The Application of Magnetic Nanoparticles as a Targeted Therapy in Cancer Treatment

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ABSTRACT

Due to the defects of traditional cancer therapies, nanotechnology has been widely applied to treat tumors. Much achievement has been achieved. Since the magnetic nanoparticles (MNPs) has been invented, many researchers have developed many MNPs. In addition, targeted drug delivery and magnetic hyperthermia are also well studied. Various breakthroughs have been made in this field. MNPs have been widely used, and both theoretical and applied research have developed rapidly. This paper discussed the research progress on MNPs. It can efficiently deliver drugs to tumor tissue in a targeted manner. Nowadays, dendrimer polymers as a promising biomedical material were used to enhance the versatility of magnetic nanoparticles to improve cancer therapies. In addition, the mechanisms of targeted drug delivery by MNPs were discussed. The current knowledge, and perspectives of application of MNPs in cancer treatment in this paper could provide a good reference for the future research of cancer diagnosis and treatment.

Keywords: *Magnetic nanoparticles, Targeted therapy, Cancer treatment, Magnetic hyperthermia.*

1. INTRODUCTION

In recent years, cancer has become is the second leading cause of death threatening human health. According to Sung et al. (2021) research, there are approximately 19.3 million cancer cases in 2020. This number will be increased to 22 million by 2030. Therefore, cancer prevention and treatment has become a very important topic. In the " China’s cancer prevention and treatment three-year action plan", the National Health Commission of the People's Republic of China mentioned that cancer screening tests and improve cancer treatment are the main measures to prevent and treat cancer [1]. There are 10 major types of cancer treatment: i.e., Biomarker Testing for Cancer Treatment, chemotherapy, hormone therapy, hyperthermia, immunotherapy, photodynamic therapy, radiation therapy, stem cell transplant, surgery, and targeted therapy [2]. The implementation of treatment for the patients usually depends on the type of cancer they have. There are pros and cons for each treatment for cancer. Therefore, choosing an appropriate treatment plays a significant role in cancer early detection and promoting cancer early diagnosis.

With the improvement of nanotechnology in the last decade, it has brought a new perspective for cancer diagnosis and treatment. There are two major defects of the original cancer treatment methods: 1) how to improve the accuracy of early cancer detection and treatment; 2) how to conduct an effective follow-up treatment and evaluate the effectiveness of treatment. These two major defects could be overcome by nanotechnology. Nanomedicine brings a new concept of integrated diagnosis and treatment to cancer treatment. Nanoparticles are designed and it can be delivered to target tumor cells. It has a relatively smaller damage on normal tissue because of a less pan-toxic effects. At present, the nanoparticles there are many nanoparticles have been developed and applied in cancer treatment such as quantum dots, magnetic nanoparticles (MNPs), liposomes and lipid nanoparticles (LNPs), and carbon nanotubes [3]. Among these nanoparticles, magnetic nanomaterials have been widely studied due to their unique superparamagnetic and magnetic responsivity as well as their properties of nanoparticles, such as a nano-level particle size and large specific surface area. Magnetic nanomaterials can aggregate in a specific part in a constant magnetic field. It also can vibrate at a high speed in an alternating magnetic field to generate heat. Its advantages allow them being a very worthwhile research and promising nanoparticle for cancer treatment as a targeted therapy.

Few studies have been conducted in this field due to the rapid growth of nanotechnology. The purpose of this study is to learn the application of magnetic nanoparticles as targeted therapy in cancer treatment. The objectives are to: 1) discuss the research progress on MNPs; 2) discuss the current knowledge and perspectives of application of MNPs in cancer treatment as a targeted therapy.

2. RESEARCH PROGRESS ON MAGNETIC NANOPARTICLES

In the past decades, MNPs (i.e., Superparamagnetic iron oxide nanoparticles) have been widely used as magnetic resonance imaging contrast agents. MNPs' medicinal applications have exploded in recent years [4]. Magnetic targeting is an advanced approach for delivering drugs to tumor tissue in a targeted manner [5]. Magnetic force can improve the retention time thereby increasing drug in combination with the surface of MNPs in tumors. MNPs can be classified as monometallic nanoparticles, bimetallic nanoparticles, and magnetic alloy nanoparticles [6]. The monometallic nanoparticles are iron nanoparticles such as Fe_3O_4 and γ-Fe_2O_3. The bimetal particles mainly include $CoFe_2O_4$, $ZnFe_2O_4$ and other substituted nanoparticles of iron tetroxide (the general formula is MFe_2O_4, in which M is mostly metals with +2 valence, such as Mn, Co, Zn, Mg, etc.). Magnetic alloys mainly are alloys of FePd, $CoPt_3$ and other platinum group metals with magnetic metal elements. Among these particles, iron oxide nanoparticles such as Fe_3O_4 and γ-Fe_2O_3 are the most commonly used. Nowadays, some researchers used dendrimer polymers to enhance the versatility of magnetic nanoparticles to provide a platform for improved therapies. Dendrimer is one of appealing materials for biomedical applications. They have a hyperbranched symmetrical structure which can be used as carriers for therapeutic cargos. Figure 1 shows the manufacturing process to generate glutamic acid-coated Fe_3O_4 nanoparticles [7].

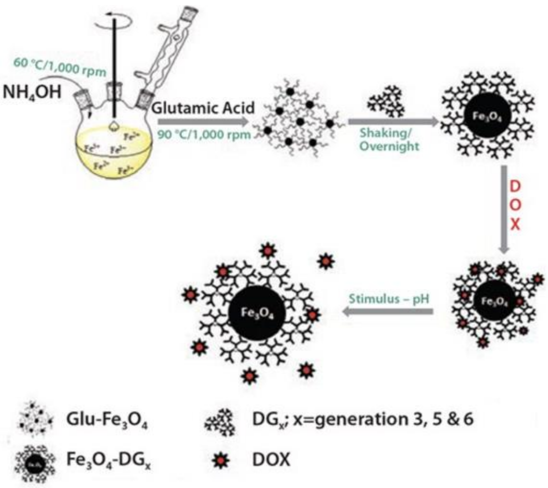

Figure 1 Manufacturing process of the glutamic acid-coated Fe_3O_4 nanoparticles [7].

3. THE APPLICATION OF MAGNETIC NANOPARTICLES IN CANCER TREATMENT

Targeted drug delivery is one of the major applications of MNPs in cancer treatment. Due to the uncertainty of the cancer's location, some tumors such as pancreatic cancer are embedded in the organs, which make it difficult for drug delivery that normally circulate in the blood to enter the lesions. Most of the anticancer drugs that have been used in clinical practice are broad-spectrum anticancer drugs, such as doxorubicin, methotrexate, cisplatin and docetaxel [8]. They usually have poor specificity and targeting and are easy to circulate continuously in the body. They can cause unnecessary damage to normal tissues during the delivery process. Therefore, an effective alternative for targeted drug delivery has become one of the hotspot research topics.

MNPs can overcome these biological barriers and limitations as an effective alternative for targeted drug delivery. Targeted drug delivery by MNPs can be divided into two categories: passive targeting and active targeting. Passive targeting means that the non-specific properties such as the charge or pH of the carrier make the nanoparticles aggregate in a specific location. Active targeting is based on the specific action of antigen-antibody reaction or external magnetic field to complete the targeting drug delivery process. Table 1 shows the advantages and disadvantages of passive targeting and active targeting for targeted drug delivery by MNPs in tumors [9]. Active targeting has received more attention due to its strong controllability and observability properties.

Table 1. Advantages and disadvantages of passive targeting and active targeting for MNPs accumulation in tumors [9].

Tumor targeting strategy	Advantages	Disadvantages
Passive targeting	Universal	Limited efficacy
	Low cost	Modest specificity
Active targeting	High efficacy	Drug resistance
	High specificity	High cost

4. MAGNETIC HYPERTHERMIA FOR CANCER TREATMENT

Magnetic hyperthermia can kill the tumor cells according to the different sensitivity of normal tissues and tumor tissues to temperature by utilizing the characteristics of magnetic nanoparticles that vibrate and generate heat in an alternating magnetic field. Due to the lack of blood supply inside the tumor tissue and the exchange of substances and energy with other normal tissues, accumulated in the tumor lesion through the targeting effect under the action of the alternating magnetic field, the magnetic field. The temperature inside the tumor cells rises rapidly after nanoparticles generate a large amount of heat. Studies indicated that necrotic mechanisms of cells are activated, thereby causing the death of cancer cells, when the temperature of tumor tissue reaches 43-47 °C. The side effects of this method are small, especially for the normal cells. In vivo studies have shown that the modified magnetic nanoparticles can effectively kill breast, prostate, colon, and brain cancers through the magnetic hyperthermia.

5. CONCLUSION

With the development of modern medicine, many cancers can be cured, even though the pathogenesis of cancer is still unknown. The application of nanoparticles in cancer treatment is being developed, underestimate exponential growth. There are more and more emerging methods for cancer treatment. One of the promising cancer treatments is MNPs as a targeted therapy. Since the MNPs has been invented, many researchers have developed many MNPs. In addition, targeted drug delivery and magnetic hyperthermia are also well studied. This paper discussed the research progress on MNPs. It can efficiently deliver drugs to tumor tissue in a targeted manner. Nowadays, dendrimer polymers as a promising biomedical material were used to enhance the versatility of magnetic nanoparticles to improve cancer therapies. In addition, the mechanisms of targeted drug delivery by MNPs (passive targeting and active targeting) were discussed. Passive targeting can use non-specific properties to aggregate the nanoparticles in a specific location. Active targeting is based on the specific action of antigen-antibody reaction to complete the targeting drug delivery process. This paper reviewed different aspects of MNPs, and it provides a good reference for the future research of cancer diagnosis and treatment.

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