IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

"Nanostructural Lipid Carriers (NLCs) As Promising Approach For Enhancing Drug Delivery In Novel Drug Delivery System (NDDS): A Systematic Review"

Mr. Abhishek R. Kale[1], Mr. Abhijit K. Banait[2], Miss. Aditi D. Jamankar[3], Mr. Achyut R. Kandalkar[4], Prof. Yashkumar A. Meshram[5]

Jagadambha Institute of Pharmacy & Research Kalamb, Maharashtra 445401, India [1,2,3,4,5]

ABSTRACT

Nanostructural lipid carriers (NLCs) are an alternate generation of lipid carriers. They've emerged as a promising class of medicine delivery systems to overcome some of the downsides of traditional formulations. NLCs offer a unique lipid matrix structure composed of both solid and liquid lipids, enhancing their medicine loading capacity, stability, and controlled release characteristics. Currently, a variety of DDS are available, which increases the medications' bioavailability in various environments and circumstances as well as their solubility in a variety of media. NLCs are a unique type of DDS that may produce concentrated dispersions and are stable in a variety of conditions. NLCs have been used in various drug delivery applications, such as oral, parenteral, optical, pulmonary, nose-to-brain, excrescence targeting, and transdermal medicine delivery. NLCs were created to address issues with solid lipid nanoparticles and are used in a variety of therapeutic methods. NLCs were originally allowed of for the delivery of lipophilic drugs, but it's now clear that they're also suitable for hydrophilic drugs.

The emergence of lipids as a viable drug delivery system is due to their biocompatibility. It was discovered to retain better lipid rates than other lipid compositions. In terms of designs, styles of manufacture, characterization, stability, and benefits over first-generation lipid nanoparticles, the major emphasis of the article is to give a comprehensive review of NLC's types, advantages, characteristics, components, method of preparation, application by different routes, biosafety & toxicology, latest advances, and future perspectives.

Keywords: Nanostructural Lipid Carrier (NLCs), Solid Lipid Nanoparticle (SLN), Drug Delivery System (DDS), Nanoparticle

1. INTRODUCTION

A completely novel type of nanoscale drug delivery system known as Nano-structural lipid carriers (NLCs) has the potential to improve the stability, solubility, and bioavailability of many medicines and bioactive substances.[1] NLCs have a liquid lipid layer around a solid lipid core, creating a heterogeneous matrix that can hold many kinds of molecules.[2] In terms of biocompatibility, scalability, adaptability, and cost-effectiveness, NLCs outperform alternative nanocarriers like liposomes, solid lipid nanoparticles, and polymeric nanoparticles in a number of ways. I'll go through the current state of the art for NLCs, their preparation procedures, characterization methods, and applications in many medical and biotechnology domains, as well as the difficulties and openings for future research and development. The composition of nanostructured lipid carriers (NLC) is depicted in figure 1.

History

Solid lipid nanoparticles (SLN), initially produced and named by two scientist s, M. Gasco from Italy and R.H. Müller from Germany, in the 1990s, were created to eliminate the use of organic solvents in the production of polymeric nanoparticles.[3] Because it offered greater stability than liposomes (previously created), solidified at body temperature to limit drug release, and was free from the harmful effects brought on by the use of organic solvents, SLN became one of the most popular systems.[4] Nanostructured lipid carriers (NLCs) are a second generation of lipid nanoparticles that overcome the shortcomings of the original generation (SLN).[5]

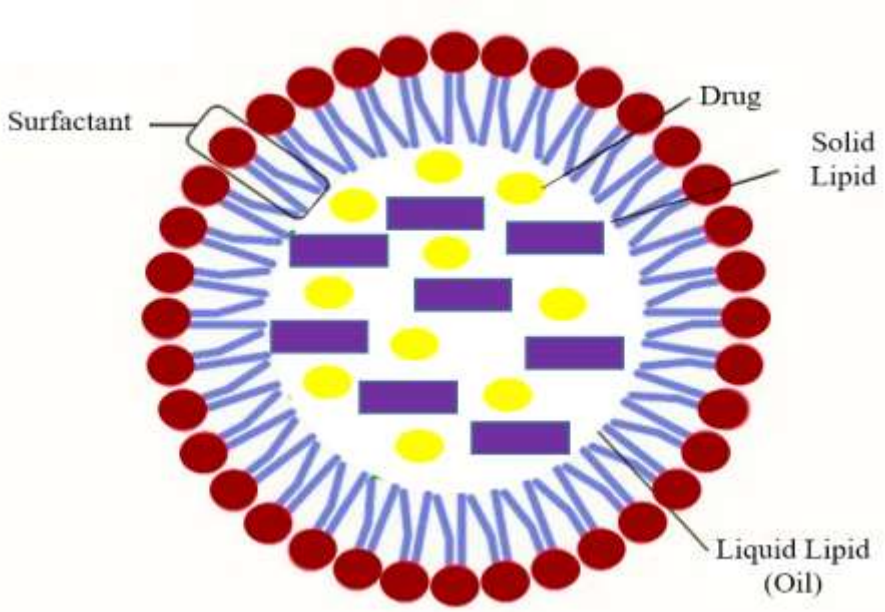

Figure No. 1: Schematic representation of 'Nanostructured lipid carriers' (NLC)

2. NLC's Types

Based on the nanostructure, content, and ratios of solid and liquid lipids, NLC has been divided into three types.

a) Type I (The imperfect type)
b) Type II (The multiple O/F/W type)
c) Type III (The amorphous type)

2.1) Imperfect Crystal Type NLCs

NLC class-I, also called imperfect crystal types, have a poorly structured solid matrix; that's why they were named Imperfect Crystal NLC. This type of NLC consists of a largely disordered matrix with numerous voids and spaces that can accommodate further drug molecules in unformed clusters. These defects in the crystal order are acquired by mixing solid lipids with an acceptable quantity of liquid lipids (oils)[6]. Glycerides are one type of fatty acid that may be employed to enhance or alter the structure. The total number of flaws in the structure is responsible and also helpful for the property of a good drug, which can be fluently increased due to the varying chain length of fatty acids and the mixture of mono-, di-, and triacylglycerol's. The matrix of NLC isn't suitable to form a largely ordered structure.

Mixing spatially different lipids increases drug payload capacity however this model offers minimum entrapment efficiency [7, 8].

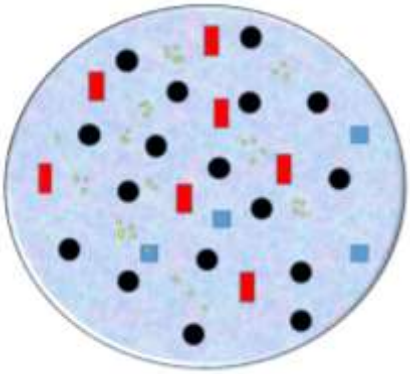

Figure 2: Imperfect NLCs

2.2) Multiple Type NLCs

Oil, lipid, and water types make up the second type of NLC, or "multiple" type. This idea leads to the creation of several types of NLC since liquid lipids have a higher solubility for lipophilic drugs than solid lipids do with a high liquid lipid concentration. The lipid matrix effectively spreads small amounts of oil molecules. Oil that is added in excess of its solubility causes phase separation, creating tiny oil Nano compartments ringed by the solid matrix. Benefits of type II models include high drug entrapment efficiency, controlled drug release, and less drug leakage. [8-9]

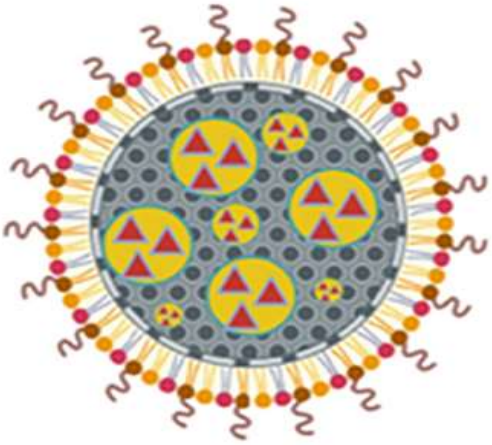

Figure 3: Multiple Type NLC's [9]

2.3) Amorphous Type NLCs

The third type of NLC is amorphous, which differs from ordinary crystalline NLCs in that it does not include lipid nanoparticles with definite crystalline structures but rather has an undefined crystalline structure and a disordered lipid matrix. These lipid-based nanocarriers are given special properties and advantages by their amorphous structure.

To prevent drug leakage as a result of crystallization, lipids are carefully combined to create amorphous-type NLC. Some lipids, including hydroxyl octacosanyl, hydroxyl stearate, isopropyl myristate, and dibutyl adipate, produce solid but non-crystalline particles. The lipid matrix is homogeneous and amorphous in nature.[7-11]

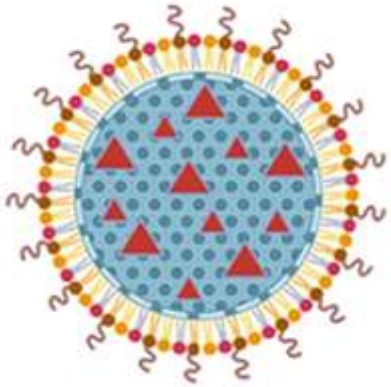

Figure No. 4: Amorphous Type NLC's [9]

3. Morphology of NLCs

Dynamic light scattering (DLS), Electron Microscopic Techniques (EMT), and Atomic Force Microscopy (AFM) are commonly used to obtain reliable information about the morphology and structural properties of Nano carriers for the characterization of nanoscale drug delivery systems also in research of NLC's. A technique like DLS provides information about the volumetric mean diameter of the particles. For NLC's, the factors affecting the preservation of structural integrity are the same for transmission electron microscopy (TEM) and scanning electron microscopy (SEM). Shrinkage of Nano systems can occur due to sample dehydration, and drying can cause structural changes, typically resulting in electron microscopic images that do not match the original morphology of the preparation.[12 -15]

In addition, in conventional electron microscopy, the use of surfactant solutions is prone to artifacts, which complicates the interpretation of the resulting images. Methods based on cryofixation can help overcome these major drawbacks.[16] Cryo-electron microscopy was developed to analyze the native structure of the nanocarrier in the frozen-hydrated state and to preserve the original morphology of the hydrated nanosample. It was successfully used to study the structural properties of NLCs. In addition, it is possible to obtain information about the internal structure of the nanocarriers (e.g., oil droplets inside the NLC). The AFM technique does not require previous sample preparation, and it is possible to measure nanoparticles in suspension, avoiding artifacts or changes in nanoparticle morphology.[17] Figure no.5 illustrates different NLC-based formulations' images obtained by AFM, TEM, Cryo-TEM and size and zeta potential distribution measured by DLS.

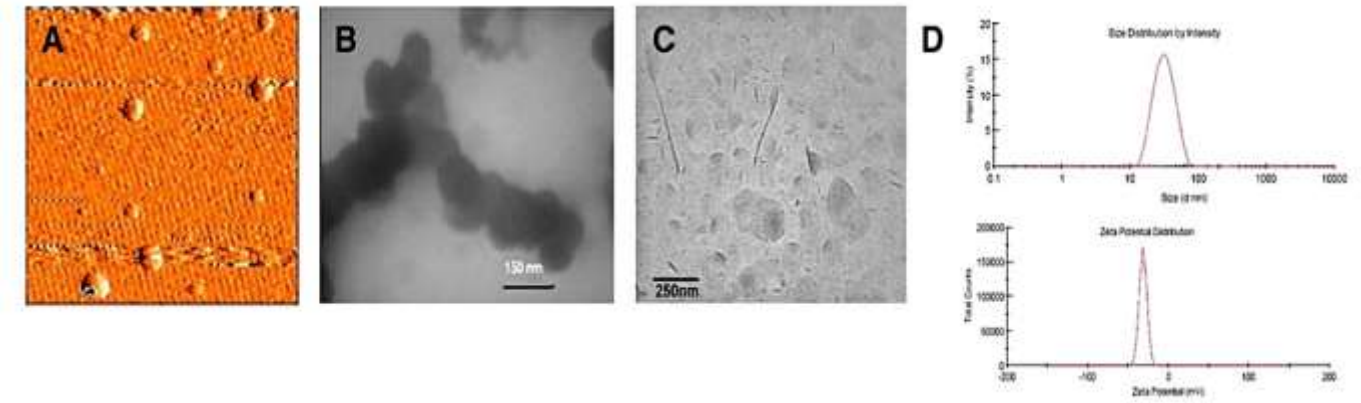

Figure 5: AFM (A) and TEM (B) images of valproic acid loaded NLCs. A Cryo-TEM image of unloaded NLCs is presented in (C). Size and zeta potential distribution of mangiferin-loaded NLCs measured by DLS (D). Images ownership belongs to Elsevier and John Wiley and Sons [18-20].

4. Advantages of NLC's

- NLC exhibits outstanding biocompatibility.[21]
- Since the techniques are water-based, organic solvents can be avoided. [22]
- NLCs are less expensive and easier to scale up than polymeric or surfactant-based carriers.[23]
- NLCs offer control and/or targeted drug release to enhance pharmaceutical stability.[24]
- Compared to other market-available carriers, NLC's deliver excellent and greater medication content.[24]
- NLCs can be more easily verified and approved by regularity agencies. [24,25,26]
- Drugs that are both lipophilic and hydrophilic may be transported simultaneously by NLC's.[27]
- The majority of lipids are biodegradable.[28]
- They enhanced physical steadiness [29]
- In an aqueous medium, NLC increased dispersability.[29]
- NLC is simple to prepare and scale up.[29]
- High lipophilic and hydrophilic drug trapping.[29]
- It also optimized benefit/risk ratio.[29]
- NLC's has controlled particle size.[29]
- It has extended medication release.[29]

5. Disadvantage of NLCs

Despite NLCs' enormous potential for targeted delivery, they have some drawbacks, such as:

- The concentration and makeup of the matrix may have cytotoxic consequences.[29,30]
- A small number of surfactants may have an irritant and sensitizing effect. [29,30]
- The use and effectiveness of protein and peptide medications and gene delivery technologies still need to be improved. [29,30]
- In the case of bone healing, nanoparticles lack sufficient preclinical and clinical research. [29,30]

6. Drug Release

NLC refers to a system in which the medicine is wrapped in a combination of solid lipid and liquid lipid, as opposed to SLN, where the molecule is encapsulated in solid lipid. Because the liquid oil increases the capability to dissolve the medicine in the NLC, this system has controlled release properties with the advantage of high medicament loading. In particular, unformed and imperfect shapes of NLCs offer fresh inflexibility to achieve the desired sustained release. A mixture of solid lipids and spatially separated liquid lipids is used to produce NLCs, which has further excrescencies in their crystal clear structure than SLNs.[31,32].

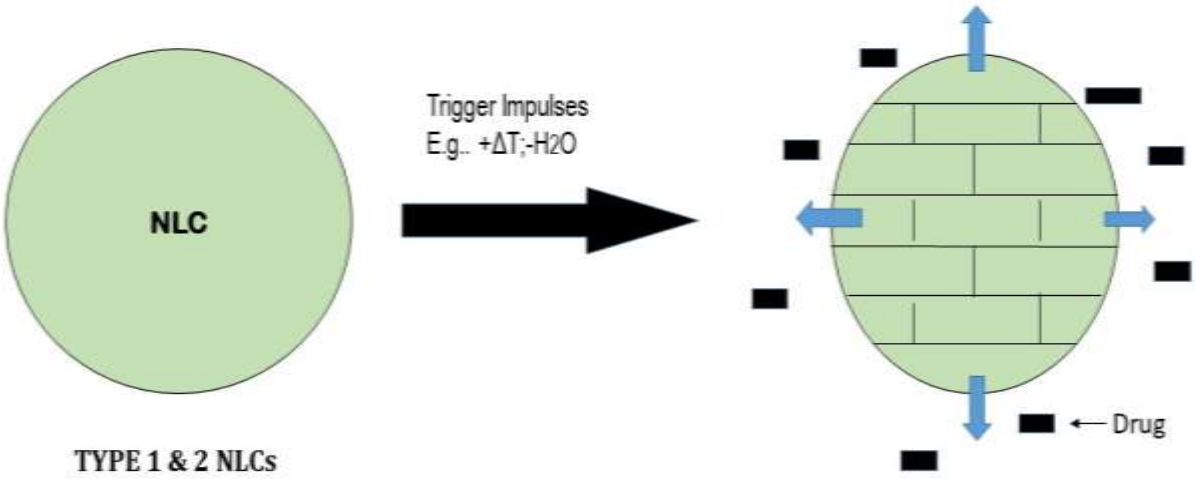

Figure 6: Release of drug from NLC by initiating the alteration from an extremely disordered lipid structure to more ordered stable modification.

The rate of degradation and diffusion in the case of Nano structural Lipid Carriers stipulates how rapidly drugs get released from a matrix. It is a release that has been meticulously controlled, beyond diffusion and degradation. A particle should be activated by an impulse when it is given for release. Due to the disorganized and disordered lipid structure of NLCs, when a particle is delivered, the release of the drug must be started by an impulse. The lipid's structure can be altered utilizing a variety of techniques and procedures, which affects the lipid molecule's structure and initiates continuous drug release, as shown in Figure 6. This approach was found to be crucial in cases where NLCs are incorporated in cream for use in the skin as well as for the treatment of different dermatological problems like psoriasis, ezema.[33] Based on this technique, these kinds of NLCs are beneficial and have highly desirable features; when rubbed, they raise the temperature and cause the water in the formulation to evaporate. To treat psoriasis, cyclosporine-lipid particles are being developed. [35-38]

Particle aggregation during long-term storage of dispersions was found to be possible in the case of SLNs.[39] The particle must be in a fixed position to prevent a collision and per kinetic flocculation, as shown in Figure 7, since the collision of the particle can lead to per kinetic flocculation in the highly concentrated NLC dispersions where the particles form a pearl-like network. [40-43]

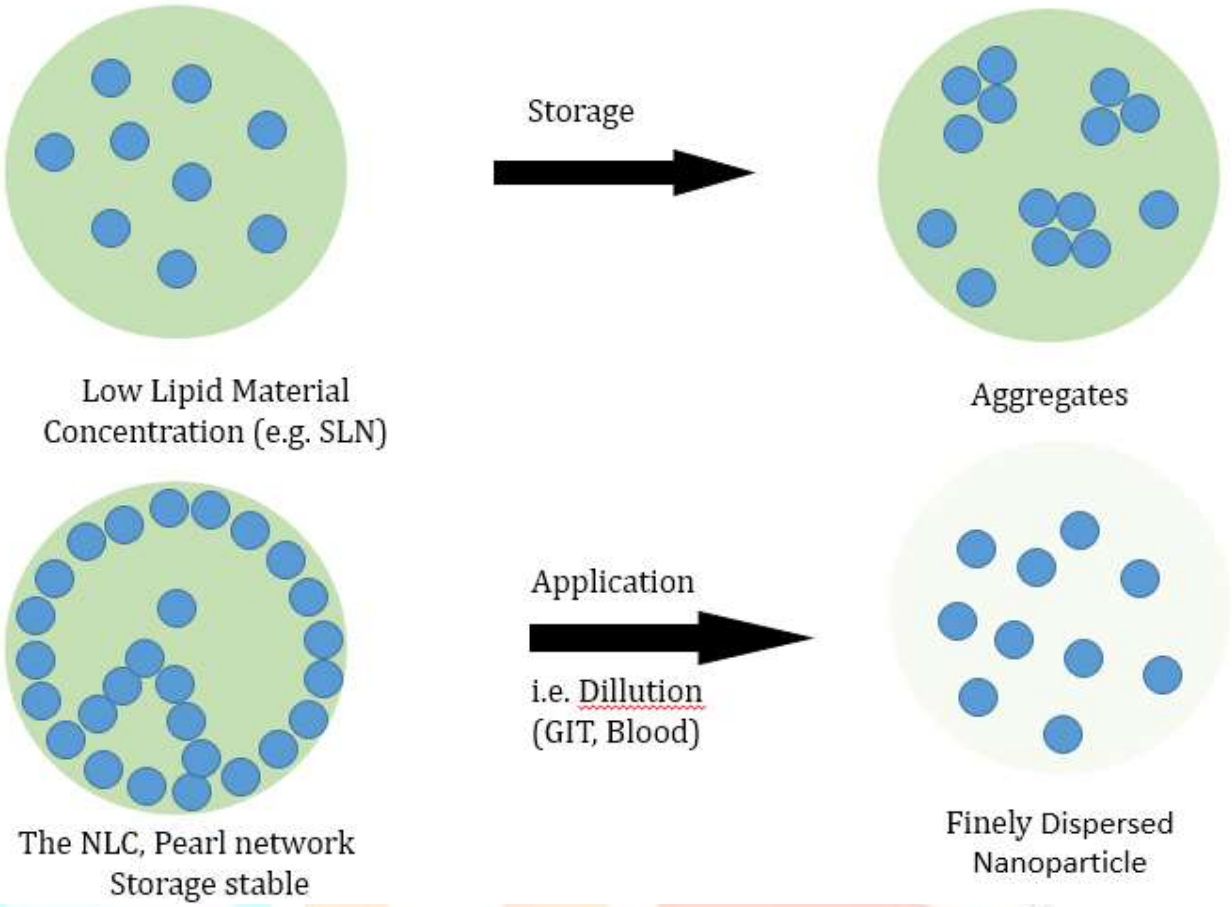

Figure 7: Aggregates formation from lipid particle after storage and pearl-like network in NLC's dispersions

7. NLC's Formulation

7.1) Composition

Nanostructural lipid carriers (NLCs) are complex lipid-based nanoparticles used in drug delivery systems. Their composition typically consists of a combination of solid and liquid lipids, surfactants, and occasionally co-surfactants. Here is a breakdown of the key components in the composition of NLC.

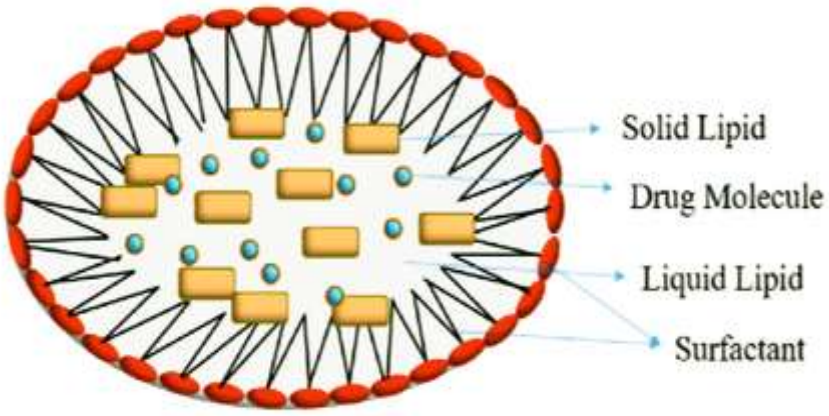

Figure 8: Components of NLC's with proper labelling of its components [44]

1. **Solid Lipids:**

Solid lipids found in NLCs are often made up of waxes, triglycerides (natural or synthetic), or other lipid substances. Solid lipids contribute to the stability and structural reliability of NLCs. Based on their melting points and suitability for the particular medicine being administered, these lipids are selected.They are a mixture of various chemicals with melting points more than 40 degrees Celsius.

Solid Lipid are well tolerated and above all they are; [45-47];

- Accepted for human use
- Also use as in-vivo biodegradable

Ex. Stearic Acid, Cutina CP 8, Beeswax, wax, Dynasan, Precifac,

2. Liquid Lipids:

NLC formulations contain liquid lipids, frequently in the form of oils such medium-chain triglycerides (MCTs), vegetable oils, or synthetic oils. These liquid lipids improve the solubility of hydrophobic medicines in the lipid matrix and increase the drug loading capacity of NLCs.

Table 1: lipids used in the preparation of nanostructured lipid carriers. [48]

Fatty acids	Dodecanoic acid, Myristic acid, Palmitic acid and Stearic acid.
Monoglycerides	Glyceryl monostearate, and Glyceryl behenate.
Diglycerides	Glyceryl palmitostearate and Glyceryl dibehenate.
Triglycerides	Caprylate triglyceride, Caprate triglyceride, Glyceryl and tribehenate/Tribehenin.
Waxes	Cetyl Palmitate, Carnauba, and wax Beeswax.
Liquid lipids	Soya bean oil, Oleic acid, Medium chain triglycerides (MCT)/caprylic- and capric triglycerides, α-tocopherol/Vitamin E, Squalene Hydroxyoctacosanyl hydroxystearate and Isopropyl myristate.
Cationic lipids	Cetyl pyridinium chloride (hexadecyl pyridinium chloride, CPC), Cetrimide (tetradecyl trimethyl ammonium bromide, CTAB.

3. Surfactants:

Due to their ability to stabilize the nanoparticles and avoid aggregation, surfactants play a significant role in NLC composition. The surfactants Tween, Span, and phospholipids are frequently utilized. Surfactants enable the formation of a homogeneous nanostructure by lowering the interfacial tension between solid and liquid lipids.

Table no. 2: Classification of surfactants and co-surfactants for the preparation of NLC's [48]

SURFACTANTS	
Ionic surfactants	**Non-ionic surfactants**
Sodium taurodeoxycholate, Sodium oleate, Sodium dodecyl sulphure	Span 20, 80, 85, Tween 20, 80, Tyloxapol, Poloxamer 188 Poloxamer 407, Solutol HS15
Amphoteric surfactants	**Co-surfactants**
Egg phospholipid (Lipoid E 80, Lipoid E 80 S) Soy	Butanol, Butyric acid
Hydrogenated soy phosphatidylcholine (Lipoid S PC-3)	
Hydrogenated egg phosphatidylcholine (Lipoid E PC-3)	
Phospholipon 80 H, Phospholipon 90 H)	

4. Co-surfactants (Optional):

Co-surfactants may be included in some NLC formulations to further optimize the characteristics of the nanoparticles. Co-surfactants enhance the stability and drug-loading capability of NLCs by collaborating with surfactants but they are the optional component used while formulation of NLCs.

5. Surface modifiers

When using advanced drug delivery techniques, surface modifiers can change the characteristics of nanoparticles to target particular molecules in different types of cells.

- Polyethylene glycol 2000, conjugated with dipalmitoyl-phosphatidyl-ethanolamine (DPPE-PEG2000).
- (DSPE-PEG2000) distearoyl-phosphatidylethanolamine-N-poly (ethylene glycol) 2000
- PEG 2000-stearic acid (SA-PEG 2000).
- (mPEG2000-C-LAA18) α-methoxy-PEG 2000-carboxylic acid-α-lipoamino acids.
- (mPEG5000-CLAA18) α-methoxy-PEG 5000-carboxylic acid-α-lipoamino acids.
- Dextran sulphate sodium salt, as an ionic polymer. [50,51]

6. Excipients for NLCs

Glyceryl behenate (Compritol® 888 ATO), glyceryl palmitostearate (Precirol® ATO 5), fatty acids, steroids, and waxes are among the solid lipids frequently utilized for NLCs. At normal temperatures, these lipids are solid. During the preparation, they melt at higher temperatures (> 80ºC). Typically, digestible oils derived from natural sources are employed as liquid oils in NLCs [51]. Table 3 lists the excipients employed in the creation of NLCs.

Ingredient	**Material**
Solid lipids	Softisan® 154, Cutina® CP, Imwitor® 900 P, Gelot® 64, Emulcire® 61, Tristearin, stearic acid, and Geleol® are some of the ingredients
Liquid lipids	Medium chain triglycerides, paraffin oil, 2-octyl dodecanol, Miglyol® 812, Transcutol® HP, Labrafil Lipofile® WL 1349, Labrafac® PG, Lauroglycol® FCC, and Capryl® 90.
Hydrophilic emulsifiers	Polyglycerol methyl glucose distearate, Solutol® HS15, polyvinyl alcohol, Tween 20, Tween 40, and Tween 80, as well as Pluronic® F68 (poloxamer 188)
Lipophilic emulsifiers	Myverol® 18-04K, Span 20,40,60.
Amphiphilic emulsifiers	Phosphatidylcholines, phosphatidylethanolamines, soy lecithin, and Gelucire® 50/13

Table 3: Excipients used for the preparation of NLC's [48]

NLCs can be made with a precise composition that is customized to the particular medication and therapeutic purpose. Hydrophobic and hydrophilic medicines are both well encapsulated by NLCs, shielding them from degradation and enabling regulated release. The versatility of this adaptable lipid-based carrier system to improve drug solubility, bioavailability, and targeted delivery has made it popular in pharmaceutical research and development. [48,53-55]

7.2) NLC's Preparation

For the preparation of NLCs, numerous approaches have been established. Following are the NLC preparation techniques based on energy input. [56]

Methods for Preparation of NLC's

❖ **High Energy Require Method**

1. High-pressure homogenization.
2. High Shear homogenization / Sonication

❖ **Low Energy require method**

1. Microemulsion technique.
2. Double Emulsification
3. Phase Inversion
4. Membrane Contractor

❖ **Very Low <u>OR</u> No Energy Require Method**

1. Emulsification-solvent diffusion
2. Emulsification-solvent Evaporation
3. Solvent Injection

Since high pressure homogenization and high shear homogenization are the two techniques that are most frequently utilized, I will mostly concentrate on HPH / HSH in this review.

High-pressure homogenization.

High-pressure homogenization is a mechanical process that involves subjecting a mixture of lipids, drug, and surfactants to high shear forces under elevated pressure. This technique is pivotal in achieving the desired physicochemical properties of NLCs. The process typically involves several stages.

- Homogenization
- Cooling / Heating (depend upon which approach is choosen)
- Further Homogenization

Generally two techniques are used to produce NLC / SLN using HPH, they are named as bellow;

a. Hot High Pressure Homogenization process
b. Cold High Pressure Homogenization process

Depending upon the requirement, the type of method is selected for the production on nanostructural lipid carrier. In both the techniques, initially, the drug is dissolved in lipid at 5–10 °C above the melting point of lipid. [57,58]

1. HIGH-PRESSURE HOMOGENIZATION PROCESS

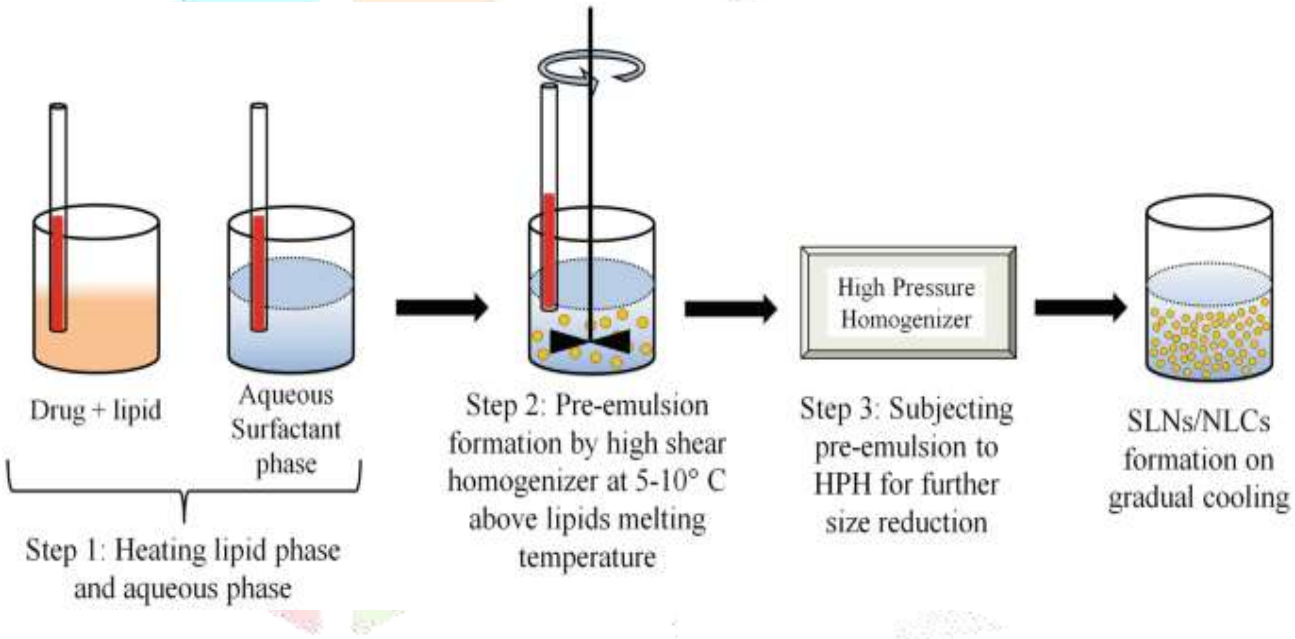

Figure 10: High-pressure homogenization process [59]

2. COLD- PRESSURE HOMOGENIZATION PROCESS

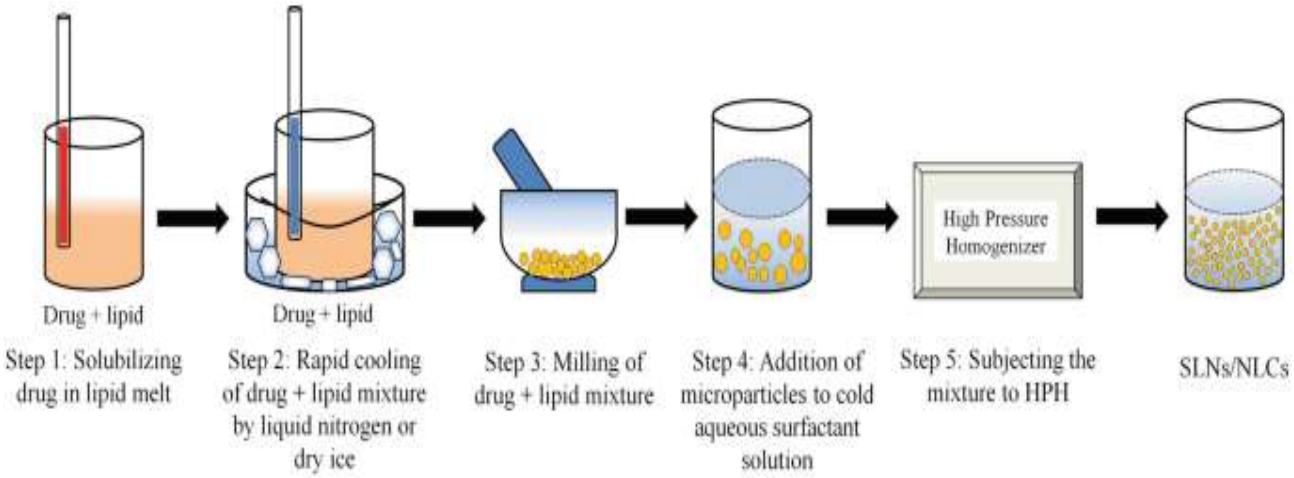

Figure 11: Cold high-pressure homogenization process [59]

High Shear Homogenization/ Sonication

The creation of Nanostructured Lipid Carriers (NLCs) relies heavily on high-pressure homogenization since it makes it possible to precisely control factors including size, drug encapsulation effectiveness, and physical stability. NLCs made through high-pressure homogenization are predicted to play an increasingly significant role in enhancing the efficacy and safety of medicines and other therapeutic agents as researchers continue to investigate novel drug delivery techniques.

In the preparation of NLC, a mixture of liquid and solid lipids, as well as a medicament and surfactants, are subjected to high shear forces. Drugs that are lipophilic are dissolved or dispersed in a mixture of molten solid and liquid lipids. To prevent recrystallization, the temperature utilized should be 10°C higher than the melting point of solid lipid. Pre-microemulsion is created by adding the aqueous surfactant solution to the lipid phase at the same temperature and stirring it vigorously. [4]

High-shear homogenizers are used to further homogenize the pre-emulsion before being treated with a probe sonicator. By using this technique, regulated particle size nanostructured lipid carriers (NLCs) will be produced, increasing the effectiveness of drug encapsulation. In order to provide NLCs the required physical properties and drug delivery capability, high shear homogenization is a crucial step. It is a crucial approach in pharmaceutical and nanotechnology applications because it permits homogenous mixing, improved medication stability, and controlled drug release. [4,60]

Microemulsion Technique

Microemulsion technique can be employed for the development of NLCs. It is prepared by similar procedure of high shear homogenization/sonication technique. After that hot microemulsion is added to cold water to form nanoemulsion, which then recrystallizes to form NLC's. [4,60]

Double Emulsion Technique

It is a method used to encapsulate hydrophilic drugs within the inner aqueous core of nanostructured lipid carriers (NLCs). It involves the creation of a double emulsion, typically water-in-oil-in-water (W/O/W), where the hydrophilic drug is dissolved or dispersed in the innermost water phase (2-10°C). High shear homogenization or sonication is then applied to form small NLCs with the drug-containing aqueous core surrounded by a lipid shell. [4,60]

Phase Inversion Technique

Phase Inversion is another method of prepration of NLC where the whole compoents mixture to 3 heating & cooling cycle.Then after that, hot mixture is shocked by dilution with cold water and at last NLC are get formed of phase inversion. [4,60]

Membrane Contractor Technique

By pressing the molten liquid against the porous membrane, tiny droplets are created using this technique. They are circulated simultaneously inside the membrane module. Following their removal from the pore, they are now cooled to room temperature. [4,60,61]

Emulsification Solvent Evaporation Technique

Emulsification Solvent Evaporation, A common technique for producing nanostructured lipid carriers (NLCs) to create a solution, lipids and a hydrophobic medication are dissolved in an organic solvent. The result is an oil-in-water (O/W) emulsion, which is created by emulsifying this solution into an aqueous phase. Following the evaporation of the organic solvent, NLCs with the medication enclosed in the lipid matrix are created. This method is useful in pharmaceutical and nanomedicine applications because it is efficient for drug loading and enables control over the particle size and drug release characteristics in NLCs.

The main drawbacks of this technology are the toxicity of the solvent residue and the diluted NLC particles caused by the insufficient solubility of the lipids in the solvents utilized. [4,62]

Emulsification Solvent Diffusion Technique

It is a technique used to create Nanostructured Lipid Carriers (NLCs). It begins by dissolving lipids and a hydrophobic drug in an organic solvent. This solution is then emulsified into an aqueous phase, forming an oil-in-water (O/W) emulsion. Over time, the organic solvent diffuses out of the emulsion into the external aqueous phase, leading to the formation of NLCs. This method allows for the encapsulation of the drug within the lipid matrix and the control of NLC size and drug release characteristics. [4,63]

Solvent Injection Technique

M. Schubert published the first report on the solvent injection method used to prepare SLNs and NLCs in 2003[61]. This approach involves dissolving medicines and lipids in a water-miscible solvent (such as acetone, methanol, ethanol, or isopropanol) or in a mixture of water-miscible solvents. Typically, an emulsifier or emulsifier mixture is added to water or a buffer solution to prepare the aqueous phase. Using a needle and constant mechanical stirring, the organic phase is then rapidly injected into the aqueous phase. This approach and the solvent emulsification-diffusion method have similar fundamental ideas. Figure 12 shows a schematic illustration of how SLNs and NLCs are formed using the solvent injection approach. [64,66]

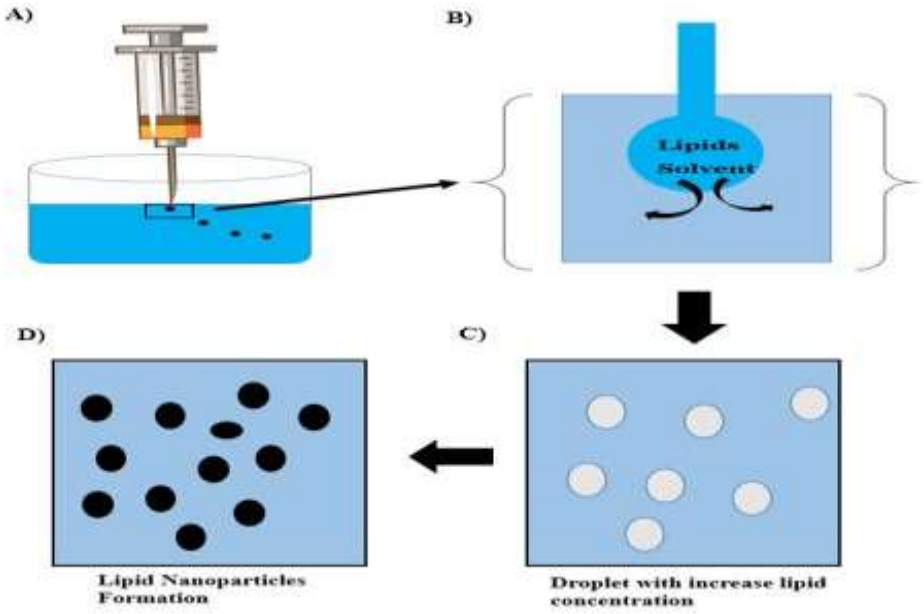

Fig.No.12: Lipid-nanoparticle production utilizing the solvent injection approach is shown schematically.

Figure 12 imparts; A) Drugs and lipids are dissolved in a water-miscible solvent (organic phase) before being injected into an emulsified aqueous phase. B) After injection, the solvent gradually diffuses into the aqueous phase, C) causing droplet division and a decrease in droplet size while an increase in lipid content. D) As a result, the emulsifiers create and stabilize solid lipid nanoparticles and nanostructured lipid carriers.

8. Application OF NLC's

Nanostructured lipid carriers (NLCs) find diverse applications across various fields, owing to their unique properties and advantages. Some of the key applications of NLCs include:

1. <u>Pharmaceuticals:</u>

Drug Delivery NLCs are frequently utilized to deliver medications with low bioavailability and solubility. Both hydrophilic and hydrophobic medicines can be encapsulated by them, enabling regulated and sustained release that boosts therapeutic effectiveness [67].

Cancer Therapy: NLCs have the potential to decrease systemic toxicity, increase chemotherapeutic efficacy, and enable targeted medication delivery to particular tumor locations. [67].

Vaccine Delivery: By defending antigens and encouraging their uptake by immune cells, NLCs can improve the durability and immunogenicity of vaccines.[68]

Transdermal Delivery: NLCs are helpful for topical therapies and dermal drug administration since they can carry medications through the skin [69]

2. Cosmetics:

Skin Care Products: To transport active chemicals like vitamins, antioxidants, and peptides to the skin, NLCs are used in creams, lotions, and serums. They increase these chemicals' stability and penetration, which increases their potency. [70]

Sunscreen Formulations: NLCs can ensure an aesthetically sophisticated texture while enhancing the UV protection and water resistance of sunscreen lotions. [71]

3. Food and Nutraceuticals:

Nutrient Delivery: Vitamins, antioxidants, and other bioactive substances can be encapsulated by NLCs to increase their stability and bioavailability in food and dietary supplements. [72]

Flavor and Aroma Enhancement: Volatile substances, like as essential oils, can be encapsulated by NLCs to maintain and release tastes and fragrances in food products. [72]

4. Agrochemicals:

Pesticide and Herbicide Delivery: NLCs can be used to create agrochemical formulations that provide nutrients to crops more effectively, have a smaller negative impact on the environment, and are more effective. [72]

5. Biotechnology:

Gene Delivery: NLCs can act as gene carriers in gene therapy, making it possible to deliver genetic material to cells effectively and selectively. [73]

6. Personal Care Products:

Fragrance Encapsulation: NLCs can encapsulate fragrances and perfumes to give personal care products a longer-lasting scent. [74]

7. Veterinary Medicine:

Animal Health: Animals' therapeutic outcomes can be enhanced by the use of NLCs to administer medications and dietary supplements to them [75]

8. Textiles: NLCs can be used to add antibacterial or water-repellent qualities to textile [76]

These applications demonstrate the versatility and potential of nanostructured lipid carriers in various industries, from healthcare and cosmetics to agriculture and beyond. As research in nanotechnology continues to advance, we can expect even more innovative uses for NLCs in the future.

9. Future Perspective & Conclusion

In conclusion, nanostructured lipid carriers (NLCs) are a viable and cutting-edge method for creating cosmetic formulations and drug delivery systems. Due to their distinctive properties, which include a high drug-loading capacity, improved stability, increased bioavailability, and the capacity to effectively encapsulate both hydrophilic and hydrophobic molecules, these adaptable nanoparticles have attracted a lot of attention. NLCs have shown promise in overcoming a number of issues with traditional drug delivery systems, including poor solubility, a lack of precise drug release control, and low bioavailability. Moreover, they are a good alternative for pharmaceutical and cosmetic applications due to their biocompatibility and very simple production techniques. Even though NLCs have several benefits, more research is needed to improve their formulation, scalability, and safety characteristics. Future research should also investigate there.

REFERENCE:

1. Tamjidi, F., Shahedi, M., Varshosaz, J., & Nasirpour, A. (2013). Nanostructured lipid carriers (NLC): A potential delivery system for bioactive food molecules. Innovative Food Science & Emerging Technologies, 19, 29-43.
2. Müller, R. H., Radtke, M., & Wissing, S. A. (2002). Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. Advanced drug delivery reviews, 54, S131-S155
3. H. Muller Rainer, Shegokar Ranjita and M. Keck Cornelia, 20 Years of Lipid Nanoparticles (SLN & NLC): Present State of Development & Industrial Applications, Current Drug Discovery Technologies 2011; 8(3). https://dx.doi.org/10.2174/157016311796799062
4. Elmowafy, M., & Al-Sanea, M. M. (2021). Nanostructured lipid carriers (NLCs) as drug delivery platform: Advances in formulation and delivery strategies. Saudi Pharmaceutical Journal, 29(9), 999-1012.
5. Syed Azhar SNA, Ashari SE, Zainuddin N, Hassan M. Nanostructured Lipid Carriers-Hydrogels System for Drug Delivery: Nanohybrid Technology Perspective. Molecules. 2022; 27(1):289. https://doi.org/10.3390/molecules27010289
6. Chauhan, I., Yasir, M., Verma, M., & Singh, A. P. (2020). Nanostructured Lipid Carriers: A Groundbreaking Approach for Transdermal Drug Delivery. Advanced pharmaceutical bulletin, 10(2), 150–165. https://doi.org/10.34172/apb.2020.021
7. Selvamuthukumar S, Velmurugan R. Nanostructured lipid carriers: a potential drug carrier for cancer chemotherapy. Lipids Health Dis. 2012;11:159. doi:10.1186/1476-511x-11-159
8. Iglic A, Kulkarni C, Rappolt M. Advances in Biomembranes and Lipid Self-Assembly. 1st ed. UK: Academic Press; 2016.
9. Dhiman N, Awasthi R, Sharma B, Kharkwal H, Kulkarni GT. Lipid Nanoparticles as Carriers for Bioactive Delivery. Frontiers in Chemistry. 2021 ;9:580118. DOI: 10.3389/fchem.2021.580118. PMID: 33981670; PMCID: PMC8107723.
10. Shah R, Eldridge D, Palombo E, Harding I. Lipid Nanoparticles: Production, Characterization and Stability. UK: Springer; 2015.
11. Ghasemiyeh P, Mohammadi-Samani S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages and disadvantages. Res Pharm Sci. 2018;13(4):288-303. doi:10.4103/1735-5362.235156.
12. Klang V, Valenta C, Matsko NB. Electron microscopy of pharmaceutical systems. Micron 2013;44:45-74.
13. Mittal V, Matsko NB. Analytical imagining techniques for soft matter characterization. 1st ed. Berlin Heidelberg: Springer-Verlag; 2012.
14. Sitterberg J, Ozcetin A, Ehrhardt C, Bakowsky U. Utilising atomic force microscopy for the characterisation of nanoscale drug delivery systems. Eur J Pharm Biopharm 2010;74:2-13.
15. Beloqui, A., Solinís, M. Á., Rodríguez-Gascón, A., Almeida, A. J., & Préat, V. (2016). Nanostructured lipid carriers: Promising drug delivery systems for future clinics. Nanomedicine: Nanotechnology, Biology and Medicine, 12(1), 143–161. doi:10.1016/j.nano.2015.09.004
16. Kuntsche J, Horst JC, Bunjes H. Cryogenic transmission electron microscopy (cryo-TEM) for studying the morphology of colloidal drug delivery systems. Int J Pharm 2011;417:120-37.
17. Saupe A, Gordon KC, Rades T. Structural investigations on nanoemulsions, solid lipid nanoparticles and nanostructured lipid carriers by cryo-field emission scanning electron microscopy and Raman spectroscopy. Int J Pharm 2006;314:56-62
18. Varshosaz J, Eskandari S, Tabbakhian M. Freeze-drying of nanostructure lipid carriers by different carbohydrate polymers used as cryoprotectants. Carbohydr Polym 2012;88:1157-63
19. . Jores K, Mehnert W, Drechsler M, Bunjes H, Johann C, Mäder K. Investigations on the structure of solid lipid nanoparticles (SLN) and oil-loaded solid lipid nanoparticles by photon correlation spectroscopy, field-flow fractionation and transmission electron microscopy. J Control Release 2004;95:217-27.
20. Liu R, Liu Z, Zhang C, Zhang B. Nanostructured lipid carriers as novel ophthalmic delivery system for mangiferin: improving in vivo ocular bioavailability. J Pharm Sci 2012;101:3833-44
21. Fretheim A, Odgaard-Jensen J, Brørs O, Madsen S, Njølstad I, et al. (2012) Comparative e ectLveness of antihypertensive medication for primary prevention of cardiovascular disease: systematic review and multiple treatments meta-analysis. BMC Med 10: 33
22. Pallerla SM, Prabhakar B (2013) A review on solid lipid nanoparticles. Int J Pharm Sci Rev Res 20: 196-206.

23. Singh P, Gupta RK, Jan R, Raina SK (2017) Original Article Adherence for medication among self-reporting rural elderly with diabetes and hypertension. J Med Soc 31: 86-89.
24. Purohit DK, Nandgude TD, Poddar SS (2016) Nano-lipid carriers for topical application: Current scenario. Asian J Pharm 10: 1-9.
25. Mottalib A, Kasetty M, Mar JY, Elseaidy T, Ashrafzadeh S, et al. (2017) Weight Management in Patients with Type 1 Diabetes and Obesity. Curr Diab Rep 17: 92.
26. Board BMA (2006) Reporting adverse drug reactions a guide for healthcare professionals. BMA Board Sci 6: 147-158.
27. Ravichandar R, Jamuna RR, Varadarajan S (2016) Article Study of adverse drug reactions in a tertiary care teaching hospital. IJBCP 5: 209-212.
28. Nguyen HM, Hwang IC, Park JW, Park HJ (2012) Enhanced payload and photo-protection for pesticides using nanostructured lipid carriers with corn oil as liquid lipid. J Micro Encapsul 29: 596-604.
29. Amandeep, & Manchanda, Rashmi & Arora, S.C.. (2019). Nanostructured Lipid Carriers: A Novel Drug Delivery System. International Journal of ChemTech Research. 12. 75-86. 10.20902/IJCTR.2019.120108.
30. Jaiswal P, Gidwani B, Vyas A. Nanostructured lipid carriers and their current application in targeted drug delivery. Artif Cells Nanomed Biotechnol. 2016;44(1):27-40. doi: 10.3109/21691401.2014.909822. Epub 2014 May 9. PMID: 24813223.
31. H Bunjes, K Westesen, and M.H. Koch, 1996. International journal of pharmaceutics, 129(1), pp.159-173.
32. Son, G.-H., Lee, B.-J., & Cho, C.-W. (2017). Mechanisms of drug release from advanced drug formulations such as polymeric-based drug-delivery systems and lipid nanoparticles. Journal of Pharmaceutical Investigation, 47(4), 287–296. doi:10.1007/s40005-017-0320-1
33. Sharma, A., & Baldi, A. (2018). Nanostructured lipid carriers: A review. Journal of Developing Drugs, 7(2), 1-15.
34. Peddinti S (2016) Nanostructured lipid carriers as a drug carrier. J Pharm Nanotechnol Nanostruc 4: 68-74.
35. Uner M (2006) Preparation, characterization and physico-chemical properties of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC): their benefits as colloidal drug carrier systems. Pharmazie 61: 375-386.
36. Zirak MB, Pezeshki A (2015) (ȣect of surfactant concentration on the particle size, stability and potential zeta of beta carotene nano lipid carrier. Int J Curr Microbiol Appl Sci 4: 924-932.
37. McEvoy SD, Sittig Dean F, Hu HT, Aaron S, Angela AI, et al. (2016) Variation in high-priority drug-drug interaction alerts across institutions and electronic health records. J Am Med Informatics Assoc 24: 331-338.
38. Anuradha K, Kumar S (2014) Development of Lacidipine loaded nanostructured lipid carriers (NLCs) for bioavailability enhancement. Int J Pharm Med Res 2: 50-57.
39. Joshi M, Pathak S, Sharma S, Patravale V (2008) Design and in vivo pharmacodynamic evaluation of nanostructured lipid carriers for parenteral delivery of artemether: Nanoject. Int J Pharm 364: 119-26.
40. Chen M, Stitt A (2016) Animal Models of Diabetic Retinopathy. Curr Diab Rep 17: 67-83.
41. López-García R, Ganem-Rondero A (2015) Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC): occlusive eȣect and penetration enhancement ability. J Cosmet 5: 62-72.
42. Carrier L (2006) Formulation and Evaluation of Nanostructured Lipid Carrier 8: 304-309.
43. Charcosset C, El-Harati A, Fessi H (2005) Preparation of solid lipid nanoparticles using a membrane contactor. J Control Release 108: 112-120
44. Kumari S, Goyal A, Sönmez Gürer E, Algın Yapar E, Garg M, Sood M, Sindhu RK. Bioactive Loaded Novel Nano-Formulations for Targeted Drug Delivery and Their Therapeutic Potential. Pharmaceutics. 2022; 14(5):1091. https://doi.org/10.3390/pharmaceutics14051091
45. Chen PC, Huang JW, Pang J (2013) An investigation of optimum NLCsunscreen formulation using taguchi analysis. J Nanomater pp: 1-11.
46. Joshi M, Patravale V (2006) Formulation and Evaluation of Nanostructured Lipid Carrier (NLC)–based Gel of Valdecoxib. Drug Dev Ind Pharm 32: 911-918.
47. Lasoń E, Sikora E, Ogonowski J (2013) Influence of process parameters on properties of Nanostructured Lipid Carriers (NLC) formulation. Acta Biochem Pol 60: 773-777.
48. Sharma, A.K., & Baldi, A. (2018). Nanostructured Lipid Carriers: A Review. Journal of Developing Drugs, 7, 0-0.

49. Fang CL, Al-Suwayeh SA, Fang JY (2012) Nanostructured Lipid Carriers (NLCs) for Drug Delivery and Targeting. Recent Pat Nanotechnol 7: 41-55
50. Kamble SS, Gambhire MS, Gujar KN (2015) Optimization and development of candesartan cilexetil loaded solid lipid nanoparticle for the treatment of hypertension. J Pharm Biosci 3: 53-64.
51. Jain NK, Ram A (2011) Development and characterization of nanostructured lipid carriers of oral hypoglycemic agent: selection of surfactants. Int J Pharm Sci Revier Res 7: 125-130.
52. Duong VA, Nguyen TT, Maeng HJ. Preparation of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers for Drug Delivery and the Effects of Preparation Parameters of Solvent Injection Method. Molecules. 2020;25(20):4781. Published 2020 Oct 18. doi:10.3390/molecules25204781
53. Shah R, Eldridge D, Palombo E, Harding I (2015) Lipid Nanoparticles: Production, Characterization and Stability. Briefs Pharm Sci Drug Dev 1: 11-23.
54. Soni K, Kukereja BK, Kapur M, Kohli K (2015) Lipid nanoparticles: future of oral drug delivery and their current trends and regulatory issues. Int J Curr Pharm Rev Res 7: 1-18.
55. Kaur S, Nautyal U, Singh R, Singh S, Devi A (2015) Nanostructure Lipid Carrier (NLC): the new generation of lipid nanoparticles. Asian 3acLfic J Heal Med 2: 76-93.
56. Uner M (2006) Preparation, characterization and physico-chemical properties of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC): their benefits as colloidal drug carrier systems. Pharmazie 61: 375-386
57. Sanap GS, Mohanta GP (2013) Design and evaluation of miconazole nitrate loaded nanostructured lipid carriers (NLC) for improving the antifungal therapy. J Appl Pharm Sci 3: 46-54.
58. Duong VA, Nguyen TT, Maeng HJ. Preparation of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers for Drug Delivery and the Effects of Preparation Parameters of Solvent Injection Method. Molecules. 2020;25(20):4781. Published 2020 Oct 18. doi:10.3390/molecules25204781
59. Vinchhi, P., Patel, J.K., Patel, M.M. (2021). High-Pressure Homogenization Techniques for Nanoparticles. In: Patel, J.K., Pathak, Y.V. (eds) Emerging Technologies for Nanoparticle Manufacturing. Springer, Cham. https://doi.org/10.1007/978-3-030-50703-9_11
60. Javed, S., Mangla, B., Almoshari, Y., Sultan, M. & Ahsan, W. (2022). Nanostructured lipid carrier system: A compendium of their formulation development approaches, optimization strategies by quality by design, and recent applications in drug delivery. Nanotechnology Reviews, 11(1), 1744-1777. https://doi.org/10.1515/ntrev-2022-0109
61. M.A. Schubert, C.C. Müller-Goymann,Solvent injection as a new approach for manufacturing lipid nanoparticles – evaluation of the method and process parameters,European Journal of Pharmaceutics and Biopharmaceutics,Volume 55, Issue 1,2003,Pages 125-131,ISSN 09396411, https://doi.org/10.1016/S0939-6411(02)00130-3
62. Shahgaldian, Patrick, Da Silva, Eric, Coleman, Anthony W, Rather, Beth, Zaworotko, Michael J, 2003. Para-acyl-calix-arene based solid lipid nanoparticles (SLNs): a detailed study of preparation and stability parameters. Int. J. Pharm. 253 (1-2), 23–38.
63. Chauhan, I., Yasir, M., Verma, M., & Singh, A. P. (2020). Nanostructured Lipid Carriers: A Groundbreaking Approach for Transdermal Drug Delivery. Advanced pharmaceutical bulletin, 10(2), 150–165. https://doi.org/10.34172/apb.2020.021
64. Vishal J. Lingayat, Nilesh S. Zarekar, Rajan S. Shendge. Solid Lipid Nanoparticles: A Review. Nanoscience and Nanotechnology Research. 2017; 4(2):67-72. doi: 10.12691/nnr-4-2-5.
65. Durán, N., & Fávaro, W. J. (2018). Nanopharmaceuticals and their applications in bladder cancer therapy: A mini review. Journal of the Brazilian Chemical Society, 29, 973-981.
66. Gerhardt, A., Voigt, E., Archer, M., Reed, S., Larson, E., Van Hoeven, N., ... & Casper, C. (2021). A thermostable, flexible RNA vaccine delivery platform for pandemic response. bioRxiv, 2021-02.
67. Bhaskar, K., Anbu, J., Ravichandiran, V., Venkateswarlu, V., & Rao, Y. M. (2009). Lipid nanoparticles for transdermal delivery of flurbiprofen: formulation, in vitro, ex vivo and in vivo studies. Lipids in health and disease, 8(1), 1-15.
68. Chen, J., Wei, N., Lopez-Garcia, M., Ambrose, D., Lee, J., Annelin, C., & Peterson, T. (2017). Development and evaluation of resveratrol, Vitamin E, and epigallocatechin gallate loaded lipid nanoparticles for skin care applications. European Journal of Pharmaceutics and Biopharmaceutics, 117, 286-291.
69. Chen, P. C., Huang, J. W., & Pang, J. (2013). An investigation of optimum NLC-sunscreen formulation using taguchi analysis. Journal of Nanomaterials, 2013, 9-9.
70. Gorantla, S., Wadhwa, G., Jain, S., Sankar, S., Nuwal, K., Mahmood, A., ... & Singhvi, G. (2021). Recent advances in nanocarriers for nutrient delivery. Drug Delivery and Translational Research, 1-26.

71. Ghosh, S., Sarkar, T., Das, A., & Chakraborty, R. (2021). Micro and nanoencapsulation of natural colors: A holistic view. Applied Biochemistry and Biotechnology, 193, 3787-3811.
72. Ahmadian, E., Eftekhari, A., Kavetskyy, T., Khosroushahi, A. Y., Turksoy, V. A., & Khalilov, R. (2020). Effects of quercetin loaded nanostructured lipid carriers on the paraquat-induced toxicity in human lymphocytes. Pesticide biochemistry and physiology, 167, 104586.
73. Dolatabadi, J. E. N., & Omidi, Y. (2016). Solid lipid-based nanocarriers as efficient targeted drug and gene delivery systems. TrAC Trends in Analytical Chemistry, 77, 100-108.
74. Pradhan, R., Santosh, S., Kharavtekar, V. J., Taliyan, R., & Dubey, S. K. (2023). 14 Nanoperfumes as a fragrance product. Nanocosmetics: Delivery Approaches, Applications and Regulatory Aspects, 293.
75. Carvalho, S. G., Araujo, V. H. S., Dos Santos, A. M., Duarte, J. L., Silvestre, A. L. P., Fonseca-Santos, B., ... & Chorilli, M. (2020). Advances and challenges in nanocarriers and nanomedicines for veterinary application. International journal of pharmaceutics, 580, 119214.
76. Caldas, A. R., Faria, M. J., Ribeiro, A., Machado, R., Gonçalves, H., Gomes, A. C., ... & Lúcio, M. (2021). Avobenzone-loaded and omega-3-enriched lipid formulations for production of UV blocking sunscreen gels and textiles. Journal of Molecular Liquids, 342, 116965.