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Self-assembly of Fe_3O_4 Nanoparticles in Chainlike Array on DNA Template, their Characterization and Cancer Cell Identification

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Abstract: We report the synthesis of DNA templated chainlike Fe_3O_4 nanoparticles. DNA being a chainlike molecule directs the growth of particles along its length due to electrostatic attraction between positively charged metal ions of salts and the negatively charged phosphate backbone of DNA chain. In our work, a series of measurements like TEM (transmission electron microscopy), XRD (X-ray powder diffractometry) and some spectroscopic analysis were done to characterize the morphology, structure and composition of the particles. Their magnetic properties were measured using a VSM (Vibrating Sample Magnetometer). A preliminary magnetic analysis of Fe_3O_4 shows superparamagnetic character. These DNA templated magnetic nanoparticles are attached to cancer cells selectively and kill most of the cancer cells. Hence this kind of material will be useful for identification of cancer as well as cancer treatment.

1. Introduction

Biological systems such as protein, DNA, enzymes, cancer cell targeting folic acid etc. combining with magnetic nanoparticles are getting much more interest because of their potential application in biological field such as in brain research, neuro-computation, prosthetics, biosensors, bio-machines etc. Therefore manufacturing of various magnetic nanoparticles combining with biological molecules is very important. But proper engineering and characterizations are necessary before their uses. For these we need to understand how bio molecule works with attachment of tiny magnetic nanoparticles. Among various biomolecules DNA has a great potentiality as a building block because it has unique molecular recognition and mechanical and self-assembling characteristics [1-2-3] more over all the natural creatures

contains DNA unit. It is known that the DNA molecule can be used to synthesize chain like nanoparticles by organizing inorganic components through mechanisms such as electrostatic interaction, Watson-Crick base pairing or covalent bonding and their modifications. Various magnetic materials, polymers, superconducting alloys, and carbon nanotubes have all been organized using DNA templates [4]. We have used DNA as template to synthesize magnetite nanoparticles. Our results indicate that DNA serves as very good templating agent for the growth of nanowires. Previously we have used micelles as template to synthesize nanoparticles [5-6-7]. We have also used DNA as template successfully in our previous work [2]. Previous material was consists of Ni and as Ni is toxic so we switch to magnetite as magnetite is not toxic.

All the reagents used were 99.9% pure and purchased from Sigma-Aldrich. Ultrapure distilled water (UPD water) DNAse, RNAse free was used in all synthesis procedures. A Stock DNA solution (1 g/L) was prepared by mixing appropriate amounts of DNA with Tris-EDTA buffer (pH 7.4) and was stirred overnight. Source of DNA was herring sperm and it was purchased from Sigma-Aldrich. The buffer solution helps to prepare a homogeneous DNA solution without any pop off of A and G bases in DNA and was stored in a refrigerator. A stock solution of ferric ammonium sulfate and ferrous ammonium sulfate in 2:1 molar ratio were made. The stock solution of ferric and ferrous ammonium sulfate was mixed with stock DNA solution at ratio 1 : 1 in volume ratio respectively and the mixture was stirred for 30 min using a magnetic stirrer. The resulting solution was then heated at about 65 to 70 oC then NaOH solution was added drop wise to synthesize magnetite nanoparticles. The solution color was turned to black, which indicates formation of magnetite nanoparticles. Then by injecting cancer cell to the mice artificially cancer was caused to mice. The cancer cells were collected from mice and treated with free magnetite nanoparticles and DNA templated magnetite nanoparticles.

From TEM image (Figure 1) it is clear that particles growth is in chain like fashion. DNA being a chain like molecules and by electrostatic attraction of positively charged iron and negatively charged phosphate backbone of DNA helps to grow the particles such chain like array.

The analysis of FTIR spectra (Figure 2) taken from only DNA (a), magnetite attached DNA (b) indicates that magnetite form bond with phosphate backbone of DNA which directs the growth of particles in chain like array. Thus DNA acts as template as well as good biologically functionalized biocompatible nanoparticles.

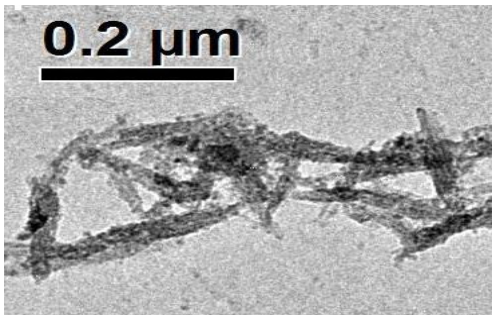

Fig. 1: TEM image of Magnetite-nanoparticles attached to DNA.

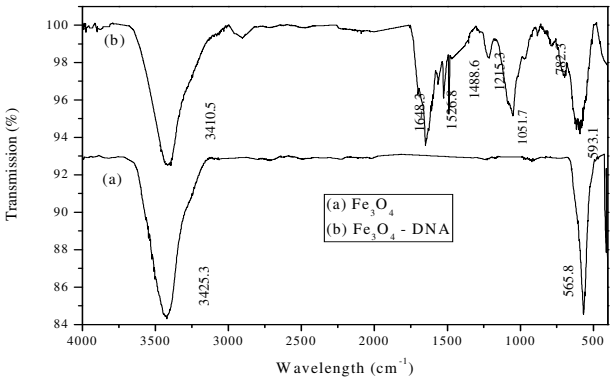

Fig. 2: FTIR spectra of pure DNA (a) and Magnetite- nanoparticles attached on DNA (b).

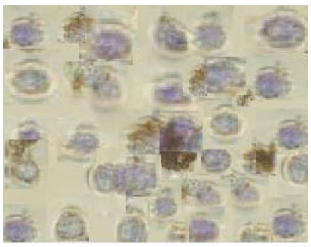

Fig.3: Image of cancer cells after treatment with DNA functionalized magnetite nanoparticles

These DNA functionalized particles are attached to cancer cell but the without DNA template nanoparticles are not attached to cancer cell. In this case we have done a control experiment. We have taken only cancer cell in 0.1% sodium chloride solution, cancer cells in 0.1% sodium chloride solution were treated with nonfunctionalized nanoparticles and in another Petri-dice cancer cells in 0.1% sodium chloride solution were treated with DNA functionalized magnetite nanoparticles. They are kept for 1 hr then all

of them treated with the dye trypan blue to check the viability of cancer cells. Here we have observed most of the cancer cells in 0.1% sodium chloride solution and treated with nonfunctionalized nanoparticles are alive (more than 70 % cells are alive) but the cells treated with DNA functionalized nanoparticles are died, almost 80 % of cancer cells are died in this case. The image of cancer cells after treatment with DNA functionalized magnetite nanoparticles is shown in Figure 3. Free magnetite particles are not getting attached to cancer cells so they can not contribute in recognition of cancer cells or to kill the cancer cells. But the particles functionalized with this DNA molecule are incorporated into cancer cells and kill most of the cancer cells about 80 %. Thus these DNA functionalized nanoparticles helps to recognize cancer cells as well as kill the cancer cells. In this case most of the cancer cells are died because those nanoparticles are causing some changes in life cycle of cancer cells or causing some interruption in life cycle of the cancer cell. We have to do some more experiments on this to understand the exact phenomenon.

2. Conclusion

We have synthesized nanochain DNA templated magnetite nanoparticles by simple chemical process where DNA successfully acts as template and able to functionalize the particles for cancer cell recognition and these particles will be useful to kill the cancer cells also. Our next experiment is to work with mice model to check the affectivity of these particles for cancer treatment and we will make a statistical study on it.

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