

REVIEW ARTICLE

Recent Advances in Drug Delivery Systems for Targeting the Blood-Brain Barrier

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Abstract: The blood-brain barrier (BBB) poses a significant challenge in treating central nervous system (CNS) disorders, limiting the efficacy of many potential therapeutic agents. Overcoming this barrier is crucial for enhancing drug delivery to the brain. Recent advancements in drug delivery systems have shown promising results in addressing this challenge. Both invasive and non-invasive strategies, including chemical modifications, colloidal systems, and biological techniques, have been developed to improve brain drug targeting. Nanoparticle-based delivery systems, such as liposomes, polymeric micelles, and dendrimers, demonstrate enhanced drug penetration and targeting capabilities. Advanced techniques like focused ultrasound-mediated BBB disruption and convection-enhanced delivery offer novel approaches to circumvent the BBB. Additionally, intranasal delivery and cell-penetrating peptides present alternative routes for CNS drug administration. These innovative approaches span a wide range of applications, from neurodegenerative diseases to brain tumors, potentially revolutionizing treatment strategies for various CNS disorders. The ongoing research and emerging trends in brain-targeted drug delivery systems provide a foundation for developing more effective therapies, offering hope for improved outcomes in patients with CNS diseases.

Keywords: Blood-Brain Barrier; Drug Delivery Systems; Nanoparticles; Focused Ultrasound; Convection-Enhanced Delivery.

1. Introduction

The central nervous system (CNS) is a complex and vital component of the human body, responsible for controlling and coordinating various physiological functions. However, treating CNS disorders remains a significant challenge in modern medicine, largely due to the presence of the blood-brain barrier (BBB) (shown in Figure 1). This highly selective barrier plays a crucial role in maintaining brain homeostasis but also presents a formidable obstacle for drug delivery to the CNS [1].

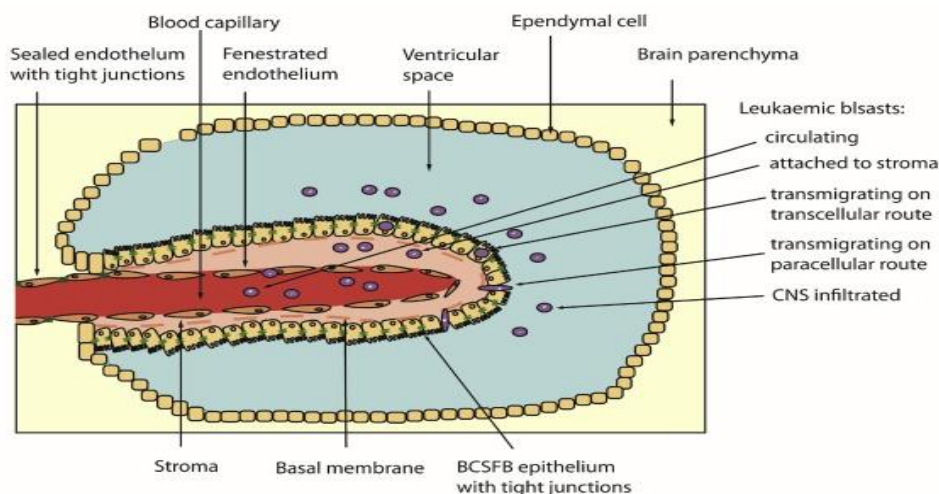


Figure 1. Blood Brain Barrier

The BBB is a specialized structure composed of brain endothelial cells, pericytes, and astrocyte end-feet, collectively forming the neurovascular unit [2]. The endothelial cells of the BBB are characterized by tight junctions, which limit paracellular transport and create a highly restrictive barrier [3]. This unique architecture allows the BBB to perform several critical functions:

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- Regulation of ion balance: The BBB maintains the ionic composition of the brain interstitial fluid, which is essential for proper neuronal function [4].
- Protection from toxins: It prevents the entry of potentially harmful substances, including pathogens and toxins, from the bloodstream into the brain [5].
- Nutrient transport: The BBB selectively allows the passage of essential nutrients through specific transport systems [6].
- Waste removal: It facilitates the efflux of metabolic waste products from the brain to the bloodstream [7].

The BBB's selective permeability is achieved through various transport mechanisms (shown in Figure 2), including:

- Passive diffusion: Limited to small, lipophilic molecules.
- Carrier-mediated transport: For specific nutrients like glucose and amino acids.
- Receptor-mediated transcytosis: For larger molecules such as insulin and transferrin.
- Adsorptive-mediated transcytosis: For positively charged molecules [8].

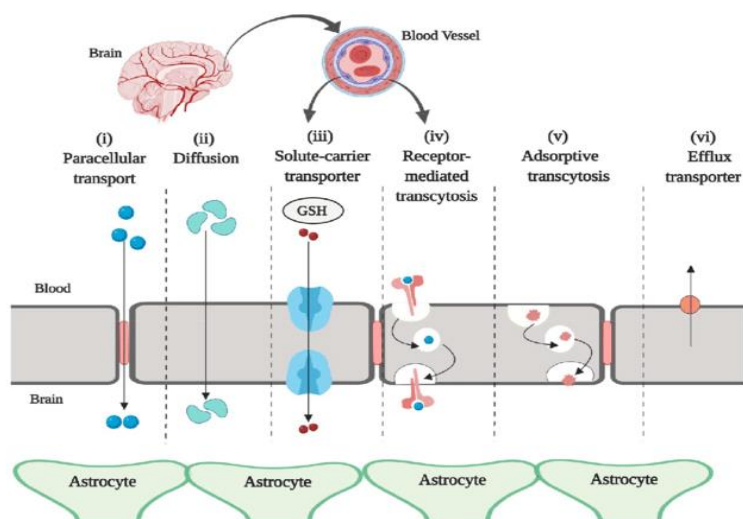


Figure 2. Transport across Blood Brain Barrier

The BBB's protective nature, while essential for normal brain function, poses significant challenges for drug delivery to the CNS. These challenges include:

- Limited permeability: Approximately 98% of small molecule drugs and nearly 100% of large molecule therapeutics are unable to cross the BBB [9]. This severely restricts the pool of potential CNS-active compounds.
- Efflux transporters: The presence of efflux pumps, such as P-glycoprotein, actively removes many drugs that do manage to cross the BBB, further reducing their effectiveness [10].
- Enzymatic barrier: Enzymes present in the BBB can metabolize drugs before they reach their target sites in the brain [11].
- Tight junctions: The presence of tight junctions between endothelial cells limits paracellular transport, making it difficult for hydrophilic drugs to pass through [12].
- Lack of lymphatic drainage: The absence of a conventional lymphatic system in the brain complicates the clearance of drugs and metabolites [13].
- Heterogeneity of CNS disorders: Different CNS diseases may require varying degrees of BBB penetration, necessitating tailored drug delivery strategies [14].
- Potential neurotoxicity: Some methods used to increase BBB permeability may lead to unwanted neurotoxic effects [15].

These challenges have spurred extensive research into novel drug delivery systems and strategies to overcome the BBB. Recent advancements in nanotechnology, polymer science, and molecular biology have opened up new avenues for CNS drug delivery, offering hope for more effective treatments of neurological and psychiatric disorders [16].

2. Barriers to CNS Drug Delivery

The central nervous system (CNS) is protected by a complex network of barriers that regulate the movement of substances between the blood and the brain or cerebrospinal fluid (CSF). These barriers play a crucial role in maintaining the homeostasis of the CNS microenvironment but also present significant challenges for drug delivery. The two primary barriers that impede the transport of therapeutic agents to the CNS are the blood-brain barrier (BBB) and the blood-cerebrospinal fluid barrier (BCSFB) [17].

2.1. Blood-Brain Barrier (BBB)

The blood-brain barrier is the most extensive and formidable obstacle to CNS drug delivery. It is a highly specialized structure composed of brain endothelial cells connected by tight junctions, forming a continuous, nearly impermeable barrier between the bloodstream and the brain parenchyma. The BBB's unique properties are maintained by the neurovascular unit, which includes pericytes, astrocytes, and neurons that interact with the endothelial cells [18].

The BBB's primary function is to protect the brain from potentially harmful substances while allowing the selective transport of essential nutrients. This selectivity is achieved through a combination of physical, transport, and metabolic barriers. The tight junctions between endothelial cells restrict paracellular diffusion, forcing most molecules to pass through the cells themselves. This transcellular route is highly regulated by various transport systems, including carrier-mediated transporters, receptor-mediated transcytosis, and ATP-binding cassette (ABC) efflux transporters [19].

The presence of efflux transporters, such as P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP), further complicates drug delivery by actively pumping many therapeutic compounds back into the bloodstream. This mechanism not only limits the brain penetration of numerous drugs but also contributes to the development of drug resistance in CNS disorders [20].

2.2. Blood-Cerebrospinal Fluid Barrier (BCSFB)

While the BBB is the primary interface between the blood and brain, the blood-cerebrospinal fluid barrier also plays a significant role in regulating the entry of substances into the CNS. The BCSFB is located at the choroid plexus, a highly vascularized structure within the brain ventricles responsible for producing cerebrospinal fluid [21].

Unlike the BBB, the capillaries in the choroid plexus are fenestrated and more permeable. However, the epithelial cells of the choroid plexus are connected by tight junctions, forming the actual barrier. These epithelial cells are also equipped with various transporters that regulate the exchange of substances between the blood and CSF [22].

The BCSFB's role in drug delivery is complex. While it may offer an alternative route for some drugs to enter the CNS, the rapid turnover of CSF and the limited surface area of the choroid plexus compared to the BBB make it a less efficient pathway for most therapeutic agents. Nevertheless, understanding and potentially exploiting the BCSFB remains an important area of research in CNS drug delivery [23].

2.3. Factors Affecting Drug Transport Across the BBB

Several factors influence a drug's ability to cross the BBB and reach its target within the CNS. Molecular size is a critical determinant, with smaller molecules generally having a better chance of penetrating the barrier. Lipophilicity also plays a crucial role, as lipid-soluble compounds can more easily diffuse through the lipid bilayer of endothelial cells. However, extreme lipophilicity can lead to nonspecific binding and reduced effectiveness [24].

The charge and polarity of a molecule significantly affect its BBB permeability. Neutral and less polar molecules tend to cross more easily than charged or highly polar compounds. Additionally, the presence of hydrogen bond donors and acceptors can impact a drug's ability to traverse the BBB, with fewer hydrogen bonds generally favoring penetration [25].

Plasma protein binding is another important factor. Highly protein-bound drugs have limited free fraction available to cross the BBB. Furthermore, the affinity of a drug for efflux transporters like P-gp can dramatically reduce its brain penetration, even if it possesses favorable physicochemical properties [26].

The physiological state of the BBB itself can also influence drug transport. Various pathological conditions, such as inflammation, tumors, or neurodegenerative diseases, can alter BBB integrity and permeability. While this may sometimes enhance drug delivery, it can also lead to unpredictable pharmacokinetics and potential toxicity [27].

3. CNS Disorders and Drug Delivery Challenges

Central nervous system disorders encompass a wide range of conditions that affect the brain and spinal cord. These disorders present unique challenges for drug delivery, primarily due to the protective nature of the blood-brain barrier (BBB) and the complex pathophysiology of each condition. Understanding the specific hurdles associated with different CNS disorders is crucial for developing effective therapeutic strategies [28].

3.1. Neurodegenerative Diseases

Neurodegenerative diseases, such as Alzheimer's disease (AD), Parkinson's disease (PD), and Huntington's disease (HD), are characterized by the progressive loss of neuronal structure and function. These conditions pose significant challenges for drug delivery due to their chronic nature and the need for long-term treatment [29].

In Alzheimer's disease, the accumulation of beta-amyloid plaques and neurofibrillary tangles leads to neuronal death and cognitive decline. Drug delivery challenges in AD include the need to target multiple pathological processes simultaneously and to maintain therapeutic concentrations of drugs in the brain over extended periods. Moreover, the BBB undergoes changes during AD progression, potentially altering drug permeability and distribution [30].

Parkinson's disease, characterized by the loss of dopaminergic neurons in the substantia nigra, presents unique drug delivery challenges. While L-DOPA remains the gold standard treatment, its efficacy diminishes over time, and motor complications develop. Delivering neuroprotective agents or growth factors directly to the affected brain regions could potentially slow disease progression but requires overcoming the BBB and achieving targeted distribution [31].

For Huntington's disease, an inherited disorder caused by a defective gene, gene therapy approaches hold promise. However, delivering large nucleic acid molecules or viral vectors across the BBB remains a significant obstacle. Additionally, achieving widespread distribution of therapeutic agents throughout the brain is crucial for addressing the global nature of HD pathology [32].

3.2. Brain Tumors

Brain tumors, both primary and metastatic, present distinct challenges for drug delivery. The BBB is often compromised in and around tumor sites, leading to the formation of the blood-tumor barrier (BTB). While the BTB is generally more permeable than the normal BBB, it is heterogeneous and unpredictable, complicating drug delivery strategies [33].

Glioblastoma multiforme (GBM), the most aggressive primary brain tumor, is particularly challenging to treat due to its infiltrative nature and rapid growth. The BBB/BTB limits the penetration of many chemotherapeutic agents, and the high interstitial fluid pressure within tumors can further impede drug distribution. Developing strategies to enhance drug penetration and retention in the tumor microenvironment is crucial for improving treatment outcomes [34].

For brain metastases, which are more common than primary brain tumors, the challenge lies in delivering therapeutic agents across both the BBB and the BTB. The heterogeneity of metastatic lesions, combined with the potential for multiple tumor sites, necessitates drug delivery approaches that can achieve widespread distribution and penetration [35].

3.3. Other CNS Disorders

Numerous other CNS disorders present unique drug delivery challenges. Epilepsy, a chronic neurological disorder characterized by recurrent seizures, requires maintaining therapeutic drug levels in the brain while minimizing systemic side effects. Achieving targeted delivery to specific epileptogenic foci could potentially improve treatment efficacy and reduce adverse effects [36].

Multiple sclerosis (MS), an autoimmune disorder affecting the myelin sheath of neurons, presents challenges related to both BBB crossing and targeting the immune components of the disease. Delivering immunomodulatory agents or neuroprotective compounds to the CNS while managing the systemic immune response requires sophisticated drug delivery strategies [37].

Psychiatric disorders, such as schizophrenia and depression, also face drug delivery hurdles. While many psychotropic medications can cross the BBB to some extent, achieving optimal brain concentrations while minimizing peripheral side effects remains a challenge. Furthermore, the complex and often poorly understood pathophysiology of these disorders complicates the development of targeted therapies [38].

Stroke and traumatic brain injury (TBI) present acute challenges for drug delivery. The time-sensitive nature of these conditions requires rapid delivery of neuroprotective agents to the affected brain regions. However, the BBB disruption that occurs in these conditions can be dynamic and unpredictable, affecting drug distribution and efficacy [39, 40]

4. Approaches for Brain-Targeted Drug Delivery

The challenges presented by the blood-brain barrier (BBB) have led to the development of various innovative approaches for brain-targeted drug delivery. These strategies can be broadly categorized into non-invasive and invasive approaches, each with its own set of advantages and limitations.

4.1. Non-Invasive Approaches

Non-invasive approaches aim to deliver drugs to the brain without physically breaching the BBB or requiring surgical intervention. These methods are generally preferred due to their lower risk profile and potential for repeated administration.

4.1.1. Chemical Techniques

Chemical techniques involve modifying the drug molecule itself to enhance its ability to cross the BBB. This approach leverages the physicochemical properties that favor BBB penetration, such as lipophilicity and molecular size.

Prodrugs: Prodrugs are bioreversible derivatives of drug molecules that undergo enzymatic or chemical transformation in the body to release the active parent drug. In the context of CNS drug delivery, prodrugs are designed to be more lipophilic, allowing easier passage through the BBB. Once in the brain, they are converted back to the active form. For example, L-DOPA, used in the treatment of Parkinson's disease, is a prodrug of dopamine that can cross the BBB more effectively than dopamine itself [41].

4.1.2. Colloidal Techniques

Colloidal drug delivery systems utilize nano-sized carriers to encapsulate drugs and facilitate their transport across the BBB. These systems can be engineered to improve drug stability, increase circulation time, and enhance BBB penetration.

Nanoparticles: Nanoparticles are submicron-sized carriers made from various materials such as polymers, lipids, or metals. They can be designed to encapsulate drugs and cross the BBB through mechanisms like receptor-mediated transcytosis. Surface modification of nanoparticles with ligands that target specific BBB transporters or receptors can further enhance their brain delivery capabilities. For instance, transferrin-functionalized nanoparticles have shown improved brain uptake due to the high expression of transferrin receptors on brain endothelial cells [42].

Liposomes: Liposomes are spherical vesicles composed of one or more phospholipid bilayers. Their amphiphilic nature allows them to encapsulate both hydrophilic and hydrophobic drugs. Like nanoparticles, liposomes can be surface-modified to target specific BBB transport systems. PEGylated liposomes have demonstrated increased circulation time and improved BBB penetration. Targeted liposomes, such as those functionalized with the OX26 antibody against the transferrin receptor, have shown promise in delivering drugs to the brain [43].

4.1.3. Biological Methods

Biological methods exploit natural BBB transport systems to facilitate drug delivery. These approaches include the use of cell-penetrating peptides, molecular Trojan horses, and exosomes. Cell-penetrating peptides, such as TAT from HIV, can be conjugated to drugs to enhance their BBB penetration. Molecular Trojan horses involve linking drugs to endogenous molecules that undergo receptor-mediated transcytosis across the BBB, such as insulin or transferrin. Exosomes, naturally occurring extracellular vesicles, are being explored as potential drug carriers due to their ability to cross biological barriers [44].

4.2. Invasive Approaches

Invasive approaches involve direct delivery of drugs to the brain, bypassing the BBB. While these methods can achieve higher drug concentrations in the CNS, they carry greater risks and are generally reserved for conditions where non-invasive approaches are ineffective.

4.2.1. Intracerebroventricular (ICV) Infusion

ICV infusion involves the direct administration of drugs into the cerebrospinal fluid (CSF) of the brain ventricles. This method allows for widespread distribution of the drug throughout the CNS but requires surgical implantation of a catheter and carries risks of infection and mechanical trauma. ICV infusion has been used successfully for the delivery of chemotherapeutics and enzymes for lysosomal storage disorders [45].

4.2.2. Intracerebral Implants

Intracerebral implants are drug-loaded devices surgically placed directly into the brain parenchyma. These implants can provide sustained, localized drug release over extended periods. Gliadel wafers, biodegradable polymeric implants loaded with carmustine, are used clinically for the treatment of glioblastoma multiforme. While effective for localized delivery, this approach is limited by the need for invasive surgery and the restricted drug distribution [46].

4.2.3. Disruption of the BBB

Techniques that temporarily disrupt the BBB have been developed to enhance drug delivery to the brain.

Osmotic Disruption: Osmotic disruption involves the intra-arterial infusion of hyperosmolar solutions, typically mannitol, to temporarily open the BBB tight junctions. This technique has been used clinically to enhance the delivery of chemotherapeutics to brain tumors. However, it is non-specific and can potentially allow the entry of harmful substances into the brain [47].

Focused Ultrasound BBB Disruption: Focused ultrasound (FUS) combined with microbubbles is an emerging technique for localized, transient BBB disruption. This method uses low-intensity focused ultrasound to oscillate intravenously administered microbubbles, creating mechanical stress on the BBB endothelium and temporarily increasing its permeability. FUS offers the advantage of being non-invasive and spatially precise. It has shown promise in preclinical studies for enhancing the delivery of various therapeutic agents, including chemotherapeutics, antibodies, and gene therapy vectors [48].

5. Recent Advances in Brain-Targeted Drug Delivery

The field of brain-targeted drug delivery has seen significant advancements in recent years, with novel approaches and technologies emerging to overcome the challenges posed by the blood-brain barrier (BBB). These innovations aim to enhance drug delivery efficiency, improve targeting specificity, and reduce systemic side effects.

5.1. Micelles

Polymeric micelles have gained considerable attention as promising nanocarriers for CNS drug delivery. These self-assembling structures consist of amphiphilic block copolymers that form a hydrophobic core capable of encapsulating poorly water-soluble drugs, surrounded by a hydrophilic shell. The small size of micelles (typically 10-100 nm) and their ability to be functionalized make them particularly suitable for crossing the BBB [49].

Recent advancements in micellar technology include the development of stimuli-responsive micelles that can release their payload in response to specific environmental cues such as pH, temperature, or enzymatic activity. For instance, pH-sensitive micelles have been designed to exploit the slightly acidic microenvironment of brain tumors, allowing for targeted drug release. Another innovative approach involves the use of dual-functional micelles that combine drug delivery with diagnostic capabilities, known as theranostics [50].

Researchers have also explored the potential of mixed micelles, which incorporate multiple types of polymers to optimize drug loading, stability, and BBB penetration. For example, a recent study demonstrated enhanced brain delivery of the anti-epileptic drug carbamazepine using mixed micelles composed of Pluronic P123 and F127 [51].

5.2. Dendrimers

Dendrimers are highly branched, star-shaped polymeric nanostructures with a well-defined architecture and narrow size distribution. Their unique structure allows for high drug loading capacity and the ability to carry multiple types of cargo simultaneously, making them versatile carriers for CNS drug delivery [52].

Recent advances in dendrimer technology for brain-targeted delivery include the development of bio-reducible dendrimers that can release their payload in response to the intracellular redox environment. This approach enhances the specificity of drug release and reduces potential toxicity. Another innovative strategy involves the use of dendrimers as a scaffold for the attachment of multiple targeting ligands, creating multivalent constructs that can engage with several BBB receptors simultaneously, thereby enhancing transcytosis [53]. Peptide-based dendrimers have also shown promise for CNS delivery. These structures combine the advantages of dendrimers with the biocompatibility and targeting capabilities of peptides. For instance, a recent study demonstrated improved delivery of doxorubicin to glioma cells using arginine-rich peptide dendrimers [54].

5.3. Polyamides

Polyamides are a class of biodegradable polymers that have gained attention for their potential in controlled drug release applications, including CNS drug delivery. These polymers undergo surface erosion, allowing for near zero-order drug release

kinetics and protection of the encapsulated drug from premature degradation [55]. Recent advancements in polyanhydride-based delivery systems include the development of nanoparticles capable of crossing the BBB. By tuning the polymer composition and surface properties, researchers have created polyanhydride nanoparticles that can exploit BBB transport mechanisms. For example, polyanhydride nanoparticles functionalized with lectins have shown enhanced brain uptake due to their ability to interact with sugar moieties on the BBB endothelium [56].

Another innovative approach involves the use of polyanhydride-based implants for local, sustained delivery of therapeutics in the brain. These implants can be designed to degrade over extended periods, providing long-term drug release directly at the target site. This approach has shown promise in preclinical studies for the treatment of brain tumors and neurodegenerative diseases [57].

5.4. Scaffolds

Three-dimensional scaffolds represent an innovative approach for localized, sustained drug delivery in the CNS. These structures can be designed to mimic the extracellular matrix, providing a supportive environment for cell growth and tissue regeneration while simultaneously delivering therapeutic agents [58].

Recent advances in scaffold technology for CNS drug delivery include the development of electrospun nanofiber scaffolds. These highly porous structures offer a large surface area for drug loading and can be engineered to release drugs in a controlled manner. For instance, a recent study demonstrated the use of poly(lactic-co-glycolic acid) (PLGA) nanofiber scaffolds for the sustained release of neurotrophic factors in a spinal cord injury model [59].

Hydrogel-based scaffolds have also shown promise for CNS drug delivery. These materials can be designed to be injectable, allowing for minimally invasive administration. Smart hydrogels that respond to specific stimuli, such as temperature or pH, have been developed to provide on-demand drug release in the brain. For example, a thermosensitive hydrogel loaded with paclitaxel demonstrated effective treatment of glioblastoma in a preclinical model [60].

5.5. Convection-Enhanced Delivery

Convection-enhanced delivery (CED) is an innovative approach that uses positive pressure to create a pressure gradient, driving the infusate through the brain interstitium. This technique allows for the distribution of therapeutics over larger volumes of brain tissue compared to simple diffusion [61]. Recent advancements in CED technology include the development of real-time imaging techniques to monitor and optimize drug distribution. Magnetic resonance imaging (MRI)-guided CED allows for precise catheter placement and visualization of the infusate spread, enabling personalized treatment strategies. Another innovative approach involves the use of nanocarriers in combination with CED to further enhance drug distribution and retention in the brain [62]. Researchers have also explored the potential of multi-catheter CED systems to achieve more uniform drug distribution in complex brain structures. This approach has shown promise in preclinical studies for the treatment of diffuse intrinsic pontine glioma, a challenging pediatric brain tumor [63].

6. Emerging Strategies

As research in CNS drug delivery continues to evolve, several emerging strategies show promise for overcoming the BBB and improving therapeutic outcomes for neurological disorders.

6.1. Intranasal Delivery

Intranasal delivery has emerged as a non-invasive route for bypassing the BBB and delivering drugs directly to the CNS. This approach exploits the olfactory and trigeminal nerve pathways, which provide a direct connection between the nasal cavity and the brain [64]. Recent advances in intranasal delivery include the development of mucoadhesive formulations to prolong residence time in the nasal cavity and enhance drug absorption. Researchers have also explored the use of nanocarriers, such as chitosan-based nanoparticles, to improve the stability and bioavailability of intranasally administered drugs [65].

Another innovative approach involves the use of cell-penetrating peptides in combination with intranasal delivery to further enhance CNS drug penetration. For instance, a recent study demonstrated improved brain delivery of the neuroprotective peptide NAP using the cell-penetrating peptide TAT as a molecular carrier [66].

6.2. Cell-Penetrating Peptides

Cell-penetrating peptides (CPPs) are short, often cationic peptides that can facilitate the intracellular delivery of various cargo molecules, including drugs and biologics. These peptides have shown potential for enhancing BBB penetration and improving CNS drug delivery [67]. Recent advancements in CPP technology include the development of activatable cell-penetrating peptides (ACPPs) that become active only in specific microenvironments, such as the acidic extracellular space of tumors. This approach

enhances the specificity of drug delivery and reduces off-target effects [68]. Researchers have also explored the potential of CPP-drug conjugates for CNS delivery. For example, a recent study demonstrated improved brain delivery of the anti-epileptic drug valproic acid using a CPP-based delivery system [69].

6.3. Exosomes and Extracellular Vesicles

Exosomes and other extracellular vesicles (EVs) have emerged as promising natural nanocarriers for CNS drug delivery. These cell-derived vesicles can cross biological barriers, including the BBB, and deliver their cargo to target cells [70]. Recent advances in EV-based drug delivery include the development of engineered exosomes with enhanced targeting capabilities. By modifying the surface proteins of exosomes, researchers have created "designer" EVs that can target specific cell types in the brain. For instance, exosomes engineered to express the rabies virus glycoprotein have shown improved neuronal targeting [71]. Another innovative approach involves the use of EVs for the delivery of therapeutic nucleic acids, such as siRNA or miRNA, to the CNS. This strategy has shown promise in preclinical studies for the treatment of neurodegenerative diseases and brain tumors [72].

7. Conclusion

Brain-targeted drug delivery remains a critical challenge in treating central nervous system disorders. Significant progress has been made in developing innovative strategies to overcome the blood-brain barrier, from advanced nanocarrier systems to novel administration routes. Emerging technologies such as cell-penetrating peptides, exosomes, and smart scaffolds show great promise for enhancing drug delivery specificity and efficacy. As our understanding of the BBB and CNS pathologies deepens, combinatorial approaches leveraging multiple technologies are likely to yield the most effective solutions. While obstacles persist, the rapid pace of innovation in this field offers hope for improved treatments and potential cures for devastating neurological conditions, paving the way for a new era in CNS therapeutics.

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Author's short biography

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