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NANOTECHNOLOGY-DRIVEN INNOVATIONS IN BRAIN TUMOR

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ABSTRACT

Brain tumours remain one of the most challenging neurological disorders to treat due to poor drug penetration across the blood–brain barrier (BBB), tumour heterogeneity, systemic toxicity, and multidrug resistance associated with conventional chemotherapy. Nanotechnology-based drug delivery systems have emerged as promising strategies to overcome these limitations by enhancing targeted delivery, improving bioavailability, and reducing adverse effects. Nanomaterials ranging from 1–100 nm, including polymeric nanoparticles, liposomes, micelles, extracellular vesicles, and inorganic carriers, enable controlled and site-specific drug release to tumour tissues.

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INTRODUCTION

Brain tumours are among the most complex and life-threatening neurological disorders due to their aggressive growth, poor prognosis, and limited response to conventional therapeutic approaches. Gliomas and glioblastomas, which account for the majority of malignant brain tumors, remain particularly difficult to treat because of rapid proliferation, tumor heterogeneity, and the development of multidrug resistance mechanisms. Despite advances in medical science, complete eradication of these tumors is rarely achieved, resulting in high morbidity and mortality rates. Conventional treatment strategies for brain tumors mainly include surgical resection, chemotherapy, and radiotherapy [1]. Surgical excision aims to remove the tumor mass; however, complete removal is often impossible due to the sensitive anatomical location of the brain and the risk of damage to surrounding healthy tissues. Chemotherapy and radiation therapy are widely employed as adjuvant treatments but are frequently associated with systemic toxicity, non-specific drug distribution, and severe adverse effects [2]. Moreover, the therapeutic effectiveness of many anticancer drugs is significantly limited by physiological barriers such as the blood–brain barrier (BBB) and the blood– brain tumor barrier (BBTB), which restrict drug penetration into the central nervous system. The BBB is a highly selective semipermeable membrane composed of endothelial tight junctions, astrocytes, and pericytes that protect the brain from harmful substances.

1. CELLULAR AND MOLECULAR MECHANISMS OF INTRACRANIAL TUMOURS AND COMPLICATION

Brain cancer arises from complex molecular and cellular abnormalities within the central nervous system that lead to uncontrolled cell growth, invasion, and resistance to therapy. Genetic mutations and epigenetic alterations disturb normal regulatory pathways governing cell division, apoptosis, and differentiation, resulting in the formation of malignant brain tumours. High-grade tumors such as glioblastoma multiforme exhibit rapid proliferation, diffuse infiltration, and marked heterogeneity, which contribute to aggressive disease behavior and poor clinical outcomes [3]. A defining aspect of brain tumor pathogenesis is the dynamic interaction between tumor cells and the tumor microenvironment (TME). The TME facilitates tumor progression by promoting immune evasion, metabolic adaptation, angiogenesis, and resistance to chemotherapy and radiotherapy. Hypoxic conditions within the tumor mass stimulate the release of angiogenic mediators, particularly vascular endothelial growth factor (VEGF), leading to the development of structurally abnormal and

functionally inefficient blood vessels. As the tumor advances, the normal blood–brain barrier (BBB) undergoes pathological remodeling, transforming into the blood–brain tumor barrier (BBTB). This altered barrier displays irregular permeability due to disrupted tight junctions, abnormal endothelial cell organization, and degradation of the basement membrane [4]. Although certain tumor. regions show increased vascular leakage, infiltrating cancer cells at the tumor margins often remain protected by an intact barrier, allowing them to escape therapeutic intervention. At the molecular level, overexpression of efflux transporters, mislocalization of astrocytic end-feet, activation of matrix metalloproteinases, and changes in water channel regulation contribute to cerebral edema, elevated interstitial pressure, and uneven drug distribution. These pathological changes impair effective drug delivery and support tumor survival and recurrence.

2. APPROACHES TO ENHANCE BLOOD-BRAIN BARRIER PERMEABILITY

The blood–brain barrier represents a major obstacle in the treatment of brain tumors due to its tightly regulated structure, which restricts the entry of most therapeutic agents. To overcome this limitation, several innovative strategies have been developed to enhance drug transport into the central nervous system. Modification of the outer characteristics of drug carriers is a widely adopted method to improve BBB traversal. By altering surface charge, hydrophobicity, or ligand attachment, nanocarriers can be designed to interact more efficiently with BBB components [5]. These modifications allow controlled interaction with endothelial cells, thereby promoting translocation across the barrier. One of the most effective BBB-crossing mechanisms involves exploiting naturally occurring receptors present on brain capillary endothelial cells. Nanocarriers are functionalized with ligands that bind to specific receptors such as transferrin, insulin, lipoprotein, or scavenger receptors. After ligand-receptor binding, the drug-loaded system is internalized and transported across the BBB via endocytosis, enabling targeted delivery to brain tissue.

3.DEVELOPMENT OF NANO ENABLED THERAPEUTIC DELIVERY PLATFORMS

Nanotechnology-based drug delivery systems represent a major advancement in pharmaceutical and biomedical sciences, offering innovative solutions to the limitations of conventional drug administration. Traditional dosage forms often suffer from inadequate bioavailability, rapid metabolism, poor tissue specificity, and high systemic toxicity. By employing nanoscale materials, drug delivery can be optimized to achieve controlled release, improved stability, and enhanced therapeutic efficiency [6]. Nanocarriers typically range from 1 to 100 nanometers in size, allowing them to interact favorably with biological systems at the molecular and cellular levels. One of the key advantages of nanotechnology-driven delivery platforms is their ability to improve drug solubility and circulation time within the body. Many potent therapeutic agents, particularly anticancer drugs, exhibit poor aqueous solubility and are rapidly cleared from systemic circulation. Encapsulation of these drugs within nanoparticles protects them from premature degradation and enables sustained release, thereby maintaining therapeutic drug concentrations for prolonged periods [7]. This approach reduces dosing frequency and enhances patient compliance. Nanotechnology-based drug delivery systems can be broadly categorized into non-targeted (passive) and targeted delivery approaches. Passive targeting primarily exploits pathological features of diseased tissues, such as abnormal vasculature and increased permeability, allowing nanoparticles to preferentially accumulate in tumor tissues. This phenomenon, known as the enhanced permeability and retention effect, facilitates higher drug concentration at the disease site compared to normal tissues, minimizing unwanted side effects. In contrast, targeted drug delivery systems utilize surface-modified nanocarriers that interact specifically with receptors or biomarkers overexpressed on diseased cells. Ligands such as peptides, antibodies, sugars, or small molecules are conjugated onto the surface of nanoparticles to enable receptor-mediated endocytosis. This strategy significantly enhances cellular uptake of therapeutic agents and improves intracellular drug localization, particularly in cancer therapy and neurological disorders. Various types of nanocarriers have been developed for pharmaceutical applications, including polymeric nanoparticles, lipid-based systems, inorganic nanoparticles, dendrimers, micelles, and extracellular vesicles. Polymeric nanoparticles formulated using biodegradable polymers such as polymeric (lactic acid) and polymeric (lactic-co-glycolic acid) are widely employed due to their excellent biocompatibility and tunable drug release profiles [8].

4. NANOMEDICINE APPROACHES FOR TARGETED BRAIN CANCER THERAPY

Brain cancer remains one of the most difficult malignancies to manage due to the restrictive nature of the blood–brain barrier and the infiltrative growth pattern of tumors such as glioblastoma multiforme [9]. Nanoparticle-based systems have emerged as a powerful solution to improve drug delivery, targeting accuracy, and therapeutic response in neuro-oncology Nanoparticles are submicron-sized carriers that can encapsulate drugs, genes, or imaging agents and transport them selectively to tumor tissues.

4.1 Lipid-Derived Nanocarriers (Liposomes)

Lipid-based vesicular systems, commonly known as liposomes, are spherical nanostructures composed of phospholipid bilayers enclosing aqueous compartments. Their structural similarity to biological membranes makes them highly biocompatible and suitable for brain-targeted delivery.

4.2 Noble Metal Nanoparticles (Gold and Silver)
Metallic nanoparticles, particularly gold and silver nanostructures, play a significant role in brain cancer nanotherapy due to their unique optical and chemical properties. Silver nanoparticles exert cytotoxic effects primarily through reactive oxygen species generation, leading to oxidative damage, mitochondrial dysfunction, and apoptosis in glioma cells.
4.3 Zinc Oxide Nanoparticles
Zinc oxide nanoparticles are inorganic nanomaterials with strong catalytic and oxidative properties. They induce cancer cell death by generating intracellular oxidative stress and DNA damage. In glioma models, zinc oxide nanostructures reduce tumor cell proliferation and promote apoptotic pathways. However, prolonged exposure may cause neurotoxicity, highlighting the need for dose optimization.
4.4 Nucleic Acid–Based Nanoparticles
Nucleic acid-loaded nanoparticles represent a promising approach for gene therapy in brain cancer. These systems deliver DNA, siRNA, or mRNA to modulate gene expression in tumor cells. Such nanocarriers enable silencing of oncogenes, restoration of tumor suppressor genes, and enhancement of chemosensitivity. They also support emerging genome-editing technologies for precision therapy.

5.INNOVATIVE TECHNIQUES TO OPTIMIZE BRAIN CANCER TREATMENT

Brain tumors, particularly glioblastoma, are among the most aggressive malignancies and remain difficult to manage because of their invasive growth pattern and resistance to conventional therapies. One of the primary limitations in brain cancer therapy is the presence of the blood–brain barrier (BBB), which restricts the entry of most chemotherapeutic agents into the brain parenchyma [10].
5.1 Passive Targeting via Tumor Vasculature Abnormalities
Passive targeting relies on the pathological characteristics of tumor blood vessels rather than specific molecular recognition. Brain tumors often exhibit irregular vascular architecture with leaky endothelial junctions.
5.2. Ligand-Mediated Active Targeting
Active targeting strategies are designed to improve specificity through receptor–ligand interactions. In this approach, nanoparticles are functionalized with molecules that selectively bind to receptors overexpressed on brain tumour cells.
5.3. Dual-Targeting Approaches.
Single-ligand systems may not sufficiently differentiate between normal and malignant brain tissues. Dual-targeting strategies incorporate two distinct ligands on a single nanoparticle system. Typically, one ligand facilitates BBB penetration while the second promotes selective tumor cell recognition.
5.4. Magnetic Targeting Strategies
Magnetic targeting employs superparamagnetic iron oxide nanoparticles to guide drug carriers using external magnetic fields. After systemic administration, an externally applied magnetic field directs nanoparticles toward the tumor region.
5.5. Stimuli-Responsive Targeting Systems
Stimuli-responsive nanocarriers release drugs in response to tumor-specific triggers. Internal stimuli include acidic pH, elevated glutathione concentration, and overexpressed enzymes within the tumour microenvironment. pH-sensitive systems exploit the acidic extracellular conditions of tumors for controlled drug release.
5.6. Cell-Mediated Targeting Strategies
Certain biological cells naturally migrate toward tumor and inflammatory sites. Immune cells such as macrophages and neutrophils can be used as carriers for nanoparticle delivery.
5.7. Biomimetic and Cell Membrane-Coated Nanocarriers
Biomimetic strategies involve coating nanoparticles with natural cell membranes. Red blood cell membrane coating prolongs systemic circulation by avoiding immune recognition. Cancer cell membrane-coated nanoparticles exploit homotypic targeting to improve glioma specificity. Such biomimetic systems enhance immune evasion and tumor accumulation simultaneously.
5.8. Self-Adaptive and Smart Nanoplatforms
Advanced nanocarriers are engineered to dynamically alter their properties in response to environmental cues. Size-switching nanoparticles shrink after reaching the tumor microenvironment, enabling deeper penetration.

6. MODERN DEVELOPMENT IN NANOMEDICINE FOR CENTRAL NERVOUS SYSTEM BRAIN TUMOUR MANAGEMENT

Neuro-oncology focuses on the diagnosis and management of tumors affecting the central nervous system (CNS), including malignant gliomas, metastatic brain tumors, and other intracranial neoplasms [11]. Despite advances in surgery, radiotherapy, and chemotherapy, therapeutic outcomes remain suboptimal due to the highly invasive nature of brain tumors and the presence of the blood–brain barrier (BBB).
6.1. Rationale for Employing Nanoparticles in Brain Cancer Therapy
One of the principal obstacles in neuro-oncology is the BBB, a tightly regulated physiological barrier that restricts the entry of most therapeutic agents into brain tissue. Conventional chemotherapeutics often fail to reach therapeutic concentrations within tumor sites.
6.2. Design Characteristics of Contemporary Nanoparticles
State-of-the-art nanosystems are developed using sophisticated engineering strategies. Key parameters

include: Particle size optimization (typically 10–200 nm), Surface charge modulation, Biocompatible material selection, Stealth coating using polyethylene glycol (PEG) These design features enhance circulation time, reduce immune recognition, and promote selective tumor cell uptake.

6.3. Lipid-Based Nanocarriers

Lipid-derived nanoparticles, including liposomes and solid lipid nanoparticles, represent another class of advanced nanoformulations. Liposomes consist of phospholipid bilayers capable of encapsulating both hydrophilic and lipophilic drugs. Their structural similarity to cellular membranes improves biocompatibility and reduces immunogenicity.

6.4.Dendritic Nanostructures for Precision Therapy

Dendrimers are highly branched, tree-like macromolecules with well-defined architecture and multiple surface functional groups. Their unique structure allows: High drug loading capacity, Surface attachment of targeting ligands, Controlled size distribution, Multimodal therapeutic functionality [12].

6.5. Inorganic and Metallic Nanoparticles

Metal-based nanoparticles such as gold nanoparticles (AuNPs) and iron oxide nanoparticles (IONPs) are utilized in advanced neuro-oncological interventions. Gold nanoparticles exhibit photothermal properties that allow tumor ablation upon near-infrared irradiation. Iron oxide nanoparticles are used in magnetic targeting and magnetic resonance imaging (MRI), making them valuable in theranostic applications.

6.6. Theranostic Nanoparticles

Theranostic nanosystems combine therapeutic and diagnostic functionalities in a single platform. These systems enable simultaneous imaging and treatment, allowing clinicians to monitor drug distribution and therapeutic efficacy in real time.

7. EVOLVING TRENDS AND TECHNICAL HURDLES

Nanotechnology-driven interventions have significantly transformed the therapeutic landscape of central nervous system (CNS) malignancies. Advanced nanoformulations have demonstrated enhanced targeting efficiency, improved drug bioavailability, and the capacity to overcome biological barriers such as the blood–brain barrier (BBB).

7.1 Personalized Nanomedicine

One of the most promising future directions involves tailoring nanoparticle systems according to patient-specific tumor genetics and molecular signatures. Brain tumors, particularly glioblastoma, exhibit profound heterogeneity.

7.2 Overcoming Drug Resistance

Nanoparticle-mediated co-delivery of multiple therapeutic agents may reduce multidrug resistance. Future strategies may incorporate efflux pump inhibitors or siRNA molecules to suppress resistance pathways in tumour cells. Emerging imaging modalities, including high-resolution MRI and fluorescence-guided surgery, may benefit from nanoparticle contrast agents.

7.3 Blood–Brain Barrier Complexity

Although nanoparticles enhance BBB permeability, complete and uniform penetration remains challenging. The heterogeneity of BBB disruption in tumors limits consistent drug distribution. The brain tumour microenvironment is highly complex, characterized by hypoxia, acidic pH, and dense extracellular matrices.

7.4 Biological Safety and Toxicity Concerns

Long-term biocompatibility and accumulation of inorganic nanoparticles remain areas of concern. Potential neurotoxicity and inflammatory responses require thorough investigation. Large-scale production of nanoparticles with consistent physicochemical properties is technically demanding [13].

7.5 Stability and Storage Limitations

Nanoparticle formulations may exhibit aggregation or degradation during storage. Stability optimization remains a significant formulation challenge. Genetic and molecular diversity within brain tumors reduces the effectiveness of single-target nanotherapies. Adaptive resistance mechanisms further complicate treatment outcomes [14].

8. CONCLUSION

Nanomedicine has significantly advanced the management of brain cancer by introducing innovative diagnostic and therapeutic strategies. Glioblastoma (GBM) and other aggressive brain tumors remain highly lethal due to their complex cellular origin and the challenge of penetrating the blood–brain barrier (BBB) for effective drug delivery. Nanotechnology-based systems have emerged as promising solutions to these challenges by enabling targeted drug transport, improved solubility, and multifunctional platforms that combine therapy with imaging. Various nanoparticles-including liposomes, dendrimers, micelles, carbon nanotubes, metallic nanoparticles, and biologically inspired carriers-have been extensively investigated, though only a limited number demonstrate strong clinical potential [15]. Emerging imaging technologies utilizing biomimetic and advanced nanoparticle systems are expanding previous limitations in diagnosis and treatment.

9. AUTHOR CONTRIBUTIONS

All authors are contributed equally.

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11. DECLARATION COMPETING INTEREST

The authors have no conflicts of interest to declare.

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NONE

13. REFERENCES

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