

Cite this article: M. Dey, S. Chakraborty, A.K. Singh, U.K. Singha, S. Hore, Lipid nanocarriers for controlled drug release in chronic diseases, *RP Materials: Proceedings* Vol. 5, Part 1 (2026) pp. 143–147.

Review Article

Lipid nanocarriers for controlled drug release in chronic diseases

Mithu Dey¹, Suchetana Chakraborty², Ankita Kumari Singh², Uday Kumar Singha², Soumyadeep Hore²

¹Department of Basic Science & Humanities (Mathematics), Asansol Engineering College, Asansol-713305, West Bengal, India

²3rd Year Student, Department of Computer Science and Business Systems, Asansol Engineering College, Asansol 713305, West Bengal, India

*Corresponding author, E-mail: mithu.maths@aecwb.edu.in

**Selection and Peer-Review under responsibility of the Scientific Committee of the 4th International Conference on Recent Trends in Materials Science & Devices 2026 (ICRTMD 2026) held at JVMGRR College, Charkhi Dadri, Haryana, India during 6–8 April 2026.

ARTICLE HISTORY

Received: 15 April 2026

Revised: 27 May 2026

Accepted: 27 May 2026

Published online: 12 June 2026

KEYWORDS

Lipid nanoparticles;
Controlled drug delivery;
Chronic diseases; Solid
lipid nanoparticles;
Nanostructured lipid
carriers.

ABSTRACT

Lipid nanocarriers (LNPs) are class of drug delivery systems that have emerged as a platform for improving the therapeutic management of chronic diseases. In contrast, the conventional drug delivery [1] methods often suffer from limitations including faster drug degradation, poor availability of biomedical, responsible for the reduction of effective treatment and may increase side effects. These nano-scale systems like Lipid-based nanocarriers [2] which includes solid lipid nanoparticles enhance system methods due to their biological compatibility, degradability and controlled drug release hence maintaining a stable drug concentration in the bloodstream over longer time which helps in the reduction of dosing frequency and strengthen patient agreement results in long-term management of chronic conditions such as cancer, diabetes and cardiovascular diseases. So, this paper explores the fundamental design methodologies, the mechanisms of drug release and therapeutic treatment applications of lipid nanocarriers in the treatment of chronic illness, hence highlighting their role as one of the best strategies for future generation drug delivery systems.

1. Introduction

Chronic diseases such as diabetes, cancer, cardiovascular diseases, arthritis and various neurological conditions are one of the major causes of death and also responsible for long-term disability worldwide. These kinds of disorders need long-term treatment and regular check-ups of medications. Traditional systems cause uneven drug concentrations in blood vessels and hence are responsible for reduction in therapeutic effectiveness and may also increase the chances of getting side effects.

In order to overcome these challenges, an effective drug delivery technology is required to deliver drugs safely and effectively in chronic patients. Controlled drug delivery systems are designed in such a way that they are biocompatible, biodegradable and stable carriers and can regulate drug levels in the patient's body for longer periods and also have the ability to target specific organs. Among various nanotechnology-based drug delivery mechanisms, Lipid Nanocarriers have evolved as a promising approaching technique and a novel drug delivery carrier.

Lipid nanocarriers [3] are the nanoscale structures composed of nano structured lipids that can upgrade the solubility of drugs and protect unstable medicinal compounds from degradation which in result enables controlled drug release. Moreover, lipid nanoparticles also exhibit low toxicity

which supports their cautious use in further medicinal applications.

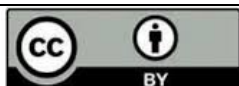
This study shows the structural and functional characteristics of lipid nanocarriers in the controlled drug delivery mechanism [4]. for the prolonged treatment of chronic diseases.

2. Materials and methods

Firstly, researches have been done on advancement of lipid-based nanocarriers [5] over last two decades for improving medical outcomes in chronic diseases. Various lipid-based systems like solid nanoparticles, nano emulsions, etc. have been under long investigation for sustained drug release. Researcher Elnady et al. examined lipid nanocarriers to copy biological structures like chylomicrons to enhance drug transport and absorption within the patient's body. Recently surface modification and ligand-based targeting techniques are under observation. These techniques help to direct lipid nanocarriers [6] toward specific tissues or cells and hence improving treatment efficiency and reducing toxicity.

3. Materials and methods

Lipid Nanocarriers are nanoscale drug delivery systems which are developed in order to enhance the therapeutic



effectiveness of drugs in the treatment of chronic diseases. These carriers are mainly formulated from physiological lipids that are safe, biodegradable and compatible with drug delivery systems [7]. These carriers can also enhance drug solubility, stability and bioavailability due to their nanoscale size and lipid structures. Lipid nanocarriers can encapsulate both hydrophilic and lipophilic drugs and enables sustained drug

release. Depending upon their composition and structural organization, lipid nanoparticles are classified into categories such as Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), Liposomes, Lipid Nanoemulsions. Among these, SLNs are one of the majorly studied Lipid Nanoparticles.

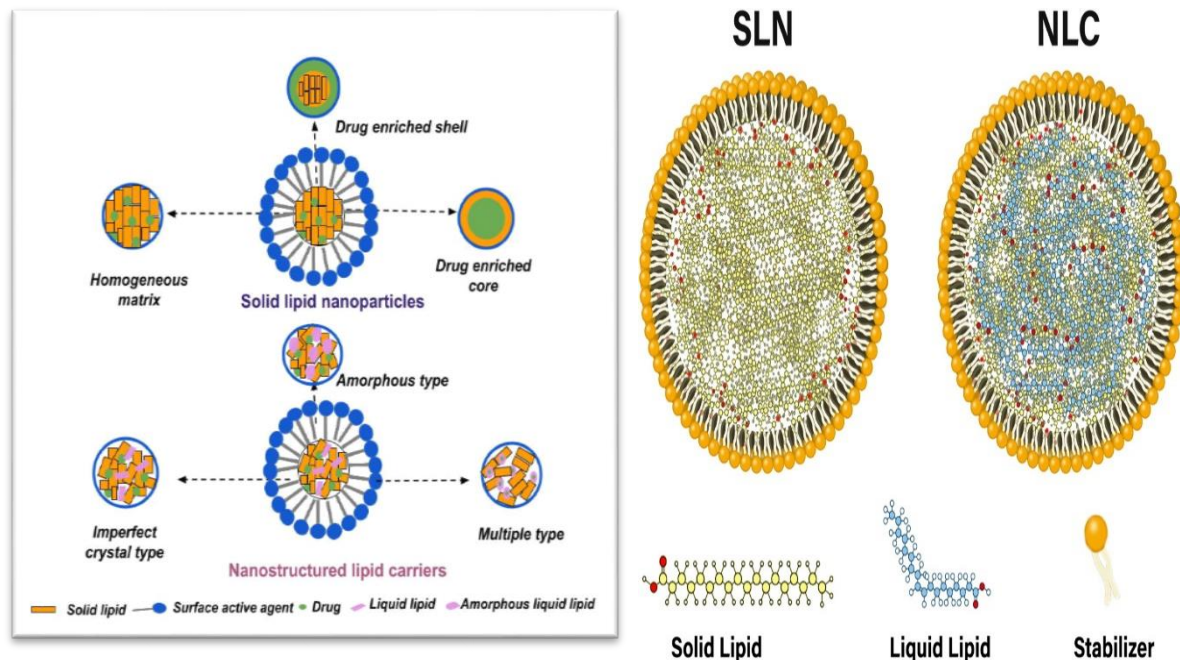


Figure 1: SLN & NLC.

3.1 Solid Lipid Nanoparticles (SLNs)

Solid Lipid Nanoparticles are colloidal carriers composed of solid lipids that remain solid at both room temperature and physiological body temperature. Surfactants or emulsifying agents are used to stabilize to maintain particle stability and prevent aggregation.

Key Characteristics

- It's formulated from physiologically compatible solid lipids like triglycerides, fatty acids, etc.
- Particle size is of 50-1000nm
- Stable in both hydrophilic and lipophilic drugs.
- Provides a solid lipid matrix that enables drug release.

3.2 Nanostructured Lipid Carriers (NLCs)

Nanostructured Lipid Carriers (NLCs) are known as the second generation of lipid nanoparticles. These are advanced to address some of the limitations related with solid lipid nanoparticles. These carriers are developed by combining solid lipids and liquid lipids (oils), makes it less ordered internal lipid structure. The imperfect lipid matrix provides voids for drug molecules and hence enhancing drug loading efficiency and reducing the risk of drug expulsion.

Key Characteristics

- It's formulated from mixture of solid lipids and liquid lipids.
- The size of the particle ranges from 50-1000nm.
- It is capable of both hydrophilic and lipophilic therapeutic agents.
- It is mainly designed to minimize drug expulsion during storage.

3.3 Liposomes

Liposomes are one of the majorly studied Lipid-based drug delivery systems used in pharmaceutical and biomedical research which are microscopic spherical vesicles [8] and consisting of phospholipid bilayers surrounding an aqueous core. The unique structure of Liposomes allows it to incorporate different therapeutic agents.

Key Characteristics

- Its spherical vesicular structures are formed by one or more phospholipid bilayers.
- Liposomes contain an aqueous inner core and are surrounded by lipid membranes.
- The size of the particle varies from nanometers to micrometers.
- These are structurally similar to biological cell membranes and hence enhancing compatibility with the patient's body.

3.4 Lipid Nanoemulsions

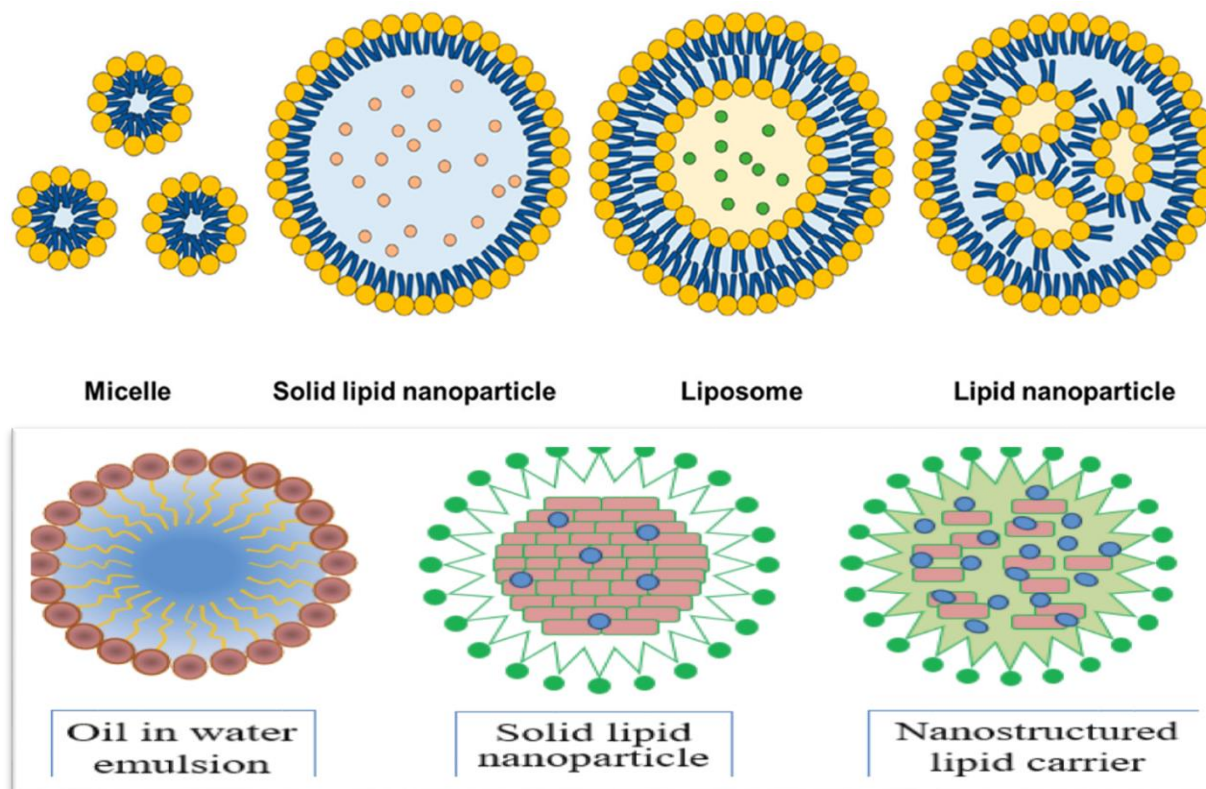
Lipid Nanoemulsions are one of the advanced colloidal drug delivery systems which are formed by tiny droplets of oil dispersed in water. These are stabilized by surfactants and co-surfactants sometimes.

Key Characteristics

- It is formed by oil droplets, aqueous phase, surfactants and co-surfactants sometimes.
- The size of the droplets ranges from 20-200nm.
- It helps in forming a stable dispersion of nanosized droplets.
- It is favorable for including poorly water-soluble drugs.

Table 1: Comparison of lipid nanocarriers.

Features	Solid Lipid Nanoparticles (SLNs)	Nanostructured Lipid Carriers (NLCs)	Lipid Nano emulsions
Physical Condition	Solid	Semisolid	Fluid
Drug Incorporation	Lipophilic Drugs	lipophilic and hydrophilic drugs	lipophilic and hydrophilic drugs
Drug Loading Capacity	Medium	Higher	Medium to higher
Toxicity	Lower	Lower	Lower

**Figure 2:** Lipid based colloidal nanocarriers.

4. Mechanism of controlled drug release in chronic diseases

There are several mechanisms to control drug release in chronic health conditions:

Diffusion: The molecules of drug slowly diffuse from the lipid matrix into the surrounding biological environment.

Lipid Matrix Degradation: Lipid matrix causes enzymatic degradation which helps in gradually releasing the encapsulated drug.

Surface Desorption: Those drugs which adsorbed on the surface of nanoparticles are rapidly released at the initial stage of the process.

Stimuli-Responsive Release: Some of the lipid nanocarriers respond to external stimuli like pH, temperature, etc.

5. Materials

- Solid lipids like Glyceryl monostearate and stearic acid are used in the formation of solid lipid matrix.
- Liquid lipids like Oleic acid and medium-chain triglycerides are used in the enhancement of drug loading efficiency and capacity.
- Surfactants like Tween 80 and Poloxamers [9] are used in stabilizing nanoparticles and preventing aggregation.

- Therapeutic drugs help in controlled delivery in chronic health conditions.
- Aqueous phase includes purified water or buffer solutions are used during the preparation of nanoparticles.
- Stabilizing agents like additional emulsifiers or stabilizers are used in the improvement of composition stability.

6. Methods of preparation

- Firstly, the favorable solid and liquid lipids are selected including the drug.
- Secondly, the selected lipids are melted at a higher above melting point temperature and lipid phase is formed.
- Thirdly, the drug is dissolved in the melted lipid phase for making a uniform mixture.
- Fourthly, the surfactants are dissolved in purified water which gradually forms an aqueous phase.
- In the Fifth step, the lipid phase is combined with the aqueous phase under high-speed stirring to form a nano emulsion.
- Sixth, high-pressure homogenization or ultrasonication is used in the reduction of particle size and hence forming lipid nanoparticles [10].

- Seventh, the Nano emulsion is then cooled down to allow the lipid phase to solidify and hence stable lipid nanocarriers are formed.
- Lastly, the already prepared nanoparticles are deeply evaluated for observing the structural behavior and characteristics.

Table 2: Methods of preparation of lipid nanocarriers.

Preparation Method	Principle	Advantages	Limitations	Nanocarriers Produced
High Pressure Homogenization (HPH)	Lipid and drug combination undergo high pressure to reduce the size of the particle.	Large scale production.	Higher energy consumption.	SNM, NLC
Ultrasonication	Ultrasonic forces help to convert lipid particles into nano droplets.	Laboratory scale preparation.	Particle aggregation.	SNM, NLC
Phase Inversion Temperature Mechanism	Temperature in phase inversion of emulsions helps in the formation of nano particles.	Very small particle size.	Sensitive to temperature	Nanoemulsions.

7. Results

Formation of stable lipid nanoparticles using selected lipids and surfactants. The methods produced small sized particles and improved drug delivery efficiency. It Shows effective drug loading capacity within the lipid matrix. It gives demonstration of gradual controlled and sustained drug release over longer periods. Lipid Nanocarriers improve drug absorption in the chronic conditioned patients. It protects drugs from degradation by encapsulation within lipid nanocarriers [7].

8. Applications

- In Cancer, Lipid nanocarriers helps in improving targeted delivery of chemotherapeutic drugs and hence reduces toxicity and improves efficiency too.
- In Diabetes, Nanocarriers increase insulin delivery and enhance the control in glucose through controlled drug release mechanism.
- In case of Cardiovascular Diseases, Lipid nanocarriers [11] enable targeted drug delivery to heart cells and tissues which improves treatment outcomes.
- In case of Neurological Disorders, Lipid nanoparticles are capable of crossing the blood-brain barrier and delivering sustained drugs for chronic conditions such as Alzheimer's disease and Parkinson's disease.
- In the situation of Arthritis, Controlled drug release procedure helps in reducing inflammation and maintaining therapeutic drug level treatment over longer periods.

9. Advantages

- Drug solubility gets improved. It has enhanced bioavailability.
- It reduces toxicity gradually.
- It helps in controlled and sustained drug release for chronic diseases [6].
- It has the capability to deliver drugs to targeted cells. It is biodegradable and biocompatible in nature.
- It protects drugs from chemical and enzymatic degradation.
- It has the ability to encapsulate both hydrophilic and lipophilic drugs.
- It has increased therapeutic efficacy of drugs. It has the potential for large-scale industrial production.
- It reduces side effects as compared to conventional methods of drug delivery systems.
- Lipid nanoparticles such as NLCs have high drug loading efficiency.
- It improves patient compliance.
- It is capable to cross blood-brain barrier.

10. Challenges and future outlook

After all the advantages there seems to be some limitations which are unavoidable. Some of the challenges are higher production cost, stability issues during storage, too much sensitive with exposure of temperature and light. Even distribution and maintaining uniform particle size is a big deal. For this research specialized equipment are required for the complex formulation methods.

After considering every research has some drawbacks, the future of this study cannot be ignored.

Gene Therapy and RNA Therapy [13] can be combined for advanced treatment.

Artificial Intelligence has been integrated for optimization and formulation development.

Large-scale production can be done and cost-effective manufacturing methods can be revised.

pH, temperature and enzyme systems can be advanced for reducing the limitations.

Multiple drugs can be used in single systems to improve treatment efficiency.

Patient-specific treatment strategies can be modernized for advanced outcomes. Hence, in the future if these systems and study are integrated with other theories and technologies then it will develop new inventions and can be used for human welfare widely.

11. Conclusions

Lipid Nanocarriers have emerged as one of the most promising tool for advanced drug delivery systems for the treatment of chronic conditions. These systems maintain stable drug concentrations in patient body and reduces drugging frequency and also side effects. Lipid Nanocarriers have drawn the interest of researchers from all over the world which also increases patient compliance and are safe in nature. With further research its potential in the pharmaceutical industry has yet to be fully explored. Thus, lipid nanocarriers play a significant role in the future of targeted and personalized drug delivery systems and can also save the lives of millions of people worldwide by treating those chronic diseases that has no other ways to cure.

Acknowledgements

I would like to convey my heartfelt thanks to our professor Dr. Mithu Dey madam for giving me the golden opportunity to do this journal which has helped me to learn a lot of things and also do a lot of research. I would extend my heartiest thanks to my friends for providing me with all the support I needed at all

time. I would like to gratefully thank my parents also for providing me with all facilities and favorable environment at home.

Authors' contributions

All authors contributed equally to the conception, design, experimental work, data analysis, interpretation of results, and preparation of the manuscript. All authors reviewed and approved the final version of the manuscript for publication.

Conflicts of interest

The author declares no conflict of interest.

Funding

This research received no external funding.

Data availability

No new data were created.

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