

Application of Lipid Nanoparticles in the Delivery and Therapeutics for Inflammation around the Body

Yue Yu^{1*}

¹The British School in the Netherlands, South Holland, Netherlands

*Corresponding Author: Rickyu5274@gmail.com

Advisor: Mary Zhao, maryz@astudentacademy.org

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Abstract

In recent years, Lipid Nanoparticles (LNPs) have become a better understood and more promising platform for enhanced drug delivery, showing many improvements over traditional methods of drug delivery. Current treatment strategies for inflammation are constrained by poor drug penetration, untargeted distribution as well as systemic toxicity. Unlike many currently existing reviews that focus on LNPs in general drug delivery, current literature provides limited overview on how LNPs address inflammatory responses in organs with highly restrictive barriers. This review concentrates on the two organ systems where drug delivery remains the most challenging, within the Blood Brain Barrier (BBB) and the lungs, highlighting how LNPs enhance the process of drug delivery. This review is based on targeted literature searches conducted between the years 2015 and 2025 using primarily PubMed and Web of Science. Search terms included combinations of keywords such as “lipid nanoparticles,” “Blood brain barrier,” and “Acute ischemic stroke.” Studies that were focusing on non-inflammatory aspects of LNP usage were generally excluded. The Blood brain barrier as well as the lungs were selected due to their current clinical importance and the significant barriers that make drug delivery especially challenging in these organs.

Keywords: Lipid Nanoparticles, Blood Brain Barrier, Acute Ischemic Stroke, Acute Respiratory Distress Syndrome, Drug Delivery

1. Introduction to Lipid Nanoparticles

LNPs are small, artificially engineered nanoparticles created from lipids, and in recent years, have begun to revolutionise and pioneer new drug delivery systems as well as slowly become a crucial part in mRNA (messenger Ribonucleic acid) and siRNA (small interfering Ribonucleic acid) based treatments and vaccines (Mehta et al., 2023).

1.1 Types of Structures of LNPs

The lipids used to create LNPs are mostly phospholipids, composed of a single hydrophilic head with two hydrophobic tails, which are either saturated or unsaturated fatty acid chains. The different sizes of their tails, as well as being saturated or unsaturated, control the size of their hydrophobic domains, which play a large role in determining the variety of complex structures and nanoparticles that can be created with them (Dowhan et al., 2016; Mehta et al., 2023).

Although LNPs are a broad class, there are some major subtypes commonly used in medicine and drug delivery, with this article primarily focusing on Liposomes and Solid Lipid Nanoparticles (SLN) structures (Mehta et al., 2023).

Liposomes are complex spherical structures that contain two phospholipid layers, creating a bilayer, and are generally made up of Lipids that have two unsaturated fatty acid tails, making the hydrophobic and hydrophilic domain similar in size. This allows them to form a circular structure with a hollow centre, as shown in Figure 1. Due to the existence of a hollow centre liposomes have a watery core, allowing for the transportation of hydrophilic drugs within

the centre, while still being able to transport hydrophobic drugs embedded within the lipid bilayers (Dowhan et al., 2016; Mehta et al., 2023).

SLNs have a similar spherical structure to Liposomes, having a singular phospholipid layer rather than a bilayer. However, rather than having a hollow core, they instead have a solid core made up of the hydrophobic domains of the phospholipid tails. Because of its solid core, SLNs are generally not well suited for carrying hydrophilic drugs. However, they are very effective in transporting hydrophobic drugs, as SLNs are specifically designed not to allow water to flow into their centre, thus protecting the encapsulated hydrophobic drugs (Mehta et al., 2023).

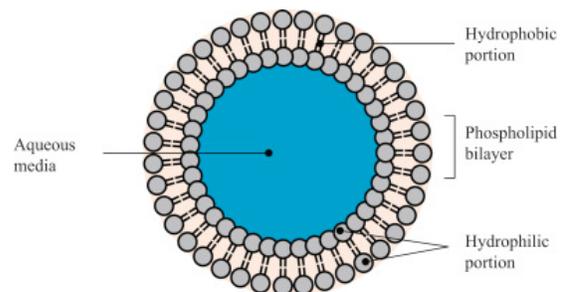


Figure 1. Structural diagram showing the composition of a Liposome (Deb et al., 2019).

1.2 Manufacturing of LNPs

The manufacturing of LNPs generally involves two main approaches. Nanoparticles can be built from molecular components or broken down from larger materials into nanoscale fragments.

The most common industrial synthesis methods include nanoprecipitation, a process where lipids are dissolved in an organic solvent and mixed with an aqueous phase under stirring to induce self-assembly into nanoparticles, and emulsification, where lipids and drugs are emulsified in water using surfactants. Upon cooling, the lipid solidifies, forming LNPs that carry the drug (Mehta et al., 2023).

Although these methods seem relatively straightforward, there are significant challenges with stability and storage in the industrial production of LNPs. Since LNPs are often highly sensitive to temperature, they can experience drug leakage or aggregation over time if not stored correctly. Many of them require ultracold temperatures, with some mRNA vaccines requiring temperatures of -80 degrees Celsius, which creates complications for drug distribution and delivery. Moreover, ensuring uniform size and drug loading for each batch of LNPs is highly difficult, especially for larger-scale continuous industrial production. To combat this, many factories have begun using real-time monitoring sensors and algorithms to maintain control, and it is a more preferred method compared to traditional batch sampling (Mehta et al., 2023).

2. Introduction to Inflammation

Inflammation is a biological immune system response triggered by the stimuli of pathogens, as well as damaged cells and toxins within the body. It primarily serves as a defence mechanism from the immune system, aiding the removal of pathogens and irritants from the body and stimulating tissue repair (Chen et al., 2017; Institute for quality and efficiency in health care (IQWiG), 2025).

Inflammation occurs through a cascade process in which harmful substances are recognised by specific receptors on the cell's membrane. These receptors can detect pathogen-associated molecular patterns from microbes and damage-associated molecular patterns released by damaged or dead cells. The detection of these substances activates signalling pathways within the cell that then induce the production of pro-inflammatory cytokines (small chemical messengers made of proteins), which lead to the inflammation of the damaged site within the body (Chen et al., 2017).

The process of inflammation involves the dilation of blood vessels, which increases blood flow to the injured tissue. This heightened blood flow enables more immune cells, such as neutrophils and macrophages, to be transported to the injured area of tissue or infection to destroy the pathogens. Moreover, more fluid is transported to the tissue, which is what causes swelling. This increased fluid also helps to physically flush the pathogens out of the body (Chen et al., 2017; Institute for Quality and Efficiency in Health Care (IQWiG), 2025).

2.1 How can inflammation cause harm to the human body

While inflammation is a powerful tool of the immune system, if it ever becomes uncontrolled or chronic, it can

lead to a wide range of further complications for the body. One common effect of an extended period of inflammation is oxidative stress, where the body possesses more free radicals than antioxidants are required to neutralise them. This leads to cell death as the lipids and molecules lining the cell membranes react with the free radicals, causing the cell to tear apart in the process (Chen et al., 2017; Zotova et al., 2023).

Although this article specifically focuses on the effects and damage caused by inflammation in the BBB and the lungs, there are numerous other organ-specific symptoms in other parts of the body, including, but not limited to, the heart, pancreas, liver, and kidneys (Alfaddagh et al., 2020; Baer et al., 2020; Koyama et al., 2017; Zheng et al., 2021).

3. Uses of Lipid Nanoparticles in the Therapeutics of Inflammation in the Blood Brain Barrier.

The BBB is a highly selective semipermeable membrane that separates the blood flow of the Central Nervous System (CNS) and the brain from the rest of the circulatory system. It is primarily formed from tightly joined endothelial cells (which are cells that line the innermost layer of blood vessels) that line the brain's capillaries, as shown in Figure 2. The BBB's highly selective nature allows it to be a protective barrier that controls the movement of substances between the bloodstream and the brain, letting useful nutrients pass through while blocking foreign objects such as toxins and pathogens. This selective permeability (Ability for substances to pass through) plays a key role in the maintenance of the controlled and delicate microenvironment of the brain (Han et al., 2024; Nong et al., 2024).

However, the BBB also acts as an obstacle for modern-day drug delivery to the brain, as a large majority of current drugs are considered harmful or foreign objects to the brain by the BBB, resulting in them being unable to cross from the bloodstream into the brain. This greatly limits options for the delivery of therapeutic drugs to the brain, making the treatment of brain diseases with drugs a significant challenge (Han et al., 2024; Nong et al., 2024).

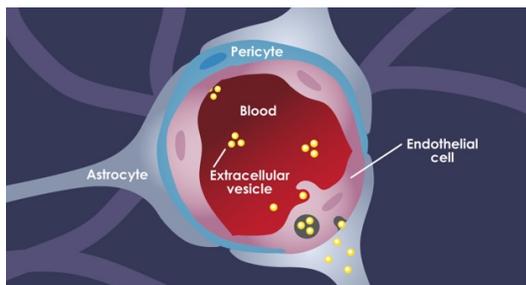


Figure 2. Structural diagram representing the endothelial cells making up the BBB, which separates the circulatory system from the blood flow of the central nervous system (National Institutes of Health, 2019).

AIS is a type of stroke that involves the physical obstruction of blood in the arteries leading to the brain, which can potentially lead to large-scale cell death. This process usually provokes an immune response that then causes a cascade of events resulting in the inflammation of the BBB due to the increased release of pro-inflammatory cytokines (Han et al., 2024; Nong et al., 2024).

Although inflammation is a useful tool for the immune system to kill off pathogens, the inflammation of the BBB is highly detrimental to the body as its selective barrier is weakened, meaning that more substances can penetrate through the BBB and enter the delicate microenvironment of the brain. This can cause a range of different further complications, including brain edema, where increased fluid

leakage into the brain, caused by a weakened BBB, results in the brain swelling, which could lead to further cell death as the brain compresses against the walls of the skull. The increased permeability of the BBB could also result in Hemorrhagic Transformation, as components and other substances in the blood leak into the already damaged brain tissue, causing blood to pool in different areas of the brain. This prevents oxygen from reaching these vital areas, leading to further cell death (Chen et al., 2017; Han et al., 2024; Nong et al., 2024).

Thus, quickly providing therapy to reduce the inflammation of the BBB after a patient suffers from an AIS could lead to a massive reduction in secondary injuries, potentially minimizing further damage to the brain and preventing possible paralysis and other brain deficits caused by the inflammation of the BBB.

3.1 Limitations of current treatments and how LNPs can be used for more effective treatment of Inflammation in the BBB

Many current drugs used to treat inflammation in the BBB depend on intravenous injection to deliver the anti-inflammatory medication directly into the bloodstream, then wait for the cardiovascular system to passively circulate

the drug throughout the body to reach the inflamed BBB without any specific targeting mechanisms, essentially hoping for the drug to accumulate within the brain at higher levels than in the rest of the body.

However, this has a very low therapeutic efficiency as the drugs lack a targeting system, meaning that very low levels of the anti-inflammatory drug accumulate within the inflamed BBB, with most of the injected drugs being dispersed randomly around the body. This means that the process is very inefficient, as to achieve the desired therapeutic effect, a much larger volume of drugs would need to be injected into the patient. However, this increased dosage of drugs could greatly increase the risk of systemic toxicity in other parts of the body, where large amounts of the drug could accumulate, causing potential side effects. Additionally, many of the patients' bodies after suffering from an AIS, would already be in critical condition and thus, would not be able to tolerate any side effects that the increased drug dosage may cause. Moreover, the unencapsulated drugs within the bloodstream have a low level of drug retention and rapid clearance as they are quickly metabolized and filtered out from the bloodstream before they have a chance to reach the brain, further reducing their therapeutic efficacy (Nong et al., 2024).

Thus, researchers have created and used LNPs to encapsulate the anti-inflammatory drugs within either a Liposome structure or an SLN before being injected into the bloodstream. The Lipid Nanocarriers (LNCs) can also have their surface layer modified to have monoclonal antibodies or targeting ligands attached to it. This results in the LNCs having an enhanced targeting system, allowing them to home onto specific cell types and giving the drugs carried by LNCs a much higher therapeutic efficiency (Nong et al., 2024).

This method of encapsulation provides multiple advantages compared to simply injecting the drugs into the bloodstream. Since the drugs are encapsulated and protected, there is a much higher level of drug protection and drug retention, as sensitive drugs, such as small molecule drugs or mRNA, can be shielded from enzymatic degradation in the bloodstream, which allows for more drugs to accumulate in the injured areas of the brain. Additionally, due to the ability of LNCs to attach antibodies and ligands to their surface, the drugs have better targeting and accumulation levels dramatically in the BBB compared to non-targeted drugs. This means that not only are fewer drugs needed to achieve the same desired therapeutic effect, but there is also a large decrease in risk of systemic toxicity and side effects. The drugs are all targeted specifically to the injured cells in the inflamed BBB, so there is a reduced chance that the drugs accumulate in dangerous levels elsewhere in the body. Moreover, better targeting means that there are fewer free unused drugs that can accumulate in other parts of the body and cause side effects, as more drugs accumulate within the BBB (Han et al., 2024; Mehta et al., 2023; Nong et al., 2024).

Therefore, by using LNCs to deliver traditional anti-inflammatory drugs, we could eliminate, or significantly reduce, a large portion of the problems that freely injected drugs hold, including the major challenge of drug volume. As typically delivered drugs would have to find a compromise between the higher required volume needed for successful treatment and the lower volume needed to prevent systemic toxicity.

3.2 Trials on Mice models

The LNPs used by researchers to create liposomes and SLNs that encapsulate drugs and mRNA therapy are typically obtained from a mouse's brain to create Brain- Lipid Nanoparticles (B-LNPs) or from liver tissues to create Liver-Lipid Nanoparticles (L-LNPs). To acquire the LNPs from the lipid tissue samples from the brain and liver, the researchers mixed 50mg of the lipid samples with 200 μ g of methanol and 500 μ g of methyl tert-butyl, shaken for 1 hour. Then, 125 μ l of deionized water was added to the mixture, which was then spun in a centrifuge for 15 minutes at 14000 rpm and 4°C. Finally, the liquid above the remaining solid is collected and dried to obtain the different types of LNPs used (Han et al., 2024).

Most trials for researching LNC use in the BBB have been performed using mouse models, specifically the transient middle cerebral artery occlusion method. This method involves blocking the mice's middle cerebral artery for 45 minutes to induce a stroke. Afterward, researchers waited 24 hours before giving different types of LNC-encapsulated drugs to see how their therapeutic efficiency differed (Nong et al., 2024).

During the experiments, researchers used three different targeting antibodies attached to the LNCs: VCAM-1 targeting antibodies, ICAM-1 targeting antibodies, and PECAM, which did not target any specific cells and acted as their control. They used two different therapeutics: Dexamethasone, a potent anti-inflammatory steroid, encapsulated

with a Liposome structure and IL-10mRNA, a strong anti-inflammatory cytokine, encapsulated with an SLN (Nong et al., 2024).

30 minutes after the injection, the researchers dissected some of the mice to observe the concentration of drugs that accumulated in the inflamed BBB. They kept the rest alive to observe them further, as well as to determine a survival rate (Nong et al., 2024).

The researchers observed that VCAM-1 targeting LNCs accumulated in the injured areas of the BBB at levels almost 50 times higher than that of their PECAM control, which had no observable bias. The ICAM-1 targeting LNCs also experienced enhanced targeting and accumulation in the brain, 16.5 times higher, but at lower levels than VCAM1, demonstrating that VCAM-1 was the most effective targeting antibody. Moreover, Dexamethasone reduced cerebral infarction by 35%, and IL-10 mRNA reduced cerebral infarction by 62% and resulted in a 100% survival rate in mice, showing that the cytokine was more effective than the steroid (Nong et al., 2024).

These mouse studies are based on previously published work, and show significant improvement compared to traditional treatment methods, with the usage of LNCs being able to obtain a much greater accumulation levels within the desired locations.

3.3 Future perspectives

In conclusion, the use of LNCs, such as Liposomes and SLNs, to encapsulate drugs and mRNA therapies offers numerous benefits and advantages over simple IV injections of free drugs.

Although all current trials have only been conducted on mouse models, the results have been very encouraging. LNCs have proven to be much more effective therapeutically than unencapsulated drugs. This suggests that using LNCs can significantly enhance patient treatment for AIS, potentially preventing secondary brain damage and paralysis that might occur due to inflammation of the BBB.

4. Uses of Lipid Nanoparticles in the Therapeutics of Inflammation in the Lungs

Inflammation in the lungs plays a key role in a range of lung diseases, such as Chronic Obstructive Pulmonary Disease, pulmonary fibrosis, and other acute lung injuries, including Acute Respiratory Distress Syndrome (ARDS) (Chen et al., 2017; Yu and Qiu, 2024).

Most lung diseases are classed as either acute or chronic. Acute lung injuries refer to short-term lung inflammation or damage, which usually only lasts for a few days or hours. The symptoms of Acute lung injuries can develop and escalate much faster compared to chronic injuries, and are often caused by infections, irritants, or allergens; however, they can typically be resolved with treatment or simply the removal of the irritant, which means that there is generally a lower chance of permanent or severe damage. On the other hand, Chronic lung injuries refer to long-term lung inflammation and damage, with symptoms slowly developing over months and years. The symptoms are often caused by constant exposure to irritants, repeated infections, or underlying diseases, and are less severe than acute cases at first, but are persistent and can possibly grow worse over time. Usually, there is no simple cure to Chronic illnesses, meaning that it is generally more challenging to treat than Acute illnesses. As a result, chronic injuries and illnesses usually result in permanent and irreversible damage to the patient's lungs (Zotova et al., 2023).

Similar to other parts of the body, inflammation of the lungs is caused by an immune response to either physical injury or an infection. However, within the lungs, inflammation can lead to a chain of events caused by the immune system that leads to the activation of fibroblasts, a type of cell that synthesis extracellular materials. The activated Fibroblasts then rapidly multiply and produce excess collagen and other extracellular materials, which leads to the scarring, thickening, and stiffening of the surrounding lung tissue and capillaries. This change in Extracellular Matrix thickness disrupts the integrity of the endothelial cells of the alveoli, leading to an increase in vascular permeability of the capillaries lining the alveoli, causing protein-rich fluids to leak into the alveoli and fill the air sacks with fluid, resulting in pulmonary edema and subsequently ARDS (Yu and Qiu, 2024).

ARDS is a life-threatening condition with very high mortality rate, 46.1% in severe adult cases, caused by severe respiratory failure and the build-up of fluid in the alveoli of the lungs, as shown in Figure 3, causing a drastically

reduced rate of oxygen uptake and carbon dioxide removal from the blood and resulting in severe hypoxemia, or Low blood oxygen levels. With the recent COVID-19 pandemic, there has been a large increase in both incidence and mortality rates of ARDS, which has generated a huge increase in demand for more effective therapeutics for the treatment of ARDS (Yu and Qiu, 2024).

4.1 Current treatments for ARDS and their limitations.

Currently, there's no definitive cure for ARDS. While various treatment options exist, they mainly provide supportive care or limited benefits, and none can fully cure the disease on their own.

Currently, the most common treatment for ARDS are Corticosteroids, which are anti-inflammatory drugs, such as the previously mentioned Dexamethasone, with the assistance of Adjuvant Agents such as Vitamin C, Ascorbic acid to act as an antioxidant therapy, and Heparin, A drug that prevents microvascular thrombosis in the lungs.

Corticosteroid is the only drug among the three treatment methods that aims to cure the underlying disease by reducing inflammation in the lungs, thereby decreasing vascular permeability and preventing severe cases of ARDS. Clinical trials show an increase in ventilator-free days and a reduction in mortality rates. However, the effectiveness of Corticosteroids depends heavily on the timing of administration, with early treatment yielding a much better therapeutic effect. This makes Corticosteroids less viable for patients in critical conditions. Additionally, responses in critically ill patients vary, and some studies even suggest that excessive use of Corticosteroids may lead to delayed recovery (Yu and Qiu, 2024).

Vitamin C, also known as Ascorbic Acid, can be used as a supportive treatment for ARDS through antioxidant therapy. The antioxidants neutralize the increased free radicals that can cause oxidative stress, potentially leading to DNA damage and lipid peroxidation, where cell membrane lipids react with radicals, damaging the membrane. In clinical trials, high doses of Vitamin C have shown a slight improvement in mortality rates for some patients. However, since Vitamin C is only a side treatment, monotherapy is highly ineffective because it only addresses one symptom of ARDS without curing the disease. Therefore, when used alongside other therapies, they may reduce symptom severity, but they offer little to no benefit in the actual treatment or cure of ARDS (Yu and Qiu, 2024).

Heparin and other adjunct agents are also secondary treatment options used to reduce the risk of further infections and complications. For example, antibiotics are administered to treat and prevent possible secondary infections, and vasodilators can be inhaled into the lungs to temporarily dilate pulmonary blood vessels to improve oxygen and blood flow. Still, they can only be used for short-term treatment (Yu and Qiu, 2024).

Therefore, many of the current treatments have severe limitations, making ARDS a very difficult disease to treat with traditional methods. The primary drugs used are too heavily dependent on the time of administration, meaning that the patients in critical condition benefit very little from them. Moreover, other treatment methods are only supportive treatments, as instead of attempting to cure ARDS and treat the underlying problem, they only seek to resolve or reduce the severity of the symptoms and secondary infections.

4.2 How LNPs can be used to improve the therapeutic efficiency of traditional treatments.

Due to the lack of therapeutic efficiency of traditional treatments, researchers have turned to LNPs in attempts to improve the efficacy of the treatments used and develop new forms of therapy.

Like drugs used to treat inflammation in the BBB, LNPs can encapsulate and deliver drugs in liposomes, providing a range of benefits. These include higher drug retention due to protection from enzymatic degradation and

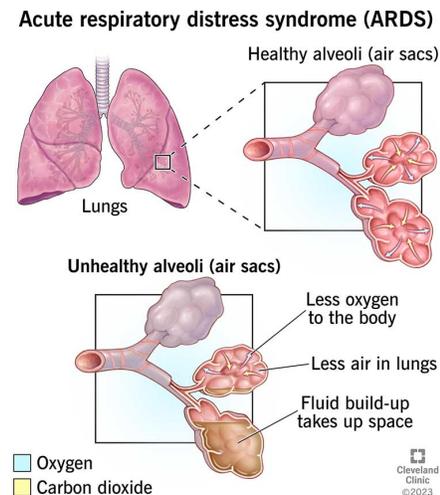


Figure 3. Visual representation diagram for ARDS, showing the buildup of fluids within the alveoli (Cleveland Clinic, 2023).

increased drug accumulation in injured areas, thanks to targeting ligands. This targeted approach reduces the risk of systemic toxicity by limiting the number of free drugs that can cause side effects elsewhere in the body. Furthermore, surface modifications can be made to trigger drug release in specific conditions, such as pH or temperature changes, enhancing targeting and allowing for patient-specific therapies. Given the limited treatment options for ARDS, having all these benefits would be highly valuable, as it would enable more effective drug delivery to injured lung areas without the risks of side effects and systemic toxicity. Additionally, surface modifications can tailor therapies to individual patients based on their conditions, such as age, disease stage, and cause, significantly increasing the therapeutic efficacy of traditional drugs (Leong et al., 2022; Mehta et al., 2023; Yu and Qiu, 2024).

Researchers have also explored the usage of mRNA and siRNA therapeutics delivered by SLNs. One example was the recent mRNA COVID-19 vaccine developed by Pfizer. By using SLNs to encapsulate the mRNA, the vaccine could successfully deliver the mRNA to muscle cells at the injection site and transport the mRNA into the surrounding muscle cells without being denatured by enzymatic degradation. The mRNA then acts as instructions for the muscle cells to produce pieces of the coronavirus antigens, which are then released into the blood stream, invoking a small-scale immune response and allowing the vaccinated patient to build up immunity to COVID-19, allowing the immune system of the vaccinated patient to react much faster if there ever were a real infection. This increased immunity would help prevent the possibility of severe infections in the future, which means that since there is a reduced stimulus, the patient would be less likely to develop a severe case of ARDS. Moreover, after the mRNA is used, it is quickly broken down as it is no longer protected by the SLNs, ensuring that there are no unwanted side effects (Mehta et al., 2023; Yu and Qiu, 2024).

Researchers have also investigated siRNA therapies as a new approach to treat ARDS and other respiratory diseases. These therapies work by silencing specific genes related to the immune response that causes inflammation. They do this by binding to mRNA molecules within cells, which leads to their degradation and prevents the translation process that creates targeted proteins. This could be highly effective for treating ARDS, as using siRNA would allow for the prevention of pro-inflammatory cytokine production, which in turn would prevent the immune system from triggering inflammation in the lungs (Leong et al., 2022; Yu and Qiu, 2024).

However, similarly to the delivery of mRNA, simple delivery systems pose significant challenges, such as a lack of targeting and cellular uptake, as well as enzymatic degradation of the siRNA molecules, thus requiring the usage of LNCs to act as its platform for delivery to achieve its desired therapeutics effects successfully (Leong et al., 2022; Yu and Qiu, 2024).

Although siRNA therapies have shown great promise in preclinical and animal trials, with LNC-delivered siRNA showing significant anti-inflammatory effects in acute lung injury models, certain challenges and safety concerns still remain. For example, delivery efficiency and cellular uptake of siRNA could heavily vary depending on factors such as nanoparticle size and surface modification. Additionally, some Cationic liposomes could trigger unwanted immune responses, leading to cytotoxicity if not managed correctly (Leong et al., 2022; Yu and Qiu, 2024).

Moreover, although siRNA therapies could potentially be a new cutting edge approach for treating ARDS, all current tests done for the usage of siRNA have been pre-clinical trials, and clinical trials are required to validate safety as well as gauge the efficacy of LNC delivered siRNA therapies for humans (Leong et al., 2022; Yu and Qiu, 2024).

Lastly, LNPs have also been researched as delivery methods for drugs in the development of new inhaled therapeutics. The primary advantages of inhaled therapies over injected therapies are that the drugs delivered are much more localised, as they are directly delivered to the targeted area of illness, instead of simply being injected into the bloodstream and waiting for the vascular system to transport them to the target area. This means that there is a reduced chance of systemic toxicity as the drugs are all localised in the lungs; moreover, this also allows for the ability to administer fewer drugs for the same therapeutic effect. However, traditional drugs used in inhaled therapies usually have similar drawbacks to normal drugs after entering the body, such as rapid clearance, low local drug accumulation, and systemic toxicity, as well as poor targeting. Due to the previous reasons and benefits mentioned, the encapsulation of the drugs in LNPs provides solutions to most of these problems. Additionally, the use of LNPs allows for inhalation of RNA therapies, which was previously impossible due to aerosolization damage (Leong et al., 2022; Yu and Qiu, 2024).

4.3 Future perspectives

Overall, similar to the brain, LNPs have huge potential for enhancing the treatment of ARDS in the future. This could lead to more personalized treatments that cater to specific patient needs and medical conditions, significantly improving the effectiveness of current medications. Additionally, LNPs have been used to develop new treatment and prevention methods, including those that use RNA, siRNA, and inhaled therapeutics. This shows that LNP technology can deliver treatments to the lungs in ways that were previously impossible.

5. Conclusions

The application of LNPs for the treatment of inflammation has seen a rapid advancement in progress, with significant potential to improve targeted drug delivery, which would not only enhance therapeutic efficacy, but also reduce chances of systemic toxicity for patients. Further research and development could possibly refine nanoparticle design, improving stability, allowing the transport of a wider range of drugs and treatments, as well as evaluating the long-term safety of the usage of LNPs

However, there are still significant limitations in this field of research, as most trials and results have been obtained solely from preclinical animal tests, although they provided promising results, there is currently still a lack of human clinical trials. Meaning although there have been significant advancements in the usage of LNPs to treat inflammation, there is still very little real-life data on humans available to support the current findings.

References

Alfaddagh, A., et al. (2020). Inflammation and cardiovascular disease: From mechanisms to therapeutics. *American Journal of Preventive Cardiology*, 4, 100130. <https://doi.org/10.1016/j.ajpc.2020.100130>

Baer, P. C., Koch, B., & Geiger, H. (2020). Kidney inflammation, injury and regeneration. *International Journal of Molecular Sciences*, 21(3), 1164. <https://doi.org/10.3390/ijms21031164>

Chen, L., et al. (2017). Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget*, 9(6), 7204–7218. <https://doi.org/10.18632/oncotarget.23208>

Cleveland Clinic. (2023, December 7). Acute respiratory distress syndrome (ARDS). <https://my.clevelandclinic.org/health/diseases/15283-acute-respiratory-distress-syndrome-ards>

Deb, P. K., et al. (2019). Protein/peptide drug delivery systems: Practical considerations in pharmaceutical product development. In R. K. Tekade (Ed.), *Advances in pharmaceutical product development and research: Basic fundamentals of drug delivery* (pp. 651–684). Academic Press. <https://doi.org/10.1016/B978-0-12-817909-3.00016-9>

Dowhan, W., Bogdanov, M., & Mileyskoykaya, E. (2016). Functional roles of lipids in membranes. In N. D. Ridgway & R. S. McLeod (Eds.), *Biochemistry of lipids, lipoproteins and membranes* (6th ed., pp. 1–40). Elsevier. <https://doi.org/10.1016/B978-0-444-63438-2.00001-8>

Han, D., et al. (2024). Selective homing of brain-derived reconstituted lipid nanoparticles to cerebral ischemic area enables improved ischemic stroke treatment. *Journal of Controlled Release*, 365, 957–968. <https://doi.org/10.1016/j.jconrel.2023.12.020>

Institute for Quality and Efficiency in Health Care (IQWiG). (2006–). In brief: What is an inflammation? *InformedHealth.org*. Updated 2025, April 11. <https://www.ncbi.nlm.nih.gov/books/NBK279298/>

Koyama, Y., & Brenner, D. A. (2017). Liver inflammation and fibrosis. *Journal of Clinical Investigation*, 127(1), 55–64. <https://doi.org/10.1172/JCI88881>

Leong, E. W. X., & Ge, R. (2022). Lipid nanoparticles as delivery vehicles for inhaled therapeutics. *Biomedicines*, 10(9), 2179. <https://doi.org/10.3390/biomedicines10092179>

Mehta, M., et al. (2023). Lipid-based nanoparticles for drug/gene delivery: An overview of the production techniques and difficulties encountered in their industrial development. *ACS Materials Au*, 3(6), 600–619. <https://doi.org/10.1021/acsmaterialsau.3c00032>

National Institutes of Health. (2019, October 1). How cancer vesicles breach the blood-brain barrier. *NIH Research Matters*. <https://www.nih.gov/news-events/nih-research-matters/how-cancer-vesicles-breach-blood-brain-barrier>

Nong, J., et al. (2024). Targeting lipid nanoparticles to the blood-brain barrier to ameliorate acute ischemic stroke. *Molecular Therapy*, 32(5), 1344–1358. <https://doi.org/10.1016/j.ymthe.2024.03.004>

Yu, Y., & Qiu, L. (2024). Nanotherapy therapy for acute respiratory distress syndrome: A review. *Frontiers in Medicine*, 11, 1492007. <https://doi.org/10.3389/fmed.2024.1492007>

Zheng, Z., et al. (2021). A narrative review of acute pancreatitis and its diagnosis, pathogenetic mechanism, and management. *Annals of Translational Medicine*, 9(1), 69. <https://doi.org/10.21037/atm-20-4802>

Zotova, N., et al. (2023). Acute and chronic systemic inflammation: Features and differences in the pathogenesis, and integral criteria for verification and differentiation. *International Journal of Molecular Sciences*, 24(2), 1144. <https://doi.org/10.3390/ijms24021144>