Review Article

www.ijrap.net (ISSN:2229–3566)

A REVIEW ON THE SECOND-GENERATION LIPID CARRIERS: NLC'S

A N Jyothsna Sree *
School of Pharmaceutical Sciences and Technologies, JNTU, Kakinada, Andhra Pradesh, India

Received on: 05/06/21 Accepted on: 02/08/21

*Corresponding author
E-mail: jyothsnasree11@gmail.com

DOI: 10.7897/2277-4343.1204130

ABSTRACT

Over the past few years, nanostructured lipid carriers became an emerging drug delivery system as lipid drug delivery systems are more focused. Within them, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) have more advantages over other lipid carriers. This article is a cumulation of structure, types, composition, formulation methodologies, drug release from NLCs, various applications of NLCs. The key aspects for promising drug delivery systems are biocompatibility, drug loading capacity, ease of preparation, non-toxicity, and stability.

Keywords: nanostructured lipid carriers, lipids, toxicity, biocompatibility, surfactants.

INTRODUCTION

In the pharmaceutical world, new inventions and new technologies are most important for the preventing, curing, and diagnosing of many diseases and infections. The development of new drugs is important, but development of new dosage forms and new drug therapy is also important as some drugs have poor solubility and permeability which retard the bioavailability of the drug. So, to overcome such problems more therapies are being invented. Solid lipid nanoparticles (SLNs) were conceptualized in the early 1990s by Professor R.H. Müller (Germany) and Professor M. Gasco (Italy). These SLNs are the first generation of lipid nanoparticles and NLCs are second-generation lipid nanoparticles. To prevent the limitations of SLNs like poor drug loading capacities and unstable systems, NLCs were prepared. NLCs have a promising carrier in ocular, pulmonary, topical routes. In recent times, brain targeting, and gene therapy were also developed.

Limitations of SLNs over NLCs

SLNs are colloidal nanocarriers that are spherical in shape and an average diameter between 10 and 1000 nm. SLNs possess a solid lipid core matrix that can solubilize lipophilic molecules whereas nanostructured lipid carriers are the colloidal nanocarriers that uses both solid and liquid lipids. Lipids used in these are biodegradable in nature. The lipid core of SLNs is stabilized by surfactants (emulsifiers). It is having a wide range of applications over peroral, parenteral, dermal, and topical routes.

- The solid lipids crystallinity has an impact on the release properties of the SLNs,
- Upon storage, there will be a transition of polymeric forms to low energy states which results in the expulsion of incorporated drug and,
- Poor drug loading capacity.
- Unpredictable gelatin tendency.[1-6]

Advantages and disadvantages of Nanoparticles

Advantages

- Carries both lipophilic and hydrophilic drugs.
- Organic solvents can be avoided.
- Control and targeted drug release formulations can be formulated.
- Have more stability when compared to SLNs.
- Drug loading capacity is more compared to other nanocarriers.
- Biodegradable lipids are used.
- Avoids the expulsion of drugs from the drug carriers during storage.
- Available at more affordable prices.
- Easier to validate and gain regulatory approval.[7-12]

Disadvantages

- Fewer cytotoxic effects due to nature of matrix and concentration of lipids.
- Some of the surfactants cause irritation
- Efficiency and the applications of protein and peptide drugs and gene delivery systems are still needed to be exploited.
- Lipid stability.

Classification of NLCs

NLCs are classified depending on the nature of lipid content and formulation parameters. These are of 3 types,

- Imperfect or disordered structures
- Amorphous structures
- Multiple structures[12-14, 16]

Imperfect Matrix/ Disordered Structures

In this type of NLCs, a low concentration of liquid lipid is used compared to solid lipid. Both the solid and liquid lipids will be in disordered states. Disordered lipid structure appears between crystal lipid and liquid lipid. So, the drug penetration capacity is increased. Liquid and solid lipids are formed into o/w nano-emulsion due to the crystallization process. This process leads to

a highly disordered, imperfect lipid matrix which offers space for drug particles.

Amorphous Type

In the amorphous type, solid lipids will not be in crystalline form but an amorphous state. The leakage of a loaded drug is reduced due to the crystalline structure. The addition of a mixture of lipids prevents crystal formation since the crystals are formed during cooldown. These crystals are formed when only liquid lipids are used.

Multiple Types

In multiple NLCs, the concentration of oil is more compared to other types. The crystallization process leads to the phase separation of two different lipids. Miscibility gap arises at some definite temperatures which lead to the precipitation of tiny oily nanocarriers. Some of the lipids might lack drug solubilizing capacity. In such conditions, more quantities of liquid lipids are added, and it may prevent drug leakage. The lipid drug has more solubility in lipid liquids which might achieve the NLCs that show slow drug release and high loading capacity.

The types of NLCs are represented in Figure 1.

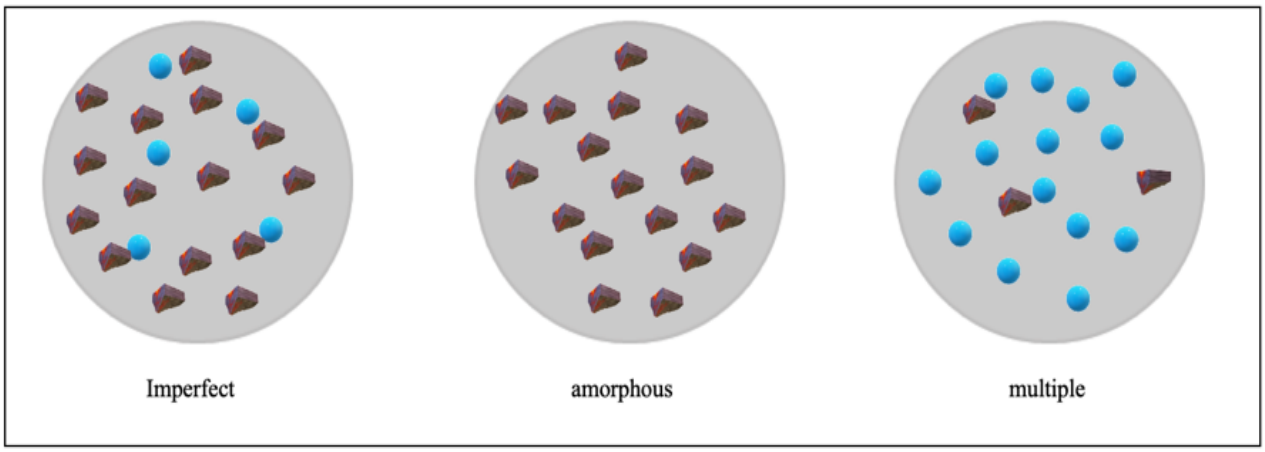

Figure 1: Types of NLCs

Excipients

NLCs are composed of a variety of LL, SL, and surfactants mixed at specific ratios and dispersed in aqueous solutions. The excipients which are used in the preparation of cancer drugs containing NLCs must be non-toxic, biocompatible.

Lipids

The most important component of NLCs responsible for the stability, drug loading capacity, and elongated action of NLCs are lipids. Two types of lipids are used in NLCs, they are solid lipids are liquid lipids.

Solid lipids include triglycerides that are mono, di, and triglycerides, fatty acids, and waxes that have been used for formulating NLC.
Liquid lipids are generally extracted from plant oils, and these are unsaturated fats.

Selection of lipids for nanoparticulate carriers is tedious work as they differ in solubility, partition coefficient, toxic grades, the solubility of the drug in the lipids on which the drug loading capacity and encapsulation efficiency are dependent. The drug entrapment capacity and efficacy can also be affected by degree of crystallization. The quality of the NLC depends on lipid crystals, hydrophilicity.[16-18]

Surfactants

Surfactants are mainly responsible for the efficacy and quality of NLC. A better selection of surfactants makes a non-toxic, stable NLC. Surfactants have a major impact on the dissolution of the drug and its permeability. These are selected depending on the HLB value, particle size, and route of administration. NLCs get solidify during the formulation which generates a tottered form of NLC. Hence, the surfactant compositions are governed to form a stable NLC.[16,17]

Other ingredients

Organic salts may be used as counter-ions in the NLC formulation to control the encapsulation of water-soluble drugs. Surface-modifiers are another category of excipients used in the formulation of NLC to minimize their phagocytic uptake by the macrophages in the reticuloendothelial system (RES). Lipid particles are coated with hydrophilic polymers like PEG, poloxamines, or poloxamers to increase the residence time of drug molecules in the systemic circulation. Surface modification may offer other advantages like enhanced physical stability and biocompatibility, drug targeting, increased transport across the epithelium.[16,17]

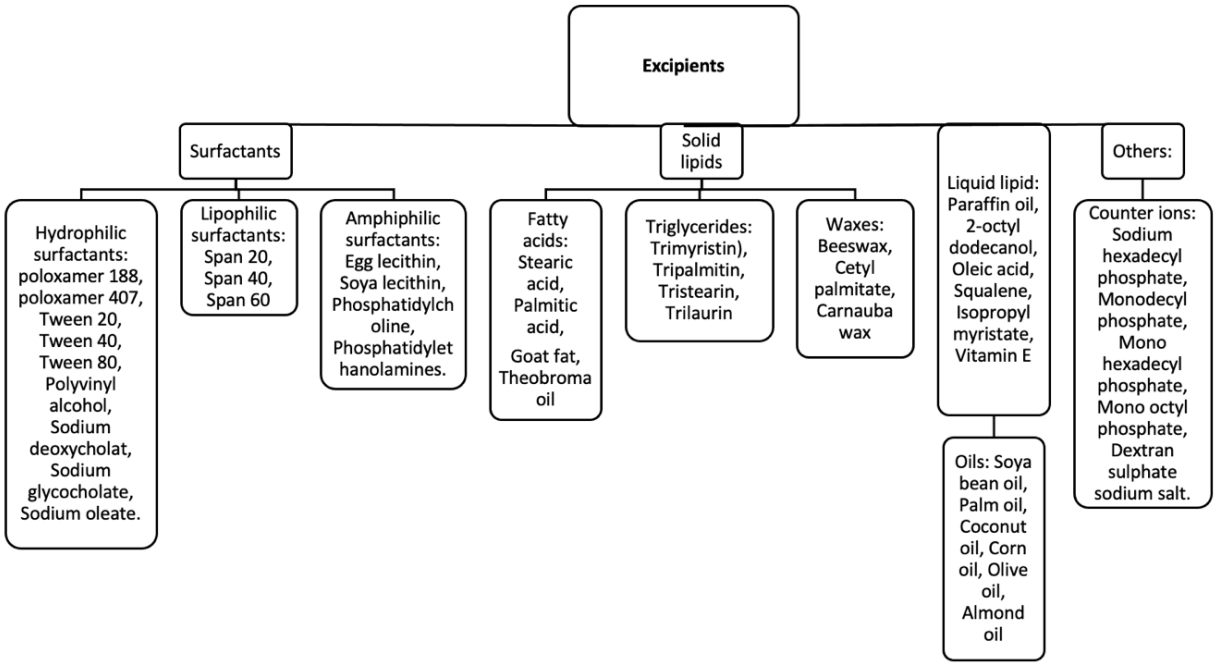

Figure 2: Excipients used in the formulation of nanostructured lipid carriers

The major components in the preparation of NLCs are surfactants and lipids.

High-Pressure Homogenization (HPH)

It is the most common method for the preparation of NLCs. It includes Hot Pressure Homogenization and Cold Pressure Homogenization

Hot High-Pressure Homogenization

This process involves the dispersion of the drug in a mixture of lipids i.e., solid lipid and liquid lipid. The hot drug molten is then mixed with the pre-heated aqueous solution of hydrophilic and/or hydrophobic surfactants by a high-pressure homogenizer (100–2000 bar) and an average of 3–5 cycles of homogenization. This result in the formation of lipid nanoparticles. The process of hot HPH is briefly described in Figure 3.[4,12,15,16,18-21]

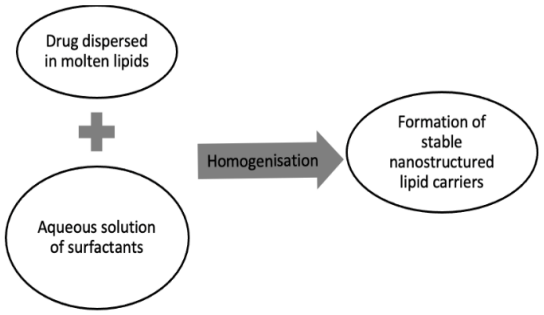

Figure 3: Hot High-Pressure Homogenization

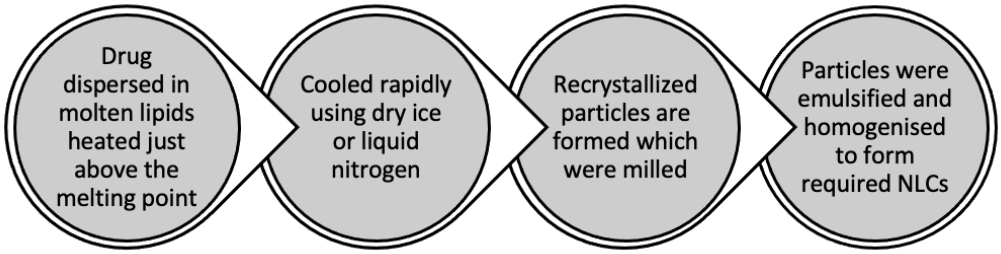

Figure 4: cold high-pressure homogenization

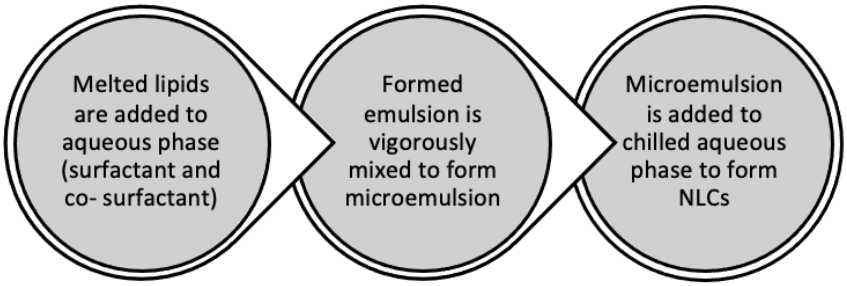

Figure 5: Microemulsions

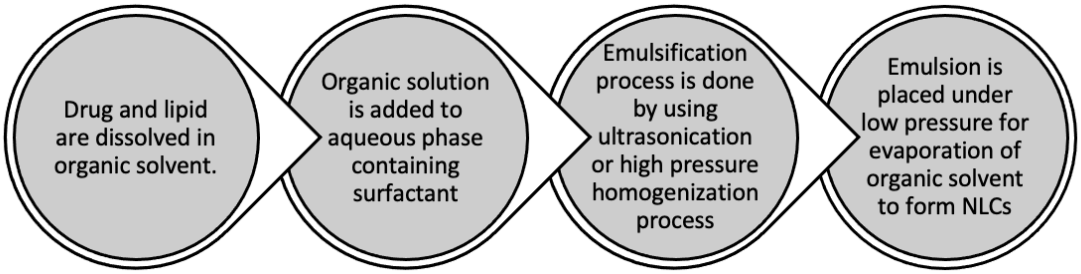

Figure 6: Solvent emulsification

Cold High-Pressure Homogenization

Hot High-Pressure Homogenization is not suitable for all drugs as the thermolabile drugs get degraded. To prevent such a problem, a Cold High-Pressure Homogenization process is used. The other disadvantage of HPH is low drug loading capacity as the drug molecules tend to move towards the aqueous phase during the crystallization of the liquid phase which can also be prevented.[4,18]

This process involves a mixture of drugs with the lipids melted just above its melting point followed by quick cooling of the mixture on dry ice or liquid nitrogen results in rapid recrystallization of SL particles. These recrystallized particles are then milled into micron range between 50–100 μm and emulsified in a cold aqueous phase using a high-pressure homogenizer to break the microparticles down into smaller NLCs. The process of Cold HPH is briefly described in Figure 4.[12,19-21]

Microemulsions

This is the most common method for the preparation of NLCs. This process involves both O/W and W/O emulsions. Melted lipids are added to an aqueous phase containing surfactant and co-surfactant to form an emulsion. The particles are broken to the micro range by mixing vigorously. This Microemulsion is then added to the chilled aqueous phase to form NLCs. The process of Microemulsions is briefly described in Figure 5.[16,17]

Solvent Emulsification/Evaporation

This process is suitable for heat-sensitive drugs. In the final product, there will be traces of the organic phase which causes toxicity after administration. This may also include more filtration steps which are not economical for larger scales. In this process, the drug and the lipid are dissolved in organic solvent (having water immiscibility) which is then emulsified with an aqueous phase containing surfactant using ultrasonication or high-pressure homogenization. This solution is then placed in low-pressure conditions (40–60 mbar) for the evaporation of the organic phase to form NLCs. The process of solvent emulsification is briefly described in Figure 6.[17,18]

Solvent Injection technique

This is a simpler technique. In this, lipids are dissolved in the hydrophilic solvent and this lipid solution is injected rapidly into an aqueous phase containing surfactant under continuous stirring. Obtained dispersion is then filtered to remove excess lipids. This process depends on the rapid diffusion of the solvent over the solvent–lipid interfaced with the aqueous phase and this physical phenomenon is critical for the precipitation of nanosized lipid particles.[17]

Phase inversion technique

This is a novel technique that involves the phase inversion from o/w to w/o emulsion. It involves two steps.

Step-1

All ingredients are taken in appropriate concentrations and are mixed properly (lipid, surfactant, and water). This mixture is stirred, and the temperature is increased from room temperature to 85°c with an increase of 4°c every time. Three temperature cycles (85–60–85-60-85°C) are applied to this system to obtain phase inversion.

Step-2

Cold water is added quickly to form NLCs. It is then stirred 5 minutes by a magnetic stirrer to prevent particle agglomeration and to form stable NLCs.[17]

Micro fluidization

The Micro fluidization process is a novel technique. This process is used for both lab-scale and production. In this technique, turbulence is generated which makes the melted lipid pass through microchannels in controlled flow rates and rapid mixing of nanolitre amounts of these reagents under highly controlled pressure. Only 2 Micro fluidization techniques are used in the present day. They are the single-channel fluidization process and

dual-channel fluidization process. The single-channel fluidization process is a two-step process whereas the dual-channel fluidization process is a one-step process. In the single-channel fluidization process wastage of lipid will be more.[16,17]

Membrane contactor technique

Membrane contactors are employed to identify membrane systems that "Keep in contact" in two phases. The lipid phase is placed in a pressurized vessel having a temperature above its melting point. It is then led to permeate through ceramic membrane pores to form small droplets under applied pressure. The aqueous phase, under continuous stirring, flows tangentially inside the membrane module and brushes away the droplets formed at the pore outlets. Lipid particles are formed by reducing the temperature. The temperature of the aqueous and lipid phase, aqueous phase tangential-flow velocity, and pressure of lipid phase, and membrane pore size are the process parameters affecting the size of lipid nanocarriers. The benefits of this new process of membrane emulsification are commercial scalability and control of particle size by fitting optimized parameters.[17,22]

Applications

Ocular administration

The ocular route has two barriers, they are static and dynamic. Static barriers consist of different segments of the eye such as the cornea, sclera, and dynamic barriers consist of choroidal and conjunctival blood flow, lymphatic clearance, and tear dilution. Both barriers affect the bioavailability of drugs[23]. These carrier systems exhibit excellent tolerability[13]. Gene therapy for retinal targeting in retinal diseases was also considered using non-viral vectors gene delivery including SLNs and NLCs[24-32]

Oral route

The oral route is the most common route of drug delivery as it has high patient compliance. But it has some disadvantages like low oral bioavailability due to low drug solubility and hepatic first-pass effect. By using NLCs oral bioavailability can be increased as they have a high solubility rate.[18,27,28]

Parenteral

This nanotechnology has a vital role in the case of parenteral. NLCs have advantages as well as disadvantages in this. These have greater biocompatibility. Controlled extended formulations can be made. Drug-loaded NLCs can be administered intravenously, subcutaneously, intramuscularly. Drug release from NLCs occurs through erosion or diffusion. new research, found the capacity of NLCs in peptides and proteins to protect them from degradations.[27,33-36]

Topical Route

Preparation of NLCs for topical route include wide aspects like biocompatibility and biodegradability, controlled and extended drug release profile, close contact and strong skin adhesion, skin hydration, and film formation to increase skin and dermal penetration. The disadvantages for the treatment of skin diseases are low drug efficacy because of poor skin penetration or skin permeation of drugs.[8,27]

Pulmonary delivery

Pulmonary drug delivery is recently developed. Using this route, the doses of the drug were reduced due to high systemic availability. More surface area of the pulmonary system increases drug permeability. They have the advantage of sustaining drug release, biocompatibility and biodegradability, lower toxicity, and better. Inhalation of drug loaded NLCs shows high bioavailability and reduces systemic adverse effects. Nanoparticles have greater bioavailability in systemic route.[18,27,37-39]

Brain delivery

Crossing drugs through the blood-brain barrier (BBB) is an important challenge. As the NLCs have a small size, high drug loading capacity, and lipid nature, they could easily pass-through BBB. Since nanoparticles can bypass the reticuloendothelial system (RES), they are suitable as brain drug delivery systems. NLCs have the advantage of increasing drug retention time in the blood of brain capillaries and inducing a drug gradient from blood to brain tissues, opening tight junctions to facilitate passage from BBB and transcytosis of drug-loaded lipid nanoparticles through the endothelium layer.[27,40-47]

CONCLUSION

NLCs are invented by transforming the SLNs to form a stable system. These systems are stable chemically and physically with more drug loading capacity compared to others. These NLCs have a wide range of applications in ocular, pulmonary, topical, oral routes. In recent years, NLCs for cancer therapy was also formed to prevent the disadvantages of present cancer treatments like high toxicity and non-compliance. More research for nanoparticles and more commercial products will pave the way to the success of nanostructures.

REFERENCES

1. Mishra V, Bansal KK, Verma A, Yadav N, Thakur S, Sudhakar K, Rosenholm JM. Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. Pharmaceutics 2018 Dec; 10(4): 191.
2. Jain V, Gupta A, Pawar VK, Asthana S, Jaiswal AK, Dube A, Chourasia MK. Chitosan-assisted immunotherapy for intervention of experimental leishmaniasis via amphotericin B-loaded solid lipid nanoparticles. Applied biochemistry and biotechnology 2014 Oct; 174(4): 1309-30.
3. Hanumanaik M, Patel SK, Sree KR. Solid lipid nanoparticles: a review. Int J Pharm Sci Res 2013; 4(3): 928-40.
4. Ekambaram P. a. Abdul Hasan Sathali and K. Priyanka. Solid lipid nanoparticles: A Review; Sci. Revs. Chem. Commun 2012; 2(1): 80-102.
5. Li H, Zhao X, Ma Y, Zhai G, Li L, Lou H. Enhancement of gastrointestinal absorption of quercetin by solid lipid nanoparticles. Journal of Controlled Release 2009 Feb 10; 133(3): 238-44.
6. Üner M, Yener G. Importance of solid lipid nanoparticles (SLN) in various administration routes and future perspectives. International Journal of Nanomedicine 2007 Sep; 2(3): 289.
7. Natarajan J, Karri VV, Anindita D. Nanostructured lipid carrier (NLC): A promising drug delivery system. Global Journal of Nanomedicine 2017; 1(5): 001-6.
8. Nanostructured Lipid Carrier (NLC) -A Promising Drug Delivery for Transdermal Application Laxmidhar sahoo J. Pharm. Sci. & Res 2020; Vol. 12(4): 475-487.
9. Nandvikar NY, Lala RR and Shinde AS. Nanostructured lipid carrier: the advanced lipid carriers. Int J Pharm Sci & Res 2019; 10(12): 5252-65.
10. Patidar A, Thakur DS, Kumar P, Verma J. A review on novel lipid based nanocarriers. International Journal of Pharmacy and Pharmaceutical Sciences 2010; 2(4): 30-5.
11. Schäfer-Korting M, Mehnert W, Korting HC. Lipid nanoparticles for improved topical application of drugs for skin diseases. Advanced drug delivery reviews 2007 Jul 10; 59(6): 427-43.
12. Sharma A, Baldi A. Nanostructured lipid carriers: A review. Journal of Developing Drugs 2018; 7(2): 1000191.

13. Shah R, Eldridge D, Palombo E, Harding I. Lipid nanoparticles: Production, characterisation, and stability. New York, NY, USA: Springer International Publishing; 2015.
14. Soni K, Kukereja BK, Kapur M, Kohli K. Lipid nanoparticles: future of oral drug delivery and their current trends and regulatory issues. Int J Curr Pharm Rew Res 2015; 7(1): 1-8.
15. Kadam VB, Dhanawade KB, Salunkhe VA, Ubale AT. Nanoparticle-novel drug delivery system. Journal of Current Pharma Research 2014 Jul 1; 4(4): 1318.
16. Haider M, Abdin SM, Kamal L, Orive G. Nanostructured lipid carriers for delivery of chemotherapeutics: A review. Pharmaceutics 2020 Mar; 12(3): 288.
17. Chauhan I, Yasir M, Verma M, Singh AP. Nanostructured lipid carriers: a Ground-breaking approach for transdermal drug delivery. Advanced pharmaceutical bulletin 2020 Jun; 10(2): 150.
18. Naseri N, Valizadeh H, Zakeri-Milani P. Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation, and application. Advanced pharmaceutical bulletin 2015 Sep; 5(3): 305.
19. Chaturvedi SP, Kumar V. Production techniques of lipid nanoparticles: A Review. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2012; 3(3): 525-41.
20. Silva AC, González-Mira E, García ML, Egea MA, Fonseca J, Silva R, Santos D, Souto EB, Ferreira D. Preparation, characterization, and biocompatibility studies on risperidone-loaded solid lipid nanoparticles (SLN): high pressure homogenization versus ultrasound. Colloids and Surfaces B: Bio interfaces 2011 Aug 1; 86(1): 158-65.
21. Parhi R, Suresh P. Preparation, and characterization of solid lipid nanoparticles-a review. Current drug discovery technologies 2012 Mar 1; 9(1): 2-16.
22. Charcosset C, Fessi H. Preparation of nanoparticles with a membrane contactor. Journal of membrane science 2005 Dec 1; 266(1-2): 115-20.
23. Sikandar MK, Sharma PK, Visht S. Ocular drug delivery system: an overview. International Journal of Pharmaceutical Sciences and Research 2011 May 1; 2(5): 1168.
24. Okur NÜ, Gökçe EH. Lipid nanoparticles for ocular drug delivery. International Journal of Ophthalmic Research 2015 Dec 29; 1(3): 77-82.
25. Li Q, Cai T, Huang Y, Xia X, Cole SP, Cai Y. A review of the structure, preparation, and application of NLCs, PNPs, and PLNs. Nanomaterials 2017 Jun; 7(6): 122.
26. Ganesan P, Karthivashan G, Park SY, Kim J, Choi DK. Micro fluidization trends in the development of nanodelivery systems and applications in chronic disease treatments. International Journal of Nanomedicine 2018; 13: 6109.
27. Ghasemiyeh P, Mohammadi-Samani S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages, and disadvantages. Research in pharmaceutical sciences 2018 Aug; 13(4): 288.
28. Garg A, Bhalala K, Tomar DS. *In-situ* single pass intestinal permeability and pharmacokinetic study of developed Lumefantrine loaded solid lipid nanoparticles. International Journal of Pharmaceutics 2017 Jan 10; 516(1-2): 120-30.
29. Balguri SP, Adelli GR, Majumdar S. Topical ophthalmic lipid nanoparticle formulations (SLN, NLC) of indomethacin for delivery to the posterior segment ocular tissues. European Journal of Pharmaceutics and Biopharmaceutics 2016 Dec 1; 109: 224-35.
30. Chetoni P, Burgalassi S, Monti D, Tampucci S, Tullio V, Cuffini AM, Muntoni E, Spagnolo R, Zara GP, Cavalli R. Solid lipid nanoparticles as promising tool for intraocular tobramycin delivery: Pharmacokinetic studies on rabbits. European Journal of Pharmaceutics and Biopharmaceutics 2016 Dec 1; 109: 214-23.
31. Sánchez-López E, Espina M, Doktorovova S, Souto EB, García ML. Lipid nanoparticles (SLN, NLC): Overcoming the anatomical and physiological barriers of the eye–Part I–Barriers and determining factors in ocular delivery. European Journal of Pharmaceutics and Biopharmaceutics 2017 Jan 1; 110: 70-5.
32. Sánchez-López E, Espina M, Doktorovova S, Souto EB, García ML. Lipid nanoparticles (SLN, NLC): Overcoming the anatomical and physiological barriers of the eye–Part II-Ocular drug-loaded lipid nanoparticles. European Journal of Pharmaceutics and Biopharmaceutics 2017 Jan 1; 110: 58-69.
33. Liu D, Liu Z, Wang L, Zhang C, Zhang N. Nanostructured lipid carriers as novel carrier for parenteral delivery of docetaxel. Colloids and Surfaces B: Bio interfaces 2011 Jul 1; 85(2): 262-9.
34. Luan J, Zhang D, Hao L, Qi L, Liu X, Guo H, Li C, Guo Y, Li T, Zhang Q, Zhai G. Preparation, characterization, and pharmacokinetics of Amoitone B-loaded long circulating nanostructured lipid carriers. Colloids and Surfaces B: Bio interfaces 2014 Feb 1; 114: 255-60.
35. Chinsriwongkul A, Chareanputtakhun P, Ngawhirunpat T, Rojanarata T, Sila-on W, Ruktanonchai U, Opanasopit P. Nanostructured lipid carriers (NLC) for parenteral delivery of an anticancer drug. Aaps Pharmscitech 2012 Mar; 13(1): 150-8.
36. Qureshi OS, Kim HS, Zeb A, Choi JS, Kim HS, Kwon JE, Kim MS, Kang JH, Ryou C, Park JS, Kim JK. Sustained release docetaxel-incorporated lipid nanoparticles with improved pharmacokinetics for oral and parenteral administration. Journal of microencapsulation 2017 Apr 3; 34(3): 250-61.
37. Cipolla D, Shekunov B, Blanchard J, Hickey A. Lipid-based carriers for pulmonary products: preclinical development and case studies in humans. Advanced drug delivery reviews 2014 Aug 30; 75: 53-80.
38. Makled S, Nafee N, Boraie N. Nebulized solid lipid nanoparticles for the potential treatment of pulmonary hypertension via targeted delivery of phosphodiesterase-5-inhibitor. International Journal of Pharmaceutics 2017 Jan 30; 517(1-2): 312-21.
39. Pardeike J, Weber S, Zarfl HP, Pagitz M, Zimmer A. Itraconazole-loaded nanostructured lipid carriers (NLC) for pulmonary treatment of aspergillosis in falcons. European Journal of Pharmaceutics and Biopharmaceutics 2016 Nov 1; 108: 269-76.
40. Kaur IP, Bhandari R, Bhandari S, Kakkar V. Potential of solid lipid nanoparticles in brain targeting. Journal of Controlled release 2008 Apr 21; 127(2): 97-109.
41. Dal Magro R, Ornaghi F, Cambianica I, Beretta S, Re F, Musicanti C, Rigolio R, Donzelli E, Canta A, Ballarini E, Cavaletti G. ApoE-modified solid lipid nanoparticles: A feasible strategy to cross the blood-brain barrier. Journal of Controlled Release 2017 Mar 10; 249: 103-10.
42. Blasi P, Giovagnoli S, Schoubben A, Puglia C, Bonina F, Rossi C, Ricci M. Lipid nanoparticles for brain targeting I. Formulation optimization. International Journal of Pharmaceutics 2011 Oct 31; 419(1-2): 287-95.
43. Tosi G, Musumeci T, Ruozi B, Carbone C, Belletti D, Pignatello R, Vandelli MA, Puglisi G. The "fate" of polymeric and lipid nanoparticles for brain delivery and targeting strategies and mechanism of blood–brain barrier crossing and trafficking into the central nervous system. Journal of Drug Delivery Science and Technology 2016 Apr 1; 32: 66-76.
44. Blasi P, Giovagnoli S, Schoubben A, Ricci M, Rossi C. Solid lipid nanoparticles for targeted brain drug delivery. Advanced drug delivery reviews 2007 Jul 10; 59(6): 454-77.

45. Montenegro L, Campisi A, Sarpietro MG, Carbone C, Acquaviva R, Raciti G, Puglisi G. *In vitro* evaluation of idebenone-loaded solid lipid nanoparticles for drug delivery to the brain. Drug Development and Industrial Pharmacy 2011 Jun 1; 37(6): 737-46.
46. Blasi P, Schoubben A, Romano GV, Giovagnoli S, Di Michele A, Ricci M. Lipid nanoparticles for brain targeting II. Technological characterization. Colloids and Surfaces B: Bio interfaces 2013 Oct 1; 110: 130-7.
47. Gastaldi L, Battaglia L, Peira E, Chirio D, Muntoni E, Solazzi I, Gallarate M, Dosio F. Solid lipid nanoparticles as vehicles of drugs to the brain: current state of the art. European Journal of Pharmaceutics and Biopharmaceutics 2014 Aug 1; 87(3): 433-44.

Cite this article as:

A N Jyothsna Sree. A Review on the Second-generation Lipid Carriers: NLC'S. Int. J. Res. Ayurveda Pharm. 2021;12(4):176-182 http://dx.doi.org/10.7897/2277-4343.1204130

Source of support: Nil, Conflict of interest: None Declared