

Efficiency of Lipid Nanoparticles in Glioblastoma Therapies

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ABSTRACT: Increasingly targeting the older population, Glioblastoma is a grade four brain tumor with less than a 10% survival rate. One major challenge in treatment is delivering drugs across the Blood-Brain Barrier (BBB) and Blood Tumor Barrier (BTB). Chemotherapy has been used as a main solution for fighting tumors, specifically in Glioblastoma; however, it can cause many side effects for patients, such as headaches and changes to mental function. Nanoparticles, and particularly lipid nanoparticles, have emerged as leading drug delivery methods to overcome those challenges. Due to their small size, they can effectively cross the BBB and can be modified with other targeted ligands. Three types of lipid nanoparticles are discussed: Solid Lipid Nanoparticles (SLNs), Liposomes, and Nanostructured Lipid Carriers (NLCs). With their liquid lipids and flexible crystallized structure, NLCs can help overcome major shortcomings of chemotherapy and improve future outcomes for Glioblastoma patients.

KEYWORDS: Cellular and Molecular Biology, Neurobiology, Glioblastoma, Blood-Brain Barrier, Lipid Nanoparticles.

■ Introduction

The impacts of cancer are everlasting and can be devastating for the body, particularly in the case of brain tumors. They can develop as a result of external factors, such as UV rays from the sun, or through genetic errors that occur during mitosis, when cells divide to create new cells. The stages of this process include:

- Interphase: the cell grows and replicates its DNA
- Prophase: chromosomes become visible
- Metaphase: chromosomes align to the center of the cell
- Anaphase: sister chromatids separate
- Telophase: cells prepare to divide

The cells cannot move on to the next stage without stopping at checkpoints. These make sure the cells go through the respective stage properly. When the mutated DNA proceeds into the cell cycle, it can bypass the checkpoints and replicate uncontrollably. The mutations created can lead to gain-of-function (GOF) phenotypes, which promote the altered genes to enhance tumor growth and formation. This action can result in tumors.

In Glioblastoma, a type of brain tumor, patients only have a 5-10% survival rate with standard treatment.¹ Because the brain is responsible for many integral functions, such as storing memory, cognitive thinking, processing emotions, movement, and regulating the body, it is crucial to implement treatments that not only effectively dissipate the tumors but also mitigate the threatening effects associated with them. Chemotherapy treatments, for instance, are often used. However, not only do they target the tumor cells, but also the healthy cells, as part of their non-selective process. Chemotherapy is inefficient because it cannot differentiate between healthy and unhealthy cells.

Due to this problem, loss of important red and white blood cells can be significant when transporting medicine through chemotherapy, which can produce side effects such as fatigue and hair loss.² Nanomedicine, however, can selectively target

only tumor cells, reducing these side effects tremendously. Within the branch of nanomedicine, nanoparticles are an important tool used especially for targeted drug delivery of medication. With the efficient applications of nanomedicine, resolving brain tumors will be associated with less stress for patients during treatments.

Nanomedicine-based treatments indeed result in improved reduction of brain tumors. According to Kumar *et al.*,³ polymeric nanoparticles have provided many positive responses in treating brain tumors. This is due to their properties of having high biodegradability, permeation in tumor cells, and a surface-to-volume ratio. The high permeation efficiency allows cells to produce further connected pore spaces, which can then allow for liquids to flow efficiently. This is useful, especially when implementing a drug-delivery system, which is a technology used to carry drugs throughout the body. These are a must for cancer therapy treatments, as that is the way to carry medicine into the brain. However, the problem arises when the drugs have to pass through the BBB (Blood-Brain Barrier) and BTB (Blood-Tumor Barrier) Complex, both of which are highly semipermeable barriers in the brain. The BBB only allows important materials into the brain, such as nutrients and oxygen, while turning away others, like pharmaceuticals. The BTB is a barrier formed due to the internal pressure within the tumor setting. However, nanoparticles (NPs) can be effectively used to cross both of the barriers. Along with their selective capabilities, they can transport multiple drugs throughout the brain, utilize many signaling pathways, and can effectively be transported across these barriers.⁴ There can be a positive correlation seen between the use of NPs and the healing of brain tumors, as the particles are effectively able to go into the brain and deliver medications successfully.

Further, nanoparticles can take advantage of the glioma EPR effect in the cell.⁵ The EPR effect is when nanoparticles can accumulate within tumor cells, and this is efficient as they will be able to target and dissipate them efficiently. Meola and

Rao emphasize the importance of their small size and shape as a beneficial contributor to delivering treatments.⁶ This property of nanoparticles helps to improve efficiency in tumor treatments, especially in the brain, where there are many small pores and barriers for medications to cross. However, Glioblastoma often retains some parts of the BBB, limiting nanoparticles from getting through. As a result, the EPR effect may not always be sufficient for lipid nanoparticles to perform drug delivery.

Additionally, a study conducted utilized the unique functionalized surface of the NPs and attached antibodies and a chemotherapy drug to them. According to the data, the NPs helped to increase the survival rate of the mouse with Glioblastoma by 50%.⁷ Researchers stated it is a crucial finding since the largest problem in medicine initially was trying to pass the chemotherapy treatments into the brain. Still, with this now, it's indeed possible.

Given the confirmed correlation between the use of nanomedicine and the efficient healing of brain tumors, NPs and nanotechnology must be implemented in treatments. The brain is one of the most important organs carrying out a multitude of vital functions; the body simply cannot function without it. Not only will NPs increase the effectiveness of delivering medication, but they will also not interfere with a patient's brain health or activities.

■ Methodology

The primary goal of this research was to determine which type of lipid nanoparticle is most efficient and compatible for treating the Glioblastoma brain tumor. This research was completed through a secondary literature review, which aims to compile multiple academic journals and primary sources, both for health and effectiveness. Studies published between 2016 and 2025 were included to capture the most recent advancements of lipid nanoparticle treatments for Glioblastoma. This time frame was selected because many recent advancements have been made, making earlier studies less representative of current data. The literature search was conducted using keywords such as “blood-brain Barrier,” “lipid nanoparticles for treatment,” and “Glioblastoma brain tumors.” Data were collected to analyze nanoparticles’ efficiency in reaching the brain and successfully treating the tumors through drug-delivery systems. The sources referenced include scientific papers published in peer-reviewed journals, clinical data, and other academic literature globally. Therefore, this literature review is derived from multiple backgrounds, leaving a well-organized, coherent review for accessing research on this specific area of study. Further research on diagnostics and other applications of lipid nanoparticles was also included. This study did not conduct experiments. Rather, it compiled and discussed data presented in the primary sources and academic literature.

The Glioblastoma Brain Tumor:

Glioblastoma is known to be one of the most common and dangerous types of brain tumors. Even with its devastating impact on the brain, there is no specific medicine known to cure the tumor completely.⁸ This aspect is crucial as the brain con-

ducts a multitude of functions, not limited to: enacting speech, movement, memory, and regulating breathing and temperature. Glioblastoma can eventually prevent the brain from performing its daily functions, not only impacting its ability to live at a higher standard but even at the cost of death.

The origins of tumor formation start in astrocytes, which are a type of glial cell. These cells support nerve cells, the spinal cord, and the brain.⁹ Astrocytes help to protect the neurons against any unneeded or toxic compounds, as well as form synapse connections within the brain. However, with glioblastoma forming from them, it can break their functions and no longer be effective. It can then go on to damage and eventually destroy the healthy cells and tissues in either the brain or the spinal cord, depending on where it started.⁸ It is possible for anyone of any age to be diagnosed with Glioblastoma, although it's more common to be present in adults, with the median age being 64 and the peak age being 75-84 years old.¹⁰ Due to the body's aging, cellular processes like genetic mutations are more likely to lose control, as well.

Glioma is a type of tumor that occurs in the brain and is categorized into two main sections: low-grade and high-grade gliomas. Low grade comprises grades 1 and 2, and high grade comprises grades 3 and 4; the order is in increments of aggressiveness. Glioblastoma is a type of glioma that is categorized as grade 4, meaning it's the most aggressive on the scale. It contains features of microvascular proliferation and necrosis (MVP), which simply emphasizes the rapidly growing glioma. Grade 4 gliomas have an average of a 5-10% survival rate, unlike grade 1, for instance, which has a 95% survival rate. The most aggressive grade 4 is the Glioblastoma *IDH* wildtype.¹¹ The effects of Glioblastoma further prove how much danger it can cause not only to the frontal and temporal lobes of the brain, where it primarily occurs, but also impacts the overall well-being of the body (Figure 1).

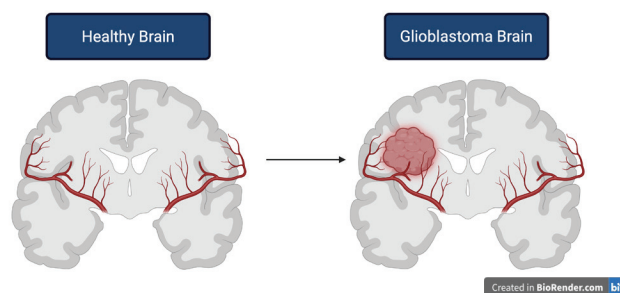


Figure 1: Healthy Brain vs. Glioblastoma Brain. This image illustrates the difference between a healthy brain and one diagnosed with Glioblastoma; the brain with Glioblastoma has a tumor present, which can affect various aspects of brain functioning. These are not limited to tumor growth, which can cause an increase in intracranial pressure due to weight distribution, as well as the breakdown of the blood-brain barrier. These chemical side effects, which will be discussed later in detail, are crucial components of the dangers of Glioblastoma on the brain, created using BioRender by Saimanasaa Viswanathan.

Causes and Symptoms:

Although there isn't a specific root cause to this tumor, mutations can be integral to contributing to the tumor's existence. Mutations happen through a single change or multiple changes occurring in a DNA sequence.¹² The DNA sequence is important as DNA communicates to the cell what to do.

However, in cancer cells, the cells will enact the mutated DNA to keep replicating; this multiplication of cancer cells, constantly replicating, forms tumors, while the healthy cells start to die off in response to the large amount of cancer cells. For instance, in the frameshift mutation, a base can either be deleted or added to the sequence. However, this can alter the entire base pairing, as proteins read bases in groups of three, known as codons. When the order shifts, different proteins will be produced. Other types of shifts include point mutations, which only affect a single nucleotide; for example, one base can be altered for another base, meaning that the entire sequence won't change. Furthermore, there are also missense and nonsense mutations, which also change the order of the DNA sequence.

Some of the key mutations present in Glioblastoma most commonly include *TP53* and/or *PTEN*. According to Olafson *et al.*, the *TP53* gene can acquire the GOF phenotypes (gain of function), which can aggravate tumor growth. Furthermore, this gene being mutated can result in a p53 altered protein, which is unable to activate apoptosis in the cells, i.e., the action of cell self-destruction.¹³ Apoptosis is important because if it doesn't happen, then the mutated or damaged DNA will continue to replicate and spread, elevating growth into a tumor.¹⁴ The *PTEN* gene contains the PTEN enzyme. PTEN mutations reduce tumor suppression activity, leading to uncontrolled cell growth. The symptoms of Glioblastoma are shown (Figure 2).

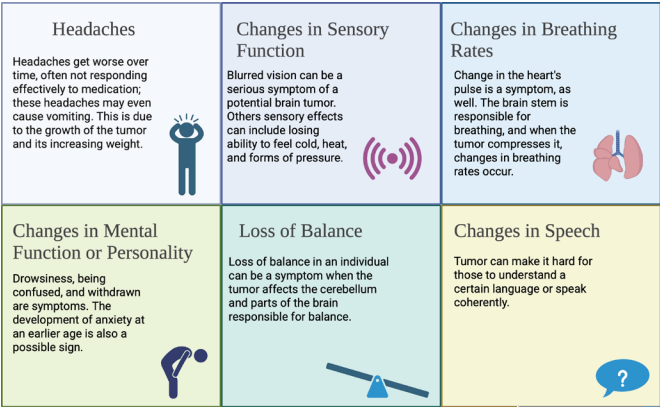


Figure 2: Symptoms of Glioblastoma in the Human Body. The symptoms of Glioblastoma start within the brain first and send signals for further action; these signs are crucial for engaging in medical treatment. Some of these are headaches, sensory changes, changes in breathing rates, changes in medical function or personality, loss of balance, and changes in speech. Information gathered from <https://www.mdanderson.org/cancer-types/glioblastoma/glioblastoma-a-symptoms.html> and created using BioRender.

Challenges to Chemotherapy:

Chemotherapy is a commonly used treatment for Glioblastoma and other cancers. However, along with its usage, multiple drawbacks prevent it from being efficient in comparison to other medications. The major consequence of chemotherapy is its inability to distinguish between cancer cells and healthy cells. Oftentimes, it is prone to targeting both cancer and healthy cells, resulting in major side effects for patients such as weight changes, fertility barriers, constipation, and appetite changes.² Its limitations are not only with these

effects but also with its ability to deliver the drugs to the body efficiently. Additionally, the size of chemotherapy drugs makes it difficult to pass medications through smaller areas such as the blood-brain barrier and blood-tumor barrier, contributing to less efficiency in transporting medication.

Blood-Brain Barrier:

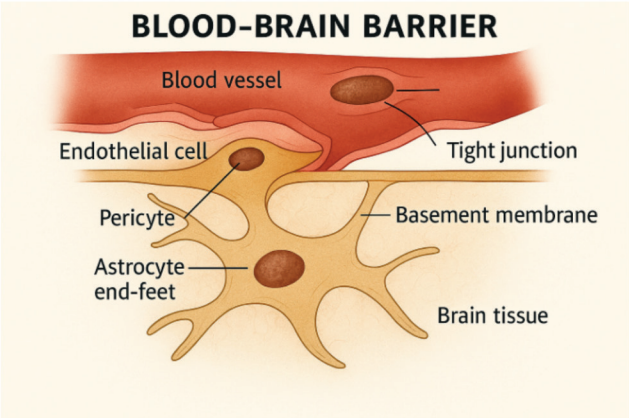


Figure 3: Blood-brain Barrier Structure. The endothelial cells form tight junctions that limit the flow of any hydrophilic substances from passing through the barrier and reaching the brain. The astrocyte endfeet help to convey signals to form the tight junctions of the blood-brain barrier. Likewise, the vascular BM (vascular basement membrane) is especially integral for being a physical support in maintaining the brain's shape as well as assisting in regulating substances. The components of the blood-brain barrier contribute to its selectivity, only allowing for particles with certain characteristics to get through, and are created using CoPilot AI.

Formation and Origin:

The blood-brain barrier (Figure 3) is a selective, semipermeable barrier containing blood vessels that regulate movement between the blood and the brain.¹⁵ It is located between the blood and extracellular space present in all regions of the brain except for the circumventricular organs (CVOs).

Implications in Treatment:

Although the blood-brain barrier can be beneficial in preventing any toxins or unneeded substances from entering the central nervous system, it can create a barrier to many drug delivery systems wanting to transport any needed biopharmaceuticals or chemical drugs for greater health purposes. According to Wu *et al.*, the blood-brain barrier excludes more than approximately 98% of small-molecule-based drugs as well as 100% of macromolecular drugs, challenging the way for these substances to pass through.¹⁶

Blood-Tumor Barrier:

Formation and Origin:

The blood-tumor barrier is a structure modified from the blood-brain barrier, specifically formed during severe tumors like Glioblastoma. The severity of the tumors can result in damage to the blood-brain barrier, resulting in the blood-tumor barrier, which is a modified form of the blood-brain barrier.¹⁷

Structural and Functional Differences Compared to the BBB:

Compared to the blood-brain barrier, the blood-tumor barrier has heterogeneous permeability, meaning the ability for substances to pass in and out varies across different locations within the tumor. This results in the inability for medications to pass through sufficiently for all locations within the tumor, as the degree of effective permeability will vary; however, compared to the blood-brain barrier, it will be more flexible in the passage of substances in and out of the membrane.

Transports and Permeability:

According to Arvanitis *et al.*, due to its heterogeneous permeability, the blood-tumor barrier also presents a challenge of increasing interstitial and intracranial fluid pressure.¹⁸ Because this barrier is constrictive compared to the blood-brain barrier, the ability for fluids to escape into the interstitial space is likely. Additionally, proteins can also pass through this space with the fluids, increasing interstitial pressure. Since this interstitial space is within the tumor itself, it will present a difficulty for such treatments to go past it with the fluids and proteins present. Likewise, intracranial fluid pressure is increased due to an increase in fluid retention and tumor mass accumulated within the skull. Because the brain skull itself cannot expand, as the tumor expands and more weight is being held upon it, the intracranial fluid pressure increases; this will present an obstacle for medical treatments to pass through to the tumors.

Implications of Treatment:

Although the blood-tumor barrier presents a series of challenges on its own, given its complexities and unevenness for medications to effectively bypass it, chemotherapy treatments still struggle to pass through it. The large size of chemotherapy treatments will be a hindrance to the small, compact, and rigid spaces within the barrier. This reasoning also advocates the need for lipid nanoparticles to be able to effectively pass through the BTB, deliver medication successfully, and minimize harm through treatment.

Drug Delivery and Resistance:

Chemotherapeutic drugs can damage healthy tissues as well, which can impact how intensive the treatment can be. Additionally, because the targeting characteristic is not present in chemotherapy drugs, cancer cells are more prone to being resistant to the drug and can advance to multi-drug resistance (MDR).¹⁹ Through this advancement, heterogeneous cancer cells adapt and grow through chemotherapeutic drugs without allowing them to be a barrier to their growth. MDR has been known for cancer cells to be able to survive a variety of anti-cancer drugs, resulting in cancer cells being mildly affected or not affected at all by the treatment due to their ability to resist such medications.²⁰

Alternatives: Why Lipid Nanoparticles?:

Nanoparticles have emerged as a widespread, efficient tool to pass medications through brain tumors to reach allocated spots effectively. Unlike chemotherapy treatments, they have targeted therapy. They can pass through the difficulties that

come with the blood-brain barrier and blood-tumor barrier, one of the most difficult pathways for drugs to get through, which chemotherapy lacks.²¹ Additionally, they are size-effective, ranging from 50-200 nm.²² Three types of lipid nanoparticles will be discussed for efficient Glioblastoma treatments: Solid Lipid Nanoparticles (SLNs), Liposomes, and Nanostructured Lipid Carriers (NLCs).

Solid Lipid Nanoparticles:

Solid Lipid Nanoparticles (SLNs) have been a promising lipid nanoparticle for the treatment of Glioblastoma brain tumors. It has managed to overcome the drawbacks that particles like liposomes, emulsions, and lipids face, such as low stability and loading capacity; through a large capacity of ligands, SLNs can deliver medication and treatments by targeting specific areas, making it widely useful when treating tumors and cancer-induced objects within the brain.²³ Having a targeting system is crucial when dealing with tumors, as the prevention of damaging healthy cells is mostly protected. The SLN's structure is shown in Figure 4.

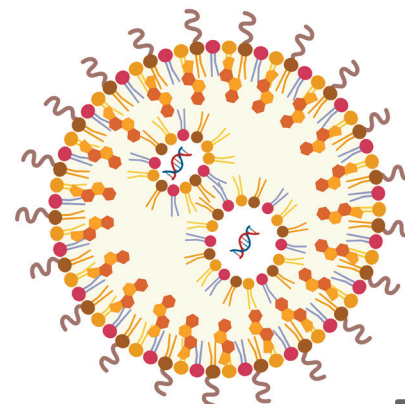


Figure 4: Solid Lipid Nanoparticles Structure. SLNs consist of solid lipids. This helps to give them a more intact, crystallized structure throughout. Drug molecules are present within. As they are lipids, they include a hydrophobic tail and a hydrophilic head, created using BioRender.

SLNs (Figure 4) have also been used to carry a variety of drugs through the drug-delivery process of medication. They can carry those with a high degree of polarity, like 5-fluorouracil, to large lipophilic molecules like taxanes; additionally, oxaliplatin and cisplatin, chemotherapeutic water-soluble drugs, are also effectively able to be loaded within SLNs.²⁵ The high versatility of these nanoparticles maximizes the potential for SLNs to transport anti-cancer drugs past the blood-brain barrier and into the targeted destination within the brain.

While SLNs have a wide spectrum of advantages and efficiency in drug delivery through Glioblastoma treatments, they tend to harden during recrystallization. This ability for these solid lipid nanoparticles to cluster together introduces an obstacle for the drugs allocated aside, making it harder for them to have space; thus, drug expulsion occurs, which is the result when there is no space left for the drug.²³ Because of their perfectly aligned, tightly packed structure, they have low drug loading efficiency, allowing space for drug molecules to fit in.²⁵

However, SLNs remain a strong candidate for Glioblastoma treatments; they are able to have high stability in water-like

environments, high drug load to carry for treatments, and can release the drug in a regulated way over the span of several weeks, instead of all at the same time.²⁶ This is important because patients receiving the treatment will not have a higher risk of side effects compared to if the drug were delivered all at once. The slow, regulated pace over this time period will not allow the body to foresee the potential adversity of side effects provided through the new medication immediately. Additionally, this improves the patients' needs more deeply. Instead of having to take daily medication or pills for treating Glioblastoma, the drugs are administered over the span of weeks, allowing the drugs to treat the patient constantly over time.

Liposomes:

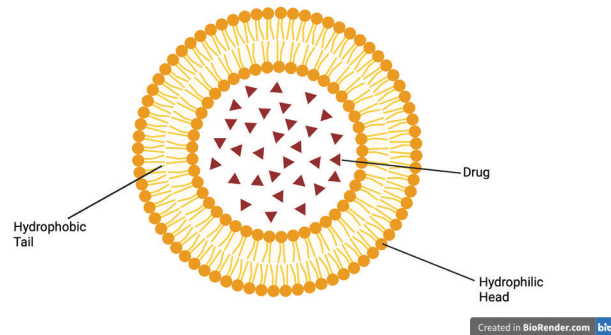


Figure 5: Liposome Structure. This figure shows how liposomes are made up of both hydrophilic heads and hydrophobic tails. They are also able to carry lipid-soluble solutions, making them efficient for the process of delivering the drugs; drugs are contained within the liposome and created using Biorender.

Liposomes (Figure 5) are another lipid nanoparticle known for their use in medical applications like drug delivery. Composed mainly of phospholipids, liposomes can either be classified as part of sphingomyelins or glycerophospholipids. There are two types of ways liposomes can load medications for drug delivery: passive or active loading methods. Within the passive loading method of water-soluble drugs, water is dissolved in the solution to form the respective liposome; likewise, in the passive loading method of hydrophobic drugs, those not compatible with water, drugs are dissolved within the lipid part of the carbon-based solvent. Then, the carbon is later evaporated, leaving just the lipid bilayers. The carbon must be evaporated because it isn't safe to keep inside the body; thus, evaporating it will leave it as the better choice. On the other hand, during active loading methods, the liposome is formed without the drug. However, for the medicine to diffuse through the lipid bilayer, mechanisms like the pH gradient technique are required for it to get inside the liposome, as a medication. Additionally, stimuli such as temperature, ultrasound, and pH have been introduced to enhance the process of drug release.²⁷ Through these processes, medications can perform in action via liposomes or lipid nanoparticles.

Liposomes contain efficient functions such as controlling the release of drugs and protecting substances from degradation. Through these passive and active methods, liposomes are selectively able to reach their highest potential dose, making it an efficient therapeutic process. However, along with their efficient physiological characteristics, they also impose some

risks regarding both their chemical compounds and manufacturing ability.²⁸

To make sure liposomes last longer in the blood, PEG chains (glycol) were introduced. Although they provide a benefit for liposomes to sustain, they introduce the PEG dilemma, which creates a barrier for liposomes to stick onto cancer cells and target them; this then makes it difficult for the liposomes to release the drug at the specific tumor sites. Although liposomes have low toxicity, high biocompatibility, and biodegradability, they come with some disadvantages: the phospholipids can suffer from lower stability and low encapsulation efficiency.²³ Additionally, the production of liposomes can be costly, and industrialization methods can be complex; this can be a challenge to process them, requiring specific equipment and methods of manufacturing.²⁹ The advantages and disadvantages of liposomes are shown (Table 1). Main methods of synthesis of liposomes for Glioblastoma tumors include Thin-Film Hydration, Reverse Phase Evaporation, and Microfluidics.

Table 1: Advantages and disadvantages of liposomes.

Advantages	Disadvantages
Encapsulation	Requires specific degrees of pH levels specifically during active loading, which increases time on waiting for the right amount.
Stability	Has shorter time frames on shelves and will need more harder storage alternatives like cold storage.
Scale-Up	Transitioning liposome production to industry is more complicated as a batch-to-batch consistency and accuracy is needed.

Nanostructured Lipid Carriers:

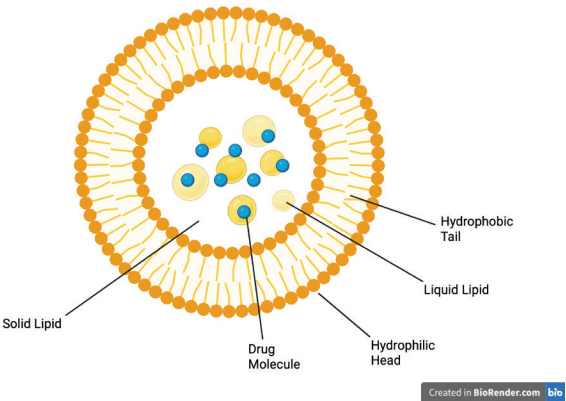


Figure 6: Nanostructured Lipid Carriers Structure. NLCs are composed of both solid and liquid lipids. The integration of liquid lipids allows the benefit of flexibility for more drug intake and carrying, giving more space for drugs to stay within the nanoparticle. As they are lipid nanoparticles, they consist of a hydrophobic tail and a hydrophilic head and were created using Biorender.

Nanostructured Lipid Carriers (NLCs) (Figure 6) are the second generation of lipid nanocarriers, having a mixture of both solid and liquid types. Because they have an imperfect crystal structure, they can have a greater efficiency in drug loading capacity; thus, because there is more space for drug delivery, there is a lower likelihood of drug expulsion.²⁵ The liquid lipids present make it possible for this flexibility. Liquid lipids found can include Capmul[®] MCM C8, sesame oil, oleic acid, and L-phosphatidyl choline (PC).²⁶ According to Xu *et al.*, NLCs have been shown in studies to not only show efficiency in drug delivery but also *in vivo* and *in vitro*. NLC

studies *in vivo*, or within an organism, show their effective nature in therapeutic efficacy and biodistribution within living organisms or the human body. NLCs are shown to be able to reach the tumor areas in need of drug delivery, as well as being effective in treating the disease. Further, they have been effective *in vitro*, in other words, studies performed outside of the organism.³⁰ As mentioned, they have a high encapsulation efficiency due to their structure, and their particle size and characteristics are suitable for stability and cellular uptake. The mixture of both solid and liquid lipids within makes it possible for high drug loading and effective measures upon transporting medication to tumors.

Additionally, studies have been made on the effectiveness of NLCs. Glioblastoma secretes many enzymes known as Matrix Metalloproteinases (MMPs). MMPs break down surrounding tissue so that the Glioblastoma tumors can spread. According to Horta *et al.*, special targeting parts were added to the NLCs, and versions were made. The version of FMBat effectively slowed down the growth of MMPs in Cancer cells and managed to cross through the blood-brain barrier.³¹ This looked promising for approaching the management of tumors. NLCs are also able to effectively carry various types of ligands such as proteins, peptides, and small molecules.³² The high ability and potential of NLCs make it possible for tumor treatments to be both efficient and promising for the needs of patients.

Although NLCs are promising treatments, they still have some limitations. Just like Liposomes, they still have to be moved to large-scale manufacturing. Keeping it consistent can be tough. Further, while they are efficient, crossing the BBB can still be a slight challenge in some circumstances due to the tight junctions present in the BBB.

Most Effective Lipid Nanoparticle:

Table 2: Comparison of Lipid Nanoparticles.

Nanoparticle	Drug Loading Capacity	BBB Penetration Efficiency	Stability	Toxicity	Scalability	Cost
Lipid Nanoparticle	Can carry hydrophilic and lipophilic drugs but moderate carrying capacity	Moderate efficiency	Relatively low- more likely to have drug leakage	Due to phospholipid composition, has low toxicity	Moderate due to complexities of lipid nanoparticles	Moderate to high levels
Solid Lipid Nanoparticle	Relatively low due to rigid structure of solid component	Moderate efficiency	High- solid matrix improves stability	Low toxicity- composed of safe lipids	High- scalability is simple and less complex	Low-moderate
Nanostructured Lipid Carriers	High- lipid matrix allows greater drug encapsulation	High efficiency	High- reduced rigid crystallization allows for minimized drug expulsion	Low toxicity- good biocompatibility	High scalability- but formation is still more complex	Moderate

While SLNs and liposomes all have their unique attributes in delivering medication for Glioblastoma brain tumors, NLCs may offer more balanced overall performance among the three systems. The comparison among the nanoparticles across drug loading capacity, BBB penetration efficiency, stability, toxicity, scalability, and cost is shown (Table 2). Having both solid and liquid lipids within their matrix allows for higher drug loading capacity compared to SLNs, for instance, which have a more rigid structure due to the composition of solid lipids. This means they are more likely to have drug expulsion as a result of not being able to have space for more drug loading. Additionally, NLCs demonstrate improved stability while maintaining lower levels of toxicity, compared to liposomes, which have a

more phospholipid structure and chemically need to be looked after and observed carefully.

However, despite these findings, limited clinical trial data on NLCs prevent the certainty that NLCs are the most effective lipid nanoparticle. Therefore, while NLCs pose improved benefits and are a promising treatment for Glioblastoma brain tumors, further clinical evidence is needed before any definitive conclusions are established.

Conclusion

With high-risk tumors like Glioblastoma, it is crucial to have medicine that will tackle the tumors effectively. While there are thorough options in healthcare to approach Glioblastoma, nanoparticles have been the most promising, specifically lipid nanoparticles. The ability of lipid nanoparticles to cross the BBB effectively, along with efficient drug delivery, has been effective in delivering targeted treatment. SLNs, Liposomes, and NLCs are all effective in their own ways. However, NLCs in particular can have a more flexible crystallized structure, allowing them to have a more targeted treatment and carry higher drug loads. Their biocompatibility and ability to cross the BBB all give them an advantage in treatments. Proceeding with NLCs for Glioblastoma treatment will not only be effective for targeting brain tumors, but also minimize the side effects for patients. Although chemotherapy can slow tumor progression, they often produce healthy tissue and can create significant side effects. Beyond improving outcomes for patients with brain tumors, advances in nanoparticle-based treatments could influence the future of cancer therapy worldwide by creating safer, more precise, and more accessible methods of drug delivery for many difficult-to-treat diseases. Future research can focus more on drug precision and the long-term safety of nanoparticles. Researchers can also focus on combining nanoparticles for immunotherapy or gene therapy to create more selective treatments for patients diagnosed with Glioblastoma.

Acknowledgments

I would like to thank Dr. Kristina Lilova and Professor Virgel Torremocha for their constant guidance throughout the research process. Their remarkable wisdom and patience will never be forgotten.

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