

# Exosome-Based Nanomedicine: An Innovative Strategy for Targeted Drug Delivery Across the Blood-Brain Barrier in Alzheimer's Disease

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**Abstract:** The blood-brain barrier (BBB) is a selectively permeable physiological barrier that regulates the passage of substances into the central nervous system (CNS). Even though they are critical in maintaining brain homeostasis, the BBB severely restricts drug delivery, one of the most serious obstacles in the treatment of neurodegenerative disorders such as Alzheimer's disease (AD). Small-molecule drugs, biologics, and gene therapies are impermeable across the BBB due to their restrictive properties, including tight junctions, efflux pumps, and metabolic enzymes. In an attempt to bypass this barrier, novel drug delivery systems have been designed. These are nanoparticle-based carriers, receptor-mediated transcytosis, targeted ultrasound with microbubbles, and lipid-based drugs. Exosome-based nanomedicine is highly promising since it naturally penetrates the BBB and can transport therapeutic drugs, including neuroprotective molecules, monoclonal antibodies, and RNA-based therapies. Engineered exosomes are a highly promising platform for targeted drug delivery with low systemic toxicity and high drug bioavailability. Even with promising advancements, there are still some challenges, such as bulk-scale production, purification, cargo loading efficiency, and targeting specificity. Future studies should focus on optimizing exosome engineering, enhancing delivery platforms, and conducting large-scale clinical trials to assess safety and efficacy. Through the development of such new drug delivery systems, scientists can uncover novel therapeutic potential for Alzheimer's disease and other CNS disorders, ultimately leading to improved patient outcomes.

**Keywords:** Blood-brain barrier (BBB), Alzheimer's disease (AD), Exosomes, Receptor-Mediated Transcytosis, Monoclonal Antibodies, Gene Therapy.

## 1. Introduction

Alzheimer's disease (AD) is among the most challenging neurodegenerative diseases, affecting millions of individuals worldwide. Despite a long record of research efforts, effective drugs reversing or arresting AD progression remain to be discovered. One of the principal hindrances in AD therapy is the presence of the blood-brain barrier (BBB), an extremely dynamic and selective interface that protects the central nervous system (CNS) by controlling the influx and efflux of molecules [1]. The barrier, though extremely crucial in ensuring neural homeostasis, is unique from drug agent delivery through the brain, and thus the bottleneck of the efficacy of the standard therapy. Disruption of BBB-based barriers is thus an inherent part towards new AD therapy discoveries. The BBB is made up of unique endothelial cells that are closely spaced apart by tight connections, preventing the passage of big macromolecules and hydrophilic compounds across the paracellular space [2]. BBB endothelial cells differ from peripheral capillaries in that they include complex networks of efflux transporters, including ATP-binding cassette (ABC) and P-glycoprotein (P-gp) transporters, a lack of fenestrations, and reduced pinocytosis. All of these traits prevent medications from passively diffusing into the central nervous system. While xenobiotics and waste products from metabolism are efficiently eliminated, glucose and amino acids are delivered in a specific form throughout the brain to the central nervous system. Despite being extremely important for protecting neurons, the BBB's limiting function is one of the main

obstacles to AD medication administration; thus, novel techniques that permit penetration into the central nervous system are vital [3]. Amyloid-beta (A $\beta$ ) plaques, tau neurofibrillary tangles, and persistent neuroinflammation are the most common signs of AD that cause cognitive impairment. These characteristics need to be maintained at high enough concentrations to demonstrate therapeutic efficacy, yet the BBB prevents traditional therapeutic compounds like peptides, monoclonal antibodies, and gene delivery vectors from efficiently entering the central nervous system [4]. Furthermore, these medicinal substances frequently encounter enzymatic and metabolic obstacles that impact them via BBB activity, resulting in their low bioavailability. These presented significant difficulties for the pharmacologist, and as a result, numerous substitute solutions emerged, including receptor-mediated transport, drug delivery systems based on nanoparticles, and, consequently, non-invasive methods to break down the blood-brain barrier to increase drug concentrations in the central nervous system [5]. Exosome-based nanomedicine presents a new avenue which may enable one to bypass BBB-related challenges. Exosomes, the endogenously secreted extracellular vesicles, have captured much scholarly attention that is because of their competence to cross the BBB and effectuate the targeted delivery of therapeutics to neuronal cells [6]. These vesicles are derived from multifarious cellular sources, such as neurons and glial cells, and are of paramount importance for cellular communication. Exosomes have a lipid bilayer that protects their cargo from enzymatic degradation while maintaining cargo stability in circulation [7]. The aim of using exosomes as the delivery vehicle for neuroprotective enzymes, RNA therapeutics, small molecules, and monoclonal antibodies in AD is to enhance their neuronal delivery. It is the overriding premise of this review that the BBB is such a concept and therefore a bottleneck in the treatment of AD, tracing an evolution of approaches centred on maximized delivery in the CNS, with that of exosome-based drug delivery systems delimiting here. Approaches to characterization and development will prove very helpful in overcoming BBB-restricted difficulties for drug delivery [8].

## **2. The Blood-Brain Barrier: A Major Obstacle in Alzheimer's Disease Therapy**

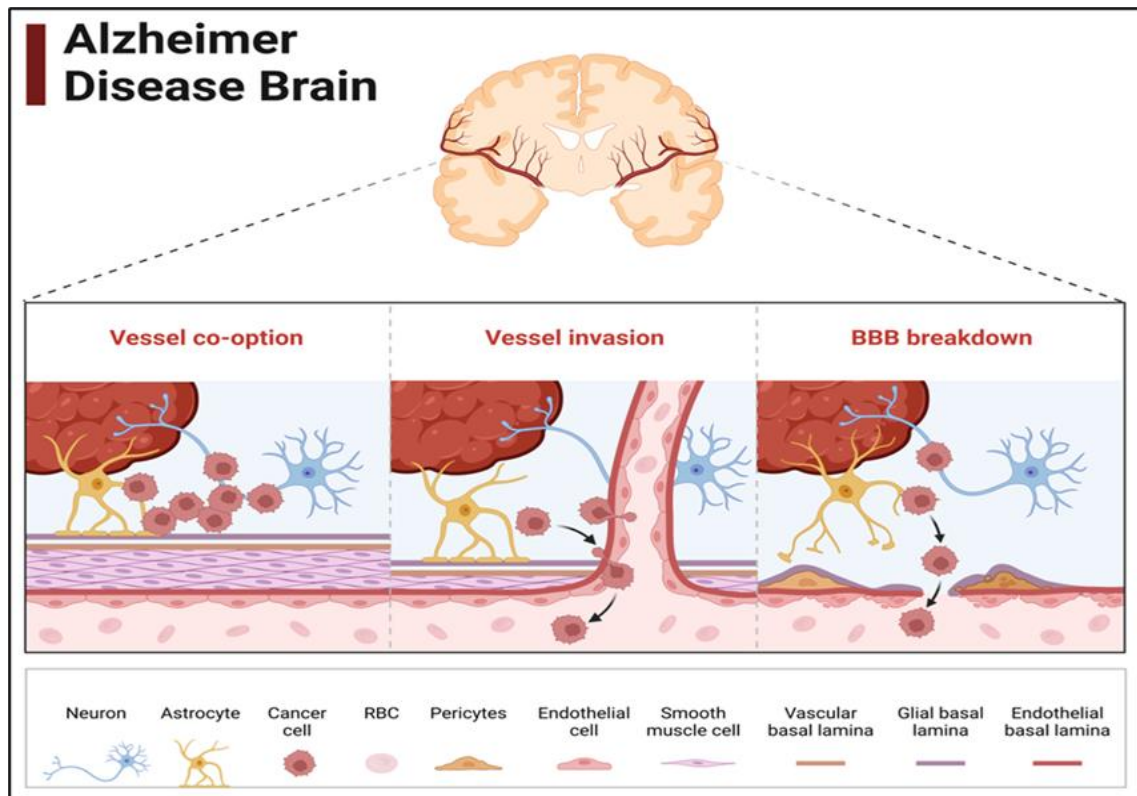
The blood-brain barrier (BBB) serves as a selective and dynamic interface essential for maintaining CNS homeostasis. This barrier consists of specialized endothelial cells connected by tight junctions, which prevent the unrestricted passage of substances from the bloodstream into the brain. The endothelial cells that constitute the capillaries in the brain lack openings known as fenestrations and exhibit minimal levels of pinocytotic vesicles. This significantly reduces passive diffusion [9]. Moreover, pericytes and the astrocytic end-feet surrounding endothelial cells play a vital role in regulating the permeability of the BBB, thus nurturing an environment that is fundamental for optimal neuronal function. The BBB selectively allows essential nutrients such as glucose and amino acids to enter the brain through specialized transport mechanisms, while also facilitating the removal of metabolic waste products and neurotoxins through active efflux processes [10]. **Figure 1** depicts the development of AD within the brain, emphasizing how vascular disruptions lead to neurodegeneration.

The upper part showcases a schematic representation of the brain with highlighted affected areas. The lower section delineates three stages: vessel co-option, vessel invasion, and breakdown of the BBB. During vessel co-option, cancer cells attach themselves to existing blood vessels without initially disrupting the BBB [11]. At this stage, neurons, astrocytes, endothelial cells, and pericytes maintain their structural integrity fairly well. As progression leads to vessel invasion, cancer cells start infiltrating blood vessel walls, which destabilizes both endothelial cells and pericytes, resulting in vascular dysfunction. Ultimately, BBB breakdown occurs in this final phase, where leakage from blood vessels happens alongside inflammation and heightened permeability that permits harmful substances into the brain. This process can cause neuronal injury, contribute to cognitive decline [12].

## **3. Exosome-Based Nanomedicine: A Novel Approach**

Exosome-based nanomedicine is emerging as a beneficial strategy in the treatment of AD as a result of its targeted capabilities toward delivering therapeutic agents, neuroprotection, and modulation of neuroinflammation [13]. They are nano-sized extracellular vesicles (30-150 nm in diameter) released from almost all cell types, including neurons, glial cells, and stem cells. Exosomes are involved in intercellular communication by transferring a variety of bioactive molecules, such as proteins, lipids, and nucleic acids, which may modulate the physiology and pathology of the targeted cells [14]. Exosomes are characterized by a lipid bilayer membrane that contributes to stability in the extracellular environment and protects against enzymatic degradation. The ability to pass through the

BBB makes exosomes especially interesting in the delivery of drugs in neurodegenerative diseases such as AD. The biogenesis of exosomes takes place through the endosomal pathway, where the inward budding of endosomal membranes results in the formation of multivesicular bodies (MVBs) [15]. Such MVBs either fuse with lysosomes for degradation or with plasma membranes to dock and release exosomes in the extracellular space. After release, exosomes can interact with target cells either through surface receptor binding, membrane fusion, or endocytosis, by which they transfer molecular cargo [16]. In AD, exosomes have arisen in highlighting both pathological and therapeutic roles, as they may mediate the spread of neurotoxic proteins like A $\beta$  and tau, which contribute to progressive disease. They also have neuroprotective properties, as they may deliver neurotrophic factors, antioxidants, and anti-inflammatory molecules that sustain neuronal survival and lessen oxidative stress [17].



**Figure 1:** Vascular Disruption and Neurodegeneration in Alzheimer’s Disease.

Among the future applications of exosomes in AD therapy, the possibility of administering drugs using exosomes opens a new avenue of promise. The attempts to find pharmaceutical remedies for this dreadful disease have not been wholly efficient owing to drug penetration barriers, poor bioavailability, and off-target effects [18]. Delivery of therapeutic drugs by exosomes provides a solution to these limitations due to their natural ability to cross the BBB and deliver the therapeutic agent with high specificity. Engineered exosomes can be loaded with small molecules, peptides, RNA-based therapeutics (siRNA, miRNA, mRNA), and CRISPR/Cas9 components to target disease-associated pathways in AD [19]. For instance, exosomes loaded with siRNA targeting BACE1, a key enzyme in A $\beta$  production, showed diminutions in amyloid pathology in preclinical models. Moreover, exosomes can also be functionalized with targeting ligands (probably peptides or antibodies) to further boost selectivity toward desired neuronal populations or disease-associated proteins [20]. Exosome-based nanomedicine can be expected to present desirable advantages, which include their biocompatibility, low immunogenicity, and the possibility to escape rapid clearance from the immune system [21]. Many challenges include scale-up culture and the method of exosomal isolation and purification to standardize cargo loading efficiency. Nonetheless, exosome-based therapeutics hold immense promise to change the status quo in AD treatment through a singular avenue in precision medicine [22]. Continuing attention toward research and industrial application may lead to innovative treatment options targeting biochemical machinery in AD, granting an enormous wish to patients suffering from this dire neurodegenerative deterioration [23]

## 4. Engineering Exosomes for Targeted Drug Delivery

Exosomes, nanosized extracellular vesicles secreted by various cell types, have emerged as promising drug delivery vehicles for neurodegenerative diseases. Their biocompatibility, ability to cross the blood-brain barrier, and potential for selective targeting make them an ideal platform for precision medicine in AD therapy [24]. Engineering of exosomes for targeted drug delivery involves three key steps: isolation and purification, loading of therapeutic agents, and surface modification for blood-brain barrier penetration and specific targeting of AD pathology [25].

### 4.1 Isolation and Purification

The isolation and purification of the exosomes from biological fluids like blood, cerebrospinal fluid, or cell culture supernatants are the first and most critical steps for their application in drug delivery. Various methods are in use today: ultracentrifugation, density gradient centrifugation, size exclusion chromatography, and precipitation methods, among which differential ultracentrifugation (the gold standard) uses several centrifugation steps to wash away larger particles and therefore concentrates exosomes; the limits of the method are low yield and purity [26]. Size-exclusion chromatography separates exosomes by size without disrupting their structure and gives more purified exosomes than ultracentrifugation. Precipitation methods lead to rapid isolation but, based on polyethylene glycol, may result in the co-precipitation of other unwanted proteins [27]. Advanced microfluidic and immunoaffinity-based techniques improve selectivity by capturing the exosomes with certain surface markers, which include CD63, CD81, and CD9, that further increase their therapeutic potential [28]

### 4.2 Loaded with Therapeutic Agents

Following their extraction, a critical next step is to efficiently load exosomes with therapeutic chemicals to treat AD. Many techniques, like as transfection, sonication, electroporation, and passive diffusion, can be used to encapsulate drugs. For exosomes to diffuse into the vesicles during the passive loading phase, they need to be treated with hydrophobic small molecules; nonetheless, this method has some efficiency limitations [29]. However, electroporation produces temporary pores in the exosome membrane that allow nucleic acids such as siRNA, miRNA, or mRNA to enter. Another option is sonication, which raises drug loading rates by momentarily dissolving membranes [30]. Furthermore, exosomes can be produced at the cellular level by introducing plasmids encoding therapeutic proteins or RNAs into donor cells. Before extraction, this technique guarantees that the components are endogenously packed into exosomes. Remarkably, lipophilic drugs with neuroprotective properties, such as curcumin and resveratrol, have been effectively loaded into exosomes meant to treat AD [31].

### 4.3 Precision Targeting and Blood-Brain Barrier (BBB) Penetration

Exosome surface modifications are conducive to specificity in AD pathology targeting and the attainment of efficient transport into the brain via the BBB. This has led to the need to develop ways to enhance exosome transport mechanisms since considerable hindrances are still presented by the BBB in the delivery of therapeutics in the CNS [32]. A competitive approach to modifying the surface of exosomes is ligand conjugation, which utilizes peptides or antibodies specific for BBB receptors-examples include those that target the transferrin receptor and the low-density lipoprotein receptor (LDLR) [33]. The RVG peptide of the rabies virus glycoprotein has also been shown to have a strong affinity for neuronal cells and aid in functionalizing exosomes to enhance their delivery into different regions of the brain. In addition, engineering efforts allow these bio-carriers to incorporate peptides or antibodies that target antigens associated with AD toxicity, such as A $\beta$  antibodies or tau-specific ligands, thereby enabling localization of delivery to neurons affected by dementia disease [34]. Stimuli-responsive coatings also allow for unabated control over the release mechanism sensitive to microenvironmental cues associated with symptoms of Alzheimer's disease, whereas PEGylation and other chemical modifications are used for stability during circulation [35]. **Table 1** illustrates the gradual neurodegenerative disorder featuring amyloid-beta plaque deposition, tau protein aggregation, oxidative stress, and neuroinflammation. Several natural and synthetic compounds have been tested for their neuroprotective roles in targeting various pathological mechanisms of AD. This table summarizes the mechanisms of action, areas of targeting, and advantages of selected drugs that may help in slowing the progression of disease and improving cognitive function.

**Table 1: Neuroprotective Drugs Targeting Alzheimer's Disease.**

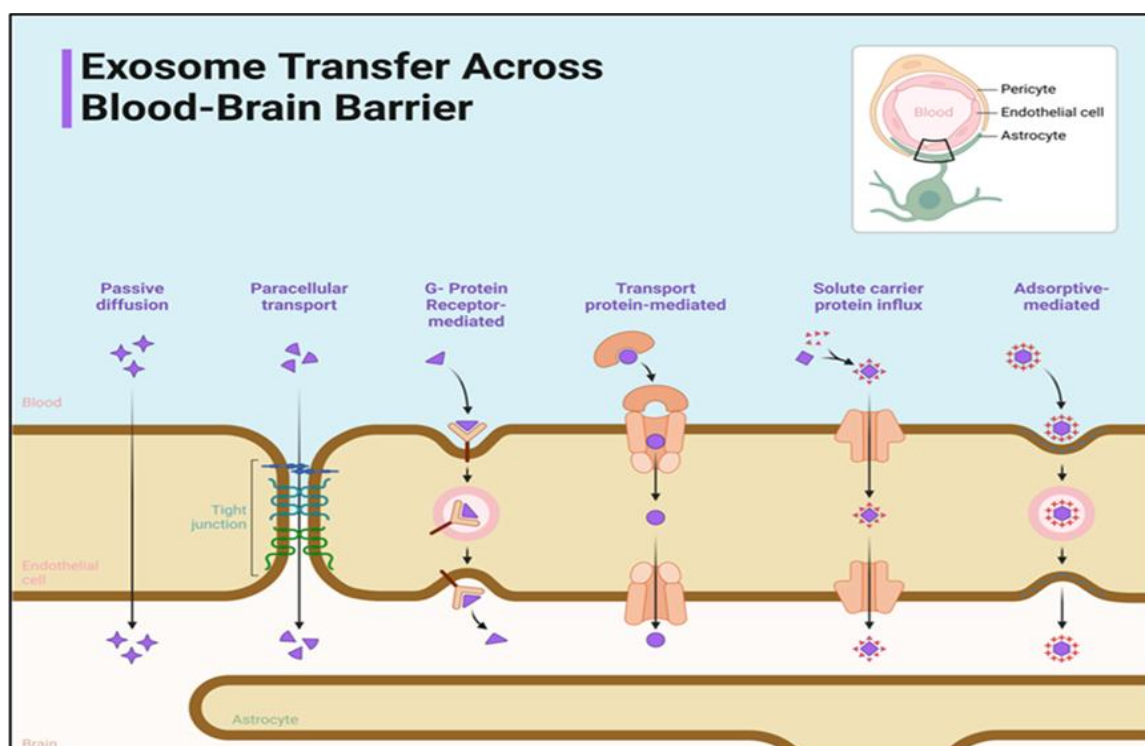
S/n	Drug	Mechanism of Action	Targeting Area	Advantages	Ref.
1	Curcumin	Anti-inflammatory, anti-amyloid	Amyloid-beta plaques	Reduces A $\beta$ aggregation, neuroprotection	[36]
2	Doxycycline	Inhibits A $\beta$ fibril formation	Amyloid-beta fibrils	Reduces neurotoxicity and inflammation	[37]
3	Resveratrol	Activates SIRT1, antioxidant	Amyloid-beta, Tau proteins	Enhances synaptic function, reduces A $\beta$	[38]
4	Epigallocatechin gallate (EGCG)	Inhibits A $\beta$ aggregation, an antioxidant	Amyloid-beta, Tau proteins	Protects neurons, enhances cognition	[39]
5	Rivastigmine	Acetylcholinesterase inhibitor	Cholinergic neurons	Improves memory and cognitive function	[40]
6	Galantamine	Acetylcholinesterase inhibitor, neuroprotective	Cholinergic synapses	Enhances neurotransmission, reduces A $\beta$	[41]
7	Donepezil	Acetylcholinesterase inhibitor	Cholinergic synapses	Slows disease progression, improves cognition	[42]
8	Memantine	NMDA receptor antagonist	Glutamatergic system	Prevents excitotoxicity, slows cognitive decline	[43]
9	Berberine	Reduces neuroinflammation, A $\beta$ clearance	Amyloid-beta plaques	Improves memory, reduces oxidative stress	[44]
10	Edaravone	Free radical scavenger, neuroprotection	Oxidative stress, Amyloid-beta	Reduces neuronal damage, protects cognition	[45]
11	Quercetin	Antioxidant, anti-inflammatory	Amyloid-beta, Tau proteins	Reduces oxidative stress, improves synaptic plasticity	[46]
12	Apigenin	Anti-inflammatory, neurogenic	Neuroinflammation, Amyloid-beta	Promotes neurogenesis, protects neurons	[47]
13	Baicalein	Antioxidant, anti-amyloid	Amyloid-beta, Tau proteins	Inhibits plaque formation, reduces oxidative stress	[48]
14	Huperzine A	Acetylcholinesterase inhibitor	Cholinergic neurons	Enhances memory, reduces neurotoxicity	[49]
15	Naringenin	Antioxidant, neuroprotective	Amyloid-beta, oxidative stress	Improves synaptic function, reduces inflammation	[50]
16	Fisetin	Neuroprotective, anti-inflammatory	Amyloid-beta, oxidative stress	Enhances cognition, protects neurons	[51]
17	Ginsenoside Rg1	Promotes neurogenesis, anti-inflammatory	Synaptic function, oxidative stress	Enhances cognition, reduces neuronal apoptosis	[52]
18	Caffeic Acid	Antioxidant, neuroprotective	Amyloid-beta, oxidative stress	Improves memory, reduces neurotoxicity	[53]
19	Luteolin	Inhibits neuroinflammation, reduces Tau phosphorylation	Amyloid-beta, microglial activation	Protects neurons, enhances cognitive function	[54]

20	Piperine	Enhances drug bioavailability, neuroprotective	Neuroinflammation, oxidative stress	Increases bioavailability of drugs, reduces neurodegeneration	[55]
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The compounds described are chemically diverse agents intended to act against AD via different mechanisms: they could act as acetylcholinesterase inhibitors, have antioxidant properties, or reduce A $\beta$  aggregation. Those emerging from preclinical and clinical studies display various efficacies and need confirmation and efforts towards optimizing bioavailability and long-term safety in patients. The treatment programs would integrate these compounds with multi-targeted approaches to alleviate neurodegeneration toward the development of AD

## 5. Mechanisms of Exosome Transport Across the BBB

Exosomes are derived from endosomal compartments and are small extracellular vesicles that are important for cellular communication by allowing diverse biomolecules, proteins, lipids, and nucleic acids to move from one cell to another. These are critical in the AD milieu since they allow toxic A $\beta$  peptides and tau proteins to cross the BBB, thereby hastening disease progression [56]. The BBB is a highly selective endothelial barrier that regulates the transference of molecules between the circulatory system and the CNS. Understanding exosome crossing of the BBB is fundamental to both tracking disease progression and designing modality profiles for therapy. Important mechanisms involved include endocytosis, transcytosis pathways, coupling of surface ligands in BBB transport, and different interactions between exosomes and the BBB in connection with AD pathogenesis [57]. **Figure 2** illustrates the various pathways by which exosomes cross the BBB, indicating their prospective role in drug delivery in Alzheimer's disease. Such comprehension of these mechanisms is important for developing targeted drug delivery approaches toward tackling neurodegeneration.



**Figure 2:** Mechanisms of Exosome Transport Across the Blood-Brain Barrier in Alzheimer's Disease.

The blood-brain barrier is a selective conduit that restricts most drugs from entering the brain, making exosome-based drug delivery a promising mechanism for AD therapies.

## 6. Release Mechanisms from Microsponges

### 6.1 Lipophilic Diffusion

Lipophilic diffusion is the passive translocation of lipid-soluble molecules through the blood-brain barrier by diffusion into the endothelial cell membrane. This route is pertinent for small, nonpolar molecules, such as oxygen and carbon dioxide and some lipophilic drugs [58].

### **6.2. Paracellular Transport**

Paracellular transport entails the passage of small molecules across the tight junctions between the endothelial cells. However, due to extremely tight junctions, this pathway is limited to only a few select substances, such as water and small ions [59].

### **6.3 Receptor-Mediated Transport**

Receptor-mediated transport occurs when exosomes or molecules bind to specific receptors on endothelial cells, triggering endocytosis. This mechanism is essential for transporting large biomolecules like insulin and transferrin, which require receptor interaction for uptake [60].

### **6.4 Transport Protein Mediated**

Transport protein-mediated mechanisms involve specific protein channels that facilitate the passage of exosomes and other molecules across the BBB. These proteins regulate the transport of essential nutrients and signaling molecules [61].

### **6.5 Solute Carrier Protein Influx**

Solute carrier protein influx is another critical transport method, where solute carrier (SLC) proteins help move nutrients, amino acids, and small molecules into the brain. This pathway is vital for maintaining neuronal function [62].

### **6.6 Adsorptive-Mediated Transcytosis**

Adsorptive-mediated transcytosis is mediated by the electrostatic interaction between the positively charged exosomes and negatively charged endothelium. This interaction fosters cell uptake and transport across the BBB, promoting drug delivery and application in therapy [63]. In AD, exosomes may serve as carriers for therapeutics directed against amyloid-beta plaques and tau tangles. Delivery via receptor-mediated and adsorptive-mediated transport may be particularly efficacious for targeted drug delivery. Exosome-based approaches may also bear promise in the reduction of neuroinflammation, stimulation of neural repair, and diagnosis via biomarker delivery [64]. Moreover, a better understanding of the transport mechanisms will enable the development of novel drug formulations to improve treatment efficacies and to slow or even reverse the development of AD [65].

## **7. Therapeutic Applications of Exosome-Based Nanomedicine in AD**

Conventional therapeutics face a host of challenges when trying to cross the BBB and be targeted for delivery. Based exosome nanomedicines have proven most efficacious against these challenges by introducing new therapeutic strategies for treating AD [66]. Exosomes, planished nanosized extracellular vesicles secreted by cell types encompass intrinsic targeted delivery properties and biocompatibility, alongside the ability to deliver therapeutic molecules, such as small molecules, biomolecules (siRNA, miRNA, and proteins), and anti-inflammatory agents, to pathological neurons [67].

### **7.1 Delivery of Small Molecules and Biomolecules**

One of the leading applications of exosomes in AD therapy is the delivery of small molecules and biomolecules that can target key pathological pathways. Exosomes can be engineered to carry siRNA-targeting genes that have been implicated in A $\beta$  production, such as BACE1, with consequent diminished A $\beta$  formation. Similarly, exosomes can deliver miRNAs with neuroprotective and anti-inflammatory activity, such as miR-124 and miR-146a, upon entry into the brain to promote neuronal survival and dampen inflammation [68]. Blasting proteins like BDNF and GDNF are another noteworthy exosomal delivery that serves to promote neuron

growth and repair synapses. This greatly augments neuronal resilience and initiates an active slowdown to the progression of the disease by repairing cellular homeostasis [69].

### **7.2 Potential for Anti-Amyloid and Neuroprotective Therapies**

Another promising area of exosome-based nanomedicine in AD is in anti-amyloid and neuroprotective strategies. Amyloid-beta plaques are among the prime pathological hallmarks of AD; targeting their formation and clearance is one of the major therapeutic objectives. Exosomes derived from mesenchymal stem cells (MSCs) and neural stem cells (NSCs) were found to contain enzymes such as neprilysin and insulin-degrading enzyme (IDE) that heteropolymerize A $\beta$  aggregates.

Besides, small molecules that mediate tau phosphorylation or A $\beta$  aggregation are loaded into the exosome and engage in different pathways that result in neurofibrillary tangle formation and amyloid burden [70]. The exosomes from genetically engineered cells could carry monoclonal antibodies against A $\beta$ , leading to targeted clearance from the brain through immune mechanisms. These types of neuroprotection go beyond the clearance of amyloid, as antioxidant and anti-apoptotic molecules delivered via exosomes can buffer oxidative versus neurodegeneration stress and death in AD patients [71].

### **7.3 Immunomodulation Approach to Reduce Neuroinflammation**

Exosome-based nanomedicine is a unique variety of an immunomodulatory approach to lessen neuroinflammation, a pivotal aspect in the progression of AD. Chronic neuroinflammation, arising from activated microglia and astrocytes, worsens neuronal damage and fasten the pathology of the disease [72]. Since exosomes derived from MSCs and immune cells contain anti-inflammatory cytokines, such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF- $\beta$ ), which modulate microglial activation and inhibit pro-inflammatory pathways, complementarity exists. Noteworthy miRNAs carried by exosomes, such as miR-21 and miR-146a, could inhibit the expression of inflammatory genes and curb the significant amount of pro-inflammatory cytokines; perhaps tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) [73]. Targeting anti-inflammatory pathways by reversing the neuroimmune environment will offer an excellent advantage to mitigate neuroinflammation and save neuronal loss in AD [74].

## **8. Future Perspectives and Challenges**

This points toward the prospects of exosome-based nanomedicines serving as targeted drug delivery to enhance treatment outcomes across the BBB in AD. With biocompatibility, suitable small sizes, and the potential to cross the BBB, exosomes represent a new means of a precise drug delivery system, minimizing systemic side effects. Future research will be concentrated on engineering exosomes for increased targeting, cargo-loading efficiencies, and prolonged circulation times [75]. Advances arising from biomolecular modifications, including ligand functionalization and surface engineering, will allow optimal exosome-mediated delivery of neuroprotective agents, including small molecules, RNA therapeutics, and monoclonal antibodies. Integration with AI and nanotechnology may improve exosome tracking and therapeutic outcomes further [76]. The challenge of clinical translation is large since this requires strict standardization, industrial-scale manufacture, and approval by regulatory bodies. However, further progress can pave the way for exosome-based nanomedicine to overhaul AD treatment by making way for efficient, non-invasive, and personalized therapeutic interventions for neurodegenerative disorders [77].

## **9. Conclusion**

One of the most important obstacles to creating efficient therapies for AD is overcoming the difficulties presented by the BBB. Drug distribution to the brain is severely limited by the selective permeability of the blood-brain barrier, which is maintained by tight junctions, efflux transporters, and metabolic enzymes. Emerging techniques provide encouraging alternatives to conventional pharmacological methods, which have trouble reaching therapeutic concentrations in the central nervous system. Focused ultrasound, receptor-mediated transcytosis, prodrug modifications, and nanoparticle-based drug carriers have all shown promise in avoiding the blood-brain barrier and improving drug bioavailability. Additionally, developments in gene therapy and biological therapies, including monoclonal antibodies, are being investigated to target tau tangles and amyloid plaques. Even with these advancements, it's still difficult to improve these delivery systems for safety, effectiveness, and low side effects. The development of Alzheimer's treatments will depend on ongoing

studies into BBB dynamics and innovative drug transport methods, which should lead to more potent treatments for this debilitating neurological disease.

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### **Conflict of interest**

It was declared to be none.

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