

Article

Effect of Surface Modification with TiO₂ Coating on Improving Filtration Efficiency of Whisker-Hydroxyapatite (HAp) Membrane

Chenning Zhang, Tetsuo Uchikoshi * , Lihong Liu, Masanori Kikuchi  and Izumi Ichinose

Research Center for Functional Materials, National Institute for Materials Science, Tsukuba, Ibaraki 305-0047, Japan; ZHANG.Chenning@nims.go.jp (C.Z.); LIU.Lihong@nims.go.jp (L.L.); KIKUCHI.Masanori@nims.go.jp (M.K.); ICHINOSE.Izumi@nims.go.jp (I.I.)

* Correspondence: UCHIKOSHI.Tetsuo@nims.go.jp; Tel.: +81-29-859-2460

Received: 17 June 2020; Accepted: 10 July 2020; Published: 13 July 2020



Abstract: Whisker-like hydroxyapatite (HAp) particles were prepared by controlling particle growth via hydrothermal synthesis. The surface modification for the hydrothermally synthesized HAp whiskers was accomplished by TiO₂ coating. After the TiO₂ modification, the zeta potential of the HAp whiskers was significantly improved from +8.6 to +21 mV at pH = 8.5. A free-standing membrane (diameter of ~4.5 cm and thickness of ~0.2 mm) was fabricated by using the TiO₂-coated HAp whiskers and was used to separate the Au nanoparticles (size = 5 nm and zeta potential = −38.6 mV at pH = 8.5) at a significantly high filtration efficiency of ~100%. The achieved high filtration efficiency was considered to be the result of effectively utilizing the electrostatic interaction between the positively-charged TiO₂-coated HAp whiskers and negatively-charged Au nanoparticles. The excellently biocompatible and highly effective TiO₂-coated HAp membrane would be potentially applied as biological and artificial separators in biotechnology processes for the biomedicine field.

Keywords: hydroxyapatite; coating; membrane; filtration; surface charge

1. Introduction

Biocompatible membranes are used as components of medical devices, implants, drug delivery systems, diagnostic assays, and bioreactor and bio-separation processes, by coming into contact with biological fluids, organs, tissues, and cells inside the human body [1]. The application of the membrane separation is a biotechnology process used for improving protein-virus separation and protein purification via high-performance filtration [2], and the biocompatibility of the membrane is its ability to perform its intended function without eliciting any local or systemic effects undesirable to the host [3].

Hydroxyapatite (HAp, Ca₁₀(PO₄)₆(OH)₂) has been very well known as a promising biomaterial for wide use as a coating of metallic implants for bone tissue regeneration and in drug-controlled release, due to its chemical similarity with the mineral component of bones and due to its biocompatible, bioactive, and thermodynamically stability in the body fluid [4–11]. In our previous work [12], the hydrothermally-synthesized HAp whiskers were used to fabricate a nest-like microstructured HAp membrane, and the fabricated membrane was applied to separate the Au nanoparticles by capturing the Au nanoparticles. Particularly, for fabricating membranes in reuse applications, HAp as hydroxide in the form of whiskers is a more suitable candidate than SiC whiskers, cellulose nanofibers, and carbon nanofibers, which are easily oxidized or burned out after heat treatment.

Recently, the importance of controlling electrostatic interactions (positive and negative charges) has been extensively reported as dominating the selectivity of membranes. Jobin et al. [13] declared

that the importance of electrostatic interactions occurred between cell-penetrating peptides and membranes, namely, cell-penetrating peptides were generally rich in positively charged residues and were thus prone to establishing electrostatic interactions with anionic membrane components. Sadeghi et al. [14] reports that the copolymer micelles membrane that was featured with a network of charged nanochannels was capable of separating anionic and neutral organic compounds based on their electrostatic charge via selective transportation. Breite et al. [15] found the domination of electrostatic forces in the interactions between polystyrene beads and the membrane surface during filtration and achieved a pH-dependent selectivity for the membrane.

Therefore, the utilization of electrostatic interaction should be considered in order to enhance the filtration efficiency of the HAp-whisker membrane. To improve the surface charge of membranes, one effective technique is surface coating, which is quite suitable as a surface modification for biomaterial membranes [16]. Since TiO_2 , which has many outstanding properties such as a superior photocatalytic activity, nontoxicity, and long-term thermal, chemical, and physical stabilities [17], has been regarded as an appropriate biocompatible coating material for alloys in biomedical applications [18–20], it seems to be one of the coating candidates for modifying the surface of HAp whisker biomaterial. Compared with many of the reported TiO_2 coating techniques, such as dipping, spin coating, and spray pyrolysis, as well as the well-known atomic layer deposition (ALD) [21], the chemical adsorption method is more facile because it utilizes the hydration reaction of the incomplete hydrolyzed TiO_2 precursor, as was reported in the literature [22].

In this work, the hydrothermal technique was used to control the particle growth of HAp in order to form a whisker shape; TiO_2 was coated around the hydrothermally-synthesized HAp whiskers by the chemical adsorption method; and a membrane was fabricated with the prepared TiO_2 -coated HAp whiskers and was applied in order to efficiently separate the negatively-charged Au nanoparticles (5 nm). The mechanism for the utilization of electrostatic interaction after TiO_2 coating as a means of improving filtration efficiency was clearly elucidated.

2. Materials and Methods

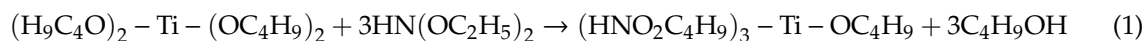
2.1. Synthesis of HAp Whiskers

In this experiment, all the reagents used were received from Nacalai Tesque Inc., Kyoto, Japan. The aqueous forms of calcium acetate monohydrate ($\text{Ca}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$), ethylene glycol ($\text{C}_2\text{H}_6\text{O}_2$), and ammonium hydrogen phosphate ($(\text{NH}_4)_2\text{HPO}_4$) were used as a calcium source (Ca^{2+} concentration = 0.5 mol/L and solution = 20 mL), complex reagent for Ca^{2+} ions (solution = 10 mL), and phosphorus source (P^{5+} concentration = 0.3 mol/L and solution = 20 mL), respectively, to prepare a precursor solution of HAp. Acetic acid ($\text{C}_2\text{H}_4\text{O}_2$) was used to adjust the pH of the prepared precursor solution to ~3.2. A Teflon-lined autoclave was used to carry out the hydrothermal treatment for the precursor solution at 180 °C for 96 h. After finishing the hydrothermal reaction, the Teflon-lined autoclave was cooled down naturally to room temperature to collect the generated white products, following washing by distilled water four times and drying at 60 °C for 12 h. The detailed experimental procedure concerning the hydrothermal synthesis has been described in the literature [23].

2.2. Preparation of TiO_2 -Coated HAp Whiskers

First of all, the precursor of TiO_2 was prepared as follows: 10 mL of Titanium (IV) Tetrabutoxide ($\text{Ti}(\text{OC}_4\text{H}_9)_4$, TTBO) (Wake Pure Chemical Industries, Ltd., Osaka, Japan) as a titanium source were added into 200 mL solvent of ethanol ($\text{C}_2\text{H}_5\text{OH}$) (99.5% purity, Nacalai Tesque Inc., Kyoto, Japan) under continuous magnetic stirring for 5 min, followed by adding 9.25 mL of Diethanolamine ($\text{HN}(\text{OC}_2\text{H}_5)_2$, DEA) (Wake Pure Chemical Industries, Ltd., Osaka, Japan) to suppress the serious hydrolysis of TTBO

with water (Equation (1)); finally, 0.55 mL of distilled water was dropped to form a stable precursor of TiO_2 (Equation (2)).



0.3 g of the hydrothermally-synthesized HAp whiskers were dispersed into the as-prepared TiO_2 precursor under vigorous ultrasonic stirring for 30 min to prepare a suspension. In this case, the TiO_2 coating layer continuously formed around the surface of the HAp whiskers after the hydration reaction between the surface hydroxyl of HAp and hydrolyzed TTBO, as illustrated in Figure 1. Herein, the origination of the hydroxyl surface group is considered from the chemical adsorption of water molecules on the HAp surface [24–26]. The prepared TiO_2 -coated HAp products were collected by using a centrifuge machine (CF16RX, Hitachi, Japan), followed by absolute-grade ethanol ($\text{C}_2\text{H}_5\text{OH}$) (99.9% purity, Nacalai Tesque Inc., Kyoto, Japan) washing four times and collection at room temperature.

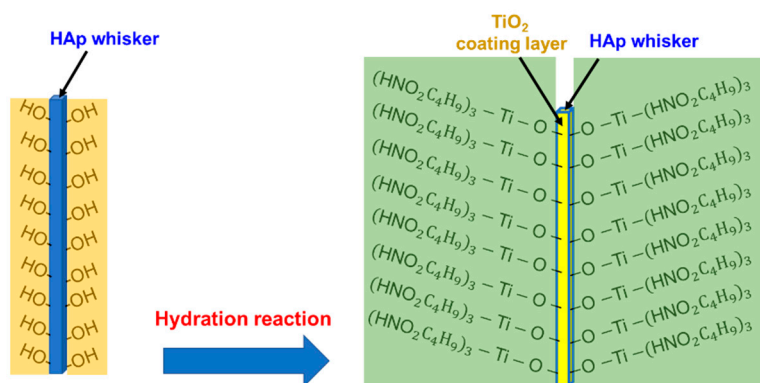


Figure 1. Diagram illustration of the formation of a continuous TiO_2 coating layer around the surface of the HAp whiskers via the hydration reaction between the surface hydroxyl of HAp and hydrolyzed $\text{Ti}(\text{OC}_4\text{H}_9)_4$.

2.3. Fabrication of TiO_2 -Coated HAp Membrane

0.15 g of the prepared TiO_2 -coated HAp whiskers were dispersed in 2-propanol (IPA, $\text{CH}_3\text{CH}(\text{OH})\text{CH}_3$) under continuous stirring with ultrasonic dispersion for 30 min. The well-dispersed suspension was poured into a vessel connected to a vacuum pump and, finally, an exfoliative and highly-flexible membrane with a diameter of ~ 4.5 cm and thickness of ~ 0.2 mm was formed onto the surface of a commercial filter paper (Grade 4A, Advantec, Co., Ltd., Tokyo, Japan) by suction evacuation.

2.4. Characterization

The phase identification was performed by X-ray diffraction (XRD) on an X-ray diffractometer (model RINT 2200, Rigaku Corp., Tokyo, Japan) under a nickel-filtered $\text{Cu K}\alpha$ radiation at 40 kV and 40 mA, with a scanning speed of $2\theta = 4^\circ/\text{min}$ and a step interval of 0.02° in 2θ in a step scan mode. Lotgering factors (a good use of the representation for the orientation degree) of the $hk0$ plane were calculated based on the XRD patterns following the below equations [27]:

$$f_L = \frac{P - P_0}{1 - P_0} \quad (3)$$

$$P \text{ and } P_0 = \frac{\sum I_{(hk0)}}{\sum I_{(hkl)}} \quad (4)$$

where $\sum I_{(hk0)}$ and $\sum I_{(hkl)}$ are the sums of the diffraction peak intensities of the $hk0$ and hkl planes, respectively. The values of P and P_0 were obtained from the synthesized HAp and HAp database (JCPDS-ICDD: 84-1998), respectively. Observations of the particle morphology and membrane microstructure were performed by field-emission scanning electron microscopy (FE-SEM) (model S-4800, Hitachi, Ltd., Tokyo, Japan). Fourier transform infrared (FT-IR) spectra were recorded by FT-IR spectroscopy (model 4200, JASCO, Tokyo, Japan), using the standard KBr method. Element mapping was detected by an energy dispersive X-ray (EDX) spectrometer (model EDAX Apollo XL, EDAX Inc., Mahwah, NJ, USA). The single TiO_2 -coated HAp whisker was observed by a scanning transmission electron microscope (STEM) (model JEM-2100F, JEOL, Ltd., Akishima, Tokyo, Japan). The zeta potential and pH were measured by a zeta potential analyzer (model Zetasizer Nano Z, Malvern Instrument Ltd., Malvern, Worcestershire, UK) and a pH meter (model ss973, Horiba, Ltd., Kyoto, Japan) equipped with a pH electrode (model 6261, Horiba, Ltd., Kyoto, Japan), respectively. Ultraviolet-visible light (UV-vis) spectra were made by a spectrophotometer (Jasco V-570, Jasco Corp., Hachioji, Tokyo, Japan) to evaluate the filtration efficiency of the membrane.

3. Results and Discussion

Figure 2a exhibits the XRD patterns of the commercial, hydrothermally-synthesized, and TiO_2 -coated HAp powders, and the unique morphologies in FE-SEM images of (Figure 2b) the hydrothermally-synthesized whisker-like and (Figure 2c) the commercial rod-like HAp particles. As seen in Figure 2a, when compared with the XRD peaks of the commercial HAp powders, the relative intensities of the XRD peaks significantly changed for the hydrothermally-synthesized HAp product. In particular, the relative intensity of the (300) peak became the strongest for the commercial HAp, instead of the strongest (121) peak; however, after the TiO_2 coating, the XRD peaks of the TiO_2 -coated HAp powders presented no appreciable change, due to the coated TiO_2 being amorphous. To explain this domination of the $hk0$ crystallographic plane for the hydrothermally-synthesized HAp (unlike that of the hkl plane for the commercial HAp), Lotgering factors were calculated for the synthesized and commercial HAp. The calculated Lotgering factor of $hk0$ for the hydrothermally-synthesized HAp is ~ 0.41 , dramatically higher than that of ~ 0 for the commercial HAp, as denoted in the XRD patterns in Figure 2a. This indicates that the HAp particles prepared by hydrothermal synthesis had a preferable growth along the c -axis, therefore leading the $hk0$ plane to be dominated. To reveal the mechanism for the preferable growth along the c -axis in the hydrothermally-synthesized HAp particle, in this work we considered Gibbs free energy as a driving force responsible for particle growth [28]. Generally, the morphology of crystal is related to the supersaturation degree of the reaction solution [29]; moreover, the pH and temperature of synthesis condition are essential in influencing the supersaturation degree in terms of the ionic strength and solubility of reaction solution [30]. Therefore, Gibbs free energy as a driving force, which is related to the difference between the supersaturation degree and equilibrium state, is dominated by the pH and temperature of the synthesis condition during the hydrothermal process. According to Cahn's theory, the crystal growth is classified into two regimes by taking into account the driving force responsible for growth during solidification [31]; that is, at a low driving force, the movement of the growing interface is only lateral, thus leading to growth by two-dimensional nucleation, while at a high driving force, the movement of the interface becomes normal, leading to a continuous growth. The tendency for the absolute value of Gibbs free energy as the driving force for HAp particle growth to apparently increase when enhancing the pH of the reaction solution [23] suggests that a higher driving force derived from a higher pH supports the continuous growth of the nucleated HAp particle in a three-dimensional direction that is preferentially along the a (b)- and c -axes; whereas, a lower driving force derived from a lower pH only sustains the preferable growth in a one-dimensional direction, mainly along the c -axis. In this experiment, the synthesis conditions of the pH (~ 3.2) for the precursor solution and temperature (180°C) for the hydrothermal synthesis ensured the prepared particle's preferable growth in one-dimension. Moreover, the preferable growth along the c -axis for the hydrothermally synthesized HAp particles consequently caused a unique morphology,

such as a whisker shape, which is quite different from the conventional shape of a hexagonal columnar for commercial HAp, as can be obviously distinguished in Figure 2b,c.

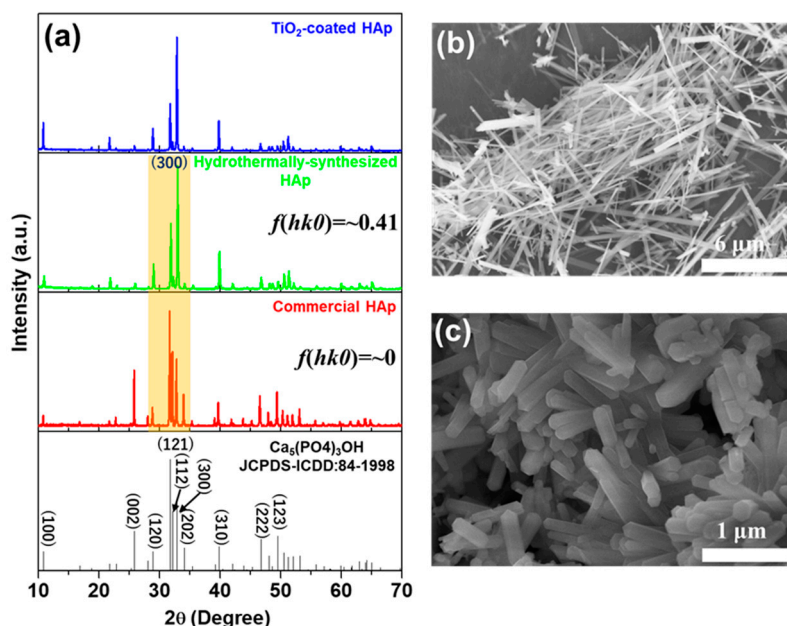


Figure 2. (a) XRD patterns of the commercial, hydrothermally-synthesized, and TiO_2 -coated HAp powders, denoting the calculated Lotgering factors of $f(hk0)$; and FE-SEM images of unique morphologies in (b) the hydrothermally-synthesized whisker-like and (c) commercial rod-like HAp particles.

Figure 3 shows the FT-IR spectra of (Figure 3a) the TiO_2 -coated HAp and (Figure 3b) hydrothermally-synthesized HAp. For the hydrothermally-synthesized HAp, the characteristic absorption bands at 1106, 1027, 962, 603, 567, and 472 cm^{-1} are assigned to the asymmetric stretching vibration of the PO_4^{3-} groups, and at 3570 and 633 cm^{-1} are attributed to the stretching and liberation vibrations of the OH^- groups [32]. For the TiO_2 -coated HAp, the band at 821 cm^{-1} is assignable to the Ti–O–Ti bond, the one at 1460 cm^{-1} is related to the Ti–O mode, and the one at 1638 cm^{-1} corresponds to the bending vibration of Ti–OH [33,34]; moreover, the 2937 and 2862 cm^{-1} bands are assignable to the C–H stretching from the remaining ethanol in the product powder [35,36], and a wide band at 3340 cm^{-1} belongs to the asymmetrical stretching vibration of the O–H group in the free water [37] from the amorphous TiO_2 coating layer.

Figure 4 shows the FE-SEM images of TiO_2 -coated HAp particles with the detection of component elements by EDX local mapping. Even though the hydrothermally-synthesized HAp particles were coated with the TiO_2 layer around their surface, their unique whisker-like shape suffered no influence and retained the initial morphology, as comparably observed in Figures 2b and 4. For the EDX mapping detection, not only were the main component elements of Ca, P, and O for HAp detected; additionally, the Ti element for the TiO_2 coating layer was spotted, indicating the existence of the TiO_2 coating layer around the HAp surface.

Figure 5 exhibits (Figure 5a) a photograph of the membrane fabricated by using TiO_2 -coated HAp whiskers, with the (a1) and (a2) insets showing the membrane images after bending, FE-SEM micrographs of (Figure 5b) surface and (Figure 5c) cross-section observations for the membrane, and (Figure 5d) STEM micrographs revealing the thickness of the TiO_2 coating layer by observing a single TiO_2 -coated HAp particle. As is clearly seen in Figure 5a, the membrane fabricated by using TiO_2 -coated HAp whiskers presents a white, free-standing, and highly flexible-like paper, even after arbitrarily bending without any damages (insets of Figure 5(a1,a2)). The surface and cross-section observation of the membrane (Figure 5b,c) show a nest-like microstructured surface and $\sim 210\text{ }\mu\text{m}$

thickness, respectively. To reveal the thickness of the TiO_2 coating layer, a STEM observation was performed upon a single TiO_2 -coated HAp particle, as demonstrated in Figure 5d. One can obviously distinguish that the coating layer was formed with a thickness of ~ 23 and ~ 19 nm for either edge of the TiO_2 coating, respectively.

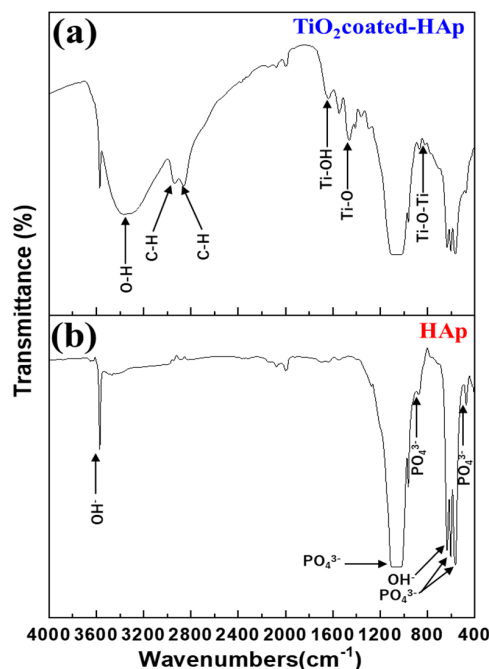


Figure 3. FT-IR spectra of (a) the TiO_2 -coated HAp and (b) hydrothermally-synthesized HAp.

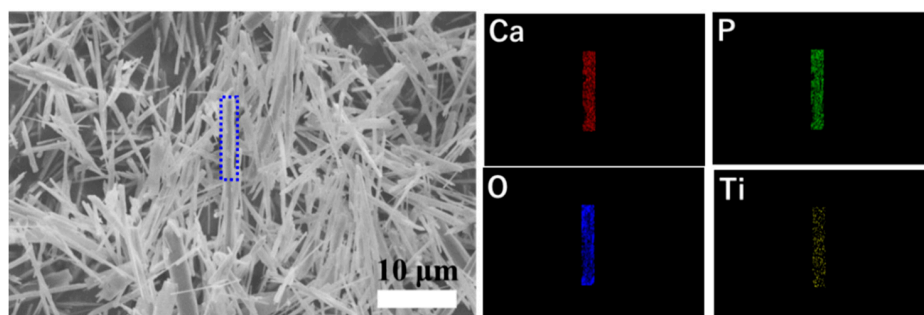


Figure 4. FE-SEM images of TiO_2 -coated HAp particles and component elements detected by EDX local mapping.

12 mL of well-dispersed Au colloidal suspension (particle size: 5 nm, number/mL: 5×10^{13} , solvent: water, and optical density: $\text{OD}_{520} = 1.0$, BBI solutions Ltd. Cardiff, UK) was poured into a vessel equipped with the TiO_2 -coated HAp membrane in order to evaluate the separation performance of the membrane. The zeta potential and pH of the Au suspension were measured at -38.6 and 8.5 mV, respectively. The intensity of the absorption peak centering at ~ 535 nm in the UV-vis spectra of the Au suspension before and after the separation was used to determine the filtration efficiency of the HAp and TiO_2 -coated HAp membranes, as exhibited in Figure 6a, and the color difference of these Au colloidal suspensions was comparably distinguished, as shown in Figure 6b. By quantitatively estimating the peak intensity, the filtration efficiency of the HAp membrane was determined as $\sim 39\%$, while that of the TiO_2 -coated HAp membrane was improved by up to $\sim 100\%$, which was also distinguishably observed by a color fade change of the Au colloidal suspensions before and after the filtration (Figure 6b). The significant improvement in the filtration efficiency after the TiO_2 coating is understood as resulting from the fact that the change in the surface situation of the HAp whiskers occurred when the TiO_2 layer

was coated around their surfaces. That is, before the coating, the zeta potential of the HAp suspension was measured as +8.6 mV at pH = 8.5, whereas after the coating the zeta potential of TiO₂-coated HAp increased by up to +21 mV at pH = 8.5. As a result, the adsorption capability of the Au nanoparticles dramatically improved after the TiO₂ coating by considering the effective utilization of the electrostatic attractive interaction between the Au nanoparticles and whisker surface, which was responsible for a high filtration efficiency of ~100%. As schematically illustrated in Figure 7, when the Au colloidal suspension fluxed through the TiO₂-coated HAp membrane, the negatively-charged Au nanoparticles (zeta potential: −38.6 mV at pH = 8.5) were effectively attracted to the positively-charged TiO₂-coated HAp whiskers (zeta potential: +21 mV at pH = 8.5) due to the electrostatic attractive interaction. The electrostatic attractive interaction was also investigated by Breite et al. [38,39] through a particle adsorption on a polyether sulfone membrane, in order to know how electrostatic interactions dominate membrane fouling. They ascribed the strong fouling of polystyrene (PS) beads for the polyethersulfone membrane as being a reason for the electrostatic attraction between cationic particles and the negatively charged membrane surface.

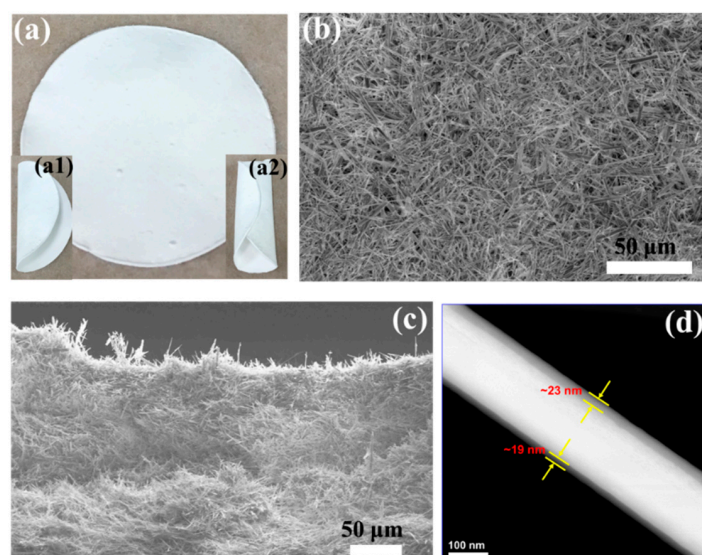


Figure 5. (a) Photograph of the membrane fabricated by using TiO₂-coated HAp whiskers, with (a1) and (a2) inset photographs of the membrane after bending, FE-SEM images of (b) surface and (c) cross-section observations of the membrane, and (d) STEM images revealing the thickness of the TiO₂ coating layer for a single TiO₂-coated HAp particle.

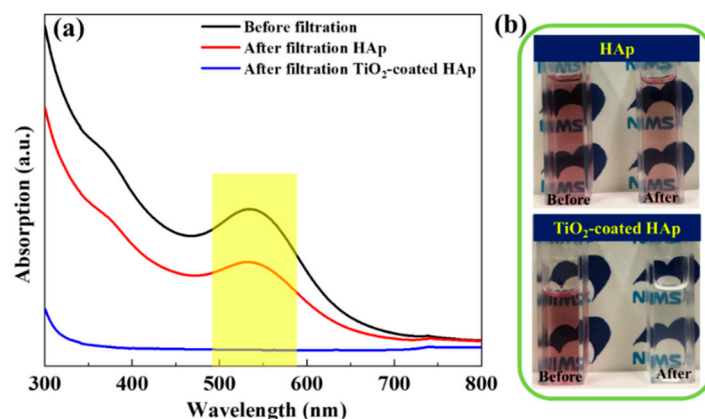


Figure 6. (a) UV-vis spectra of the Au colloidal suspensions before and after the filtration by using the membrane fabricated by the HAp and TiO₂-coated HAp whiskers; (b) photographs showing the color difference of these Au colloidal suspensions.

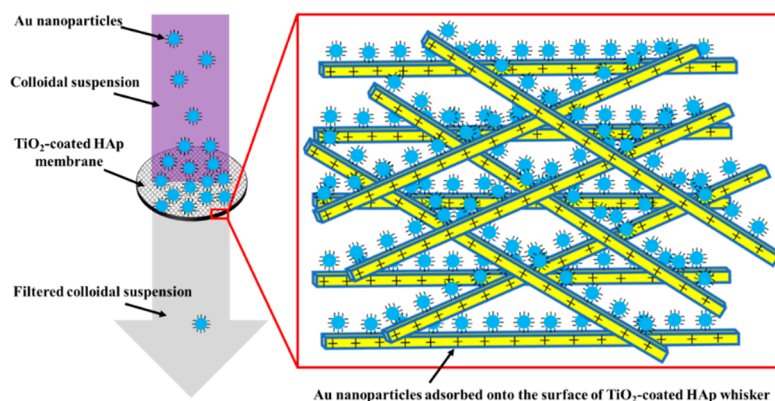


Figure 7. Schematic illustration of the Au colloidal suspension filtered by the TiO_2 -coated HAp membrane, with a locally enlarged schema to illustrate the adsorption of Au nanoparticles onto the surface of the TiO_2 -coated HAp whisker as a result of the electrostatic attractive interaction of their negative and positive surface charges.

Figure 8 shows the FE-SEM micrograph of the surface of the TiO_2 -coated HAp membrane after the filtration using EDX element mapping to detect, in particular, the captured Au nanoparticles. After the filtration, the separated Au nanoparticles could not be distinguishably seen from the FE-SEM observation on the surface of the TiO_2 -coated HAp membrane; however, the EDX element mapping not only detected the main component elements of Ca, P, and O for the HAp whiskers and that of Ti for the TiO_2 coating layer, but also, more evidently, that of Au was clearly detected for the adsorbed Au nanoparticles.

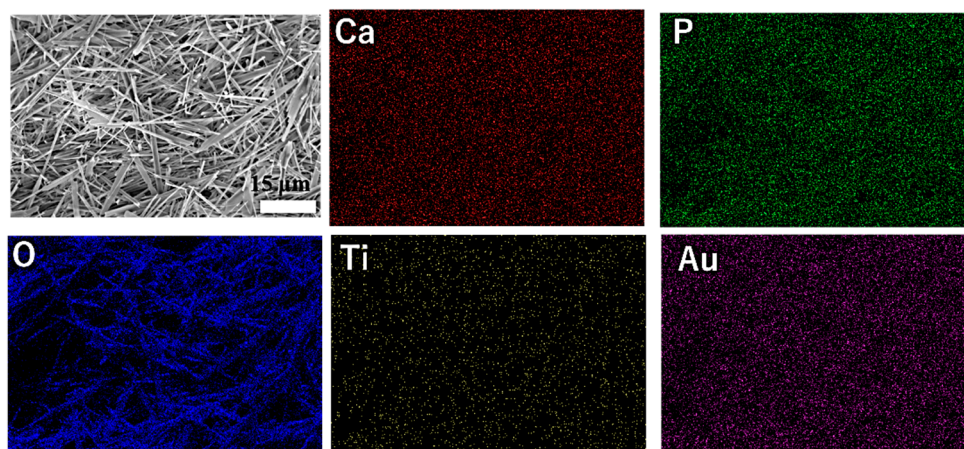


Figure 8. FE-SEM micrograph showing the surface of the TiO_2 -coated HAp membrane following Au nanoparticle separation and EDX element mapping to detect, in particular, the captured Au nanoparticles.

4. Conclusions

The particle growth of HAp was controlled so as to have them grow along the *c*-axis and then form whisker shapes via hydrothermal synthesis. TiO_2 was coated around the surface of the hydrothermally synthesized HAp whiskers, and therefore the surface charge of the HAp whiskers was improved from +8.6 to +21 mV after the TiO_2 modification. A free-standing membrane with a high flexibility was successfully fabricated by using the TiO_2 -coated HAp whiskers and then was used to effectively separate the Au nanoparticles (size = 5 nm and zeta potential = −38.6 mV) with a high filtration efficiency of ~100%, which is dramatically higher than that of ~39% that results from using the uncoated HAp membrane. The high separation performance was considered to be due to the effective

utilization of the electrostatic attractive between positively-charged TiO₂-coated HAP whiskers and negatively-charged Au nanoparticles.

Author Contributions: Writing—original draft preparation, C.Z.; Writing—review and editing and supervision, T.U.; Formal analysis, L.L.; Investigation, M.K.; Project administration, I.I. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

- Williams, D.F. On the nature of biomaterials. *Biomaterials* **2009**, *30*, 5897–5909. [[CrossRef](#)] [[PubMed](#)]
- Wang, Z. *Membrane Biotechnology*; Springer: Berlin/Heidelberg, Germany, 2015.
- De Bartolo, L. *Membrane Biocompatibility*; Springer: Berlin/Heidelberg, Germany, 2015.
- Habibovic, P.; Barrere, F.; van Blitterswijk, C.A.; de Groot, K.; Layrolle, P. Biomimetic hydroxyapatite coating on metal implants. *J. Am. Ceram. Soc.* **2002**, *85*, 517–522. [[CrossRef](#)]
- Bhadang, K.A.; Gross, K.L.A. Influence of fluorapatite on the properties of thermally sprayed hydroxyapatite coatings. *Biomaterials* **2004**, *25*, 4935–4945. [[CrossRef](#)]
- Zhang, J.; Wang, Q.; Wang, A. In situ generation of sodium alginate/hydroxyapatite nanocomposite beads as drug-controlled release matrices. *Acta Biomater.* **2010**, *6*, 445–454. [[CrossRef](#)]
- Fan, L.; Zang, J.; Wang, A. In situ generation of sodium alginate/hydroxyapatite/halloysite nanotubes nanocomposite hydrogel beads as drug-controlled release matrices. *J. Mater. Chem. B* **2013**, *1*, 6261–6270. [[CrossRef](#)]
- Zhou, H.; Jaebeom, L. Nanoscale hydroxyapatite particles for bone tissue engineering. *Acta Biomater.* **2011**, *7*, 2769–2781. [[CrossRef](#)] [[PubMed](#)]
- Sergo, V.; Sbaizero, O.; Clarke, D.R. Mechanical and chemical consequences of the residual stresses in plasma sprayed hydroxyapatite coatings. *Biomaterials* **1997**, *18*, 477–482. [[CrossRef](#)]
- Forsgren, J.; Svahn, F.; Jarmar, T.; Engqvist, H. Formation and adhesion of biomimetic hydroxyapatite deposited on titanium substrates. *Acta Biomater.* **2007**, *3*, 980–984. [[CrossRef](#)] [[PubMed](#)]
- Murugan, R.; Ramakrishna, S. Bioresorbable composite bone paste using polysaccharide based nano hydroxyapatite. *Biomaterials* **2004**, *25*, 3829–3835. [[CrossRef](#)]
- Zhang, C.; Uchikoshi, T.; Liu, L.; Kikuchi, M.; Ichinose, I. Nest-like microstructured biocompatible membrane fabricated by hydrothermally-synthesized hydroxyapatite (HAP) whiskers. *J. Eur. Ceram. Soc.* **2020**, *40*, 513–520. [[CrossRef](#)]
- Jobin, M.L.; Alves, I.D. On the importance of electrostatic interactions between cell penetrating peptides and membranes: A pathway toward tumor cell selectivity? *Biochimie* **2014**, *107*, 154–159. [[CrossRef](#)] [[PubMed](#)]
- Sadeghi, I.; Kronenberg, J.; Asatekin, A. Selective Transport through Membranes with Charged Nanochannels Formed by Scalable Self-Assembly of Random Copolymer Micelles. *ACS Nano* **2018**, *12*, 95–108. [[CrossRef](#)]
- Breite, D.; Went, M.; Prager, A.; Kuhnert, M.; Schulze, A. Charge Separating Microfiltration Membrane with pH-Dependent Selectivity. *Polymers* **2019**, *11*, 3. [[CrossRef](#)] [[PubMed](#)]
- Taubert, A.; Mano, J.F. *Biomaterials Surface Science*; John Wiley & Sons: Hoboken, NJ, USA, 2013.
- Fujishima, A.; Zhang, X.; Tryk, D.A. TiO₂ photocatalysis and related surface phenomena. *Surf. Sci. Rep.* **2008**, *63*, 515–582. [[CrossRef](#)]
- Ng, B.S.; Annergren, I.; Soutar, A.M.; Khor, K.A.; Jarfors, A.E.W. Characterisation of a duplex TiO₂/CaP coating on Ti₆Al₄V for hard tissue replacement. *Biomaterials* **2005**, *26*, 1087–1095. [[CrossRef](#)]
- Amaravathy, P.; Sathyanarayanan, S.; Sowndarya, S.; Rajendran, N. Bioactive HA/TiO₂ coating on magnesium alloy for biomedical applications. *Ceram. Int.* **2014**, *40*, 6617–6630. [[CrossRef](#)]
- Araghi, A.; Hadianfard, M.J. Fabrication and characterization of functionally graded hydroxyapatite/TiO₂ multilayer coating on Ti-6Al-4V titanium alloy for biomedical applications. *Ceram. Int.* **2015**, *41*, 12668–12679. [[CrossRef](#)]
- Rauwel, E.; Willinger, M.-G.; Ducroquet, F.; Rauwel, P.; Matko, I.; Kiselev, D.; Pinna, N. Carboxylic Acids as Oxygen Sources for the Atomic Layer Deposition of High-κ Metal Oxides. *J. Phys. Chem. C* **2008**, *112*, 12754–12759. [[CrossRef](#)]

22. Zhang, C.; Uchikoshi, T.; Xie, R.-J.; Liu, L.; Sakka, Y.; Hirosaki, N. Significantly improved photoluminescence of the green-emitting beta-sialon:Eu²⁺ phosphor via surface coating of TiO₂. *J. Am. Ceram. Soc.* **2019**, *102*, 294–302. [\[CrossRef\]](#)
23. Zhang, C.; Uchikoshi, T.; Liu, L.H.; Kikuchi, M. Controllable Design of Various Microstructures for Hydroxyapatite Coatings by Electrophoresis Deposition Process for Biomedical Applications. *J. Electrochem. Soc.* **2019**, *166*, D700–D706. [\[CrossRef\]](#)
24. Ruiz Hernandez, S.E.; Streeter, I.; de Leeuw, N.H. The effect of water on the binding of glycosaminoglycan saccharides to hydroxyapatite surfaces: A molecular dynamics study. *Phys. Chem. Chem. Phys.* **2015**, *17*, 22377–22388. [\[CrossRef\]](#)
25. Prakash, M.; Lemaire, T.; Di Tommaso, D.; de Leeuw, N.; Lewerenz, M.; Caruel, M.; Naili, S. Transport properties of water molecules confined between hydroxyapatite surfaces: A Molecular dynamics simulation approach. *Appl. Surf. Sci.* **2017**, *418*, 296–301. [\[CrossRef\]](#)
26. Wang, X.; Zhang, L.; Liu, Z.; Zeng, Q.; Jiang, G.; Yang, M. Probing the surface structure of hydroxyapatite through its interaction with hydroxyl: A first-principles study. *RSC Adv.* **2018**, *8*, 3716–3722. [\[CrossRef\]](#)
27. Lotgering, F.K. Topotactical Reactions with Ferrimagnetic Oxides Having Hexagonal Crystal structures—I. *J. Inorg. Nucl. Chem.* **1959**, *9*, 113–118. [\[CrossRef\]](#)
28. Viswanath, B.; Ravishankar, N. Controlled synthesis of plate-shaped hydroxyapatite and implications for the morphology of the apatite phase in bone. *Biomaterials* **2008**, *29*, 4855–4863. [\[CrossRef\]](#) [\[PubMed\]](#)
29. Li, S.; Xu, J.; Luo, G. Control of crystal morphology through supersaturation ratio and mixing conditions. *J. Cryst. Growth* **2007**, *304*, 219–224. [\[CrossRef\]](#)
30. Judge, R.A.; Jacobs, R.S.; Frazier, T.; Snell, E.H.; Pusey, M.L. The effect of temperature and solution pH on the nucleation of tetragonal lysozyme crystals. *Biophys. J.* **1999**, *77*, 1585–1593. [\[CrossRef\]](#)
31. Cahn, J.W. Theory of crystal growth and interface motion in crystalline materials. *Acta Metall.* **1960**, *8*, 554–562. [\[CrossRef\]](#)
32. Koutsopoulos, S. Synthesis and characterization of hydroxyapatite crystals: A review study on the analytical methods. *J. Biomed. Mater. Res.* **2002**, *62*, 600–612. [\[CrossRef\]](#)
33. Zeidler, V.A.; Brown, C.A. The Infrared Spectra of Some Ti-O-Si, Ti-O-Ti and Si-O-Si Compounds. *J. Phys. Chem.* **1957**, *61*, 1174–1177. [\[CrossRef\]](#)
34. Nadica, D.; Abazovic, M.; Comor, M.; Dramicanin, D.; Jovanovic, S.; Jovan, M. Photoluminescence of Anatase and Rutile TiO₂ Particles. *J. Phys. Chem. B* **2006**, *110*, 25366–25370.
35. Sivakesava, S.; Irudayaraj, J.; Demirci, A. Monitoring a bioprocess for ethanol production using FT-MIR and FT-Raman spectroscopy. *J. Ind. Microbiol. Biot.* **2001**, *26*, 85–190. [\[CrossRef\]](#) [\[PubMed\]](#)
36. Smith, B.C. IR Spectral Interpretation Workshop Alcohols The Rest of the Story. *Spectroscopy* **2017**, *32*, 19–23.
37. He, Y.J.; Peng, J.F.; Chu, W.; Li, Y.Z.; Tong, D.G. Black mesoporous anatase TiO₂ nanoleaves: A high capacity and high rate anode for aqueous Al-ion batteries. *J. Mater. Chem. A* **2014**, *2*, 1721–1731. [\[CrossRef\]](#)
38. Breite, D.; Went, M.; Thomas, I.; Prager, A.; Schulze, A. Particle adsorption on a polyether sulfone membrane: How electrostatic interactions dominate membrane fouling. *RSC Adv.* **2016**, *6*, 65383–65391. [\[CrossRef\]](#)
39. Breite, D.; Went, M.; Prager, A.; Schulze, A. The critical zeta potential of polymer membranes: How electrolytes impact membrane fouling. *RSC Adv.* **2016**, *6*, 98180–98189. [\[CrossRef\]](#)

