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Mini Review

DEVELOPING ORGANIC AND INORGANIC NANOMEDICINE FOR CANCER THERAPY

Xinwei Cheng*

Department of Biomedical Engineering, The Ohio State University, Columbus, OH 43210, USA

ABSTRACT

The application of nanomedicines has proved to be effective for the therapy of various types of cancer compared to conventional treatments such as chemotherapy and radiation therapy. The nanomedicines can treat various cancers with the precise target without affecting the normal cells. In addition, by utilizing of enhanced permeability and retention (EPR) effect, nanomedicines can selectively targeting disease site and yield very promising therapeutic results for cancer treatment. Among all available nanomedicines, organic materials such as polymers are widely used in recent decades as biomaterials for their favorable properties like excellent biocompatibility, easy design and preparation, several types of structures and interesting biomimetic character, which warrants the further evaluations on these kinds of innovative material. Inorganic nanoparticles such nanogold also demonstrated the ability to target cancer and can be employed as both therapeutic and imaging agents. This mini-review will give a brief discussion of using inorganic and organic nanoparticles for the treatment of cancer.

Keywords: Nanomedicine, self-assembly, drug delivery, nanoparticle, nanogold, anticancer drugs

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*Address for Correspondence

Department of Biomedical Engineering, The Ohio State University, Columbus, OH 43210, USA; Tel.: 614-286-3918.
E-mail: cheng.726@buckeyemail.osu.edu

INTRODUCTION

Cancer has become one of the most deadly diseases due to its fast abnormal cell growth. Change in the DNA sequence by mutation and thereby altering the genetic expression is the root cause of cancer. This mutation could result from several external factors like exposure to UV light or other carcinogenic compounds like tobacco. DNA methylation occurs because of the mutation, in which a methyl group is added to the cytosine and adenine of DNA.

At present, chemotherapy is the most common and widely used treatment for cancer¹⁻⁴. Nanomedicines, use the latest nanotechnology for many medical applications⁵⁻⁷. According to Heim & Mitelman⁸, nanomedicines have been proven effective in treating and preventing cancer compared to other forms of treatments⁹. The drugs used in the nanomedicines are prepared in nanometers and thus can be directed to the site of cancer accurately without many side effects^{10,11}.

CURRENTLY USED METHODS FOR TREATING CANCER

In order to treat cancer effectively, it is quite necessary to diagnose cancer at the early stage¹². Due to the relatively immature diagnose technique, it is hard to detect the cancer at an early stage¹³. Fortunately, there are multiple potent therapeutic techniques available for cancer treatment.

Surgery is one of the most common approaches used for removing the tumor at an early stage, which prevents the tumor cells from spreading to other normal organs. Chemotherapy, radiation therapy, hormonal therapy, and immunotherapy are conventional therapies for cancer treatment¹⁴. During chemotherapy, many anti-cancer drugs, such as docetaxel, doxorubicin, cyclophosphamide, etc, are administered into the human body to inhibit cell proliferation and metastasis¹⁵. Depending on the different characteristics of cancer, various drugs are applied to the patients during the treatment. This kind of therapy is usually

combined with some other form of treatments, such as radiation therapy to improve the efficacy.

The effectiveness of this treatment also depends on the type of cancer and what stage of cancer has entered¹⁶. Flygare et al believed that if the treatment has been given at an early stage, cancer would be sensitive to many kinds of treatments¹⁷. Leukemia, a type of cancer occurring in the bone marrow, which causes a rise in the number of white blood cells, can be treated with chemotherapy with a good outcome. However, during the treatment of brain and skin tumors, chemotherapy has not been reported to be very effective¹⁸. This may be due to the poor permeability of Blood- Brain Barrier (BBB) and the drug resistance produced by p-glycoprotein.

In addition, it is essential to have the “perfect” dosage of the drugs that are incorporated into chemotherapy¹⁹. As these drugs are very toxic and efficient, overdosage can be very harmful to normal organs of cancer suffering patient. While low dosage may not even have effects on the cancerous cells and tissues. Therefore, it is significant to have this “perfect” drug dosage, which highly depends on the stage of cancer, body surface area, body mass, height, and age of a patient²⁰. It has been reported that the chemotherapy often related to some side effects without the targeting, which will cause damage to other normal organs²¹. In most circumstances, patient receiving this treatment often suffer from a headache, nausea, diarrhea, constipation and abdominal pain. Moreover, the immune system is usually impaired by this non-targeting effect shown as the vastly decreasing white blood cells. Hair loss is another common side effect resulted from the inhibition of hair cells from dividing normally.

Radiation therapy is another technique that can be applied to the treatment of cancer. Briefly, the cancerous cells are exposed to ionizing radiation that can potentially kill those cells. According to Mi²², this therapy is effective if the cancer is localized to a restricted area without metastasis. This therapy causes damage to the DNA of the cancerous cells and thereby inhibits the cell proliferation.

Radiation therapy can be painless, which is different from chemotherapy. Nevertheless, common side effects, such as nausea, damage to the epithelial tissues, and infertility, are still presented.

USEFULNESS OF NANOMEDICINES FOR CANCER THERAPY BASED ON EPR EFFECT

The Enhanced Permeability and Retention (EPR) effect is a unique property. To be more specific, due to the differences of pathophysiological and anatomical in solid tumors, nanosize drugs tend to leak out of the loose tumor blood vessel easily and accumulate in solid tumors²³. The EPR based cancer treatment has become highly effective and offered a broad range of potentiality to the patients²⁴.

The side effects are similar to other common cancer treatment²⁵. According to Cha²⁶, the small sizes of nanomedicines with targeting ligand facilitate their binding to the cancerous cells accurately and thus can yield satisfactory result compared to conventional treatments.

The tumor cells have their own characteristics. They are able to attract the blood vessels to provide nutrition and oxygen, which will boost angiogenesis. In addition, tumors have a poor lymphatic drainage system that leads to the variable retention rate produced by high interstitial pressure. Due to these merits, nanomedicines often easily leak out of the blood vessel and enter the actual tumor tissues²⁷. Eventually, because of the high retention rate of the tumor, once the tumor tissues have taken up the nanomedicines, it is tough to escape from the tumor again²⁸.

USE OF POLYMER NANOPARTICLE FOR TREATING CANCER

In the field of smart drug delivery, polymer plays an important role, in its ability to deliver therapeutic agents directly to the site of action with high efficiency^{29,30}. Thus, the delivery system of the smart drug has become successful by the application of advanced polymer science in the field of nanobiotechnology^{31,32}. It possesses some valuable features, such as sustained and controlled release, targeted delivery^{33,34}. There are several micro-scale and nano-scale sized particles that are utilized in biological applications³⁵⁻³⁸.

In addition, many polymeric nanoparticle delivery systems are used in the therapeutic treatment of cancer³⁹⁻⁴¹. According to Kim et al⁴², the properties of the nanoparticle systems need to be adjusted according to the characteristics of the tumor. The types of nanoparticle systems explored for applications in cancer therapy include the dendrimers, polymers as well as the polymeric nanoparticles. The increasing number of interests in modifying the polymeric chemical systems gives them a direction for the targeted and therapeutic aspects⁴³. Several polymeric systems have been developed into therapeutic platforms, which include the solid polymeric nanoparticles and polymeric micelle. The function of the nanoparticles was to assist achieving the extended circulation time of drug and reducing the nonspecific tissue distribution. The negatively charged nanoparticles are more efficient than the positively charged ones and the size of these particles range from 1-100 nm that help to increase the phagocytic capability of the cell and thereby enhancing the drug delivery system.

USE OF GOLD NANOPARTICLE FOR CANCER THERAPY

Nanoparticles have been developed as it possesses valuable impact on the treatment of various diseases⁴⁴⁻⁴⁶. It has been reported that gold nanoparticles are able to absorb a certain wavelength of light and produce greatly increased temperature⁴⁷. This is one of the very effective thermal therapies. Due to their increased atomic mass, the absorption wavelength

can also shift. This is quite different from the soft tissue cells that are not able to absorb the extensive amount of radiation during the treatment. Thus, as per Hainfeld et al stated, an increase in the dose of radiation is possible using the gold nanoparticles for treating tumors and cancers when gold nanoparticles are heated up⁴⁸.

In the field of nanotechnology, nanoparticles are optimized on their surface, size, zeta and the inner phase to treat various types of cancer⁴⁹. With specific surface medication, drugs have increased their potential in targeting the site of action without causing much side effects. As stated by Maeda et al³³, a 5-nm gold nanoparticle has been conjugated to cetuximab covalently along with gemcitabine for the treatment of pancreatic cancer. In order to decrease the possibility of affect normal healthy cells during the treatment, gold nanoparticles are usually coated with an antibody that is able to recognize specific receptor on target cancer cell. According to Alhasan et al⁵⁰, the particle size of PEG-coated gold nanoparticles around 130 nm in diameter are observed to be utilized for treating cancer-based on the EPR effect⁵¹. Effect of gold nanoparticles during cancer treatment is evaluated based on the color and distance. It is generally believed that gold nanoparticles are not toxic, which enhances their use in the various treatment processes⁵². Also, gold nanoparticles have also been employed as imaging modalities to detect cancer cells due to the enhanced scattering ability upon absorbing of radiation. Another positive impact of gold nanoparticles is by utilizing antibody for Epidermal Growth Factor Receptor (EGFR), which is a protein

that expressed on the surface of cancer cells. This facilitates the interaction with cancer cells other than the normal cells. It has been reported that gold nanoparticles have the ability to heat the cancer cells in a rapid manner compared to the normal cells based on the property of heat-conductor exhibited by gold⁴². Eventually, Gold nanoparticles with cell penetrating peptide enhance their ability to be uptake by the cancer cells, which will essentially increase their accumulation in the tumor based on the EPR effect.

CONCLUSION

The application of nanomedicines has proved to be effective for cancer treatment compared to conventional chemotherapy and radiation therapy. The nanomedicines can treat various cancers with the precise target without affecting the normal cells. In addition, by utilizing of enhanced permeability and retention (EPR) effect, nanomedicines can yield a very promising result for cancer treatment.

Moreover, polymers are widely used in recent decades as biomaterials for their favorable properties like excellent biocompatibility, easy design and preparation, several types of structures and interesting biomimetic character, which warrants the further evaluations on these kinds of innovative materials.

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