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Review Article

## Lipid-Based Nanocarriers for Enhanced Oral Bioavailability: A Review of Recent Advances and Applications

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### ABSTRACT

The development of innovative oral drug delivery systems is crucial for improving the bioavailability of poorly soluble drugs. This review focuses on lipid-based nanocarriers, including solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and lipid-polymer hybrid nanoparticles (LPHNPs). These nanocarriers have shown promise in enhancing the solubility, permeability, and bioavailability of poorly soluble drugs. SLNs, NLCs, and LPHNPs have been designed to overcome the limitations of traditional oral drug delivery systems, offering improved stability, targeted delivery, and controlled release of drugs. The applications of these nanocarriers in cancer therapy, anti-inflammatory and analgesic drugs, antiviral and antibacterial agents, and cardiovascular and neurological disorders are also discussed. Despite the advantages of these nanocarriers, challenges such as stability, regulatory considerations, and scaling up production need to be addressed.

**Keywords:** Nanocarriers, Nanoparticles, Oral drug delivery, Bioavailability.**ARTICLE INFO:** Received 27 Nov 2024; Review Complete 28 Dec. 2024; Accepted 19 Jan. 2025. ; Available online 15 Feb. 2025**Cite this article as:**Aboli P. Mangle AP, Dr. Ravindra L. Bakal, Pooja R. Hatwar, Jitendra A. Kubde, Lipid-Based Nanocarriers for Enhanced Oral Bioavailability: A Review of Recent Advances and Applications, Asian Journal of Pharmaceutical Research and Development. 2025; 13(1):71-80, DOI: <http://dx.doi.org/10.22270/ajprd.v13i1.1506>

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### INTRODUCTION:

The percentage of a given medication that enters the systemic circulation in an active state and is accessible for therapeutic action is known as bioavailability. Pharmacokinetics, the area of pharmacology that studies how medications are absorbed, distributed, metabolized, and excreted, is based on this concept<sup>1</sup>. Due to its ease of usage and patient acceptability, oral administration is among the most conventional methods. However, because of the strong obstacles the GI tract presents, many biological therapies that are poorly soluble, poorly permeabilized, and/or poorly stable in the GI environment also have low oral bioavailability and are rarely employed for oral drug administration<sup>2</sup>. The advantages of improved medication absorption, particularly in terms of increasing bioavailability, have been demonstrated using nanoformulation. In recent

years, there has been a notable surge in the use of nanoformulations for oral administration systems<sup>3</sup>.

#### Challenges with poorly soluble drugs

Among these strategies, polymeric micelles (PMs) have drawn a lot of interest in the past 20 years as a multipurpose nanotechnology-based drug delivery method for medications that are not highly soluble in water<sup>4</sup>. Therefore, increasing the solubility and rate of dissolution of poorly water-soluble medications and boosting the permeability of poorly permeable pharmaceuticals are two fields of pharmaceutical research that concentrate on increasing the oral bioavailability of active substances<sup>5</sup>. In drug discovery, poorly water-soluble drug candidates lead to a growing number of issues with inconsistent and poor bioavailability. About 70% of novel chemical entities are thought to be

poorly soluble in aqueous media, and many of them are even poorly soluble in organic media. Drug distribution benefits from nanotechnology, especially when it comes to oral medications. It makes it possible to administer drugs that are not particularly soluble in water<sup>4</sup>. Because of their low solubility and sluggish rates of dissolution, poorly soluble medications with notable pharmacological activity frequently fall short of their full therapeutic potential, which can result in problems including the requirement for higher doses of the drug in clinical settings<sup>6</sup>. It is difficult to encapsulate and precisely control the release of hydrophilic medications due to their highwater solubility, which makes it difficult to stop drug leakage into the aqueous phase<sup>7</sup>. To improve the solubility of medications that are not very soluble in water, the co-solvency approach has been used to a wide range of solvent combinations<sup>8</sup>.

### Overview of lipid-based nanocarriers

A flexible and promising platform for medication administration, gene therapy, and diagnostics is lipid-based nanocarriers. These nanocarriers improve stability, bioavailability, and targeting capabilities by encapsulating medicinal chemicals in naturally occurring lipids. The stability, targeting capability, and general effectiveness of the nanocarriers can all be improved by these changes<sup>9</sup>. Phospholipids are used to create liposomes. In contrast to liposomes, which are made up of phospholipid bilayers like cell membranes, vesicle-based micelles are composed of a single layer of phospholipids, with the head group facing the exterior and the hydrophobic tails forming the micelle core in a hydrophilic atmosphere, such as blood<sup>10</sup>. Lipid-based nanoparticles are employed in RNA-release therapy for the treatment of cancer and as drug carriers<sup>11</sup>.

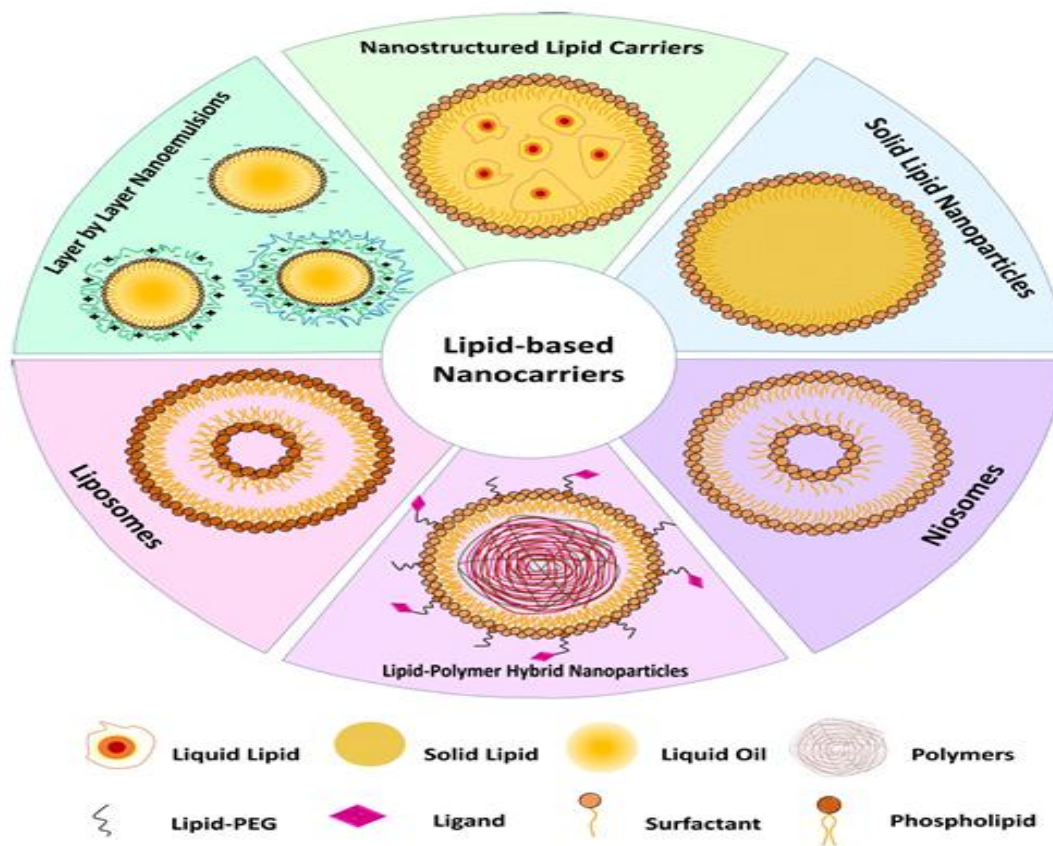


Figure 1: The main lipid-based nanocarriers<sup>12</sup>.

Drug release from lipid-based formulations is primarily governed by four fundamental principles: solubility, dispersion, digestion, and absorption<sup>13</sup>.

### Advantages<sup>12</sup>

- Increasing the solubility of bioactive compounds.
- Delivering chemicals in significant amounts.
- The used lipids' biodegradable nature.
- Including the lipophilic and hydrophilic biomolecules.
- More affordable as compared to other delivery options.

- Water-based technique that eliminates organic solvents.
- Controlled and extended release of bioactive substances.
- Extensive production because of the ease of preparation.
- Accurate particle size.
- Stronger physical stability.

### LIPID-BASED NANOCARRIERS

#### Solid Lipid Nanoparticles (SLNs)

Since their creation in 1991, SLNs have dominated the market for drug and other payload delivery modules<sup>14</sup>.

Previously known as lipospheres, solid lipid nanoparticles (SLNs) are a potential class of pharmacological nanocarrier intended for the regulated release of drugs<sup>15</sup>. With an average size range fluctuation of 10 to 1,000 nm, SLNs are also spherical in form<sup>14</sup>. Solid lipid nanoparticles can stabilize sensitive components chemically and physically while combining particle form and integrity<sup>16</sup>. In the arsenal of oral drug delivery systems, SLNs that combine the benefits of several carrier systems have become advantageous carriers. In the arsenal of oral drug delivery systems, SLNs that combine the benefits of several carrier systems have become advantageous carriers<sup>17</sup>. SLNs have been identified as preferable carriers, notably, for the lipophilic pharmaceuticals

for the high-yielding, efficient, and optimal drug delivery of the encapsulated/entered medications with increased bioavailability<sup>14</sup>. Solid lipids, mostly physiological lipids, distributed in an aqueous solution with a surface stabilizer<sup>15</sup>, make up the majority of SLNs. Due to their superior penetration through anatomical constraints, prolonged, and to a lesser degree, chrono-controlled delivery, SLNs have also become a viable alternative to liposomal deliveries<sup>14</sup>. The key ingredients of SLN formulations include lipids, which are in the solid state at room temperature, emulsifiers and sometimes a mixture of both, active pharmaceutical ingredients (APIs) and an adequate solvent system<sup>18</sup>.

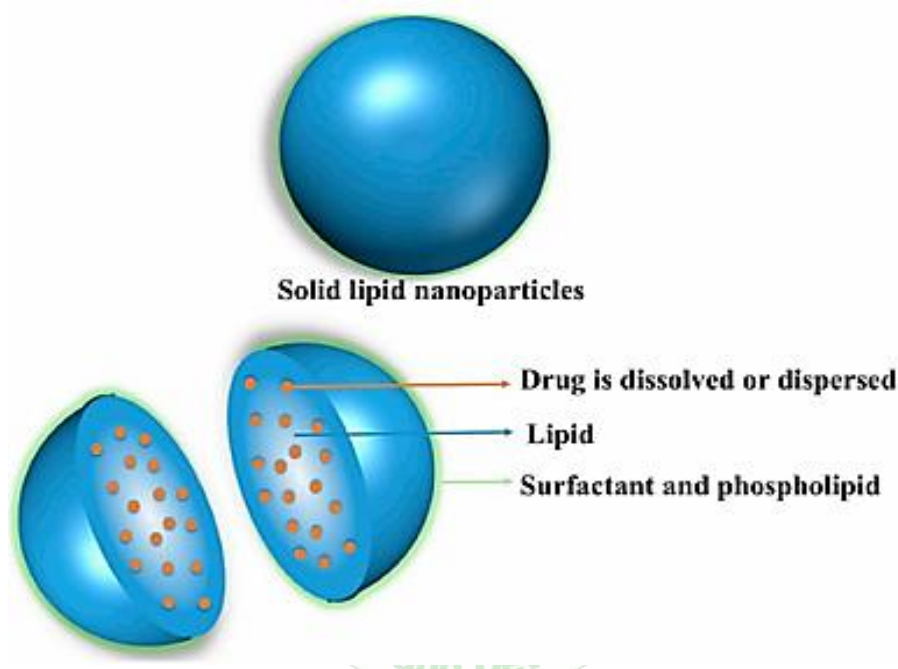


Figure 2: Structure of solid nanoparticle<sup>19</sup>.

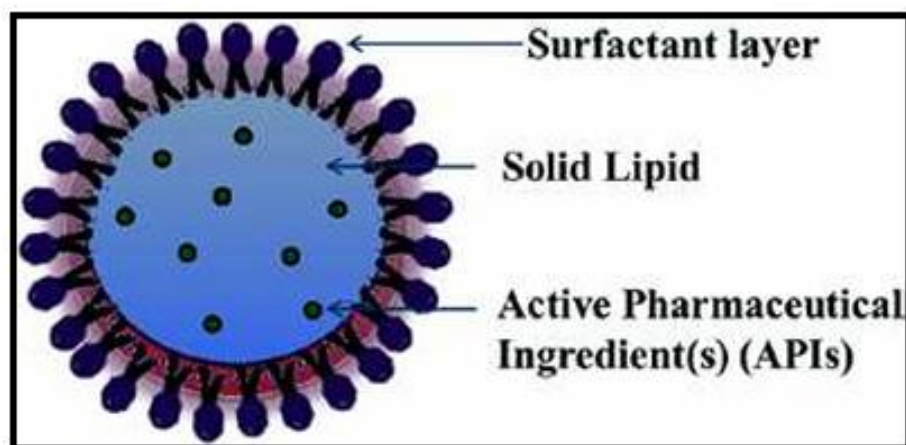


Figure 3: Structure solid lipid nanoparticles<sup>16</sup>.

### Synthesis

The diameter of spherical SLNs ranges from 10 to 1000 nm. These nanoparticles' solid lipid core structure allows them to

dissolve lipophilic drugs. Emulsifiers (surface activators) can stabilize the lipid matrix, which is used according to the method of intake and is more limited for injection. It is a

solid hydrophobic core matrix covered with phospholipids. In this regard, we will review some methods used to prepare SLN-based drug delivery platforms, such as i) Homogenization at high pressure, ii) micro-emulsion technology, iii) membrane contactor technique iv) probe/bath

ultrasonication, v) spray drying technique vi) double emulsion method vii) super crystal fluid method viii) solvent emulsification diffusion method shows some techniques for the synthesis of SLNs<sup>20</sup>.

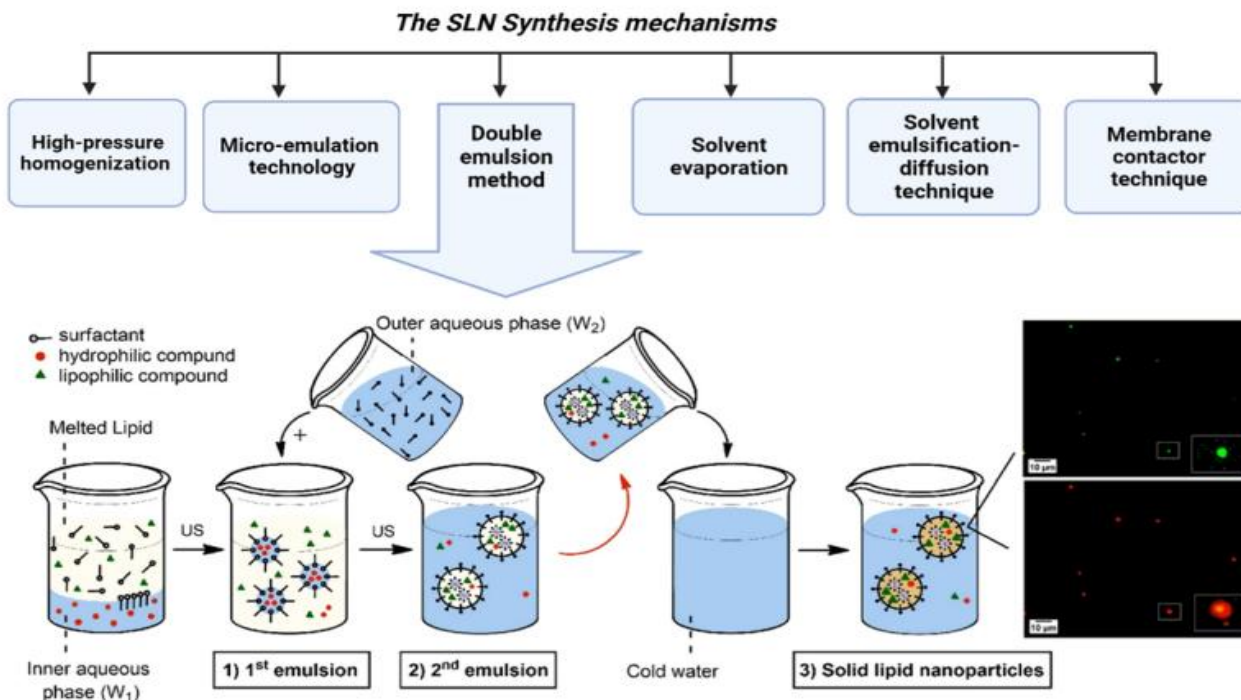


Figure 4: The Solid lipid synthesis mechanisms<sup>20</sup>.

### Advantages

- SLNs provide several benefits in DDSs by acting as efficient carriers for a range of active ingredients. There are several ways to administer these carriers. By bypassing biological barriers, the physiological nature of SLN compounds enables tailored administration, lowering the risk of acute and chronic toxicity. There are many advantages to using SLNs for medication delivery<sup>15</sup>.
- Sensitive medications are shielded from chemical, oxidative, and photochemical deterioration by immobilizing drug molecules into solid lipids, which also reduces drug leakage. Drying by lyophilization is feasible<sup>16</sup>.
- Reticuloendothelial system cells can bypass liver and spleen filtration because they cannot absorb solid lipid nanoparticles due to their nanosized range<sup>19</sup>.
- Increase the stability of medications<sup>19</sup>.
- Drying by lyophilization is feasible<sup>19</sup>.

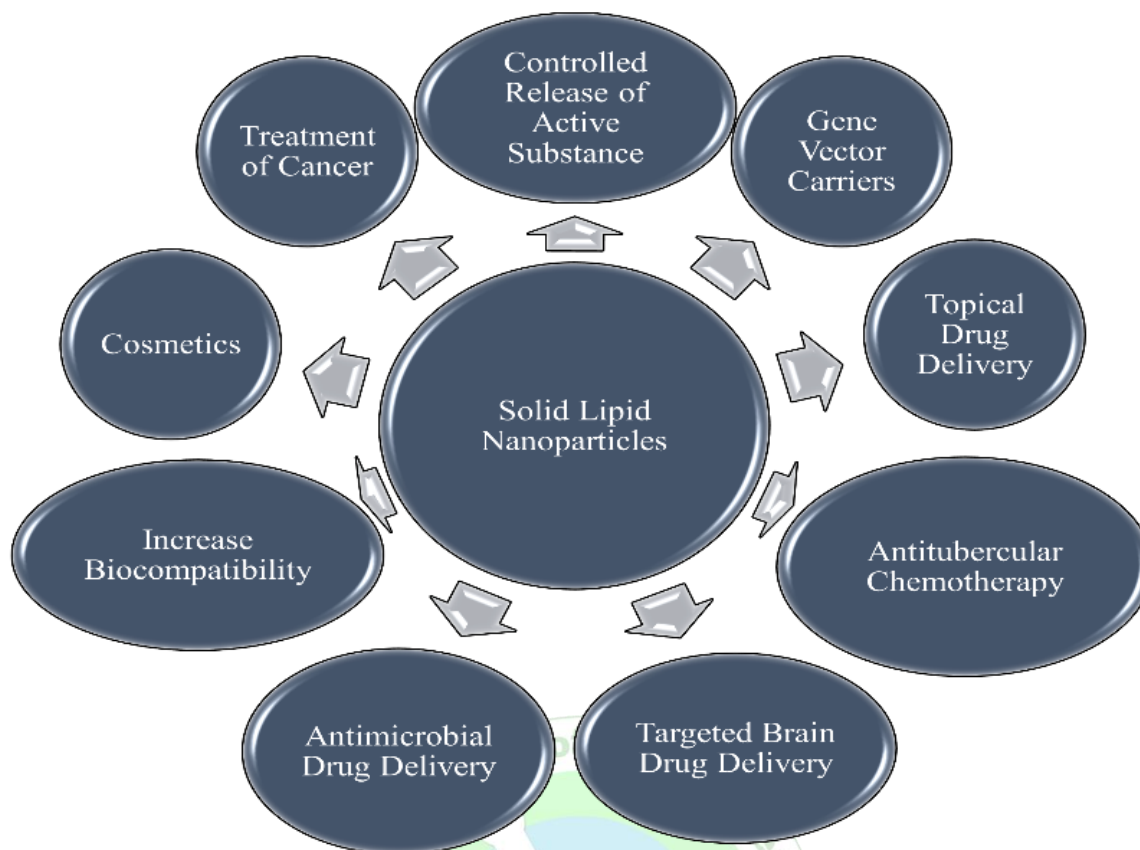
### Disadvantages

- SLNs do, however, have several drawbacks. The production process is costly and intricate, including certain tools and supplies. Drugs being ejected during

- storage or changes in the lipid structure that impact dependability are examples of stability problems<sup>15</sup>.
- During storage, drug release occurs following polymeric transformation. The water concentration of the dispersion particles is high, ranging from 70 to 90%<sup>16</sup>.
- Inadequate ability to load drugs<sup>19</sup>.
- The type of gelation tendencies might vary<sup>19</sup>.
- The water content of the dispersion is comparatively greater, ranging from 70 to 99.9%<sup>19</sup>.

### Applications

The wide range of applications for SLNs and the ongoing research into additional possible applications demonstrate their adaptability and therapeutic effectiveness. Using Compritol 888 ATO, Soy Lecithin/Pluronic F68, or Soy Lecithin/Tween 80 via HPH, for example, can be used to formulate  $\alpha$ -trans retinoic acid into SLNs. This formulation greatly improved oral bioavailability and gastrointestinal absorption, both of which are important for treating acne and several types of cancer<sup>15</sup>. There are various Applications of Solid Lipid Nanoparticles widely used SLN Listed below<sup>16</sup>.



**Figure 5:** Applications of Solid Lipid Nanoparticles <sup>16</sup>.

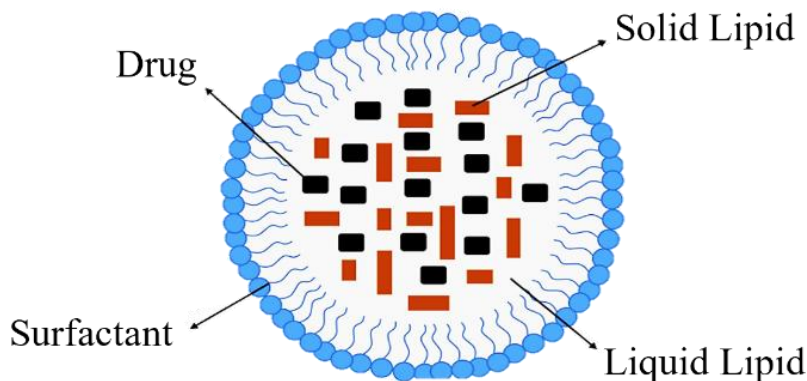
### Nanostructured Lipid Carriers (NLCs)

The purpose of NLCs, also known as the second generation of LBNPs, is to get around the drawbacks of SLNs. They are classified as colloidal drug delivery systems because their core matrix contains both liquid and solid lipids <sup>21</sup>. NLCs as the name suggest are nanosized multiparticulate system in the size range of 50 nm to 500 nm. The particle size distribution of NLC depends on nanoparticles manufacturing process and composition <sup>22</sup>. It was once thought that these second-generation lipid nanoparticle systems could only load lipophilic medications, making it difficult to load water-

soluble ones. To solve this issue, lipid-drug conjugates were later developed, and NLCs are still the ideal method for loading hydrophilic pharmaceuticals <sup>23</sup>. A mixture of solid and liquid lipids that stay solid at body temperature is used to make NLC <sup>24</sup>.

### COMPOSITION

NLCs are carrier systems made up of lipids that are both liquid and solid. Within NLCs, the physical characteristics, melting points, and crystalline features of solid and liquid lipids may be used to distinguish between them <sup>25</sup>.



**Figure 6:** Composition Nanostructured Lipid Carriers (NLCs) <sup>25</sup>.

With a melting point that is usually higher than 37°C, solid lipids- such as stearic acid, glyceryl behenate, and glyceryl palmitostearate maintain their solidity during physiological and environmental temperatures, guaranteeing structural integrity in NLC formulations<sup>25</sup>.

### Advantages

- Prevent drug deterioration.
- Keep medication safe from stomach enzymes and pH.
- Stomach mucosa adhesion.
- By reducing the release of loaded unstable chemicals from the lipid structure and preserving the topical formulations' physical quality throughout storage, NLCs improve the chemical stability of active components<sup>26</sup>.

### limitations

There are many difficulties and barriers when using nanostructured lipid carriers (NLCs) technology for topical wound healing. The regulatory structure controlling the

creation of drugs at the nanoscale is one important concern. Usually, guidelines for testing and quality control procedures are created for straightforward, unaltered medications. The ingredients utilized in the formulation of NLCs also provide constraints for their utilization<sup>25</sup>.

- Enhanced drug physical stability and extended release<sup>27</sup>.
- Preparation and scaling up are easy.
- Enhanced dispersibility of aqueous media.
- Notable trapping of hydrophilic and lipophilic drugs<sup>13</sup>.

### Applications

Active compounds have been included into NLCs in a number of studies, underscoring the important role these carriers play in wound medication delivery. NLCs greater bioadhesive qualities are the mechanism underlying the improved wound healing they enable. Research by Saporito et al. provides supporting data, showing that NLCs had the highest amount of bioadhesion when compared to both control and unloaded medicines<sup>25</sup>.

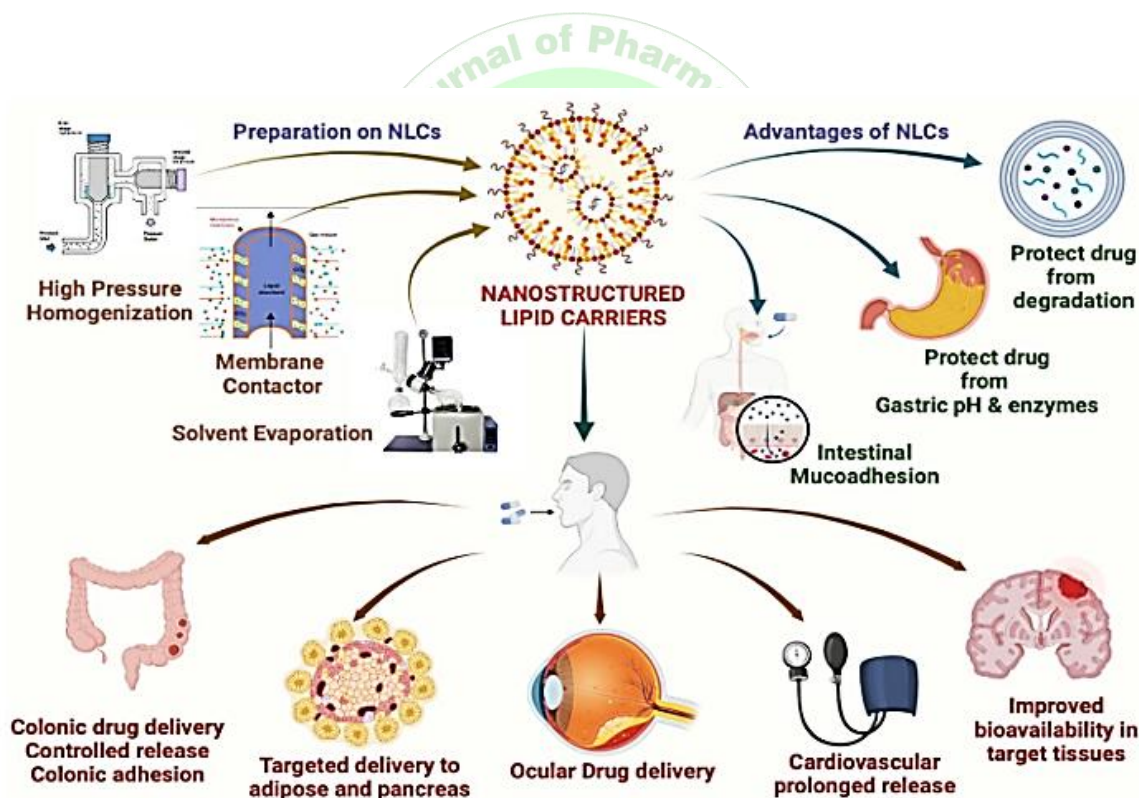


Figure 7: Applications of Nanostructured Lipid Carriers<sup>25</sup>.

### Lipid-Polymer Hybrid Nanoparticles

By combining polymeric nanoparticles with liposomes, the lipid polymer hybrid nanoparticles are a novel formulation that successfully addresses the shortcomings of each substance when utilized separately<sup>9</sup>. A lipid layer envelops a polymer core in polymer-lipid hybrid nanoparticles (PLNPs). These were created with the idea that mixing polymeric NPs

with liposomes would be superior to employing only pure lipids or polymers<sup>28</sup>. By combining the beneficial qualities of liposomes with polymeric nanoparticles, LPHNPs offer a step forward in nanoparticle technology. These PLHNPs combine biomimetic lipids and biocompatible polymers, giving them exceptional adaptability in the delivery of chemotherapeutic drugs with a variety of physicochemical characteristics<sup>29</sup>.

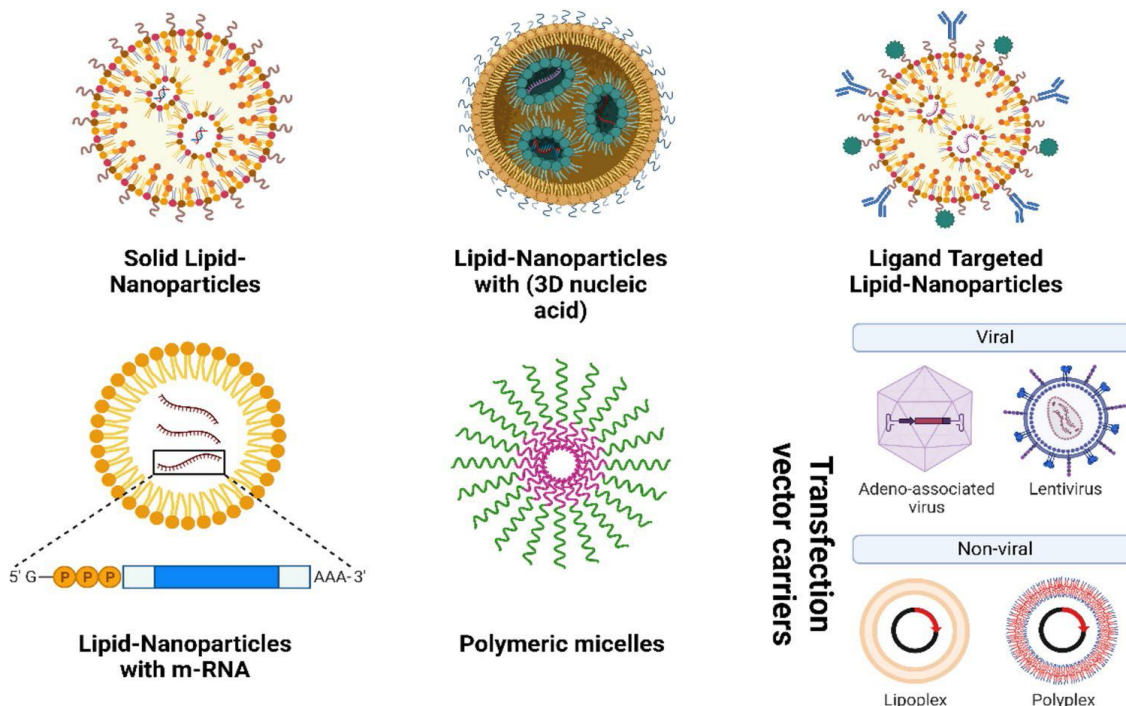


Figure 8: Various types of lipid nanoparticles <sup>30</sup>.

## COMPOSITION

Four fundamental lipid components are commonly found in LNP composition: cholesterol, zwitterionic phospholipids, polyethylene glycol (PEG) lipids, and localizable cationic lipids <sup>31</sup>.

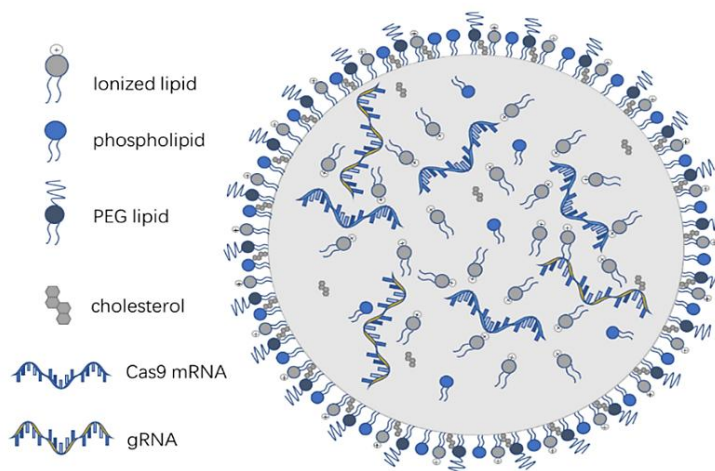


Figure 9: Composition Lipid-Polymer Hybrid Nanoparticles <sup>31</sup>.

## Applications <sup>31</sup>

- Gold Nanoparticles Encapsulated in Lipids.
- Monosized Lipid-Coated Stellate Mesoporous Silica Nanoparticles (LC-MASNs) that are biocompatible.
- Messenger RNA nanoparticles with biodegradable lipids.
- Nanoparticles of Mulberry Leaf Lipids.
- Phenylboric acid-derived lipid nanoparticles.
- The technology of lipid-polymer hybrid nanoparticles is limited to the destruction of microbubbles by ultrasound.
- PEG-b-PLGA nanoparticles aided by cationic lipids.
- Multi-Valent Lipid Nanoparticles of N-Acetylgalactosamine (Gal NAc).

## MECHANISMS OF ENHANCED ORAL BIOAVAILABILITY

### Improved solubility and dissolution rate

A solid, liquid, or gaseous chemical component known as a solute's ability to dissolve in a solvent and create a homogeneous solubility is a feature that is mostly dependent on the solvent employed, as well as on temperature and pressure <sup>5</sup>. The saturation concentration, at which the addition of more solute does not raise the concentration of the solute in the solution, is a measure of a substance's degree of solubility in a particular solvent <sup>32</sup>. Their solubility or dissolution rate determines the pace at which they are

absorbed in the gastrointestinal tract<sup>13</sup>. A drug's solubility behavior is one of the most important factors affecting its oral bioavailability. It has always been challenging to develop an oral administration formulation with good bioavailability due to the solubility of some medicinal compounds<sup>27</sup>. Tacrolimus's pharmacokinetics and bioavailability depend on a number of parameters, such as its poor solubility and status as a substrate for the CYP3A and P-gp enzymes. Tacrolimus's low water solubility and strong hydrophobicity make it challenging to formulate for oral delivery<sup>33</sup>. A key physicochemical characteristic that influences drug absorption and therapeutic efficacy is solubility<sup>34</sup>.

### Enhanced permeability and absorption

High permeability indicates that the medication product is stable in the gastrointestinal tract and that more than 90% of the prescribed dosage is absorbed. Permeability is the ability to pass through biological membranes and migrate from the place of administration (the gastrointestinal tract) to the systemic circulation. Permeability is dependent on drug absorption, which is dependent on several chemical characteristics, receptors, biological membranes, transport modes, respectively<sup>24</sup>. The amount of a medicine that enters the systemic circulation depends on its capacity to pass through biological membranes, including the gut wall, how a medication enters the bloodstream from the place of administration. The presence of food, the pH of the gastrointestinal tract, and the formulation of the medicine all affect absorption. The processes of drug absorption and the variables affecting permeability across biological membranes require more investigation. Examining the function of enzymes, transporters, and gastrointestinal disorders is part of this<sup>1</sup>.

### Targeted delivery to specific tissues

Among the many significant benefits of targeted drug delivery of LNPs are (i) protection of healthy cells from cytotoxic compounds, (ii) enhanced drug accumulation in the tumor, which lowers dose-related cytotoxicity to normal healthy cells, and (iii) enhanced bioavailability and therapeutic efficacy<sup>29</sup>. Targeted liposomes have been developed with ligands on their surface to help them find and bind to certain cell receptors (such the folate receptor). The surface of LNPs is commonly modified using peptides, monoclonal antibodies, or small molecule ligands to produce tailored liposomes. The great loading capacity and adaptability of liposomal delivery methods in modifying their physical, chemical, and biological characteristics have drawn a lot of interest as therapeutic carriers<sup>30</sup>.

## APPLICATIONS

### Cancer therapy

Chemotherapy, which involves injecting drugs into the body, has been the most popular cancer treatment up to this point. Surgery may not be the best option for all cancer types.

Chemotherapy, radiation therapy, immunotherapy, phototherapy, and hormone therapy have all advanced, but their fundamental drawback is that they have detrimental side effects that kill both healthy and injured body cells, making them poor choices<sup>35</sup>. Many traditional medicines, including as immunotherapy, hormone therapy, chemotherapy, and radiation therapy, are now used to treat breast cancer. Radiation treatment can be utilized to eradicate cancer cells that might not be seen after surgery, reducing the chance of a local cancer recurrence<sup>36</sup>. Micelles and liposomes, which are lipid-based nano-carriers, have advanced the treatment of breast cancer. When loaded with cisplatin, Andey et al. have shown that the lipid-conjugated estrogenic derivative (ESC8) is more efficacious, particularly in a xenograft mice model. Their research has also demonstrated the potential of lipid nanocarriers in the treatment of malignancies that are resistant to drugs<sup>37</sup>. This section discusses the most important developments in the use of LBNP for the treatment of the most common kinds of cancer<sup>07</sup>.

### Anti-inflammatory and analgesic drugs

Patients with a variety of illnesses and conditions frequently utilize non-steroidal anti-inflammatory medicines (NSAIDs), such as aspirin, diclofenac, ibuprofen, or celecoxib, which are widely accessible both with and without a prescription<sup>38</sup>. The chronic illness known as inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), results in inflammation of the digestive system. The gastrointestinal tract is harmed by persistent inflammation and immunological dysfunction<sup>39</sup>.

### Antiviral and antibacterial agents

The most research and development of technology that makes use of the antibacterial characteristics of nanoparticles has been done in the domains of health and medicine. Nano drug delivery systems have a lot of potential to enhance medication therapy since they can sustain drug release and prevent drug degradation. Bacterial infections and the repercussions they may produce are a major and frequent cause of death<sup>11</sup>. In the treatment of non-small-cell lung cancer, these nanoparticles demonstrated improved bioavailability and therapeutic effectiveness, suggesting a viable path toward maximizing bedaquiline's use in cancer therapy<sup>40</sup>. Commonly used skincare treatments and formulations have a number of disadvantages, such as limited skin effectiveness and toxicity. As a result, gold and silver nanoparticles have become popular because of their broad antifungal and antibacterial capabilities<sup>41</sup>.

One of the greatest pathogens of human disease in documented human history has been found to be viruses. Viral diseases, such as HIV, Ebola, Marburg, Spanish influenza, and, most recently, the COVID-19 pandemic of 2020, are a major danger to human health despite their



apparent structural simplicity. When viruses attach to and enter host cells, they can cause damage <sup>11</sup>.

### Cardiovascular and neurological disorders

The term "neurological disorders" refers to a broad category of illnesses that impact the brain, spinal cord, and peripheral nerves. Debilitating deficits in motor function, cognition, behavior, and general quality of life may arise from these illnesses. Epilepsy, multiple sclerosis, Parkinson's disease, Alzheimer's disease, neuropathic pain, and anxiety disorders are a few prevalent neurological conditions <sup>42</sup>.

## CHALLENGES AND FUTURE DIRECTIONS

### Stability

For bacterial nanocarriers to be used safely and effectively in medication delivery applications, stability and biocompatibility are essential factors. To guarantee dependable and constant therapeutic results, bacterial nanocarriers must preserve their structural integrity and drug-loading ability throughout administration, storage, and transit. Physical stability (e.g., aggregation, sedimentation, or degradation), chemical stability (e.g., drug degradation or release), and biological stability (e.g., vulnerability to enzymatic destruction or immunological recognition) are some of the components that make up stability <sup>43</sup>.

### Regulatory considerations

Since there are no established standards or assessment criteria, it might be difficult to get regulatory clearance for ethosomal herbal preparations. To prove the safety, effectiveness, and quality of ethosome-based products, regulatory bodies could need a lot of preclinical and clinical evidence, which would take longer to approve (Bhatt, 2018) <sup>44</sup>. Nanomedicine's regulatory environment is complex and constantly changing. MNPs' special qualities provide difficulties for regulatory approval even if they are beneficial for medication delivery. Nanoparticles frequently display distinct toxicity and pharmacokinetics <sup>45</sup>. Guidelines and regulations must be updated in response to new scientific discoveries and developing technology, which requires constant communication between researchers and regulatory bodies. By doing this, regulatory frameworks are kept current and encourage creative thinking <sup>01</sup>.

### Future research directions

Future research directions should focus on addressing the challenges associated with lipid-based nanocarriers, such as stability, regulatory considerations, and scaling up production. The development of novel lipid-based nanocarriers with improved stability, targeted delivery, and controlled release of drugs is essential. The application of these nanocarriers in various diseases, including cancer, inflammatory disorders, and infectious diseases, should be explored. Additionally, the development of lipid-based nanocarriers for personalized medicine and gene therapy is an

area of future research. The use of artificial intelligence in the design and optimization of lipid-based nanocarriers is also a promising area of research. Furthermore, the development of novel analytical techniques for the characterization of lipid-based nanocarriers is essential for their therapeutic purpose.

## CONCLUSION:

Lipid-based nanocarriers have shown great potential in enhancing oral bioavailability of poorly soluble drugs. These nanocarriers offer improved solubility, permeability, and targeted delivery of drugs, making them a promising tool for various therapeutic applications. However, stability and regulatory considerations remain significant challenges that need to be addressed. Future research directions should focus on developing novel lipid-based nanocarriers with improved stability, targeted delivery, and controlled release of drugs.

## REFERENCE

- Bhandare A and Nannor KM. Bioavailability in drug design and development: A comprehensive review. *World Journal of Pharmaceutical Research* 2024;13(17):145-168.
- Zhang L, Wang S, Zhang M and Sun J. Nanocarriers for oral drug delivery. *Journal of Drug Targeting* 2013; 21(6): 515–527.
- Preeti, Sambhakar S, Malik R, Bhatia S, Harrasi AA, Saharan R, Aggarwal G, Kumar S, Sehrawat R and Rani C. Lipid Horizons: Recent Advances and Future Prospects in LBDDS for Oral Administration of Antihypertensive Agents. *Hindawi International Journal of Hypertension* 2024;1: 1-54.
- Xu W, Ling P, and Zhang T. Polymeric Micelles, a Promising Drug Delivery System to Enhance Bioavailability of Poorly Water-Soluble Drugs. *Hindawi Journal of Drug Delivery* 2013;1:1-15.
- Bagwan JA, Adhav DU, Ade DD, Bhalerao DD and Avdhut MS. A review on solid dispersion technique for enhancing solubility of poorly soluble drugs. *World Journal of Pharmaceutical Research* 2024;13(8):87-106.
- Liu Y, Liang Y, Yuhong J, Xin P, Jia Li Han, Du Y, Yu X, Zhu R, Zhang M, Wen Chen & Yingjie Ma. Advances in Nanotechnology for Enhancing the Solubility and Bioavailability of Poorly Soluble Drugs. *Drug Design, Development and Therapy* 2024;18:1469–1495.
- Waheed I, Ali A, Tabassum H, Khatoun N, Wing-Fu Lai and Zhou X. Lipid-based nanoparticles as drug delivery carriers for cancer therapy. *Frontiers in Oncology* 2024;14:1296091.
- Balmanno A, Falconer JR, Ravuri HG and Mills PC. Strategies to improve the Transdermal Delivery of Poorly Water-Soluble Non-Steroidal Anti-Inflammatory Drugs. *Pharmaceutics* 2024;16:675.
- Anwar DM, Hedeya HY, Ghozlan SH, Ewas BM and Khattab SN. Surface-modified lipid-based nanocarriers as a pivotal delivery approach for cancer therapy: Application and recent advances in targeted cancer treatment. *Beni-Suef Univ J Basic Appl Sci* 2024;13:06.
- Patel P, Garala K, Singh S, Prajapati BG and Chittasupho C. Lipid-Based Nanoparticles in Delivering Bioactive Compounds for Improving Therapeutic Efficacy. *Pharmaceutics* 2024;17: 329.
- Falke PB, Shelke PG, Hatwar PR, Bakal RL and Kohale NB. A comprehensive review on Nanoparticle: Characterization, classification, synthesis method, silver nanoparticles and its applications. *GSC Biological and Pharmaceutical Sciences* 2024;28(01):171–184.
- Abbasi A, Hashemi M, Kafil HS, Astamal MA, Lahouty M, Tajani AG, Hosseini H, Nasirifar SZ. A Critical Review on the Bioavailability Promotion of the Food Bioactive Compounds: Nano Lipid Carriers Perspective. *Pharmaceutical Sciences* 2024;30(3):282-303.

13. Kesharwani R, Jaiswal P, Patel DK, Yadav PK. Lipid-Based Drug Delivery System (LBDDS): An Emerging Paradigm to Enhance Oral Bioavailability of Poorly Soluble Drugs. *Biomedical Materials & Devices* 2022. <https://doi.org/10.1007/s44174-022-00041-0>
14. Mohammed HA, Khan RA, Singh V, Yusuf M, Akhtar N, Sulaiman GM, Albukhaty S, Abdellatif AH, Khan M, Mohammed SA, and Al-Subaiyel AM. Solid lipid nanoparticles for targeted natural and synthetic drugs delivery in high-incidence cancers, and other diseases: Roles of preparation methods, lipid composition, transitional stability, and release profiles in nanocarriers' development. *Nanotechnology Reviews* 2023; 12:20220517.
15. Krishnan MN, Sangeetha S, Ranjani PS, Narayanasamy D. The Science of Solid Lipid Nanoparticles: From Fundamentals to Applications. *Cureus* 2024; 16(9): e68807.
16. Phalak S, Bodke V, Yadav R, Pandav S, Ranaware M. A systematic review on nano drug delivery system: solid lipid nanoparticles (SLN). *International Journal of Current Pharmaceutical Research* 2024;16(1):10-20.
17. Harde H, Das M and Jain S. Solid lipid nanoparticles: an oral bioavailability enhancer vehicle. *Expert Opin. Drug Deliv.* 2011; 8(11):1407-1424.
18. Duan Y, Dhar A, Patel C, Khimani M, Neogi S, Sharma P, Kumar NS and Vekariya RL. A brief review on solid lipid nanoparticles: part and parcel of contemporary drug delivery systems. *RSC Adv.*, 2020; 10: 26777–26791.
19. Munir M, Zaman M, Waqar MA, Khan MA & Alvi MN. Solid lipid nanoparticles: a versatile approach for controlled release and targeted drug delivery. *Journal of Liposome Research* 2024;34(2):335-348.
20. Arabestani MR, Bigham A, Kamarehei F, Dini M, Gorjikhah F, Shariati A, Hosseini SM. Solid lipid nanoparticles and their application in the treatment of bacterial infectious diseases. *Biomedicine & Pharmacotherapy* 2024; 174:116433.
21. Eker F, Duman H, Akda E, Bolat E, Sarita S, Karav S and Witkowska MA. A Comprehensive Review of Nanoparticles: From Classification to Application and Toxicity. *Molecules* 2024; 29:3482.
22. Khan S, Sharma A, Jain V. An overview of Nanostructured Lipid Carriers and its application in drug delivery through different routes. *Adv Pharm Bull.* 2023 Jul;13(3):446-460. doi: 10.34172/apb.2023.056. Epub 2022 Sep 18. PMID: 37646052; PMCID: PMC10460807.
23. D. Pranitha, Velraj M. Advancing oral drug bioavailability: A comprehensive review of Nanostructured Lipid Carriers. *International Journal of Chemical and Biochemical Sciences* 2023;24(12):96-103.
24. Godase SS, Kulkarni NS, Dhole SN. A Comprehensive Review on Novel Lipid-Based Nano Drug Delivery. *Adv Pharm Bull* 2024;14(1):34-47.
25. Wathoni N, Suhandi C, Elamin KM, Lesmana R, Hasan N, Mohammed AFA, Ali El-Rayyes and Wilar G. Advancements and Challenges of Nanostructured Lipid Carriers for Wound Healing Applications. *International Journal of Nanomedicine* 2024;19: 8091–8113.
26. Fitriani EW, Avanti C, Rosana Y, Surini S. Nanostructured lipid carriers: A prospective dermal drug delivery system for natural active ingredients. *Pharmacia* 2024; 71:1–15.
27. Mishra R, Devi. Solid dispersion: An overview of different methodology and techniques. *International Journal of Research and Analytical Reviews* 2024; 11(1):392-400.
28. Albakr L, Hongyuan Du, Zhang X, Kathuria H, Anwar-Fadzil AF, Wheate NJ, and Kang L. Progress in Lipid and Inorganic Nanocarriers for Enhanced Skin Drug Delivery. *Adv. Nano Biomed Res.* 2024;4: 2400003.
29. Chaudhary AA, Fareed M, Salah-Ud-Din Khan, Lina M. Alneghery LM, Aslam M, Arockia Alex, Md. Rizwanullah. Exploring the therapeutic potential of lipid-based nanoparticles in the management of oral squamous cell carcinoma. *Explor Target Antitumor Ther.* 2024; 5:1223–46.
30. Dhayalan M, Wang W, S. U. Mohammed Riyaz, Dinesh RA Shanmugam J, Irudayaraj SS, Stalin A, Giri J, Mallik S, Ruifeng Hu. Advances in functional lipid nanoparticles: From drug delivery platforms to clinical applications. *3 Biotech* 2024; 14:57.
31. Zhang T. Applications of Lipid Nanoparticles in CRISPR Technology. *Dean & Francis.* 2024; 1(7):1-5.
32. Nasikkar Z, Tiwari S, Vishwakarma R, Tarmale P, Verma N and Turerao M. Solid dispersion: A review. *World Journal of Pharmaceutical Research* 2024; 13(9) 271-287.
33. Sajjadi S, Shayanfar A, Kiafar F, Siah-Shadbad M, Tacrolimus: Physicochemical stability challenges, analytical methods, and new formulations. *International Journal of Pharmaceutics: X* 2024; 8:100285.
34. Motwani A, Hatwar PR, Dr. Bakal RL. Advances in Solubility Enhancement of Poorly Soluble Drugs in Pharmaceutical Development: A Review of Current Techniques and Strategies. *International journal of pharmaceutical sciences.* 2024; 2(11):138-148.
35. Anjum S, Hashim M, Malik SA, Khan M, Lorenzo JM, Abbasi BH and Hano C. Recent Advances in Zinc Oxide Nanoparticles (ZnO NPs) for cancer diagnosis, target drug delivery, and treatment. *Cancers* 2021; 13:4570.
36. Fatima A, Naseem N, Md Haider F, Md Rahman A, Mall J, Saifi MS, Akhtar J. A comprehensive review on nanocarriers as a targeted delivery system for the treatment of breast cancer. *Intelligent Pharmacy* 2024; 2(3):415–426.
37. Alharbi HM. Exploring the Frontier of Biopolymer-Assisted Drug Delivery: Advancements, Clinical Applications, and Future Perspectives in Cancer Nanomedicine. *Drug Design, Development and Therapy* 2024; 18:2063–2087.
38. Sokolowska P, Bleibel L, Owczarek J, Wiktorowska-Owczarek A. PPAR $\gamma$ , NF- $\kappa$ B and the UPR pathway as new molecular targets in the anti-inflammatory actions of NSAIDs: Novel applications in cancers and central nervous system diseases? *Advances in Clinical and Experimental Medicine.* 2024:1899–5276.
39. Kim SH, Keum B, Kwak S, Byun J, Shin JM, and Kim TH Therapeutic Applications of Extracellular Vesicles in Inflammatory Bowel Disease. *Int. J. Mol. Sci.* 2024; 25:745.
40. Omidian H, Gill EJ and Cubeddu LX. Lipid Nanoparticles in Lung Cancer Therapy. *Pharmaceutics.* 2024; 16:644.
41. Chakraborty SS, Panja A, Dutta S, Patra P. Advancements in nanoparticles for skin care: a comprehensive review of properties, applications, and future perspectives. *Discover Materials* 2024; 4:17.
42. Singh K, Bhushan B, Chanchal DK, Sharma SK, Rani K, Yadav MK, Porwal P, Kumar S, Sharma A, Virmani T, Kumar G and Noman A. Emerging Therapeutic Potential of Cannabidiol (CBD) in Neurological Disorders: A Comprehensive Review. *Hindawi Behavioural Neurology* 2023; 1:1-17.
43. Sisodiya D, Madhavalatha B, Bandigari P, Katual KM, Gupta N, Krosuri P, Vishvakarma P, Negi SS. Bacterial Nanocarriers for Site-Specific Drug Delivery: Harnessing Microorganisms for Precision Medicine. *African Journal of Biological Sciences* 2024; 6(9):2400-2420.
44. Anita A, Jain T, Saini C, Devi N, Boora N, Kandukuri KM, Lal S and Aggarwal D. Enhanced delivery of herbal medications by using Ethosomes. *Enhanced delivery of herbal medications by using ethosomes* 2024; 24(1):541-552.
45. Zhuo Y, Zhao YG and Zhang Y. Enhancing Drug Solubility, Bioavailability, and Targeted Therapeutic Applications through Magnetic Nanoparticles. *Molecules* 2024; 29:4854.