Research Article www.pharmaresearchlibrary.com/ajmps **ISSN: 2348-0165**

Asian Journal of Medical and Pharmaceutical Sciences

Superparamagnetic Iron Oxide Nanoparticles in the Diagnosis and Treatment of Cancer

J. Jayabarath*[1], T. Karthick[2], M. Aniskumar[2], E.Menaga[2], A. Catherin Sangeetha[2], R. Yuvashri, K. Gobika

Head[1], Asst. Professor[2], Department of Biotechnology, Pasvendar Bharathidasan College of Engineering and Technology, Mathur, Trichy-24, India*

NCADDD, 25 July 2014, Organized by Department of Pharmaceutical Technology, Anna University, BIT Campus, Tiruchirappalli–620024, Tamil Nadu, India

Abstract

During the last decade, significant scientific research efforts have led to a significant growth in understanding of cancer at the genetic, molecular, and cellular levels providing great opportunities for diagnosis and treatment of cancer diseases. The hopes for fast cancer diagnosis and treatment were significantly increased by the entrance of nanoparticles to the medical sciences. Nanoparticles are attractive due to their unique opportunities together with negligible side effects not only in cancer therapy but also in the treatment of other ailments. Among all types of nanoparticles, surface-engineered super-paramagnetic iron oxide nanoparticles (SPIONs) have been attracted a great attention for cancer therapy applications. This review covers the recent advances in the development of SPIONs together with their opportunities and challenges, as theranosis agents, in cancer treatment.

Keywords: Super-paramagnetic iron oxide nanoparticles (SPIONs), cancer therapy, theranosis agents.

Contents

***Corresponding author**
J. Jayabarath
Head, Department of Biotechnology,
Pavendar Bharathidasan College of Engineering and Technology, Mathur, Trichy-24,
Manuscript ID: NCADDD2014-AJMPS2281

PAPER QR-CODE

1. Introduction

Cancer known medically as a malignant neoplasm, is a broad group of diseases involving unregulated cell growth and remains one of the most deadly diseases in the world. In cancer, cells divide and grow uncontrollably, forming malignant tumors, and invade nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Studies have showed that Super Paramagnetic Iron Oxides Nanoparticles (SPIONs) can be used in the diagnosis and treatment of cancer. Superparamagnetic iron oxide nanoparticles (SPIONs), with a mean diameter as low as 10 nm and superior magnetic properties, have proven to be among the most capable candidates . In the field of drug delivery, SPIONs particles are considered as small, thermally agitated magnets in carrier liquids, which are called “ferrofluids". A distinguishing feature of SPIONs for drug delivery is their applicability for both alternatives (i.e. magnetic properties and antibody attachment) and consequently developing a targeting capability. In our research, SPIONs are synthesized by the method of co-precipitation and are used in the diagnosis and treatment of cancer.

2. Materials and Method

Synthesis of SPIONs by co-precipitation

$FeCl_2$ and $FeCl_3$ was dissolved in 50ml of deionized water with molar ratio of 2/3 and the solution concentration was varied from 250mmol to 12.5mmol by adding ferric and ferrous ions at 250,200,150,100,75,50,25 and 12.5mmol respectively. 15ml of freshly prepared NaOH was added to 50ml mixture of ion salts under vigorous mechanical stirring at 15000 rpm. The reaction was carried out for 30 min at 20ºC in air medium. After the reaction was over, the precipitate was washed 3 times with distilled water and was dried in an oven to obtain the powder. To prevent destabilization, it was coated with dextran.

Characterization of the sample: The sample was then characterized by XRD patterns of the nanoparticles, Fourier transform infrared spectroscopy (FT-IR) for the confirmation of formation of iron oxide nanoparticles, and TEM analysis for the determination of the morphology and size of the synthesized nanoparticles.

Diagnosis and treatment of cancer using SPIONs

The synthesized SPIONs were used as diagnostic tools for cancer detection through Magnetic Resonance Imaging (MRI). Normally hydrogen atoms in water have a property called spin. MRI generates a magnetic pulse that aligns all of the spins in a certain direction. The magnetic resonances of the nuclei will cause differences in how they return to their normal spin state. The MRI machine records the energy released as they realign at different times and generates an image. Cancer was treated using SPIONs by the method of hyperthermia. It is the method in which high temperature under controlled conditions was used to destroy the cancerous cells. The synthesized nanoparticles were injected intravenously and an external rotating or alternating magnetic field was applied.

3. Results and Discussion

Characterization of The Sample:

XRD patterns:

Experiments were carried out by adjusting the amount of iron ion in the solution while keeping the other parameters constant. It was observed that the color of the samples changed from black to reddish-brown as the amount of iron ion in the medium decreased from 250 mmol to 12.5 mmol. This change may indicate the phase transform of magnetite to another iron oxide phase (maghemite, hematite) and/or iron oxyhydroxides since the color of magnetite is black while it is reddish-brown for others. The XRD patterns of samples (S1–S8) in Fig. 1(a) are corresponding to nanoparticles synthesized with the total amount of iron ion at 250, 200, 150, 100, 75, 50, 25, and 12.5mmol, respectively, see also Table I. S1–S5 samples have the characteristic (220), (311), (400), (422), (511), (440), and (533) peaks of a face-centered cubic spinel structure at around 2 theta ≈ 30º , 35º , 43º , 53º , 57º , 63º , and 74º respectively. Whereas in patterns of S6–S8, the intensity of (311) and (440) peaks were reduced and the other peaks observed in previous patterns disappeared as seen from Fig. 1(a). Thus, it can be concluded that the decrease of total iron ion concentration results in a remarkable broadening and weakening of the peaks. Fig. 1(b) show the experimentally observed peak profile fit of sample S1 which was fitted by using pseudo-Voigt function that is a linear combination of Gaussian and Cauchy functions.

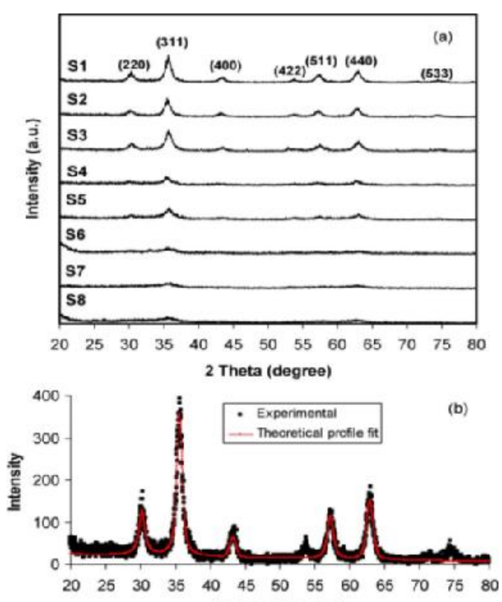

Figure 1: (a) XRD patterns of nanoparticles. (b) Theoretical profile fit of XRD pattern for S1.

Fourier transform infrared spectroscopy

FT-IR analysis was performed to confirm the formation of iron oxide nanoparticles. FT-IR spectra of the samples in the 1200–400cm^{-1} region are shown in Fig.2. A broad band was detected at about 560–580cm^{-1} which was related to the vibrations of Fe-O bond. A shoulder peak was observed in the spectrum of samples S1–S4 at around 620cm^{-1} indicating the maghemite phase. In all samples, Fe-O vibration band was widened and weakened with the decrease of iron ion concentration. In the spectrum of S4, two weak peaks around 790 and 890cm^{-1} were observed. Since these two peaks indicate iron oxyhydroxide phase [40], it can be said that the samples from S4 to S8 have an additional FeOH phase with main iron oxide phase. Fe-O vibrations deduced and weak Fe-O(OH) vibrations appeared with the decrease of iron ion concentration which is consistent with the XRD results.

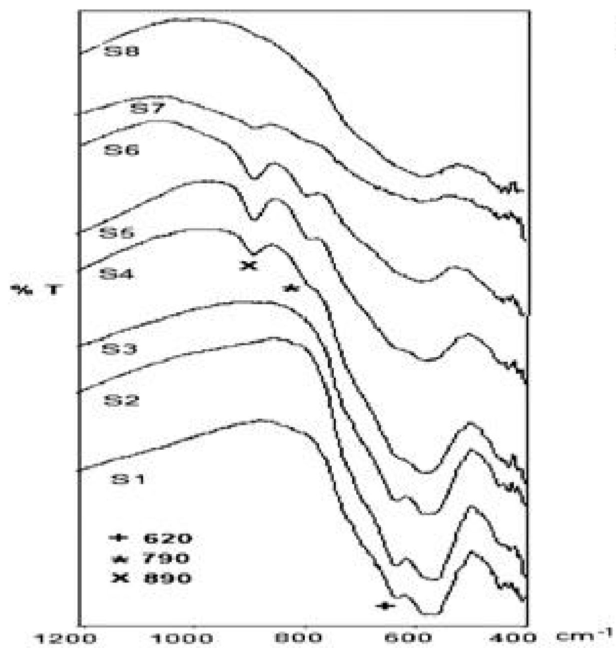

Figure 2: FT-IR spectra of SPIONs

Transmission electron microscope

TEM pictures of the samples were taken to determine the morphology and size of the nanoparticles and compare them with the particle sizes obtained using other techniques. The TEM images of samples S2 and S6 are given in Fig.3(a) and (b), respectively. In the image of S6 rod-like particles some of formations may be in amorphous phase as no peaks of another phase were observed in the XRD pattern of the sample. The particle sizes are found to be around 8 nm.

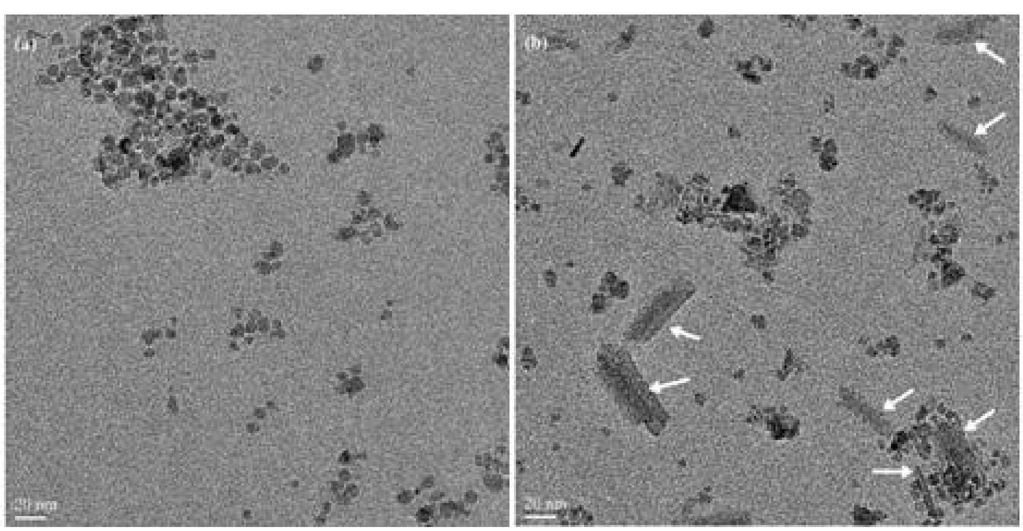

Figure 3: TEM images of nanoparticles: (a) sample S2,
(b) Sample S6. (Arrows show the amorphous by-products of co-precipitation.)

Diagnosis and treatment of cancer through MRI

MRI relies on the nuclear magnetic resonance signal from protons of hydrogen nuclei within water and lipid molecules in tissues. A set of images were generated at certain small time intervals after the pulse sequence and the image showing the cancerous cells was obtained.

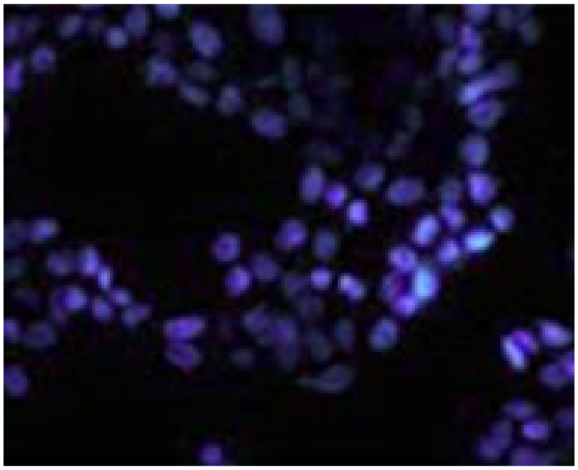

Figure 4: MRI image

The application of external rotating or alternating magnetic field followed by the injection of SPIONs caused the magnetic nanoparticles to vibrate and generate heat which ultimately destroyed the cancerous cells.

4. References

1. Anand P, Kunnumakara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, Sung B, Aggarwal BB; "Cancer is a Preventable Disease that Requires Major Lifestyle Changes". Pharm Res. 2008; 25:2097–116.
2. "Nanoparticles (SPIONs): Development, surface modification and applications in chemotherapy". Advanced Drug Delivery Reviews. **2011**, 63:24–46.
3. Means GE, Feeney RE; "Chemical Modifications of Proteins: History and Applications". Bio-conjugate Chemistry. **1990**, 1:2–12.
4. Chau Y, Dang NM, Tan FE, Langer R; "Investigation of targeting mechanism of new dextran-peptide-methotrexate conjugates using bio-distribution study in matrix-metalloproteinase-over-expressing tumor xenograft model". Journal of Pharmaceutical Sciences. **2006**, 95:542–51.
5. Gregoriadis G; "Engineering liposomes for drug delivery: Progress and problems". Trends in Biotechnology. **1995**, 13: 527–37.
6. Adams ML, Lavasanifar A, Kwon GS; "Amphiphilic block copolymers for drug delivery". Journal of Pharmaceutical Sciences. **2003**, 92: 1343–55.
7. Rosler A, Vandermeulen GWM, Klok HA; "Advanced drug delivery devices via self-assembly of amphiphilic block copolymers". Advanced Drug Delivery Reviews. **2001**, 53: 95–108.
8. Wu GH, Milkhailovsky A, Khant HA, Fu C, Chiu W, Zasadzinski JA; "Remotely triggered liposome release by near-infrared light absorption via hollow gold nanoshells". Journal of the American Chemical Society. **2008**, 130: 8175–7.
9. Son SJ, Bai X, Lee SB; "Inorganic hollow nanoparticles and nanotubes in nanomedicine". Part 1. Drug/gene delivery applications. Drug Discovery Today. **2007**, 12: 650–6.
10. Akerman ME, Chan WCW, Laakkonen P, Bhatia SN, Ruoslahti E; "Nanocrystal targeting in vivo". Proceedings of the National Academy of Sciences of the United States of America. **2002**, 99: 12617–21.
11. Uhrich KE, Cannizzaro SM, Langer RS, Shakesheff KM; "Polymeric systems for controlled drug release". Chemical Reviews. **1999,** 99: 3181–98.
12. Veronese FM, Pasut G; "PEGylation, successful approach to drug delivery". Drug Discovery Today. **2005**, 10: 1451–8.
13. Richardson TP, Peters MC, Ennett AB, Mooney DJ; "Polymeric system for dual growth factor delivery". Nature Biotechnology. **2001**, 19: 1029–34.
14. Vinogradov SV, Bronich TK, Kabanov AV; "Nanosized cationic hydrogels for drug delivery: preparation, properties and interactions with cells". Advanced Drug Delivery Reviews. **2002**, 54:135–47.
15. Gupta P, Vermani K, Garg S; "Hydrogels: from controlled release to pH-responsive drug delivery". Drug Discovery Today. **2002**, 7:569–79.

16. Qiu Y, Park K; "Environment-sensitive hydrogels for drug delivery". Advanced Drug Delivery Reviews. **2001**.
17. Santini JT, Cima MJ, Langer R; "A controlled-release microchip". Nature. **1999**, 397: 335–8.
18. LaVan DA, McGuire T, Langer R; "Small-scale systems for in vivo drug delivery". Nature Biotechnology. **2003**, 21: 1184–91.
19. Grayson ACR, Choi IS, Tyler BM, Wang PP, Brem H, Cima MJ, Langer R; "Multi-pulse drug delivery from a resorbable polymeric microchip device". Nature Materials. **2003**, 2: 767–72.