



## NOVEL NANO PARTICLES APPROACHES IN TRAGETED THERAPY OF BRAIN CANCER

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### ABSTRACT

Brain cancer, particularly glioblastoma, remains one of the most aggressive and difficult-to-treat malignancies due to the restrictive nature of the blood–brain barrier (BBB) and blood–brain–tumour barrier (BBTB). The reviewed articles collectively highlight the transformative role of nanotechnology in improving the diagnosis, imaging, and treatment of brain tumours. Nanoparticles (NPs), including lipid-based, polymeric, metallic, carbon-based, virus-based, and biomimetic nanomaterials, demonstrate enhanced permeability, targeted delivery, and multifunctional capabilities. Their nanoscale size, high surface area, and modifiable surfaces enable efficient BBB penetration, tumour-specific targeting, drug encapsulation, and controlled release. In addition to therapeutic applications, nanostructures offer optical, magnetic, and photodynamic properties that significantly enhance imaging precision and multimodal diagnostics. While nanotechnology presents substantial clinical promise, concerns regarding neurotoxicity and long-term safety necessitate standardized toxicological evaluation. Current research emphasizes improving specificity, minimizing adverse effects, and developing biocompatible and cell membrane-coated systems for safer clinical translation. Overall, nanotechnology-based platforms represent a rapidly advancing strategy that integrates targeted therapy and advanced imaging, offering improved efficacy and potential breakthroughs in brain cancer management while underscoring the importance of safety optimization.

**Keywords:** Brain cancer, Glioblastoma, Nanoparticles, Blood–brain barrier, Drug delivery, Nanotechnology, Tumour targeting, Nanomedicine, Neurotoxicity, Diagnostic imaging

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### INTRODUCTION

The brain, which is made up of the cerebrum, cerebellum, brain stem, and four lobes (frontal, parietal, occipital, and temporal), is the most important and remarkable three-pound organ that is protected inside the skull. It controls memory, sensitive motor functions, and many other processes. Together with the cerebrum, which is functionalized for muscle, posture, and movement coordination, the cerebellum is the largest section of the brain and works with the right and left hemispheres to conduct higher sensory and motor tasks as well as command motions. Additionally, the appropriate propagation of behavioral processes is linked to the brain's four important lobes

[1]. An abnormal mass of tissue that grows abnormally in the brain and has the potential to directly kill healthy brain cells is called a brain tumor or intracranial tumor. Globally, brain tumours are the primary cause of illness and death. 10.82 cases of brain cancer are reported for per 100,000 people annually on average [2]. Medical diagnosis and treatment have been transformed by nanomedicine, which has also shown promise in improving the pharmacological and pharmacokinetic pattern of unstable anticancer medications and facilitating their passage across the blood-brain barrier [3]. In the current paper, we reviewed the most recent published papers on various nanomaterials applicable in the diagnosis and treatment of brain cancer. This was done in relation to all of the information above and in continuation of our research group's efforts regarding the synthesis of nanomaterials and investigation about their potential bio applications [4].

Nanomaterials can be classified as zero-dimensional (such as nanoparticles and quantum dots), one-dimensional (such as nanofibers, nanotubes, and nanowires), or two-dimensional (such as graphene and

graphene oxide) based on their structural characteristics. On rare occasions, certain materials might be positioned on the edge of these groups. Furthermore, nanoparticles can be produced chemically, physically, physiologically, or mechanically, or they can be found in nature [5]. Nanoparticles, the focus of this review, have been described by the All three exterior dimensions are present in the nanoscale International Organization for Standardization (ISO) as nano-objects. Furthermore, if the lengths of the longest and shortest axes differ significantly-typically by more than three times-the names nanorod or nanoplate may be applied [6]. A variety of forms and sizes of nanoparticles, including spheres, cylinders, cubes, triangles, rings, and disks with varied dimensions, are available.

The use of nanoparticles for a range of biomedical applications has gained popularity in recent years. Therefore, the most significant applications relate to the diagnosis and treatment of various diseases using photoablation therapy, biosensors, targeted drug delivery, bioimaging, and hyperthermia [7].

### 1. DESCRIPTION OF MNP

The most prevalent component of MNPs is ferromagnetic iron oxide (Fe<sub>3</sub>O<sub>4</sub>). They usually have a diameter of 1–100 nm and are invisible to the human eye. By altering their surface and adding a peptide or antibody unique to cancer cells, MNPs can be made to specifically target cancer [8]. They can administer tailored therapy to particular body parts for use in biomedical applications. By applying an external magnetic field, MNPs can be targeted and systemically injected into the bloodstream. When the particles reach their destination, a medicine that has been designed into them can be released. The effects of MNPs in a magnetic field on glioma cells have been demonstrated in in vivo investigations to last for up to 100 minutes after exposure. In a different investigation involving rabbits, squamous cell carcinoma tumours were permanently remitted after receiving an intravenous injection of specifically made MNPs and then being exposed to an external magnetic field 2 [9]. The BBB continues to be a significant obstacle for systemic delivery of medicines for the treatment of brain tumours, even if intravenous administration is possible for tumours in other areas of the body. Direct intratumoral administration minimizes systemic toxicity while offering the highest therapeutic dosage for patients with GBMs.

### 2. MNP FOR THE DIAGNOSIS OF BRAIN CANCER

The most intricate and specialized bodily system is the central nervous system, which is made up of hundreds of different, extremely ordered subtypes of neurons and glia. In a similar vein, diseases of the central nervous system are equally complicated, resulting in a variety of behavioral abnormalities that can be definitively diagnosed. As a result, only a little quantity

of medication reaches the central nervous system, which is insufficient to cure brain disorders. Therefore, in order to effectively treat illnesses of the central nervous system, new methods for delivering therapeutic drugs to the brain-such as nanotechnology approaches-are required. Since nanoparticles have several benefits, including targeting efficiency, non-invasiveness, biodegradability, stability, and controllability to load and release drugs, there has been a lot of interest in using them to diagnose brain diseases or help deliver medications across the blood-brain barrier [10].

#### Nanoparticle Applications for Brain Tumours

Because brain tumours are so common, scientists are focusing on developing new applications for their diagnosis and treatment. The most frequent intracranial metastases are from meningiomas, gliomas, and systemic malignancies; these patients need extensive multidisciplinary therapy, involving medical oncology, radiation oncology, and neurosurgery. There have been reports of using a variety of nanoparticle kinds in bioimaging techniques to identify brain cancers. As a result, research reports using iron oxide nanoparticles that have been covalently linked to phosphonate polyethylene glycol to the cycle RGD peptide sequence as contrast agents for magnetic resonance imaging because of its magnetic characteristics [11].

#### Nanoparticle Applications for Neurodegenerative Disorders

Because of their rising incidence, age-dependent neurodegenerative diseases constitute a serious threat to human health. Alzheimer's disease and Parkinson's disease are the two most prevalent neurodegenerative illnesses, and they have a wide range of pathophysiology's, such as memory loss, cognitive deficits, locomotor dysfunction, and emotional and behavioral issues [12].

#### Nanoparticle Applications for Stroke

symbolizes a serious medical situation that may cause death or incapacity. There are two different kinds of stroke: haemorrhagic stroke, which is brought on by a cerebral blood vessel rupturing, and ischemic stroke, which happens when a cerebral blood artery is blocked. Severe neurological symptoms, inflammation, and neurological death are the outcomes of the more common kind of stroke, known as an ischemic stroke [13].

### 3. MNP FOR TREATMENT OF BRAIN CANCER

Nanomedicine is significantly impacted by the quick advancement of nanotechnology for biological applications. By making it easier to synthesize and manipulate materials at the nanoscale, nanotechnology aids in the creation of new instruments for biological system monitoring, control, diagnosis, and treatment. A group of substances with any external dimension at the nanoscale or with an internal or surface structure at the nanoscale, roughly between 1 and 100 nm, are referred to as nanomaterials [14].

### Liposomes

Liposomes are spherical vesicles made up of aqueous compartments and biodegradable natural or synthetic phospholipid bilayers. Phospholipids' amphiphilic nature allows for the spontaneous formation of these nanospheres. Depending on the synthesis techniques and post-formation processing, they can be classified as either unilamellar vesicles (ULVs) or multilamellar vesicles (MLVs). MLVs (two or more concentric lipid bilayers organized like an onion skin, 1–5  $\mu\text{m}$ ) preferentially encapsulate lipid-soluble pharmaceuticals, while ULVs (one lipid bilayer, 50–250 nm) contain a big aqueous core and are appropriate to entrap hydrophilic medications. While unilamellar liposomes, which have two to three lamellar bilayers and a hydrodynamic diameter of 250 nm, show a significantly faster release rate than MLVs, MLVs often have a larger entrapped volume than ULVs. In order to deliver medications [15].

By altering the surface of the liposomes with transferrin (Tf) and peptide-penetratin (Pen) for receptor-mediated transcytosis and enhanced cell penetration, respectively, Lakkadwala et al. [16] developed and described a dual-functionalized liposome-based nanotherapeutic system

### Nano-Micelles

Above a certain critical concentration (also known as the critical micelle concentration), amphiphilic molecules in water self-aggregate to form micelles, an intriguing family of amphiphilic spherical nanostructures. Both hydrophilic and hydrophobic regions can be found in micelles. The hydrophilic portion of the molecules encloses the micelle shell, whilst the hydrophobic portion makes up the cores, which contain lipophilic bio actives. Chemotherapeutics designed to target site-specific ovarian cancer can be loaded into these potential nanocarriers with notably high capacities. Micelles are one type of nanocarrier that has garnered a lot of interest lately as a means of delivering drugs precisely to treat brain tumours. [17].

### Dendrimers

A class of well-ordered, hyper-branched, nanoscale polymers is known as dendrimers. Over the past few decades, researchers have created a vast array of dendrimers, and they are still designing and creating new types. Glycosylation, PEGylation, acetylation, and amino acid functionalization are surface modifications that can enhance the biocompatibility of dendrimer polymers and offer safe therapy to healthy cells. The surface of dendrimers can be adorned with targeting ligands that promote cancer cell rearrangement without compromising the viability of normal cells, thereby achieving targeted delivery and selectivity of brain Chemo sensors 2020, 8, 117 8 of 31 tumor cells [18].

### Carbon Nanotubes and Carbon Dots

Carbon nanotubes (CNTs) are Because of their unique mechanical, electrical, and surface characteristics, pharmaceutical researchers are increasingly interested in using carbon nanotubes (CNTs), which are

cylindrical nanostructures, to deliver therapeutic compounds and medications. CNTs are more biocompatible because the reactivity of their surface makes it easier for guest molecules to attach. These innovative nanocarriers are mostly used for cancer treatment and tumor cell targeting, and they can be functionalized with polymers, carbohydrates, peptides, and organic compounds based on the specifications [19].

### 4.SYNTHESIS OF MNP

Both solid-inorganic (magnetic  $\text{Fe}_3\text{O}_4$  NPs, gadolinium NPs, gold NPs, and semiconductor quantum dots [QDs] and organic-based (dendrimer hydrogel and polymer) NPs have been used as imaging and delivery agents in brain cancer research. Naturally, each system will have a very different synthetic route. However, a brief examination of common synthetic techniques is made possible by a number of unifying approaches based on whether the final product is primarily inorganic or organic. Here, we give a brief overview of the general processes for creating both organic and inorganic NPs before looking at how active targeting is necessary for these forms to be used in brain cancer treatment. The solid core material of inorganic nanoparticles (NPs) can be a semiconductor or metallic framework, or it can be a magnetic metal oxide. Magnetic  $\text{Fe}_3\text{O}_4$  NPs are the most widely used inorganic motif for brain tumor imaging, according to a survey of the last ten years' literature [20].

The basis for creating targeted NPs, whether they are classified as inorganic or organic, is the capacity to chemically alter polymer structures. In order to incorporate a wide range of targeting ligands to the NP scaffold, such as EGF-related targets, transferrin, lactoferrin, trans-activating transcriptional activator, aptamers, and many other peptides, condensation processes have been widely used in the literature [21].

### 5. APPLICATION OF MNP FOR BRAIN CANCER

The primary application of Magnetic Nanoparticles (MNPs) in brain cancer-especially in aggressive tumours like Glioblastoma-is targeted therapy and imaging. They are mainly used in the following ways:

#### 1 Targeted Drug Delivery Across the Blood–Brain Barrier (BBB)

One of the biggest challenges in treating brain cancer is the blood–brain barrier.

MNPs can

- Be coated with chemotherapy drugs.

- Be guided magnetically toward the tumor site.

- Release drugs directly inside tumor tissue.

- Reduce systemic side effects.

This improves delivery of drugs like temozolomide used in Glioblastoma treatment.

#### 2.MRI Contrast Enhancement

MNPs (especially iron oxide nanoparticles) act as MRI contrast agents.

They help

Improve tumor visualization.  
 Define tumor margins.  
 Monitor treatment response.  
 MRI is the primary imaging technique used in brain cancer diagnosis.  
 3. Theragnostic (Combined Therapy + Diagnostics)  
 MNPs can combine  
 Imaging (MRI)  
 Drug delivery  
 Hyperthermia  
 This integrated approach is called theragnostic, allowing personalized treatment.

## 6. LIMITATION

Novel magnetic nanoparticles—especially those investigated for tumours like Glioblastoma—show strong potential in hyperthermia, drug delivery, and theragnostic. However, several scientific, technical, and clinical limitations still restrict their widespread use.

### 1. Blood–Brain Barrier (BBB) Challenges

Even though MNPs are designed to cross or bypass the BBB:

- Many nanoparticles still fail to efficiently penetrate the intact BBB.
- Tumor BBB disruption is heterogeneous, meaning some tumor regions remain protected.
- Magnetic guidance from outside the skull has limited depth and precision.

Result: Incomplete drug delivery to infiltrative tumor cells.

### 2. Limited Tumor Penetration

- Brain tumours like Glioblastoma are highly infiltrative.
- Nanoparticles may accumulate mainly near the injection site.
- Interstitial pressure inside tumours limits diffusion.
- This reduces overall therapeutic effectiveness.

### 3. Heat Control Issues (Magnetic Hyperthermia)

## 7. FUTURE DIRECTION OF NP-BASED BRAIN CANCER THERAPY

Targeting agents and imaging agents will likely be used more frequently in the future of NPs for the treatment of brain tumours, along with the simultaneous delivery of medications. Because many medications can be delivered at the same time, treatment can be customized for each patient. NPs are essentially delivery vehicles that can be used to provide drug mixtures. The increased use of targeted medicines will improve therapeutic efficacy by increasing accumulation in brain tumours and decreasing accumulation in normal brain tissue. Additionally, the growing use of imaging agents will assist monitor brain tumours during a treatment regimen and diagnose cancer at an earlier stage for the highest chance of survival.

The development of complex systems requires an understanding of the different parts that comprise the delivery vehicle as a whole, hence this future is still difficult. A thorough understanding of how each component functions will

be necessary for future NP delivery systems that can use simultaneous drug administration, targeting to certain brain tumor surface indicators, and/or simultaneous imaging of their distribution in order to accomplish such aims. [22].

## 8. CONCLUSIONS

Since the application of nanoparticles, defined as nano-objects with all three external dimensions in the nanoscale, in the diagnosis and treatment of brain diseases, including brain tumors, neurodegenerative disorders, and stroke, is continuously and rapidly emerging, the need for understanding both their beneficial and negative impacts on brain health is imperative. Although nanoparticles possess unique physicochemical properties that justify their broad use in application for the central nervous system, they can also manifest neurotoxic effects, including oxidative stress, resulting in cell apoptosis and autophagy, immune responses, and neuroinflammation, which will affect the blood brain barrier function. Thus, the development of standardized toxicological studies is crucial for the improvement of brain applications.

## 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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