International Journal of Advance Research in Science and Engineering
Vol. No.5, Issue No. 01, January 2016
www.ijarse.com
IJARSE
ISSN 2319 - 8354

# Iron Oxide Nanoparticles Synthesis, Characterization and Application

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**ABSTRACT**

*Formaline and aniline based iron oxide magnetic nanoparticles are synthesized and formulated that can be loaded easily with high doses of water-insoluble anticancer agents. Neither the formulation components nor the drug loading affected the magnetic properties of the core iron oxide nanoparticles. Sustained release of the incorporated drug is observed over 2 weeks under in vitro conditions. The nanoparticles further demonstrated sustained intracellular drug retention relative to drug in solution and a dose-dependent antiproliferative effect in breast and prostate cancer cell lines. This nanoparticle formulation can be used as a universal drug carrier system for systemic administration of water-insoluble drugs while simultaneously allowing magnetic targeting and/or imaging.*

***Keywords: Sustained release; water-insoluble drugs; cellular uptake; targeting; tumor***

## I. INTRODUCTION

Magnetic nanoparticles offer exciting new opportunities toward developing effective drug delivery systems, as it is feasible to produce, characterize, and specifically tailor their functional properties for drug delivery applications[1-5]. An external localized magnetic field gradient may be applied to a chosen site to attract drug-loaded magnetic nanoparticles from blood circulation. Drug targeting to tumors, as in other pathological conditions as well, is desirable since anticancer agents demonstrate nonspecific toxicities that significantly limit their therapeutic potentials[6-17].

The use of magnetic nanoparticles for drug delivery vehicles must address issues such as drug-loading capacity, desired release profile, aqueous dispersion stability, biocompatibility with cells and tissue, and retention of magnetic properties after modification with polymers or chemical reaction[18-20]. Magnetic nanoparticles generally are coated with hydrophilic polymers such as starch or dextran (to impart aqueous dispersity to particles), and the therapeutic agent of interest is either chemically conjugated or ionically bound to the outer layer of polymer[21-23]. This approach is complex, involves multiple steps, and usually results in limited drug-loading capacity, and the bound drug dissociates within hours. Rapid dissociation of drug from the carrier system may be less effective, especially in tumor therapy where chronic drug retention in the target tissue is required for therapeutic efficacy.

In this paper, we report on the synthesis, characterization, in vitro and in vivo biological/radio evaluation Formaline and aniline based iron oxide magnetic nanoparticles and their formulation.

## II. MATERIALS AND METHODS

All chemicals used in present study of analytical grade purchased from Sigma, Aldrich and Merck chemical Co. All the solvents were used after distillation. TLC was run on the silica get coated aluminium sheets (silica gel 60 $F_{254}$, E Merck, Germany) and visualized in UV light. Melting points were determined by using Thomas Hoover apparatus and are uncorrected. IR spectra were recorded on the FT-IR perking Elmer spectrum BX spectrophotometer. NMR spectra were obtained by using Brucker NMR instrument 300 MHz. The FAB-MS spectra were recorded from JEOL SX 102/DA-6000 spectrometer using m-Nitro benzyl alcohol as matrix. EI-MS spectra were recorded on a JEOL SX102/DA (KV 10 mA) instrument. Elemental analysis was done on elementar analysen system Gmbh variable system. Radio complexation and radio chemical purity was checked by instant strip chromatography (silica gel impregnated paper chromatography) with IILC-SG (Gelman sciences, Ann arbar, MI, USA).

### 2.1 Synthesis of Magnetic Nanoparticles

Aqueous solutions of 0.1 M Fe(III) (30 mL) and 0.1 M Fe(II) (15 mL) were mixed, and 3 mL of 5 M NaOH sol, was added dropwise over 1 min with stirring on a magnetic stir plate. The stirring continued for 20 min under a nitrogen-gas atmosphere. The particles obtained were washed 3 times using ultracentrifugation (30000 rpm for 20 min at 10 °C) with nitrogen purged water. The iron oxide nanoparticle yield, determined by weighing of the lyophilized sample of the preparation, was 344 mg.

### 2.2Transmission Electron Microscopy (TEM).

A drop of an aqueous dispersion of nanoparticles was placed on a Formvar-coated copper TEM grid (150 mesh, Ted Pella Inc. Redding, CA) and was allowed to air-dry. Particles were imaged using a Philips 201 transmission electron microscope (Philips/FEI Inc., Briarcliff, Manor, NY). The NIH ImageJ software was used to calculate the mean particle diameter from the TEM photomicrograph. Diameters of 50 particles were measured to calculate the mean particle diameter.

### 2.3 pharmacokinetics of nano Conjugates

0.03 nM solution of the compounds dissolved in DMSO was taken in a shielded vial and 60µl of $1x10^{-2}$ M $SnCl_2 .2H_2O$ (dissolved in $N_2$ purged 1mL (10% acetic acid) was added followed by addition of (<1h) freshly eluted Saline solution of Sodium pertchnetate. The pH of the reaction mixture was adjusted to 6.5 with 0.1 M $NaHCO_3$ solution and shook to mix the contents. The vial was allowed to stand for 45 minutes at room temp. Compound l purity as well as $R_f$ was determined by ITLC-SG strips using 0.9% NaCl aqueous solution (saline) as developing solvent and simultaneously in acetone and PAW(Pyridine, acetic acid and water in 3:5:1.5 ratio ) as mentioned earlier. Each TLC was cut in 0.1 cm segments and counts of each segment were taken.

### 2.4 Blood kinetic measurement

In normal rabbit weighing about 2 to 2.5 kg, nano material was administered intravenously through the dorsal ear vein of the animal. At different time interval starting from 5 min to 24 h persistence of the activity in terms of percentage administered dose in samples at different time intervals was calculated using gamma counter.

### 2.5 In-Vitro serum Stability Assay

The fresh serum was prepared by allowing blood collected from healthy volunteers to clot for 1h at 37°C in a humidified incubator maintained at 5% carbon dioxide, 95% air. Then the sample was centrifuged at 400 rpm and the serum was filtered through 0.22 micron syringe filter into sterile plastic culture tubes. Percentage of free

pertchnetate at a particular time point that was estimated using Saline and Acetone as mobile phase, represented percentage dissociation of the complex at that particular time point in serum

## III. ACKNOWLEDGEMENT

The authors like to thank VC DSMNRU, Mohaan road Lucknow for constant encouragement to do research work. The authors are also thankful to Director, INMAS, for providing all the facilities and for his deep interest during the course of the study.

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