanoparticles (e.g., Abraxane®), Polymeric nanoparticles/micelles, Liposomes, SLNs, NLCs	Nanocrystal formation (Abraxane), Encapsulation in hydrophobic core (polymers, lipids), Reduced particle size, Altered surface properties	Nanocrystal formation (Abraxane), Encapsulation in hydrophobic core (polymers, lipids), Reduced particle size, Altered surface properties	70
Curcumin	Anti-inflammatory, Antioxidant,	Extremely poor aqueous solubility	Liposomes, SLNs, NLCs, Polymeric Nanoparticl	Encapsulation in hydrophobic core, Protection from degradation,	Encapsulation in hydrophobic core, Protection from degradation, Increased surface	71

	Anticancer		es, Nanoemulsions	Increased surface area for dissolution, Amorphization within matrix	area for dissolution, Amorphization within matrix	
Amphotericin B (AmB)	Antifungal (systemic)	Very poor aqueous solubility & stability; rapid metabolism	Liposomes (e.g., AmBisome®), Lipid complexes (e.g., Abelcet®)	Liposomes (e.g., AmBisome®), Lipid complexes (e.g., Abelcet®)	Encapsulation within lipid bilayer/matrix, reducing free drug concentration, altered biodistribution to fungal sites, reduced toxicity.	72
Ritonavir	Antiviral (HIV protease inhibitor)	Extremely poor aqueous solubility, high toxicity in conventional form	Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)	Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)	Maintaining drug in solubilized state within nano-droplets upon dispersion in GI fluid, enhanced surface area, facilitated lymphatic transport.	73
Vericonazole	Antifungal	Low aqueous solubility (BCS Class II)	Nanoparticle	Nanoparticle	Improve in Solubility& and Dissolution rate	74
Dexibuprofen		Low Bioavailability and Toxicity	PLGA nanoparticles		PEG increased interaction with corneal membrane; improved drug release for ocular inflammation	75

V. CONCLUSION

the use of biocompatible and biodegradable lipids, these lipid-based Nano carriers have gained tremendous interest during the past two decades. Lipid Nano carriers are preferred over polymeric nanoparticles. Lipid nanoparticles can resolve the challenges associated with polymeric nanoparticles, such as cytotoxicity and lack of suitable methods for large-scale production. Lipid nanoparticles can substantially improve the solubility, bioavailability, pharmacokinetic parameters, intestinal absorption, skin penetrability, and ocular residence time of drugs which

helps the molecule to cross the physiological barriers and decrease its side effects. Thus, these drug delivery carriers demonstrate significant potential in pharmaceutical or medical applications.

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