



The Applications of Gold Nanoparticles in Cancer Diagnostics and Treatment

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Cancer is one of the most dangerous and rapidly spreading diseases where cells divide uncontrollably at a rapid speed and the orderly cell division process breaks down and mutations form (National Cancer Institute, 2021). Gold nanoparticles can be used in the fight against cancer as contrast agents for medical diagnostics. Their high x-ray attenuation properties make them a favorable candidate for x-ray imaging (Hainfeld et al. 2014). AuNPs or gold nanoparticles, compared to other popular contrast agents such as iodine-based compounds have higher contrast and longer imaging times. Gold nanoparticles can also be used as a drug delivery tool in the human body (Farooq et al. 2018). It has the potential to transport chemotherapy drugs to tumor sites because of its large surface area. Besides this, AuNPs can also deliver genes for gene therapy (Hu et al. 2020). Using gold nanoparticles to transport healthy genes into mutated cancer cells could potentially halt the spread of cancer by causing cell death. Hence, though there are no current cures for cancer, gold nanoparticles hold tremendous potential in treating and opposing cancer.

INTRODUCTION

Cancer is one of the leading causes of death worldwide with more than 10 million individuals dying from the disease every year (National Cancer Institute, 2020). Surgery, chemotherapy, and radiation therapy are some of the most common treatments for cancer nowadays. These treatments help combat cancerous cells by slowing their spread through the body. However, some setbacks of these current treatments are that they cause physical pain, hair loss, and soreness throughout the body. New treatments such as nanotechnology have emerged that can be used to overcome some of the setbacks present in current treatment methods. Nanotechnology is essentially the manipulation of matter at a nanoscale and can be used to treat diseases such as cancer (National Nanotechnology Initiative, n.d.). The progression of nanotechnology has paved the way for possibilities of treatment and diagnostics for cancer. Gold nanoparticles, also known as AuNPs, are small colloidal nanoparticles that can be utilized as a contrast agent for the diagnosis of cancer to help doctors determine the size and location of the tumor (Hainfeld et al. 2014). They can also be used as a potential treatment for cancer by being a drug delivery system because of its unique physical and chemical properties (Farooq et al. 2018). They allow therapeutic substances such as chemotherapy drugs or healthy genes to selectively reach the tumor site and destroy the cancer cells (Hu et al. 2020). Understanding the complete properties of gold nanoparticles is crucial if AuNPs are to reach their full potential as contrast agents and drug delivery molecules. AuNPs can potentially lead us to biomedical advancements in the treatment and therapy of the various types of cancer. In this review article, we summarize certain applications of gold nanoparticles in the research and fight against cancer.

GOLD NANOPARTICLE'S USE IN CANCER DIAGNOSTIC

The application of gold nanoparticles as contrast agents for cancer imaging is an area of interest in the anticarcinogenic (i.e., preventing and delaying the development of cancer) scientific community. Colloidal gold nanoparticles (AuNPs) are biocompatible, highly functional, have low toxicity, and can be easily synthesized through a chemical reaction (Yeh et al. 2012). Gold nanoparticles have been intensely studied as contrast agents for biomedical imaging because of those unique properties (Hu et al. 2020). Diagnostic scans and medical imaging display the internal skeleton of the human body including tissues and bones. Contrast agents, also known as contrast materials or contrast media, increase the contrast and enhance the visibility between those different bodily tissues (RadiologyInfo, 2020). They “contrast” certain areas of the body from other normal tissues or structures, making them appear differently on scans and images. Contrast materials can be swallowed or injected into the body and the high contrast levels help doctors distinguish and recognize abnormalities within tissues.

AuNPs have a number of other properties that have encouraged their use in biomedical imaging. For example, AuNPs can be also used by scientists as computed tomography (CT) imaging contrast agents because of their high x-ray attenuation properties (Hainfeld et al. 2014). CT is a medical examination involving x-ray equipment to produce diagnostic images of the body (Mayo Clinic, 2022). CT combines a series of x-ray images and creates cross-sectional images of the body. CT scans show a tumor's shape, size, and location. It also has the capability of developing 3D images with high spatial resolution while being cost-efficient. While an x-ray travels through the body, scattering and photoelectric absorption occurs and affects the intensity of the beam (Thomsen et al. 2005). Each x-ray photon interacts with an atom of the material it penetrates through and completely



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disappears, thus decreasing the beam's intensity. This can also be known as attenuation, the reduction of the intensity of an x-ray beam. Having a high attenuation means that doctors can separate normal tissues and bones and those with possible tumors. Two properties that determine a substance's attenuation properties are its density and atomic number (Z). Dense materials are known to attenuate more x-ray photons. Similarly, materials with a high atomic number can also attenuate more x-ray photons. Hence, AuNPs being both dense and having an atomic number of 79, has great x-ray attenuation properties. Thus, because of AuNPs high x-ray attenuation properties, they have been widely suggested as contrast agents for CT.

IODINE-BASED AGENTS VS AUNPS

As contrast agents, gold nanoparticles have overcome some of the setbacks caused by standard contrast agents such as iodine-based compounds (Jain et al. 2012). The way contrast agents work on CT imaging is that healthy and diseased tissues have different densities (Mayo Clinic, 2022), and this property is used by contrast agents such as iodine-based compounds to help distinguish normal and abnormal tissues or cells (Wang et al. 2017). In short, the contrast between soft tissues is poor on CT scans and hence, iodinated molecules are injected to identify tumors from healthy tissues. As discussed before, the atomic number of the element contributes to x-ray attenuation through photoelectric absorption. As iodine has a high atomic number (53), injecting iodine-based compounds will help produce image contrast (Hainfield et al. 2014). Furthermore, iodine's k-shell binding energy is 33.2 keV, close to the mean energy of most diagnostic x-ray beams (Bell et al. 2022). As the atomic number (Z) of a material increases, so does the k-shell binding energy (expressed in keV). When the k-shell binding energy is high, the K-edge energy, which is the sudden increase of photoelectric absorption in x-ray photons, also increases. Photoelectric absorption is more likely to happen when the x-ray energy is close to the K-edge energy of the atom it interacts with. Thus, because iodine has a K-edge or k-shell binding energy of 33.2 keV, which is close to the average energy of x-rays, photoelectric absorption (x-ray attenuation) is likely to occur. However, iodinated contrast agents also have many limitations including short imaging times, quick renal clearance, low sensitivity, poor contrast in large patients, and high toxicity (Jain et al. 2012). Therefore, it is crucial that we turn to new technology and explore other materials that can be used as contrast agents for x-ray imaging such as AuNPs. In the last few years, scientists have wondered if AuNPs can overcome the limitations of iodine-based contrast agents. Firstly, gold nanoparticles have higher photoelectric absorption than iodine, causing higher contrast with a lower x-ray dose (Bell et al. 2022). Moreover, Hainfield et al. demonstrated that when gold nanoparticles of 1.9 nm (in diameter) were injected intravenously into mice, it resulted in longer retention times, unusual clarity, and no toxicity after 11 and 30 days (Hainfield et al. 2006). Because AuNPs clear the blood slower than iodine agents (slower renal clearance), they

will have a longer imaging time unlike iodine-based compounds. Also, because the mice's organs such as kidneys and tumors were seen with unusual clarity, gold nanoparticles achieved superior contrast. These animal studies suggest that gold nanoparticles are viable x-ray contrast agents compared to current agents. In summary, AuNPs are non-toxic, allow higher contrast, and have longer imaging times than iodine-based agents.

DELIVERY CARRIERS

Besides the application of gold nanoparticles as contrast agents for cancer imaging, AuNPs can also be used in anticarcinogenic drug delivery systems because of their large surface area which increases the loading capacity (amount of drug loaded per unit weight of nanoparticle) (Farooq et al. 2018). The most common cancer treatment is chemotherapy, which targets cells that divide rapidly. However, the drawback is that chemotherapy is administered to the entire body and will target all cells that divide at a high speed, including healthy hair and skin cells (National Cancer Institute, 2021). Traditional drug delivery systems such as oral administration for chemotherapy is also limited because only parts of the drug will reach the tumor site and the rest will be circulating through the body (Hu et al. 2020). Thus, the inability to target specific cells has become a barrier in cancer research and treatment. There are many different drug delivery systems (DDS) such as liposomes, liquid crystals, and polymers. However, because of AuNPs' special properties such as vast surface area, gold nanoparticles have the potential to become a viable anticarcinogenic drug delivery system (Farooq et al. 2018). AuNPs can become a targeted drug delivery system by delivering chemo to target specific cells at tumor sites in comparison to other DDSs (Hu et al. 2020). Moreover, modified AuNPs help lower toxicity and the chances of cancer cells developing resistance. For example, Wójcik et al. showed using the MTT assay that GSH-AuNPs (glutathione-stabilized AuNPs) were non-covalently modified with doxorubicin (DOX) are more active than the activity of unmodified gold nanoparticles against feline fibrosarcoma cell lines (Wójcik et al. 2015). Besides using AuNPs as a drug delivery service to treat or prevent cancer, gold nanoparticles have also been suggested for the delivery of genes (Hu et al. 2020). Gene therapy alters or replaces a mutated gene with a healthy version of that particular gene (Wang et al. 2017). Although in the early stages of development, AuNPs as delivery agents have the potential to be an alternate treatment for cancer in the future. New and healthy genes have the potential to be administered into a cancerous cell via gene therapy and prevent the spread of cancer by causing cell death. Gold nanoparticles are recognized as a potential gene delivery service because of their high biocompatibility with DNA or RNA and their optical properties (Mendes et al. 2017). For example, Shahbazi et al. developed a nano formulation utilizing colloidal gold nanoparticles that contained guide RNA and nuclease on the surface (Shahbazi et al. 2019). They displayed the non-toxic delivery of the entire "cargo" into human blood stem cells.



CONCLUSION

Cancer is one of the most common terminal diseases in the world and accepted treatments include chemotherapy, surgery and radiation (National Cancer Institute, 2020). However, as it is in cancer's nature to advance structurally and biologically, newer treatments such as gold nanoparticles must also emerge. Gold nanoparticles hold incredible potential in cancer research as they can be used as contrast agents for biomedical imaging. Quality contrast agents have high diagnostic value in medical imaging and can better help doctors find cancer and show the tumor's size and location (Hainfeld et al. 2014). AuNPs delivers better contrast and longer imaging time compared to other mainstream contrast agents such as iodine (Jain et al. 2012). Furthermore, because of AuNPs special properties such as increased surface area, they can serve as a drug delivery system that can deliver chemotherapeutic drugs to cancer cells (Farooq et al. 2018). Targeting specific cells has always been an area of improvement in cancer therapy and using gold nanoparticles to deliver chemotherapeutic drugs help target specific cells in tumor sites instead of affecting the entire body (Hu et al. 2020). Using AuNPs in gene therapy by delivering healthy genes into cancer cells is another possibility of delivery services with gold nanoparticles. Over the last decade, extensive research in the application of gold nanoparticles in cancer research and treatment has paved the way for ample possibilities. However, the specifics of using AuNPs have not yet been clinically tested and proven to be safe for the human body. Factors such as long-term toxicity, specific targeting, and safety for each specific synthetic formula are still areas of active research (Wang et al. 2017). Overcoming these challenges will help gold nanoparticles reach their full potential in combating cancer and stem further research into the applications of AuNPs for treatment and therapy.

REFERENCES

- Bell, D. J. (2022, May 17). Iodinated contrast media. *Radiopaedia*. Retrieved from: <https://radiopaedia.org/articles/iodinated-contrast-media-1?lang=us#:~:text=Iodine%20has%20a%20particular%20advantage,is%20more%20likely%20to%20occur>
- Dentalcare.com. *Radiographic Contrast*. Retrieved from: <https://www.dentalcare.com/en-us/ce-courses/ce571/radiographic-contrast>
- Farooq, M. U. (2018, February 13). Gold Nanoparticles-enabled Efficient Dual Delivery of Anticancer Therapeutics to HeLa Cells. *Nature*. Retrieved from: [https://www.nature.com/articles/s41598-018-21331-y#:~:text=Colloidal%20gold%20nanoparticles%20\(AuNPs\)%20are,and%20functionality%20through%20surface%20chemistries](https://www.nature.com/articles/s41598-018-21331-y#:~:text=Colloidal%20gold%20nanoparticles%20(AuNPs)%20are,and%20functionality%20through%20surface%20chemistries)
- Hainfeld, J. F. (2014, February 13). Gold nanoparticles: a new X-ray contrast agent. *The British Institute of Radiology*. Retrieved from: <https://www.birpublications.org/doi/abs/10.1259/bjr/13169882?journalCode=bjr#:~:text=Gold%20has%20higher%20absorption%20than,agents%2C%20permitting%20longer%20imaging%20times>
- Hu, Xiaopei. (2020, August 13). Multifunctional Gold Nanoparticles: A Novel Nanomaterial for Various Medical Applications and Biological Activities. *Frontiers*. Retrieved from: <https://www.frontiersin.org/articles/10.3389/fbioe.2020.00990/full#B157>
- Jain, S. (2012, February). Gold nanoparticles as novel agents for cancer therapy. *National Library Of Medicine*. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3473940/>
- Knoll, G. F. Radiation measurement. *Britannica*. Retrieved from: <https://www.britannica.com/technology/radiation-measurement>
- Mahan, M. M. (2018, March 07). Advanced Nanomaterials for Biological Applications. *Journal of Nanomaterials*. Retrieved from: <https://www.hindawi.com/journals/jnm/2018/5837276/>
- Mayo Clinic. (2022, January 6). *CT Scan*. Retrieved from: <https://www.mayoclinic.org/tests-procedures/ct-scan/about/pac-20393675>
- Mendes, R. (2017, March 2). Gold Nanoparticle Approach to the Selective Delivery of Gene Silencing in Cancer—The Case for Combined Delivery? *National Library Of Medicine*. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5368698/>
- Nanoprobes.com. (2011, March). Can Gold Cure Cancer? *Gold Nanoparticles in Radiation Therapy*. Retrieved from: https://www.nanoprobes.com/newsletters/Vol11_Iss03_gold-nanoparticles-in-radiation-therapy.html#discussion
- National Cancer Institute. (2020, September 25). Cancer Statistics. Retrieved from: <https://www.cancer.gov/about-cancer/understanding/statistics#:~:text=Cancer%20is%20among%20the%20leading,related%20deaths%20to%2016.4%20million>
- National Cancer Institute. (2021, May 5). What is Cancer? Retrieved from: <https://www.cancer.gov/about-cancer/understanding/what-is-cancer>
- National Nanotechnology Initiative. *About Nanotechnology*. Retrieved from: <https://www.nano.gov/about-nanotechnology/what-is-so-special-about-nano>
- Nett, B. X-ray attenuation of tissues [thickness, atomic number] for Radiologic Technologists. How Radiology Works. Retrieved from: <https://howradiologyworks.com/x-ray-attenuation-of-tissues/#:~:text=Lower%20energy%20x%20rays%20form,in%20the%20lower%20energy%20image>
- RadiologyInfo.org. (2020, June 15). Contrast materials. Retrieved from: <https://www.radiologyinfo.org/en/info/safety-contrast>
- Thomsen, V. (2005, August 31). Tutorial: Attenuation of X-Rays By Matter. *Spectroscopy*. Retrieved from: <https://www.spectroscopyonline.com/view/tutorial-attenuation-x-rays-matter>
- Wang, S, Lu, G. (2017, May 9). Applications of Gold Nanoparticles in Cancer Imaging and Treatment. *Intech Open*. Retrieved from: <https://www.intechopen.com/chapters/57037>
- Wójcik, M. (2015, April 30). Enhancing anti-tumor efficacy of Doxorubicin by non-covalent conjugation to gold nanoparticles - in vitro studies on feline fibrosarcoma cell lines. *PLoS One*. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/25928423/>
- Yeh, Y. C. (2012, March 21). Gold Nanoparticles: Preparation, Properties, and Applications in Bionanotechnology. *National Library Of Medicine*. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4101904/>



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