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Blood compatibility improvement of titanium oxide film modified by doping La_2O_3

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Abstract La_2O_3 doped titanium oxide (TiO_2) films with different concentration were deposited by means of the Radio-Frequency magnetron sputtering technique. The microstructure and surface properties of TiO_2 films were characterized by X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS) and contact angle test. The blood compatibility of the specimens was evaluated by tests of platelet adhesion. Results show that pure rutile phase is formed in doped samples and La_2O_3 incorporation significantly improves the wettability and hemocompatibility of TiO_2 films. Our studies demonstrate that La_2O_3 doped TiO_2 films are potentially useful biomaterials with good blood compatibility.

1 Introduction

TiO_2 thin films have been widely investigated in photocatalysis application fields such as hydrophilicity, self-cleaning and purification of air and toxic gases, etc. Recent studies have shown that TiO_2 films are suitable as surface coatings on biomedical applications due to its good hemocompatibility [1, 2] and researches concerning biomedical aspects are widely increasing [3–5]. Besides the pure TiO_2, doping TiO_2 films with selective elements is an attractive method to enhance the biological properties of TiO_2 [6, 7]. Rare earth elements exhibit relatively low toxicity, anticoagulant, antiemetic, antiseptic, immunomodulatory and antineoplastic properties, which have aroused considerable interest in medicine application due to these and other pharmacological effects [8]. However, there have rarely been reported on the haemocompatibility of rare earth oxide or/and materials doped with rare-earth elements [9, 10]. In this work, TiO_2 films doped with La_2O_3 were prepared using RF-magnetron sputtering. The effects of La_2O_3 incorporation on the structural properties and the hemocompatibility of TiO_2 films were studied. The unique hemocompatibility properties of La_2O_3 doped TiO_2 films reveal the potential applications in blood-contacting biomedical materials.

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2 Experiment

The La_2O_3 doped TiO_2 films were deposited on silicon substrates using RF-magnetron sputtering. The targets were mechanically composted by using TiO_2 powder (in purity 99.9%) and La_2O_3 powder (in purity 99.5%) with the La_2O_3 molar concentration of 0%, 1%, 2% and 3%, respectively. Using argon (99.99%) as a sputtering gas, the work pressure was set at 4 Pa. The samples were prepared in room temperature and the RF power of 200 W was applied in the sputtering process. The sample 1, 2, 3 and 4 are prepared using the targets with a doped La_2O_3 molar content of 0%, 1%, 2% and 3%, respectively.

The microstructures were evaluated by X-ray diffraction (XRD) with a Cu-K_α source under an applied voltage of 40 KV and a current of 40 mA. The compositions were analyzed by X-ray photoelectron spectroscopy (XPS). The contact angle measurement was conducted in atmospheric conditions at room temperature using an OCA20 Optima device. Distilled water and glycol were used in our tests to determine the surface energy and interfacial tension of the samples. Each sample was measured five times on different locations to obtain statistical averages. The experiment of the platelet adhesion was performed to identify the blood compatibility of all the specimens. The reference samples are Chrono flex used in clinical application and glass with good and bad haemocompatibility, respectively [11]. In this experiment, fresh blood of rabbit was centrifugalized at 3000 rpm for about 20 min to prepare platelet-rich plasma, and then 0.2 ml of platelet-rich plasma was dropped onto the surface of the samples and incubated at 37°C for 1 h. After incubation, the samples were fixed for 3 hours in glutaraldehyde, critical-point dried with CO_2 and gold coated for examination in a scanning electron microscope. Ten different regions were randomly chosen for each sample to obtain good statistical results.

3 Results and discussion

3.1 XPS characterization

The chemical states of La_2O_3 doped TiO_2 films were investigated by XPS. All the doped samples display the similar results and typical XPS spectrum was shown in Fig. 1. Results indicate that the La 3d spectrum possesses two doublets and the peaks appearing on the high energy side of the $3d_{5/2}$ and $3d_{3/2}$ peaks are satellite peaks. The most intense peak of La $3d_{5/2}$ is at approximately 835.3 eV, the energy difference between the La $3d_{3/2}$ and $3d_{5/2}$ states is approximately 17 eV, which is agree well with the character values La_2O_3 [12]. The main peak at 530.5 eV in the O1s spectrum corresponds to O^{2-} of the metal oxide. Hence, the XPS results show that La is La $^{3+}$ oxidation state, which means that the La exists as La_2O_3 in TiO_2 films. The La_2O_3 content calculated from XPS spectra for the La_2O_3-doped sample 2, 3 and 4 are approximately 1.56%, 2.31%, and 3.64%, respectively, which are much higher than the content in their corresponding target. The reasons maybe is caused by the difference of sputtering rate between the TiO_2 and La_2O_3 during deposition.

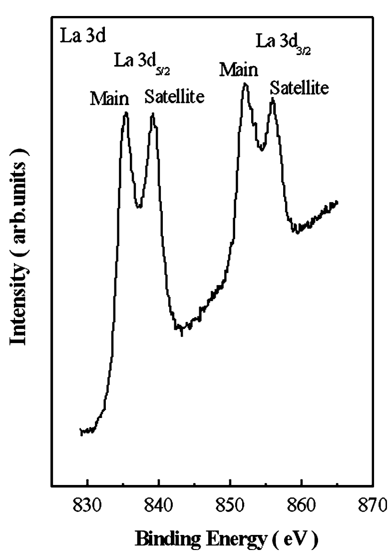

Fig. 1 Typical La 3d high-resolution XPS spectrum of La_2O_3 doped TiO_2 films with a content of 2.31 at.%

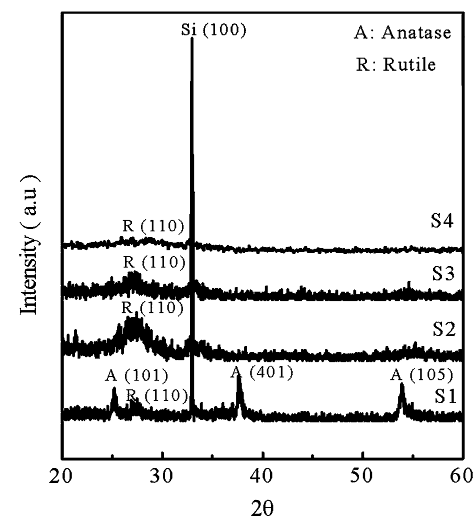

Fig. 2 XRD pattern of titanium oxide films doped La_2O_3 with different concentration

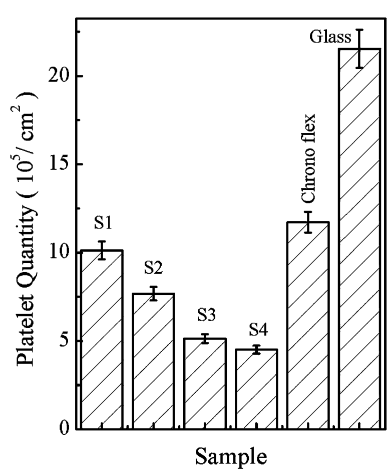

Fig. 3 Number of platelet adhered on the surface of the undoped and La_2O_3-doped TiO_2 films with different content

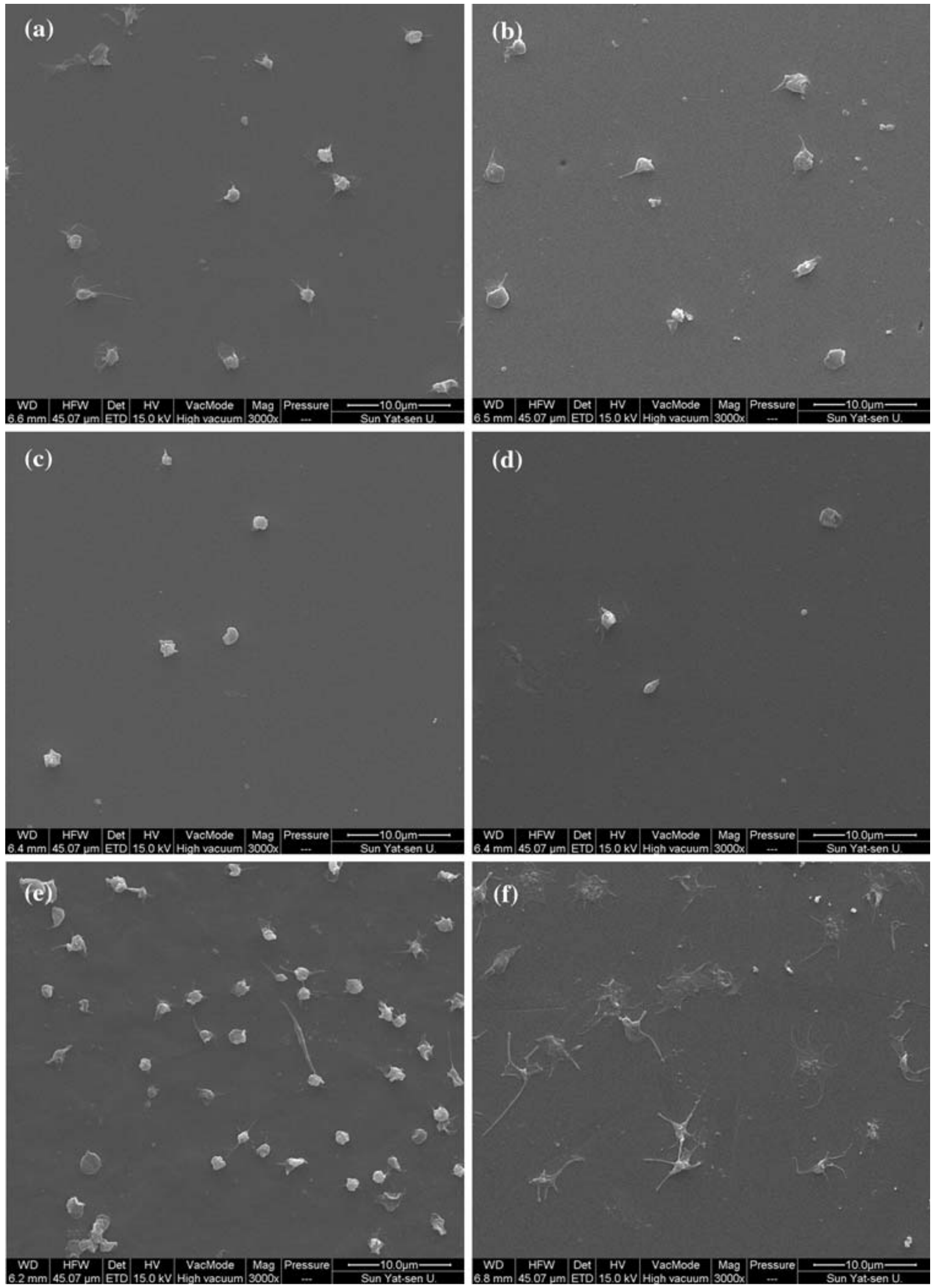

Fig. 4 Typical SEM images of platelets adhering on the surface of **a** Sample 1; **b** Sample 2; **c** Sample 3; **d** Sample 4 and reference samples of **e** Chrono flex; **f** Glass

3.2 XRD analysis

The X-ray diffraction patterns acquired from samples on Si substrate are displayed in Fig. 2. The film on S1 is composed of primarily anatase TiO_2 (101), (401) and (105), however, pure rutile TiO_2 (110) can be detected in La_2O_3-doped samples except the Si peak and the width of rutile phase peak becomes much broader with increasing La_2O_3 content, indicating that La dopant not only greatly promotes the phase transfer from anatase to rutile and enhances the crystal phase of TiO_2 with preferential growth in the direction of (110), but also can refine grain size of TiO_2.

3.3 Platelet adhesion

The experiments of platelet adhesion have been performed to observe the number and shape of platelet adhered on the surface of the samples. Generally, the sample with less platelet adhered on its surface has better haemocompatibility. The number of platelet adhered on the surface of samples was counted and the statistical results were shown in Fig. 3. The S1, S2, S3 and S4 are the TiO_2 films with a doped La_2O_3 molar content of 0%, 1.56%, 2.31% and 3.64%, respectively. Results indicate that there is less platelet adhered on the doped TiO_2 films, exhibiting the excellent haemocompatibility. Typical SEM images of the samples with the adhesion of platelets were shown in Fig. 4. Compared to the undoped TiO_2 film and the Chrono flex, the La_2O_3 doped samples exhibit fewer platelets aggregation and pseudopod, suggesting that La_2O_3 doped TiO_2 films are potential in application of blood-contacting biomedical materials.

3.4 Surface energy and interfacial energy results

The first step after blood contacting with the biomaterial is adsorption of plasma protein, which will determines the anticoagulation property of the biomaterial [13]. Adsorption of human fibrinogen (HFG) and human serum albumin (HSA) are two primary factors related to haemocoagulation. It has been proven that adsorption of HFG will promote the adhesion of platelets and activate the platelets, whereas adsorption of HSA does the opposite thing [14]. Therefore, it is important to investigate the interaction between the material surface and plasma proteins. The interfacial tension (Γ_{HSA}, Γ_{HFG}) between different proteins (HSA, HFG) and different surfaces were calculated referring to the method in our previous work [11]. In addition, γ_{sp}^{p} and γ_{sp}^{d} represent the polar component and dispersive component of the interfacial tension, respectively. The ratio of $\gamma_{sp}^{p}/\gamma_{sp}^{d}$, which represents the contribution of the polar and dispersive components to the interfacial tension, was evaluated. The calculated results are listed in Table 1.

As shown in Table 1, the contact angles of water decrease with increasing La_2O_3 concentration, indicating that the doped samples become more hydrophilic with increasing La_2O_3 content. In addition, the ratio of $\gamma_{sp}^{p}/\gamma_{sp}^{d}$ is from 235.1 to 296.8 in adsorption process of HFG and samples, indicating that polar component $\left(\gamma_{sp}^{p}\right)$ is dominant in the interfacial tension compared to dispersive component. Whereas the ratio of $\gamma_{sp}^{p}/\gamma_{sp}^{d}$ is from 1.6 to 12.53 in adsorption process of HSA and samples, suggesting that polar component $\left(\gamma_{sp}^{p}\right)$ and dispersive component $\left(\gamma_{sp}^{d}\right)$ have almost the same contribution to the interfacial tension. According to the study of C.P. Sharma [15], when the polar and dispersive components have the same contribution to the interfacial tension, the adsorption between protein and biomaterial surface is strong. However, one of the polar and dispersive components is leading in the interfacial tension, the adsorption between protein and biomaterial surface is weak. Therefore, albumin preferentially adsorbs on the doped samples. The result agrees with that of platelet adhesion.

Table 1 Contact angle, surface energy components and interfacial tension towards plasma proteins

Samples	Contact angle (degrees)	Interfacial tension(dyn/cm)			
		Γ_{HSA}	$\gamma_{sp}^{p}/\gamma_{sp}^{d}$	Γ_{HFG}	$\gamma_{sp}^{p}/\gamma_{sp}^{d}$
Sample 1	83.1	9.97	12.53	11.85	235.1
Sample 2	81.6	9.46	1.6	11.69	259.9
Sample 3	78.3	7.82	17.7	9.49	279.4
Sample 4	76.5	7.96	10.8	10.8	296.8

4 Conclusions

La_2O_3 doped TiO_2 films were deposited using RF-magnetron sputtering. In undoped TiO_2 film, a mixed phase comprising of anatase and rutile was formed. However, in doped TiO_2 films, pure rutile phase was formed. All doped specimens exhibit more hydrophilic surfaces than undoped sample. The better blood compatibility was observed on the La_2O_3 doped TiO_2 films in comparison with undoped TiO_2. This may attribute to different contribution of the polar and dispersive components to interfacial tension between materials and proteins. However, more basic studies are needed.

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