Fabrication of Hydroxyapatite/Tantalum Composites by Pressureless Sintering in Different Atmosphere

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ABSTRACT: The effect of sintering atmosphere (air and Ar) and temperature (1100, 1200, 1300 °C) on the microstructure, mechanical properties, and bioactivity of hydroxyapatite/tantalum (HA/Ta) composites were systematically investigated by pressureless sintering of the mixture of HA and Ta powders. It shows that the sintering atmosphere greatly impacts the phase composition and microstructure of the HA/Ta composites. The higher diffusion of atoms promotes shrinkage and causes deeper reaction fusion between the HA matrix and Ta, which improved the interfacial binding of the HA/Ta composites. The refined grain structure and improved interfacial binding obtained within the Ar atmosphere compared to the air atmosphere benefit the mechanical properties. The maximum bending strength and shrinkage observed for the composites sintered at 1300 °C in the Ar atmosphere are 27.24 MPa and 6.65%, respectively. The cell counting kit-8 (CCK-8) method was used to investigate the in vitro cytocompatibility of HA/Ta composites. The results revealed that the HA/Ta composites sintered with different conditions have no cytotoxicity. The simulated body fluid (SBF) soaking results showed that all of the studied composites possess desirable bioactivity, as demonstrated by their ability to form calcium-deficient carbonate apatite layer on the surfaces. For composites sintered at 1300 °C, the surface apatite layer coverage of the composites obtained in the Ar atmosphere was increased by 139.7% than the ones obtained in air, which confirmed an enhanced bioactive mineralization ability. The results indicated that the HA/Ta composites sintered at 1300 °C in Ar possess desirable mechanical properties and bioactivity. This work opens up the new possibility for preparing HA-based composites and is of great value in biomedical applications.

1. INTRODUCTION

Recent research progress has shifted the focus from monoliths to composites because multiphase materials are able to maximize the properties of the single materials, especially hydroxyapatite (HA)-based composite materials. Being the main inorganic component of bones, hydroxyapatite (Ca_{10}(PO_4)_6(OH)_2, HA) has been preferred as a viable prospect for bone implants. Numerous attempts have been made to fabricate hydroxyapatite bioceramic bone implants due to their high biocompatibility and excellent osteoconductivity. Nevertheless, HA ceramics have insufficient mechanical properties (fracture strength and toughness) for long-bearing applications.

The combination of HA and biocompatible metals (such as titanium, Ti6Al4V, and 316L stainless) to fabricate biocomposites with both mechanical properties and bioactivity is considered an efficient way to overcome the previously mentioned disadvantages of HA. Except for these metals, tantalum (Ta) is also considered a promising candidate due to its excellent corrosion resistance, high fracture toughness, and prominent biocompatibility. Moreover, Ta demonstrates no remarkable inflammatory response and is reported to possess the ability to support the attachment, growth, and differentiation of human osteoblasts. Pressureless sintering is a commonly used method to prepare dense ceramics, while hot pressing and hot isostatic pressing are more complex and expensive. In general, vacuum sintering and atmosphere sintering (typically Ar atmosphere) are used to prevent adverse reactions between different components. For example, the sintering of HA/Ti composites is usually carried out in an argon atmosphere to prevent the oxidation of Ti.

Obviously, it is essential to evaluate the effect of atmosphere on the sintering process of HA/Ta composites, which has not yet been reported systematically.
The present investigation is an attempt to investigate the influences of sintering atmospheres and temperatures on the properties of HA/Ta ceramic composites. The phase composition, microstructure, and mechanical performance of the sintered composites as well as the in vitro bioactivity have been studied. The work opens up the new possibility for preparing HA-based composites and is of great value in biomedical applications.

2. RESULTS AND DISCUSSION

2.1. Characterization of HA/Ta Composites. 2.1.1. Morphology and Phase Analysis. Figure 1 exhibits the X-ray diffraction (XRD) patterns of the composites fabricated in air and Ar atmosphere. Table 1 shows the phase composition of HA/Ta composites after sintering in different conditions. The disappearance of tantalum peaks in Table 1 indicates the reaction between tantalum and HA, and the formation of a third phase is inevitable. It can be observed that in all test temperatures, peaks corresponding to CaTa₂O₆ appeared. There are two possible explanations of the formation for CaₓTa₂O₆₊₅n. One is in connection with the Ca²⁺ diffused from HA. It is reported that the formation of tantalum oxidation is inevitable even for sintering within argon (>99.99%).¹⁷ Tantalum oxide (usually refers to Ta₂O₅) reacts with Ca²⁺ at the interface, leading to the formation of calcium tantalum oxides. The other is the calcium oxide, from the HA decomposition (reaction 1), reacts with Ta₂O₅ to form calcium tantalum oxides (reaction 2). However, the CaO pattern is absent in Figure 1, indicating that the generation of CaₓTa₂O₆₊₅n is related to the diffusion of Ca²⁺ in HA.

\[
\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \rightarrow 3\text{Ca}_3(\text{PO}_4)_2 + \text{CaO} + \text{H}_2\text{O} \tag{1}
\]

\[
m\text{CaO} + n\text{Ta}_2\text{O}_5 \rightarrow \text{Ca}_m\text{Ta}_{2n}\text{O}_{m+5n} \tag{2}
\]

It was reported that there is no decomposition for pure HA in air and argon when sintered at temperatures below 1200 °C.²⁰ The characteristic diffraction peaks for Ca₃(PO₄)₂ (β-TCP) are observed in HA_Ta1100 composites in both atmospheres, which indicates that the presence of Ta accelerated the decomposition of HA. A similar finding that Ta made HA phase more unstable was reported by Dhal et al.²¹ The formation of CaₓTa₂O₆₊₅n reduces the ratio of Ca/P of HA, which contributes to the formation of TCP due to a lower Ca/P ratio for TCP. For HA_Ta1100 and HA_Ta1200 composites, HA and β-TCP peaks are observed in both atmospheres. However, with increasing sintering temperature to 1300 °C, HA peaks disappeared while β-TCP peak remained and α-TCP peaks appeared. Figure 2 represents the XRD patterns of HA_Ta1300 composites fabricated in different atmospheres (Ar and air). The relative intensities of the α-TCP diffractions increased when sintered in Ar, which would be considered that the transition of HA to phosphate is more favorable when sintering in an Ar atmosphere.

Fracture surfaces of HA/Ta composites sintered in different conditions are shown in Figure 3. Many pores are observed at the boundaries and grain junctions. The presence of calcium tantalum oxide and HA thermal decomposition products (e.g., β-TCP) as secondary phases impeded the densification process of HA, which leads to plenty of pores remaining in the structure. Moreover, the formation of pores may also be attributed to the densification process of HA during sintering.²³

Table 1. Phase Developed after the Sintering Process

| sample code | sintering atmosphere | phase                                      |
|-------------|----------------------|--------------------------------------------|
| HA_Ta1100   | air                  | β-TCP + CaTa₂O₆ + HA + Ca₂Ta₂O₇            |
| HA_Ta1200   | air                  | β-TCP + CaTa₂O₆ + HA                      |
| HA_Ta1300   | air                  | β-TCP + CaTa₂O₆ + α-TCP                   |
| HA_Ta1100   | Ar                   | β-TCP + CaTa₂O₆ + HA                      |
| HA_Ta1200   | Ar                   | β-TCP + CaTa₂O₆ + Ha                      |
| HA_Ta1300   | Ar                   | β-TCP + CaTa₂O₆ + α-TCP                   |

Figure 1. XRD results of HA/Ta composites sintered in (a) air and (b) Ar atmosphere.

Figure 2. XRD patterns of HA_Ta1300 composites sintered in air and Ar atmospheres.
Average grain sizes of HA/Ta composites sintered in Ar and air atmospheres are listed in Table 2. The grains grow up gradually with the increase of the sintering temperature. In an air atmosphere, the grain size of the composite samples is 0.89 ± 0.22, 1.23 ± 0.25, and 1.98 ± 0.55 μm for HA_Ta1100, HA_Ta1200, and HA_Ta1300 samples, respectively. Also, finer grain sizes are found in Ar atmosphere, which are 0.53 ± 0.11, 0.85 ± 0.17, and 1.18 ± 0.25 μm for HA_Ta1100, HA_Ta1200, and HA_Ta1300 samples, respectively. It is clear that the composite samples sintered in an Ar atmosphere show a finer grain size than the samples sintered in an air atmosphere.

| sintering atmosphere | HA_Ta1100 (μm) | HA_Ta1200 (μm) | HA_Ta1300 (μm) |
|----------------------|----------------|----------------|----------------|
| Ar                   | 0.53 ± 0.11    | 0.85 ± 0.17    | 1.18 ± 0.25    |
| air                  | 0.89 ± 0.22    | 1.23 ± 0.25    | 1.98 ± 0.55    |

Two phases with different grain morphologies of HA_Ta1200 composites sintered in Ar can be observed from Figure 4a. Energy-dispersive spectrometry (EDS) results from these two different areas are shown in Figure 4A,B. Flower-like grains are visible and surrounded by matrix grains in the microstructures and show high-intensity peaks of Ta, Cα, and O atoms, which are essentially the signs of the CaTa2O6 phase. The EDS intensity collected from matrix grains shows the presence of Ca, P, and O atoms, which represent the calcium phosphate phase. The EDS analyses from different areas of the microstructures confirm the presence of calcium phosphate phase and CaTa2O6.

Fracture surfaces of HA_Ta1200 composites sintered in air and Ar are represented in Figure 4a,b, respectively. A large area of gaps is distributed around CaTa2O6 at the junction of the HA matrix and Ta when composites are sintered in air. However, for composites sintered in Ar, the pore area at the junction decreases, and this difference in interfacial bonding may be related to the diffusion of atoms in different atmospheres. Since there is no element P in the phase of CaTa2O6 and no element Ta in the phase of calcium phosphate, the presence of P atoms and Ta atoms in the Ta-rich regions and Ca-rich regions, respectively, are the result of atomic diffusion. Figure 4A,C shows the EDS results in the Ta-rich area of HA_Ta1200 composites sintered in Ar and air, respectively, where the atom ratios of P are 8.30 and 5.97%, respectively, indicating that the diffusion rate of HA toward the Ta area when sintering in Ar is 39% higher than that in air. Figure 4B,D shows EDS in the Ca-rich area when sintering in Ar and in air, respectively. The results show that the diffusion of Ta to HA area increases by 22% compared with that in air. These results indicate that the diffusion between HA and Ta phases in Ar sintering is higher than in air sintering.

2.1.2. Shrinking and Bending Strength. Figure 5 shows the linear shrinkage of the sintered HA/Ta composites. As listed in Figure 5, with an increase in sintering temperature, HA/Ta composites show an increase in shrinkage. The results show that HA/Ta composites sintered in an Ar atmosphere
exhibit a higher shrinkage than those in air regardless of the sintering temperature. When sintered in Ar atmosphere, the shrinkage of HA_Ta1100, HA_Ta1200, and HA_Ta1300 is 2.32, 5.52, and 6.65%, respectively. The composite HA_Ta1300 (sintered in Ar atmosphere) has maximum shrinkage of about 6.65%, which increased by 13.48% compared with those composites sintered in air. It is well known that the shrinkage of ceramics is the process by which the pores in the structure are filled by grains. According to the EDS analysis, the lower diffusion of P can be observed in the Ta-rich area for composites sintered in air. As a result, the possibility of HA filling the pores in the composites caused by the diffusion of HA is reduced, which leads to a decrease in the shrinkage of the composites sintered in air.

Figure 6 shows the bending strengths of HA/Ta composites under different sinter conditions. It can be observed in Figure 6 that an increase in the sintering temperature increases the bending strength of HA/Ta composites in both sintering atmospheres. Composites sintered in an Ar atmosphere show a higher bending strength than composites sintered in air. The bending strength of HA_Ta1100 in Ar is about 22.76 MPa, which is 87.01% higher than that of air. For HA_Ta1200 and HA_Ta1300 composites, the bending strength obtained in an Ar atmosphere is also increased by 31.44 and 1.57%, respectively, compared with the composites sintered in air.

According to the EDS analysis, for HA_Ta1200 composites sintered in Ar, the proportion of P in the Ta-rich area and the proportion of Ta in the P-rich area are increased by 39 and 22%, respectively, compared with air sintering. The mutual diffusion of a higher proportion of Ta and P makes the reaction between HA and Ta more intense, which can be evidenced by Figure 1, where the relative intensity of the CaTa2O6 diffraction peak during sintering in argon is higher. The deeper reaction fusion when sintered in Ar causes a tight bonding between the HA matrix and Ta, which improves the interfacial bonding of HA/Ta composites. Ceramic mechanical properties depend upon grain sizes, shapes, and grain
arrangement. For this work, the enhancement of the bending strength for the HA/Ta composites sintered in Ar is probably associated with the decrease in grain size (Table 2). In the microstructure, the size of the crystals has the utmost importance in preventing the propagation of cracks in the whole structure. According to the Hall–Petch effect, as the grain size decreases, the strength and toughness of the material increases. The deeper reaction fusion and the finer grain size in argon sintering result in higher bending strength. As for HA_Ta1300 composites, abnormal grain growth and decomposition of HA may lead to less improvement in its mechanical properties. Combining Figures 4–6, it can be concluded that HA/Ta composites sintered in an Ar atmosphere have enhanced mechanical properties than those sintered in air.

2.1.3. Wettability Analysis. Distilled water is used to measure the contact angles on the HA/Ta composites, and the results are shown in Figure 7. The composites sintered in air and Ar have the same order in terms of the contact angle: HA_Ta1200 > HA_Ta1300 > HA_Ta1100. Obviously, sintering temperature has a great impact on the contact angle of the HA/Ta composites. There are two main reasons for the higher contact angle in HA_Ta1200 and HA_Ta1300. One of these two could be explained by the closure of some surface pores with the increase in sintering temperature. Shrinkage is governed by the rate of densification and through the reduction in porosity. In Figure 5, HA/Ta composites show an increase in shrinkage when the sintering temperature is increased, which could result in the closure of some surface pores, extenuates the fluid penetration and consequently enhances the contact angle. The second reason is associated with the phase composition. It has been reported that the contact angle increases with the increasing TCP concentration in the case of biphasic ceramic consisting of HA and β-TCP. The increase of sintering temperature promotes the decomposition of HA, which enhanced the concentration of β-TCP. Compared with the HA_Ta1100 composites, a higher concentration of β-TCP in HA_Ta1200 and HA_Ta1300 composites also explained the increase in contact angle. However, the closure pores and higher concentration of β-TCP are not the reasons for the decrease in contact angle of HA_Ta1300 composites. CaTa2O6 is also a secondary phase that we cannot ignore; as the sintering temperature enhanced, the intensity of the diffraction peak of CaTa2O6 gradually increased, improving the concentration of CaTa2O6 in the structure. We speculate that a higher CaTa2O6 concentration may lead to a decrease in the contact angle of HA_Ta1300 composites. The HA_Ta1100 composite sintered in an Ar atmosphere shows a minimum contact angle value of 16.76°, whereas the surface contact angle is 59.13° when it is sintered in air. Also, for HA_Ta1200 composites, sintering in Ar atmosphere gives a lower contact angle. Usually, for calcium phosphate, the contact angle decreases with the decrease in grain size. A finer grain size of composites sintered in Ar (Table 2) explains the smaller contact angle values.

2.2. In Vitro Bioactivity Analysis. 2.2.1. In Vitro Cell Activity of HA/Ta Composites. Figure 8 reveals the cell proliferation of MC3T3-E1 for HA/Ta composites over time. Cell proliferation increased for all of the composites with increasing incubation duration. In general, HA/Ta composites have no cytotoxicity. After 1 and 3 days of incubation, according to the one-way analysis of variance (ANOVA) test, there is no significant difference in proliferation between the composites sintered in different conditions. However, after 5 days of incubation, cell proliferation is statistically significantly higher on HA_Ta1100 composites sintered in Ar compared to those sintered in air. Previously, it had been reported that the hydrophilic surface supports better cell adhesion and spread. Hence, the current results show that cell adhesion was enhanced on a more hydrophilic surface for HA_Ta1100 composites sintered in Ar.

2.2.2. In Vitro Mineralization of HA/Ta Composites. The bioactivity of HA/Ta composites was measured by immersion in simulated body fluid (SBF) for 14 days. As observed in Figure 1, HA peaks disappeared only for HA_Ta1300 composites. Therefore, the HA_Ta1300 composite sintered in Ar is selected to accurately analyze the phase compositions of the mineralized layer to remove the interference of the HA phase in the HA/Ta composites. XRD patterns on the surface of HA_Ta1300 composites sintered in an Ar atmosphere before and after soaking in SBF solutions are shown in Figure 9. The characteristic peaks of hydroxyapatite (JCPDS 86-0740) are newly detected after immersion in SBF, indicating that the deposited layer could be HA crystals.

Figure 10 shows the results of X-ray photoelectron spectroscopy (XPS) analysis, which provides detailed information on the mineral phase on the biomineralized composites. XPS spectra of the samples exhibit the presence of O, Ca, P, Mg, Na, C, and Ta elements. The O 1s peaks are located at 531.3 and 532.8 eV, as shown in Figure 10c. The
first peak at 531.3 eV corresponds to O 1s in PO$_4^{3−}$.

The second peak at 532.8 eV is attributed to the Ta−OH group, which is suggested as an effective functional group for inducing apatite nucleation. Figure 10d indicates that the location of Ca 2p$_{1/2}$ and Ca 2p$_{3/2}$ is 347.4 and 351.0 eV, respectively, which is the fingerprint for Ca 2p in the standard HA. The intensity of the P 2p peak at 133.2 eV is assigned to the PO$_4^{3−}$ groups. The C 1s peaks show a double peak configuration. The lower binding energy peak around 284.8 might contribute to carbon contamination from composite preparation. The higher binding energy peak at 287.7 is assigned to the CO$_3^{2−}$ groups, which indicates the presence of carbonate in the apatite layer. It is reported that the carbonate groups are contained within biological calcium phosphates. Therefore, the apatite grown on the surface of HA/Ta composites in this work resembles the biological apatite.

The SEM photographs of the HA/Ta composites surface after immersion in the SBF for 14 days are selected to represent long-term biomineralization characterization. The corresponding morphology and distribution of the mineralized apatite characterized via SEM are presented in Figure 11. Globular particles are observed to deposit on the surfaces of all tested composites from Figure 11. The thick precipitate layer is composed of many tiny nanocrystals (average particle size is 18.86 ± 2.97 nm). This bone-like apatite layer with globular particles was also reported by Uchida et al. There are two possible explanations for the generation of this apatite layer. One of these two is reported by Kim et al. After immersion in SBF, the OH$^−$ and PO$_4^{3−}$ anions from the composite surface are able to attract Ca$^{2+}$ cations from the surrounding SBF, which, in turn, attracts PO$_4^{3−}$ ions to create nucleation centers and the growth of calcium phosphates. And then, the formation of Ta−OH groups could be the second explanation. According to Miyazaki et al., the Ta−OH groups with negative charges, consuming Ca$^{2+}$ ions to form calcium tantalate, and then combined with PO$_4^{3−}$ ions to form amorphous calcium phosphate. The process continues with the combination of the large amount of Ca$^{2+}$ ions and PO$_4^{3−}$ ions to build up the apatite layer.

SEM results show that, for HA_Ta1100 composites, the surface particle size of the mineral (sintered in an Ar atmosphere) is 0.81 ± 0.19 μm, which is finer than that sintered in an air atmosphere (1.14 ± 0.41 μm; Figure 11a). The improved wettability (Figure 7) might be attributed to a rapid apatite formation rate. For HA_Ta1300 composites, sintered in an Ar atmosphere, the surface is completely covered with HA particles while the composites obtained in an air atmosphere are composed of many tiny nanocrystals (average particle size is 18.86 ± 2.97 nm).
atmosphere coverage rate is only 41.71%. This result illustrates that the concentration of the apatite layer deposits appeared to be higher on the surface prepared in an Ar atmosphere.

The corresponding EDS element analysis is demonstrated in Figure 12. Ca, P, C, O, Ta, Na, and Mg elements are detected in all samples. The Na⁺ and Mg²⁺ cations are considered to substitute Ca²⁺ ions and combine with the newly formed apatite layer. The Ca/P ratio of the HA/Ta composites is around 1.17−1.50, which is lower than the Ca/P ratio of HA (1.67). Owing to the incorporation of these ions, the newly formed apatite is a calcium-deficient apatite layer and contains CO₃²⁻ ions. The atomic ratio of Ca/P for HA_Ta1100, HA_Ta1200, and HA_Ta1300 (sintered in air) is 1.17, 1.34, and 1.25, respectively. Also, a higher Ca/P atomic ratio of the composites sintered in an Ar atmosphere is found to be 1.41, 1.50, and 1.27 for HA_Ta1100, HA_Ta1200, and HA_Ta1300, respectively. Compared to the samples sintered in an air atmosphere, the composites sintered in an Ar atmosphere coverage rate is only 41.71%. This result illustrates that the concentration of the apatite layer deposits appeared to be higher on the surface prepared in an Ar atmosphere.

Figure 11. SEM pictures of HA/Ta composites soaked for 14 days: (a–c) HA_Ta1100, HA_Ta1200, and HA_Ta1300 composites sintered in air atmosphere, respectively, and (d–f) HA_Ta1100, HA_Ta1200, and HA_Ta1300 composites sintered in an Ar atmosphere, respectively.

Figure 12. Typical EDS spectra of the HA/Ta ceramic soaked in the SBF solution for 14 days: (a)−(c) HA_Ta1100, HA_Ta1200, and HA_Ta1300 composites sintered in air atmosphere, respectively, and (d)−(f) HA_Ta1100, HA_Ta1200, and HA_Ta1300 composites sintered in an Ar atmosphere, respectively.
atmospheres. The results of Figures 11 and 12 demonstrate an enhanced apatite-inducing ability for composites sintered in Ar, which might be attributed to enhanced wettability and finer particle size.37

3. CONCLUSIONS

The present work is carried out to investigate the effect of sintering atmosphere and temperature on tantalum and hydroxyapatite composites in terms of microstructure, mechanical properties, and bioactivity. The HA/Ta composites sintered in an Ar atmosphere showed improvement in mechanical properties and bioactivity compared with those in an air atmosphere. The maximum bending strength and shrinkage of the HA/Ta composites sintered in an Ar atmosphere were 27.24 MPa and 6.65%, respectively, which were higher than those in an air atmosphere. SEM results show that grain sizes of HA/Ta composites increase in both atmospheres as the temperature rises. Consequently, the bending strength and shrinkage increase with an increase in the sintering temperature. CCK-8 results show that HA/Ta composites sintered in different conditions have no cytotoxicity. For HA_Ta1100 composites, higher cell activity was observed after 5 days of incubation for Ar sintering, which may be attributed to the more hydrophilic surface. SBF soaking results reveal that all of the studied samples are biologically active. The composites sintered in an Ar atmosphere produce a higher ability for inducing apatite precipitation, as demonstrated by finer particle sizes of the mineral and higher concentrations of the apatite layer. The combined influence of the refined microstructure and improved wettability for composites obtained in an Ar atmosphere benefited the biomineralization ability of HA/Ta composites. In conclusion, HA/Ta composites sintered in an Ar atmosphere (especially HA_Ta1100) were found to exhibit better mechanical properties and improved bioactivity, which would provide the feasibility of HA/Ta composites as a bone implant material in clinical applications.

4. MATERIALS AND METHODS

4.1. Preparation of HA/Ta Composites. The conventional powder metallurgy method was selected to prepare HA/Ta composites. A planetary ball mill was used to mix and mill the 90% HA powder (99.9%, d (0.5) = 39.8 μm) and the 10 wt % Ta powder (99.9%, d (0.5) = 122.5 nm) at a speed of 250 rpm for 2 h. Moreover, extra 2 wt % hydroxypropyl methyl cellulose (HPMC) was selected as a binder. After the drying process and powder sieving, the HA/Ta powders were compacted into rectangular bar samples, and subsequently cold isostatic pressed at 200 MPa. The debinding process was carried out at 600 °C for 2 h in air and Ar, respectively. The debinding composites were consolidated by pressureless sintering at various temperatures, ranging from 1100 to 1300 °C (the composites were labeled as HA_Ta1100, HA_Ta1200, and HA_Ta1300) and a heating rate of 5 °C/min in Ar and air atmospheres.

4.2. Characterization. The phase analysis of the sintered composites was performed by X-ray diffraction (XRD, Empyrean). The microstructure of the composites was examined by a scanning electron microscope (SEM, JSM-7500F). ImageJ software was used to determine the average grain size from SEM images; at least 100 grains were measured. The grain size results were reported as mean ± standard deviation for each group of composites. The sintered composites were cut into bars with dimensions of 3 × 4 × 35 mm³ (ISO 14704-2000). An electronic universal testing machine (Instron 5967) was selected to measure the bending strength using a three-point bending test. The linear shrinkage of the composites was also measured. The contact angle of the sintered sample was measured by a contact angle goniometer (DSA100L) to evaluate the surface wettability.

4.3. In Vitro Biocompatibility and the SBF Immersion Test of HA/Ta Composites. To measure the cell viability percentage, an extraction process was done according to the ISO 10993-12 extraction standard. With a surface area of 6 cm², composites were sterilized by immersion in 75% ethanol for 30 min, then hydrated and thoroughly rinsed with phosphate-buffered saline (PBS). The conditioned media were obtained by incubating the scaffolds in 2 mL of Roswell Park Memorial Institute (RPMI)-1640 medium in an incubator at 37 °C for 24 h. A similar amount of the culture medium was kept in the same condition to be used as a control. The conditioned media were filtered before use. MC3T3-E1 cells were cultured in an α-minimal essential medium (MEM-α, Hyclone), supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin solution in a humidified atmosphere at 5% CO₂ and 37 °C. Cells were seeded at a density of 1 × 10³ cells/well on 96-well tissue culture polystyrene plates the day before experiments and then incubated with 100 μL of the conditioned media. At each defined time point (1 and 3 days), cell viability was assessed by CCK-8 assay according to the manufacturer’s instructions. The optical density (OD) was measured on a Thermo LabSystems microplate reader (MK3) at 450 nm and corrected by subtracting the OD from blank wells containing only unseeded composites. The * denotes a statistically significant difference with p <0.05.

The bioactivity of HA/Ta composites was measured by immersion in a simulated body fluid (SBF) for 14 days. SBF was prepared according to the research reported by Kokubo and Takadama.38 The ion concentrations (mM) of this solution are 142 Na’, 5 K’, 1.5 Mg²⁺, 2.5 Ca²⁺, 147.8 Cl⁻, 4.2 HCO₃⁻, 1 HPO₄²⁻, and 0.5 SO₄²⁻, which are close to that of body fluid. With a surface area of 1 cm², the samples were soaked in 20 mL of SBF at 37 °C. SBF was renewed every 2 days to maintain its composition. The morphology and microstructure of the sample surface were observed by SEM. Energy-dispersive spectroscopy (EDS, X-Max N80) was performed for the surface elemental analysis. The chemical composition of surfactant deposits was analyzed by XRD (Empyrean) and X-ray photoemission spectroscopy (XPS, ESCALAB 250Xi).

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