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Colloidal strategies for electrophoretic deposition of organic-inorganic composites for biomedical applications

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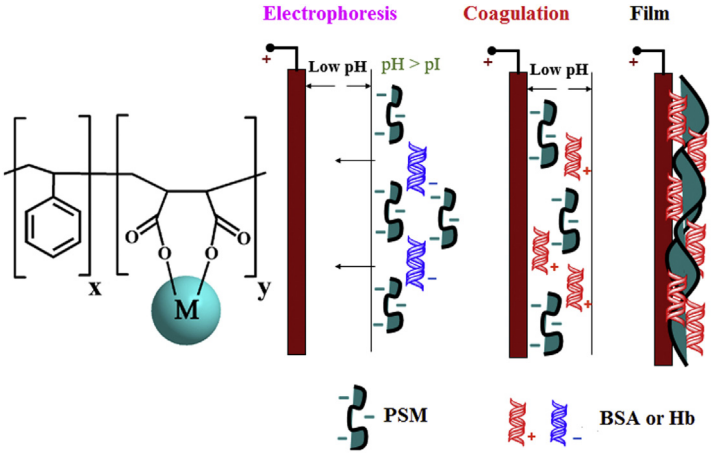
HIGHLIGHTS

- Poly(styrene-alt-maleic acid) (PSM) was used as a chelating dispersant for particles.
- PSM allowed for electrophoretic deposition (EPD) of biomaterials and composites.
- Hydroxyapatite, bioglass, TiO_2, Al_2O_3 and carbon nanotubes were deposited.
- Methods for co-deposition of PSM with albumin and hemoglobin were developed.
- PSM adsorption, EPD mechanisms, film morphologies and applications are discussed.

GRAPHICAL ABSTRACT



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ABSTRACT

Poly(styrene-alt-maleic acid) (PSM) exhibits a number of unique properties, which are important for diverse biomedical applications. A conceptually new strategy has been utilized for dispersion, charging and electrophoretic deposition (EPD) of advanced materials for biomedical applications, such as hydroxyapatite, bioglass, TiO_2 and Al_2O_3 using PSM. The approach is based on the use of chelating properties of maleic acid monomers, which created multiple bonds with surface atoms on the particle surface and allowed strong PSM adsorption and efficient particle dispersion. The deposition kinetics and mechanism have been investigated and the advantages of PSM have been discussed. Our new findings in the colloidal electrochemistry allowed for the co-deposition of PSM with hemoglobin and albumin, which have been utilized as model proteins for the development of the deposition mechanism. Another major finding was the possibility of efficient deposition of various composites, containing PSM, hydroxyapatite, bioglass, TiO_2, Al_2O_3, proteins and carbon nanotubes. Comprehensive electron microscopy data was used for the analysis of film morphologies at different experimental conditions. The results of this investigation paved the way for EPD of composite films, utilizing properties of different functional biomaterials.

1. Introduction

Electrophoretic deposition (EPD) is gaining increasing interest as a colloidal processing technique for a variety of technical applications [1,2]. This method can be combined with other

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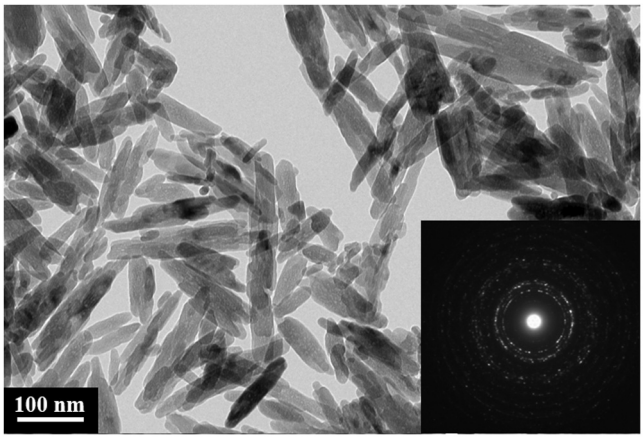

Fig. 1. TEM image of HA particles, prepared by a chemical precipitation method. Inset shows a selected area electron diffraction pattern.

electrochemical strategies [3–5] for the deposition of composite films and coatings with advanced functionality. EPD offers many advantages for the deposition of films for biomedical applications [6–8]. Organic–inorganic biocomposite films have attracted substantial attention due to the possibility of combining the properties of organic and inorganic components [9]. Many investigations focused on the co-deposition of biocompatible polymers with inorganic particles [6,10]. The progress in EPD of biocompatible polymers and composites offers important opportunities in the development of advanced films and coatings for biomedical implants and devices [10–12].

Recently significant interest has been generated in the biomedical applications of poly(styrene-alt-maleic acid) (PSM) [13,14]. Nanoparticles of PSM were utilized as colloidal carries for anticancer agents. It was found that PSM and its derivatives allow for significant improvement in the pharmacological properties of various drugs [13,15]. The PSM formulated drugs showed high tumor targeting efficiency and low toxicity [13,14]. The relatively strong bonding of various drugs to PSM was beneficial for controlled drug release. Another important finding was the strong non-covalent bond between albumin and PSA, which allowed improved PSM particle stability in blood plasma [13]. The analysis of PSM interactions with phospholipids resulted in the synthesis of PSM-phospholipid complexes, which showed promising properties for various biomedical applications [16]. PSM was used for the immobilization of hemoglobin and the fabrication of biosensors [17]. Ag loaded PSM composites with antiseptic properties have been developed for biomedical devices [18]. PSM interactions with proteins showed that PSM is beneficial for the surface modification of various biomaterials [19].

Of particular interest are the important structural features of PSM, which the literature has not paid sufficient attention to. The structure of the maleic acid monomer includes two carboxylic groups (Fig. 1A), which make PSM a strong complexing agent. The two adjacent carboxylic groups form complexes with metal ions in solutions [20,21]. The chelating PSM polymer has been used for the removal of heavy ions from water [22,23]. It has also been reported that the PSM complexes exhibit valuable luminescence properties [24]. The chelating properties of PSM were utilized for the synthesis of inorganic materials. Particles with different morphologies were prepared by chemical precipitation methods in the presence of PSM [25–27]. A polymer mediated mineralization method was developed using the chelating PSM polymer for the fabrication of mesoscale-organized particles with unusual superstructures [28]. PSM has been utilized for the fabrication of one-dimensional nanostructures by hydrothermal synthesis [29]. New techniques for template synthesis have been developed based on the chelating properties of PSM [30,31].

The chelating properties and biocompatibility of PSM are of particular interest for application in EPD of biomaterials. Particles of inorganic biomaterials must be well dispersed and charged in suspensions for EPD [10,32]. The adsorption of a dispersant is important for the fabrication of stable suspensions, because a non-adsorbed ionic dispersant promotes particle coagulation and sedimentation [33]. Previous investigations [33] showed the advantages of small organic dispersant molecules, containing chelating groups. Such molecules adsorbed on inorganic particles by chelating bonding to the metal atoms on the particle surface. However, the single chelating groups provided relatively weak bonding to the particle surface. In contrast, substantial improvement in adsorption and dispersion may be possible using chelating polymers, such as PSM. The chelating monomers of PSM can provide multiple adsorption sites for strong PSM adsorption on inorganic particles. Moreover, compared to small dispersant molecules, PSM offers the advantages of electrosteric stabilization.

The goal of this investigation was EPD of biomaterials using PSM as a charging and dispersing agent. We targeted the deposition of films of advanced inorganic materials for biomedical implants, such as hydroxyapatite, bioglass, TiO_2 and Al_2O_3. The analysis of experimental data provides an insight into the influence of PSM structure on the polymer adsorption, particle dispersion and EPD yield. The results presented below indicated that the use of PSM allows for EPD of inorganic materials at high deposition rates. Moreover, we report that PSM can be used for the deposition of other functional biomaterials, such as albumin and hemoglobin. We demonstrate that the problem of protein charge reversal, related to pH changes at the electrode surface, can be avoided and propose a mechanism, explaining EPD of albumin and hemoglobin. Another important finding was the possibility of co-deposition of different materials using PSM as a co-dispersant and formation of composite films. Comprehensive electron microscopy data was used for the analysis of film morphologies at different experimental conditions.

2. Experimental procedures

Poly(styrene-alt-maleic acid) (PSM), TiO_2 (anatase, 25 nm), human hemoglobin (Hb), bovine serum albumin (BSA), $Ca(NO_3)_2{\cdot}4H_2O$, $(NH_4)_2HPO_4$, NH_4OH (Aldrich, Canada), Al_2O_3 (0.13 μm, Baikowski, USA), multiwalled carbon nanotubes (MWCNT, ID 4 nm, OD 13 nm, length 1–2 μm, Bayer,Germany) were used in this work. Bioactive glass powder (45S5 Bioglass®) of composition (wt%): 45% SiO_2, 24.5% Na_2O, 24.4% CaO and 6% P_2O_5 and average particle size ~5 μm was supplied by MO-SCI Corporation, USA.

The procedure for the preparation of stoichiometric hydroxyapatite (HA) nanoparticles for EPD was based on that described in a previous work. Precipitation was performed at a temperature of 70 °C by a slow addition of 0.6 M $(NH_4)_2HPO_4$ solution into 1.0 M $Ca(NO_3)_2$ solution. The pH of the solutions was adjusted to 11 with NH_4OH. Stirring was performed for 8 h at 70 °C and 24 h at room temperature. The precipitate was washed with water and finally with isopropyl alcohol. It has been previously reported that this method resulted in the formation of crystalline HA. Fig. 1 shows a TEM image of HA particles, which exhibit a needle-like morphology with a typical length of 150 nm and aspect ratio of about 8. The electron diffraction pattern (Fig. 1, inset) confirms the HA crystallinity.

The electrochemical cell for EPD included a stainless steel substrate and Pt counter electrode. The distance between the substrate and counter electrodes was 15 mm. The deposition voltage was varied in the range of 5–30 V. The deposition time was varied in