Colloids and Surfaces A 555 (2018) 80–87

Contents lists available at ScienceDirect

Colloids and Surfaces A

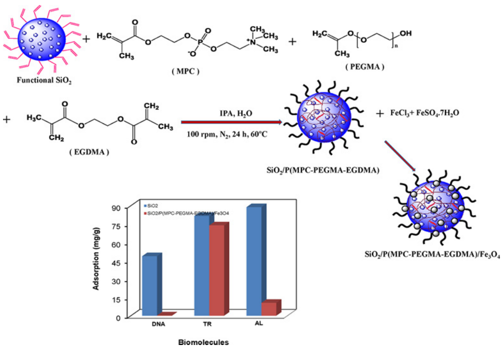
journal homepage: www.elsevier.com/locate/colsurfa

Zwitterionic poly(2-(methacryloyloxy) ethyl phosphorylcholine) coated mesoporous silica particles and doping with magnetic nanoparticles

Taslima Hossain[a], Mohammad A. Alam[a], Mohammad A. Rahman[a], Mostafa K. Sharafat[a], Hideto Minami[b], Muhammad A. Gafur[c], Sheikh M. Hoque[d], Hasan Ahmad[a,*]

[a] *Department of Chemistry, Rajshahi University, Rajshahi, 6205, Bangladesh*
[b] *Graduate School of Engineering, Kobe University, Kobe, 657-8501, Japan*
[c] *Pilot Plant and Process Development Centre, BCSIR, Dhaka, 1205, Bangladesh*
[d] *Materials Science Division, Bangladesh Atomic Energy Commission, Dhaka, Bangladesh*

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Poly(2(methacryloyloxy) ethyl phosphorylcholine) (PMPC)
Zwitterion
Magnetic property
Adsorption
Biomolecule

ABSTRACT

Poly(2(methacryloyloxy) ethyl phosphorylcholine) (PMPC) a zwitterionic biopolymer has been used to prepare hybrid inorganic/organic/inorganic tri-layered magnetic composite particles. Mesoporous SiO_2 particles of average diameter 284.8 nm are first prepared by sol-gel technique in presence of cetyltrimethylammonium bromride (CTAB) as template to generate porosity. The surface of mesoporous SiO_2 particles is then functionalized to introduce vinyl functionality using silane coupling agent, 3-(trimethoxysilyl) propyl methacrylate (MPS). Finally grafting of MPC is carried out on the surface of mesoporous SiO_2 particles by carrying out seeded copolymerization in presence of monomethoxy-capped poly(ethylene glycol) methacrylate (PEGMA) as a reactive steric stabilizer and ethylene glycol dimethacrylate (EGDMA) as a cross-linker. The prepared composite polymer particles named as SiO_2/P(MPC-PEGMA-EGDMA) are finally doped with magnetic iron oxide nanoparticles (Fe_3O_4) via simultaneous in situ precipitation of Fe^{2+} and Fe^{3+} from alkali solution. The final composite particles possessed moderate paramagnetic property having magnetic susceptibility (2.22×10^{-5}) which is just one order less than that of reference Fe_3O_4 nanoparticles (1.00×10^{-4}). A comparative adsorption behaviour of biomolecules suggested that surface of SiO_2/P(MPC-PEGMA-EGDMA) composite particles resist protein adhesion whereas after doping with Fe_3O_4 nanoparticles the surface has tendency to adsorb proteins.

---

* Corresponding author.
E-mail address: hahmad@ru.ac.bd (H. Ahmad).

https://doi.org/10.1016/j.colsurfa.2018.06.020
Received 5 April 2018; Received in revised form 26 May 2018; Accepted 8 June 2018

1. Introduction

Zwitterionic polymers bearing fixed pairs of positive and negative charges are known to possess antifouling properties and generally used as bioinert blood compatible surface. It is believed that zwitterionic polymer surfaces form hydration layer via electrostatic interaction and hydrogen bond [1] and lead to a strong repulsion to protein adsorption [2,3]. Such zwitterionic polymer surfaces are therefore considered useful to prevent nonspecific protein adsorption, cell adhesion and bacterial attachment for various biomedical applications [4–10], such as drug or gene delivery carriers [11,12], filtration membranes [13,14], diagnostic biosensors [15,16], soft contact lenses [17,18], low biofouling coating on urological devices [19], tympanostomy tube implants [20] and blood contacting implanted devices [21–23]. Additionally they are also useful in coatings on mobile and stationary structures immersed in sea water for prevention of biofouling [24] and chemical separation membrane [25,26].

During the last twenty years 2-(methyacryloyloxy)-ethyl phosphorylcholine (MPC), a biomimetic commercial zwitterionic monomer has been widely used to produce a wide range of polymer coatings [27–32]. MPC based polymers are highly hydrophilic and reportedly incorporate 22 water molecules per MPC repeat unit [33,34]. Though most zwitterionic polymers exhibit good flexibility and membrane-forming property but they have poor mechanical strength and thermal stability. These limitations had restricted their applications in harsh conditions such as higher temperature, strongly oxidizing environments, alkaline media and organic solvents. Preparation of inorganic/organic hybrid materials can effectively improve mechanical strength and thermal stability and also can produce improved properties of individual inorganic and organic components. However, only few researches have been carried out on the preparation of poly(MPC) or PMPC based inorganic/organic hybrid composite particles. For example, Cho et al. prepared MRI-active Gd_2O_3 core/SiO_2 shell/PMPC corona composite nanoparticles for cancer and neutron capture therapy [35]. They prepared Gd_2O_3 nanoparticles, functionalized with SiO_2-Br and finally carried out atom transfer radical polymerization (ATRP) to form a biomimetic layer of PMPC. Yuan et al. synthesized Fe_3O_4 nanoparticles using diblock copolymer of PMPC-*b*-poly(glycerol monomethacrylate) [36]. In another recently published article Pan and his group discussed the preparation of poly(ethyl methacrylate)/SiO_2 hybrid colloidal spheres and grafted with hydrophilic diblock copolymer of PMPC-*b*-poly[3(trimethoxysilyl)propyl methacrylate)] (PMPC-*b*-PMPS) through the reaction of silanol groups of SiO_2 and the methoxy groups of MPS [37].

In the present investigation submicrometer-sized mesoporous SiO_2 particles have been used as core materials to produce tri-layered magnetic iron oxide (Fe_3O_4) doped zwitterionic composite polymer particles. The preparation scheme is depicted in Scheme 1. Mesoporous SiO_2 particles with well-defined pore structures are considered to have some excellent properties such as high water dispersibility, chemical inertness and thermal stability, resistance to pH, mechanical tension, biocompatibility and high loading capacity [38–41]. Seeded copolymerization of MPC is carried out in 90/10 isopropanol (IPA)/water mixture to prevent the solubilization of PMPC. This is already reported that PMPC is soluble in both lower alcohols and water but becomes insoluble in certain alcohol-rich alcohol/water mixtures [42–46]. During seeded copolymerization monomethoxy-capped poly(ethylene glycol) methacrylate (PEGMA) and ethylene glycol dimethacrylate (EGDMA) are used as reactive steric stabilizer and cross-linker respectively. Finally in situ simultaneous co-precipitation of Fe^{2+} and Fe^{3+} is carried out to prepare SiO_2/P(MPC-PEGMA-EGDMA)/Fe_3O_4 composite polymer particles. These magnetic composite particles with zwitterionic PMPC moiety would particularly find applications in drug delivery, hyperthermia application due to their selective heating capacity without damaging healthy tissues, body implant devices, contrast enhancement in magnetic resonance imaging (MRI) and separation of biochemicals.

2. Materials and methods

2.1. Materials

MPC, PEGMA both from Sigma-Aldrich, USA and EGDMA from Fluka, Biochemica, Switzerland were of monomer grade and used without purification. Tetraethylorthosilicate, TEOS (Sigma Chemical Company, USA), cetyltrimethylammonium bromide, CTAB (Fluka, Biochemica, Switzerland) and 3-(trimethoxysilyl) propyl methacrylate, MPS (Alfa Aesar, UK) were used as received. 2,2’-Azobis(isobutyronitrile) (AIBN) was recrystallized from ethanol solution and preserved in the refrigerator before use. Trypsin, TR (Merck, Germany), albumin, AL (LOBA Chem., India) and deoxyribonucleic acid, DNA (Sigma-Aldrich, USA) were used as biomolecules. Diethyl amine (DEA), $FeCl_3$, $FeSO_4.7H_2O$, oleic acid, ethanol, NH_4OH, 2-propanol (IPA) and other chemicals were of analytical grade. Deionized water was distilled using a glass (Pyrex) distillation apparatus.

2.2. Preparation of mesoporous SiO_2 particles

At first requisite amount of CTAB (4.38 g), DEA (0.12 g) and 27% (v/v) aqueous ethanol were taken in a three-necked round flask and dipped in a thermostat water bath at 60 °C. The mixture was stirred under a N_2 atmosphere for 30 min. Then, TEOS (4.38 g) was added drop-wise into the mixture. The mixture was stirred for another 4 h and the solution was cooled to room temperature. The solution gradually turned white. The as-prepared mesoporous SiO_2 particles were separated and washed repeatedly with ethanol.

In order to extract CTAB, washed SiO_2 particles were refluxed by dispersing SiO_2 particles (3.0 g) in ethanol (693.0 mL) containing 37% HCl (27.7 mL) at 80 °C for 48 h. Finally mesoporous SiO_2 particles were washed three times with double distilled H_2O using a desk-top centrifuge machine (TG16-WS, China). Finally, the product was dried overnight under vacuum.

2.3. Functionalization of SiO_2 particles by MPS

Dried SiO_2 powders (1.0 g) were dispersed in ethanol (2–5 mL) by ultrasonication and transferred into a three necked round flask with MPS (1.5 g) to introduce vinyl groups at the surface. The mixture was magnetically stirred (400 rpm) for 24 h at 25 °C under a nitrogen atmosphere. The dispersion media comprised water-ethanol mixture containing 12.5% (w/w) water. The prepared functional SiO_2 particles were washed and used as seed particles for further surface modification by seeded copolymerization.

2.4. Preparation of SiO_2/P(MPC-PEGMA-EGDMA) composite polymer particles

MPC (0.704 g), PEGMA (0.08 g), EGDMA (0.016 g) and 90/10 IPA/water mixture (100 g) were taken into a three necked round flask containing 1.0 g functional SiO_2 particles. The flask was transferred to a thermostat water bath and temperature was raised to 60 °C. Oil soluble AIBN (0.036 g) was added and the polymerization was continued for 24 h in a nitrogen atmosphere. The prepared composite polymer particles were washed three times with 90/10 IPA/H_2O mixture and finally collected in IPA/water mixture. It is worthwhile to mention that SiO_2/P(MPC-PEGMA-EGDMA) composite polymer particles could not be washed with distilled water because PMPC was partially soluble despite the formation of crosslinked network.

2.5. Doping of composite polymer particles with Fe_3O_4 nanoparticles

SiO_2/P(MPC-PEGMA-EGDMA) composite polymer particles were doped with Fe_3O_4 nanoparticles by simultaneous precipitation of Fe^{2+} and Fe^{3+} (molar ratio 1:2). For this composite polymer particles (0.7 g),