

## BIOCOMPATIBLE MAGNETIC MICROPARTICLES: A COLLOIDAL STABILITY STUDY

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*Abstract.* This work addresses a method for preparing magnetic crosslinked polyvinyl alcohol (PVA)-chitosan (CS) microspheres (BMM) specifically tailored/functionalised to bind blood toxins, optimization of the synthesis parameters and characterization of the products. Some experiments concerning the BMM dispersability in aqueous/ethyl alcohol-water media, using different surfactant systems, have been made.

*Key words:* magnetic particles, polyvinyl alcohol (PVA)-chitosan (CS) microspheres.

### INTRODUCTION

In recent years, magnetic nano and microparticles received a lot of attention related to their use in biomedical applications, such as: diagnostics, separation and purification of biomolecules, carriers for drug delivery and MRI contrast enhancement agents [2]. Among these applications, the possibility of using magnetic particles to detoxify blood in patients suffering from hepatic/renal deficiencies receives a considerable interest. The most common magnetic material is iron oxide (magnetite,  $\text{Fe}_3\text{O}_4$ ) used as a core covered with a shell or uniformly dispersed within a matrix containing a natural or a synthetic polymer [1]. Chitosan (CS) is frequently used due to its biocompatibility and advantageous functional groups [3]. Polyvinyl alcohol (PVA) is also attractive because it prevents coagulation of particles and adds stability and monodispersity [4]. The composite BMM were produced by an emulsion crosslinking method, the following synthesis parameters being studied: CS/PVA ratio, crosslinking concentration and the type of oil soluble surfactant. Zeta potential and potentiometric titration analysis

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Received November 2009;  
in final form February 2010.

qualitatively demonstrated the presence of the amino functional groups on the surface of the BMM.

Dispersability of the particles is typically critical to their performance in medical field. Thus, we made some studies concerning the dispersability of the obtained particles by determination of their size distribution in aqueous / ethyl alcohol-water media, using different surfactant systems.

## MATERIALS AND METHODS

Colloidal magnetite particles were prepared by the co-precipitation method from an aqueous solution containing  $\text{Fe}^{3+}/\text{Fe}^{2+}$  ions with molar ratio of 2:1, upon addition of aqueous sodium hydroxide 2.66 M. The particles were stabilized in suspension by adding a 2% aqueous solution of a non ionic biocompatible surfactant (Pluronic F127). This suspension (containing 1.45% w/v magnetite) was used for the obtaining of composite magnetic particles. The composite particles were produced by an emulsion crosslinking method. The aqueous phase was prepared by mixing a 5% aqueous solution of PVA, a 1% solution in acetic acid 0.5% of CS (in various ratios) and the previously prepared magnetite stabilized suspension (1/10 w/w magnetite/polymers ratio). The aqueous phase was dispersed in an oil phase consisting of vegetable oil and  $2.23 \times 10^{-3}$  moles of oil soluble surfactants (Tween 20, Span 65, Span 85, oleic acid) using a high speed homogenizer (Ultraturrax –  $10^4$  rpm). Glutaraldehyde aqueous solution with variable concentrations (6.25–25 %) was added as a crosslinker in the presence of HCl 1 N solution. The mixture was homogenized further for 2 minutes and then aged twenty minutes. The particles were cleaned repeatedly with heptane, acetone and distilled water and dried in air. The following synthesis parameters were studied: CS/PVA ratio, PVA molecular weight, crosslinking concentration and the type of oil soluble surfactant (Table 1). The products were characterized regarding properties such as: size distribution (Laser Diffraction Analysis, TEM), structure (FTIR), magnetic properties (magnetization), concentration of surface functional groups (potentiometric titration, Zeta potential).

The experimental procedure for the evaluation of the dispersability was as follows: 1 mL of the particles suspended in  $\text{NaH}_2\text{PO}_4/\text{Na}_2\text{HPO}_4$  2 M buffer solution (pH 6.2) was treated with 0.5 mL of one dispersing agent (0.2% aqueous solution of PVA 72000 totally hydrolyzed, PVA 70000 partially hydrolyzed, 0.25% sodium dodecyl sulphate aqueous solution, 0.02% Pluronic F127 aqueous solution or a HCl 2N solution) and 10 mL bidistilled water. In other systems, the obtained particles were suspended in ethyl alcohol-water media, without any dispersing agent. The size distribution for the particles dispersed into these systems had been made using laser diffraction analysis (Nanotracc, Microtracc Inc., USA).

*Table 1*  
Synthesis parameter study

Batch	Water/oil phase ratio (v/v)	PVA Mw	CS/PVA ratio (w/w)	Surfactant	GA conc. (%)	Average diameter ( $\mu\text{m}$ )	Zeta potential (mV)	Magn. (emu/g)
1	11.3/150	67000	1/1	Tween Ac. oleic	12.5	0.027	9.27	6.89
2	11.3/150	72000	1/1	Tween Ac. oleic	12.5	0.454	4.76	6.33
3	11.3/150	205000	1/1	Tween Ac. oleic	12.5	0.680	1.15	6.31
4	22.52/150	72000	0/1	Tween Ac. oleic	12.5	0.33	-1.7	6.17
5	22.52/150	72000	1/0	Tween Ac. oleic	12.5	0.413	4.41	6.2
6	22.52/150	72000	1/1	Tween Ac. oleic	12.5	0.410	2.06	5.73
7	22.52/150	72000	1/1	Tween Ac. oleic	6.25	0.657	-3.8	4.5
8	22.52/150	72000	1/1	Tween Ac. oleic	25	0.515	-0.806	6.8
9	22.52/150	72000	2/1	Tween Ac. oleic	12.5	0.654	4.3	4.84
10	22.52/150	72000	1/2	Tween Ac. oleic	12.5	4.926	-0.860	4.7
11	22.52/150	72000	1/1	Span85	12.5	0.511	2.3	6.3
12	22.52/150	72000	1/1	Span80	12.5	0.414	2.21	6

## RESULTS

The size analysis of the particles synthesized with PVA having different molecular weights (67000, 72000 and 205000) confirmed the fact that a higher molecular mass of the polymer means a higher average diameter for the particles. The size distribution of the particles diameters for different PVA types showed that the narrowest distribution of the particles diameters was obtained using PVA 72000.

Figure 1 shows transmission electron microscopy of batch 6 dispersed in ethyl alcohol-water media. It suggests that the prepared particles are well dispersed and have a relatively narrow size distribution with the mean size of about 100 nm. The image showed that the magnetic particles are dispersed in a polymeric crosslinked matrix.

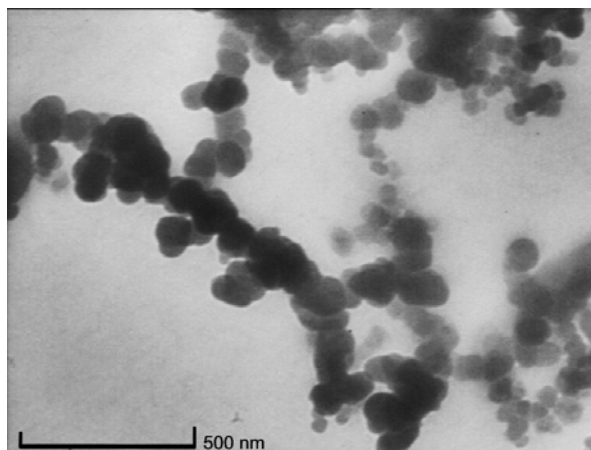


Fig. 1. Transmission electron microscopy of batch 6.

The positive values of the Zeta potential (water as dispersion medium) qualitatively confirmed that the use of CS leads to functional amino groups on the particles surface. Conductimetric titration for the batch 6 demonstrated the presence of  $3.457 \times 10^{-4}$  amino Eg/g particles (Fig. 2).

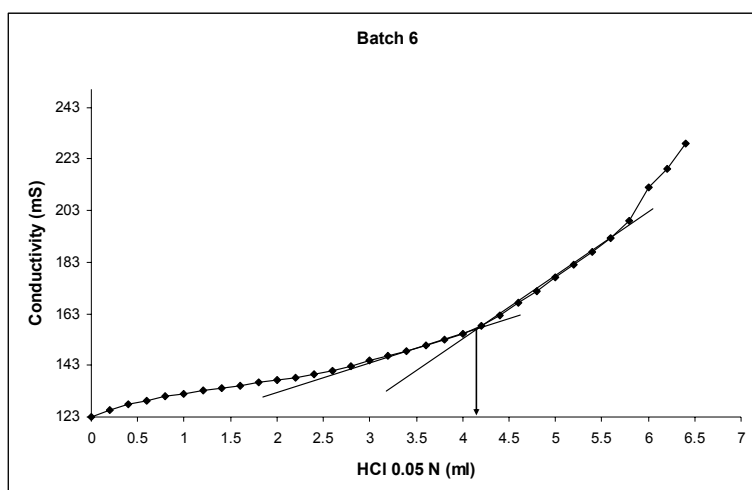


Fig. 2. Conductimetric titration curve for the batch 6.

The magnetizations of the magnetite stabilized with Pluronic F127 and for the obtained particles were measured, using a magnetometer Lakeshore VSM 7400 (Fig. 3). The magnetization of saturation for the pure magnetite is 90 emu/g; the magnetization of saturation for the magnetite stabilized with Pluronic F127 being 53 emu/g demonstrated the fact that the magnetite presented a stabilizing layer (Pluronic F127) on his surface. The magnetization of saturation for the obtained particles (batch 6) was 5.73 emu/g. Considering the fact that the rate magnetite/polymers was maintained at the same value for all samples (1/10 w/w stabilized magnetite/polymers ratio), it can be concluded that the entire quantity of feed magnetite was included in the particles.

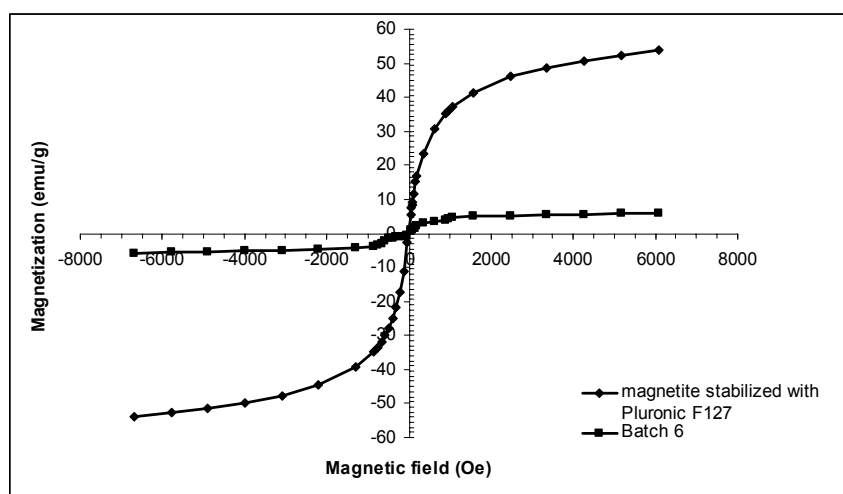


Fig. 3. Magnetization curve for stabilized suspension of magnetite and batch 6.

FTIR spectra of CS, PVA 72000, magnetite stabilized with Pluronic F127, batch 4 and batch 6 were shown in Fig. 4.

The spectrum of PVA showed the peaks around 3040.35, 2941.44 and 1095.56  $\text{cm}^{-1}$ , indicating the stretching of OH, aliphatic CH and CO respectively. There was also a band at 1442.75  $\text{cm}^{-1}$  due to CH bending vibration. The spectrum of CS showed peaks around 3439.07, 2924.08, 1382.96 and 1089.78  $\text{cm}^{-1}$ , indicating the stretching of OH and aliphatic CH, bending of CN and CO respectively. The amine group of CS has a characteristic peak in the region of 3000–3500  $\text{cm}^{-1}$ , which has been masked by the peak due to OH group. CS also presented a characteristic absorption peak at 1637.56  $\text{cm}^{-1}$  due to its amide group. The spectrum of the stabilized magnetite showed peaks at 3425.57  $\text{cm}^{-1}$  (OH groups of Pluronic F127) and 567.07  $\text{cm}^{-1}$ , indicating the presence of magnetite.

The presence of a new peak in the batch 4 spectrum (1130.28  $\text{cm}^{-1}$ ) was a band of acetal group, formed due to the reaction of glutaraldehyde with OH group

of PVA. Besides this peak, in the spectra of batch 6 can be seen a peak at  $1078.21\text{ cm}^{-1}$  occurred due to hydrogen bonds between  $\text{NH}_2$  or/and OH groups of CS and OH groups of PVA. Moreover, a new peak at  $1631\text{ cm}^{-1}$  was due to the formation of CN as a result of crosslinking reaction between amino groups.

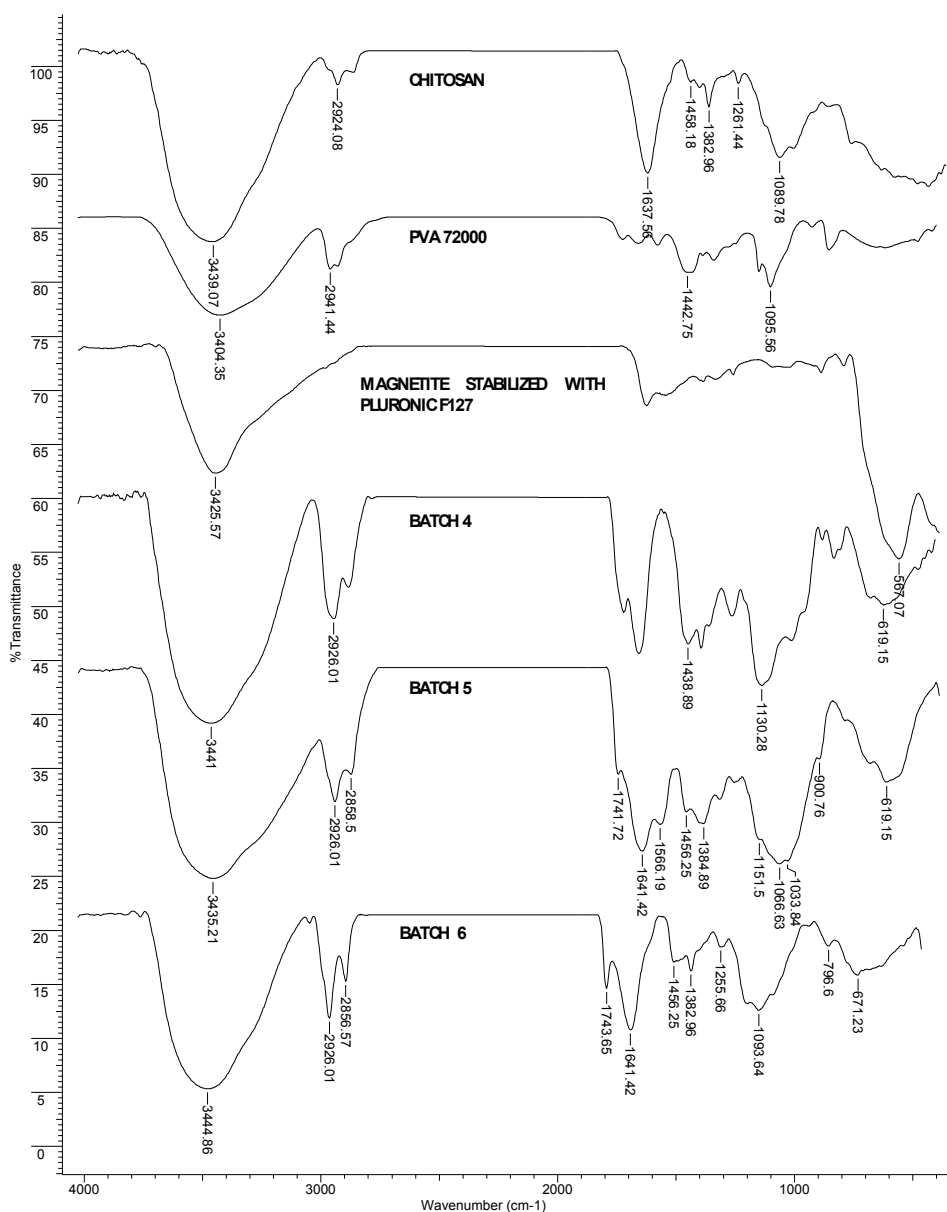


Fig. 4. FTIR spectra.

The average particle size is an important factor that determines dispersability. The particles are optimally dispersed when they are easily separated into discrete aggregates; the smaller are the dispersed particles the better is the dispersability. The results concerning the average size for the particles dispersed in different media are presented in Table 2. The experimental data suggested that in aqueous media the particles were agglomerated irrespective of dispersant agent used. The particles showed a good dispersability in ethyl-water media.

Table 2

Dispersability study

Batch / Average diameter of BMM using different dispersants ( $\mu\text{m}$ )	PVA 72000	PVA 70000	SDS	Pluronic F127	HCl 2N	Ethyl alcohol-water
Batch 5	26	0.8	0.3	26	0.3	0.413
Batch 6	37	45	34	49	167	0.41
Batch 7	1.5	1.51	5.6	0.85	0.45	0.657
Batch 8	1.89	1.88	1.88	1.88	1.42	0.515
Batch 9	201	59	32	34	208	0.654
Batch 10	36	36	39	43	179	4.926
Batch 11	4.9	26	19	25	28	0.511
Batch 12	0.4	4.8	4.7	0.49	4.67	0.414

In conclusion a method for the preparation of magnetite/CS/PVA composite particles with surface functionality using the emulsion crosslinking method was developed and optimized. Due to surface amino groups and their magnetic properties, the obtained particles have potential application in blood detoxification methods.

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