Original Research Article

Gold Nanoparticles In Diagnosis & Management Of Oral Cancer & Pre-Cancerous Lesions.

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ABSTRACT:-

Gold is one of the first metals to have been discovered; the history of its study and application spans at least several thousand years. In particular, the optical properties of GNP are determined by their plasmon resonance, which is associated with the collective excitation of conduction electrons and localized in the broad region. The application of nanotechnology for the treatment of cancer is mostly based on early tumor detection and diagnosis by nanodevices capable of selective targeting and delivery of chemotherapeutic drugs to the specific tumor site. The nanotechnology-based detection and diagnostic methods used are Magnetic resonance imaging (MRI), Optical coherence tomography (OCT), Photoacoustic imaging, Surface plasmon resonance scattering, Surface-enhanced Raman spectroscopy, Diffusion reflection imaging, Quantum dots imaging, and Nano-based ultrasensitive biomarker detection. Due to the remarkable properties of gold nanoparticles, they have long been considered a potential tool for the diagnosis of various cancers and for drug delivery applications. Recent advances in nanomedicine make it auspicious for cancer diagnosis and treatment. The attractive properties of gold nanomaterials, particularly, anti-angiogenic properties, are highly useful in a variety of cancer studies. In addition, they can bind many proteins and drugs and can be actively targeted to cancer cells by over-expressing cell surface receptors and they are biocompatible in nature with a high atomic number, which directs to greater absorption of kilovoltage X-rays and provides greater contrast than standard agents. Nano-based contrast agents for MRI, OCT, and photoacoustic imaging have lower toxicity, prolonged blood circulation half-life, and the ability to target unique cell surface molecules. The nano agents exhibit better image contrast properties and improved penetration depth than routine contrast agents. They can provide molecular-targeted imaging, analyze biomarkers at the nano-scale, enable intraoperative identification of surgical resection margins, and monitor oral cancer prognosis after treatment. Using nano-based techniques can help clinicians to detect and better monitor diseases during different phases of oral malignancy. This review will focus on such current modalities in the diagnosis & management of oral cancer and pre-cancerous lesions using gold nanoparticles.

Keywords: Gold nanoparticles, GNP diagnostics and therapeutics, Cancer cells, Oral cancer, Precancerous lesions.

INTRODUCTION

Cancer is a critical public health problem worldwide that has brought a great burden to society. According to a survey in 2016, an estimate of 1.6 million new cases was reported and 5.9 lakh cancer death occurred in the United States only and amongst it 31910 new cases of oral cancer and 6,490 deaths occurred due to it. The formation of oral cancer is a multifactorial and a multi-step process. Thus, early detection of OMPD and oral cancer is critical for the prognosis of diseases[1]. To date, scalpel biopsy and histopathological examination are still the standard diagnostic procedures applied to ascertain the oral potentially malignant and malignant lesions. However, the biopsy procedure is often invasive, which may cause patient anxiety and discomfort[2]. The selection of resection margins depends largely on the histopathological assessment and the result can be affected by the quality of the specimen and pathologists subjective judgements. In the past few decades, a variety of pain free diagnostic strategies have been developed, amongst which is nanotechnology and nanomedicine.

According to the US National Nanotechnology Initiative, Nanotechnology Initiative, nanotechnology refers to the manipulation of matter with length scale of 1-100nm in at least one diamension. Among many other pure metals like platinum, silver, titanium, zinc, cerium, iron and thallium. Gold nanoparticles bound with biomolecules seems to be a good choice, given their multifuctionality, optical and photothermal properties and biocompatible nature. They are synthesized with different surface coatings to conjugate drug compounds and improve the pharmacokinetics by admisistering through oral and parentral route.[3]

Various size like gold nanorods, nano cages, nano shells and assemblies can be used. Due to low absorption of water and haemoglobin. Gold nanmaterial have a deeper penetration depth in the tumor therapy and imaging and can be used as a photothermal agents, imaging agents and therapeutic agents. According to Lee et at 2017, compared with other shapes, elongated nanoparticles have better affinity, greater diffusion and transmembrane rates, they can penetrate the tumors rapidly and accumulate extremely.[4]

The range of GNP use in modern medical and biology studies is extremely wide. In particular, it comprises genomics, biosensorics, immunoanalysis, clinical chemistry, detection and photothermolysis of microorganisms and cancer cells; the targeted delivery of drugs, DNA and antigens; optical bioimaging and the monitoring of cells and tissues using modern registration systems.[5] It has been argued that gold nanoparticles could be used in almost all medical applications: diagnostics, therapy, prevention, and hygiene.

1. NANOTECHNOLOGY BASED DIAGNOSTIC METHODS

1.1 Visualization and bioimaging

Gold nanoparticles have recently been in active use in the identification of chemical and biological agents. The use of high-resolution instruments (high-resolution transmission electron microscope – HRTEM) and systems of digital recording and the processing of images are examples of the modern application of electron microscopy equipment. The main use is in modern medico-biological studies is for the identification of causative agents of infectious diseases and their surface antigens. In addition to the conventional colloidal gold with quasi-spherical particles (nanospheres), non-spherical particles, such as nanorods, nanoshells, nanocages, nanostars, and other types of particles (this group of particle were named “plasmon resonance particles of noble metals”) have recently been used. These techniques are based on detecting micro-objects using an optical microscope in which the object's luminescence is excited due to the simultaneous absorption of two (or more) photons; the energy of each of them being lower than that required for fluorescence excitation.[6] The use of two-photon luminescence of gold nanoparticles allows to visualize (amongst other objects) on comarkers on the surface or inside a cell.

With the advancement in nanotechnology, various types of nanoparticles have been applied as specifc MRI contrast agents for cancer screening. Nano-contrast agents have the ability to recognize unique cell surface markers and prolonged blood circulation half-life, exhibiting better MRI contrast properties. Nano-contrast agents have also been studied in oral cancers. For example, Shanavas et al. combined the folate preconjugated chitosan and magnetic poly (lactide-coglycolide) (PLGA) nanoparticles to create an MRI contrast agent.[7] The overall T2 relaxation time was shortened, and the nanoparticle relaxivity was enhanced thereby providing better imaging contrast. Meanwhile, the folate receptor positive KB oral cancer cells showed increased nanoparticle uptake and caused signifcant enhancement in cytotoxicity. This nano agent not only provided high contrast cancer imaging but also simultaneously provided cancer therapy.[8]

1.2 Gold nanoparticles as drug carriers

Gold nanomaterials are promising nanomaterials in medicine, especially for the targeted drug delivery. Due to their varying structure, small size, easy synthesis method, and surface modifcations, they are emerging as a new class of targeted drug delivery systems.[9] Many methods have been developed for drug loading in the AuNPs, including direct conjugation involving Au–S or –N linkages, capping ligands, electrostatic interactions, van der Waals forces, and hydrogen bonding.

2. NANOTECHNOLOGY BASED CANCER THERAPY

2.1 Photothermal therapy

Photothermal killing of a cancerous cell is a promising technique in cancer treatment. During PTT, the AuNPs become hot when they reach their maximum absorption in the visible or near infrared region, leading to cell death (Kennedy et al. 2011).[10] Thus, laser-irradiated AuNPs could act as a therapeutic agent without the presence of a drug. Selectively inducing cell death is possible by adjusting the size, shape, particle number, and laser energy. This property makes AuNPs potentially useful in PTT and treating other diseases. Gold nanostructures are promising candidates for PTT of cancer and other diseases. However, there are still some drawbacks and unanswered questions regarding PTT, such as material stability, biocompatibility, physiochemical interactions, and blood circulation time. The killing mechanisms of PTT with gold nanomaterials need to be investigated in more detail. The high cost of gold may also play a major role in limiting its use in PTT (Dykman and Khlebtsov 2012; Yang et al. 2015)[11,12]

2.2 Photodynamic therapy

The use of photosensitizer drugs that are activated by visible light of a particular wavelength for the treatment of diseases is called photodynamic therapy (PDT). Affected cancer cells are irradiated with a wavelength of laser light, corresponding to the peak of drug absorption (Dykman and Khlebtsov 2012).[11] In addition to the aforementioned heat therapy, another mechanism plays a role, namely the photochemical generation of oxygen free radicals, which induces necrosis and apoptosis in cancer cells (Wilson 2008).[13] Gold nanomaterials have received considerable attention in the PDT field. When the AuNPs absorb light, electrons transfer to the excited state and lead to overproduction of reactive oxygen species (Negishi et al. 2006)[14]

Two important properties of gold-based photosensitizers are that they can penetrate to the depth needed for effective cancer treatment, and they are more stable than the organic dyes (Vankayala et al. 2014).[15] Recently, Hwang et al. confirmed that GNR have a high potential to destroy cancer cells by irradiation of laser light at 915 nm. Along with gold, nanoconjugates composed of, for example, peptides, proteins, photoactive substances, nanoshells, nanoechinus, and nanocages are also useful for PDT (Dykman and Khlebtsov 2012; Yang et al. 2015).[11,12] However, the photosensitizer should persist in the targeted area for a long time, and the heating should be low for the dye alone

CONCLUSION

In this review, we enlighten on the recent advances in the development and application of gold nanoparticles in cancer diagnostics and treatment. Nano-based diagnostic methods act as a promising tool to provide real-time, convenient. Gold nanoparticles' optical properties, easy synthesis, possible control over size and shape, colloidal stability, and the ability to tune the surface chemistry to achieve easy conjugation with biological moieties make them favorable for biomedical applications. Millions of functionalized gold nanoparticles can be released into the blood stream and bind to specific cancer cells, and in turn either aid in treatment via PTT or enable photoimaging for the successful removal of the tumor by operation. Despite these advances with gold nanoparticles, there is still a requirement for more cost-effective gold nanoparticle-based systems, which will allow cancer diagnosis and treatment at an early stage with a high level of specificity.

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