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Development of Gold Nanoparticles of Various Morphologies for Targeted Drug Delivery

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Introduction

Combining advantages of nanotechnology with anticancer drugs represents an efficient, logical and alternative approach for cancer treatment [1]. Targeted drug delivery is already an emerging topic and it's all set to be the next generation of drug delivery agents. Meanwhile it has been recently discovered that natural molecules like curcumin, etc. have anti-cancer properties [2]. In this aspect we have combined the advantages of both nanotechnology and natural drug molecules to develop novel nanodrug delivery systems where ultrasound waves will trigger the drug release from the surface of nanoparticles. As a carrier we have chosen gold nanoparticles which have properties like inertness, high surface to volume ratio and low toxicity. We have developed a one pot green method for the synthesis of gold nanocrystals in presence of trisodium citrate which does not require mechanical stirring, organic solvents or high temperatures.

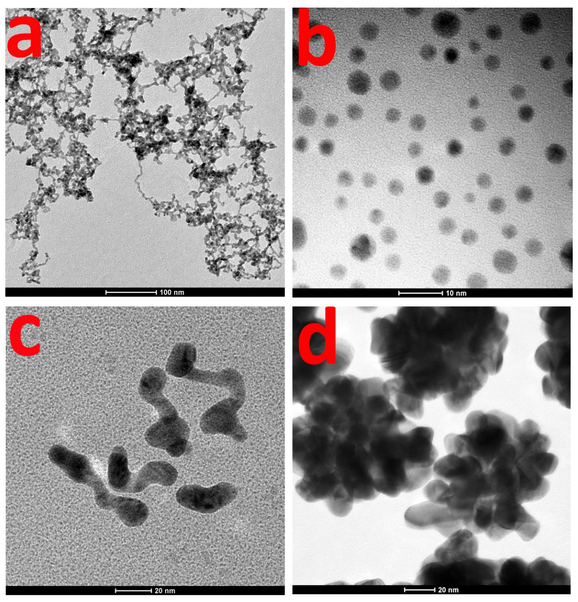


Figure 1: TEM micrographs of gold nanocrystals.

Green Synthesis of GNPs

GNPs loaded with an anticancer molecule curcumin were synthesized by a green one pot protocol which involved addition micromolar amounts of ethanolic solution of curcumin to an aqueous solution of auric chloride followed by aqueous solution of trisodium citrate. Trisodium citrate is a weak reducing agent and reduces chloroauric acid very slowly at room temperature to form a black colloidal solution comprising of 2-D nanowire network [3] (Figure 1a). Introduction of a third molecule like curcumin, L-tyrosine or polyvinylpyrrolidone (PVP) has a drastic change in the morphology which can also be seen visually as change in the color of colloidal solution [4-6]. For example, with adding micromolar amounts of curcumin or PVP resulted in bright red colloidal solution [4] (Figure 1b) while with L-tyrosine black and blue color sol were obtained [5,6] (Figure 1c & d). The main advantage of the process was that no high temperatures were needed for the reaction as such even temperature sensitive molecules can be loaded on the surface of particles.

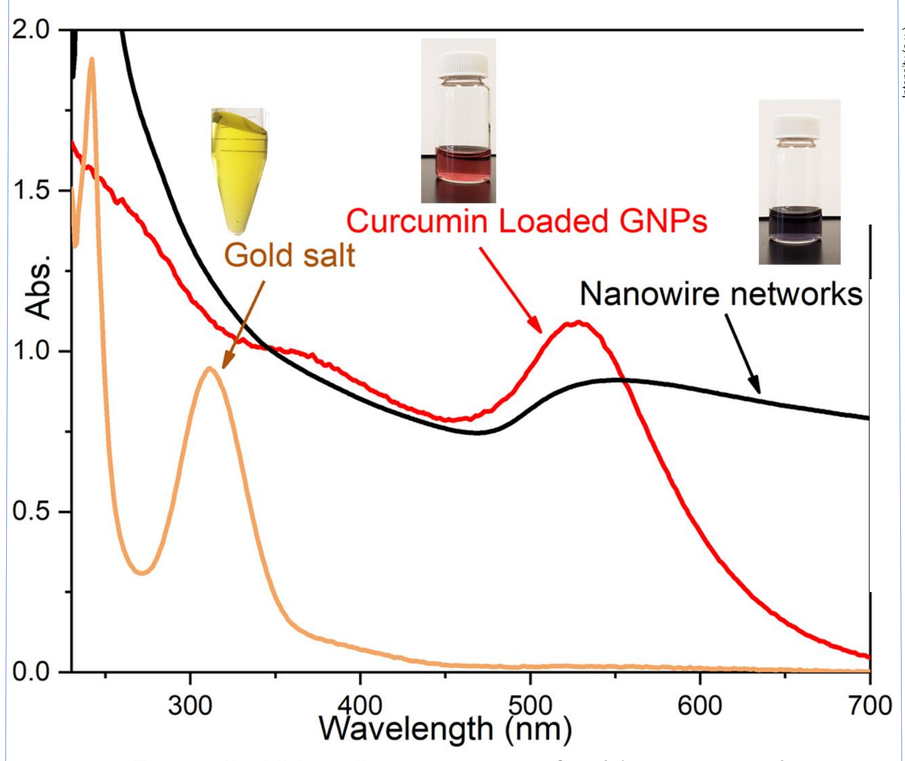


Figure 3 : UV-vis Spectroscopy of gold nanocrystals.

LIPUS Results

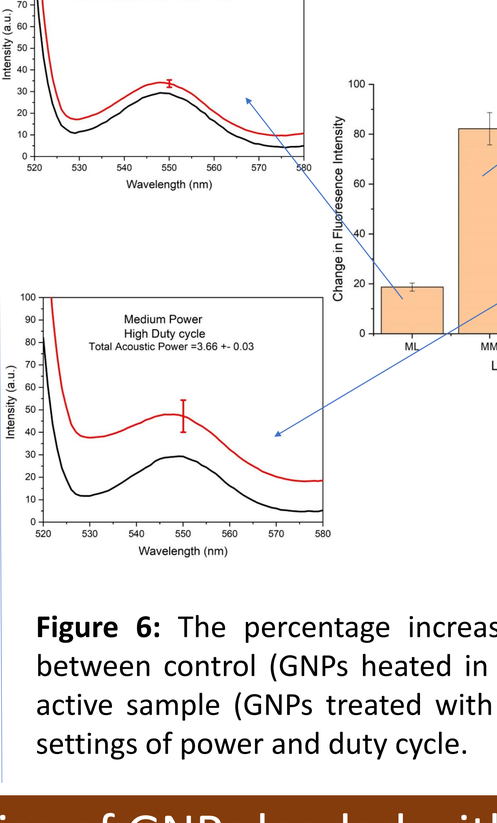


Figure 4: Initial and Final temperature of colloidal solution of Au-Curcumin nanoparticles inside tissue at different Power and Duty Cycle of LIPUS. Max Time 5 Min.

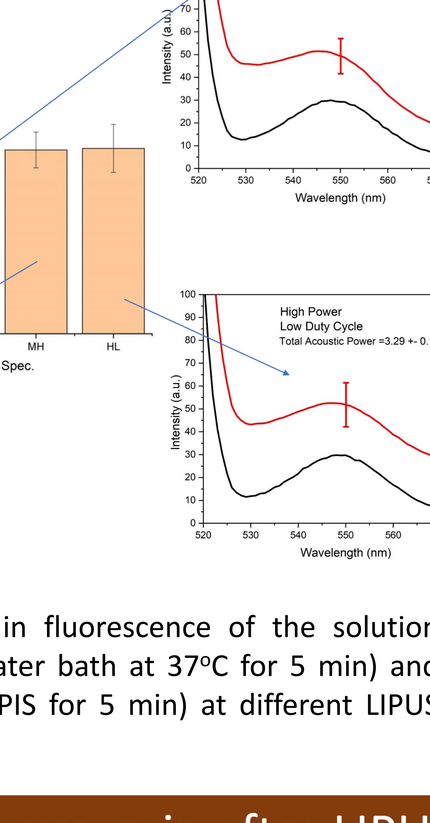


Figure 5: Increase of temperature with respect to time of colloidal solution of Au-Curcumin nanoparticles at different setting of LIPUS.

Figure 6: The percentage increase in fluorescence of the solution between control (GNPs heated in water bath at 37°C for 5 min) and active sample (GNPs treated with LIPIS for 5 min) at different LIPUS settings of power and duty cycle.

Set-up of Experiment

For all experiments an in-house experimental set up was designed which consisted of a sample holder placed inside a tissue block (pork chop). A LIPUS device capable of pulsed ultrasound at 1 MHz with Power selection: Three levels: Low (L), Medium (M) and High (H) and Pulsed duty cycle: 33%, 50% and 100% (continuous) was used. The temperature of sample as well as tissue was measured by thermometer equipped with needle thermometer. The water bath temperature was maintained at 37°C which was equivalent to human body temperature.

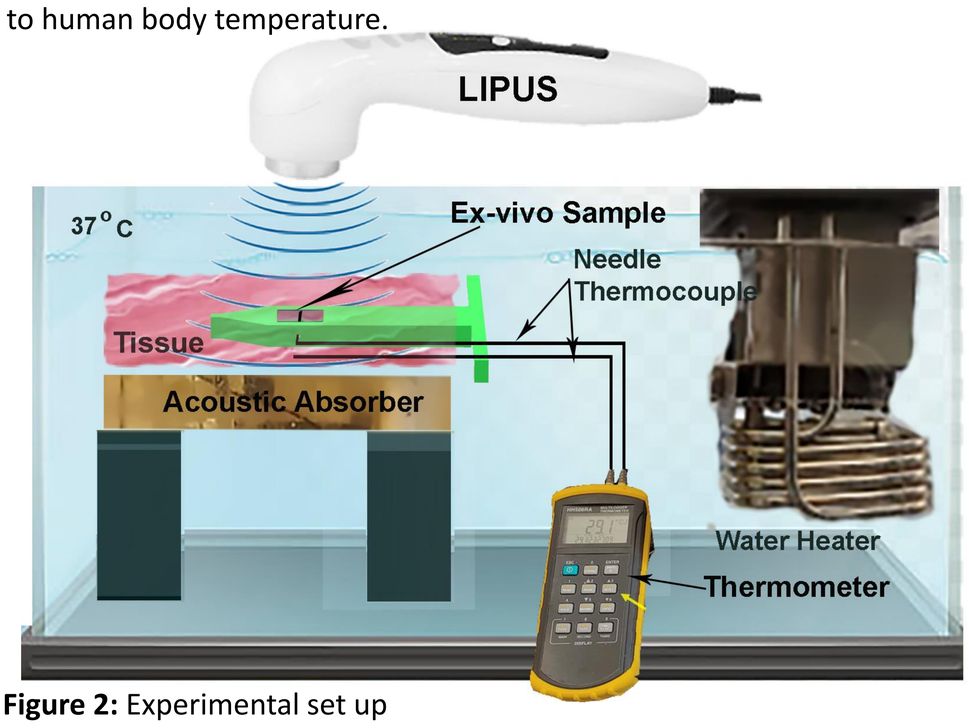
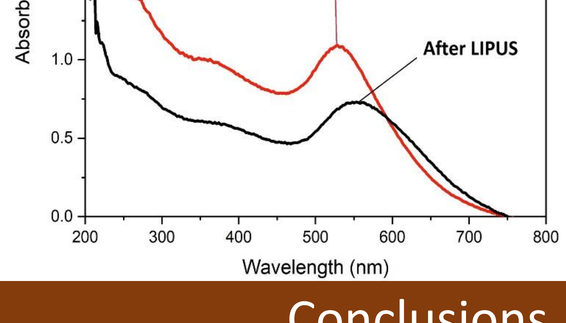


Figure 2: Experimental set up

Change in properties of GNPs loaded with curcumin after LIPUS

Figure 7: GNPs displayed a plasmon band at around ~525 nm which became broader and red shifted towards higher wavelength after interacting with pulsed ultrasound for just 5 minutes. Visually the color of colloidal solution changed from wine red to pinkish. All these changes suggest a change in surface properties and morphology of gold nanoparticles after the release of curcumin and citrate from the nanoparticle. surface.



Conclusions

- In summary we have successfully loaded gold nanoparticles with a natural anticancer molecule curcumin.
- Curcumin interacted non-covalently with the surface of gold nanoparticles.
- These non-covalent interactions could be easily broken down by short pulsus of ultrasound.
- This release was evident by change in surface properties of gold. nanoparticles and measurement of fluorescence of released curcumin.

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Partial Funding through a research contract from TOKI and Toronto Poly Clinic is acknowledged. Partial support from an Ontario Research Fund-Research Excellence (ORF-RE) grant was used toward development of the experimental setup.

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