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Research Article

Challenges in the Production of Titanium–based Scaffolds Bio–functionalized with Hydroxyapatite by Powder Metallurgy Technique

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Abstract

Recently, titanium and its alloys have remarkable interest for researchers due to their advanced mechanical, surface and biological properties. Researchers are investigating new materials, especially in the field of health, and perhaps material design is the most important criteria that exhibit the low Young's modulus of bone. Along with these criteria's most preferred are composite materials reinforced with hydroxyapatite (HA). Porous materials are preferred because they exhibit Young's modulus close to the bone. The aim of the study, the problems encountered in the production of titanium/hydroxyapatite (Ti/HA) composite scaffolds and the solutions will be emphasized. These are briefly; porogen removal, usage of different sintering furnaces, sintering atmosphere, material thickness, crack formation-propagation as a result of excessive or insufficient pressing pressure, and agglomeration of porogens during mold filling. It has been proven that the use of vertical tube furnaces under the Ar gas atmosphere has successful results compared to the use of horizontal tube furnaces and different atmospheres (vacuum or Ar gas). It has been concluded that in the composite scaffolds that have been successfully produced, micropores are formed as well as macropores, which may result from insufficient neck growth and pressing pressure. In addition, results showed that bi-modal (macro/micro porosity) pore structures may contribute to bone tissue orientation in possible biomaterial use.

Keywords: Powder metallurgy (PM), titanium, hydroxyapatite, composite scaffolds, porous materials.

Hidroksiapatit ile Biyo-fonksiyonelleştirilmiş Titanyum-esaslı Yapı İskelelerinin Toz Metalurjisi Tekniği ile Üretimindeki Zorluklar

Öz

Son zamanlarda titanyum ve alaşımları gelişmiş mekanik, yüzey ve biyolojik özellikleri nedeniyle araştırmacıların ilgisini çekmektedir. Araştırmacılar, özellikle sağlık alanında yeni malzemeleri araştırmakta ve belki de malzeme tasarımı, düşük Young modülü sergilemesinden dolayı, en önemli kriterdir. Bu kriterler içerisinde en çok tercih edilen ise hidroksiapatit (HA) ile güçlendirilmiş kompozit malzemelerdir. Gözenekli malzemeler, Young modülünü kemiğe yakın sergiledikleri için tercih edilmektedirler. Çalışmanın amacı, titanyum/hidroksiapatit (Ti/HA) kompozit yapı iskelelerinin üretiminde karşılaşılan sorunlar ve çözüm önerileri üzerinde durulacaktır. Bunlar kısaca; porojen giderimi, farklı sinterleme fırınlarının kullanılması, sinterleme atmosferi, malzeme kalınlığı, aşırı veya yetersiz presleme sonucu çatlak oluşumu-yayılması ve kalıp doldurma sırasında porojenlerin aglomerasyonu. Ar gazı atmosferi altında dikey tüp fırınların kullanılmasının, yatay tüp fırınların ve farklı atmosferlerin (vakum veya Ar gazı) kullanımına kıyasla başarılı sonuçlar verdiği kanıtlanmıştır. Başarıyla üretilen kompozit iskelelerde makro gözeneklerin yanı sıra yetersiz boyun büyümesi ve yetersiz pres basıncından kaynaklanabilecek mikro gözeneklerin de oluştuğu sonucuna varılmıştır. Ek olarak, sonuçlar bi-modal (makro/mikro gözeneklilik) gözenek yapılarının olası biyomateryal kullanımında kemik dokusu yönlenmesine katkıda bulunabileceğini göstermiştir.

Anahtar Kelimeler: Toz metalürjisi (TM), Titanyum, Hidroksiapatit, Kompozit doku iskelesi, Gözenekli malzeme.

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1. Introduction

Due to its high specific strength (strength/specific gravity), titanium (Ti) is frequently used in the medical implant industry, especially in hip prostheses. The enhanced corrosion resistance of Ti is due to the thin titanium oxide layer it forms on itself and thanks to this feature, its biocompatibility increases [1]. Also, Ti is a metal that is mechanically more rigid and more resistant than other metals such as aluminum, steel etc. The most important known disadvantage of Ti is that it is expensive compared to other elements. The structure of bone tissue in the body and the structure of Ti differ from each other in terms of properties such as strength, hardness, toughness and most importantly Young's modulus (E). Although considered to be sufficiently biocompatible, scientists are trying to increase this biocompatibility by using bone-like structures. These can be briefly explained as the modification of bone and/or similar structures by various methods (coating, composite structure, etc.) [2,3].

Human bone consists of mostly calcium (Ca) and phosphate (P) elements especially, tooth enamel, cortical bone and other spongy bones. Various bioceramics were used by researchers to mimic bone tissue such as calcium phosphates, bioglasses, zirconia (Y-TZP), inert Al_2O_3, MnO_2 etc. [4]. Hydroxyapatite is in the calcium phosphate class and reflects similar properties with the basic minerals that make up the bone structure, especially chemically. Elementally, the chemical composition of HA is $Ca_{10}(PO_4)_6(OH)_2$, the Ca:P ratio, which is the measure of the proximity of bioceramics to bone tissue, is 1.67 [5]. Besides, due to its porosity, HA is used in orthopedic or dental implant applications due to its ability to improve bone tissue orientation. HA, which can be obtained both naturally and artificially in the laboratory environment, is frequently used in orthopedic applications due to its chemical structure resembling natural hard tissues, high biocompatibility and bioactivity. İt's known that Ti/HA composites also have high Young's modulus than cortical bone structure [6]. Researchers are working on reducing Young's modulus to prevent the stress-shielding effect. This phenomenon was firstly explained by Wolf (which also known as Wolf's law) and simply explain the load-carrying capacity difference between bone and implant materials [7]. One can be done by researchers was produce porous materials which have low Young's properties for better load distribution and enhanced bone transformability to the implant's inside (osseointegration). Various methods have been developed to increase the osseointegration behaviors by modifying the implant surfaces or the implant itself for the bone tissue to act as a whole with the implant. One of them is that the implant surface or the whole has a porosity and the tissue development progresses towards these pores. In these ways, many researchers have used numerous pore-agent for pore-forming with food-grade powders such as sodium chloride, sucrose, dextrin corn starch and tapioca starch [8]. Any reaction between the pore-forming particles and the base powders can impair the mechanical properties of the produced material. Besides, when biocompatibility is taken into account in biomaterials, reaction formation between pore-forming particles and powders should be avoided. Since rapid removal of pore-forming particles from the material prevents contamination of the material, the ability to remove or dissolve should be considered in the selection of the pore-forming particle [9]. Another critical factor is the strength properties of the pore-forming particle to be selected, an important feature to prevent the core powders from breaking during pressing. Also, porogen has to be more commercial as well as inexpensive such as NaCl which reported by Topuz *et al.* [10]. In this study, the difficulties encountered and their possible causes will be discussed to guide researchers who will work on Ti/HA porous scaffolds. Moreover, the problems encountered in the production of scaffolds and the possible sources and possible solutions to these problems will be emphasized. The sub-aims of the study can be summarized as follows; producibility of Ti/HA composite scaffold materials, the importance of sintering conditions, and pore homogeneity.

2. Material and Method

Commercial pure Ti with an average size –325 mesh (~45 µm) with irregular shape was procured from Merck (Darmstadt, Germany) and hydroxyapatite with an average size of 3–5 µm was used to compaction. NaCI powders have cracked non-cracked and partly spherical forms. Also, it has a size range between 150–600 µm which is suitable porosity dimensions for biomedical application. Ethanol was used as a binder to Ti and HA powders, and enhance the homogeneity of powder mixing. Then, NaCl powders were added and mixed for 4 h to obtain homogenous porosity. Cylindrical hot work tool steel with 20 mm in diameter and 10 mm height was pressed at 700 MPa for 5 min with the help of a 100 tons' capacity hydraulic press machine. To remove the NaCl powders in the composite materials from the structure and obtain scaffolds, different water-leaching techniques (stirring, vacuum impregnation etc.) have been tried. At the end of salt-leaching trials stirring for 4 h at 70 °C in hot distilled water.

The most important stage of Ti/HA scaffold producibility is sintering. For the sintering stage of scaffolds, different sintering approaches were carried out. Firstly, sintering was tried in a horizontal furnace that can work both vacuum and inert atmosphere. The vacuum was the first tried conditions. As we know that, at high temperature, the melting temperature of NaCl was getting lower and consequently not need any salt-leaching procedure. So the first trial was carried out at 1200 °C for 2 h at ~60 mtorr vacuum. The second trial was at the same furnace vacuum-inert gases (Argon: Ar) procedure. This is carried out with vacuum–filling inert gases–vacuum and sintering at 1200 °C for 2 h. The third trial in a horizontal furnace was a continuous flow of inert gases at 1200 °C for 2 h. The last and final trials were done in a vertical furnace with able to vacuum an inert atmosphere. These trials carried out at 1000 °C for 1 h in a continuous flow of Ar atmosphere. Ar was used for the whole sintering atmosphere due to the high reactivity of Ti to other small atomic sized elements such as; O, N, H etc. and resulted in possible TiO_2, TiN and TiH_2 formation. After the sintering stage, scaffolds were examined for further tests or analyses. Microstructural characteristics (especially neck formation and growth) of the sintered scaffolds were investigated by optical microscopy (OM). From OM images, both cell size, wall thickness and interconnectivity of pores were examined. Further microstructure investigation on sintered scaffolds was carried out with scanning electron microscopy (SEM) which attached with an energy dispersive spectroscopy (EDS) device. Observed problems related to pre-sintering conditions and post-sintering were discussed in the next section.

3. Results and Discussion

Before the sintering stage, NaCl particles must be removed to prevent any reaction between Ti/HA and NaCl in the scaffold. In this way, a couple of salt dissolving processes were carried out, respectively; i) soaking in pure water for 4 h, ii) vacuum empegrenation process in pure water for 30 min, and finally, iii) dissolving in a magnetic stirrer in pure water at 70 °C for 4 h. The scaffolds presented in Figure 1 and kept in distilled water caused scaffold transverse cracks due to internal stresses following the dissolution of NaCl particles over time.

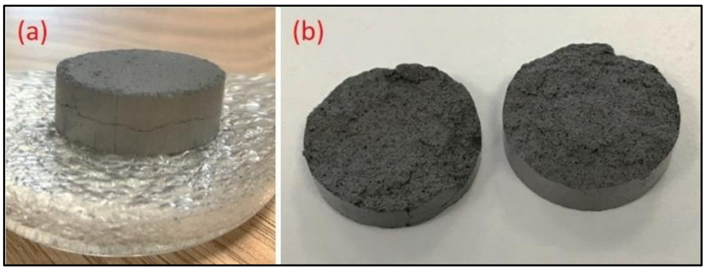

Figure 1. Soaked scaffolds in distilled water for 4 h; (a) during soaking and (b) after soaking scaffolds

In the vacuum impregnation process, which is the other salt dissolving process, wear was observed from the scaffold corners over time and this method was eliminated because the scaffolds could not keep their shape [11]. The reason for this can be shown as the insufficient pressure distribution in the sharp corners of scaffolds and exposure to excessive vibration during vacuum. The last method and the resulting method is salt dissolving in a magnetic stirrer. The purpose here is to ensure continuous circulation in pure water rather than stagnation in the scaffold during the dissolution of NaCl particles in water. All the mentioned NaCl dissolving processes were carried out in all sintering trials.

The representive image of the first trial setup used in the sintering part is presented in Figure 2. Figure 2a shows the furnace which used in experiments while Figure 2b represent semi-sintered scaffolds.

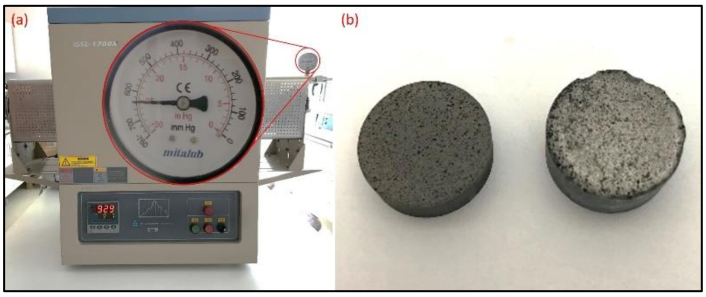

Figure 2. First sintering trial setup; (a) horizontal furnace with vacuum gauge and (b) semi-sintered scaffolds

While most of the literature studies are generally carried out in vertical furnaces under Ar gas, it is thought that the possible low vacuum melting point of NaCl particles will decrease and the salt can be removed by heat rather than dissolving in water [12]. As a result of evacuating the atmosphere in the furnace, the lower part of the scaffolds, which has alumina ceramics on the lower part of it, is sintered in micron thickness, since the scaffolds are sintered by heat conduction, while the upper part is not sintered (Fig. 2b). As another phenomenon, the possibility of air entering as a result of excess components used in the furnace design or the insufficient power of the vacuum pump. The semi-sintering phenomenon was revealed when scaffolds were cut along the section after sintering [13].

Following the unsuccessful results of the first method, Ar gas was tried to be used in the same furnace setup represented in Figure 3. In this test method, the ppm level of oxygen in the furnace (which may react with Ti) was purified first by vacuum, then with Ar gas and finally under vacuum again.

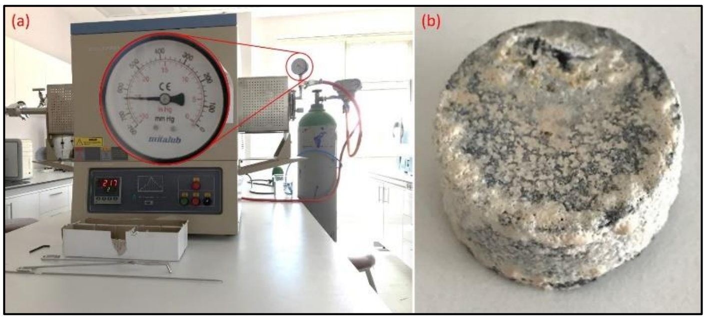

Figure 3. Second sintering trial setup; (a) horizontal furnace with Ar gases modification and (b) oxidized scaffold

As can be seen from Figure 3b, it is seen that TiO_2 and other unknown phases are obtained as a result of a reaction with oxygen on the surface and inner parts of scaffolds obtained as a result of the sintering process. It has been observed that the oxidized scaffolds obtained are the result of the fact that the furnace is horizontal due to its structure and Ar gas is heavier than air, and that oxygen is present in the upper part of the horizontal tube furnace, where it sweeps only the lower part. It is thought that there may be air leakage after vacuuming.

The last sintering stage performed by sweeping under Ar gas with a horizontal tube furnace is presented in Figure 4. Continuous sweeping operation under Ar gas was applied in this experiment to sintering scaffolds in the second trial.

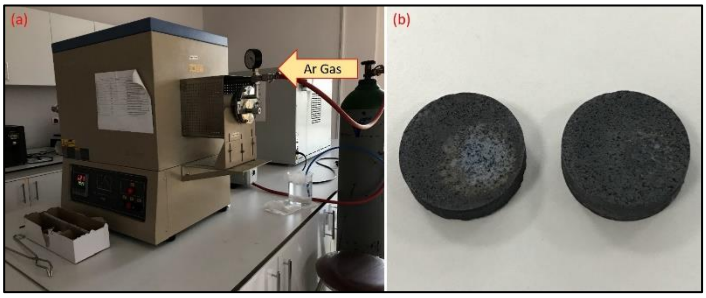

Figure 4. Third sintering trial setup; (a) horizontal furnace with Ar gases sweeping and (b) non-sintered scaffolds

The idea here can be summarized as follows: Ar gas to sweep the continuous medium by introducing into a horizontal tube furnace are intended to be permanent under Ar gas. However, another fact that was overlooked that the scaffolds were not sintered again as a result of the permanent heat environment could not be provided with an environment of continuous Ar gas (Fig. 4b). This can be shown as the absence of time to heat the scaffold during Ar gas sweeping. Because the Ar gas was cold, may not be sufficiently heated until it leaves the furnace.

Another experiment was carried out with a thinner scaffold to obtain positive results in this trial. As can be seen in Figure 5, in thin prepared scaffolds which to keep the sample completely in the Ar gas, an oxidized layer and an inward oxide structure are seen on the surface. Moreover, as the scaffolds get thinner too much, cracks are seen on the surface, which may occur from the sintering speed, atmosphere and cooling rate.

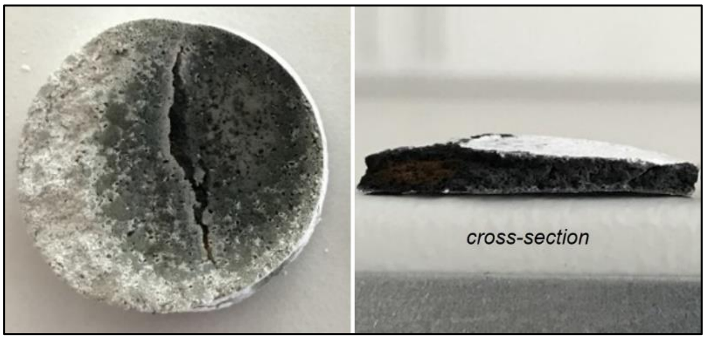

Figure 5. Scaffold which obtained with a second sintering trial with a cross-sectional image

Composite scaffolds were successfully sintered in the vertical tube furnace setup (Fig. 6), where Ar gas was used to sweep the atmosphere and was frequently used in studies [14,15].

Figure 6. Final sintering trial setup; vertical furnace with Ar gases sweeping from bottom to top and successfully sintered scaffolds

As it is known, since Ar gas is heavier than air, the inner part of the furnace is filled with Ar gas from the lower part and discharged to the top, and any problem encountered in heat transfer in the sintering process. The water used in the setup was used to reduce the excess temperature occurring at 1000 °C in the sintering stage of the scaffolds for preventing deterioration of the silicone plug which mounted on top of the furnace for insulation from oxygen.

Figure 7 shows the progress of the cracks that started in the inner parts of the scaffolds caused by excessive water dissolution during the salt dissolution process to the surface after the sintering process [16].

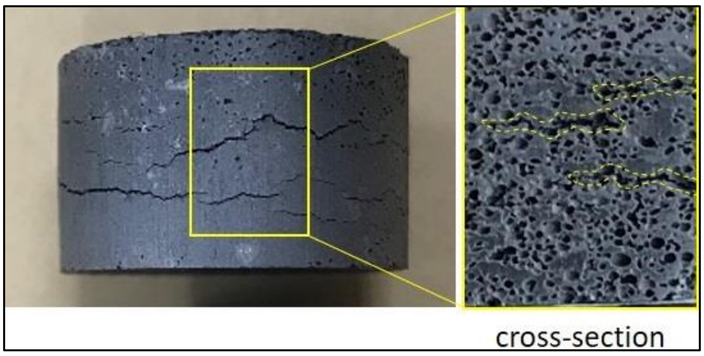

Figure 7. Horizontal cracking after sintering and cross-section

It can be concluded that distilled water can penetrate the interior of the scaffold during the NaCl leaching due to the pores interconnectivity. Moreover, the regions indicated by dashed yellow lines in the cross-sectional view prove the accuracy of this phenomenon (Fig. 7).

Figure 8 showed that excessive porogen agglomeration during the powder compaction stage. The reason for this is that during the filling of the powders into the mould, NaCl particles were collected in a certain part may a result of vibration applied to the mould several times during powder stacking into the mould.

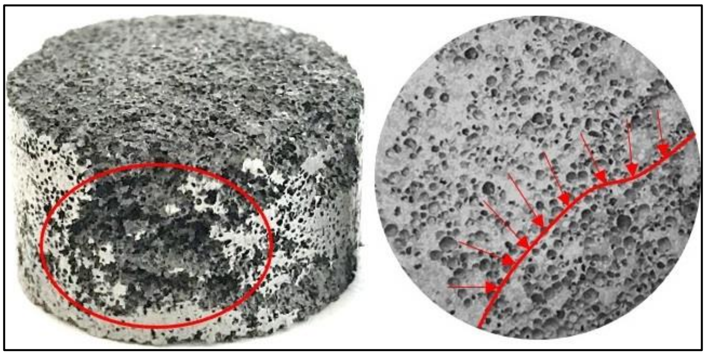

Figure 8. Excessive porogen agglomeration during powder stacking to mould

Moreover, as can be seen from the figure, a porogen orientation was seen towards the part marked with an arrow in the red area. This problem can have reduced by using a binder during the pellet preparation phase from powders to prevent the agglomeration between the NaCl particles [17].

Optical microscope (OM) images of Ti/HA composite scaffolds sintered successfully are presented in Figure 9 by different magnification, ×50, ×100 and ×200 respectively.

As can be seen from the OM results, unlike the pure and/or alloy scaffolds mentioned in the literature, micropores, as well as macropores, were found in composite scaffolds. It is thought that this may be due to the difference in the thermal expansion coefficient of Ti and HA powders. Moreover, the combination of Ti with each other to form a neck instead of covering the HA during sintering results in such results. On the other hand, micropores can form due to insufficient cold bond formation between Ti and HA as a result of the low pressing pressure during pressing. Besides the desired macropores, the obtained micropores are very important especially for materials that are considered to work in corrosive media. Because it is known that such unusual porosities can be affected more rapidly in corrosive media [15]. The reason for this is that since the contact surface of the scaffold with the corrosive media will increase, the corrosion mechanism will proceed faster. On the other hand, it has been stated by many researchers that such spontaneously formed micropores can contribute to bone tissue orientation in the use of biomaterials [18].

SEM micrographs of sintered scaffold's cell walls were given in Figure 10 with EDS analyses. EDS analyses confirmed that regions #1 were Ti particles and regions #2 were HA particles (Fig. 10). According to this, HA particles in the cell walls of the pores are located homogeneously. Such a homogenous dispersion indicates successful mixing of the powders before pressing, while at the same time evidence that enhanced biocompatible zones. On the other hand, such dense HA ceramics surrounding Ti will reduce the sinterability of Ti [11]. Therefore, the reinforcement fraction is very important because of its sinterability of Ti and the possibility of decomposition of HA particles at high temperatures during the sintering stage.

Figure 9. Optical microscopy of Ti/HA 50% porous scaffolds, ×50, ×100 and ×200 respectively

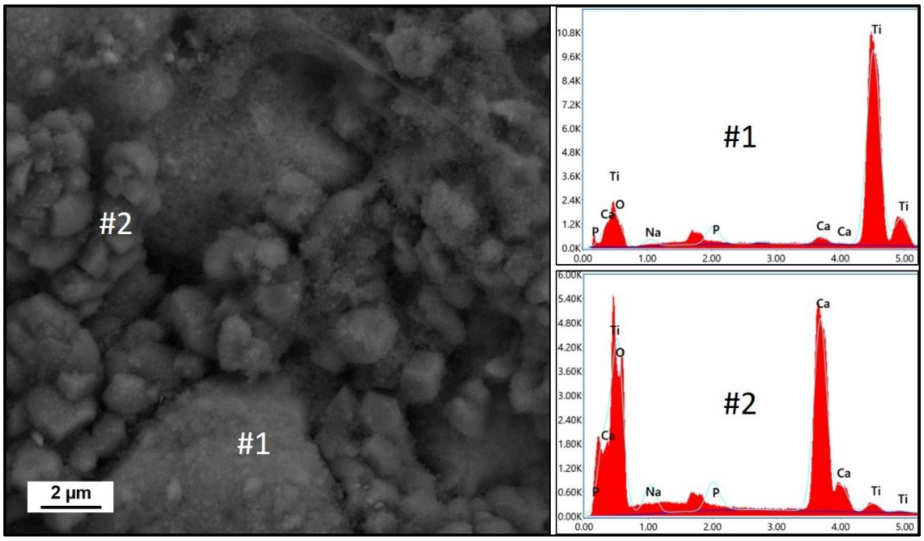

Figure 10. SEM micrograph of sintered scaffolds with different areas EDS result

4. Conclusions and Recommendations

The problems encountered in the production of Ti/HA composite scaffold and their possible causes and partial solutions were mentioned. In general, these problems can be listed as follows; i) difficulties encountered during NaCl dissolving studies applied to prevent possible phases between Ti/HA and NaCl, ii) restrictions in the use of horizontal tubes, iii) failures in the use of vacuum and Ar gas, iv) insufficient pressing pressure and v) nonhomogeneous distribution of porogens. The findings as a result of the studies have shown that successful sintering can be achieved in the vertical tube under Ar gas instead of the horizontal tube that does not have a high vacuum capacity besides basic sealing. Moreover, it has been concluded that processes such as the preparation of powder and porogen mixture, pressing and desalting are very important during or after sintering. The most important outcome of the study is considered to be a guide to other researchers who will work on the composite scaffolds.

5. Acknowledge

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References

[1]. H.L. Yao, C. Yang, Q. Yang, X.Z. Hu, M.X. Zhang, X.B. Bai, H.T. Wang and Q.Y. Chen, ''Structure, mechanical and bioactive properties of nanostructured hydroxyapatite/titania composites prepared by microwave sintering,'' Mater. Chem. Phys. vol. 241, 122340, 2020. https://doi.org/10.1016/j.matchemphys.2019.122340.

[2]. B. Dikici, M. Niinomi, M. Topuz, Y. Say, B. Aksakal, H. Yilmazer and M. Nakai, ''Synthesis and Characterization of Hydroxyapatite/TiO_2 Coatings on the β-Type Titanium Alloys with Different Sintering Parameters using Sol-Gel Method,'' Prot. Met. Phys. Chem. Surfaces. vol. 54, pp. 457–462, 2018. https://doi.org/10.1134/S2070205118030255.

[3]. K. Niespodziana, ''Synthesis and Properties of Porous Ti-20 wt.% HA Nanocomposites,'' J. Mater. Eng. Perform. vol. 28, pp. 2245–2255, 2019. https://doi.org/10.1007/s11665-019-03966-8.

[4]. D. Ragurajan, M. Golieskardi, M. Satgunam, E. Hoque, A.M.H. Ng, M. Jameelah and A. Kamal, ''Advanced 3Y-TZP bioceramic doped with Al_2O_3 and MnO_2 particles potentially for biomedical applications: study on mechanical and degradation,'' Integr. Med. Res. pp. 1–11, 2017. https://doi.org/10.1016/j.jmrt.2017.05.015.

[5]. B. Dikici, M. Niinomi, M. Topuz, S.G. Koc and M. Nakai, ''Synthesis of biphasic calcium phosphate (BCP) coatings on β–type titanium alloys reinforced with rutile-TiO_2 compounds: adhesion resistance and in-vitro corrosion,'' J. Sol-Gel Sci. Technol. vol. 87, 2018. https://doi.org/10.1007/s10971-018-4755-2.

[6]. C. Chu, X. Xue, J. Zhu and Z. Yin, ''Mechanical and biological properties of hydroxyapatite reinforced with 40 vol. % titanium particles for use as hard tissue replacement,'' J. Mater. Sci. Mater. Med. vol. 15, pp. 665–670, 2004. https://doi.org/10.1023/B:JMSM.0000030207.16887.f2.

[7]. A. Arifin, A.B. Sulong, N. Muhamad, J. Syarif and M.I. Ramli, ''Material processing of hydroxyapatite and titanium alloy (HA/Ti) composite as implant materials using powder metallurgy: A review,'' Mater. Des. vol. 55, pp. 165–175, 2014. http://dx.doi.org/10.1016/j.matdes.2013.09.045.

[8]. B. Lee, T. Lee, Y. Lee, D.J. Lee, J. Jeong, J. Yuh, S.H. Oh, H.S. Kim and C.S. Lee, ''Space-holder effect on designing pore structure and determining mechanical properties in porous titanium,'' Mater. Des. vol. 57, pp. 712–718, 2014. http://dx.doi.org/10.1016/j.matdes.2013.12.078.

[9]. B. Zhao, A.K. Gain, W. Ding, L. Zhang, X. Li and Y. Fu, ''A review on metallic porous materials: pore formation, mechanical properties, and their applications,'' Int. J. Adv. Manuf. Technol. vol. 95, pp. 2641–2659, 2018. https://doi.org/10.1007/s00170-017-1415-6.

[10]. M. Topuz, B. Dikici and M. Gavgali, ''Titanium-based composite scaffolds reinforced with hydroxyapatite-zirconia: Production, mechanical and in-vitro characterization,'' J. Mech. Behav. Biomed. Mater. vol. 118, 104480, 2021. https://doi.org/10.1016/j.jmbbm.2021.104480.

[11]. X. Fan, ''Preparation and performance of hydroxyapatite/Ti porous biocomposite scaffolds,'' Ceram. Int. vol. 45, pp. 16466–16469, 2019. https://doi.org/10.1016/j.ceramint.2019.05.178.

[12]. Y. Torres, J.J. Pavón and J.A. Rodríguez, ''Processing and characterization of porous titanium for implants by using NaCl as space holder,'' J. Mater. Process. Technol. vol. 212, pp. 1061–1069, 2012. https://doi.org/10.1016/j.jmatprotec.2011.12.015.

[13]. N.K. Tolochko, S.E. Mozzharov, I.A. Yadroitsev, T. Laoui, L. Froyen, V.I. Titov and M.B. Ignatiev, ''Balling processes during selective laser treatment of powders,'' Rapid Prototyp. J. vol. 10, pp. 78–87, 2004. https://doi.org/10.1108/13552540410526953.

[14]. P. Balbinotti, E. Gemelli, G. Buerger, S.A. de Lima, J. de Jesus, N.H.A. Camargo, V.A.R. Henriques and G.D. de A. Soares, ''Microstructure development on sintered Ti/HA biocomposites produced by powder metallurgy,'' Mater. Res. vol. 14, pp. 384–393, 2011. https://doi.org/10.1590/S1516-14392011005000044.

[15]. L. Zhang, Z.Y. He, Y.Q. Zhang, Y.H. Jiang and R. Zhou, ''Rapidly sintering of interconnected porous Ti-HA biocomposite with high strength and enhanced bioactivity,'' Mater. Sci. Eng. C. vol. 67, pp. 104–114, 2016. http://dx.doi.org/10.1016/j.msec.2016.05.001.

[16]. C. Popa, V. Simon, I. Vida-Simiti, G. Batin, V. Candea and S. Simon, ''Titanium - Hydroxyapatite porous structures for endosseous applications,'' J. Mater. Sci. Mater. Med. vol. 16, pp. 1165–1171, 2005. https://doi.org/10.1007/s10856-005-4724-5.

[17]. M.R. Raza, A.B. Sulong, N. Muhamad, M.N. Akhtar and J. Rajabi, ''Effects of binder system and processing parameters on formability of porous Ti/HA composite through powder injection molding,'' Mater. Des. vol. 87, pp. 386–392, 2015. http://dx.doi.org/10.1016/j.matdes.2015.08.031.

[18]. R.F. Prado, G.C. Esteves, E.L. De, S. Santos, D.A.G. Bueno, C.A.A. Cairo, L. Gustavo, O.D. Vasconcellos, R.S. Sagnori, F. Bastos, P. Tessarin, F.E. Oliveira, L.D.D. Oliveira, M. Fernanda, L. Villaça-Carvalho, V.A.R. Henriques, Y.R. Carvalho and L.M.R.D. Vasconcellos, ''In vitro and in vivo biological performance of porous Ti alloys prepared by powder metallurgy,'' PLoS One. vol. 13, pp. 1–22, 2018. https://doi.org/ 10.1371/journal.pone.0196169.