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Gold Nanoparticles as Nanocarriers in Cancer Targeted Therapy

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Abstract

Functionalized gold nanoparticles are being used extensively for many biomedical applications and research has shown an abundant use in targeted delivery. AuNPs are small gold particles that have a diameter between 1nm to 100nm. More lately, these unique optoelectronic properties have been researched and employed in high technology applications like organic photovoltaics, sensory probes, therapeutic agents, drug delivery in biological and medical applications, electronic conductors and catalysis. The optical and electronic properties of gold nanoparticles are tunable by altering the size, shape, surface chemistry, or aggregation state. This review will provide a comprehensive review of recent advances and future perspectives of AuNp's in targeted therapy and diagnostics.

Keywords: Gold Nanoparticles; Nanoparticles; Nanocarriers; Targeted Therapy

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Introduction

Cancer is one of the leading causes of death in history in current society. The cause of a disease can be lifestyle, genetics and it varies from person to person. There are many treatments in the diagnosis of cancer to either ease the pain of the patient or to reduce the tumor altogether. Chemotherapy, Radiation therapy, Immunotherapy, targeted therapies are currently in use to treat cancer. Targeted therapy has found prominence in current medicine due to applications to activate the required size of the tumor. This has provided a wide application in treatment. Metals like Zinc, Silver, Gold, and Titanium are widely considered as carriers for the same in which gold nanoparticles have shown prominent results.

AuNps are being used extensively in biological, biotechnology, diagnostics and mainly in targeted therapy. Their unique properties are providing versatile applications to carry antibodies, proteins and can provide multiple applications in biomedical applications. The use of gold in medicine has been seen in history and it has shown some prominent results [1]. The reason for extensive use also is due to its ease in synthesizing, being economical and reliable. They can be easily modified to any shape by changing conditions. And due to highly reactive surfaces, they can bind the molecules, drugs and make them valuable carriers.

And a most important reason for the researcher using gold nanoparticles for binding with molecules is its non-toxic nature and its biocompatible nature. Recent studies have shown the use of gold nanoparticles has enormous potential to improve treatment in cancer biology [2]. Functionalized gold nanoparticles have a high level of biocompatibility and predictable biodistribution patterns, making them ideal candidates for usage as the basis of new cancer therapies [2].

Cancer Therapies

A study by Farooq MU, et al. (2018) [3], has demonstrated an efficient dual delivery of anti-cancer therapeutics to HeLa cells. The paper has demonstrated a design of a stable BLM-capped DOX complex on PEG-AuNPs for efficient drug delivery. PEG-AuNPs (S1) Nanocarriers can be used to deliver multiple anticancer medicines to HeLa cells using an active targeting method at lower doses while still retaining drug cytotoxicity. This study has shown prominently in ovarian cancer treatments.

Colloidal gold exhibits Localized Plasmon Surface Resonance (LPSR), which means gold nanoparticles may absorb light at specific wavelengths, resulting in photoacoustic and photothermal properties that could be useful in cancer treatments. Changing the size and shape of gold nanoparticles can change their LPSR photochemical activities, as well as their photoacoustic and photothermal properties, allowing them to use other wavelengths of light, such as near-infrared light. It is possible to passively transport gold around the body in a Nanoscale framework, where it can localize in tumors (tumors with leaky blood vessels) and be safely eliminated through the urinary system [4].

Computed tomography (CT) is a widely used diagnostic imaging modality for cancer. It can obtain 3D images to understand the tumor

size and provide spatial resolution and is cost-effective. Here, it becomes important to provide a contrast between regular tissue and effective tissue [5]. So, constrict agents, mainly iodine-based agents are injected into the required site. Gold particles have shown good results in providing high-resolution images. As X-ray images are attenuated by the atomic number of the element, the accumulation of AuNps has increased X-ray resolution and provided high contrast between healthy and affected tissues [6].

The ion beams generate surface Plasmon's, increasing the production of secondary electrons, which is one of the hypothesized processes for the radiosensitization of gold nanoparticles. Li S, et al. (2016) [7], has compared the effects of gold nanoparticles of different sizes (5 and 10 nm) and proton beams of varied LET (10 and 25 keV m1) on gold nanoparticles. The radiosensitization effects of gold nanoparticles (GNPs) (5 or 10 nm) have been investigated in vitro in combination with a proton beam of different linear energy transfer due to the appealing physical properties of protons and the emerging evidence of biological relevance of the use of gold nanoparticles (GNPs) (LET).

Although gold nanoparticles are an appealing foundation for developing revolutionary cancer imaging and therapeutic techniques, their toxicity in human applications must be thoroughly investigated [6]. Although gold is mostly inert to bio tissues, these nanoparticles tend to persist in the body for a long period, especially in the liver and spleen. As a result, the long-term toxicity of nanoparticles is a worry for their use in humans. Because the size, shape, and coating of gold nanoparticles affect their biodistribution and toxicity, it appears that the safety of gold nanoparticles is dependent on some factors that must be explored for each synthetic formula and application.

Photothermal therapy (PTT) is an application of GNPs in cancer treatment. Gold nanoparticles absorb incident photons and convert them to heat to destroy tumor cells. Due to their unique optical properties as a result of LSPR, gold nanoparticles absorb light with extremely high effectiveness, which ensures efficient PTT at fairly low radiation energy [6]. The abnormal vascular structure of the tumor is ineffective in dissipating heat, therefore the tumors are more sensitive to hyperthermia than healthy tissues. When irradiated by light, the heat generated by gold nanoparticles causes biomolecule denaturation and cellular membrane disturbance and kills tumor cells.

In vitro studies

Initial biological studies of gold dose enhancement were carried out with monolayers of C3H 10T1/ 2 murine cells grown on thin layers of a gold foil [8]. Regulla DF, et al. (1998) [9], demonstrated massive DEFs of 55-114 when sensors were placed next to gold foil boxed in polymethylmethacrylate (PMMA) and irradiated with mean X-ray energies of 33-100 kV. With 80 kV X-rays, the secondary radiation dropped exponentially with the distance from the gold foil and was negligible at 30 μm. Herold DM, et al. (2000) [10], examined improvement with 3 μm diameter gold microparticles in vitro and in vivo. The dose improvement with 1 gold microparticles in solution without cells was determined using chemical Fricke dosimetry and observed to be 1.42 for 200 kVp X-rays. Chithrani DB, et al. (2010) [11], investigated the impact of GNP size, concentration and radiation energy on in vitro radiosensitization in Hela cells.

An in vitro study utilized 30-nm citrate or thioglucose- coated GNPs with DU145 cells irradiated with 200-kVp X-rays after 24 h GNP exposure [12]. A threefold rise in GNP uptake was observed in glucose-limited GNPs, reducing cellular proliferation with exposure to either GNP medication. The combination of GNPs with radiation was largely additive, while citrate GNPs with 2-Gy radiation have less effect on cellular proliferation than glucose-limited GNPs.

In vivo studies

Despite the rapid-fire increase of GNP publications in recent times and an accelerating number of in vivo studies investigating the uptake and distribution of GNPs, there remains a deficit of studies of in vivo radiosensitization with GNPs. These studies will be critical for the successful translation of this approach to the clinic. In the first trial, Balb/ C mice bearing EMT-6 murine breast cancer tumors received a single dose of 30 Gy using 250-kVp radiation alone or in combination with high attention of GNPs (1.35 g of Au kg-1) injected intravenously 5 min before irradiation [8]. The Gd enabled in vivo monitoring of GNP biodistribution, demonstrated maximum tumor uptake at 10 min when 13.5 mg of gold was injected, with a tumor-to-muscle ratio of 3:1. Mice were exposed to GNPs alone or in combination with 10 Gy, 150 kVp X-rays 20 min after GNP injection. There was no difference in survival times with median survivals of 17 days and 14 days respectively, in the GNP and radiation group compared with radiation alone [8]. Numerous other studies present the in vivo factors that are leading the exploration of GNPs to better improve the applications and the effectiveness.

Conclusion

GNPs have numerous properties that are fascinating for use in cancer therapy. They're small and can pierce extensively throughout the body, preferentially accumulating at tumor spots owing to the EPR effect. Importantly, they can bind numerous proteins and drugs and can be actively targeted to cancer cells overexpressing cell face receptors. While they're biocompatible, it's clear that GNP preparations can be toxic in vitro and in vivo systems. GNPs have a high atomic number, which leads to greater absorption of kilovoltage X-rays and provides greater contrast than routine agents. They reverberate when exposed to the light of specific energies, producing heat that can be used for tumor-selective photothermal therapy. GNPs have been shown to cause radiosensitization at kilovoltage and megavoltage photon energies. The exact routine remains to be seen but it may be physical, chemical, or biological [8]. There's huge potential to use nanoparticles in cancer therapy. With intense global interest in nanotechnology and especially in nanomedicine, many of these questions will likely be addressed in the near future.

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