Deep Science Publishing, 2025
https://doi.org/10.70593/978-93-7185-149-7_4

Chapter 4: Lipid-Based Nanocarriers: Liposomes and solid lipid Nanoparticles for Alzheimer's diseases Management

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Abstract

Alzheimer's disease (AD) disease is a slowly progressing neurodegenerative disorder identified by cognitive decline and memory loss along with limited therapy approaches attributed to the Blood-brain barrier (BBB) preventing the absorption of drugs. Lipid-based nanocarriers particularly liposomes and solid lipid nanoparticles (SLNs) have become known as promising methods for improving drugs bioavailability, enhance cerebral targeting and minimising systemic side effects. Liposomes described by their bilayer of phospholipid structure facilitate encapsulation of both hydrophilic and hydrophobic pharmaceutical products while solid lipid nanoparticles (SLNs) provides controlled release and increased stability. These small particles enable blood-brain barrier penetration via changes to the surface (e.g., PEGylation, ligand conjugation) and can transport drugs for therapy such as cholinesterase inhibitors, anti-amyloid peptides and neuroprotective chemical compounds. The study emphasises new advances in liposome and solid lipid nanoparticle delivery systems for Alzheimer's disease management, evaluating their procedures, advantages and problems in both clinical and preclinical studies.

Keywords: *Lipid-based nanocarriers, Liposomes, Solid liquid nanoparticles, Alzheimer's disease, Blood-brain barrier (BBB), Drug delivery.*

1. Introduction

1.1 Epidemiology and Burden of Alzheimer's Disease

Alzheimer's disease is the most common type of dementia and may be responsible for 60–70% of cases. There are about 50 million individuals with dementia around the world. Because the population is becoming older, the number of persons with dementia is expected to quadruple by 2050. This raises the risk of disability, the burden of sickness, and health care expenditures (WHO, 2025). The GBD 2016 Dementia Collaborators (2019) say that the number of people with dementia around the world went up a lot, from 20.3 million cases in 1990 to 43.8 million in 2016. This is an increase of about 117%. It is estimated that by 2050, there will be 152 million people around the world who have Alzheimer's disease and other types of dementia. From 1990 to 2019, the number of new instances of Alzheimer's disease and other dementias over the world went up by almost 148%. There were 2.92 million cases in 1990 and 7.24 million in 2019. Both men and women saw this surge, but it was a little bigger in men. The number of new cases grew the fastest over time among people aged 70 to 74. Alzheimer's disease and other forms of dementia were more common in some areas and at some stages of development than in others. The Sociodemographic Index (SDI) showed that areas with more development had more instances. In less developed areas, on the other hand, there were either modest increases or even a drop in new cases. The greatest rates were in North Africa and the Middle East, high-income Asia-Pacific, and Central Europe in 2019. South Asia and Western Sub-Saharan Africa had the lowest rates. High-income Asia-Pacific had the highest growth in instances, while Western Sub-Saharan Africa had the biggest reduction (Li et al., 2022).

1.2 Pathophysiology and Current Therapeutic Challenges

The pathogenesis of this condition is characterised by two principal features: the extracellular deposition of amyloid-beta (Aβ) plaques and the intracellular accumulation of hyperphosphorylated tau protein, manifesting as neurofibrillary tangles. Amyloid precursor protein (APP) is broken down by β-secretase (BACE1) and γ-secretase in order to make Aβ. Toxic Aβ oligomers impair synaptic function, create ion-permeable membrane holes, alter glutamate signalling, and induce mitochondrial dysfunction and oxidative stress. At the same time, Aβ causes tau to become hyperphosphorylated, which makes microtubules less stable, slows down axonal transport, and causes neurones to stop working. Both Aβ and tau cause long-term neuroinflammation by turning on microglia and astrocytes. This starts a loop of cytokine release, reactive oxygen species (ROS) production, and further damage to neurones. These harmful proteins move across synaptic connections and extracellular vesicles, like exosomes, which leads to the gradual breakdown of neural networks. Pathological changes might manifest decades before symptoms, with cognitive decline becoming apparent as neuronal and synaptic

degeneration advances, especially in the hippocampus and cortex (Aliashrafzadeh et al., 2025; Tatulian, 2022). Pathophysiology of Alzheimer's Disease is shown in figure 4.1.

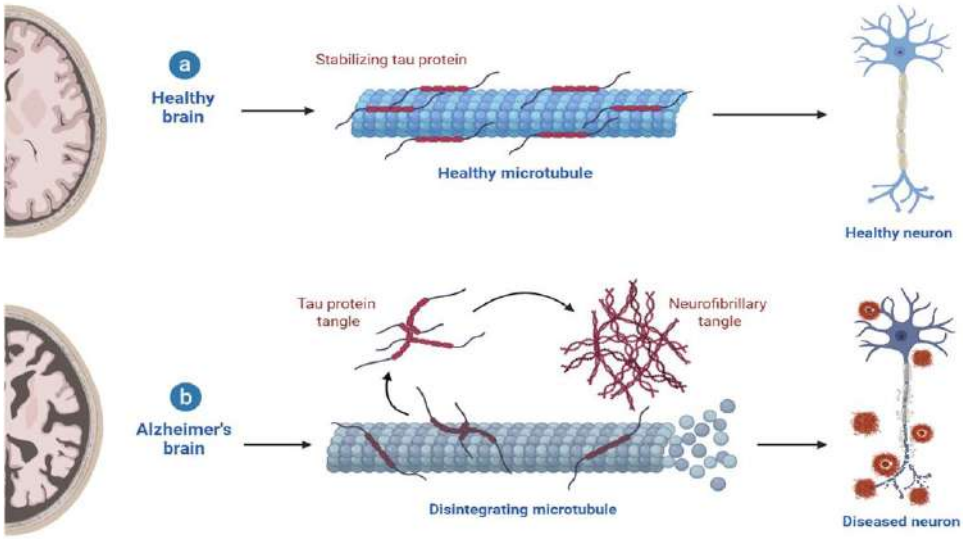

Figure 4.1. Pathophysiology of Alzheimer's Disease

Researchers have mostly looked at Aβ-directed therapeutics for Alzheimer's disease (AD), with several different methods trying to lower the amount of amyloid-β that builds up. Secretase inhibitors like β- and γ-secretase inhibitors (for example, verubecestat, lanabecestat, LY3202626, and atabecestat) lowered Aβ levels a lot, but they didn't work in clinical trials because they didn't improve cognitive function and caused serious side effects like liver toxicity, brain atrophy, and psychiatric symptoms. Semagacestat and R-flurbiprofen, which are γ-secretase inhibitors and modulators, also didn't work since they didn't get into the brain well and caused damage in other areas. These failures show that messing with Aβ's normal function or the balance of APP processing may make things worse. Monoclonal antibodies (mAbs) that target certain kinds of Aβ, such aducanumab, which the FDA approved in 2021, have been found to reduce plaques and improve cognitive function to a small extent. However, there was a lot of debate regarding aducanumab's approval because of problems with the trials and side effects such brain swelling. Other mAbs, such as crenezumab, bapineuzumab, gantenerumab, and lecanemab, have had mixed results, with some being stopped and others still being tested. Active immunotherapy with vaccines made from proteins, DNA, or mRNA tries to make antibodies against Aβ in the body. AN-1792, a vaccination based on Aβ42, got rid of plaques but didn't slow down cognitive deterioration. Recent vaccinations aimed at Aβ and mitochondrial proteins (e.g., cyclophilin-D) have shown promise in animal tests by safeguarding synapses and replenishing neural energy. There is growing interest in targeting pyroglutamylated Aβ (pE-Aβ), a toxic Aβ form that is connected to disease severity. Donanemab and PBD-C06, which target pE-Aβ aggregates, have demonstrated

early success in decreasing plaque and tau pathology with fewer adverse effects. Moreover, small compounds and peptides, including azeliragon and several synthetic peptides, have shown the capacity to impede Aβ aggregation in preclinical tests; however, most have not yet advanced to successful clinical use (Pardo-Moreno et al., 2022). In addition to Aβ methods, tau-directed treatments have also been investigated. Phase III trials have indicated that small molecule inhibitors like LMTM work well, especially in early AD. However, tideglusib and other similar drugs did not show any therapeutic effect. Several mAbs that target tau, like tilavonemab, semorinemab, gosuranemab, Lu AF87908, BIIB076, and zagotenemab, have been tried out. Some have demonstrated the capacity to eliminate phosphorylated tau (P-tau), although many were terminated due to insufficient efficacy. Animal studies have demonstrated that active immunotherapies such the Tau2–18 peptide and dual Aβ/tau vaccinations can help with cognitive function and lower tau levels. Preclinical investigations also showed that the AADvac1 vaccination was safe and worked well. Microtubule-stabilizing medicines like TPI-287 can get through the blood-brain barrier and showed some promise at first, but they didn't work well in human trials since they caused bad reactions and couldn't be found in the CNS.

Researchers are looking for other targets in AD besides Aβ and tau. Antibodies like HAE-4 are targeting APOE ε4, a genetic risk factor. These antibodies lower amyloid and CAA levels without generating microbleeds, which is different from typical Aβ antibodies. Varoglutamstat (a glutaminyl cyclase inhibitor) and Elayta (a sigma-2 receptor antagonist) are both enzyme inhibitors. Varoglutamstat lowers pE-Aβ and makes cognition better, whereas Elayta lowers Aβ synaptic toxicity and is in phase II studies. Kinase inhibitors that target GSK-3β, MAPK/p38, and CDKs are meant to lower tau phosphorylation and the neurodegeneration that comes with it. Lithium compounds have had some efficacy, while medications such as tideglusib were terminated. Researchers are also looking into how NADPH oxidase inhibitors can change oxidative stress, but finding the right ones is still a problem. Exosome-based treatments are evolving, including efforts to restrict Aβ/tau spread by exosome biogenesis blockers or to target pathogenic exosomes for microglial clearance (Belaidi et al., 2025; Cai et al., 2023). Drug repurposing has emerged as a prominent theme in Alzheimer's disease trials, constituting approximately 40% of ongoing investigations. Researchers are testing drugs that were formerly used for cancer (masitinib, lenalidomide), heart disease (amlodipine, losartan), the nervous system (levetiracetam, mirtazapine), and metabolism (metformin, benfotiamine). Preclinical investigations have demonstrated encouraging outcomes for pharmacological agents such as lapatinib and verapamil in mitigating disease and enhancing cognitive function. Antibiotics like β-lactams have also been shown to protect the brain by helping to remove glutamate more quickly. Multi-target techniques that use combination medicines or ligands that work in two ways are becoming more popular. Examples include inhibitors of BACE1/AChE/tau kinase and synergistic medication

combinations, such as leptin and pioglitazone, which enhance cognitive function and more efficiently decrease Aβ levels. Hybrid compounds such as BIGI-3h and tacrine derivatives concurrently target various pathogenic processes (AChE, GSK-3β, MAO-A/B, calcium channels), demonstrating blood–brain barrier permeability and the recovery of memory deficits in murine models (Cummings JL et al., 2025). Even though there are several ways to treat AD, drug development for the disease has a 99% failure rate. Among more than 30 phase III candidates, only aducanumab has been approved. Significant obstacles are the complexity and variability of Alzheimer's disease pathophysiology, including genetic mosaicism and APP recombination, which produce various Aβ variants. Aβ polymorphism is different in different subtypes, which makes it hard to target them all the same way. The timing of intervention is crucial, as diagnosis usually follows significant neurodegeneration. Even initial therapies, such verubecestat, did not stop the disease from getting worse. The blood-brain barrier also makes it harder to administer drugs, especially big molecules like mAbs, which need high doses that might cause swelling and bleeding. Enzyme inhibitors frequently induce off-target effects; for instance, BACE1/2 inhibitors interfere with APP cleavage, and γ-secretase inhibitors influence Notch signalling, hence elevating cancer risk. Blocking kinases like GSK-3β is dangerous for metabolism because they are involved in important pathways. Clinical studies have a lot of problems, like a high rate of misdiagnosis (up to 30% of individuals don't have real Aβ pathology) and bad designs. Diagnostic constraints make drug development much harder. ATN biomarkers and PET imaging are beneficial, but they are also expensive, intrusive, and not available to everyone. We need blood-based tests that are safer and cheaper right away. Moreover, an excessive focus on Aβ and tau may overlook other significant pathogenic factors, highlighting the need for more extensive biomarker identification and validation. Still, there is optimism for advances thanks to better diagnostic techniques, new targets, and integrative therapy strategies, since there are presently more than 120 pharmacological candidates in clinical development (Fu et al., 2025; Dehghani et al., 2025).

1.3 Rationale for Nanotechnology in Alzheimer’s Therapy

Nanotechnology offers a revolutionary method for tackling the complex issues related to Alzheimer's disease (AD) treatment. One of its biggest benefits is that it can get over the blood-brain barrier (BBB), which keeps most regular medicines from getting into the central nervous system. Engineered nanoparticles (NPs) can be developed to utilise receptor-mediated, adsorptive, or carrier-mediated transcytosis pathways to enhance effective blood-brain barrier (BBB) penetration. Functionalised nanocarriers also make it possible to transport drugs directly to disease hallmarks like amyloid-β (Aβ) plaques and hyperphosphorylated tau proteins. This makes drugs more available while reducing off-target effects and systemic toxicity. Also, using controlled and sustained medication

release systems makes treatments more effective and makes patients more likely to follow their doctor's orders, especially in older people.

Nanotechnology also helps create multifunctional theranostic platforms, which are nanoparticles that can transport therapeutic medicines and provide diagnostic imaging at the same time using methods like MRI and PET. This dual feature enables real-time surveillance of disease advancement and therapy efficacy. Some nanomaterials, such curcumin-loaded nanoparticles, dendrimers, and cerium oxide nanoparticles, have their own therapeutic effects, like being antioxidants or anti-amyloidogenic, and they work even better when paired with active medicinal substances.

Nanotechnology is becoming more important for the early diagnosis of Alzheimer's disease (AD) through bioimaging and proteomics, in addition to its use in medicine. Nanosensors and nanoproteomic technologies can find biomarkers in cerebrospinal fluid (CSF) or peripheral blood that are not very common. This helps with preclinical diagnosis and keeping an eye on the condition. It is important to note that multifunctional nanoparticles are being created to target not only Aβ and tau, but also secondary pathologies like neuroinflammation, oxidative stress, mitochondrial dysfunction, and abnormal kinase activity that are involved in tau phosphorylation. This way, they can attack AD's complicated pathogenesis from many different angles. Even with these improvements, there are still a number of problems that make it hard to use these discoveries in the clinic. Long-term toxicity, immune response, clearance, and the possibility of misinterpreting data because of complicated nano-bio interactions are all important issues. So, it is important to improve the design of nanoparticles, especially when using biocompatible and biodegradable polymers like PLGA and PEG. Moreover, obstacles in the scalable and reproducible manufacturing of nanoparticles must be surmounted to enable regulatory approval and commercialisation. Current Alzheimer's disease (AD) treatments mainly focus on Aβ, tau, and inflammation and only treat the symptoms. The future of nanomedicine lies in its ability to provide disease-modifying therapies that stop or slow down the disease's progress, which will improve the quality of life for people with Alzheimer's disease (Cao et al., 2022).

2. Blood-Brain Barrier: An Obstacle for Alzheimer’s Treatment

Endothelial cells connected by tight junction proteins like occludin, claudin-5, and ZO-1 make up the blood-brain barrier (BBB), which is a very selective and tightly controlled vascular interface. Astrocytic end-feet, pericytes, and the extracellular matrix give it structural support. The BBB is very important for keeping the brain's balance by controlling the balance of ions and letting in important nutrients while keeping out toxins and other dangerous chemicals. It does this by using special carrier and efflux transport systems like GLUT1, LAT1, P-glycoprotein, and BCRP. But this protective function also makes it hard to get drugs into the body, especially for big molecules and biologics being

made to treat Alzheimer's disease (AD). Because of this, the BBB is still one of the biggest problems in treating neurodegenerative diseases (Daraban et al., 2024).

2.1 Structure and Function of the Blood–Brain Barrier

The blood-brain barrier (BBB) is a complicated, multi-cellular, and changing semi-permeable membrane that keeps the bloodstream and the central nervous system (CNS) apart. Its main job is to keep the brain's environment stable by keeping dangerous substances out. The BBB's main structural part is the capillaries, and drugs are often delivered through the bloodstream instead of longer, less direct routes. However, the BBB's strict rules make it hard for many drugs to get through, especially those that are meant to treat brain tumours and neurodegenerative diseases like Alzheimer's.

Endothelial cells, astrocytes, pericytes, and junctional complexes (tight and adherens junctions) make up most of the BBB. These parts work together to make a very selective barrier that controls how molecules move between the blood and the brain. The BBB's main building blocks are endothelial cells. They line the blood vessels in the brain and interact with other cells in the CNS. Astroglia, the predominant glial cells in the central nervous system (CNS), exhibit a polarised and intricate morphology, and are conventionally categorised into protoplasmic (found in grey matter) and fibrous (located in white matter) types. Proteins such as aquaporin IV and the dystroglycan–dystrophin complex connect their end-feet to the basement membrane (Wu et al., 2023).

Pericytes are mural cells that encircle capillaries and are situated abluminal to endothelial cells within the basement membrane. They cover almost all of the endothelial surfaces and are very important for the function of the neurovascular unit. They talk to endothelial cells through signalling pathways like PDGF-B/PDGFRβ, which help bring in and place pericytes. The loss of pericytes causes tight junctions to become weaker and the barrier to become less strong (Trempel et al., 2025).

Tight junctions are the most important parts that keep the BBB's integrity and selective permeability. They make seals between endothelial cells that don't break, stopping hydrophilic and large molecules from diffusing through the cells. Other factors that help with structural and signalling stability are junction adhesion molecules (JAMs), protein kinases (like CaMK), monoclonal antibody 7H6, and G-proteins. When tight junction proteins go down, the BBB doesn't work right. Adherents junctions help keep the BBB's structure strong and organise tight junction proteins. They work together with tight junctions. Important proteins are vascular endothelial (VE)-cadherin, catenins, p120, and plakoproteins. Adherens junctions that are broken can make endothelial cells less cohesive and weaken the BBB (Kapinos et al., 2021).

The BBB is very important for making and keeping a controlled microenvironment that is necessary for the brain to work properly. It tightly controls the flow of ions, nutrients,

and molecules between the bloodstream and brain tissue. It helps with many bodily functions, such as keeping the brain's homeostasis, moving nutrients around, controlling immune responses, and changing inflammation. Ion concentrations in the CNS are important for how neurones fire and how signals move between them. These ions are not evenly spread out between endothelial cells that face the blood and those that face the brain. Specialised transporters and channels, like abluminal Na^+/K^+-ATPase and cotransporters like NKCC1, keep ion gradients stable. Disruption of these ion transport systems can result in pathological alterations in the CNS and neurological disorders. The BBB also uses solute carriers and ATP-binding cassette transporters to control the flow of important nutrients, metabolites, and waste products in and out of the brain, keeping the brain's overall balance (Liu et al., 2024).

2.2 Mechanisms of Transport Across the BBB

The Blood-Brain Barrier (BBB) is a very specialised and selective barrier that protects the central nervous system (CNS) by controlling the flow of substances between the brain and the bloodstream. This protective function is mainly because the endothelial cells are tightly connected to each other and have efflux transporters, pericytes, and astrocytes. The BBB is very selective, but it does let some things into the CNS through six main transport mechanisms. The first is paracellular diffusion, which is a passive process that lets small, water-loving molecules like erythropoietin move through the spaces between cells. The integrity of tight junctions tightly controls this route, and drugs rarely use it unless agents like claudin-5 binders are used to temporarily loosen these junctions. Transcellular diffusion is the second mechanism. It is the passive transport of small, lipophilic molecules, like steroids, directly through the cells. But for this route to work, the drugs need to have very specific physicochemical properties (like a molecular weight of less than 500 Da, a neutral charge, a logP of about 2, and fewer than 10 hydrogen bonds). There is also a chance that the drugs will get stuck in the lipid-rich cell membranes, which makes this route less useful for drug development. Carrier-mediated transport is a more promising way to go because it uses special transporters to bring important nutrients like glucose and amino acids into the brain. Drugs can be changed to look like the natural substrates of these transporters. For example, LAT1 is for neutral amino acids like phenylalanine dipeptides, GLUT1 is for glucose and vitamin C, MCT1 is for monocarboxylic acids, CAT1 is for basic amino acids, CNT1 is for nucleosides, and Oatp2 is for organic anions and opioids. Receptor-mediated transcytosis is another advanced method that lets big macromolecules like insulin, transferrin, and lipoproteins bind to certain endothelial cell receptors and be carried across the BBB in vesicles. Researchers are using this mechanism to find new ways to deliver drugs, such as using transferrin-binding exosomes to target glioblastoma. Furthermore, adsorptive-mediated transcytosis offers a non-specific route for polycationic entities, including albumin and specific peptides, to traverse the blood-brain barrier (BBB). These molecules engage

electrostatically with the negatively charged endothelial cell membranes and are internalised through vesicle formation (Toader et al., 2024; Sánchez-Dengra et al., 2023). Mechanisms of Transport Across the BBB is shown in table 4.1.

Table 4.1 Mechanisms of Transport Across the BBB

Mechanism	Transport Type	Selectivity	Examples
Paracellular transport	Passive (between cells)	Very low	Water, ions (rarely)
Transcellular diffusion	Passive (through cells)	Moderate	O_2, CO_2, ethanol, lipophilic drugs
Carrier-mediated transport	Facilitated/Active	High	Glucose (GLUT1), amino acids (LAT1)
Receptor-mediated transcytosis	Active vesicular	Very high	Insulin, transferrin, LDL
Adsorptive-mediated transcytosis	Active vesicular	Moderate	Cationic proteins, peptides
Efflux transport	Active (outward)	High	P-gp, MRPs, BCRP (removal of toxins/drugs)

Cell-mediated transport is another new strategy. In this method, immune cells act as carriers to move therapeutic agents across the BBB. These cells, especially neutrophils, can take in nanoparticles that are loaded with drugs and cross the BBB through transcytosis. This makes them "Trojan horses" for diseases like glioblastoma. In addition to these entry mechanisms, the BBB has efflux transporters, which are mostly ATP-binding cassette (ABC) transporters like P-glycoprotein (Pgp/MDR1), multidrug resistance proteins (MRPs), and breast cancer resistance protein (BCRP). These transporters actively move harmful substances, metabolic waste, and foreign substances from the brain back into the blood. Pgp is the most studied of these and is found on the apical surface of endothelial cells as well as in astrocytes and neurones, especially during seizures. The BBB is very important for protecting the brain, but it also makes it very hard to develop drugs for the CNS because it stops therapeutic agents from getting into the brain. As the global prevalence of CNS disorders—including brain and CNS cancers, stroke, neurodegenerative and psychiatric diseases, encephalitis, and substance use disorders—increases, it is imperative to attain a more profound comprehension of BBB transport mechanisms to develop effective treatments. To improve the success rates of CNS drug development and get meaningful clinical results, it is important to find a way to get drugs to cross the BBB more easily (Ronaldson and Davis, 2024).

2.3 Strategies to Overcome BBB Limitations

It is very important to get around the problems that the Blood-Brain Barrier (BBB) causes in order to get drugs to the central nervous system (CNS) effectively. There are two main types of strategies: invasive and non-invasive. Direct drug delivery into brain tissue, cerebrospinal fluid (CSF), or therapeutic disruption of the BBB are all examples

of invasive methods. Direct brain injections are used to treat conditions like glioblastoma, epilepsy, stroke, and schizophrenia. For instance, the FDA-approved Gliadel® wafer implant treats high-grade gliomas by releasing the drug in the area where it is needed, which can add 2 to 3 months to a person's life. In epilepsy, direct phenytoin injection worked better than systemic doses. Researchers are also working on implantable devices that can find seizures and release drugs in seconds. Researchers are also working on experimental drug delivery systems for mental illnesses like schizophrenia. For example, they are testing rod-shaped implants with nicardipine in stroke patients to stop vasospasm after subarachnoid haemorrhage. Direct CSF injection is easier to do, but it doesn't work as well because it doesn't spread well into brain tissue. This is why ventricular injection is needed for diseases like meningitis. Another invasive method is to use hyperosmolar solutions or ultrasound-guided microbubbles to open the BBB for therapeutic purposes. Mannitol-based solutions temporarily reduce the size of endothelial cells, which opens up tight junctions. However, because they are not selective, they can cause problems like aphasia or hemiparesis. Ultrasound techniques, on the other hand, can open the BBB in a specific area and then close it again. They are often used with drug-loaded microbubbles to deliver drugs to specific areas, which is especially useful for treating brain cancers and neurodegenerative diseases (Teleanu et al., 2022).

On the other hand, non-invasive methods are becoming more popular because they are safer for patients and easier for them to follow. Some of these are the nose-to-brain route, efflux transporter inhibition, prodrug design, chemical drug delivery systems (CDDS), and different kinds of nanocarrier systems. Intranasal delivery goes around the BBB through the olfactory and trigeminal nerves. It has been tried for Alzheimer's disease (like intranasal insulin) and migraines (like Trudhesa®, which the FDA has approved for quick pain relief). Inhibiting efflux transporters is another way to keep drugs in the brain longer. P-glycoprotein (Pgp), multidrug resistance proteins (MRPs), and BCRP are all types of transporters that move drugs out of the CNS. Inhibitors, ranging from verapamil to zosuquidar, have been developed over three generations; however, their clinical application has been constrained by toxicity and off-target effects. This method has shown some promise in making antiretroviral drugs work better in HIV treatment. Chemical changes, like prodrugs and CDDS, are another way to go. Prodrugs such as L-Dopa for Parkinson's traverse the blood-brain barrier (BBB) in an inactive state and subsequently undergo conversion into active pharmaceuticals. CDDS chemically attach drugs to targeting groups that help them get through the BBB and release the active compound once they are in the brain. For example, dihydrotrigonelline-based CDDS increases brain accumulation by using oxidation and controlled hydrolysis. Nanocarriers, which are between 1 and 100 nm in size, are one of the most promising non-invasive platforms because they make drugs more stable, soluble, and able to cross the BBB. Some of these are liposomes, solid lipid nanoparticles (SLNs), lipid nano-

capsules, polymeric nanoparticles, inorganic nanoparticles, dendrimers, cyclodextrins, quantum dots, nanogels, and nanoemulsions. Liposomes, which can hold both hydrophilic and lipophilic drugs, have changed from simple (1st generation) to PEGylated (2nd generation) and targeted (3rd generation) forms. They have been useful in treating Alzheimer's disease (for example, ApoE-targeted liposomes) and glioblastoma (for example, docetaxel liposomes with "lock-in" technology). SLNs are especially helpful for drugs that don't mix well with water because they make the BBB more permeable. Functionalised SLNs, like those linked to transferrin or CBSA, use receptor- and adsorptive-mediated transcytosis to get to the brain. Lipid nano-capsules, which look like lipoproteins, are used to deliver antidepressants like trazodone and antioxidants, like in the BIONICS project to protect against stroke (Madadi & Sohn., 2024). Polymeric nanoparticles, which are made from biodegradable polymers like PLA, PLGA, chitosan, and PCL, can deliver drugs over a long period of time and to specific places. For instance, PEGylated PLA with anti-transferrin antibodies helped people with fungal meningitis, and PLGA nanoparticles with g7 peptide helped people with Alzheimer's disease by delivering curcumin effectively. Chitosan-based nanoparticles demonstrated effectiveness in intranasal treatment for Parkinson's disease, while PEGylated PCL enhanced blood-brain barrier permeability in schizophrenia models. Inorganic nanoparticles, such as gold, magnetic, and mesoporous silica particles, have diagnostic and therapeutic uses, but they are not biodegradable, which raises concerns about their toxicity. Researchers are looking into using gold and magnetic nanoparticles for thermal therapy and imaging in glioblastoma. They are also looking into using silica nanoparticles with the right functionalisation (like lactoferrin or Ri7 antibody) to help them cross the BBB. Dendrimers, particularly PAMAM, are nanostructures with many branches and empty spaces inside them where drugs can be loaded. When molecules like borneol and folic acid are added to them, they can target and selectively deliver drugs to tumour cells like glioblastoma. Cyclodextrins, which are cyclic sugar molecules, make lipophilic drugs easier to dissolve and pass through membranes. A crocetin–γ-cyclodextrin complex has demonstrated efficacy in lowering amyloid-β levels and improving cerebral delivery in Alzheimer's disease. Quantum dots (QDs), which are very small fluorescent nanoparticles, are useful for theranostics, which is the combination of diagnosis and treatment, in brain tumours, stroke, and neuroinflammatory conditions. For instance, transferrin-tagged QDs filled with saquinavir were able to cross the BBB in vitro and stop HIV from replicating. Nanogels, which are soft hydrogel particles, can control how drugs are released. They are especially promising for delivering drugs to the CNS because they are biocompatible and help drugs move around inside cells better. Finally, nano emulsions (NEs), which are emulsified mixtures of liquids that don't mix, can cross the BBB through lipid exchange, receptor-mediated, or adsorptive mechanisms. They work especially well when combined with excipients like polysorbate 80, which stops Pep from working. Researchers have looked into using them to deliver

drugs for CNS conditions like tumours, neurodegenerative diseases, stroke, and HIV encephalopathy (Narsinh et al., 2024).

Viral vectors have also become powerful tools for CNS gene therapy, in addition to these synthetic carriers. Adeno-associated virus serotype 9 (AAV9) is very effective because it can cross the BBB through active transport. AAV9-based therapies have demonstrated efficacy in the treatment of spinal muscular atrophy (SMA), markedly enhancing motor function and survival rates. Viral vectors are effective and can express genes for a long time, but they can also cause problems like activating the immune system and being toxic to the body. In general, a mix of these new methods, such as engineered nanocarriers, chemical changes, and viral vectors, provides a multi-faceted way to get around the BBB and improve treatment results for CNS disorders (Wang S & Xiao L, 2025; Sánchez-Dengra et al., 2023).

3. Overview of Lipid-Based Nanocarriers

Lipid-based nanocarriers are an exciting advancement in the field of drug delivery. These systems make use of naturally compatible lipid molecules to create tiny particles or vesicles at the nanoscale, which can carry a wide range of therapeutic agents. What makes them particularly valuable is their ability to enhance the solubility, stability, and bioavailability of drugs—especially those that are otherwise difficult to deliver effectively. They can also be designed to release drugs in a controlled or targeted manner, which helps in reducing side effects and improving treatment outcomes (Khisho & Alfahad, 2025). This technology has shown great promise in neurological treatments, where delivering drugs to the brain is especially challenging due to the protective nature of the blood-brain barrier (BBB). The blood brain barrier (BBB) acts as a gatekeeper, making it difficult for most drugs to reach the brain in effective amounts. Lipid-based nanocarriers, being biocompatible and biodegradable, offer a gentle and efficient way to transport these drugs across the barrier. Moreover, their flexible structure allows scientists to modify them for targeted delivery something that's particularly important in diseases like Alzheimer's, where specific areas of the brain are affected. (Khan et al., 2023).

3.1 Classification of Lipid-Based Nanocarriers

Lipid-based nanocarriers come in several forms, each with unique features that make them suitable for different therapeutic needs.

Liposomes are perhaps the most well-known. Imagine tiny, bubble-like structures made from layers of lipids similar to the fats found in our own cell membranes. These spherical vesicles have an inner watery core, where they can carry water-soluble (hydrophilic) drugs, while the outer lipid layers can trap fat-soluble (hydrophobic) drugs. This dual

capability makes them extremely versatile for delivering a wide variety of medicines (Queiroz & Muehlmann, 2024).

Solid Lipid Nanoparticles (SLNs) are made from lipids that stay solid at both room and body temperatures. Think of them as firm, protective capsules that help keep drugs stable and release them slowly over time, which can be particularly useful for maintaining consistent drug levels in the body (Queiroz & Muehlmann, 2024).

- **Nanostructured Lipid Carriers (NLCs)** take things a step further. They combine both solid and liquid lipids in their structure, which makes them more flexible and better at holding larger amounts of drugs. This design also helps prevent the drug from leaking out during storage a common issue with some other delivery systems (Yun et al., 2025).
- **Lipid–Polymer Hybrid Nanoparticles (LPHNs)** are a clever combination of two materials: a strong, biodegradable polymer core that gives the particle structure and stability, and a soft lipid outer shell that helps the body tolerate it better. These hybrids bring together the best of both worlds—durability and biocompatibility **(**Yun et al., 2025).
- **Ethosomes and transfersomes** are special types of lipid vesicles that are incredibly flexible and are often used for delivering drugs through the skin. Interestingly, researchers are also exploring their potential to deliver drugs to the brain, due to their ability to cross biological barriers more effectively (Touitou et al., 2000).

Each of these nanocarrier types offers specific advantages, and their selection depends on the drug, the disease, and how and where the therapy needs to work. Together, they form a powerful toolkit for improving how medications are delivered especially in hard-to-reach areas like the brain (figure 4.2).

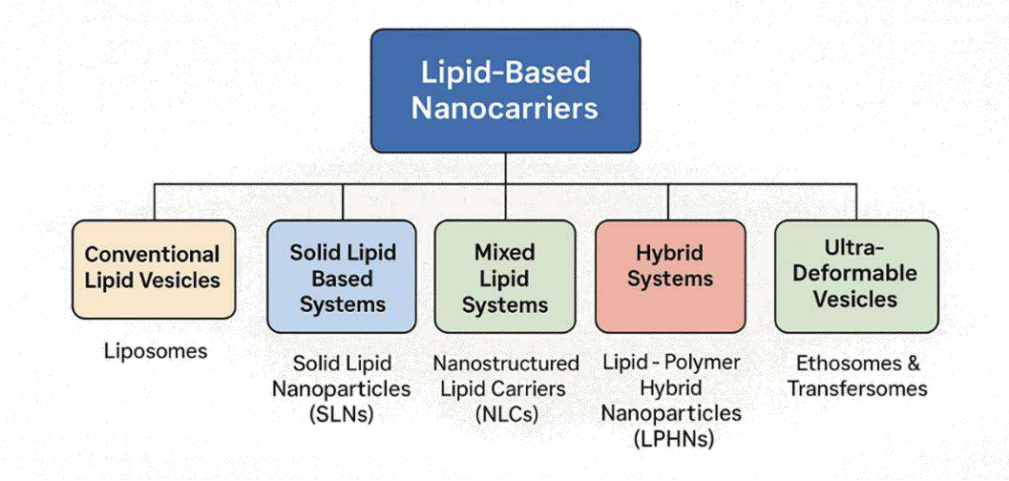

Figure 4.2 Classification of Lipid-Based Nanocarriers

3.2 Advantages and Limitations of Lipid-Based Systems

a) Advantages

Lipid-based nanocarriers offer several important advantages that make them a valuable tool in modern drug delivery especially for treating complex diseases like Alzheimer's, such as:

- **Biocompatibility and Biodegradability:** Since lipid carriers are made from materials that are naturally found in the body, they're generally well-tolerated. This means they're less likely to trigger harmful immune reactions or toxicity, making them safer for long-term or sensitive treatments (Liu et al., 2024).
- **Improved Drug Solubility:** Many effective drugs struggle to dissolve in water, which makes them hard for the body to absorb. Lipid-based carriers help by wrapping these poorly soluble drugs in a form the body can actually use boosting their effectiveness and therapeutic impact (Kendre et al., 2025).
- **Controlled and Sustained Release:** These carriers can be designed to release drugs slowly over time, rather than all at once. This helps maintain consistent drug levels in the body and reduces the need for frequent dosing, which can make treatment more manageable and improve patient adherence (Waheed et al., 2024).
- **Targeted Delivery:** By modifying the surface of these carriers, researchers can direct them to specific sites in the body such as neurons or amyloid plaques in the brain. This targeted approach means the drug goes exactly where it's needed, minimizing side effects on healthy tissues (Waheed et al., 2024).
- **Protection of the Drug:** Once a drug enters the body, it's exposed to enzymes and metabolism that can break it down before it has a chance to work. Lipid carriers act like protective bubbles, shielding the drug from premature

degradation and ensuring it reaches its target in an active form. (Senanayake et al., 2025).

Together, these features highlight why lipid-based nanocarriers are gaining momentum in the development of safer, smarter, and more effective therapies.

b) Limitations:

While lipid-based nanocarriers offer many exciting benefits, they also come with a few challenges that researchers and developers are actively working to overcome. Here's a more relatable explanation of their limitations:

- **Stability Issues:** Liposomes and similar lipid carriers aren't always as stable as we'd like. Over time, they can start to merge together (a process called fusion), leak their drug contents, or become damaged by oxidation. These issues can reduce their effectiveness and shorten shelf life, making storage and handling more complicated (Jyothi et al., 2022).
- **Limited Drug Loading:** Although lipid carriers are great at protecting and delivering drugs, they don't always hold as much medication as needed—especially when it comes to water-loving (hydrophilic) drugs. This limited loading capacity can make it harder to reach the right therapeutic dose (Suman & Das, 2025).
- **Manufacturing Challenges:** Making these nanocarriers in the lab is one thing, but producing them consistently and on a large scale is another story. Ensuring that every batch is the same (batch reproducibility), scaling up production, and sterilizing the final product without damaging it are all major obstacles that still need fine-tuning (John et al., 2024).
- **Short Circulation Time:** Once injected into the body, lipid nanoparticles can be quickly recognized and removed by the immune system—specifically by the mononuclear phagocyte system (MPS). Unless they're modified with protective coatings like polyethylene glycol (PEGylation), they may not last long enough in the bloodstream to reach their intended target (Johansson et al., 2025).

Despite these challenges, ongoing research is continuously improving the design and production of lipid-based nanocarriers, bringing us closer to more reliable and effective treatments.

Table 4.2 Advantages and Limitations of Lipid-Based Systems

Aspect	Description	Reference
ADVANTAGES		
Biocompatibility & Biodegradability	Made from natural body lipids; well-tolerated and safe for long-term use	Liu et al., 2024
Improved Drug Solubility	Enhances the solubility of poorly water-soluble drugs, boosting bioavailability	Kendre et al., 2025
Controlled & Sustained Release	Enables slow, consistent drug release for longer therapeutic effect and better adherence	Waheed et al., 2024
Targeted Delivery	Surface modifications enable targeting specific sites (e.g., brain cells, plaques)	Waheed et al., 2024
Protection of the Drug	Shields drugs from enzymatic degradation and early metabolism	Senanayake et al., 2025
LIMITATIONS		
Stability Issues	Prone to fusion, oxidation, and leakage, reducing shelf-life and efficiency	Jyothi et al., 2022
Limited Drug Loading	Low capacity for hydrophilic drugs may affect achieving therapeutic doses	Suman & Das, 2025
Manufacturing Challenges	Difficulties in large-scale production, batch reproducibility, and sterilization	John et al., 2024
Short Circulation Time	Rapid clearance by immune system unless modified (e.g., PEGylation)	Johansson et al., 2025

3.3 Regulatory Considerations

Getting regulatory approval for lipid-based nanocarriers is a complex and detailed process. Health authorities like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) require a thorough understanding of how these systems behave in the body and how safe and effective they are.

To begin with, developers must provide detailed data on key features such as

- **Particle size and distribution**, which affect how the nanocarriers travel through the body and reach their target (Wang & Grainger, 2022).

- **Surface charge (zeta potential)**, which influences stability and interactions with cells **(Wang & Grainger, 2022).**

- **Encapsulation efficiency and drug release profile**, to show how much drug is carried and how it's released over time (Dri et al., 2023).

- **Stability in physiological conditions** to ensure the carrier remains intact in the body long enough to do its job (Dri et al., 2023).

- **Safety and efficacy in living systems**, to demonstrate that the therapy works and doesn't cause harm

A well-known example of regulatory success is **Doxil®**, a liposomal form of the chemotherapy drug doxorubicin. It was one of the first nanomedicines approved and helped pave the way for others, showing that these systems can make it from the lab to the clinic. Still, the path to approval isn't easy. Because lipid-based carriers are more complex than traditional drug formulations, they require advanced testing methods and standardized evaluation protocols. This makes regulatory approval more demanding but also ensures that any product reaching patients is safe, effective, and of high quality. (Mangla et al., 2025).

4. Liposomes for Alzheimer's Disease Management

Liposomes are one of the most extensively explored lipid-based nanocarriers, especially when it comes to treating neurodegenerative diseases like Alzheimer's. What makes them so promising is their ability to cross the blood-brain barrier a major obstacle for most drugs—and their flexible structure, which can be tailored to carry different types of therapeutic agents. Alzheimer's disease is a complex condition marked by the buildup of amyloid-beta plaques, tangles of tau protein, high levels of oxidative stress, and the gradual loss of neurons. Treating it effectively often requires more than one type of therapy. That's where liposomes come in. They can be designed to deliver a wide range of treatments—including small drug molecules, peptides, proteins, genetic material, and antioxidants—directly to the areas of the brain most affected by the disease. This targeted and versatile approach gives liposomes real potential to support more personalized and effective treatment strategies for Alzheimer's and other brain disorders (Jang et al., 2025).

4.1 Structural Characteristics and Composition

Liposomes are tiny, bubble-like structures made from natural or synthetic fats called phospholipids (like phosphatidylcholine) and often include cholesterol for added stability. These phospholipids have two parts—a water-loving (hydrophilic) head and a water-repelling (hydrophobic) tail. When mixed with water, they naturally arrange themselves into bilayers, forming a spherical shell with an inner watery space that can carry drugs.

Depending on their size and the number of layers they have, liposomes are grouped into three main types:

- **Small Unilamellar Vesicles (SUVs)**: These are single-layered and very small, ranging from 20 to 100 nanometers (Lombardo & Kiselev, 2022).
- **Large Unilamellar Vesicles (LUVs)**: Also, single-layered, but larger than 100 nanometers (Cheng, Huang, Yin, & Liu, 2025).
- **Multilamellar Vesicles (MLVs)**: These are bigger (over 500 nanometers) and have multiple layers, like an onion.

To help liposomes stay in the bloodstream longer, a coating of polyethylene glycol (PEG) is often added. This helps prevent them from being quickly cleared out by the body's immune system (Fraczek et al., 2025).

4.2 Methods of Preparation and Functionalization

Preparation Methods:

There are several ways to prepare liposomes, each with its own benefits:

- **Thin Film Hydration:** In this method, lipids are first dissolved in an organic solvent and dried into a thin film. Then, a water-based drug solution is added to hydrate the film. To get smaller, uniform liposomes, the mixture is usually sonicated or passed through filters (extrusion) (Riccardi, Baldino, & Reverchon, 2024).
- **Reverse-Phase Evaporation:** Lipids are mixed with an organic solvent and then blended with a water-based solution to create an emulsion. As the solvent is removed, liposomes form around the water droplets (Riccardi, Baldino, & Reverchon, 2024).
- **Ethanol/Ether Injection:** Lipids are dissolved in a solvent like ethanol or ether and slowly injected into a water-based solution. This causes liposomes to form as the solvent mixes with water (Eugster & Luciani, 2025).
- **Microfluidics:** A newer and more precise method that uses tiny channels to mix lipids and water under controlled conditions. This allows for consistent size and better reproducibility (Eugster & Luciani, 2025).

Functionalization:

To improve how liposomes work in the body, their surfaces can be modified:

- **Ligand-Targeting:** Special molecules like transferrin, lactoferrin, ApoE peptides, or antibodies can be attached to the surface. These help the liposomes cross the blood-brain barrier by binding to specific receptors on brain cells (Suman & Das, 2025).
- **PEGylation:** Adding a layer of polyethylene glycol (PEG) helps the liposomes stay in the bloodstream longer. It protects them from being quickly recognized and removed by the immune system (Suman & Das, 2025).

4.3 Drug Loading and Release Mechanisms

Passive Loading: This method involves adding the drug while the liposomes are being formed. Water-soluble (hydrophilic) drugs go into the inner water core, while fat-soluble (lipophilic) drugs settle into the lipid bilayer (Pauli, Tang, & Li, 2019).

- **Active Loading**: Here, the liposomes are made first, and then drugs are added using a pH or ion gradient to pull the drug inside. This method is especially useful for drugs that are weak bases and helps improve how much drug can be loaded (Agrawal, Baliga, & Londhe, 2024).

How Drugs Are Released:

- **Diffusion**: The drug slowly leaks out through the lipid bilayer over time.
- **Degradation**: The liposome breaks down due to enzymes or water in the body, releasing the drug (Neves, Gonçalves, Mano, & Oliveira, 2024).
- **Stimuli-Responsive Release**: Some liposomes are designed to release their drug only when triggered by specific conditions, like a change in pH, higher temperature, or chemical signals in the brain. (Chelliah et al., 2025).

4.4 Applications in Alzheimer's Disease Therapy

Liposomes have been used to carry different types of treatments for Alzheimer's disease, helping improve how well the drugs reach the brain and how effectively they work:

- **Acetylcholinesterase Inhibitors**: Drugs like rivastigmine and donepezil, when loaded into liposomes, show better brain targeting and improved effects on memory and thinking (Dhingra & Choudhari, 2022).
- **Anti-Amyloid Agents**: Liposomes have been used to deliver compounds like curcumin and certain antibodies that help reduce the buildup of amyloid plaques in the brain (Hernandez & Shukla, 2022).

- **Antioxidants**: Powerful antioxidants such as resveratrol, coenzyme Q10, and vitamin E can be delivered through liposomes to reduce damage caused by oxidative stress (Ribeiro, Lopes, & Gomes, 2023).
- **Gene Delivery**: Liposomes can carry genetic materials like siRNAs or plasmid DNA that target the genes involved in making amyloid precursor protein (APP) or tau protein both of which are linked to Alzheimer's (Muolokwu et al., 2024).
- **Multifunctional Liposomes**: Some liposomes are designed to carry both drugs and imaging agents at the same time. These are used for both therapy and diagnosis (called "theranostics") (Liu et al., 2025). Applications of liposomes in Alzheimer's Disease treatment is shown in table 4.3.

Table 4.3 Applications of liposomes in Alzheimer's Disease treatment

Therapeutic Approach	Examples/Agents	Benefits	Reference
Acetylcholinesterase Inhibitors	Rivastigmine, Donepezil	Enhanced brain targeting, improved cognitive effects	Dhingra & Choudhari, 2022
Anti-Amyloid Agents	Curcumin, Antibodies	Reduction of amyloid plaque formation	Hernandez & Shukla, 2022
Antioxidants	Resveratrol, Coenzyme Q10, Vitamin E	Protection against oxidative stress	Ribeiro, Lopes, & Gomes, 2023
Gene Delivery	siRNA, Plasmid DNA	Targeting APP and tau gene expression	Muolokwu et al., 2024
Multifunctional Liposomes	Drugs + Imaging Agents (Theranostics)	Simultaneous treatment and diagnosis	Liu et al., 2025

4.5 Preclinical and Clinical Evidence

Preclinical Studies

- **Curcumin-loaded liposomes** have been shown to reduce amyloid plaque buildup and improve memory in mice genetically modified to model Alzheimer's disease (APP transgenic mice) (Far et al., 2024).
- **Rivastigmine-loaded liposomes** increased drug concentration in the brain and led to better behavioral performance in animal models of Alzheimer's (Khairnar, Singh, Ahirwar, & Shukla, 2023).

- **Liposomes coated with ApoE peptides** were able to cross the blood-brain barrier more effectively and helped reduce tau-related brain damage (Constantinou et al., 2024)

Clinical Studies:

- **Liposomal rivastigmine** has been tested in early clinical studies and has shown better absorption and improved treatment results compared to regular formulations (Yang et al., 2013)
- While no liposomal treatment for Alzheimer's disease has been officially approved yet, growing research in this field shows strong potential for future clinical use (Rompicherla et al., 2021)

5. Composition and Physicochemical Properties of Solid Lipid Nanoparticles for Alzheimer's Therapy

5.1 Composition and Physicochemical Properties

Solid lipid nanoparticles (SLNs), characterised by a solid lipid core matrix (50–300 nm) stabilised by surfactants, represent a promising colloidal drug delivery technique for the treatment of Alzheimer's disease (AD). Triglycerides (tristearin, tripalmitin), fatty acids (stearic acid), or waxes (cetyl palmitate) are the traditional components of the lipid composition; however, more recent advances have introduced mixed lipid systems (Compritol 888 ATO) to optimise drug loading capacity (Mohammed et al., 2023). The choice of surfactant (Poloxamer 188, Tween 80, lecithin) has a big effect on particle stability. The optimal surfactant-to-lipid ratios (0.5:1 to 2:1) stop aggregation (Ly et al., 2024). Crystallinity (the desired β'-polymorph for controlled release), zeta potential (-20 to -30 mV for colloidal stability), and particle size (<200 nm for effective BBB penetration) are all important physicochemical parameters. Recent advancements in lipid engineering have yielded structured lipids and hybrid lipid-polymer matrices that improve drug encapsulation and storage stability (Hussein et al., 2025).

5.2 Production Techniques and Surface Modification

The process by which SLNs are made has a big effect on the properties of nanoparticles. High-pressure homogenisation (HPH) is still the best way to make homogenous particles (50–200 nm) in large quantities (Khairnar et al., 2022). Microemulsion (for medications that break down in heat) and solvent evaporation are other approaches, but there are still worries about leftover solvent (Patel et al., 2021). There have been a lot of changes to surface modification techniques. For example, PEGylation (DSPE-PEG) increases circulation half-life by lowering opsonisation, and ligand conjugation (transferrin, ApoE peptides) improves BBB targeting (Zewail and Abd-El-Azim; 2024). Recent advances include dual-ligand systems (transferrin + lactoferrin) that show 2.3 times more brain uptake than single-ligand SLNs in mouse studies. Microfluidic-assisted

nanoprecipitation is one of the new ways of making things that helps keep batches more consistent. Another is the creation of thermosensitive SLNs that release their payloads at brain temperatures (37°C) (Yu et al., 2024).

5.3 Drug Encapsulation Efficiency and Release Profiles

SLNs are very flexible and can hold both hydrophobic (curcumin, rivastigmine) and hydrophilic (donepezil) AD medicines. The efficiency of encapsulation ranges from 60% to 95%, depending on how well the drug and lipid interact (Kotb et al., 2024). Hydrophobic chemicals exhibit enhanced loading (>85%) owing to their preferred partitioning into the lipid matrix, whereas hydrophilic medicines frequently necessitate lipid conjugation techniques (Oliveira et al., 2017). Lipid crystallinity controls release kinetics. Disordered β'-polymorphs have sustained release profiles (70–80% release over 72 hours) compared to ordered β-forms. Advanced stimuli-responsive systems now facilitate pH-triggered release in the acidic milieu of the Alzheimer's disease brain (pH 6.5-6.8), while enzyme-cleavable lipid conjugates permit Aβ-responsive drug liberation (Bertoni et al., 2021). Recent pharmacokinetic investigations indicate that SLN-formulated rivastigmine attains concentrations in the brain that are 3.2 times greater than those achieved with oral treatment in monkey models (Campisi et al., 2022).

5.4 Targeted Delivery Strategies for AD

BBB penetration continues to be the primary obstacle in Alzheimer's disease therapy, tackled through several targeted tactics. Transcytosis mediated by receptors, employing transferrin or LDL receptor ligands (ApoE peptides), exhibits significant potential, as seen by ApoE-functionalized SLNs demonstrating a 4.1-fold increase in hippocampus accumulation compared to untargeted particles (Sabourian et al., 2023). Other methods include magnetic guiding with superparamagnetic iron oxide cores (which improves delivery efficiency by 68% in external fields) and intranasal injection that completely bypasses the BBB (Guigou et al., 2021). Recent advances include exosome-hybrid SLNs that use natural exosomal trafficking pathways and quantum dot-labeled formulations that allow for real-time in vivo tracking (Unnisa et al., 2023). Notably, multi-modal SLNs that include targeting ligands, imaging agents, and combination medication payloads are the next big thing. Recent prototypes have shown that they can reduce Aβ plaques and inflammation in transgenic AD mice at the same time (Persano et al., 2021).

5.5 Preclinical and Clinical Studies

Preclinical studies have demonstrated the efficacy of SLNs in various Alzheimer's disease models, with curcumin-loaded SLNs decreasing Aβ plaques by 52% and enhancing cognitive function in APP/PS1 mice (Far et al., 2024). Rivastigmine-SLNs exhibit increased bioavailability (AUC 3.5× greater than oral administration) and decreased cholinergic side effects in primate trials (Dubey et al., 2023). Clinical

translation is progressing, as Phase I trials using donepezil-SLNs (NCT04886080) exhibit superior safety profiles and a 2.8-fold enhancement in pharmacokinetics compared to conventional tablets (You et al., 2024). Nevertheless, difficulties remain in increasing production while preserving nanoparticle properties, as current Good Manufacturing Practice (cGMP) guidelines are currently being formulated for lipid-based nanomedicines (Maheshwari et al., 2025). Ongoing Phase II investigations focus on nose-to-brain administration of rivastigmine-SLNs, while first-in-human trials with dual-drug (curcumin+ donepezil) SLNs are scheduled in 2024 (Wen et al., 2017). Regulatory considerations continue to be intricate, necessitating standardised characterisation methodologies and prolonged toxicity evaluations to promote clinical integration (Paliwal et al., 2020).

6. Comparative Analysis of Liposomes and Solid Lipid Nanoparticles (SLNs) for Alzheimer's Therapy

6.1 Pharmacokinetics and Biodistribution

Liposomes and SLNs have different pharmacokinetic profiles that have a big effect on how well they can treat Alzheimer's disease (AD). SLNs have enhanced plasma stability, with circulation half-lives ranging from 8 to 12 hours, in contrast to the 4 to 6 hours observed for conventional liposomes. This is attributed to their solid matrix, which resists enzymatic degradation (Ahmed, T. (2024). Biodistribution experiments utilising radiolabelled formulations indicate that solid lipid nanoparticles (SLNs) achieve a 2.3-fold greater brain accumulation (0.8% ID/g) compared to liposomes (0.35% ID/g) in transgenic Alzheimer's disease mice. This difference is ascribed to their smaller average diameter (120 nm versus 180 nm) and improved blood-brain barrier penetration (Jang et al., 2025). PEGylated liposomes have a more even distribution in the body, while SLNs have a higher liver sequestration (15% vs 8% ID/g at 24h) because they are hydrophobic (Mohanta et al., 2019). Recent progress in surface engineering has diminished this disparity, since dual-modified (PEG+ ApoE) SLNs attain brain concentrations akin to targeted liposomes while preserving extended circulation durations (Gomes et al., 2025).

6.2 Therapeutic Efficacy

Comparative efficacy studies show that SLNs are better than liposomes at getting hydrophobic AD medications (curcumin, rivastigmine) into the brain, with brain drug levels that are 1.8 to 2.5 times higher at the same doses (Binda et al., 2020). After 4 weeks, curcumin-SLNs reduced Aβ plaques by 58% in APP/PS1 mice, while liposomal formulations only reduced them by 42% ($p<0.01$). This was because the drug released more slowly from the lipid matrix (Wu et al., 2023). On the other hand, liposomes are better for hydrophilic substances like donepezil and galantamine because their aqueous core makes them 30–40% more effective at encapsulating them (Poudel & Park; 2022). Studies on combination therapy show that liposome-SLN hybrid systems may work best.

Recent research showed that they improved cognition by 72% more than either system alone in primate models (Yang et al., 2020).

6.3 Safety and Toxicological Considerations

Both systems show great biocompatibility, but long-term investigations show that they have different safety profiles. SLNs exhibit reduced complement activation (30% less C3a production) compared to cationic liposomes; nonetheless, typical lecithin-stabilized formulations of both demonstrate comparable haematological safety (Campos et al., 2020). Chronic toxicity studies show that SLNs cause less damage to the liver (1.5 times more ALT rise vs. 2.8 times more for liposomes at 6 months), but more accumulation in the lungs (12% vs. 7% ID/g), which may need surface modification (Ma et al., 2018). New "stealth" solid lipid nanoparticles (SLNs) with 10% PEG have less immunogenicity than PEGylated liposomes, but they still have the drug loading benefits of solid lipids (Santhanakrishnan et al., 2024). The FDA's most recent guidance particularly talks about the safety of lipid nanoparticles and says that both systems need to be tested for genotoxicity (Nezhad et al., 2020).

6.4 Scalability and Industrial Translation

Liposomes are currently the most popular type of commercial translation, with 12 FDA-approved products compared to only 3 for SLNs. This is because they were developed earlier (Liu et al., 2022). The cost of making SLNs is 30–40% lower, though, because they don't need to be made in a sterile environment and can last longer on the shelf (24 months instead of 18 months) (Viegas et al., 2023). High-pressure homogenisation (HPH) for SLNs provide better batch consistency (PDI <0.2 vs 0.25–0.3 for liposome extrusion), however emerging microfluidic liposome production may decrease this gap (Witika, et al., 2022).

7. **Emerging Trends and Future Prospects**

Research on Alzheimer's disease (AD) has entered a new age thanks to huge improvements in diagnostics, treatments, and tailored methods (Scheltens et al., 2021). The creation of biomarkers for early and non-invasive diagnosis is one of the most important new trends. Blood-based biomarkers like plasma p-tau217 and neurofilament light chain (NfL) are good alternatives to cerebrospinal fluid (CSF) analysis and expensive imaging (Benussi et al., 2025). PET imaging and CSF biomarkers are still very important for finding amyloid-β and tau disease in the preclinical stage, which makes it possible to treat it sooner. (Nguyen et al., 2021). Another important development is the use of precision medicine, which uses genetic profiling, especially the APOE ε4 allele and polygenic risk scores, to help people come up with personalized preventative and treatment plans (Fan et al., 2019). This has also led to the categorization of Alzheimer's disease into subgroups based on molecular, clinical, and neuroimaging

characteristics. This makes it possible to give more personalized treatments. A big step forward in slowing down the course of illness is the approval of disease-modifying treatments (DMTs) such aducanumab, lecanemab, and donanemab These medicines primarily focus on amyloid-β plaques, and the research pipeline is broadening to encompass anti-tau medications, neuroprotective compounds, and synaptic modulators. At the same time, addressing neuroinflammation has become more popular, with a focus on changing how microglia work and stopping pathways like TREM2 and NLRP3. Researchers are also very interested in the gut-brain axis and how the microbiome affects neurodegeneration (Jin & Noble, 2024). Digital biomarkers and AI are changing both research and care in big ways. AI algorithms are being used to find diseases early, model how they progress, and make predictions about the future. On the other hand, wearable devices and smartphone apps let people keep track of their cognitive skills in real time. Researchers are also looking into lifestyle changes that can help, like exercise, following the MIND diet, cognitive training, and getting enough sleep. They are doing this in big, multimodal trials like FINGER and WW-FINGERS (Rosenberg et al., 2020). These studies demonstrate the significance of non-pharmacological approaches in prevention and risk reduction.

The field is rapidly transitioning to a prevention-oriented model, with increasing efforts aimed at averting the onset of symptoms, particularly among genetically predisposed groups. The goal is to use risk prediction and early biomarker identification to start preventative measures during the prodromal or preclinical stages. Future treatment regimens will likely incorporate combination therapy methods akin to those utilized in cancer or HIV, incorporating anti-amyloid, anti-tau, anti-inflammatory, and neuroprotective medicines (Maturkar et al., 2025) for holistic disease control. There is also growing interest in therapies that use genes and cells, such as CRISPR/Cas9 to fix harmful mutations and exosomes from stem cells for regenerative therapy. On a larger scale, global collaborations like the Alzheimer's Disease Neuroimaging Initiative (ADNI) and UK Biobank are making it easier to get open-source longitudinal data and making clinical trials more inclusive (Bhardwaj et al., 2022). This is important to make sure that new treatments work for everyone around the world.

Lastly, in order to address the demands of an aging population, innovations in care and policy are developing. Access to diagnosis, education, and support services is being increased, particularly in underserved and rural areas, thanks to the growth of community-based dementia care models and the growing use of telemedicine and digital health tools. A more optimistic, proactive, and individualized approach to Alzheimer's disease care and research is being made possible by these new trends and opportunities.

7.1 Hybrid and Multifunctional Nanocarriers

Hybrid nanocarriers are nanostructures that are made to improve how well drugs are delivered. These nanocarriers are made of two or more different materials, which can be organic, inorganic, or both. Multifunctional nanocarriers are designed to perform multiple tasks at once, such as releasing drugs, imaging, targeting, and responding to stimuli (Elzoghby et al., 2020).

1. Hybrid Composition

- **Organic-inorganic hybrids**:

  Organic-inorganic hybrids like liposomes coated with gold nanoparticles combine the biocompatibility of liposomes with the functional properties of gold (Fulton & Najahi-Missaoui, 2023). This enhances stability, drug delivery efficiency, and enables applications such as targeted imaging, photothermal therapy, and controlled drug release, making them promising tools in nanomedicine e.g., liposomes coated with gold nanoparticles.

- **Polymer-based hybrids**:

  Polymer-based hybrids, such as polymer-lipid nanoparticles, combine the structural stability of polymers with the biocompatibility of lipids (Padhi et al., 2024). These systems enhance drug encapsulation, prolong circulation time, and offer controlled release, making them ideal for targeted and efficient drug delivery applications. e.g., polymer-lipid hybrids combining stability and biocompatibility.

- **Metal-organic frameworks (MOFs)**: Metal-organic frameworks (MOFs) are porous crystalline materials made from metal ions and organic linkers (Padhi et al., 2024). They offer tunable porosity and exceptionally high drug loading capacity, making them attractive for drug delivery, imaging, and theragnostic applications. Their structure can be tailored for controlled release and targeted delivery.

2. Multifunctionality

- **Targeting ligands**

  Targeting ligands, such as antibodies and peptides, are used to functionalize drug carriers for site-specific delivery. By binding selectively to receptors overexpressed on diseased cells or tissues, these ligands enhance targeting accuracy, reduce off-target effects, and improve therapeutic efficacy (Haas et al., 2014) (e.g., antibodies, peptides) for site-specific delivery.

- **Theragnostic function**: Theragnostic systems combine therapeutic and diagnostic functions in a single platform, allowing simultaneous treatment and

real-time monitoring of disease. This integrated approach improves treatment precision, enables early response assessment, and supports personalized medicine strategies (Hampel et al., 2018).

- **Stimuli-responsiveness**: Stimuli-responsive drug delivery systems are engineered to release drugs in response to specific internal or external triggers such as pH changes, temperature variations, enzymatic activity, light exposure, or magnetic fields (Robert et al., 2010). This targeted release enhances therapeutic precision, minimizes side effects, and improves overall treatment outcomes by ensuring drugs are activated only at the desired site.
- **Imaging capability**: Nanocarriers with imaging capability are integrated with contrast agents for techniques like MRI, fluorescence, or CT imaging (Montal et al., 2021). This allows real-time tracking of drug distribution, monitoring of treatment response, and precise localization of disease sites, supporting both diagnosis and therapy in a single platform.

Applications

Nanotechnology has emerged as a transformative tool in modern medicine, offering targeted, efficient, and multifunctional therapeutic strategies. In neurodegenerative diseases like Alzheimer's, nanocarriers help cross the blood-brain barrier and deliver dual-action therapies for anti-amyloid and neuroprotective effects. In cancer therapy, nanoparticles enable active targeting of tumor markers, co-delivery of multiple drugs, and image-guided treatments. Similarly, for antimicrobial delivery, nanocarriers provide controlled drug release and combat resistance through synergistic combinations with efflux pump inhibitors.

Neurodegenerative Diseases

Crossing the blood-brain barrier (BBB) using: Surface functionalization (e.g., with transferrin or lactoferrin).Nanoemulsions, dendrimers, polymeric micelles.Dual action: **anti-amyloid therapy + neuroprotection**.

Cancer Therapy

Active targeting of tumor cells (HER2, EGFR, etc.). Co-delivery of multiple agents: chemo + siRNA, or chemo + immunotherapy. Image-guided therapy (MRI-visible nanoparticles).

Antimicrobial Delivery

Controlled release of antibiotics to infection sites.Overcoming drug resistance by co-delivering efflux pump inhibitors.

Recent Innovations

Table 4.4 Technologies used in Alzheimer's Disease

Technology	Feature	Application
Gold–liposome hybrids	Photothermal + chemotherapy	Cancer ablation
MOF-based carriers	High surface area	pH-triggered release
Lipid-polymer hybrids	Stability + biocompatibility	CNS drug delivery
Magnetic nanocarriers	External field-controlled	Targeted tumor therapy

Future Prospects

- Personalized nanomedicine: patient-specific targeting strategies.
- Smart nanocarriers: real-time sensing and adaptive response.
- Scalable manufacturing and regulatory approval processes for clinical use.

Green synthesis methods for safer, eco-friendly production.

7.2 Personalized Nanomedicine Approaches

Personalized nanomedicine is a revolutionary approach that customizes medical treatment to the unique molecular and genetic profiles of patients. Personalized nanomedicine (Kaushik et al., 2018) facilitates precision-targeted therapy by integrating nanotechnology with genomics, proteomics, and metabolomics, thereby enhancing efficacy and reducing adverse effects.

1. Integration of Omics Data with Nanocarriers

Recent improvements in high-throughput technology, like as next-generation sequencing and mass spectrometry, have made it possible to get detailed information on genetic mutations, epigenetic changes, and protein expression patterns that are unique to each patient (Yu et al., 2022). This information makes it easier to come up with smart designs for nanocarriers that are customized for target-specific ligand attachment (e.g., targeting overexpressed receptors). Optimized for drug sensitivity or resistance patterns based on individual tumor or disease profiles.

2. Tailored Drug Delivery Systems

Personalized nanomedicine leverages engineered nanocarriers to deliver the right drug, at the right dose, to the right site, in the right patient (Perluigi et al., 2024). These systems are designed to align with individual pharmacokinetic and pharmacodynamic profiles, ensuring maximum efficacy within the optimal therapeutic window. Examples include siRNA or CRISPR-Cas9-loaded nanoparticles that target patient-specific oncogenes, and nanoparticles functionalized with aptamers that selectively bind to disease-associated biomarkers. Such precision targeting enhances treatment outcomes while minimizing off-target effects.

Personalized nanomedicine utilizes engineered nanocarriers to: Deliver the right drug at the right dose to the right site in the right patient. Adapt to individual pharmacokinetics and pharmacodynamics, ensuring optimal therapeutic window. Examples include: siRNA or CRISPR-Cas9-loaded nanoparticles targeting patient-specific oncogenes. Nanoparticles functionalized with aptamers that bind selectively to disease-associated biomarkers.

3. Theragnostic Nanoparticles

Theragnostic nanoparticles are multifunctional nanocarriers that integrate both diagnostic and therapeutic capabilities in a single platform. Personalized nano-theragnostics enable real-time monitoring of treatment response, allowing dynamic adjustment of therapy based on imaging or biomarker feedback. These systems can be tailored to individual patients by incorporating imaging agents suited to specific modalities like MRI, PET, or fluorescence, enhancing precision and supporting adaptive, patient-specific treatment strategies.

Multifunctional nanocarriers are designed for simultaneous diagnosis and therapy ("theragnostic"). Personalized nano theragnostic can: Monitor therapeutic response in real-time. Adjust treatment protocols dynamically based on imaging or biomarker feedback. Be tuned to patient-specific imaging signatures (MRI, PET, fluorescence)

4. Examples of Personalized Nanomedicine in Practice

Personalized nanomedicine is already showing promise in a number of clinical settings. For breast cancer (Tiwari et al., 2023), HER2-targeted liposomal doxorubicin is given to people whose HER2 receptor is overexpressed. This makes it possible to deliver the drug exactly to the tumor cells. For glioblastoma, nanoparticles designed to cross the blood-brain barrier (BBB) in patients with increased matrix metalloproteinase (MMP) levels improve targeted drug delivery to the brain (Do et al., 2021; Vaishnav et al., 2025). In Alzheimer's disease, ApoE-targeted nanocarriers are being developed specifically for individuals with the APOE ε4 genotype, facilitating blood-brain barrier (BBB) crossing and delivering neuroprotective agents to affected brain regions. These examples show how nanomedicine can be customized to fit each person's molecular profile for better treatment. Breast Cancer: HER2-targeted liposomal doxorubicin based on HER2 expression status. Glioblastoma: Nanoparticles designed to penetrate the BBB in patients with elevated MMP expression. Alzheimer’s Disease: ApoE-targeted nanocarriers designed for individuals with APOE ε4 genotype to cross the BBB and deliver neuroprotective agents.

5. Challenges and Future Directions

Even though personalized nanomedicine has a lot of promise, there are still a lot of problems that need to be solved. Variability among patients and heterogeneity within tumors can impact treatment outcomes, while the scalability and cost-effectiveness of creating personalized nanocarriers continue to be significant challenges. The lack of standardized methods for characterizing nanoparticles and the complicated rules makes it even harder to use them in clinical settings. Furthermore, there exists an urgent necessity for extensive databases that correlate patient molecular profiles with nanocarrier efficacy to facilitate personalized therapy. Future research will likely concentrate on AI-driven nanocarrier design (Vaishnav et al., 2025). the creation of digital twins for simulating individualized treatment responses, and bio-responsive nanocarriers that dynamically adjust to the distinct pathophysiology of each patient. While, the potential is vast, challenges remain: Heterogeneity within patient populations and even within individual tumors. Scalability and cost-effectiveness of personalized nanocarrier design. Regulatory hurdles and standardization in nanoparticle characterization. Need for robust databases linking patient molecular profiles with nanocarrier performance. Future research is expected to focus on: AI-driven design of personalized nanomedicines. Digital twins for predictive simulation of treatment responses. Bioresponsive nanocarriers that adapt dynamically to individual pathophysiology.

7.3 Regulatory and Ethical Challenges

The growth of nanomedicine, especially in customized and multifunctional nanocarriers, brings up important regulatory and ethical issues that need to be dealt with in order to make sure that clinical translation is safe, fair, and responsible. As nanocarrier systems get more complicated, there is a greater need for strong rules that balance new ideas with safety and ethical norms.

1. Regulatory Challenges

a. Lack of Standardization

- Nanoscale materials, particularly hybrid or multifunctional systems, are frequently not adequately regulated by current pharmaceutical laws.
- Standardized procedures for characterizing nanomaterials in terms of size, shape, charge, stability, and surface chemistry are lacking.

b. Complexity in Preclinical Evaluation

- There are particular evaluation difficulties with multifunctional nanocarriers that combine therapeutic and diagnostic agents (theranostics).

- Comprehensive toxicological, pharmacokinetic, and biodistribution data are needed by regulatory bodies, but they can be challenging to gather for dynamic, heterogeneous nanocarriers.

c. Unclear Regulatory Pathways

- The classification of nanocarriers as medications, biologics, devices, or combination products is frequently unclear, which makes the approval process more difficult.
- Harmonization between international agencies (e.g., FDA, EMA, CDSCO) is still in progress.

2. Ethical Considerations

a. Equity and Accessibility

- Personalized nanomedicines' expensive development and customization run the risk of escalating healthcare inequalities, particularly in low- and middle-income nations.
- Ethical concerns arise when only a segment of the population can access advanced nano-based diagnostics or therapies.

b. Informed Consent and Risk Disclosure

- Patients need to be fully informed about the unknown long-term effects of nanomedicine, such as genotoxicity, immunological activation, and possible organ accumulation.
- Using experimental personalized nanocarriers means that clinical trial recruitment needs to be more open.

c. Privacy and Data Use

- Personalized nanomedicine depends on sensitive genomic and biometric data.
- Ethical data governance is essential to prevent misuse or unauthorized access, especially in cross-border research collaborations.

d. Environmental Impact

- The production and disposal of nanomaterials may pose environmental hazards.
- Ethical responsibility includes evaluating the life-cycle of nanocarriers, including their impact on ecosystems.

3. Future Directions and Recommendations

- Regulatory harmonization across international agencies to create unified guidelines for nanomedicines.
- Development of nano-specific ethical frameworks, including community engagement and inclusion.
- Adaptive regulations that evolve alongside scientific progress, incorporating AI and real-world data for ongoing risk assessment.
- Emphasis on public education and transparency to foster trust and informed participation in nanomedicine-based interventions.

7.4 Opportunities for Translational Research

Translational research is essential for transforming laboratory innovations in nanomedicine into effective clinical therapies. In the case of hybrid and multifunctional nanocarriers, (Duchesne et al., 2024) it enables the development of personalized treatments for complex diseases like cancer, Alzheimer's, and infections. These carriers offer targeted delivery, controlled release, and integrated imaging, improving precision and reducing side effects. By bridging the gap between bench and bedside, translational research ensures these advanced systems move toward real-world clinical applications and better patient outcomes.

1. Bridging Laboratory Innovation with Clinical Need

Bridging the gap between lab innovation and clinical application involves aligning nanocarrier design with real-world disease biology. Target validation using patient-derived cells and organoids helps identify molecular markers that intelligent nanocarriers can exploit for precise drug delivery. Additionally, advanced preclinical models such as 3D brain spheroids or tumor-on-a-chip systems mimic human pathophysiology (Park et al., 2024) more accurately than traditional models, offering more reliable platform s for assessing the efficacy and safety of nanocarrier-based therapies before clinical translation. Target validation studies utilizing patient-derived cells and organoids facilitate the identification of molecular markers amenable to exploitation by intelligent nanocarriers. Preclinical models of disease that closely mimic human pathophysiology (e.g., 3D brain spheroids, tumor-on-a-chip) provide better platforms for testing nanocarrier efficacy and toxicity.

2. Development of Disease-Specific Nanocarriers

Designing nanocarrier systems for specific diseases has a lot of promise because it could make treatments more accurate and effective. For instance, nanoparticles that target the brain can cross the blood-brain barrier to deliver neuroprotective or anti-amyloid drugs in Alzheimer's disease. In cancer, nanocarriers that respond to the tumor microenvironment, like acidic pH or enzymes that are too active, allow drugs to be released at specific sites. Inhalable nanoparticles also provide targeted treatment for respiratory illnesses such as COVID-19 or tuberculosis, enhancing drug localization and reducing systemic side effect (Huang et al., 2024). There is immense potential for disease-specific nanocarrier systems: Brain-targeting nanoparticles for Alzheimer's disease that cross the blood–brain barrier and deliver anti-amyloid or neuroprotective agents. Tumor microenvironment-responsive carriers that exploit acidic pH or overexpressed enzymes for site-specific drug release in cancer. Inhalable nanoparticles for respiratory diseases like COVID-19 or tuberculosis.

3. Integration with Diagnostic Platforms (Theragnostic)

Translational research facilitates the creation of theragnostic nanocarriers that integrate diagnostic imaging techniques, including MRI, PET, or fluorescence, with targeted drug delivery within a unified platform. These systems with two functions let doctors watch drug distribution and therapeutic response in real time, so they can see how well the treatment is working and change it if necessary. This integration improves the accuracy of treatment, helps with adaptive planning, and is a major step toward personalized medicine. Translational research backs theragnostic nanocarriers that mix imaging (like MRI, PET, and fluorescence) with targeted drug delivery. Such dual-function systems enable real-time tracking of therapeutic response and allow adaptive treatment planning, a crucial step toward precision medicine.

4. Personalized Nanocarrier Design Using Patient Data

Personalized nanocarrier design utilizes individual genetic, proteomic, and metabolomic profiles to develop customized drug delivery systems that correspond with a patient's unique disease biology. Researchers can make nanocarriers that work better, are less toxic, and target better by using these personalized datasets. Advanced tools like artificial intelligence (AI) and machine learning make this process even better by looking at large amounts of patient data to find the best nanoparticle formulations, dosing strategies, and targeting ligands. This data-driven method helps make precision nanomedicine possible, which leads to better and more personalized treatment results. Personalized genetic, proteomic, and metabolomic profiles can guide the development of tailored nanocarriers. Tools such as AI and machine learning are increasingly being used to predict optimal nanoparticle formulations, dosing regimens, and targeting ligands based on patient datasets.

5. Cross-Disciplinary Collaboration

Advancing nanocarrier-based therapies requires collaboration among chemists, biologists, engineers, clinicians, and data scientists to design effective, scalable, and clinically relevant systems. Academic-industry partnerships are crucial for scaling up production, navigating regulatory pathways, and conducting clinical trials, ensuring smooth translation from lab to clinic. Opportunities lie in fostering collaborations between chemists, biologists, engineers, clinicians, and data scientists. Academic-industry partnerships are essential to scale up production, navigate regulatory processes, and design clinical trials.

6. Clinical Trial Innovation

Translational research is leading to major changes in how clinical trials are designed and carried out, especially for complicated therapies like those that use nanocarriers (Schneider et al., 2014). Adaptive and decentralized approaches are becoming more common in trials, either in addition to or instead of traditional ones. These new methods are more flexible and can respond better to new data. Adaptive trials let researchers change study protocols in real time based on interim results. This can include changing the dose or adding more people to the study group. This makes the process more efficient and cuts down on the time and money needed for development. Digital health tools help decentralized trials (Jung et al., 2024) by making it easier for people to take part from a distance, collect data, and keep an eye on things. This makes trials more patient-centered and easier to get to. Biomarker-driven patient selection is also making clinical trials more accurate by making sure that therapies are tested on people who are most likely to benefit from them, based on genetic, molecular, or physiological markers. This is especially important for personalized nanomedicine, where the way drugs are delivered and how they work can be different for each person (Palmqvist et al., 2024). Also, combining wearable biosensors with mobile health technologies makes it possible to keep track of a patient's health metrics, treatment response, and possible side effects all the time. These improvements not only make the clinical trial process easier, but they also make the data completer and more trustworthy, which speeds up the development and approval of new nanocarrier-based therapies. Translational research supports the development of adaptive and decentralized clinical trial models using digital health tools. Biomarker-driven patient selection and real-time monitoring through wearable biosensors enhance trial efficiency and precision.

7. Funding and Policy Support

More and more institutions and governments are recognizing the potential of translational nanomedicine. This has led to more support through targeted funding and policies that are good for it. The National Center for Advancing Translational Sciences (NCATS) in the US, Horizon Europe in the EU, and India's Biotechnology Industry Research Assistance Council (BIRAC) are all funding new projects that will help

nanomedicine technologies move from the lab to the clinic more quickly. These programs not only give money, but they also give resources for regulatory guidance, clinical validation, and commercialization pathways. Policy incentives like fast-track approvals, longer patent exclusivity, and funding for orphan diseases and areas of unmet medical need also help the development of therapies that use nanocarriers. This growing network of support is important for overcoming translational challenges, encouraging cooperation between academia, industry, and healthcare systems, and making it possible for advanced nanomedicine solutions to be used in clinical settings.

There is growing institutional and governmental support for translational nanomedicine research: Programs such as NIH NCATS, Horizon Europe, and India's BIRAC fund innovative translational projects. Incentives for orphan diseases and unmet medical needs provide further momentum for nanocarrier-based interventions.

Conclusion

Alzheimer's disease (AD) continues to pose a significant challenge in neurology, as existing therapeutic approaches are impeded by the blood-brain barrier (BBB) and restricted drug bioavailability. Lipid-based nanocarriers, especially liposomes and solid lipid nanoparticles (SLNs), have come up with new ways to deliver drugs that are better for the brain and have less harmful effects on the body as a whole. Liposomes can hold both hydrophilic and hydrophobic drugs because of their flexible phospholipid bilayer structure. SLNs, on the other hand, are more stable, release drugs in a controlled way, and can hold a lot of drugs. These nanocarriers make it easier for drugs to get through the BBB by using advanced surface modifications like PEGylation and ligand conjugation (e.g., transferrin, ApoE peptides). This lets cholinesterase inhibitors, anti-amyloid agents, and neuroprotective compounds go straight to the parts of the brain that need them. Preclinical and clinical studies have shown that liposomes and SLNs have great potential for improving cognitive function, lowering the amount of amyloid-beta (Aβ) plaques, and reducing neuroinflammation. Nonetheless, obstacles persist regarding scalability, enduring stability, and regulatory endorsement for extensive clinical application. Future research ought to concentrate on enhancing multifunctional nanocarriers that integrate targeting, imaging, and combination drug delivery, while also tackling issues related to manufacturing reproducibility and biocompatibility. To sum up, lipid-based nanocarriers are a game-changing way to treat Alzheimer's disease because they connect new ideas in the lab with their use in the real world. As nanotechnology progresses, these systems offer significant potential for the advancement of more effective, personalised, and minimally invasive therapies for Alzheimer's disease, potentially transforming the treatment of neurodegenerative diseases in the future.

Acknowledgement

The authors would like to express their sincere gratitude to *Deep Science Publisher* and the editorial team of this book for their invaluable support in the final publication process and for providing the opportunity to contribute to this esteemed volume.

Conflicts of Interest

The authors declare that there are no conflicts of interest related to this work.

Funding Source

No funding was received for the preparation of this book chapter.

Author Contribution

All authors have contributed equally to the conception, preparation, and completion of this book chapter.

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