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Brain Cancer: Nanoparticle Based Drug Delivery System

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ABSTRACT

Brain cancer is the consequence of abnormal growths of cells in the brain and fourth most common cause of cancer death. Nanotechnology is the promising options in the treatment of brain cancer. Nanoparticle (NP) based drug delivery system has been reported scientifically for the treatment of brain cancer. Therefore nanoparticles are attracted increased attention for treating brain cancer. This review provides to present the reader with an overview of brain cancer and achievements of nanoparticles (NPs) based drug delivery system for treating brain cancer.

Key words: Brain cancer, Nanotechnology, Nanoparticles, Drug delivery system

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INTRODUCTION

A cancer is a mass of abnormal cells. Brain tumors are classified as primary tumor and secondary tumor. The primary tumor occurs in the brain and can be noncancerous (benign) or cancerous (malignant). The secondary tumor arises in another part of the body and spread to the brain and secondary tumor is more common in the people. The brain tumors may require treatment because it can grow on normal brain structures in the confined space inside the skull. The signs and symptoms of brain tumor are headaches that often are worse in the morning, seizures (convulsions), loss of feeling in the arms or legs, abnormal eye movements and changes in speech. Treatment for a brain tumor generally involves surgery, radiation therapy and chemotherapy [1, 2]. Surgery is the most common treatment and neurosurgeon performs a craniotomy, which involves making an opening in the skull in the patient. The surgeon can perform a biopsy, in which a small piece of the tumor can be removed. Radiation therapy can be useful to destroy tumor tissue that cannot be removed with surgery or to kill cancer cells that may remain after surgery. Chemotherapy can kill cancer cells [3].

Brain Cancer: Nanotechnology

In 'hole-in-the-skull' method, brain cancers are inoperable due to their location within critical brain regions or because they are too small to detect. Nanotechnology offers a platform for a smart drug approach to fighting brain tumors. Nanoparticulate drug delivery could be the delivery of the drug payload into the brain. But, crossing the brains protective shield (blood-brain barrier) is a major challenge [4]. The targeted Nanoparticle based drug delivery systems that are able to cross blood-brain barrier and ability of drug loaded nanoparticle can destroy brain cancer cells. This review article expresses the achievement of nanoparticulate drug delivery for the treatment of brain cancer.

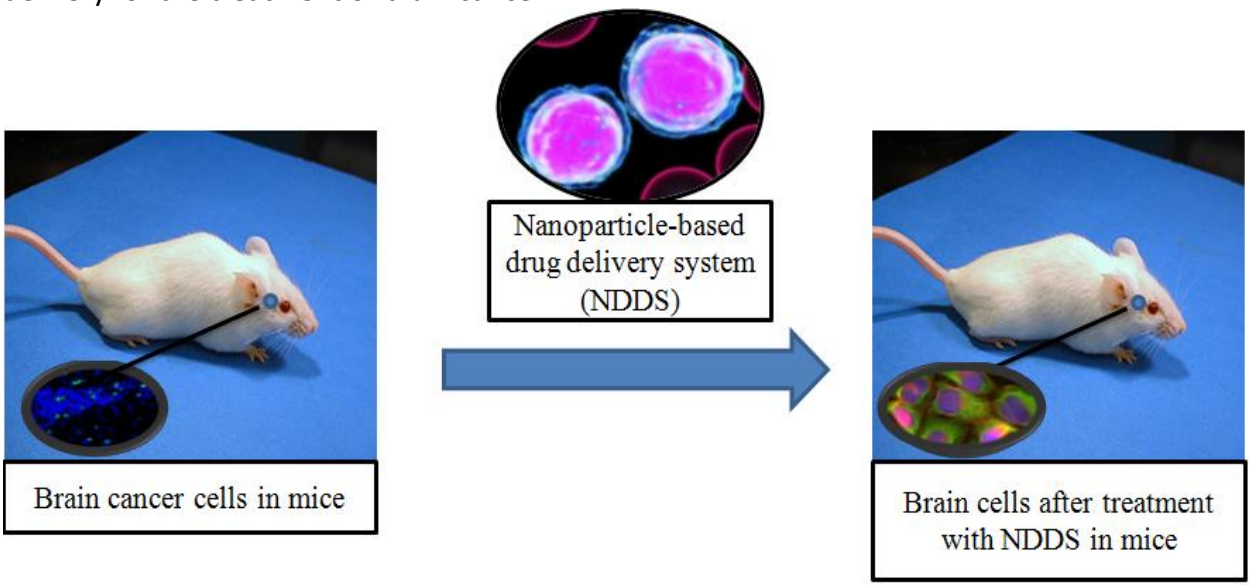

Figure 1: Nanoparticles-based drug delivery system

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Nanoparticle based drug delivery system for brain cancer

Glioblastoma multiforme (GBM) is the most common malignant primary brain tumor in humans. The effect of TNF-related apoptosis inducing ligand (TRAIL) conjugated nanoparticles (NP) was investigated on the glioma cells. TNF-related apoptosis inducing ligand (TRAIL) was conjugated to magnetic ferric oxide nanoparticles (NP) by binding the TRAIL primary amino groups to activated double bonds present on the nanoparticle surface. The results indicated that conjugation of TRAIL to NP increased its apoptotic activity against human U251 glioma cell, as compared with free recombinant TRAIL. In addition, NP-TRAIL was found in the tumor site and induced a significant increase in glioma cell apoptosis, a decrease in tumor volume, and increased animal survival. Therefore, NP-TRAIL could be used as a targeted anticancer agent for the treatment of glioblastomas [5]. Noscapine can be used for the treatment of brain cancer. Because, it can crosses blood-brain-barrier and inhibits proliferation of glioblastoma cells. But, short plasma half-life of noscapine required the administration of multiple injections for successive chemotherapy. Therefore, Noscapine conjugated with poly (ethylene)-glycol solid lipid nanoparticles (N-PEG-SLN) were developed and studied for its anticancer activity in U87cells and plasma half life of (N-PEG-SLN) also studied. The study expresses that enhanced subG1 population were observed in U87cells. Plasma half-life of N-PEG-SLN was enhanced up to ~11-fold. So, N-PEG-SLNs could be useful for the management of brain cancer [6]. Early detection of brain tumors is great importance for improving treatment outcomes. Magnetic resonance imaging (MRI) is a prominent, clinically-relevant imaging modality because of its excellent tissue contrast resolution. MRI utility can be enhanced with the use of magnetic iron oxide nanoparticles, which can function as both a contrast agent for imaging and as a drug delivery vehicle for treating brain cancer [7].

Therapeutic effect of glioma is limited due to poor permeability of drugs across the Blood-Brain Barrier (BBB).Paclitaxel loading ANG-PEG-NP was developed as a dual targeting drug delivery system for glioma treatment based on low density lipoprotein receptor related protein (LRP) receptor. This paclitaxel loading-ANG-PEG-NP could across BBB through LRP-mediated transcytosis and then targeted the glioma via LRP-mediated endocytosis. Further, there is no acute toxicity with intravenous administration with a dose of 100 mg/kg blank ANG-PEG-NP per day for a week. This study indicated that paclitaxel loading ANG-PEG-nanoparticle could be a considerable brain targeting drug delivery system for glioma treatment [8]. FePt nanoparticles with different surface coatings and components were synthesized using oleic acid/oleylamine (OA/OA) as capping agent. The surface coatings and components of the FePt nanoparticles on the proliferation of glioma cells was investigated through MTT assay using glioma cell lines such as glioma U251 cells, neuroglioma H4 cell and astrocytoma U87 cells as in vitro models. The results expressed that the proliferation of glioma cells was suppressed by lipophilic FePt-OA/OA nanoparticles in a time- and/or dose-dependent manner, The IC_{50} value of FePt-OA/OA NPs on the three glioma cell lines was approximately 5-10 μg mL^{-1} after 24 hours incubation. Therefore, it indicates the engineering of the surface coating, FePt nanoparticles can be developed as therapeutic agents for malignant gliomas [9]. Nano-drug delivery system plays a major role by delivering the contrast agent in a targeted manner to specific tumor cells, leading to improvement in the visualization of tumor cells. Targeted MR contrast agent,

transferrin-conjugated superparamagnetic iron oxide nanoparticles (Tf-SPIONs) was developed for brain glioma detection. MR imaging indicated that contrast change of brain glioma before and after administration of Tf-SPIONs in C6 glioma rat model. Enhancement of brain glioma was clearly seen even 48 h post injection, due to the retention of Tf-SPIONs in cytoplasm of tumor cells which was proved by Prussian blue staining. These results suggested that Tf-SPIONs could be used for targeting MR contrast agent for brain glioma [10]. Polysorbate-80 coated temozolomide-loaded PLGA-based superpara-magnetic nanoparticles (P80-TMZ/SPIO-NPs) were developed as diagnosis agent for malignant brain glioma. The mean particle size of P80-TMZ/SPIO-NPs was found to be 220 nm. Anti-proliferative effect of P80-TMZ/SPIO-NPs was investigated in C6 glioma cells. Further, cellular uptake of P80-TMZ/SPIO-NPs was determined in C6 glioma cells by fluorescence microscopy, Prussian blue staining and atomic absorption spectrophotometer. In vitro MRI scanning analyses expressed that P80-TMZ/SPIO-NPs could be employed as a MRI contrast agent. The results suggested that Polysorbate 80 coated temozolomide-loaded PLGA-based superparamagnetic nanoparticles could be used as diagnostic carrier of brain cancer [11]. Curcumin is an herbal drug and can induce apoptosis of glioma cells. The greatest challenge of curcumin is exhibiting low bioavailability. Curcumin-loaded glyceryl monooleate (GMO) nanoparticles (NP) coated with the surfactant Pluronic F-68 and vitamin E D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) was developed for brain delivery. The results indicated that curcumin-loaded nanoparticles induced a greater percentage apoptotic cell death in glioma cells and enhanced bioavailability of curcumin in blood serum and brain tissue when delivered by curcumin-loaded GMO NPs in a rat model. This study suggested that curcumin-loaded GMO NPs could be a considerable approach for glioblastoma therapy [12].

CONCLUSION

Despite considerable advancements in the treatment of brain cancer in recent years with modern radiation, surgical techniques as well as chemotherapy, treatment results are mostly unsatisfactory. Nanoparticle (NP) based drug delivery system showed a greater achievement in the treatment of brain cancer. Nanoparticle based drug delivery system has been well studied in animal model or using brain cancer cell lines. However, still nanoparticle based drug delivery system for way from clinical trial applications. Therefore, clinical trial studies of nanoparticle based drug delivery system may be mainly considered for the treatment of brain cancer to get sufficient scientific data for clinical applications.

REFERENCE

[1] Dearlove JV, Fisher PG, Buffler PA. J Pediatr Hematol Oncol 2008; 30(1): 8-14.
[2] Bobek-Billewicz B, Jurkowski MK, Romanowicz G. Przegl Lek 2005; 62(1): 54-60.
[3] Dhermain F, Ducreux D, Bidault F, Bruna A, Parker F, Roujeau T, Beaudre A, Armand JP, Haie-Meder C. Bull Cancer 2005; 92(4): 333-42.
[4] Nduom EK, Bouras A, Kaluzova M, Hadjipanayis CG. Neurosurg Clin N Am 2012; 23(3): 439-449.

[5] Perlstein B, Finniss SA, Miller C, Okhrimenko H, Kazimirsky G, Cazacu S, Lee HK, Lemke N, Brodie S, Umansky F, Rempel SA, Rosenblum M, Mikklesen T,Margel S, Brodie C. Neuro Oncol 2013; 15(1): 29-40.
[6] Madan J, Pandey RS, Jain V, Katare OP, Chandra R, Katyal A. Nanomedicine. 2012 (*In Press*).
[7] Wang J, Huang Y, David AE, Chertok B, Zhang L, Yu F, Yang VC. Curr Pharm Biotechnol 2012; 13(12): 2403-2416.
[8] Xin H, Sha X, Jiang X, Zhang W, Chen L, Fang X. Biomaterial 2012, 33(32): 8167-8176.
[9] Sun H, Chen X, Chen D, Dong M, Fu X, Li Q, Liu X, Wu Q, Qiu T, Wan T, Li S. Int J Nanomedicine 2012; 7: 3295-3307.
[10] Jiang W, Xie H, Ghoorah D, Shang Y, Shi H, Liu F, Yang X, Xu H. PLoS One 2012; 7(5): 373-376.
[11] Ling Y, Wei K, Zou F, Zhong S. Int J Pharm 2012; 430(1-2): 266-75.
[12] Kundu P, Mohanty C, Sahoo SK. Acta Biomater 2012; 8(7): 2670-87.