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A Review on Novel Nano Drug Delievery System for Brain Tumor Treatment

1) Mr.Yogesh K Dheple , 2) Dr.D.K.Vir , 3) Mr. Sominath A Badak , 4) Mr. Bhagwat N Ghuge , 5) Mr. Mayur K Jadhav.6) Miss.Ashwini R Borade
1)Student, 2) Principal (Guidance), 3) Student, 4) Student, 5) Student, 6) Student
Department of pharmacology, shree goraksha college of pharmacy and researchcentre khamgaon

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ABSTRACT:
Cancer is one ailment with a complex pathological mechanism. Current chemotherapy has issues with cytotoxicity, lack of selectivity, multidrug resistance conformation, and stem-like cell growth. Nanomaterials are accessories with unique optical, glitzy, and electrical properties that range in size from 1 to 100 nm. Nanomaterials used to treat cancer can be categorized into a wide variety of major orders. These nanomaterials, which target cancer cells, the excrescence medium, and susceptible systems, have been altered for a range of cancer treatments in an effort to improve specificity, decrease toxicity, and increase medication capacity and bioavailability. The primary factors impeding the brain's ability to receive remedial medications are the blood-brain barrier (BBB), the diversity of excrescence, and the high infiltration rates of its cells.

I. INTRODUCTION:

One serious illness that poses a threat to life and health is cancer. According to the WHO report on cancer 2020, cancer was the second biggest cause of death globally in 2018 with 18.1 million diagnoses and 9.6 million deaths. By 2040, the frequency and mortality rate of cancer could almost double due to the growing worldwide burden of the disease. According to the World Health Organization, there are 20 to 60 cases of multiple sclerosis for every 100,000 people in Iran. The primary step in treating neurological disorders is the prolixity of medications across the blood-brain barrier. One of the best ways to address neurological diseases is to deliver medication mixtures to the central nervous system in a safe, effective, and focused manner. Because of their anatomical location and the presence of the blood-brain barrier (BBB), which prevents and regulates the penetration and accumulation of medications, brain excrescences provide additional levels of complication.

History:

Sir William Macewenz performed the first known brain tumor surgery in 1879 utilizing Lister's antisepsis methods.The patient survived for an additional eight years until passing away from Bright disease, an unrelated illness, which was caused by a meningioma tumor.Over the past century, brain tumor surgery has expanded rapidly thanks to advancements in technology, globalization, and training programs.Brain surgery started out cautiously but quickly gained traction thanks to advancements in cerebral localization, antisepsis, anesthetic, and hemostasis.Cerebral localization-based brain tumor surgery was first performed in the 19th century, predating imaging methods like computed tomography, magnetic resonance imaging, and X-rays.Formal neurosurgery began in India in 1949 at CMC, Vellore, during the post-independence period.

A significant turning point in the history of brain tumor surgery was the introduction of micro neurosurgery in the late 1960s, which improved safety profiles and results. Prognosis and survival have also been enhanced by developments in brain tumor imaging, surgical equipment (neuronavigation and intraoperative imaging), adjuvant therapy, and molecular tumor profiling. Using five historical development epochs—premodern (before to 1879), incubational (1879–1919), modern (1919–1967), microsurgical (1967–1999), and new millennial (from 2000 onward)—we analyze the rich history of brain tumor surgery from both a global and Indian viewpoint. Brain tumor surgery has a number of groundbreaking developments ahead of it, which will improve surgical results and patient quality of life. Rapmune and Mylotarg were both released in 2000. Additionally, the National Nanotechnology

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Initiative was launched in 2000 by the U.S. government, which the rest of the globe quickly adopted.

- **Diagnosis Of Brain Tumor:**

Tumors of the brain The WHO's GLOBOCAN Design 2008 assessment states that the prevalence of terrible brain cancer is around 3.5 per 100,000 people worldwide.Because of its poor prognosis, difficult control, and wide age distribution, brain excrescence poses a very serious risk to mortal health .Better individual CT and MRI procedures, a lower level of neurosurgeon vacuity, shifting patterns of access to medical care, individual changes, and changing medical approaches toward senior cases haveall contributed to the difficulty of interpreting increases in the prevalence of primary nasty brain excrescences, especially among the elderly .Although it has long been thought that a neural stem cell could eventually develop into a brain excrescence, no projected insulation of stem cells has been carried out. in excrescences from the brain. The neural stem cell marker can be expressed by brain excrescence cells.

> Brain Tumor Diagnosis Imaging Relevant brain imaging and histology are necessary to form an opinion on a suspected brain excrescence .Because of its resolution and enhancement with discrepancy agents, gadolinium-enhanced magnetic resonance imaging (MRI) is the preferred modality .Head and chine computed tomography (CT) is a good alternative to magnetic resonance imaging (MRI) if MRI is not possible (for example, due to metallic implants, bedded bias, or claustrophobia).However, CT has a lower resolution than MRI and is unable to detect lesions in the posterior fossa and chine.For opinion and staging, new imaging that resembles fluorodeoxyglucose positron emigration tomography, glamorous resonance spectroscopy, or glamorous resonance perfusion may be required.

- **Drug Delivery Systems Based on Nanotechnology Design:**

Nanoparticles can be utilized in targeted medication distribution at the site of complaint to improve medication bioavailability, targeted medication delivery to a specific spot, and uptake of medications that are not properly responsive . Untargeted and targeted pharmaceutical delivery systems are schematically compared. Using nanomaterials, some anti-cancer medications have been effectively developed, such as doxorubicin ,5-fluorouracil dexamethasone and paclitaxel . The glucocorticoid dexamethasone, which acts intracellularly, has been synthesized using polylactic/glycolic acid (PLGA) and polylactic acid (PLA) grounded nanoparticles. The chemotherapy drug dexamethasone has anti-inflammatory and anti-proliferative properties. Cytoplasmic receptors are bound by the medication, and the posterior medicine-receptor complex iscarried to the nexus where specific genes that regulate cell proliferation are expressed .The growth of vascular smooth muscle cells was completely suppressed by these drug-loaded nanoparticle formulations that deliver sophisticated drug boluses over an extended period of time.Similar to liposomes, micelles, or nanoparticles, colloidal medication delivery techniques have been widely used .

- **Cancer Treatment Using Nanomaterials:**

A)Nanoparticles Nanoparticles continue to have a great potential for the active delivery of medicines.Moreover, conjugating medications with nanocarriers enhances their bioavailability by shielding them from chemical or metabolic changes as they travel to the intended cells.Various kinds of inorganic nanocarriers were merged with colorful systems in this review.The various compositions of organic, carbon nanotube, and quantity blotches, as well as physical and chemical parcels, have been used for drug delivery operations.

(B) Particles that have a nanoscale size are known as nanoparticles.Nanoparticles (NPs) that have been extensively studied include metallic nanoparticles, extracellular vesicles (EVs), polymeric nanoparticles (PNPs), and monoclonal antibodies (mAbs) .Because of the versatility of polymeric nanoparticle-based therapies, they hold considerable promise for treating a variety of illnesses.

(c) Vesicles outside of cells Bilayer phospholipid vesicles, or EVs, typically have a size between 50 and 1000 nm. Colorful cell types continuously bury EVs, which vary in size, origin, and content. EVs are categorized into three main types based on their origin: apoptotic bodies, microvesicles, and exosomes. Exosomes are nanoscale patches between 40 and 200 nm. EVs are used in long-distance deployments and contain DNA, RNA, and protein . Exosome NPs may easily incorporate with target cells and evade vulnerable surveillance because their membranes include similar lipids and motes to those of their original cells. Additionally, exosome NPs are natural carriers that can be mixed with anti-tumor compositions and styles. In order

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to treat cancer, gene remedies use DNAs and RNAs.

A number of methods areinvestigated in gene therapy, such as the restoration of a shifted proto-oncogene resembling p53. Phosphatase and tensin homolog (PTEN), growth 4 (ING4), and gene editing employing the clustered regularly interspaced short palindromic reprises (CRISPR)-associated proteins (Cas) system, which inhibits important oncogenes.

(D) Nanomaterials based on lipids Lipid-grounded nanomaterial research is booming, and three primary ordersliposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs)—are receiving a lot of interest in both current research and clinical studies. Considered the first enclosed bitsy phospholipid bilayer nanosystem, liposomes were authorized in 1965.

Liposomes are globular vesicles that are mostly made of uni- or multi-lamellar phospholipids. They typically range in size from 20 nm to more than 1 um.We use lipid-grounded bandy in this chapter.

- **Techniques to Get Pass the Blood-Brain Barrier :**

A) Surface Alteration to Get Past the BBBSimilar to paracellular routes, receptor-intermediate transport, transporter-intermediated transport, adsorption-intermediated transport, cell-piercing peptides, etc., there are many different transport mechanisms for substances moving across the blood-brain barrier.Different face variants can be used to fluently control the appropriate BBB crossing capability of nanomedicine carriers, which have fluently controllable face packages .With their great particularity and selectivity, receptor-intermediated endocytosis (RMT) nano-drug delivery devices are among the most developed brain-targeting techniques.Similar to transferrin receptors (TRs), scavenger receptors (SRs), insulin receptors (IRs), and lipoprotein receptors (LPRs), some receptors have limited or no expression in normal tissue but are highly expressedin the blood-brain barrier, brain excrescence cells, or associated blood arteries.

- **Techniques for Improving the Targeting of Brain Tumor Cells:**

The targeting of brain nano medication delivery systems to brain tumor regions should be improved in order to lessen the harm that nanomedicines do to the immune system and normal brain function. At the moment, active targeting techniques are mostly used to target brain tumors, whereas passive targeting techniques are used to increase medication accumulation at tumor sites [48]. Passive, active, and magnetic targeting will be the main topics of this section.

(A) Targeting Passively Enhancement of permeability and retention (EPR) products is essential for passive targeting of brain excrescences. In the pathogenic state of brain excrescences, edema, swelling, and elevated brain pressure may cause some disruption of the blood-brain barrier.

(B) Targeting Actively Targeting by ligand-ligand-receptor-specific relationships between a medication or medication carrier and the target is sometimes referred to as "active targeting." There are some receptors that are almost connected to the growth of excrescence. They are either not expressed at all or expressed at low levels in other apkins, but they are mostly expressed in brain excrescence cells or in blood arteries close to brain excrescences. Therefore, the receptors can direct medications or drug carriers to enter excrescence cells or total at brain excrescences by altering the appropriate ligands on their faces.Although this research also discussed the receptor-intermediated targeting method in the prelude of the brain targeting strategy, these receptors are expressed in the blood-brain barrier and brain excrescences, whichincreases the brain targeting of medications;

- **Crossing the Blood-Brain Barrier with Nanomedicine Delivery:**

By coating NPs with polysorbate (Tween) surfactants, nano-reprised medications can be spread across the blood-brain barrier.The delivery of therapeutic drugs to the brain is more effectively accomplished by cationic liposome carriers than by neutral or anionic liposomes.Anionic and cationic NPs with high attention, however, compromise the integrity of the BBB, but neutral and anionic **NPs** with low attention do not have any detrimental effects.Chitosan-derived NPs have the ability to relax the BBB's tight junctions.Similar to sodium dodecyl sulfate, a number of surfactants can cause the blood-brain barrier to breach.The BBB flashes open when toxins delivered by surfactants or nanocarriers are present.

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- **Treating Field (TTFields):**

"Optune" (NovoTTF-100A Device) was created to deliver an interspersing electric field at a frequency of 100–300 kHz.For direct operation on the shaved head,

TTFields uses two pairs of flexible transducer array panels, each of which includes nine insulated electrodes.Through mitotic arrest, aberrant spindle conformation, apoptosis, and stalling cell mitosis in interphase (G1/S/G2) over an extended period of time, TTFields prevent cell growth.

TT Field is used as a monotherapy for intermittent GBM after all other alternatives, including surgery and radiation, have been exhausted.

- **Personalized Nanocarrier Systems for Brain Tumor Treatment Methods:**

1. Carbon Nano Tubes (CNT) PEGylated oxidized multi-walled carbon nanotubes with glioma-bearing male Balb/c mic Doxorubicin IN order to provide doxorubicin for the treatment of brain malignancies, these oxidized MWNTs possess important dual-targeting carriers.
2. Dendrimers' Mice with Brain TumorsDNA NPs, PAMAM-PEG-Argiope Temozolomide A non-viral delivery method for gene therapy for brain tumors is dendrimers.
3. Paclitaxel-loaded microbes U87MG glioblastoma-bearing naked mice c(RGDyK)-PEG-Paclitaxel the treated mice's survival rate was noticeably higher than that of the comparable treatment options.
4. The 3D mathematical model of tumor growth for liposomes

TemozolomideDrugs encapsulated in liposomes have decreased toxicity and increased bioavailability

- **Current Methods for Brain Cancer Compared to Nanotheranostic Surgical excision is one of the conventional methods of treating cancer:**

Cancer is traditionally treated with chemotherapy, radiation therapy, and surgical excision.

With the advancement of current technology, several treatment modalities, including gene therapy, photodynamic therapy, vulnerable therapy, angiogenesis impediments remedy, and hyperthermia remedy, have recently been investigated.

The ultimate goal is to identify and describe illnesses early on.When diagnosing brain cancer, magnetic resonance imaging (MRI) is the most efficient method.While CT or CAT scanning can also be used, MRI has mainly taken its position due to its high temporal and spatial resolution and incalculable anatomical features.

Positron emigration tomography, or PET, has been used in conjunction with molecular imaging in more recent times.

PET can more effectively describe brain excrescences by examining metabolic processes like blood input, oxygen metabolism, DNA conflation or enzyme exertion, and receptor list.

Cancer is also one of the most diverse diseases, with a wide range of phenotypic manifestations at various organ locations, when compared to other illnesses.

The main obstacles to the complete eradication of this horrible ailment are the inability of efficient individual instruments to detect excrescences in the early stages with efficient treatment modalities and many venom.

- **Symptoms:**

The signs and symptoms of a brain tumor can vary and are mostly determined by the tumor's size, location inside the brain, and rate of growth. *A headache * Difficulty thinking, speaking, or finding the right words * Muscle weakness or fatigue * Disorientation or confusion in daily situations * Sensory alterations, such as hearing and vision problems or loss of smellLoss of memory

II. CONCLUSION:

Due to its aggressive nature and poor prognosis, gliomas are still difficult to completely cure.Even though chemotherapy is an indispensable method for treating brain excrescences in clinical settings, the BBB and BBTB remain the primary barriers.

Nanotechnology-based medication delivery systems can significantly improve medication delivery efficiency and lower the high levels of toxic side effects brought on by traditional chemotherapy.Accurate medication delivery can be achieved by incorporating a discrepancy agent into the medication delivery system, which can also aid see the brain excrescence therapy process.

Nevertheless, medication failure is likely to occur since glioma cells are resistant to medications.Furthermore, some drug delivery

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systems struggle with the body's natural chemicals, which results in poor drug delivery efficacy.

Rapid-fire declination accessories are commonly utilized in nanoparticle design to decrease the toxicity of the medicine carrier itself.

This will also cause the medications to decelerate before they reach the action location.Therefore, the primary trend at the moment is the creation of multifunctional and multi-targeted nanomedicine therapeutic systems.

Certain gene therapy and antiangiogenic therapy approaches can be employed as tactics to combat glioma's resistance to medication.

Because of its high biocompatibility, inherent capacity to cross the blood-brain barrier, and structural and functional complexity similar to the original natural patron, a biomimetic nanomedicine system can successfully protect the medication from declination. It has great potential as a medication carrier.

III. SUMMARY:

Cytotoxicity and multidrug resistance are obstacles to cancer treatment.By enhancing medicine delivery and focusing on cancer cells, nanomaterials provide hope.The blood-brain barrier and tumor variety make brain cancer especially difficult.Current therapies have serious adverse effects and are not very successful.

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