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Surface functionalization of gold nanoparticles for targeted drug delivery

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Abstract: Despite rapid advancements in the field of medical sciences, the current therapeutic modalities still face several challenges like; lack of efficacy, lack of specificity to the tissue/cellular environment, inability to penetrate the endosomal barriers, reduced bioavailability etc. In order to circumvent these issues nanoparticle based drug delivery systems can be novel and intriguing in the near future.Gold nanoparticles have peculiar and extraordinary properties which are of profound interest in diverse fields of applications. Due to their unique sub cellular size(quantum size effects), high surface area to volume ratio, enhanced optoelectronic properties, excellent surface chemistry and enhanced bio compatibility they are promising candidates in advanced drug delivery systems. These subcellular particles can effectively penetrate the endosomal barriers. They can be used as pro drugs or drug carriers that can selectively deliver the administered dosage of the drug to the targeted tissue. They exhibit enhanced permeation and retention rate. This paper highlights various methods for the synthesis, functionalization and characterization of gold nanoparticles. Gold nanoparticles were synthesized using wet chemical method by citrate reduction process and through green synthesis using lemon grass broth as a reducing agent. Surface functionalization of the synthesized particles was done with chitosan,polysorbate 80 and polyethylene glycol.
Keywords:- Gold nanoparticles, endodomal barrier, targeted drug delivery.

Introduction

Gold nanoparticles are quantum confined sub cellular particles of gold having dimensions in the range of 1-100nm.At the nanoscale regime these particles exhibit unique and extraordinary characteristics when compared to their bulk counterparts. They are complex multi-electron systems where reduced sizes and the quantum confinement of their electrons and phonons that lead to their fascinating properties that are tunable with their shape and size distribution surface chemistry and aggregation state. At the nanoscopic level the number of surface atoms become predominant and larger proportion of the atoms occupy in the corners of the crystal. The surface energy possessed by these atoms increases to manifold as a result of which the chemical reactivity of every atom is nearly 400 fold times higher than a bulk atom of gold. Surface functionalization is the technique of surface modification incorporating functional moieties onto the surface of nanostructures. The

purpose of surface functionalization is to control the reactivity of nanoparticles, reduce the toxicity, stabilize their symmetry and morphology in order to enhance the tissue biocompatibility and rate of uptake of nanoparticles by the cells in the biological environment. Surface functionalization using chitosan, polysorbate 80 and polyvinyl alchohol are described in this paper[1-8].

Materials and methods[1-8]

2.1Citrate synthesis of gold nanoparticles

The method used for the synthesis of gold nanoparticles is the citrate reduction method/Turkevich method. This method is based on the reduction of chloroauric acid by surfactant addition which causes Au^{3+} ions to be reduced to neutral gold atoms.When more gold atoms form the solution becomes supersaturated and gold begins to precipitate into sub nanometer particlesA capping agent or a stabilizing agent is added to facilitate monodispersion and prevent agglomeration.Reagents used 0.01M chloroaurate trihydrate, trisodium citrate,chitosan, glacial acetic acid, Polyvinyl alchohol, milliq water

Procedure

1ml from the prepared 0.01M stock solution (chloroaurate trihydrate) was taken in a clean beaker and 100ml of deionized water was added to it. The solution was stirred in a magnetic stirrer at desired speed and heated gradually upto 80°C.After it had reached the desired temperature 1% trisodium citrate solution was added drop wise to the heated solution after every 5 minutes. The addition of trisodium citrate the boiling chloroaurate solution resulted in pale pink colouration which was the end point.

The solution was subsequently cooled to room temperature followed by the addition of 1ml of 5% PVA solution as a capping agent. The beaker containing the solution was sealed tightly with parafilm and stored in refrigeration unexposed to light

$$2HAucl4+Na3C6H5O7 \longrightarrow 2Au+C5H6O5+3Nacl+Co2$$

Fig 2.1 Pale pink coloured colloidal gold after citrate reduction

2.2 Preparation of chitosan-gold nanoparticle suspension

3%w/v of chitosan was prepared in 2%v/v of glacial acetic acid solution. A fine suspension of chitosan in glacial acetic acid was obtained after magnetic stirring overnight5ml of this prepared suspension was added to 10ml of the colloidal gold solution in the ratio1:2 .The prepared suspension is stored in a sterile glass vial and was kept for magnetic stirring overnight until the chitosan complex was completely dissolved in the colloidal gold solution

2.3 Green synthesis using lemongrass broth

Fresh leaves of the lemon grass plant were taken and rinsed thoroughly in distilled water and air dried.The leaves were cut uniformly and weighed up to 1.5g.The finely cut leaves were placed in a beaker with 100ml of deionized water and heated in a hot plate till the temperature reached 100°CThe solution was cooled to room temperature and was filtered thoroughly using whattman filter paper. The clarified solution of lemon grass broth was used as reducing agent for the synthesis of gold nanoparticles

Reduction process

1ml from the stock solution of chloroauric acid was taken and subsequently made into solution by added 100ml of DI water. The solution was heated to 80°C in a hot plate and was subject to magnetic stirring To this boiling solution the prepared lemon grass broth was added drop wise after every 5minsThe addition of reducing agent was stopped when the solution turned purple due to the reduction of Au 3+ to Au 0The solution was cooled to room temperature and 1ml of 5% PVA was added as a stabilizing agent soon after the reduction process the solution was kept for overnight stirring till a very fine dispersion was obtained

Fig2.3.2 green synthesized colloidal gold

1% (w/v) chitosan was prepared and dissolved in 2%(w/v)L-ascorbic acid. The solution was kept for magnetic stirring overnight until a very fine suspension of chitosan was obtained5ml of this suspension was added to 10ml of the green synthesized colloidal gold solution in the ratio 1:2.The solution was stored in a clean glass vial and kept at 4°C unexposed to light.Polysorbate 80 commonly referred to as tween 80 is a non-ionic hydrophilic surfactant derived from polyethoxylated sorbitan and oleic acid. It is a synthetic viscous liquid which is soluble in water. It has a critical micelle concentration of 0.012mM.

1ml of tween 80 was taken using a micropipette and added to 100ml of deionized milliq water in a beaker making 1% v/v solution.The solution was stirred overnight at room temperature to obtain a very fine suspension5ml of the prepared 1% Tween 80 solution was added to 10 ml of the green synthesized colloidal gold solution.The solution was subsequently stored in a clean glass vial and kept at 4°C unexposed to light.

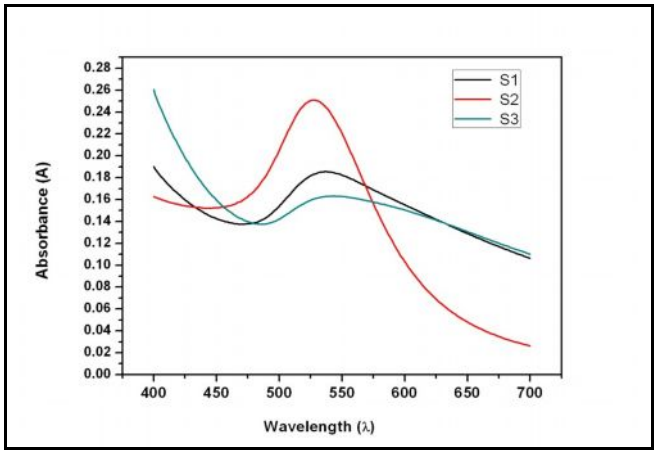
Characterization Techniques

Uv-vis spectroscopy was taken to confirm the characteristic absorption peak, The wavelength of illuminating light was set from 400-700nm. X-ray Fluorescence Spectroscopy was taken graphical data between energy of X-ray fluorescence and excitations per second is obtained that determines the elemental existence of gold.ATR-FTIR Spectroscopy was taken and the wavelength is set in the IR region and the result is a graph obtained between wave number and absorbance that displays the vibrational bands(stretching and bending) corresponding to the functional groups .Dynamic Light Scattering Spectroscopy and Zeta Potential was taken.The size and zeta potential of the gold nanoparticles was determined by Malvern Zetasizer device. This device measures a phase change in light scattered by the particlesunder the influence of an applied electric field(200V).The field emission scanning electron microscope used was Carl Zeiss SUPRA™ 55. A drop of the samples was placed in a silicon substrate and was air dried. The ultra -high vaccum is turned on an hour before sampling

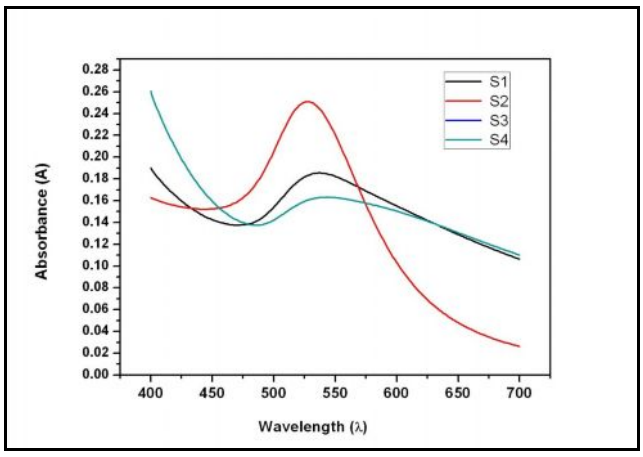
Results and Discussion

UV-Visible spectroscopic data

S1 denotes the 3%chitosan functionalized gold nanoparticles S2 denotes standard (control gold nanoparticles), S3 denotes 5%PVA capped gold nanoparticles**.** The maximum plasmon absorption peak for all the samples was found to lie between 500-570nmsuggesting the longitudinal surface plasmon resonance when compared with the reference SPR peaks for gold nanoparticles. The longitudinal plasmon resonance peak shifts to longer wavelength when the surface to volume ratio of the nanoparticles increases.



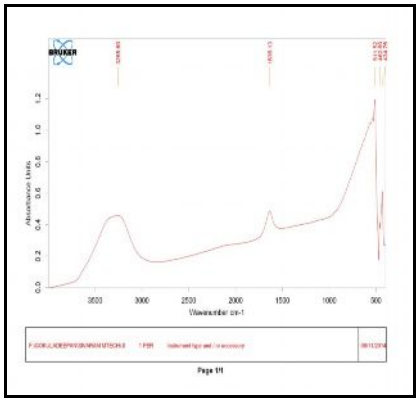
Fig;4.1.1 UV-VIS Spectroscopic data for citrate synthesized gold nanoparticles



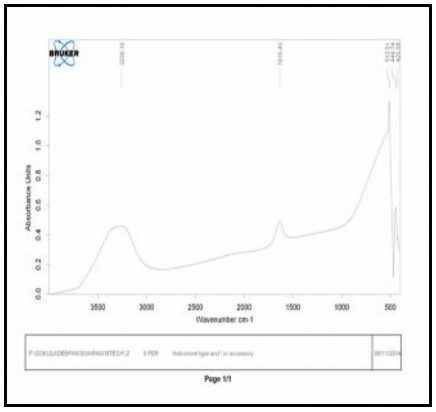
Fig;4.1.2 UV-VIS Spectra for Gold nanoparticles synthesized using lemon grass broth as reducing agent

ATR Spectrum for gold nanoparticles

There was a broadening of peak at 3225cm-1that indicates the stretching modes of the amide bonds and the symmetric stretching of the C=O bonds was observed at 1636cm-1 and a very sharp asymmetric stretching of the vibrational bands were observed at 511.52 and bending of the vibrational bands was observed at 462cm-1.



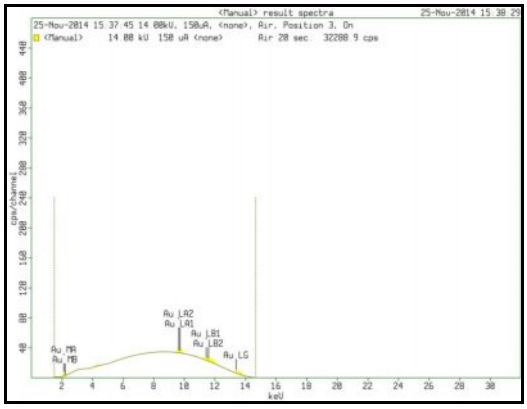
Fig;4.2.1 1% chitosan functionalized green synthesized colloidal gold



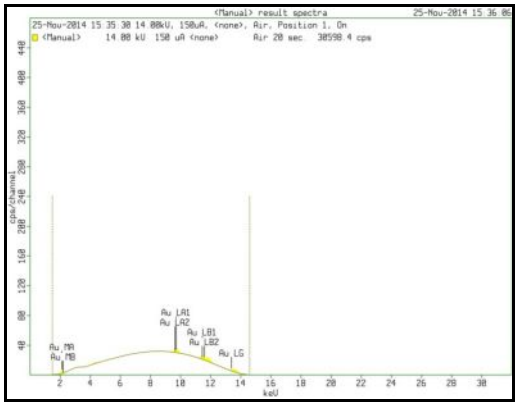
Fig;4.2.2 5%PVA functionalized colloidal gold

The peaks at 1635cm-1 is indicative of O-H groups and C-H deformation vibration in PVA . A broad absorption band at 3256cm-1 is noticed which can be attributed to the O-H stretching vibrations and hydrogen bonded hydroxyl groups.

XRF Spectrum In both the cases the X-Ray fluorescence yield of for the L -shell of the gold nanoparticles was found to be greater than the corresponding M-shell. The maximum fluorescence yield was found to be at 9KeV energy.

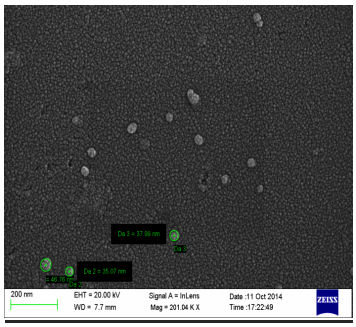


Fig; 4.3.1 1% chitosan functionalized gold nanoparticles



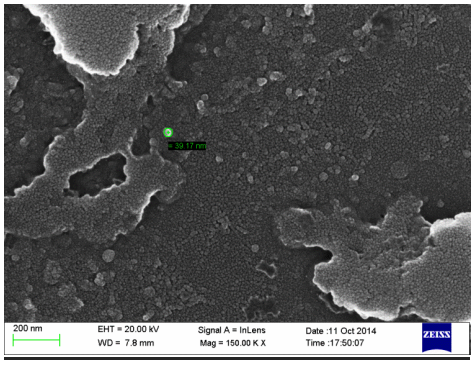
Fig; 4.3.2 5% PVA functionalized gold nanoparticle

FESEM imaging



Fig;4.4.1 Citrate synthesized gold nanoparticles

At 200nm scale imaging at 201KX magnification the morphologies of the gold nanoparticles were found to be spherical. The hydrdyanamic radius of the gold nanoparticle was found to be 35.07nm.



Fig;4.4.2 Chitosan functionalized gold nanoparticles

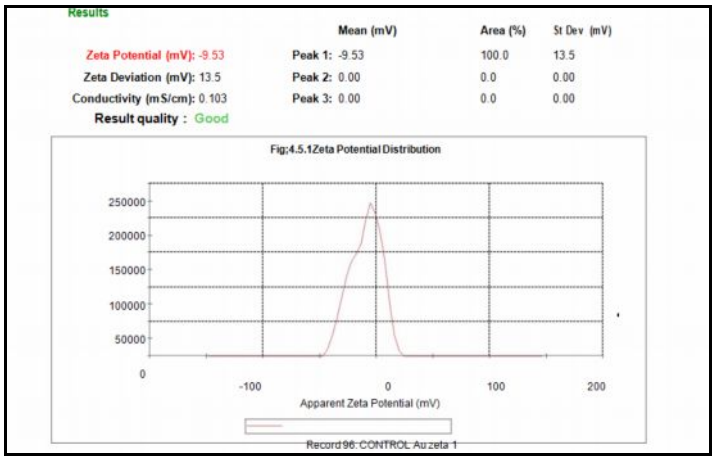
Most of the subcellular particles of gold formed clusters due to the addition of chitosan with irregular morphologies. Some agglomerated particles can also be visualized which is attributed to genuine aging of the chitosan-gold complex. The average particle size was found to be 39.07nm

DLS Spectroscopy and Zeta potential Report

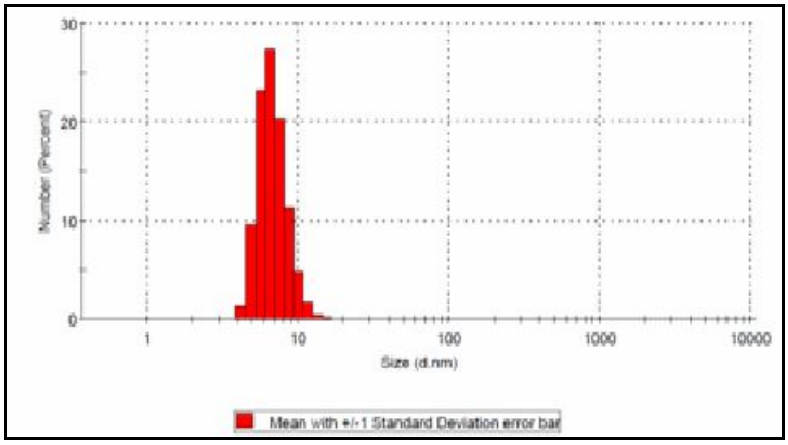
The mean zeta potential of the gold nanoparticles was negative which indicates that the surface charge is negative.

For control gold nanoparticles

Temperature (°C):	25.0	**Zeta Runs:**	12
Count Rate (kcps):	379.1	**Measurement Position (mm):**	4.50



Z-Average (nm): 95.70748 **Derived Count Rate (kcps):** 4400.3479935925



Fig;4.5.2 Graph indicating particle size distribution

For 1% chitosan functionalized gold nanoparticles

The positive value of the mean zeta potential indicates the positive surface charge of the chitosan functionalized gold nanoparticles. This attributes to the high stability of the chitosan-colloidal gold complex.

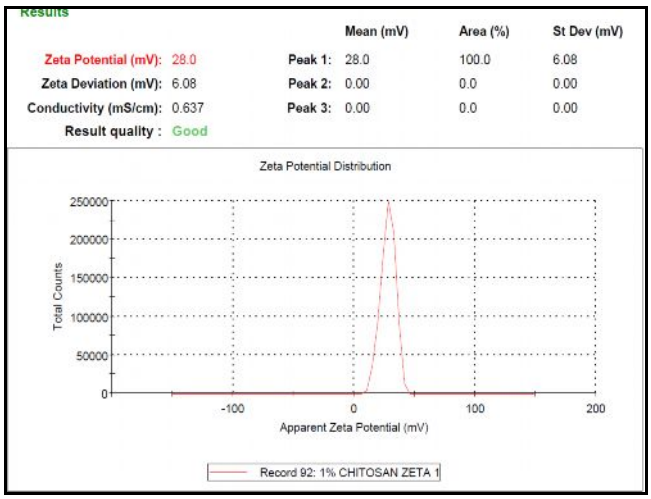


Fig 4.5.3 Graph of zeta potential distribution

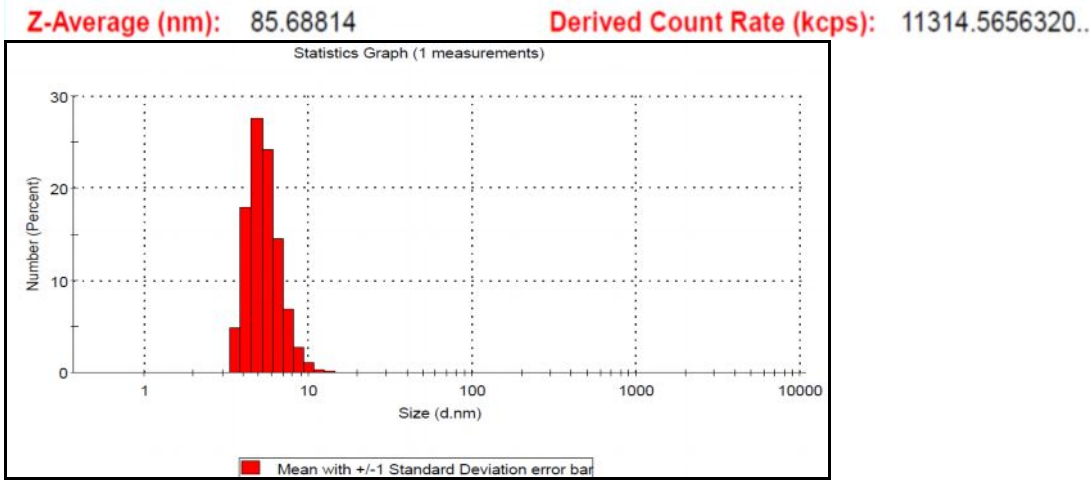
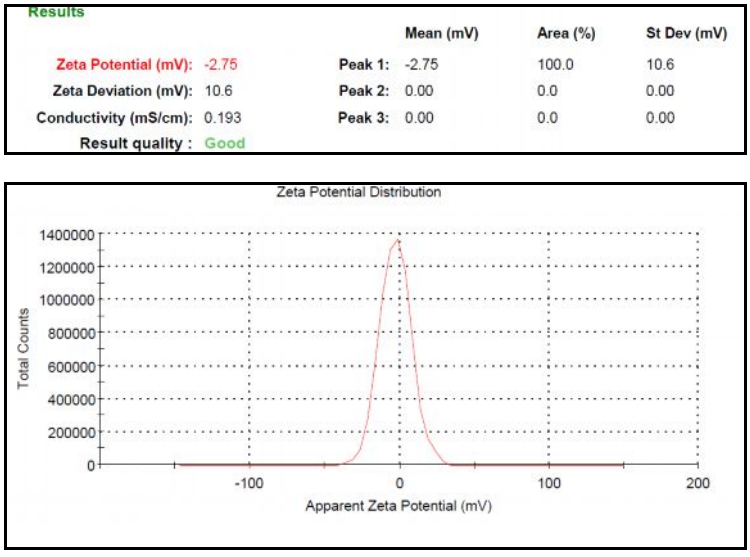


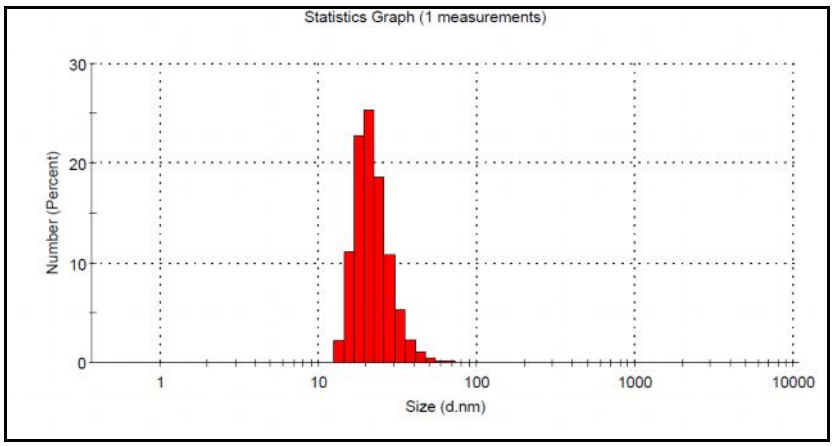
Fig 4.5.4 Particle size distribution

For PVA functionalized gold nanoparticles

The negative zeta potential indicates the negative surface charge of the colloidal particles. There was average particle size is increased due to aggregation of particles



Fig;4.5.6 Graph of particle size distribution



Fig;4.5.5 Graph of zeta potential distribution

Conclusions

Gold nanoparticles were synthesized using citrate reduction and Lemon grass as reducing agent. Various characterization techniques were employed to quantitatively and qualitatively analyse the gold nanoparticles. Simple surface functionalization was done using chitosan polyvinyl alchohol and polysorbate 80.The particle size distribution and Zeta potential measurements revealed the surface charge of the particles.

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