Application of gold nanoparticles in Medicine and Biology

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Abstract:
Nanotechnology is formidably powerful technology. Nanoparticles are the simplest form of structures with sizes within the nanometer (nm) range. The US National Nanotechnology Initiative defined the nanoscale is a range from 1 to 100 nm, in this range particles are included which are naturally occurring, such as smoke particles, volcanic ash, sea spray, and from anthropogenic sources. Nanotechnology proposals unique styles to review a variety of medical and biological methods that occur at nanometer scales, and is anticipated to own a revolutionary impact on biology and medication. Among the approaches for exploiting nanotechnology in medicine, nanoparticles offer some unique advantages as image enhancement, delivery agents and sensing. Many style of nanoparticles with biomedical relevance are available including, liposomes, quantum dots, polymeric nanoparticles, dendrimers, metal nanoparticles, nanoassemblies and micelles. To additional the applying of nanoparticles in therapy and disease diagnosis, it is important that the systems are biocompatible and capable of being functionalized for recognition of specific target sites within the body after systemic administration. We have explained some important applications of gold nanoparticles in this review.

Keywords: *gold nanoparticle, drug delivery, cancer cells, cellular targating, biocompatible, photothermal*

1. Introduction

Gold is a soft transition metal and its configuration is [Xe] $4f^{14}$ $5d^{10}$ $6s^{1}$. It is highly reactive and one of the least chemically active elements. Gold is considered a "boring" element in terms of chemistry because it is an inert element in its purest form so it does not react with other chemicals/elements easily. Gold nanoparticles express different size and shape related properties from 1-100nm in size. These properties offer many uses for gold nanoparticles in field of electronics, photonic, medicine, chemistry, etc. Gold salts have potent anti-inflammatory properties and have been administered to reduce pain and swelling associated with rheumatoid arthritis and tuberculosis **[10]**. The applications of gold are further extended by colloidal gold which are submicrometer size particles of gold. Over the years, gold solutions were found to be used across different parts of the world for treating variety of ailments such as syphilis **[11]**, alcoholism **[12]**, and easing suffering in cancer patients **[13]**. Michael Faraday also discovered that its color is due to the size of the gold particles, it mean gold particles have properties that differ from bulk gold **[17]**.

Arabian, Chinese and Indian scientists can be found initial information on colloidal gold in treatises who tried as early as in the fifth- fourth centuries BC to attain gold and they utilized it for medicinal (Indian "liquid gold", Chinese "golden solution") and other functions. Paracelsus wrote about the curative properties of gold quintessence- "quintaessentiaauri", which he detected by the reduction of gold chloride by vegetables dig outs in alcohols or oils and used the "potable gold" for healing a number of metal diseases and syphilis **[1]**. Giovanni Andrea utilized "aurum potabile" for leprosy plague,epilepsy and diarrhea as a therapy for patients. When the doctor to Louis XIII of France recommended, the alchemist David de Planis- campy, served his "Longevity elixir", a colloidal

solution of gold in water. Gold nanoparticles are flexible agents with a selection of biomedical applications including use in highly sensitive analytical assessments, ablation thermal and radiotherapy development as well as drug and gene delivery **[2-7]**. According to Recent studies we can see a wide variety of applications of gold nanoparticles. Over the last decade, areas of medicine, biology and electronics has attracted a lot of attention in range of applications. Biocompatible, non-cytotoxic, optical, electrical and magnetic properties allow many uses for gold nanoparticles **[12]**.

2. Applications in Medicine & Biology

2.1 Cancer/tumour treatment

Generally, Cancer treatment is extremely challenging. There is vast improvements in micro cancer cells (micro tumours), medicinal surgery even but still remain a serious threat. Some residual tumour cells get left behind even when severe cancers get treated through a complete tumour treatment. These residual tumour cells which get left behind might gradually experience growth and eventually reintroduce cancer if untreated. At times these tumour cells are strongly bind to the critical organs of the body so they are difficult to remove. In order to find a method to detect and eliminate these residual cancer cells, researches have been going on, even some are showing good results. To detect and eliminate these residual cancer cells, the concept of Plasmonic Nano Bubble nanosurgery often known as PNB method use. Studies show that reintroduction of cancer is prevented by this surgical method and this Nano surgery was considered more effective than standard surgical methods and it gave 100% tumor-free survival. In gaseous state, Plasmonic Nano bubbles are basically temporal Nano sized bubbles and via short laser pulses these nano bubbles are arose around clusters of Gold Nanoparticles. Via non-stationary plasmonic mechanism, Gold nanoparticles cluster absorb the laser pulses and convert the energy absorbed into heat energy when they hit by short Laser pulses. Fluids that are located around these cells evaporates into small nano sized bubbles by the converted heat energy and expands within itself and at the best collapses in nanoseconds. Through a process, around the cancer cells these large clusters of gold nanoparticles are formed, known as endocytosis. Basically, materials transport in and out of cells through this method. Against the receptors of the cancer cells this clinically certified gold colloids are attached to the antibodies. Without causing harm to nearby healthy cells, allows selective targeting of the cancer cells and this surgical method improves the surgical results and reduces errors. Chemotherapy and radiation therapy in such type of methods, selective targeting of cancer cells are not possible. Moving onto another aspect, determining a single residual cancer cell may be very difficult but clusters of cancer cells can be easily detected by gold nanoparticles method. Hence, it can be said that detection of cancer cells and their elimination both are possible through this method **[14].**

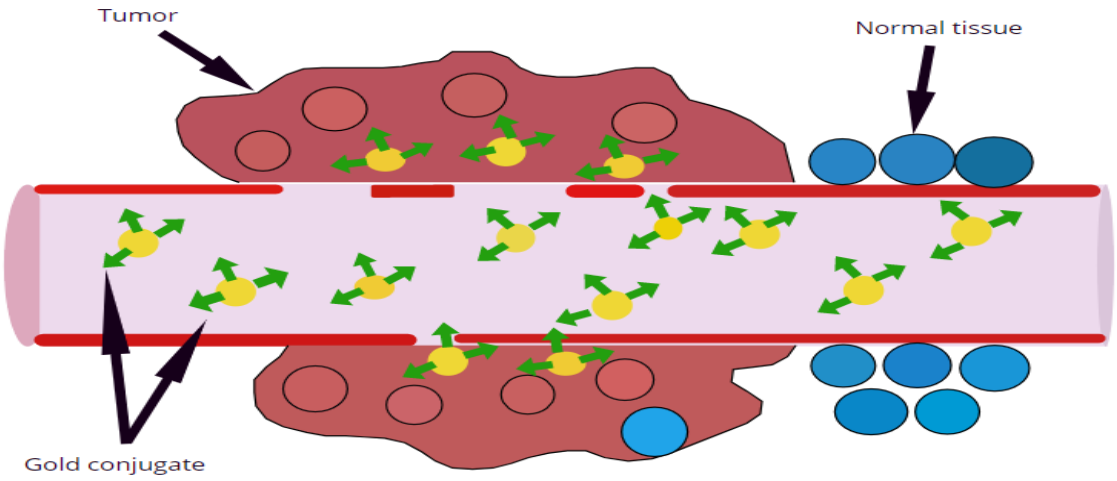

Figure 1 Systematic Delivery of gold nanoparticles to the tumour cells via leaky blood vessels [14].

Solidified tumour cells often tend to have leaky blood vessels and leaky blood vessels of cancer cells leak out and bind around the tumour cells as clusters of gold colloids are inserted in the patient's blood via systematic delivery. They generally target only the tumour tissues and avoid normal healthy tissues. This is about by this surgical method how the healthy cells remain unaffected. While they get hit by short near infra-red laser pulses inside the tumour cells, to destroy the cancer cells, fluid surrounding the cells gets heated. Across centimeters of tissues without harming them this short laser pulses are penetrable. Some normal healthy tissues also contain some of these gold nanoparticles and these normal cells containing gold nanoparticles might get destroyed while short laser pulses are shot in the process, this one can be a problem. Another shortcoming, normal cells surrounding the cancer tissues that infrared light from the laser pulse transmitting on it. This whole experiment has been conducted only on mice so to carry out on humans instead of mice, researchers and clinical experts are setting up working on the procedures. A massive decrease in the number of cancer patients if it shows positive results on humans but this will take some more years. In cases this method could come in very handy when it becomes impractical where practically removing an entire tumour. Cancer cells common in human head and neck tumours, squamous cell carcinoma of human is first inserted into mice. These are not easy to deal with standardized treatments. Gold Nanoparticles coated with immune protein antibodies after insertion into mice. On the surface of squamous cells these antibodies attaches with receptors. Hence clusters that formed by concentrated particles, surrounding and also inside the cancer cells. This time, instead of shooting continuous laser beams they shot ultra-short infrared pulses so causing heat is not able to reach the normal tissues, only they succeeded into cancer cells. In regions containing large clusters of gold nanoparticles temperatures increase by the heat.

2.2 Targeted drug delivery

Doubtlessly uses of gold nanoparticles is Targeted drug delivery. Gold nanoparticles works as a non-toxic carrier of drugs **[16, 17].** Advancement of very delicate organ (tumor) directed diagnostics and treatments show in the creating field of nanotechnology. Without question, the blending of material science and tumor science is provoking the headway of innovative vectors with the capacity of achieving the since quite a while ago searched after goal of tumor-focused on drug delivery, where we can get the drug delivery specialist precisely where it is required, which is at the strong tumor. Luckily, bio-nanotechnologists have manufactured compelling techniques to overcome this obstruction related issues. Lately, GNPs have been gathered into platforms and utilized in biosensors and utilized in deoxyribonucleic acid (DNA) diagnostics. Some historical data, along with some data from Good Laboratory Practices (GLP) toxicology studying rabbits, shows that gold nanoparticles are comparatively inert and biologically suitable carriers. **[18]**

Gold nanoparticles can convey huge biomolecules, without themselves going about as transporters for simply little molecular drugs. Their extraordinary usefulness alongside their tunable size makes them a suitable framework for productive acknowledgment and conveyance of enormous biomolecules. They have shown fulfillment in conveyance of peptides, proteins, or nucleic acids like DNA or RNA. Gold Nanoparticles also provide themselves as appealing contenders in Gene Delivery **[19]**.

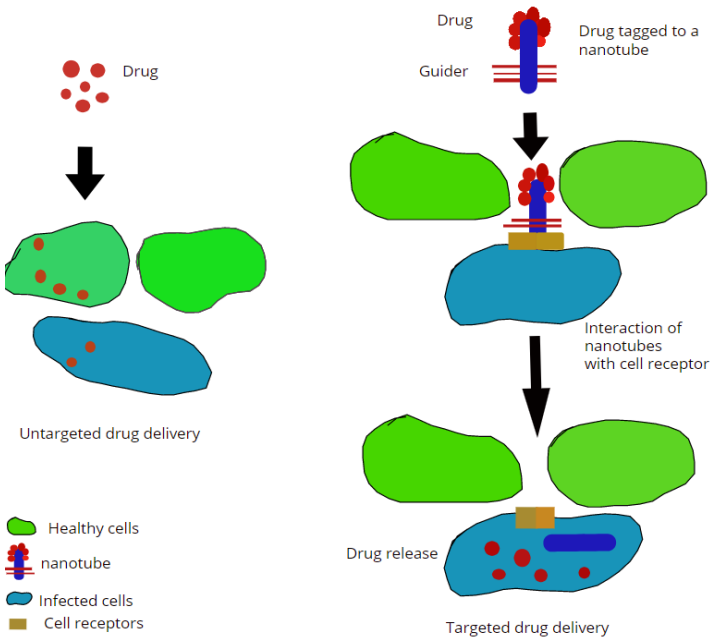

Figure 2 Nanotechnology- based drug delivery system

Cells themselves, normally, accomplish a decent work in shielding their significant substance, and along these lines, it is extraordinarily difficult to invade their film dividers so as to convey medications, supplements or biosensors without hurting or beating the cell. A suitable strategy for doing as such, is utilizing colloidal gold nanoparticles being secured with a flimsy layer of an uncommon polymer. All the while, scientists previously covered the gold nanoparticles with the slight layer of the polymer and join them with lipids - a classification of regular fats, waxes and nutrients that gives the cell wall its shape. Scientists also showed a furthest cutoff on the measured particles that can enter the cell wall. This breaking point is dictated by the particles' covering creation.

This covering includes a mix of hydrophobic and hydrophilic sections shaping a monolayer, a one atom thick layer on the outside of the molecule. Catching X-beam radiates is likewise a valuable side of Gold nanoparticles. On the off chance that they could be made to enter cancer cells, and if heat was concerned them by X-beam radiates, they could obliterate those cells from within. "So the fact that it's gold may be useful," says Irvine, a professor of materials science and engineering and biological engineering and member of the Koch Institute for Integrative Cancer Research. An expected use of this examination could be in embedding and appending biosensing particles on or into explicit cells. Thusly, scientists could recognize or screen specific biochemical markers, for instance, proteins that show the beginning or lessening of a malady or metabolic cycle.

2.3 Cancer imaging

As I have just revealed in an earlier area, the dispersing properties of gold colloids rely upon the size, shape and structure of the nanoparticles. Commonly, particles of 30–100 nm distances across disperse strongly and can be handily identified by an occupational magnifying instrument (microscope) under dim field light conditions. Actually, 40 nm AuNPs can be effectively identified by eye down to an element concentration of 10^{-14} M. Likewise, the scattering from a 60 nm AuNPs is 10^5 stronger than the emission of a fluorescein molecule **[21]**.The high dispersing cross-areas of AuNPs along with their greater photostability (when contrasted with natural colors) make them very encouraging for cell imaging.

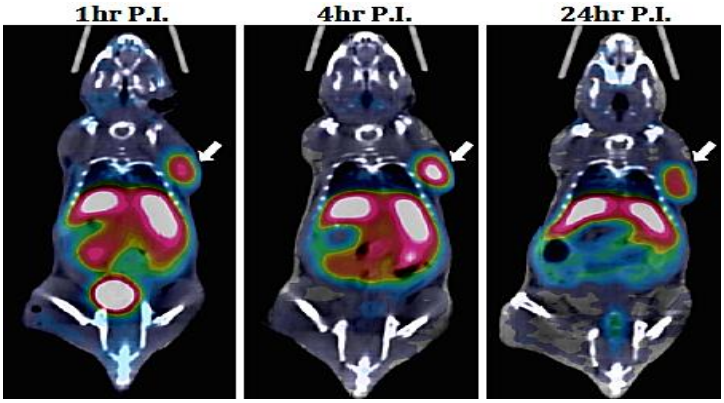

Figure 3 Some sample PET/CT images from the Small Animal Imaging Resource at UT Southwestern (UT-SAIR)

Standard clinical imaging modalities, for example, X-beam based computed tomography (CT), magnetic resonance imaging, and ultrasound can give fundamental data with respect to tumor area, size and spread. . However, these methods are not efficient in detecting tumors and metastases smaller than 0.5 cm and they can barely distinguish between benign and cancerous tumors **[22]**. On the other hand, gold induces a strong X-ray attenuation, having unique physical, chemical, and biological properties, which make them an ideal candidate for CT contrast agents **[23, 24].** In expansion, AuNPs give a serious amount of adaptability as far as functional groups for covering and focusing on and have additionally end up being harmless and biocompatible in vivo. Gold induces a strong X-ray attenuation, as was first demonstrated, inadvertently, by Wilhelm Roentgen, in the first X-ray human image (Figure 1).

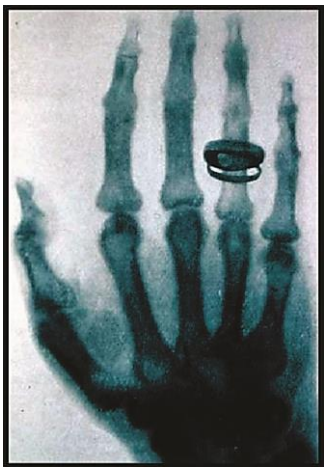

Figure 4 First ever medical X-ray image (1895) taken by Roentgen. “Hand with Ring” print of Wilhelm Roentgen’s first “medical” X-ray, taken on 22 December 1895. It dramatically showed the bones of her fingers; however the real size of her finger’s soft tissue could be garnered from the clearly visible gold ring on her finger. Likewise, below we show that “ringing” the tumor cells with gold nanoparticles makes it effectively more visible to CT. Note that the size of the ring maps the width of the finger’s soft tissue. Radiology Centennial, Inc. copyrighted in 1993.

An improvement of the cancer imaging based on the scattering properties of AuNPs was made by El-Sayed et al. using dark field microscopy in 2005 **[26]**. For this situation, the nanoparticles are energized by the white light from a halogen lamp which is additionally a similar light utilized for lucent field imaging. As the nanoparticles scatter light most strongly at the wavelength of the SPR maximum, the nanoparticles appears in brilliant color that depends on the size and shape of the particles **[27]**.

2.4 Cellular targeting

In vivo particle imaging and targeted therapy the focused-on delivery of nanoparticles to strong tumors is a key errand in the advancement of cancer nanomedicine. "Passive" and "active" focusing on are two methodologies utilized for tumor focusing on. Active targeting relies on specific recognition of the ligands that are displayed on nanoparticles by cell surface receptors, often followed by receptor mediate endocytosis and nanoparticle internalization **[29]**. Biomolecules of intrigue may include at least one of the accompanying: peptides, proteins and antibodies; catalysts, oligonucleotides and aptamers; drugs or other organically dynamic little atoms; journalist particles or differentiation mediators, e.g., radiolabels or fluorescent colors. On the other hand, in the passive mode, nanoparticles without targeting ligands are accumulated and retained in the tumor interstitial space mainly through the enhanced permeability and retention effect **[30, 31]**.

In both mechanisms, a common feature is that nanoparticles in the blood stream must first move across the tumor blood vessels (usually leaky vasculatures) and extravasate into the tumor interstitium or the perivascular region **[32]**. Nam et al. utilized cyclic RGD-PEGylated AuNPs with straight categorized radioactive iodine as atomic imaging tests for tumor spots, exploiting that radioactive iodine has an affectability of 10^{-10}-10^{-11} M for in vivo imaging, and discovering that the tests can target tumor spots by means of integrin receptor acknowledgment simply after 10 min from circulatory vaccination. Interestingly, TEM and radio-TLC analysis of urine samples suggested the ability of these nanoparticles to go through renal filtration and be excreted from the body **[34]**.

El-Sayed and co-workers in their recent paper report on the prostate cancer targeting: AuNPs conjugated with antiandrogen chemotherapeutics target membrane androgen receptor and androgen-sensing G protein-coupled receptor, involved in prostate cancer growth and progression **[35]**. Finally, DNA- and RNA-conjugated AuNPs were found to be taken up by HeLa cells in serum-free culture by a process involving receptor-mediated endocytosis primarily mediated by scavenger receptors, a class of pattern recognition receptors **[37]**. Here we have selected just most significant instances of AuNPs application in biology and nanomedicine: this field is constantly being expanding and, ideally, before long will bring to in vivo tests on people.

3. Conclusion

It is currently wide accepted that GNP conjugates are excellent labels for determination the issues of bioimaging, which might be employed using different optical technologies, together with resonance scattering dark-field microscopy, confocal laser microscopy, completely different variants of two-photon luminescence of GNP, optical coherence tomography, acoustic tomography, etc. Modern instrumental methods such as surface enhanced Raman spectroscopy, LISNA, IR Fourier spectroscopy, etc. and the use of simple solid-phase or homo phase procedures like dot analysis, immune chromatography are methods on which GNP conjugates have found application in analytic studies based on. Finally, there is a necessity to continue and broaden studies on the biodistribution and the toxicity of GNP. First a coordinated program which might expose the correlations between particle parameters like size, shape, functionalization with various molecular probes, experimental parameters like model, doses, method, and administration scheme, organs, cells, subcellular structures under study, etc., and the observed biological effects. Coordinated efforts within the introduction of standards for the particles and methods used for the testing of nanomaterial toxicity are needed **[38-44]**.

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