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REVIEW ON GOLD NANO PARTICLE FOR NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

Drug delivery technologies are patent protected formulation technologies that modify drug release profile, absorption, distribution and elimination for the benefit of improving product efficacy and safety, as well as patient convenience and compliance .Delivery devices already exist that can release two drugs, but the timing of the release must be built into the device and it cannot be controlled from outside the body. But the new system gold nanoparticles are controlled externally and theoretically could deliver up to three or four drugs. When a drug is administered, the dosage must be carefully calculated so that the body can use the drug, which requires a drug delivery system which allows for precise dosing. Drug delivery systems also need to consider the way in which a drug is metabolized by the body. For example, some drugs are destroyed in the intestinal tract, which means that they cannot be introduced to the body in this way. Others may be dangerous in large amounts, which mean that a time release method should be used to deliver the drug for patient safety.

Keywords:

Novel drug delivery system,
Nano particle in medicine,
Gold nano particle,
Cancer treatment with Gold nano particle,
HIV Block with nano particle

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INTRODUCTION: Nanotechnology is the study, design, creation, synthesis, manipulation, and application of materials, devices, and systems at the nanometer scale (One meter consists of 1 billion nanometers). It is becoming increasingly important in fields like engineering, agriculture, construction, micro-electronics and health care to mention a few. The application of nanotechnology in the field of health care has come under great attention in recent times. There are many treatments today that take a lot of time and are also very expensive.

Using nanotechnology, quicker and much cheaper treatments can be developed. By performing further research on this technology, cures can be found for diseases that have no cure today. We could make surgical instruments of such precision and deftness that they could operate on the cells and even molecules from which we are made - something well beyond today's medical technology. Therefore nanotechnology can help save the lives of many people. Nanotechnology, when used with biology or medicine, is referred to as Nanobiotechnology.

This technology should be used very carefully because the lives of human beings are being dealt with. If used properly, it can be very effective in providing treatments with minimal side-effects. Nanomedicine, an offshoot of nanotechnology, refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve.

A nanometer is one-billionth of a meter, too small to be seen with a conventional lab microscope. It is at this size scale- about 100 nanometers or less- that biological molecules and structures inside living cells operate.

Nanotechnology involves the creation and use of materials and devices at the level of molecules and atoms. Research in nanotechnology began with discoveries of novel physical and chemical properties of various metallic or carbon-based materials that only appear for structures at nanometer-sized dimensions. Understanding these nanoscale properties permits engineers to build new structures and use these materials in new ways. The same holds true for the biological structures inside living cells of the body.

Nanotechnology in medicine currently being developed involve employing nano-particles to deliver drugs, heat, light or other substances to specific cells in the human body. Engineering particles to be used in this way allows detection and/or treatment of diseases or injuries within the targeted cells, thereby minimizing the damage to healthy cells in the body.

Nanotechnology can be defined as the science and engineering involved in the design, synthesis, characterization, and application of materials and devices whose smallest functional organization in at least one dimension is on the nanometer scale or one billionth of a meter. At these scales, consideration of individual molecules and interacting groups of molecules in relation to the bulk macroscopic properties of the material or device becomes important, since it is control over the fundamental molecular structure that allows control over the macroscopic chemical and physical properties.

Applications to medicine and physiology imply materials and devices designed to interact with the body at subcellular (i.e., molecular) scales with a high degree of specificity. This can potentially translate into targeted cellular and tissue-specific clinical applications designed to achieve maximal therapeutic affects with minimal side effects. In this review the main scientific and technical aspects of nanotechnology are introduced and some of its potential clinical applications are discussed.

The future of health care is closely intertwined with developments in nanotechnology, stem cells, genomics and proteomics. Nanotechnology is here with us today and is being used in an evolutionary manner to improve the properties of many therapeutics and healthcare products.

The application of stem cells in regenerative medicine and in drug screening is set to grow. Advances in genomics and proteomics are fuelling the shift towards predictive, preventive and personalized medicine. How these technologies will evolve and be used safely for all our benefit will be one of the great scientific adventures of the first half of the 21st century and one in which pharmacists will play an important role.

Nanotechnology and Drug Bioavailability: Drug bioavailability is a related problem with potential nanotechnology solutions. Again, biodegradable polymer capsules show promise. Hydrophobic drugs such as paclitaxel or 5-fluorouracil can be encapsulated in polymers or liposome's with nanoscale cavities that improve drug absorption and bioavailability. The opportunity exists to systematically look at both successful and failed drugs to see which ones might benefit from novel delivery vehicles. In some cases, reformulation of a drug with smaller particle size may improve oral bioavailability.

Nanotechnology is being used to create new diagnostic pharmaceuticals for use in medical imaging. The class of compounds known as superparamagnetic iron oxides (SPIOs), also known as monocrystalline iron oxide nanoparticles, or MIONs, has shown promise for a number of magnetic resonance (MR) imaging applications both as naked particles and as magnetic labels.

Application of Nanotechnology in Medicine

1. While most applications of nanotechnology in medicine are still under development nanocrystalline silver is already being used as a antimicrobial agent in the treatment of wounds.

2. Qdots that identify the location of cancer cells in the body.

3. Nanoparticles that deliver chemotherapy drugs directly to cancer cells to minimize damage to healthy cells.

4. Nanoshells that concentrate the heat from infrared light to destroy cancer cells with minimal damage to surrounding healthy cells. For a good visual explanation of nanoshells

5. Nanotubes used in broken bones to provide a structure for new bone material to grow.

6. Nanoparticles that can attach to cells infected with various diseases and allow a doctor to identify, in a blood sample, the particular disease.

Nanotechnology in Health Care: Traditionally nanotechnology in pharmacy has been associated with drug delivery, where the size of the delivery vehicle, whether it be a liposome, a polymer or even a metallic nanoparticle and its consequent ability to evade many of our bodies' natural defences has been the main attraction. We have recently seen the launch of the first nano-delivery system (DOXIL; Ortho-Biotec), a reformulated version of the anticancer agent doxorubicin.

Here, the drug is encased within polyethylene glycol (PEG)-coated liposomes less than 200nm in diameter. Because of the sustained release of the drug from the liposome and its long circulation time from the "stealth" ability conferred by the PEG, intravenous treatment is only required every four weeks. The use of PEG to mask a drug from our natural defences has also been used for antibody based therapeutics. Other delivery routes have also benefited. For example, VivaGel - a topical anti-HIV formulation - is one of the first drug products based upon nanoscale molecules called dendrimers (hyper-branched polymeric macromolecules, 2-10nm in size).

Looking ahead, a recent report suggests that the efficiency of inhaled drug delivery could be improved eight-fold using magnetic fields to guide drugs mixed with magnetic nanoparticles.

Although the lead time required to bring products to the market in the health care sector is longer than in other areas, it is clear that the steady stream of launches which led to 38 products on the market in 2004 is shortly to increase dramatically, and not only in drug delivery.

The implications of nanotechnology go much further, including for example:

- Superparamagnetic iron oxide nanoparticles for magnetic resonance imaging
- Nanopowders to increase bioavailability of poorly soluble drugs
- Wound dressings and medical devices using antimicrobial nanosilver
- Magnetic and optically active materials for cancer treatment
- Nanohydroxyapatite for implant coatings and bone substitution
- Nanosensors for point-of-care diagnostics

Some of the most far-reaching consequences of nanotechnology we can foresee are still in the research laboratory. Although the idea of nano-engineered robots circulating our systems like minisubmarines killing diseased cells are fantasy, the ability to make use of and modify biomolecular machines and motors- the proteins and nucleic acids that make life possible is real. For example, recently, a synthetic molecular motor capable of autonomous nanoscale transport inspired by bacterial pathogens was demonstrated. This new biomolecular motor operates by polymerizing a double-helical DNA tail and is hence powered by the free energy of DNA hybridization. Other researchers are using the coded nature of DNA binding to assemble large complex structures, even being able to produce letter shapes which form spontaneously. The exact applications of such work may not be obvious but these are clearly important steps on the path to radical new applications in health care

Nanomedicine:

Future Applications: Nanomedicine refers to future developments in medicine that will be based on the ability to build nanorobots.

In the future these nanorobots could actually be programmed to repair specific diseased cells, functioning in a similar way to antibodies in our natural healing processes.

1. The elimination of bacterial infections in a patient within minutes, instead of using treatment with antibiotics over a period of weeks.
2. The ability to perform surgery at the cellular level, removing individual diseased cells and even repairing defective portions of individual cells.
3. Significant lengthening of the human lifespan by repairing cellular level conditions that cause the body to age.

Nano Drug Delivery System based on Gold Particles: Colloidal gold particles in nanometer sizes were first prepared by Michael Faraday more than 150 years ago, but were never referred to or associated with nanoparticles or nanotechnology until recently. About three decades ago, colloidal gold particles were conjugated with antibody for target specific staining, known as immune-gold staining such an application may be considered as a precursor of recent explosive applications of gold particles in nanotechnology.

The importance of nanotechnology in drug delivery is in the concept and ability to manipulate molecules and supramolecular structures for producing devices with programmed functions Gold nanoparticles offer so many advantages because that they're nanometer-size systems that can get into the bloodstream and around cells.

Multi-functional gold nanoparticles have been demonstrated to be highly stable and versatile scaffolds for drug delivery due to their unique size, coupled with their chemical and physical properties. The ability to tune the surface of the particle provides access to cell-specific targeting and controlled drug release.

Massachusetts Institute of Technology (MIT) researchers are reporting on a new multi-drug delivery system based on an interesting type of gold nanoparticles. Drugs attached to their surface are released when the gold nanoparticles dissolve after exposure to a specific frequency of infrared light. The infrared frequency is related to the nanoparticle shape and allows for the targeted release of drugs.

Nanoparticles of different shapes respond to different infrared wavelengths, so just by controlling the infrared wavelength, we can choose the release time for each drug. However, the infrared wavelength necessary to melt any particular nanoparticle depends on the particle's shape. The MIT researchers created two shapes of gold nanoparticle.

Wavelengths of 1,100 nanometers melt 'nanobones,' as the team calls them, while radiation at 800 nanometers melts 'nanocapsules' (**fig. 1**). The team envisions creating up to four differently shaped particles to carry drugs into patients that physicians could release at appropriate times by using different infrared wavelengths with a lot of diseases, especially cancer and AIDS.

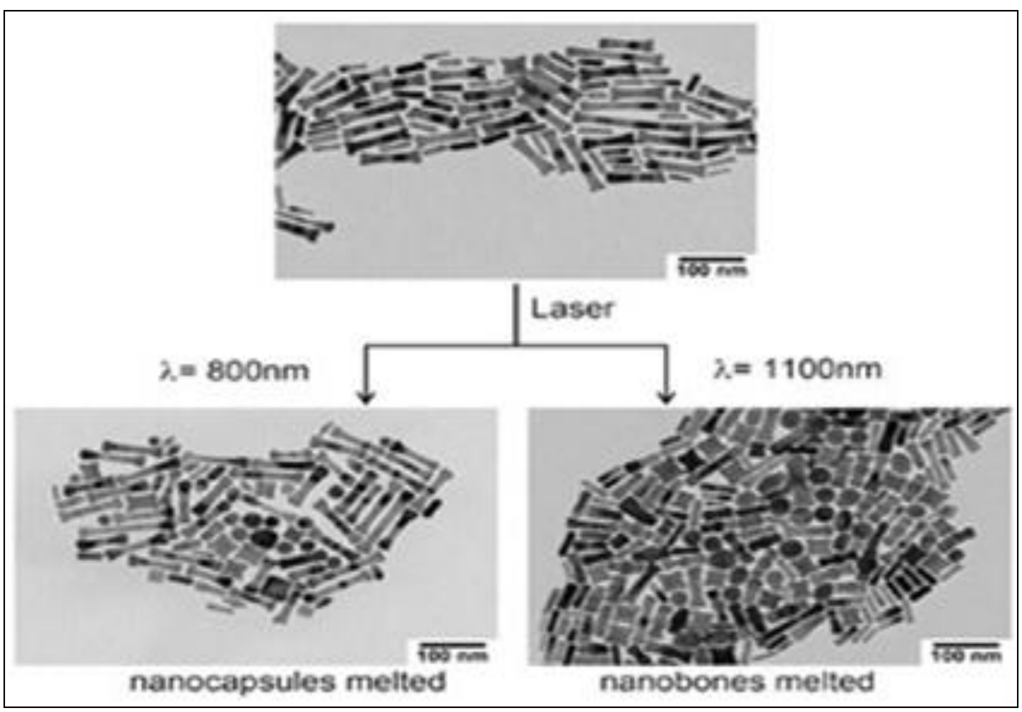

FIG. 1: THE TOP IMAGE SHOWS A MIXTURE OF GOLD NANOPARTICLES. THE LONGER PARTICLES ARE CALLED NANOBONES, AND THE SMALLER ARE NANOCAPSULES. BOTTOM LEFT: AFTER THE NANOPARTICLES ARE HIT WITH 800 NANOMETER WAVELENGTH INFRARED LIGHT, THE NANOCAPSULES MELT AND RELEASE THEIR PAYLOAD. NANOBONES REMAIN INTACT. RIGHT: AFTER THE NANOPARTICLES ARE HIT WITH 1100 NANOMETER WAVELENGTH INFRARED LIGHT, THE NANOBONES MELT AND RELEASE THEIR PAYLOAD. NANOCAPSULES REMAIN INTACT.

The research teams have applied other shapes of gold nanoparticles to the destruction of tumors. In each, the particles first seek out cancer cells. Then, when exposed to near-infrared light, the particles destroy the cells by heating them. Because the heating is localized, it spares healthy cells. "This class of particle provides the most efficient method of specifically depositing energy in tumors.

Hollow Nanospheres: The nanospheres have very distinct and unusual properties, in that they can be constructed to absorb light strongly, or narrowly. That is to say, the distance between them can be modified in the growing process, so that the end-result would consist of tighter-packed objects on the same amount of space (**fig. 2**). The formations could be successfully used to target tumors in the photo thermal cancer.

Nanospheres structure special is the combination of the spherical shape, the small size, and the strong absorption in visible and near infrared light. The absorption is not only strong; it is also narrow and tunable. All of these properties are important for cancer treatment. The heat that kills the cancer cells depends on light absorption by the metal nanoparticles, so more efficient absorption of the light is better. The hollow gold nanospheres were 50 times more effective than solid gold nanoparticles for light absorption in the near-infrared. It is a unique structure that offers true advantages over other nanostructures, so it has a lot of potential.

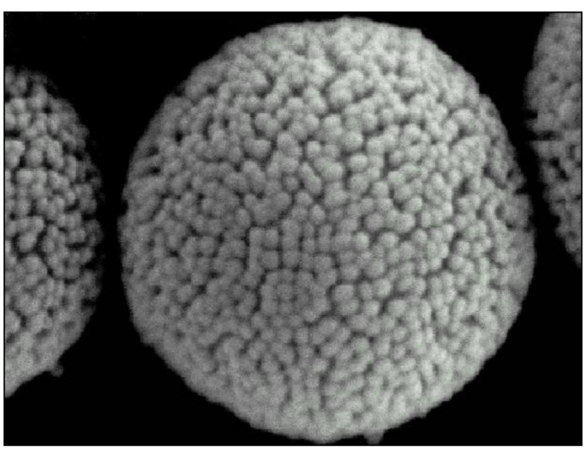

FIG. 2 : HOLLOW NANOSPHERES

Star-Shaped Gold Nanoparticles: The star shape nanoparticles can enhance the reflected lights in comparison to other shapes nanoparticles and therefore can be suitably used for various applications including as a contrast agent or a tracer. Further, as these star shape nanoparticles significantly affect the reflected light spectrum, gold nanostar (**fig. 3**) can be used as labels for detecting or identifying the particular molecule or compound and therefore can be used for controlled synthesis. Durham, NC have used these nanostars for enhancing the signal of Raman Spectrum, which is also known as SERS (surface-enhanced Raman Scattering) and found that if the target molecule is coupled with metal nanostructure, the response is greatly enhanced and sometimes more than a million times. SERS could be used for detecting various chemicals including pollutants, markers of diseases and carcinogens.

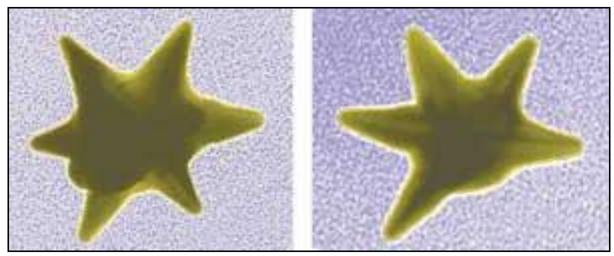

FIG. 3 : STAR-SHAPED GOLD NANOPARTICLES

Smart Gold Nanocage: The smart nanocage is designed to be filled with a medicinal substance, such as a chemotherapy drug or bactericide. Releasing carefully titrated amounts of a drug only near the tissue that is the drug's intended target, this delivery system will maximize the drug's beneficial effects while minimizing its side effects.

Cancer Treatment by using Gold: Gold is used in the treatment of prostate cancer. Using small gains of gold (about the size of a grain of rice); doctors can accurately identify the position of the patient's prostate during treatment. The improved accuracy allows for a more precise radiation dose and a more targeted area for the treatment of the tumor. Gold is the material of choice for the positioning grains because it is dense and opaque to X-rays.

An alternative approach is being pursued by the US Company Nanospectra who are focused on the development of Aurolase Therapy to selectively destroy solid tumors. Nanospectra use gold nanoshells (tiny particles of gold wrapped around silica) rather than sold gold nanoparticles, but these are injected into the body.

After the particles accumulate in a tumor, the area is illuminated with a near-infrared laser at wavelengths chosen to allow the maximum penetration of light through tissue. Unlike solid gold nanoparticles, Auroshell particles are designed to specifically absorb this wavelength, converting the laser light into heat. This results in the rapid destruction of the tumor along its irregular boundaries.

Hot Gold Nanoparticles can cook Cancer Cells: There are many possible ways to kill a cancer cell, and one of them is to cook them to death. There are nanoparticles worth their weight in gold to do just that. Researchers at the Niels Bohr Institute at the University of Copenhagen are experimenting with tiny gold particles' ability to melt the lipid membranes surrounding cells, paving the way for pinpoint precision when attacking tumors.

The researchers used optical tweezers, which is focused laser light that can trap and hold the gold nanoparticles. "The particles can be heated using infrared light from the optical tweezers and by turning the light up and down you can control the heat
To measure how hot the gold nanoparticles got, they were moved closer and closer toward an artificial cell membrane composed of lipids. When the lipids melted, they could calculate the temperature. It turns out that the gold particles are able to reach several hundred degrees at a light intensity of less than 1 watt. Melt the lipids in a cell membrane, and the cell dies -- but only that cell, since the heat dissipates at a cell's length away.

Gold Nanoparticles in DNA Technology: Gold nanoparticles have been used in the development of self-assembling DNA nanotubes that could provide a new method for delivering drugs to specific cells. The researchers of McGill University in Montreal assembled double-stranded DNA nanotubes to create three-dimensional triangular chambers of different sizes. When built in the presence of different sized gold nanoparticles, the metal molecules were trapped in the matching capsule "like peas in a pod". In effect, the nanotubes act like sieves and select the correct sizes to encapsulate. The researchers added strands of DNA that specifically complement the strands used to trap the particles to release them.

This system could be used to carry cancer treatments in the body before releasing them when they are near diseases tissue.

Gold Nanoparticles to help in faster detection of Meningitis: Gold nanoparticles enable faster detection of meningococcal meningitis and minimize fatalities. Meningitis progresses rapidly and can cause death if left untreated. Symptoms include fever, chills, headache, vomiting, stiff neck, rash, confusion, seizures, and coma, stiffness in knees and hips and shock.

The Royal Melbourne Institute of Technology (RMIT) developed a method to notes change in the color of gold nanoparticle solution to indicate the presence of meningococcal DNA. The change is read by the naked eye and the technique is being fine tuned for use in a point-of-care clinical setting. In the future, this will hopefully lead to more rapid detection of meningococcal disease and earlier treatment, which will ultimately result in fewer deaths and less severe complications. By diagnosing the disease early, it is possible to prevent death or severe complications by giving patients the most appropriate treatment.

Gold Nanoparticles to block HIV: Now it is believe that gold nanoparticles may breathe new life into once-promising drug candidates, in particular a compound designed to stop the spread of HIV (human immunodeficiency virus) that was shelved because of side effects.

The compound, TAK-779 was first proposed by researchers in 1996 and proved effective at blocking the virus from infiltrating body's immune system. But it was scuttled by 2005; because recipients suffered severe irritation at injection sites and oral doses were ineffective because of ammonium salt molecules in the compound triggered the bad reaction. Now it was found during lab tests that attaching 12 molecules of TAK-779 modified to exclude ammonium salt molecules to one gold nanoparticle restored the drug's ability to prevent HIV infection. The size of the gold particles is two nanometers (two billionths of a meter) in diameter, is comparable to that of the HIV proteins they are trying to block. This should make them well suited to stop viral proteins from coming in contact with key receptors (**fig. 4**).

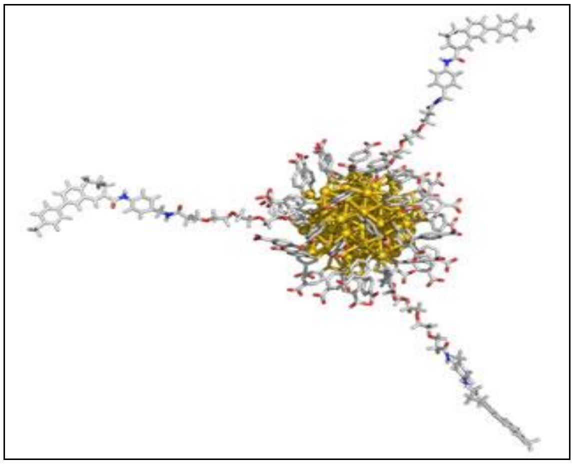

FIG. 4: PROCESS OF SUBSTITUTING OF AMMONIUM SALT MOLECULES WITH GOLD NANOPARTICLES CAN CREATE A COMPOUND THAT BLOCKS HIV FROM INFECTING RECEPTOR PROTEINS WITHOUT HARMFUL SIDE EFFECTS

CONCLUSIONS: Today the nanotechnology carries have a major role in the pharmaceutical research for detecting various diseases. The new system gold nanoparticles are play a major role in controlled drug delivery system externally and theoretically could deliver up to three or four drugs. With a lot of diseases, especially cancer and AIDS, it is possible to get a synergistic effect with more than one drug, so the gold nanoparticles drug delivery system could provide multiple drugs in the treatment of cancer or aids. Nanoparticles of different shapes respond to different infrared wavelengths, so just by controlling the infrared wavelength, we can choose the release time for each drug. Such a system could one day be used to provide more control when battling diseases commonly treated with more than one drug,

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