| JMATPRO | Journal of Advanced Materials and Processing<br>12 (45): 15-24, Winter 2024<br>https://sanad.iau.ir/journal/jmatpro<br>Doi: 10.71670/jmatpro.2024.1213562 |
|---|---|

Research Paper

# Fabrication of Polycaprolactone/Nano Hydroxyapatite/Silver Composite Scaffolds by Freeze-Drying Method

**Ghazale Salmanian, Arash Yazdani*, Esmaeil Salimi**

*Faculty of Chemical and Materials Engineering, Shahrood University of Technology, Shahrood, Iran, P.O. Box 3619995161*

**ARTICLE INFO**

*Article history:*

Received 30 July 2025
Revised: 22 September 2025
Accepted 9 December 2025
Available online 5 January 2024

*Keywords:*
*Bone tissue engineering*
*Freeze-drying*
*Hydroxyapatite*
*Bioactive.*

**ABSTRACT**

Regarding the natural structure of bone tissue, synthetic polymer-ceramic composite scaffolds have attracted great attentions for bone replacement applications. So, the present research tried to prepare nanocomposite scaffolds based on polycaprolactone (PCL) as the biocompatible and biodegradable polymeric matrix, hydroxyapatite nano (n-HA) particles as the bioactive and reinforcing filler and silver particles as the antibacterial agent. Porous scaffolds with different compositions have been prepared by using the freeze-drying method, which have been characterized by Scanning electron microscopy (SEM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), porosimetry and mechanical analysis. Additionally, the in vitro bioactivity of the scaffolds has been evaluated by soaking the samples in Simulated Body Fluid (SBF) for 21 days, where the formation of an apatite layer has been observed by SEM analysis. The compressive strength of the scaffolds as well as their bioactivity have been increased by increase in the content HA and silver particles. The obtained FESEM images have demonstrated the interconnected pores with around 73-81% porosity, as measured by the Archimedes test, which can provide appropriate conditions for osteoblast cells adhesion and proliferation. Therefore, the prepared PCL/n-HA/Ag nano-composite scaffolds can be considered as an alternative solution for the replacement of the damaged bone tissue.

**Citation**: Salmanian, Gh.; Yazdani, A.; Salimi, E. (2024). Fabrication of Polycaprolactone/Nano Hydroxyapatite/Silver Composite Scaffolds by Freeze-Drying Method, Journal of Advanced Materials and Processing, 12 (45), 15-24. Doi: 10.71670/jmatpro.2024.1213562



* **Corresponding Author:**
E-Mail: ayazdani@shahroodut.ac.ir

## 1. Introduction

Bone tissues can be regarded as composite materials consist of inorganic hydroxyapatite and organic phase (mainly collagen). Bone injuries can significantly impact the patient's quality of life. Musculoskeletal diseases such as bone fractures, osteoporosis, bone infections and tumors are rapidly increasing due to the aging of the world's population [1]. Bone grafting can be used to strengthen the existing bone or stimulate the formation of new bone tissue, which can facilitate the repair of bone fractures, replacement or reconstruction of the damaged bone [2]. However, due to the immunogenic challenges, bone grafts may not always be able to meet the demands for bone substitute materials [3]. Therefore, synthetic alternative compounds that can match the performance of the autologous bone grafts is a persistent issue in bone replacement Scaffolds are synthetic structures that can support living tissues and serve as platform for the cells adhesion, growth and proliferation [4]. There are different methods for producing scaffolds, such as sol-gel [1], freeze-drying/lyophilization [1], self-assembly, fiber bonding, solvent casting and particulate leaching (SCPL), the gas foaming method and etc.[4].

PCL is a bioresorbable polyester approved by the FDA for tissue engineering and medical devices [2]. Compared to other polymers, PCL has a long degradation period of up to four years, make it more suitable for long-term degradation applications such as bone void filler. Sobhani et al. added wollastonite powders to PCL in different concentrations to evaluate the effect of the amorphous or crystalline particles on the bioactivity of the obtained nanocomposite films [5]. Hydroxyapatite is a ceramic material that forms the mineral part of the bone, and its chemical formula is $Ca_{10}(PO4)_6(OH)_2$, in which the Ca/P ratio is equal to 1.67. One of the main advantages of using hydroxyapatite as a bone graft substitute is to create a strong bond between hydroxyapatite and bone. Considering that more than 70% of bone weight is composed of hydroxyapatite, this substance is used as the mineral phase and scaffolds reinforcement material.

In 2010, Boontharika et al. produced polycaprolactone/ hydroxyapatite composite scaffolds by using a combined solvent casting and particulate leaching method. Porosity, water absorption and compressive modulus of the scaffolds were measured. Culture of primary bone stem-cells on the PCL/HA scaffolds disclosed improved osteogenic cells differentiation compared to the cell cultured on the PCL scaffold [6]. In 2016, Sharon et al. prepared composite scaffolds by using the freeze-drying method. They applied electrical stimuli around the damaged bone to accelerate its regeneration. They added polypyrrole to polycaprolactone and hydroxyapatite to create electrical conductivity in the scaffolds. The SEM results showed the 50-250 micrometer pores size, which decreased after addition of higher amount of HA and polypyrrole. The electrical conductive PCL/HA/PPY scaffolds were recognized as a suitable candidate for bone tissue engineering applications [7]. Hoover et al. conducted a study on absorbable tricalcium phosphate scaffolds with silver particles for use in bone grafting (i.e., reconstruction of jaw and facial bones). Since there is a risk of infection in all surgical operations, the release of silver ions from the scaffolds can play an important and effective role in reducing the risk of infections and strengthen antibiotics against resistant bacteria. In continuation of evaluation of the samples, human osteoblast cells were cultured on the scaffolds to measure toxicity and proliferation of the cells. They concluded that the scaffolds porosity can increase bone conduction since the growth and proliferation of the cells had been doubled. Moreover, the samples (even the sample containing 2 wt% of silver oxide) did not cause any toxicity. The results of this research study showed that silver particles can be released from the scaffolds in a long period of time, but they have no negative effect on the biocompatibility of scaffolds [8]. In another study by our group, HA has been blended with alginate and carbon quantum dots to develop photoluminescent nanocomposites for bone filling applications [9]. Since composite scaffolds consist of different materials can represent wider and more suitable properties in terms of biocompatibility, bioactivity, and mechanical properties than polymeric scaffolds. So, this research tried to combine the bioactivity of HA with the biocompatibility of PCL to prepare porous nanocomposite scaffolds and compare their mechanical, structural and physical features.

## 2. Materials and methods

### 2.1. Materials

Polycaprolactone with an average molecular weight of Mn: 80,000 was obtained from Sigma-Aldrich. Hydroxyapatite nano powder, silver nanoparticles and acetic acid were obtained from Merck. All chemicals used were of the analytical grade and used without purification.

### 2.2. Scaffold production method

First of all, PCL was dissolved in acetic acid and stirred for several hours to create a uniform solution. Then, different quantities of the HA and Ag were added to the polymer solution while agitating the solution. Table 1 showed the weight percentage of the materials used in the preparation of scaffolds. The whole process was carried out under vigorous stirring

to inhibit agglomeration and form a homogenous solution, The final solutions were then poured into vials, covered with aluminum foils, placed in the freeze-dryer (OPERON FDB-5503), frozen at -18°C for 12 hours and then lyophilized leaving porous matrix.

**Table 1.** The quantity of the used materials

| Sample | Silver | | Nano hydroxyapatite | | Polycaprolactone | | Acetic acid |
|---|---|---|---|---|---|---|---|
| | (g) | %wt | (g) | %wt | (g) | %wt | (g) |
| **PCL** | 0 | 0 | 0 | 0 | 2.405 | 100 | 24.045 |
| **PCL/15 HA** | 0 | 0 | 0.399 | 15 | 2.261 | 85 | 22.608 |
| **PCL/20 HA** | 0 | 0 | 0.551 | 20 | 2.206 | 80 | 22.059 |
| **PCL/15 HA/3 Ag** | 0.082 | 3 | 0.410 | 15 | 2.244 | 82 | 22.436 |
| **PCL/20 HA/3 Ag** | 0.085 | 3 | 0.568 | 20 | 2.186 | 77 | 21.864 |
| **PCL/15 HA/6 Ag** | 0.169 | 6 | 0.423 | 15 | 2.225 | 79 | 22.253 |
| **PCL/20 HA/6 Ag** | 0.176 | 6 | 0.585 | 20 | 2.166 | 74 | 21.656 |

## 3. Characterization

The morphology of the prepared scaffolds as well as the size of pores were observed by field emission scanning electron microscopy (FESEM) (FESEM, Zeiss HV-300-Germany) associated with the energy dispersive X-ray analyzer (EDS, Oxford AZtec1-England). In order to identify the phases in the prepared scaffolds, x-ray diffraction technique was performed by using a machine (PW1730, PHILIPS X'Pert Pro, Netherland) and Cu as the X-ray source with a wavelength of 1.5406 A˚. Chemical bonds and functional groups in the prepared scaffolds were identified by FTIR analysis (Bruker-Tensor 27) in the range of 400 to 4000 $cm^{-1}$. The compressive strength of the cylinder-shaped scaffolds was measured by a universal device (Hounsfield Test Equipment Model HS-KS) at cross-head speed of 2 mm/min and load unit of 500 newton. Three samples were evaluated for each composite and the reported data was the average of the obtained results.

### 3.1. In-vitro bioactivity test

In order to study the *in-vitro* bioactivity of the scaffolds, they were cut into the same size and then placed in 30 cc of SBF at 37°C for 21 days. Then, the morphology of the scaffolds surface was examined by using FESEM analysis. The bioactivity of the scaffolds was evaluated through the formation of an apatite layer on their surface after being placed in SBF. The SBF solution used in this test was prepared following the usual method [10, 11].

### 3.2. Archimedes porosimetry

Due to the importance of porosity in the growth, proliferation and differentiation of cells, the percentage of the porosity in the scaffolds was measured by employing the Archimedes method. To do so, ethanol (96%) was used instead of water (due to the hydrophobic nature of PCL) for the immersion of samples. The weight of the scaffolds was measured in the dry state, and then they were placed in the weighing basket in ethanol medium to obtain the weight of the submerged state. Finally, the surface of the submerged scaffolds was dried, and the weight was measured again to obtain the weight of the saturated state. Three samples were evaluated for each composite and the reported data was the average of the obtained results. The percentage of porosity of each scaffold was calculated based on the Eq. 1 [12].

$$\text{Porosity percentage} = \frac{W_w - W_d}{W_w - W_s} \times 100 \qquad \text{Eq. 1}$$

$W_d$: The sample weight in the dry state
$W_s$: The sample weight in the saturated state
$W_w$: The sample weight in the submerged state

## 4. Results and discussion

### 4.1. SEM analysis

The porous structure of the prepared scaffolds could be seen in the SEM images in Fig. 1. Upon removal of solvent during the freeze-drying process, an interconnected porous structure was formed. In general, scaffolds with a pore size of 20 to 150 micrometers were used in tissue engineering [13]. The size of pores in the spongy bone is about 300 to 600 micrometers, while the dense bone contains pores in the range of 10 to 50 micrometers. It is known that the minimum required pore size in an implant for effective growth of bone cells is around 100 μm. The ImageJ software was used to calculate the size of the pores in the SEM images of the

prepared. In Fig. 1a, uniform distribution of pores with an average size of 116 µm could be seen. The PCL/15 HA scaffold in Fig. 1b represented 123 µm pores, where the presence of HA particles was also observed on the pores walls, distributed uniformly. The interconnection of the pores is quite evident for all samples, which is one of the requirements of scaffolds, allowing the cells to migrate and proliferate and receive the continuous flow of nutrients. The calculated pore size was around 117, 128, 135, 120 and 114 µm, derived from the samples images in Fig. 1c, d, e, f and g. To evaluate the chemical composition of the samples, EDX analysis (area scan) was employed. The obtained data in Fig. 2 confirmed the presence of calcium and phosphorus elements with the Ca/P ratio of about 1.6, which could verify the presence of HA in the composite. Other elements such as carbon, oxygen and silver were also observed, ascribing to the polymeric matrix and Ag nanoparticles in the scaffolds. In addition, gold peak was also detected, which was related to gold sputtering in the sample preparation process for SEM analysis to make the surface of the scaffolds conductive.

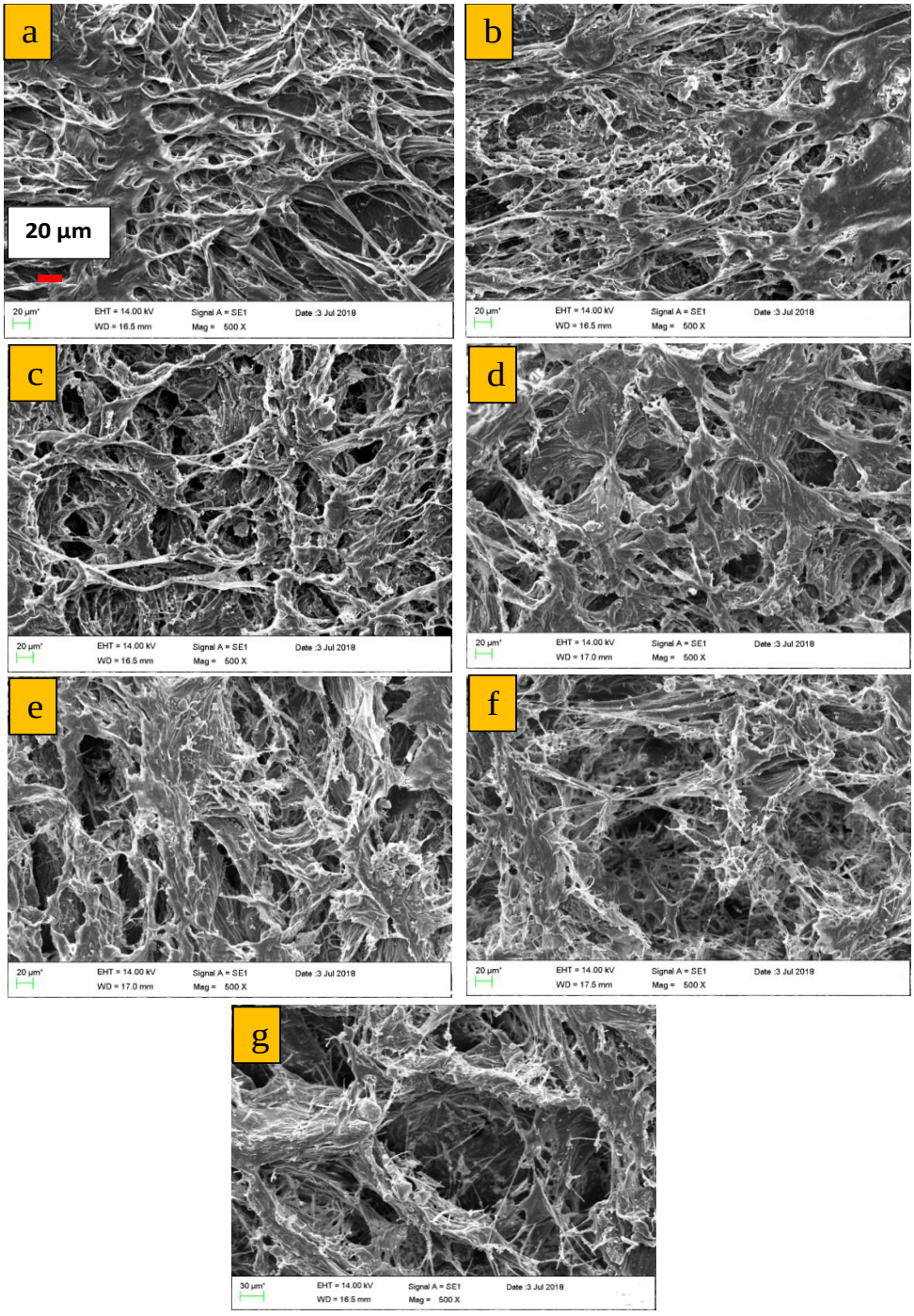


**Fig. 1.** SEM images of the a) PCL/, b) PCL/15 HA, c) PCL/20 HA, d) PCL/15 HA/3Ag, e) PCL/20 HA/3 Ag, f) PCL/15 HA/6 Ag and g) PCL/20 HA/6 Ag samples.

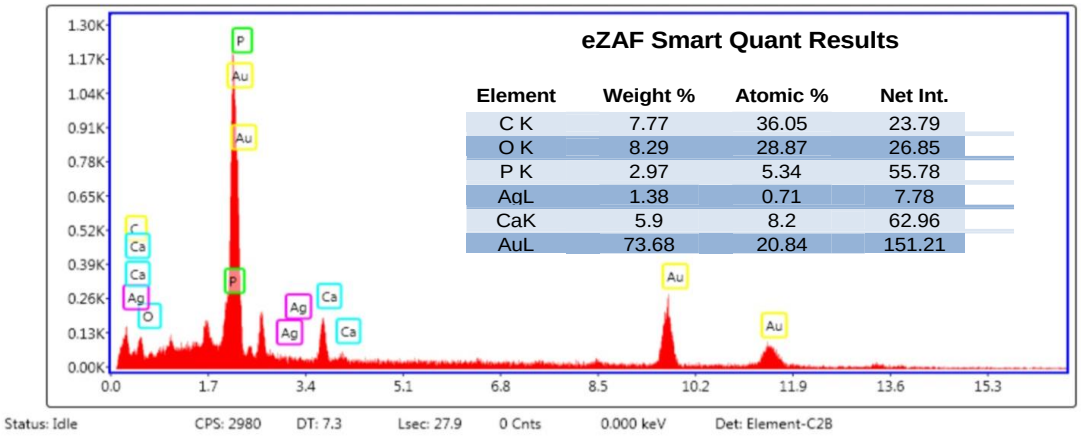


**Fig. 2.** EDX (area scan) results of the PCL/15 HA/3 Ag scaffold.

## 4.2. Bioactivity test

The SEM images obtained from the surface of the scaffolds after immersion in the SBF could be observed in Fig. 3. Fig. 3a was corresponded to the PCL sample. The absence of nano-HA particles in the composition of the scaffold was limited the growth of apatite after being placed in the BSF.

According to Kokubo et al., The formation of an apatite layer on a material's surface in SBF can predict its in-vivo bioactivity and capacity to create interfacial links with living bone [14]. This feature was not found in non-bioactive compounds [15]. Researches have highlighted the possibility of integrating bioactive ceramics and polymers to develop bioactive composites bone filler [16, 17].

In Fig. 3b, which was related to the PCL/15 HA sample, a layer of apatite with cauliflower structure could be detected, which was completely different from the HA particles in the composite. Higher magnification image in the right corner of Fig. 3b clearly indicate the precipitation of apatite crystals on the surface of scaffold. Since the quantity of nano-HA particles was increased to 20% in the PCL/20 HA scaffold, shown in Fig. 3c, more amount of the precipitated apatite could be observed, indicated the high bioactivity of the scaffold, which was in consistent with the reported results by Nirmala et al. [18], The PCL/15 HA/3 Ag sample (Fig. 2d ) with 15 wt% of HA in the composition represented lower degree of bioactivity compared with PCL/20 HA one In general, it could be said that all of the prepared scaffolds presented high in-vitro bioactivity, when an white cauliflower-like apatite layer was formed on the surface after being placed in SBF. However, more apatite crystals could nucleate on the surface of the samples with higher quantity of HA in the composition, suggested their higher bioactivity and potential in forming strong bonds with bone tissue.

## 4.3. XRD analysis

The XRD results of the prepared scaffolds could be seen in Fig. 4. The characteristic peaks of PCL were appeared around 2θ= 21.3º and 23.7º, which could be detected in all patterns. The observed peaks around 2θ= 26º, 29.3º, 32.2º, 46.6º and 49.4º could be ascribed to the crystalline HA phase in the composite, as reported in the standard JCPDS file number 09–0432 [19, 20]. It was observed that the intensity of the PCL peaks was reduced, where the quantity of HA was increased. In the XRD patterns of PCL/15 HA/3 Ag, PCL/20 HA/3 Ag, PCL/15 HA/6 Ag and PCL/20 HA/6 Ag scaffolds, new peaks about 2θ= 36.4º and 55.5º were appeared, indicated the presence of Ag in the samples.

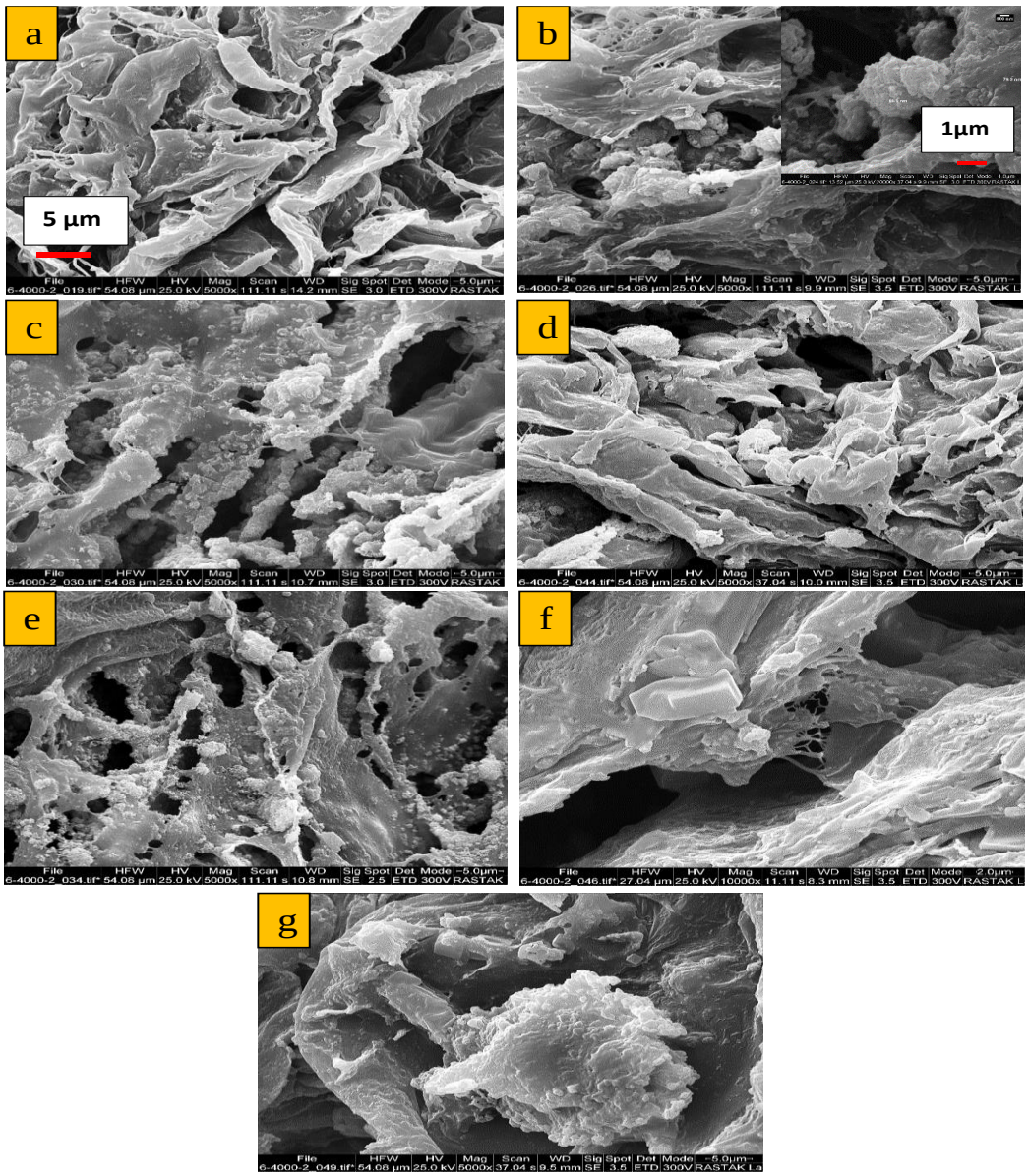


**Fig. 3.** SEM images of the scaffolds after immersion in the SBF for 21 days, a) PCL/, b) PCL/15 HA, c) PCL/20 HA, d) PCL/15 HA/3Ag, e) PCL/20 HA/3 Ag, f) PCL/15 HA/6 Ag and g) PCL/20 HA/6 Ag samples

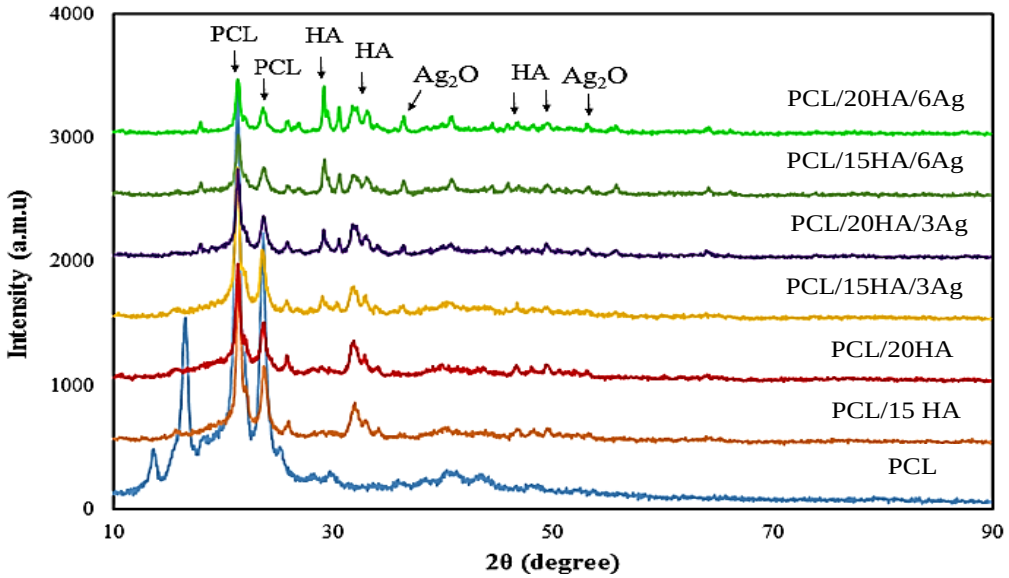


**Fig. 4.** The X-ray patterns of the prepared samples.

### 4.4. FTIR analysis

Fig. 5 shows the FTIR spectra of PCL, PCL/20 HA and PCL/20 HA/6 Ag scaffolds, where the related vibrational bonds appeared at different wavelengths are given in Table 2. So, according to the obtained data, the carbonyl bond (stretched C=O) appeared in the range of 1721 $cm^{-1}$, related to the aliphatic ester. The bonds at 1365 and 1470 $cm^{-1}$ could be ascribed to the C-H groups. The bonds at 1293, 1107 and 1396 $cm^{-1}$ could be related to the C-O stretching vibrations, while the bonds at 1044, 1065 and 1418 $cm^{-1}$ indicated the C-C groups. The corresponding C-O-C stretching vibrations observed at 960, 1238 and 1168 $cm^{-1}$. All mentioned vibrations could be related to the PCL chemical structure. Furthermore, the characteristic vibrations of phosphate group in the HA structure were appeared in the range of 600-1500 $cm^{-1}$ at 980, 961, 1031, 1042 and 1092 $cm^{-1}$. The peak observed around the frequency 671 $cm^{-1}$ can also be related to the OPO bending vibrational mode. A weak bond was seen in the range of 3565 $cm^{-1}$, which could be related to the OH groups in HA or absorbed water on the surface. It was reported that $CO_3^{2-}$ ions may be detected in the HA structure, which originate from $CO_2$ in the air. These $CO_3^{2-}$ ions can easily replace $OH^-$ or $PO_4^{2-}$ in the network; so the observed peaks in the range of 1500-1545 $cm^{-1}$ could be correspond to the carbonate groups. The appeared bonds around 862, 1222 and 1118 $cm^{-1}$ could be related to the $HPO_4^{2-}$ ions in the HA [21].

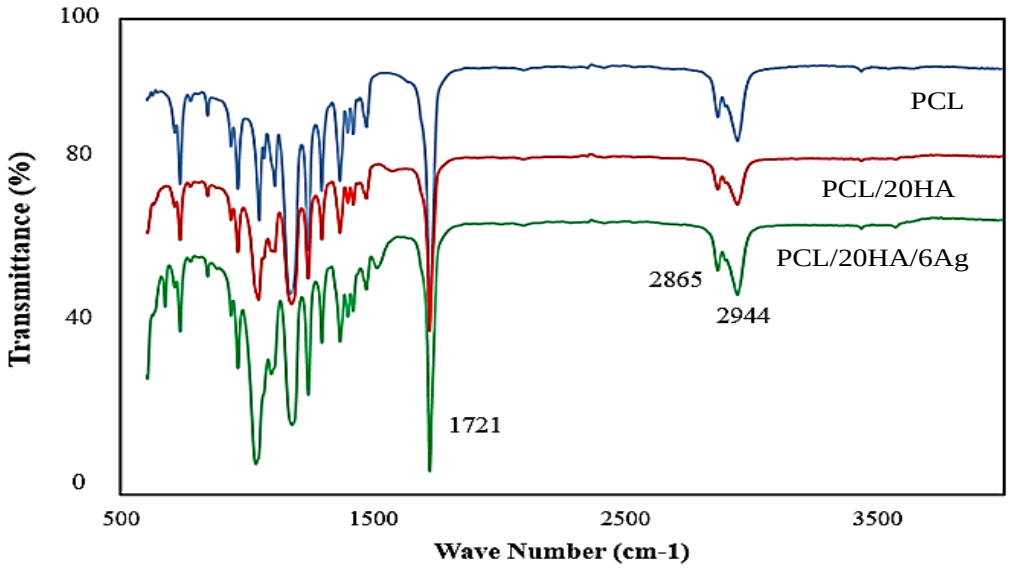


**Fig. 5.** FTIR spectra of PCL, PCL/20 HA/ and PCL/20 HA/6 Ag scaffolds.

**Table 2.** The related chemical bonds in the FTIR spectra of samples

| Kind of chemical bond | Vibration frequency ($cm^{-1}$) |
|---|---|
| $CH_2$ | 731 |
| C-O-C (Symmetric stretch) | 960 |
| C-C | 1044 |
| C-C | 1065 |
| C-O | 1107 |
| O-C-O | 1168 |
| C-O-C (Asymmetric stretch) | 1238 |
| C-C and C-O | 1293 |
| C-H | 1365 |
| C-O | 1396 |
| C-C | 1418 |
| C-H | 1470 |
| C=O | 1721 |
| $CH_2$ | 2865 |
| $CH_2$ | 2944 |
| O-H | 3436 |

### 4.5. Porosimetry analysis

The cancellous bones possess 75-85% porosity, while the dense bones have 5-10% porosity in their structure. The percentage of porosity of the prepared scaffolds obtained from the porosimetry test can be seen in Fig. 6. The results indicate that the scaffolds contain about 73-81% porosity, which is suitable for bone tissue engineering applications. According to the data in Fig. 6, it can be concluded that increase in the quantity of HA particles from 15% to 20 wt% in the scaffolds composition, reduced the percentage of scaffolds porosity. Moreover, addition of Ag particles to the scaffolds structure could have an effective role in reducing porosity of the scaffolds. These results were in agreement with the reported data by Asefnejad et al. [22], where they showed that increase in the amount of HA in the polymer structure reduced the porosity of the scaffold and increased its compressive strength.

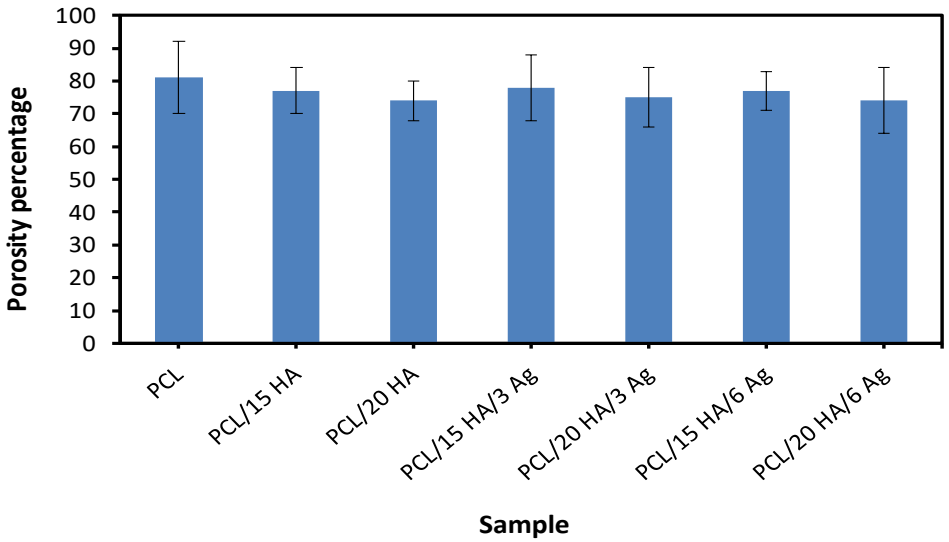


**Fig. 6.** Porosity percentage of the prepared scaffolds calculated by Archimedes method (n=3).

### 4.6. Compressive strength

The mechanical strength of the prepared samples was reported in Fig. 7. It is known that the fabricated scaffold by conventional freeze-drying methods can represent a maximum compressive strength of 0.4 MPa, which is much lower than what is found in hard tissues (10-1500 MPa) and also many soft tissues (0.4-350 MPa) [13]. It can be seen in Fig. 6 that the measured compressive strength of all samples was lower than 0.2 MPa. Moreover, the compressive strength of the scaffolds was increased with increase in the weight percentage of HA particles from 15% to 20%. The PCL/20 HA/6 Ag sample with 20 wt% HA and 6 wt% Ag had the highest strength among other samples, which could be related to the higher amount of inorganic phase in the composite. However, the PCL/20 HA/3 Ag sample with 20 wt% HA and 3 wt% Ag showed a low value of mechanical strength. The agglomeration of nanoparticles (as viewed by using microscope) in the composite structure could be the regarded as the main reason for this deterioration.

It is worth mentioning that there are two types of damage, *i.e.*, adhesion and cohesion, and their occurrence is strongly correlated to the homogeneous dispersion of particles in the matrix. Therefore, the adhesion strength can be affected by physical and chemical reactions between the polymer and filler materials. It is well known that the due to the small size of nanoparticles, they possess higher surface area with more active sites, which improve their interactions with the polymeric matrix. So, the shear strength of nanocomposites increase by crease in the content of fillers. However, inadequate dispersion within the composite matrix and agglomeration of the fillers may have led to weaker interface bonding between the matrix and the fillers and decrease the shear strength of specimen.

In conclusion, it could be suggested that the fabricated porous scaffolds via freeze-drying method can not withstand the comprehensive load in bone tissues, but they can be an appropriate candidate for bone filling applications.

The ideal synthetic bone filling material should possess a low cost, be simple to apply, facilitate the development of an osteoconductive and osteoinductive extracellular matrix microenvironment. Besides the exceptional mechanical features, they have to be biocompatible and capable of facilitating cell adhesion and proliferation. So, the obtained porous structure in this study can fill the bone cavity for a short time and motivate the immigration and regeneration of bone cells. Moreover, the release of Ag ions a hinder the progress of infection in the defect.

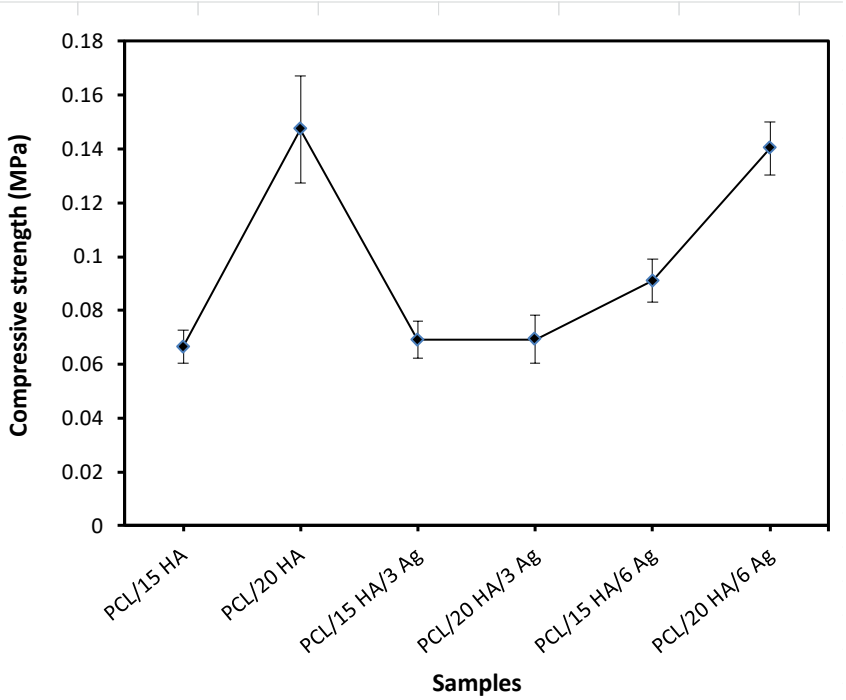


**Fig. 7.** Compressive strength of the prepared scaffolds (n=3).

## 5. Conclusion

In the present research, nano composite scaffolds of PCL/HA/Ag were prepared by using the freeze-drying method and were investigated in terms of physical, chemical, mechanical, morphology and bioactivity by using various analyses. The final results and discussions can be summarized briefly, as follows:

1. The results of the mechanical evaluation showed that the prepared scaffolds possess low compressive strength, which is not suitable for repairing bones with large voids or damaged area, as well as load bearing applications, however, they can be a potential candidate to fill small injuries in the bone tissue.
2. The SEM images exhibited porous scaffold with interconnected pores with non-uniform surface that is suitable for cell adhesion. Moreover, the average size of these pores was around 114-135 μm, which is suitable for cell growth and proliferation.
3. The results of the Archimedes porosimetry test showed 73-81% porosity in the scaffolds structure, which decreased by increase in the content of HA and Ag nano particles.
4. The results of the in-vitro bioactivity analysis disclosed highly bioactive scaffolds, where the precipitated apatite crystals were found on the surface upon placing the scaffolds in the SBF solution for 21 days. It was observed in the SEM images that the samples with higher amount of HA had higher bioactivity.
5. The PCL/20 HA/6 Ag sample (PCL/20 wt% HA/6 wt% Ag) can be suggested as a suitable candidate for bone tissue engineering applications in terms of bioactivity and compressive strength.

## Acknowledgment

The author would like to appreciate all supports from the Shahrood University of Technology.

**Competing interests:** The authors declare no competing interests.

**Data Availability Statement**: The data that support the findings of this study are available on request from the corresponding author.

## 6. References

[1] L. Roseti, V. Parisi, M. Petretta, C. Cavallo, G. Desando, I. Bartolotti, B. Grigolo, Scaffolds for Bone Tissue Engineering: State of the art and new perspectives, Materials Science and Engineering: C 78 (2017) 1246-1262. https://doi.org/https://doi.org/10.1016/j.msec.2017.05.017.

[2] L. Polo-Corrales, M. Latorre-Esteves, J. Ramirez-Vick, Scaffold Design for Bone Regeneration, Journal of nanoscience and nanotechnology 14 (2014) 15-56. https://doi.org/10.1166/jnn.2014.9127.

[3] V. Marx, Organs from the lab, Nature 522(7556) (2015) 373-377. https://doi.org/10.1038/522373a.

[4] Z. Hashemi, M. Soleimani, Tissue Engineering Scaffolds: History, Types and Construction Methods, Journal of Iranian Anatomical Sciences (2011).

[5] A. sobhani, E. Salimi, Nanocomposite films of polycaprolactone and amorphous/sintered wollastonite nanoparticles for potential biomedical applications, Ceramics International 50 (2024). https://doi.org/10.1016/j.ceramint.2024.04.417.

[6] B. Chuenjitkuntaworn, W. Inrung, D. Damrongsri, K. Mekaapiruk, P. Supaphol, P. Pavasant Polycaprolactone/hydroxyapatite composite

scaffolds: Preparation, characterization, and in vitro and in vivo biological responses of human primary bone cells, Journal of Biomedical Materials Research Part A 94A(1) (2010) 241-251. https://doi.org/https://doi.org/10.1002/jbm.a.32657.
[7] S. Ufere, N. Sultana Phd Ceng Csci, Fabrication and characterization of pcl/ha/ppy composite scaffold using freeze-drying technique, Jurnal Teknologi Vol. 78 (2016). https://doi.org/10.11113/jt.v78.10072.
[8] S. Hoover, S. Tarafder, A. Bandyopadhyay, S. Bose, Silver doped resorbable tricalcium phosphate scaffolds for bone graft applications, Materials Science and Engineering: C 79 (2017). https://doi.org/10.1016/j.msec.2017.04.132.
[9] A. Kargar nigje, E. Salimi, M.J. Molaei, M. Ghatee, A potential trackable bone filler: Preparation and characterization, International Journal of Applied Ceramic Technology 18(6) (2021) 1921-1929. https://doi.org/https://doi.org/10.1111/ijac.13832.
[10] M.I. Sabir, X. Xu, L. Li, A review on biodegradable polymeric materials for bone tissue engineering applications, Journal of materials science 44(21) (2009) 5713-5724. https://doi.org/10.1007/s10853-009-3770-7.
[11] F. Yang, J. Wolke, J.A. Jansen, Biomimetic Calcium Phosphate Coating on Electrospun Poly(ε-caprolactone) Scaffolds for Bone Tissue Engineering, Chemical Engineering Journal 137 (2008) 154-161. https://doi.org/10.1016/j.cej.2007.07.076.
[12] D.R. Askeland, P.P. Fulay, W.J. Wright, The Science and Engineering of Materials, SI Edition, Cengage Learning2011.
[13] Q.L. Loh, C. Choong, Three-Dimensional Scaffolds for Tissue Engineering Applications: Role of Porosity and Pore Size, Tissue engineering. Part B, Reviews 19 (2013). https://doi.org/10.1089/ten.TEB.2012.0437.
[14] T. Kokubo, S. Ito, Z.T. Huang, T. Hayashi, S. Sakka, T. Kitsugi, T. Yamamuro, Ca, P-rich layer formed on high-strength bioactive glass-ceramic A-W, Journal of Biomedical Materials Research 24(3) (1990) 331-343. https://doi.org/https://doi.org/10.1002/jbm.820240306.
[15] L.L. Hench, H.A. Paschall, Histochemical responses at a biomaterial's interface, Journal of Biomedical Materials Research 8(3) (1974) 49-64. https://doi.org/https://doi.org/10.1002/jbm.820080307.
[16] A.H. Hoveidaei, M. Sadat-Shojai, S. Mosalamiaghili, S.R. Salarikia, H. Roghani-shahraki, R. Ghaderpanah, M.H. Ersi, J.D. Conway, Nano-hydroxyapatite structures for bone regenerative medicine: Cell-material interaction, Bone 179 (2024) 116956. https://doi.org/https://doi.org/10.1016/j.bone.2023.116956.
[17] m. khorshidsavar, m. khakbaz, g. mir mohammad sadeghi, m. moradi, Porous nanocomposite scaffolds prepared from gelatin and hydroxyapatite for bone tissue engineering: direct mixing and biomimetic, Journal of Textiles and Polymers 11(1) (2023) 13-26. https://doi.org/10.48302/jtp.2023.361289.1255.
[18] R. Nirmala, K.T. Nam, D.K. Park, B. Woo-il, R. Navamathavan, H.Y. Kim, Structural, thermal, mechanical and bioactivity evaluation of silver-loaded bovine bone hydroxyapatite grafted poly (ε-caprolactone) nanofibers via electrospinning, Surface and Coatings Technology 205(1) (2010) 174-181.
[19] E. Salimi, Development of bioactive sodium alginate/sulfonated polyether ether ketone/hydroxyapatite nanocomposites: Synthesis and in-vitro studies, Carbohydrate Polymers 267 (2021) 118236. https://doi.org/10.1016/j.carbpol.2021.118236.
[20] S. Abd-Khorsand, S. Saber-Samandari, S. Saber-Samandari, Development of nanocomposite scaffolds based on TiO2 doped in grafted chitosan/hydroxyapatite by freeze drying method and evaluation of biocompatibility, International Journal of Biological Macromolecules 101 (2017) 51-58. https://doi.org/10.1016/j.ijbiomac.2017.03.067.
[21] D. Verma, K. Katti, D. Katti, Bioactivity in in situ hydroxyapatite–polycaprolactone composites, Journal of Biomedical Materials Research Part A 78A(4) (2006) 772-780. https://doi.org/https://doi.org/10.1002/jbm.a.30774.
[22] A. Asefnejad, A. Behnamghader, M.T. Khorasani, B. Farsad, Polyurethane/fluor-hydroxyapatite nanocomposite scaffolds for bone tissue engineering. Part I: morphological, physical, and mechanical characterization, International Journal of Nanomedicine 6 (2011) 93-100. https://doi.org/10.2147/ijn.s13385.