A REVIEW ON RECENT ADVANCES IN NANOTECHNOLOGY- GOLD NANOSHELLS SYNTESIS AND ITS APPLICATIONS

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***Abstract*: Gold Nanopshells: Nanoshells are the nano particles with dielectric core which is covered by thin metallic shell usually gold these are nanoshell plasmon that means nanoshells involve in quasiparticles , the nanoshell plasmon have collective excitation or quantum plasma oscillation means that the electrons simultaneously oscillate with respect to ions.These nanoparticles, seen in transmission electron micrograph image, they have solid core. Researchers at north western university are using gold particles to develop ultra-sensitive detection systems for DNA and protein markers associated with many forms of cancer, including breast prostate cancer. Gold nanoshells are unique in that they combine many ideal features in a single particle. As a direct result of nanoscale resonance phenomena, gold nanoshells have very large optical absorption and scattering cross - sections, which render them highly suitable as contrast agents for imaging. They can be tuned to preferentially absorb or scatter light at specifi c wavelengths in the visible and near - infrared (NIR) regions of the spectrum. In the NIR ' tissue window ' , light penetration into tissue is optimal. Nanoshells tuned to absorb NIR radiation are particularly useful as mediators of photothermal cancer therapy because they effi ciently convert absorbed radiation into heat, and are thermally stable at therapeutic temperatures. Furthermore, nanoshells preferentially accumulate at tumor sites due to their nanoscale dimensions. The inert gold surface of nanoshells provides several advantages, including biocompatibility, noncytotoxicity, and it also facilitates conjugation to monoclonal antibodies or other biomolecules for both active tumor targeting and biosensing applications.**

***Index Terms:* Nanoshells, collective excitation, ultra-sensitive, nanotubes, biomolecules.**

I.INTRODUCTION:

Gold nanoshells are spherical particles with diameters typically ranging in size from 10 to 200 nm. They are composed of a dielectric core covered by a thin gold shell. As novel nanostructures, they possess a remarkable set of optical, chemical and physical properties, which make them ideal candidates for enhancing cancer detection, cancer treatment, cellular imaging and medical biosensing. Gold nanoshells are unique in that they combine many ideal features in a single particle. As a direct result of nanoscale resonance phenomena, gold nanoshells have very large optical absorption and scattering cross - sections, which render them highly suitable as contrast agents for imaging. They can be tuned to preferentially absorb or scatter light at specifi c wavelengths in the visible and near - infrared (NIR) regions of the spectrum. In the NIR ' tissue window ' , light penetration into tissue is optimal. Nanoshells tuned to absorb NIR radiation are particularly useful as mediators of photothermal cancer therapy because they effi ciently convert absorbed radiation into heat, and are thermally stable at therapeutic temperatures. Furthermore, nanoshells preferentially accumulate at tumor sites due to their nanoscale dimensions. The inert gold surface of nanoshells provides several advantages, including biocompatibility, noncytotoxicity, and it also facilitates conjugation to monoclonal antibodies or other biomolecules for both active tumor targeting and biosensing applications. The fi rst Stage I clinical trials using nanoshells as therapeutic agents to treat head and neck cancers are set to commence in 2008 [2] . Over the past few years, the pace of research in this fi eld has accelerated rapidly, as have the number of potential biomedical applications for nanoshells. It has been the present authors ' best attempt to keep abreast of new developments in the fi eld but, given the pace of progress, this chapter will be partially outdated by the time it hits the press – which is good news! The chapter is designed with two distinct audiences in mind: researchers already in the fi eld who may use it as a quick reference; and ' early - stage ' researchers, who can use it as a first read to gain a broader understanding.

Advantages;

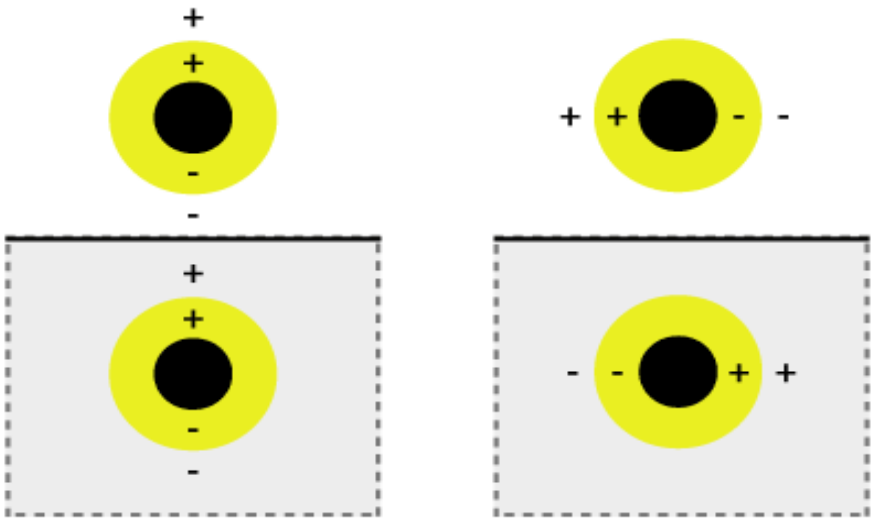
Nanoparticles provide massive advantages regarding drug targeting, delivery and release and, with their additional potential to combine diagnosis and therapy, emerge as one of the major tools in nanomedicine. The main goals are to improve their stability in the biological environment, to mediate the bio-distribution of active compounds, improve drug loading, targeting, transport, release, and interaction with biological barriers. The cytotoxicity of nanoparticles or their degradation products remains a major problem, and improvements in biocompatibility obviously are a main concern of future research.

1. New drug delivery systems can provide improved or unique clinical benefits such as Improvement in patient's compliance Improved out comes.
2. Reduction of adverse effect, Improvement of patient's acceptance of treatment, Avoidance of costly interventions such as laboratory services.
3. Allowing patients to receive medications as out patients and possibly. v Reduction in overall use of medicinal resources.

4. Nano-drug delivery systems that deliver large but highly localized quantities of drugs to specific areas to be released in controlled ways, Controllable release profiles, especially for sensitive drugs, Materials for nanoparticles those are biocompatible and biodegradable.
5. Architectures / structures, such as biomimetic polymers, nanotubes. v Technologies for self-assembly.
6. Functions (active drug targeting, on-command delivery, intelligent drug release devices/ bioresponsive triggered systems, self-regulated delivery systems, systems interacting with the body, smart delivery).
7. Virus-like systems for intracellular delivery, Nanoparticles to improve devices such as implantable devices / nanochips for nanoparticle release, or multi reservoir drug delivery-chips.
8. Nanoparticles for tissue engineering; e.g. for the delivery of cytokines to control cellular growth and differentiation , and stimulate regeneration; or for coating implants with nanoparticles in biodegradable polymer layers for sustained release.
9. Advanced polymeric carriers for the delivery of therapeutic peptide/proteins (biopharmaceutics) and also in the development of: Combined therapy and medical imaging, for example, nanoparticles for diagnosis and manipulation during surgery (e.g. thermotherapy with magnetic particles)
10. Universal formulation schemes that can be used as intravenous, intramuscular or preoral drugs
11. Cell and gene targeting systems & Devices for detecting changes in magnetic or physical properties after specific binding of ligands on paramagnetic nanoparticles that can correlate with the amount of ligand. v Better disease markers in terms of sensitivity and specificity.

II. NANOSHELLS

Nanoshells are the nano particles with dielectric core which is covered by thin metallic shell usually gold these are nanoshell plasmon that means nanoshells involve in quasiparticles , the nanoshell plasmon have collective excitation or quantum plasma oscillation means that the electrons simultaneously oscillate with respect to ions.



Polarisation reaction

III. MATERIALS REQUIRED FOR PRODUCTION OF NANOSHELLS:

- Tetraethyl orthosilicate
- Ammonium hydroxide
- Hydroxylamine HCL
- 3-amino propyl trisilicate
- Hydrogenated tetrachloroaurate (111) trihydrate
- Tetrakis(hydroxymethyl) phosphonium chloride
- NAOH
- Potassium carbonate
- Ethanol
- Ultra pure water

IV. GENERAL METHODS FOR PREPARATION OF NANOSHELLS:

1. By preparation through microfluidic device fabrication**:**

➢ In this method microfluidic device is fabricated with silicon wafers by standard photolithography the device is moulded in PDMS for 70 degrees centigrade for 4 hours the silicon coated wafers are peeled & cut and cleaned.

➢ Then the inlet and outlet holes are punched into the device and the microchannels were irreversibly bonded to a glass slide those are precooled with thin layer of PDMS and then it is plasmon treatment.
➢ Finally the microchannels are have rectangular cross section and are 300micrometers wide 155micrometers deep and 0.45mters long.

2. Pumping silicon oil method:

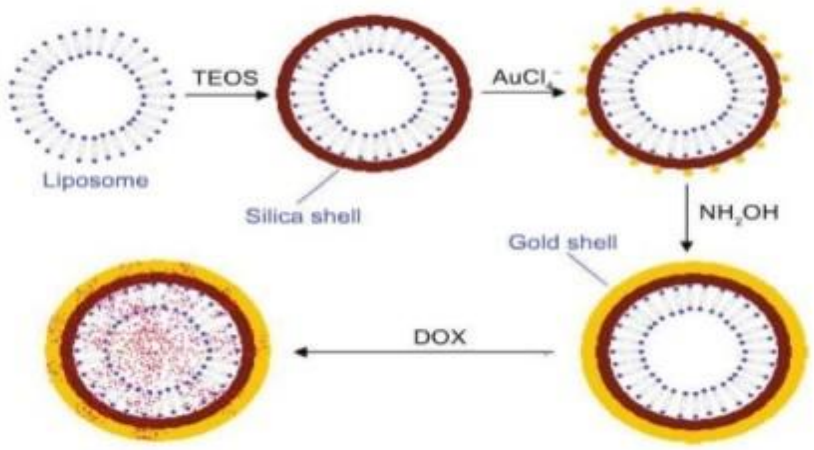
➢ In this method a mixture of gold and seeded silica particles and gold plating solution and reducing solution was coated on a microfludic device while nitrogen was delivered from cylinder.
➢ The plating solution was then left to age, in a controlled environment, for longer then 24 hours.
➢ After, the completion of aging process the fluid is collected from the microfluidic device and placed in centrifuge.
➢ The resulting liquid has a layer of oil on the surface with a solution below that contains the nanoshells.

3. Another method for preparation of gold nanoshells;

In this method it involves 3 steps they are

1. **Silica-coated liposomes (**nano composities synthesis):
Soya bean lecithin (120mg) and cholesterol (8mg) were dissolved in chloroform(1ml) in a conical flask and the distilled water is added to the flask to hydrate the dried lipid film, and the liposome dispersion was extruded through the polycarbonate membrane filters.the liposome suspension was diluted with water and NAOH is added and gently stirred at room temperature for 24 hours and stirring was stopped and liposome suspension was taken and stored at 4 degrees centigrade at refrigerator.
2. **Gold nanoshell synthesis:**
The distilled water diluted with KH550(amino propyl trithoxy silane (20micro liter,6ml/L) was mixed with liposome/ Sio2 suspension (200µl) for about 2hours.HAUCl4(AU chloride tetra hydrate) aq.solution and NH2OH aq.solution were added ,afterv that reaction solution was continuously stirred for 10 minutes and centrifuged and the precipitate was washed with water and freeze dried about 72 hours.
3. **Fabrication of DOX loaded liposomes/Sio2/AU:**
The liposome Sio2/AU precipitate (5mg) was added to DOX aq.solution and incubate at room temperature and after 12 hours and suspension was precipitated by centrifugation and washed once with water to remove the free DOX and finally washed precipitate is resuspended in a serum free RPMI 1640 medium before cell experimentation,

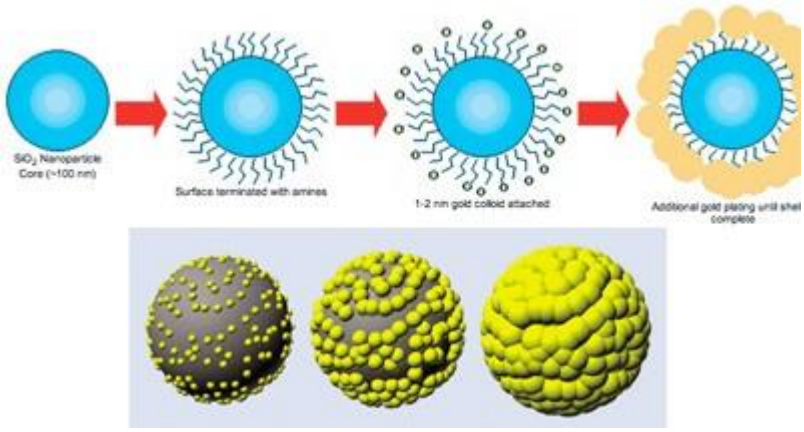
Formation of DOX loaded nanoshells



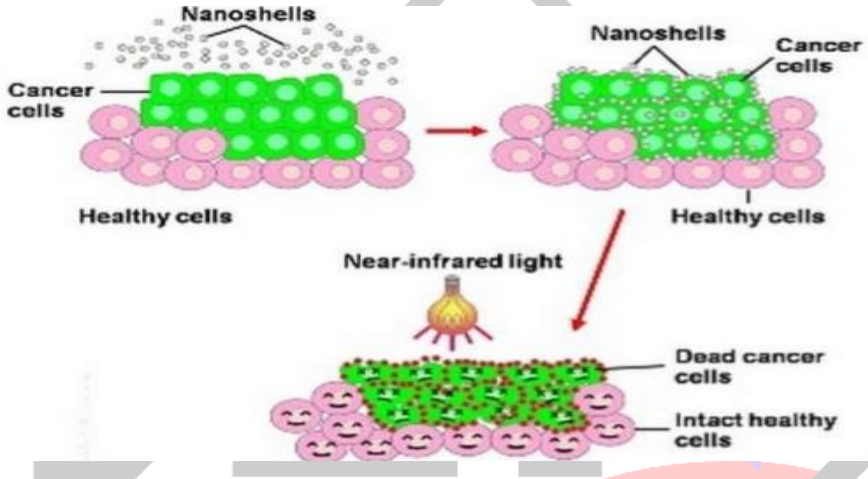
V. MAIN MECHANISM OF GOLD NANOSHELLS:

In this main use of nanoparticles act by two mechanisms they are

*1.**Electrochemical detection***; in this method the standard electrode is coated with chitosan ,a complex sugar obtained from crab and shrimp shells and then with gold nanoparticles in first step to provide the electrical conductivity surface upon in which cancer cell can stick without damaging the cells and the cancer cells are taken from the patient and suspended in a suitable growth solution after that cells were allowed to bind to the electrode and two monoclonal antibodies are added to assay solution and the fist antibody binds to glycoprotein and the second antibody cause the electrochemical reaction , but only the first antibody has bound to any glycoprotein ,the electrochemical reaction triggers of cells with glycoprotein present on the cell surfaces.



photothermal therapy: In this potothermal therapy the photon energy is converted in to heat to damage and destroy the cancer cells,theis therapy uses conductive nanomaterials like gold particles and gold shells and carbon nanotubes.



VI.TOXICITY STUDIES OF GOLD NANOSHELLS:

No comprehensive studies evaluating long - term toxicity of gold nanoshells has been reported. All available proof shows that at physiological doses, gold nanoshells are not cytotoxic and do not cause any short-term health risks. Gold has been universally recognized as the most biologically inert of metals. Silica nanospheres have been shown to be nontoxic in a murine mouse model. The safety of gold nanospheres has been well documented; in experiments performed in vitro, a gold nanosphere incubated with macrophages was found to be both noncytotoxic and nonimmunogenic. A nanosphere was also found to reduce production of both Reactive Oxygen Species (ROS) and nitrite radicals, and does not stimulate secretion of inflammatory cytokines. Numerous in vivo studies that were conducted in mice have provided best evidence that nanoshells are not only nontoxic but also safe. Although a prolonged respiratory exposure to high doses of crystalline silica have been linked to lung cancer in epidemiological studies, the carcinogenic potential of gold nanoshells is minimal because silica used in nanoshells is completely obscured from the host by gold shell, which is not carcinogenic.

VII. APPLICATIONS OF NANOSHELLS:

- *optical characteristics;* the optical property of nanoshells is due to the plasma resonance of dielectric gold interface ,the most important characteristic is tunability it is the position of resonance extention peak selectively tuned from 600nm to greater then 1000nm,especially the normal wavelength of nanoshells ranges from 700nm-900nm the nanoshells can develop high scattered light with in the desired spectrum.
- *Tissue welding;* nanoshells represents a rapid means of treating lacerations in emergency room settings ,the nanoshells has exogenous NIR absorber for welding tissue wounds ,they have high and effective penetration depths ranges from few mellimeters to several centimeters depending on the tissue type.
- *Drug delivery or targetting*: Because of small size, gold nanoshells are taken by cells where large particles would be excluded or cleared from the body A gold nanoshell carries the pharmaceutical agent inside its core, while its shell is functionalized with a 'binding' agent. Through the 'binding' agent, the 'targeted' nanoparticle recognizes the target cell. The functionalized nanoparticle shell interacts with the cell membrane.The nanoparticle is ingested inside the cell, and interacts with the biomolecules inside the cell. The nanoparticle particles breaks and the pharmaceutical agent is released.

- *Diagnosis and sensing;*every cell has a specific unique molecular structure to detect the healthy and sick tissues , a nanooshell can be functionalized to diagnoise the infected tissue and targets to a specific infected tissue by using biomarker ,thuus the detection of nanoparticle is linked to the detection of the biomarker and to the diagnosis of disease.
- *Metal nanoshells for biosensing applications:*Biosensors are analytical tools that help to detect the presence of several chemical and biological agents like viruses, drugs, or bacterium in biological or ecological systems.Nanoshell biosensors work by emitting a signal that is characteristic of the virus, toxin, or bacteria to be measured, thus identifying the presence or absence of the material. The ratio between the thicknesses of the gold nanoshell to the non-conductive, silicon core determines the signal to be emitted. Gold is used because of its non-reactive properties and conductive nature, allowing the nanoparticle to absorb specific frequencies of infrared or ultraviolet light.
- *Gold nanoshells vs. alzheimer:*Alzheimer and other degenerative diseases are caused by the clustering of amyloidal beta (Aβ) protein. Gold nanoparticles canbe functionalized to specifically attach to aggregates of this protein (amyloidosis). The functionalized gold nanoparticles specifically attach to the aggregate of amyloidal protein. The microwaves of certain frequency are irradiated on the sample. Resonance with the gold nanoshells increases the local temperature and destroys the aggregate
- *Cancer imaging and therapy:* Nanoshells has rigid structure due to their metallic nature they offers more stability to improve the biocompatibility they are coated with stealthing polymer like gold . Nanoshells of 120nm diameter silica core produce peak absorption.Therapy of SKBr3 breast cancer cells along with antiHER2 when irradiated destroy the cancer cell.

The gold nanoshell of 10nm diameter core and 10nm thick gold shell absorb light in NIR region having absorbance of820nm destroys the cancer cells and also by scattering and absorption of light bioimaging at optical frequencies is obtained.

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