

## SYNTHESIS OF POLYETHYLENE MAGNETIC NANOPARTICLES

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**INTRODUCTION:** Polymer-based nanoparticles have been synthesized in the last few decades for biomedical applications, mostly in drug delivery, immunoassay and cell separation. Non-magnetic and water-insoluble polyethylene, polypropylene and polystyrene particles are being used as components in cleansing agents in the cosmetic industry and to study the effect of body fluids on polymer particles in vitro. In most cases polymer composite particles and encapsulated particles are prepared by emulsion polymerization, solvent evaporation, hot melt method etc. A convenient way of forming encapsulated particles is to dissolve the polymer and the inorganic particles in a solvent or water and then forming an oil in water emulsion and stabilizing the particles either by chemical crosslinking or by heat. Recently a method has been described by Wunder et al [1] to prepare UHMWPE particles to be used for in vitro study. Their method was based on the concept of nonsolvent and temperature induced crystallization. This method is much easier and less complicated for the preparation of particles with crystalline polymers. In this study the above method is modified to produce composite particles. A method of solvent-nonsolvent temperature induced crystallization, coupled with ultrasonication using an ultrasound probe is reported in this paper. No direct interaction of sound field with molecular species takes place during ultrasound application; moreover, the acoustic cavitations at the transient high temperature and high pressure cause chemical effects and give rise to nanostructured materials. Ultrasound mixing of the polymer with maghemite in the solvent and further mixing with the nonsolvent caused the formation of a homogeneous emulsion with a well-dispersed phase of polymer with maghemite. Initially, the emulsion was formed by mixing the solvent, polymer with maghemite and nonsolvent at high temperature using ultrasound. The ultrasonication caused the formation of microdroplets, which formed a microphase-separated system while cooled rapidly and consequently a macrophase-separated system was formed separating two liquids. Polymer crystallized with lowering of temperature and the polymer along with magnetic particle was distributed in the nonsolvent medium separating two liquids.

Our study focuses on the effect of different solvents and amplitudes of sonication during particle formation. The two solvents with high boiling points were Decalin and OMCTS and the nonsolvent was tetraglyme. The polymer used in this study was low molecular weight polyethylene with broad distribution. The polymer had a wax like appearance and softness. The particles formed with this polymer are non-toxic and can be used for in vitro applications and also as an efficient medium for transdermal drug delivery. These polyethylene magnetic particles were further modified to bind avidin for biomedical applications such as cell separation and immunoassays. The protein coupling efficiency was measured. The magnetic properties were also investigated, since these submicron composite particles are designed for biomedical applications where an external magnetic field will induce a force to separate them.

**METHODS:** Very low molecular weight polyethylene wax (number average molecular weight 700 g/mole) was obtained from the Honeywell Corporation. This product is not hazardous under OSHA Hazard communication. Decalin and tetraglyme were obtained from Sigma-Aldrich, octamethylcyclotetrasiloxane from Dow Chemical Company, sodium oleate from Sigma-Aldrich. All solvents and nonsolvents were used as received.

Iron oxide particles with an average diameter range of 5 nm -10 nm were synthesized by a combination of the widely used coprecipitation method along with ultrasonication [2]. These particles were modified with sodium oleate (an anionic surfactant) to attach them to polyethylene. Iron oxide powder was mixed with sodium oleate (30% of weight of polymer) in water, stirred at moderate speed for about 2 hours, dried and then used in a mixture with the polyethylene wax.

A dilute (0.05% w/w) solution (10 ml) of the polyethylene wax and iron oxide mixture was made using Decalin at 150°C in a 25 ml screw cap scintillation vial by ultrasonication. Ten ml of tetraglyme at same temperature was added and sonicated at 50% amplitude for 30 seconds. After dissolution and mixing at 150°C, the mixture was immediately cooled at 0°C temperature. An emulsion formed within a few minutes. Within 45 minutes to one hour at room temperature,

polyethylene particles along with maghemite formed. The suspension was then kept at  $-10^{\circ}\text{C}$  in the refrigerator for about half an hour. A very thin reddish brown layer was observed in the junction of two liquids. The top and the bottom layer of liquids were extracted with the help of micropipette and syringe. The particles were then centrifuged in a microcentrifuge to isolate it from rest of the solvent mixture. The remaining solvent was removed and particles were washed with acetone. Six different batches of particles were made using two solvents at two different speeds of sonication and with two different concentrations of polymers in each of two solvents.

Appropriate amounts of the ligand avidin were dissolved in the adsorption buffer (sodium acetate/ acetic acid, pH 5). The polyethylene magnetic particle suspension (in the same buffer, 10% solid) was added to above protein solution and mixed gently for 1-2 hours. After 2 more hours at room temperature, the mixture was centrifuged and the protein concentration in the supernatant was measured using a Turner spectrophotometer (SP 830) at a wavelength of 562 nm, using BCA protein assay kit.

One drop of polyethylene composite particles in acetone was placed on a carbon coated copper grid, dried and observed under a JEOL 2010 Transmission Electron Microscopy microscope operated at 200 KV. Bright field imaging technique was used to image the samples by selecting the transmitted diffraction spot to form the image.

A D 3000 Nanoscope from Digital Instruments was used in tapping mode. One drop of sample was placed on cleaved Mica surface and observed under the microscope. Micrographs were taken in both height and amplitude mode.

A Quantum Design MPMS5 DC Superconducting Quantum Interference Device (SQUID) was used to study the magnetic properties of the maghemite particles and the polyethylene magnetic particles. Weighed amount of sample were packed in gel capsules and placed tightly in the glass tube ensuring no movement in either direction and the magnetic properties were measured.

A Perkin Elmer DSC 7 equipped with a 3700 data station was used for Differential Scanning Calorimeter and the instrument was calibrated with an Indium standard. Approximately 4 mg of pure polyethylene wax sample was heated first to a temperature of  $150^{\circ}\text{C}$  then quenched to room temperature and kept there for 10 minutes to ensure complete crystallization and then reheated at a rate of  $10^{\circ}\text{C}/\text{min}$  to  $150^{\circ}\text{C}$ . Similarly pure polyethylene particles and polyethylene composite particles both

formed by solvent-nonsolvent and temperature induced crystallization when heated in aluminum pans from  $40^{\circ}\text{C}$  to  $150^{\circ}\text{C}$  at same heating rate. The peak temperature in the endotherm was considered as the melting temperature and the crystallinity values were calculated based on the standard heat of fusion value of polyethylene ( $\Delta H_u = 290\text{J/g}$ ).

**RESULTS AND DISCUSSION:** The polyethylene magnetic composite particles were formed under the experimental conditions summarized in Table 1. High boiling solvents and nonsolvent were chosen in order to increase the undercooling, which enhanced the crystallization process. Particle morphology is dependent on the choice of solvent as evident from the micrographs.

Table 1: Experimental conditions and results.

Polymer conc (w/v) %	Solvent: Nonsolvent	% maghemite	Morphology (av. diameter (nm))
0.05	Decalin/TG	50	Spherical/elliptical ~300 nm
0.05*	Decalin/TG	50	Spherical/elliptical ~370 nm
0.1	Decalin/TG	30	Spherical/elliptical ~200 nm
0.1*	Decalin/TG	30	Spherical/elliptical ~360 nm
0.05	OMCTS/TG	50	Spherical ~300 nm
0.1	OMCTS/TG	30	Spherical ~250 nm
0.1*	OMCTS/TG	30	Not well formed

\*Amplitude of sonication was set at 80%, while all other samples were set at 50%

Transmission electron micrographs (Figures 1 and 2) obtained for particles formed under different experimental conditions showed that the particles have diameters in the range of 50 - 500 nm with two types of distinct morphology, spherical and elliptical. It was found that an increase in the amplitude of ultrasonication produced smaller particles after crystallization. However, there was a lack of attachment for the iron oxide particles with the polymer and the mostly irregular shaped particles were formed under that condition irrespective of the type of solvent. Most particles were nicely formed using 50% amplitude with both types of solvents.

The polymer concentration had no significant effect on particle size. In fact, when polymer crystallized from the solvent in the nonsolvent medium, it had maghemite on the surface, which affects the particle growth and final shape.

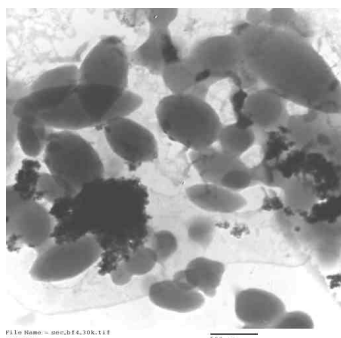


Fig. 1. TEM of polyethylene particles.

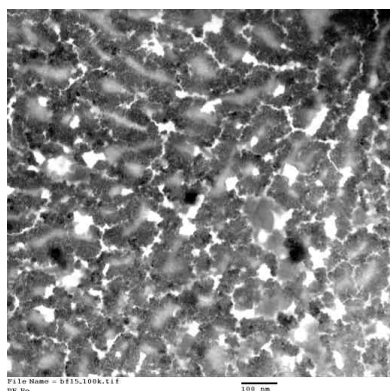


Fig. 2. TEM of polyethylene composite.

Particles formed from the OMCTS/tetraglyme emulsion showed mostly spherical morphology under different experimental conditions (Fig. 3), but the particles formed from the decalin/tetraglyme system have both elliptical and spherical morphology. The low molecular weight polyethylene used in this study has a very wide distribution of molecular weights (300-700 g/mole). It has been reported [3] that fractionations occur for solution grown crystals of polyethylene with shorter molecules concentrated towards the edges of lamella within the crystal. This could be one of the reasons for the changes in particle morphology. The solvent effects on particle morphology are still under investigation. The whole system after addition of a nonsolvent becomes a phase-separated system, which leads to precipitation of a swollen polymer and is used in fractionation and recrystallization. The lower value of crystallinity for the solution crystallized pure particles and composite particles as obtained from differential scanning calorimetry studies might be additional evidence for fractionation and recrystallization. The effect of ultrasonication at the dissolution and mixing step where interparticle collision occurred due to ultrasonication needs to be considered. Particles are not well formed when used 80% amplification.

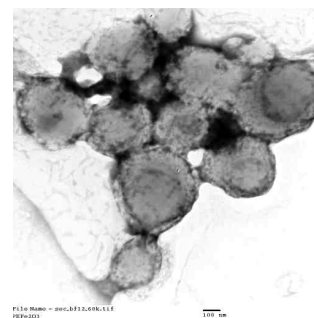


Fig. 3. TEM of polyethylene particles.

An atomic force micrograph for the polyethylene avidin-coated particles is shown in Figure 4. Particles are found to be agglomerated after protein adsorption on their surface due to protein-protein interaction. In these micrographs, both spherical and elliptical particles were observed.

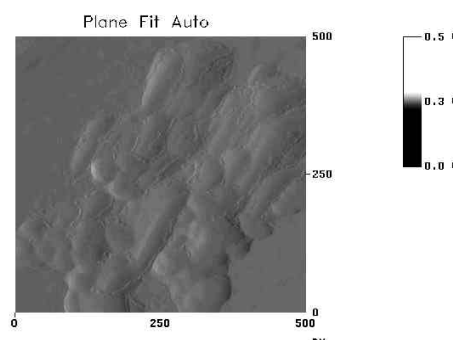


Fig. 4. AFM of avidin coated polyethylene particles.

Degree of crystallinity values for the pure polymer, polymer crystallized from solvent-nonsolvent emulsion (without iron oxide) and composite particles were obtained from their heat of fusion values. As expected the composite particles showed lowest value of crystallinity indicating the presence of another material with the polymer. Polymer particles formed without maghemite also showed lower crystallinity compared to the pure polymer indicating fractionation by the effect of dissolution and recrystallization process. Their crystallinity values are tabulated in Table 2 along with the melting points.

Table 2. Degree of Crystallinity

Sample	Melting point (°C)	Degree of Crystallinity (%)
PE wax	85.3	74.2
PE particles (nonmagnetic)	87.5	53.4
PE particles (magnetic)	85.4	16.7

Magnetization was measured using a SQUID at 5 K and at 300 K (Figures 5 and 6). It was found at 5

K that the hysteresis was rather large with a coercive field. The hysteresis loop is symmetric, showing the characteristics of superparamagnetic behavior. Magnetization curves at 300 K showed no hysteresis and the typical superparamagnetic behavior of the composite particles.

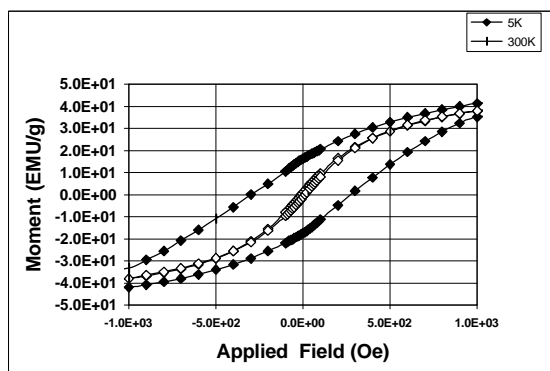


Fig. 5. Hysteresis curve at 5 K and 300 K.

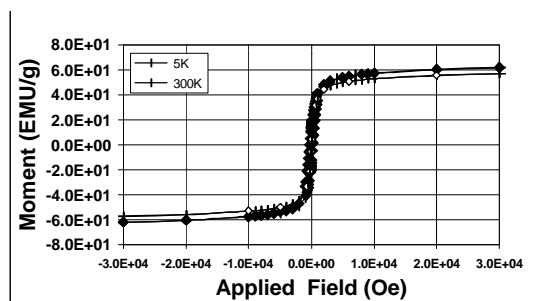


Fig. 6. Hysteresis curve at 5 K and 300 K.

The protein coupling efficiency was measured for the composite particles. Avidin was used as ligand as it has strong bond forming ability with various ligands used in immunoassays. Composite particles were coated with avidin. It had been found only 30% of the calculated amount of avidin required for monolayer formation on polyethylene particles is used to coat the particles and remaining portion remained unadsorbed.

**CONCLUSIONS:** Polyethylene magnetic composite particles have been fabricated in submicron range using nonsolvent-temperature-induced crystallization coupled with ultrasonication. The particles formed have spherical and elliptical morphology depending on the nature of solvent for a certain time of crystallization. Polymer concentration and amplitude of ultrasonication have large effects on the size of the microdroplets of polymer with iron oxide in solvent-nonsolvent emulsion. The final size of the particles is dependent on the size of the microdroplet formation. Smaller particles (30-50 nm) with irregular shapes are formed at high amplitude of ultrasonication. Unmodified maghemite showed no coupling with

polyethylene under any of the reaction conditions. The decrease in crystallinity for the composite particles shows the presence of iron oxide in the polymer. Lower magnetic moments support the above conclusion. Lower blocking temperatures show that the particles are coated with polymer, as has been also shown in the transmission electron micrographs. Composite particles are superparamagnetic in nature as observed in the magnetization experiment. Composite particles can be effectively coated with ligands such as avidin and could thus be used for biomedical applications.

**REFERENCES:** <sup>1</sup> Y. Yaravoy, G. Baran, S. Wunder and R. Wang (2000) *J. Biomed. Mat. Res.* **53**:152. <sup>2</sup> J. Chatterjee, Y. Haik, and C.-J. Chen (2001) *J. Mag. Magn. Mat.* **225**:21. <sup>3</sup> D. Bassett in Principles of Polymer Morphology. R. Cahn, M. Thompson and I. Ward Eds. (1981) Cambridge University Press.

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