Original Article

Gold Nanoparticles Modified with Different Capping Agents - a Comparative Study for Drug Delivery Application

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Abstract

Background: Nanoparticles have been extensively used in the field of medicine due to the remarkable ability in delivering therapeutic agents specifically at the site of action. Massive research is carried out using nanomaterials with multiple applications such as imaging, drug targeting and sensing.

Objectives: Gold nanoparticles can be designed with variable shape and size to tune optical properties for the applications in biomedicine.

Materials and Methods: Gold nanoparticles are non-toxic, can be conjugated with different types of biological agents such as oligonucleotides, DNA, amino acids, enzymes and antibodies to be used as drug delivery vehicles. In the present study, gold nanoparticles were prepared and capped with citrate and bis(p-sulfonatophenyl) phenylphosphine dihydrate.

Results: The efficacy of gold nanoparticles in delivering therapeutic agents has been controlled by modifying their surface with appropriate ligands.

Conclusions: The size and properties of the prepared gold nanoparticles were compared to determine their use in drug delivery.

Key words : Gold nanoparticle, citrate, bis(p-sulfonatophenyl)phenylphosphine dihydrate, insulin

Introduction

Current research in medicine is focused on developing novel medications that can treat diseases efficiently without eliciting any side effect.[1] Although enormous development has been seen in the area of drug discovery, transporting drugs exactly to the site of target is the chief problem associated with conventional drugs.[2] Controlled drug delivery systems can be used to protect drugs from quick degradation or clearance and improve the amount of drugs distributed at the site of action.[3] In recent years, nanotechnology has seen exceptional advancements in areas of engineering and medicine as it deals with nanostructures that possess distinctive physical and chemical properties. Nanoparticles are solid or colloidal materials with their size ranging from 1 to 100 nm. Various research groups have reported the significance of different types of nano particles such as liposomes, carbon nanostructures, dendrimers, metal and polymeric nanoparticles as drug delivery vehicles.[4] Gold Nano Particles (GNP) are one of the most widely used nanostructures in the field of medicine, due to their tremendous characteristic properties and numerous surface functionalities. Different therapeutic agents such as drugs, antibodies, oligonucleotides, proteins can be loaded onto GNP for drug delivery applications.[5-7] GNP can be employed for either passive or active mode of drug targeting applications. In passive mode, GNP accumulates within the tumor through tumor's irregular vasculature whereas in active mode, specific ligands are attached on to the surface of GNP.[8,9] They can be used to sense biomolecules, deliver therapeutics and improve contrast in computed tomography.[10-12] In the present study, GNP were prepared and functionalized using various

capping agents and their efficacy and delivering insulin was studied.

Materials and Methods

Materials

Gold chloride, trisodium citrate, tannic acid, bis(p-sulfonatophenyl)phenylphosphine dihydrate (BSPP) and cysteine were purchased from Sigma Aldrich Chemicals Pvt Ltd. All other chemicals used were of analytical grade.

Methods

Citrate capped gold nanoparticles (C-GNP)

250 µl of 1% gold chloride was mixed with 25 ml of distilled water and the solution was allowed to boil under constant stirring. 15 ml of 1% trisodium citrate was added and the colour of solution turned from yellow to wine red.[13,14]

BSPP capped gold nanoparticles (BSPP-GNP)

5 mg of BSPP was added to citrate stabilized GNP and stirred overnight. The mixture was then centrifuged to remove unreacted compounds and used for further characterization.[15,16]

Insulin coated C-GNP (I-C-GNP)

0.1 ml of human insulin (I) was added to the 0.9 ml of 0.5 mg of C-GNP. The mixture was incubated for 6 hours and centrifuged at 12,000 rpm for 30 minutes. Supernatant was removed and the pellet was re-suspended in1 ml of phosphate buffer saline and used as I-C-GNP. Similar procedure was used to prepare insulin coated BSPP-GNP (I-BSPP-GNP).

Characterization

The prepared nanoparticles were characterized using Malvern-DLS Zetasizer Nano series for size determination. Shimadzu-UV spectrophotometer was used to perform UV-Vis spectroscopic measurements of the nanoparticles. Alpha-E FTIR spectrophotometer was used to determine the functional groups present in the nanoparticles.

Insulin release profile

The amount of insulin released from the nanoparticles was determined by treating 5 mg of test samples in 1 ml of PBS. The solution was placed inside dialysis membrane and dialyzed against PBS buffer solution (pH 7.4). The buffer was collected at specific time interval and subjected to UV absorption. The percentage of drug entrapped was calculated as follows;

Entrapment efficiency = (Amount of insulin in the nanoparticles / Total amount of feeding insulin) x 100 %

Results and discussion

Characterization

In the present study, GNP was prepared with capping agents and insulin was loaded onto the nanoparticles to compare their efficacy in drug delivery. Insulin was directly attached onto the surface of empty GNP via hydrogen bonds. DLS measurement showed the size of I-C-GNP and I-BSPP-GNP as 147 nm and 120 nm respectively. The size of the nanoparticles plays a significant role in interaction with cells and imparting toxicity. When the size of the particle reduces, their delivery efficiency increases due to increased surface area.

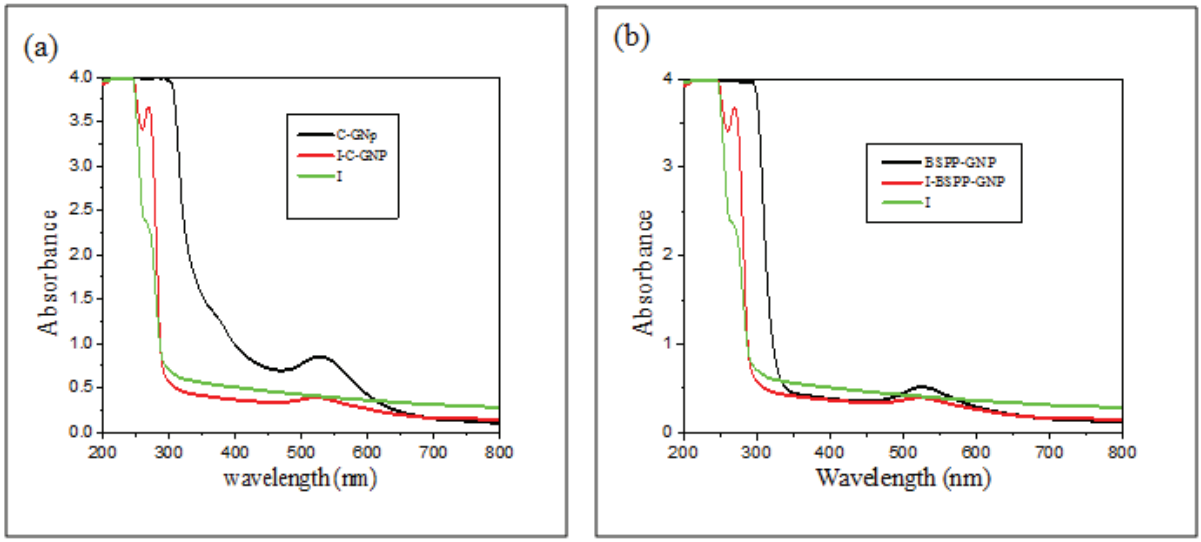

Figure 1: UV spectroscopic analysis of (a) I-C-GNP and (b) I-BSPP-GNP respectively

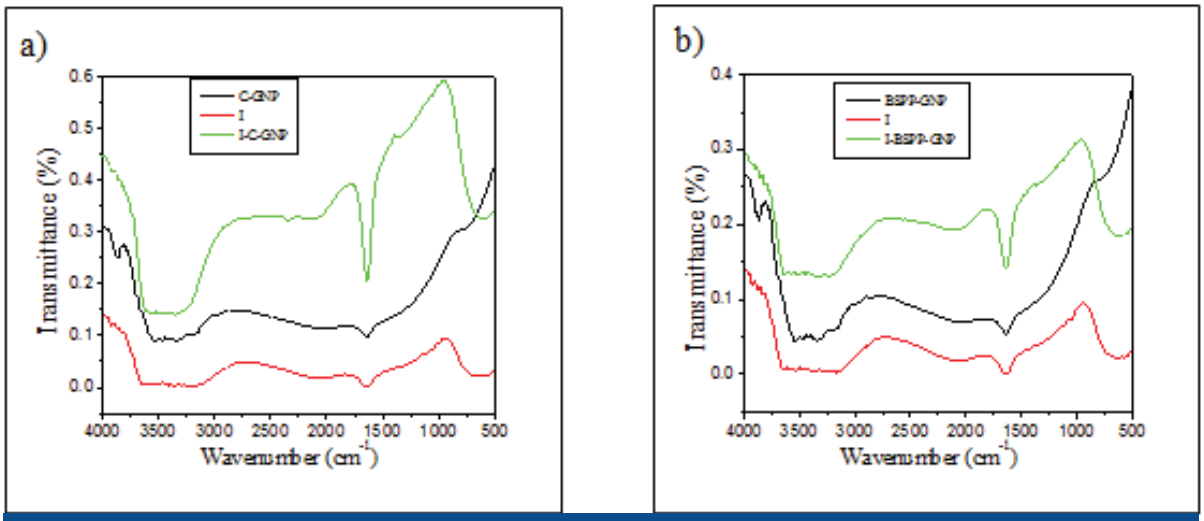

Figure 2: FTIR spectra of (a) I-C-GNP and I-BSPP-GNP respectively.

Previous reports exist on GNPs to act as insulin carrier through mucosal layer.[17] In the present study the size of the nanoparticles is less than 150 nm proving their potency in the field of drug delivery. The UV spectra (Figure 1) of I-C-GNP and I-BSPP-GNP showed absorption in the range of 520 -530 nm corresponding the GNP and at 270 nm corresponding to insulin.

The FTIR peaks (Figure 2) of I-C-GNP and I-BSPP-GNP show bands at around 3306 cm-1 and 1001 cm-1 that can be attributed to the GNP and bands at 1650 cm-1 indicating the amide III peak of insulin.

Insulin release profile

Figure 3 shows the release kinetics of insulin from GNP. I-C-GNP showed the sudden burst release of drug at higher concentration when compared with BSPP-GNP. From these results, it is evident that BSPP-GNP are better when compared with C-GNP for drug delivery applications.

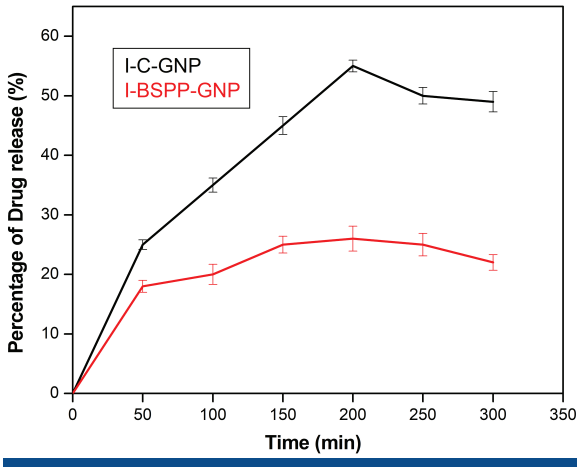

Figure 3: Insulin Release Profile from nanoparticles

Conclusion

In the present study, gold nanoparticles functionalized with various capping agent was prepared and characterized using various techniques like UV spectroscopy, dynamic light scattering and FTIR spectroscopy. The size of nanoparticles ranged from 30-150 nm. The prepared nanoparticles were loaded with insulin and its release profile was analyzed. The prepared nanoparticles can be used for biomedical applications with further experiments and characterization.

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