Adsorption of Maleic Acid Monomer on the Surface of Hydroxyapatite and TiO₂: A Pathway toward Biomaterial Composites

Mitchell Albert, Amanda Clifford, Igor Zhitomirsky,* and Oleg Rubel*©

Department of Materials Science and Engineering, McMaster University, 1280 Main Street West, Hamilton, Ontario L8S 4L8, Canada

ABSTRACT: Poly(styrene-alt-maleic acid) adsorption on hydroxyapatite and TiO₂ (rutile) was studied using experimental techniques and complemented by ab initio simulations of adsorption of a maleic acid segment as a subunit of the copolymer. Ab initio calculations suggest that the maleic acid segment forms a strong covalent bonding to the TiO₂ and hydroxyapatite surfaces. If compared to vacuum, the presence of a solvent significantly reduces the adsorption strength as the polarity of the solvent increases. The results of first-principles calculations are confirmed by the experimental measurements. We found that the adsorbed poly(styrene-alt-maleic acid) allowed efficient dispersion of rutile and formation of films by the electrophoretic deposition. Moreover, rutile can be codispersed and codeposited with hydroxyapatite to form composite films. The coatings showed an enhanced corrosion protection of metallic implants in simulated body fluid solutions, which opens new avenues for the synthesis, dispersion, and colloidal processing of advanced composite materials for biomedical applications.

KEYWORDS: maleic acid monomer, hydroxyapatite, rutile, surface adsorption, density functional theory, electrophoretic deposition, coating, corrosion protection

1. INTRODUCTION

Investigations of adsorption of organic molecules at the surface of nanomaterials and their colloidal behavior allowed for the development of novel strategies for the surface modification, dispersion, and advanced synthesis of nanoparticles. Studies of mussel adsorption on inorganic surfaces provide important chemical and physical insights into development of covalent anchoring mechanisms. It was found that the strong mussel adhesion involves protein macromolecules that contain a catecholic amino acid L-3,4-dihydroxyphenylalanine (L-DOPA). The adhesion mechanism of mussels is attributed to the complexation or bridging bidentate bonding between metal atoms on material surfaces and hydroxyl groups of catechol. These studies have generated interest in the investigation of chelating molecules from the catechol family has driven investigations of natural aliphatic compounds with carboxyl groups, which can provide strong chelating or bridging polydentate bonding to inorganic materials. Of particular interest are fumaric and maleic acid (MA) isomers, containing trans and cis carboxyl groups, respectively. These acids showed strong adsorption on various oxides. The cis conformation of MA provides an ideal orientation for coordination via both carboxylate groups in a strong tetradentate interaction. It is in this regard that many dispersant molecules described in the literature provide a relatively weak monodentate bonding to the particle surface. Clearly, tetradeatate interactions of MA with oxide surfaces offer advantages for surface modification of materials. Significantly stronger interactions with inorganic surfaces can be expected using MA polymers or copolymers. The individual MA monomers of such polymers can provide multiple chemical bonds with substrates. Poly(maleic acid) showed a strong adsorption on alumina particles and allowed for their efficient dispersion. Poly(acrylic acid-co-maleic acid) exhibited a strong affinity to BaTiO₃ and clay minerals. The adsorption properties of the poly(styrene-alt-maleic acid) (PSMA-h) copolymer (Figure 1) have been utilized for the synthesis of inorganic particles with different morphologies and unusual superstructures. PSMA-h is a biocompatible polymer, which is currently under investigations for many biomedical applications, such as drug delivery, antimicrobial materials, and implants. PSMA-h demonstrated a strong affinity to hydroxyapatite (HA), bioglass, and bioceramics and allowed their electrophoretic deposition (EPD) and codeposition with proteins. Colloidal techniques, such as EPD, have a high potential in the...
Theoretical results are obtained using DFT. The neutron diffraction experimental data for TiO$_2$ and HA are taken from Refs 51 and 52.

<table>
<thead>
<tr>
<th>compound</th>
<th>a (Å)</th>
<th>c (Å)</th>
<th>u</th>
<th>a (Å)</th>
<th>c (Å)</th>
<th>u</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO$_2$ (rutile)</td>
<td>4.664</td>
<td>2.966</td>
<td>O (0.3046, 0.3046, 0)</td>
<td>4.594</td>
<td>2.959</td>
<td>O (0.3048, 0.3048, 0)</td>
</tr>
<tr>
<td>hydroxyapatite</td>
<td>9.549</td>
<td>6.934</td>
<td>Ca$_{9}$ (1/3, 2/3, 0.0016)</td>
<td>9.432</td>
<td>6.881</td>
<td>Ca$_{9}$ (1/3, 2/3, 0.0014)</td>
</tr>
</tbody>
</table>

“Theoretical results are obtained using DFT. The neutron diffraction experimental data for TiO$_2$ and HA are taken from Refs 51 and 52.”

Figure 1. Styrene-MA copolymer.
terminated carbon atoms were added to the MA molecule such that they mimic a polymer chain (Figure 3e,f). As a result, the sp² double bond between two carbon atoms in MA transforms into an sp³ single bond in the MA segment. It is assumed that the individual MA segment can represent an MA residue as a part of copolymer and can serve as a basis for studying its adsorption at inorganic surfaces. This choice is driven by the necessity to make our model computationally feasible at the first-principles level. At the same time, we admit that this approach omits some details of the copolymer conformation that can limit the exposure of MA residues to the solvent/surface and possible interactions between phenyl group and the surfaces.

The adsorption of MA monomer and MA segment is modeled as an inner-sphere surface complex. The molecules were initially positioned at the surface in such a way that the distance and arrangement between the metal ion and oxygen atoms of the ligands resembles that in the bulk. The structural optimization is performed until Hellmann–Feynman forces acting on atoms dropped below 20 meV/Å. Crystallographic information files (CIFs) with atomic structures used in calculations can be accessed through the Cambridge crystallographic data centre (CCDC deposition numbers 1582972–1582992).

2.2. Experimental Section. Titanium foil (0.127 mm), TiO₂ (rutile, particle size less than 100 nm), PSMA-h, Ca(NO₃)₂·4H₂O, (NH₄)₂HPO₄, NH₄OH, and Hank’s balanced salt solution (CaCl₂ 0.14 g L⁻¹, KCl 0.40 g L⁻¹, KH₂PO₄ 0.06 g L⁻¹, MgCl₂·6H₂O 0.10 g L⁻¹, MgSO₄·7H₂O 0.10 g L⁻¹, NaCl 8.00 g L⁻¹, NaHCO₃ 0.35 g L⁻¹, Na₂HPO₄ 0.048 g L⁻¹, glucose 1.00 g L⁻¹, and phenol red 0.01 g L⁻¹, Sigma-Aldrich, Canada) were used for the following experiments. Stoichiometric HA was synthesized using wet chemical precipitation, by the slow addition of 0.6 M (NH₄)₂HPO₄ solution to 1.0 M Ca(NO₃)₂ solution while continuously stirring at 70 °C. The solution was stirred for 8 h at 70 °C, followed by 24 h of stirring at room temperature, and the pH was adjusted to 11 using NH₄OH. The resulting precipitate was washed using water and ethanol and then dried. Crystalline needle-shaped HA nanoparticles have been obtained using this method. The transmission electron microscopy (TEM) micrograph presented in Figure 4 shows a needle-shaped HA particle morphology. HA particles had an aspect ratio of approximately eight and an average length of 150 nm.
physiological conditions. A scan rate of 1 mV/s was used to obtain the potentiodynamic polarization curves.

A JEOL 7000F scanning electron microscope and an FEI Tecnai Osiris transmission electron microscope were used for electron microscopy. A Nicolet 12 diffractometer with monochromatized Cu Kα radiation was used for X-ray diffraction (XRD). Fourier-transform infrared (FTIR) spectroscopy studies were performed on a Bruker Vertex 70 spectrometer.

3. RESULTS AND DISCUSSION

We begin with examining surfaces of rutile and HA. The specific surface energy is defined as

\[ \gamma = \frac{E_{\text{tot}}(\text{slab}) - E_{\text{tot}}(\text{bulk})}{2A} \]  

(1)

where \( E_{\text{tot}} \) is the DFT total energy of the slab and the bulk material, \( A \) is the planar surface area, and the factor of 2 accounts for the presence of two surfaces at the top and bottom of the simulation slab. Results for the surface energy are presented in Table 2, which also includes the values of the surface energies reported in the literature for comparison. A large scattering of literature values, in particular for HA, can be typically for the HA(011) surface energies. The presence of a polar solvent (water) significantly affects the surface energy, in particular for HA. The disparity between the surface energies of TiO\(_2\) and HA vanishes in the solvent.

The MA molecule and MA segment adapt a three-dimensional structure as shown in Figure 3a,b and e,f, respectively. Some adsorption configurations require a structural deformation (flattening) of the MA molecule or MA segment. The flattening occurs via rotating the carboxyl groups to align both groups to a common plane, as illustrated in Figure 3c,d and g,h, respectively. The associated deformation energy is on the order of 0.15 eV as evaluated by DFT calculations, which is 1 order of magnitude less than typical adsorption energies. The ability of MA to easily adapt its structure to the surface of interest can be attributed to its aliphatic nature.

Figure 5 shows the lowest energy configuration of the MA monomer adsorbed on TiO\(_2\) and HA surfaces. Adsorption to the TiO\(_2\) surface takes place via an inner-sphere bonding to a pair of Ti atoms (a bridge bidentate coordination), as illustrated in Figure 6a, rather than chelate bidentate bonding to a single Ti site at the surface. This result can be explained by a dense packing of Ti atoms at the TiO\(_2\) surface and is reminiscent of catecholate adsorption on TiO\(_2\). In the case of HA, the spacing between Ca atoms at the surface is too large. Therefore, chelation is a preferable type of bonding on HA (Figure 6b,c). The adsorption of MA is accompanied by deprotonation of both carboxyl groups. Those protons are readily attracted to passivate oxygen dangling bonds at the surface PO\(_4\) tetrahedra and to restore the charge balance perturbed by the newly formed Ti-O or Ca-O bonds. Regarding H\(^+\) placement on the HA(0110) surface, there are several alternatives to the top of PO\(_4\) tetrahedra, which include O atoms in the base of PO\(_4\) tetrahedra as well as the \(\equiv\text{Ca}_2\text{OH}_2\) groups present at the surface. It turns out that \(\equiv\text{Ca}_2\text{OH}_2\) is the second most favorable scenario from the DFT total energy point of view.

The affinity of MA to the surfaces is characterized by the adsorption enthalpy, which is defined as

\[ \Delta H_{\text{ad}} \approx E_{\text{tot}}(\text{MA ads.}) - E_{\text{tot}}(\text{MA}) - E_{\text{tot}}(\text{slab}) \]  

(2)

where \( E_{\text{tot}}(\text{MA ads.}) \) is the total energy of a slab with the molecule adsorbed on its surface (Figure 5), \( E_{\text{tot}}(\text{MA}) \) is the total energy of the molecule or segment in its ground state configuration (Figure 3a or e), and \( E_{\text{tot}}(\text{slab}) \) is the energy of the slab. The approximate sign reflects neglecting a zero-point energy change upon adsorption and finite temperature effects. This approximation is justified in an earlier study of catalytic reactions because the sum of zero-point energies is approximately constant during the traversing of regions with energy barriers.

The adsorption enthalpies of MA on TiO\(_2\) and HA surfaces are summarized in Table 2. Here, we list the results obtained

Table 2. Calculated Surface Energy and Adsorption Energy of MA at TiO\(_2\) and HA Surfaces

<table>
<thead>
<tr>
<th>surface</th>
<th>surface energy (J/m(^2))</th>
<th>adsorption enthalpy (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO(_2)(110)</td>
<td>0.63/0.48/0.44</td>
<td>-1.3/-0.7/-0.6</td>
</tr>
<tr>
<td>HA(0001)</td>
<td>0.90/0.53/0.45</td>
<td>-3.4/-1.3/-1.2</td>
</tr>
<tr>
<td>HA(0110)</td>
<td>0.96/0.59/0.51</td>
<td>-4.7/-2.5/-2.1</td>
</tr>
</tbody>
</table>

Values are presented for various solvent conditions: vacuum/mixture 80% ethanol + 20% water/100% water, respectively. 

Figure 5. (a) Maleic acid monomer at the (110) surface of TiO\(_2\), (b) at the HA(0001) surface, and (c) at the HA(0110) surface.
for different solvents (water and a mixture of water and ethanol) as well as for the vacuum because effects of the solvent are often neglected in studies of a molecular adsorption. The values of the adsorption enthalpies in Table 2 suggest that the binding energies of molecules to the surface are comparable to gas phase energy (1.1 to 1.5 eV for the TiO2 (rutile) particles) as well as for the vacuum because of the reduction in the voltage drop in the bulk of the suspension, containing 10 g L−1 TiO2 (rutile) suspensions without PSMA-h showed the formation of cathodic deposits. The low cathodic EPD yield indicated that particles were weakly positively charged. PSMA-h films were deposited anodically and showed strong adhesion to the substrates. The film adhesion corresponded to 5B classification (ASTM D3359). The addition of PSMA-h to the TiO2 suspensions resulted in a significant improvement of the suspension stability and the formation of anodic deposits. The formation of anodic films signified a particle charge reversal due to the adsorption of the negatively charged PSMA-h. The deposition mass increased with increasing deposition time at a constant applied voltage (Figure 7). The experimental results indicated that the film thickness can be controlled and varied. The deposition yield data showed a relatively high deposition rate. A decrease of deposition rate with time was observed due to the adsorption of the negatively charged PSMA-h formed anodically and showed strong adhesion to the substrates. The low cathodic EPD yield indicated that particles were weakly positively charged. PSMA-h films were deposited anodically and showed strong adhesion to the substrates. The film adhesion corresponded to 5B classification (ASTM D3359). The addition of PSMA-h to the TiO2 suspensions resulted in a significant improvement of the suspension stability and the formation of anodic deposits. The formation of anodic films signified a particle charge reversal due to the adsorption of the negatively charged PSMA-h. The deposition mass increased with increasing deposition time at a constant applied voltage (Figure 7).

Figure 6. Maleic acid and neighbor atoms of the adsorption complex (a) at the (110) surface of TiO2, (b) at the HA(0001) surface, and (c) at the HA(0110) surface. Bond distances between the MA and surface metal atoms are shown in Angstroms for an aqueous environment.

Figure 7. Deposit mass vs deposition time for 5 g L−1 TiO2 suspension, containing 10 g L−1 PSMA-h at a deposition voltage of 15 V.
It was found that the variation of TiO$_2$ concentration in the suspension resulted in changes of film microstructure. The SEM image of a film prepared from 5 g L$^{-1}$ TiO$_2$ suspension, containing 10 g L$^{-1}$ PSMA-h showed TiO$_2$ particles in a PSMA-h matrix (Figure 9a). The SEM image of a film prepared from 10 g L$^{-1}$ TiO$_2$ suspension (Figure 9b), containing 10 g L$^{-1}$ PSMA-h, showed mainly TiO$_2$ particles, which formed a porous film. The film porosity resulted from the packing of TiO$_2$ particles. The comparison of the SEM images, shown in Figure 9a,b, indicated that the increase of TiO$_2$ concentration in the 10 g L$^{-1}$ PSMA-h solution resulted in the increasing TiO$_2$ content in the deposited film.

The composite TiO$_2$–PSMA-h coating prepared from 5 g L$^{-1}$ TiO$_2$ suspension, containing 10 g L$^{-1}$ PSMA-h, was studied in Hank’s balanced salt solution, which acted as a simulated body fluid. Tafel plots comparing the electrochemical behavior of the coated and uncoated titanium are shown in Figure 10. From the Tafel plots, it can be seen that the deposited TiO$_2$–PSMA-h coating allowed a reduction of the corrosion current, compared to an uncoated titanium. Moreover, the coated substrate showed a higher corrosion potential. These results demonstrated that the coating acted as a protective layer and provided corrosion protection of the titanium substrates. Therefore, the TiO$_2$–PSMA-h coating containing the bioactive TiO$_2$ rutile phase offers additional benefits of corrosion protection of underlying metallic substrates for biomedical implant applications.

The XRD pattern showed TiO$_2$ (rutile) peaks, corresponding to the JCPDS file 021-1276, and peaks of HA, corresponding to the JCPDS file 046-0905. This confirmed that HA and TiO$_2$ were codeposited using PSMA-h, and thus composite HA-rutile-PSMA-h films were formed. The results of SEM studies (Figure 12) provided additional evidence of the formation of composite coatings. The SEM image presented in Figure 12 shows needle-shaped HA particles in addition to the TiO$_2$ particles. Therefore, PSMA-h can be used as a codispersing and dispersant for the codeposition of TiO$_2$ (rutile) and HA to fabricate composite rutile-HA coatings. A suspension containing 5 g L$^{-1}$ HA, 5 g L$^{-1}$ TiO$_2$, and 10 g L$^{-1}$ PSMA-h was used for anodic EPD, and subsequent films were studied using XRD. The resulting XRD pattern is shown in Figure 11.
chemisorption is favorable at both surfaces in vacuum, which agrees with previous studies. However, the presence of solvent not only reduces the magnitude of interaction but also changes the surface receptivity. As evident from Table 3, the enthalpy of dissociative adsorption of water molecules at the HA(0110) surface in aqueous environment is positive, indicating that its chemisorption is unlikely. When reflected onto experimental conditions, this result implies that the surface of rutile particles is likely to be terminated with hydroxyl groups during a reaction with PSMA-h, whereas the surface of HA is not. As a benchmark for the solvation model, we also computed the vaporization enthalpy of water molecule +0.32 eV versus the experimental value of +0.46 eV, which sets error bars of the calculation.

The absence of a strong dissociative bond between water and HA allows us to assume the coexistence of the hydrated \( \text{CaOH} \) and \( \text{OH}^- \) surface sites with unhydrated \( \text{Ca}^{2+} \) and \( \text{O}^{2-} \) sites. The ligand exchange reaction in this case proceeds through the following steps:

\[
\text{CaOH} + \text{OH}^- + 2\text{H}^+(aq) \\
\rightarrow \text{CaOH}_2^+ + \text{OH}^{2-}(aq) \\
\rightarrow \text{CaOH}_2^+ + \text{Ca}^{2+} + L^2-(aq) \rightarrow \text{Ca}_2L^{2-1} + H_2O
\]

The corresponding enthalpy is strongly negative (see Table 3), indicating that, unlike in the case of TiO\(_2\), there is no competition between water chemisorption and MA adsorption at the surface of HA.

### 4. CONCLUSIONS

PSMA-h adsorption on HA and TiO\(_2\) (rutile) was studied using experimental techniques and corroborated by ab initio simulations of adsorption of a MA segment as a subunit of the copolymer. Ab initio calculations suggest that the MA segment adsors on the TiO\(_2\) surface via an inner-sphere bridge bidentate bonding to a pair of Ti atoms. Chelation is a preferable type of bonding for the MA monomer and the segment is comparable to that of catecholates. Solvent effects play a twofold role when providing quantitative evaluation of the adsorption energetics...
and thus cannot be neglected. First, it significantly reduces the adsorption strength (by almost a factor of 2 if compared to vacuum) as the polarity of the solvent increases. Second, a water chemisorption at the surface hinders the adsorption of MA at the surface of rutile. The results of first-principles calculations were confirmed by the experimental measurements. We found that adsorbed PSMA-h allowed efficient dispersion of rutile and formation of films by the EPD. We investigated the deposition yield and morphology of the films. Moreover, it was found that rutile can be codispersed and codeposited with HA to form composite films. The coatings obtained by the EPD showed corrosion protection of metallic implants in simulated body fluid solutions, which is a favorable characteristic for biomedical applications.

■ AUTHOR INFORMATION

Corresponding Authors
*E-mail: zhitom@mcmaster.ca. Phone: +1 905 5259140 ext. 24295 (I.Z.).
*E-mail: rubelo@mcmaster.ca (O.R.).

ORCID
Oleg Rubelo: 0000-0001-5104-5602

Notes
The authors declare no competing financial interest.

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