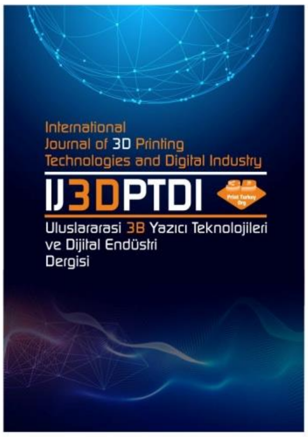

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DESIGN AND STRUCTURAL ANALYSIS OF 3D-PRINTED POROUS POLYLACTIC ACID/HYDROXYAPATITE SCAFFOLDS

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ABSTRACT

Different designs of three-dimensional (3D) structures have gained increasingly significant in bone tissue engineering. For scaffolds, having appropriate porosity and adequate mechanical properties is crucial. The porosity and mechanical properties of scaffolds are higly influenced by their 3D modeled design. By evaluating the mechanical properties of scaffolds with various designs, it can be confirmed that they could serve as an important platform for the regeneration of damaged bone tissue. In this study, a diverse range of unit cells and lattice structures featuring different pore structures of polylactic acid (PLA)/hydroxyapatite (HA) based scaffolds were modeled and designed. Structural analyses of the designed models were conducted in a simulation environment and their mechanical properties were compared with similar studies. The results suggest that PLA/HA-based scaffolds with different designs hold high potential for applications in bone tissue engineering.

Keywords: Polylactic Acid, Scaffold, Design, Structural Analysis, Mechanical Strength.

1. INTRODUCTION

Bone tissue defects that occur owing to many reasons such as trauma, metabolic disorders, and aging are important health problems that greatly affect the patients' quality of life [1]. Bone is one of the most commonly transplanted tissue for biomedical therapy [2]. However, bone transplantation poses a significant clinical difficulty in practice due to its many disadvantages, such as causing new bone damage in the body and requiring a second surgical procedure for the patient, inability to obtain sufficient grafts for the treatment of major damage, and difficulties in shaping the graft. At this point, scaffolds that have emerged in order to overcome the limitations of existing methods aim at functional bone regeneration based on the interaction of biomaterials, cells and biosignal molecules [3].

In the fabrication of scaffolds, in order to best imitate bone, which is a natural composite material, biopolymers with biocompatible and biodegradable properties and bioactive ceramics, that have the ability to bond with living bone by creating an apatite interface layer with their osteoinductive properties are used together to make them structurally more compatible materials are being developed. Polylactic acid (PLA) is a polymeric scaffold material that has been widely investigated for bone tissue applications and has been approved by the US Food and Drug Administration (FDA) for clinical trials [2,5]. PLA attracts much attention with its excellent biocompatibility, bioabsorbability and biodegradability with non-toxic by-products [2, 6-9]. Additionally, it has multifunctional applications in different fields such as drug delivery systems, antimicrobial products, medical implant devices, and 3D printed scaffold manufacturing for bone tissue applications [9].

However, PLA's lack of ability to facilitate cell adhesion and proliferation on its surface due to its weak cellular binding ability restricts its wider applications [2, 5]. In addition, the low mechanical strength of polymeric materials is insufficient to transmit mechanical force in load-bearing applications. In studies conducted to overcome this situation, the surface properties of the produced scaffolds were examined and it was determined that they needed a hard surface for the attachment and proliferation of anchorage-dependent primary cells, and when they were reinforced with calcium phosphate-based bioceramic materials, modification of the surface topology and improved mechanical strength were determined. Hydroxyapatites (HA), which are frequently used among calcium phosphates, are promising as scaffold materials with their excellent biological behavior such as high osteoconductivity and osteoinductivity, as well as promoting cell attachment of scaffolds, exhibiting bioactive properties with their reactive surfaces, and high osteoconductivity and osteoinductivity [2, 13].

Lattice structures are 3D structures consisting of unit cells that repeat each other regularly and are most preferred in the biomedical field today [14]. When the studies on additive manufacturing are examined, it has been seen that the interest in lattice structures has increased in recent years due to their high strength/weight ratio and homogeneous porosity distribution [15]. Computer-aided design programs such as AutoCAD, SolidWorks and 3DS are used for 3D modeling of these lattice structures with complex geometries [16-17]. Structures with mechanical properties close to native bone and in which porosity can be controlled easily developed using the additive manufacturing method [18]. Li et al. [19] produced Ti6Al4V implants with a honeycomb lattice structure using the electron beam melting method, which is one of the additive manufacturing method. According to their results, they stated that the produced implants have high strength with an elasticity modulus close to that of human bone and can be used in implant applications. However, the most advanced simulation method used in static analysis in bone tissue design is the finite element model. In this model, ANSYS analyzes that can create approximate values close to reality come to the fore. In the study conducted by Chethan et al. [20], static analyzes were carried out with ANSYS finite element software on the hip prosthesis stem design, and the optimum material and geometric design were determined by determining the tensile deformations.

Production of properly designed scaffolds using appropriate materials is critical for bone tissue applications. Although porosity, pore size and pore morphology have a significant effect, the scaffolds produced with a porous structure also allow bone growth and attachment [21-22]. In addition, scaffolds with inter-connected and highly porous structure can be obtained by a wide variety of methods such as solvent casting, particle leaching, gas foaming, solvent evaporation, laser beam processing and freeze drying [22-23]. However, the fact that the scaffolds produced have a closed pore morphology is a disadvantage of traditional methods. Moreover, it has been observed that PLA-based scaffolds produced with these methods have less internal connections between pores due to their low degradation rate, poor permeability and non-uniform structure [23]. On the other hand, 3D printing method enables the rapid, accurate and reliable fabrication of scaffolds that can fill the defective area in the desired geometries, where control of the pore size in the tissue scaffolds, homogeneous porosity distribution and an open porosity structure are obtained [4, 24]. Designing alternative structures with improved mechanical properties is very important for bone tissue applications. Structural analysis of the scaffolds designed with these features can be carried out in a simulation environment and structures with properties similar to natural bone can be obtained in a practical way. The predictability of the calculations made with this method is quite advantageous as it can obtain results close to experimental studies.

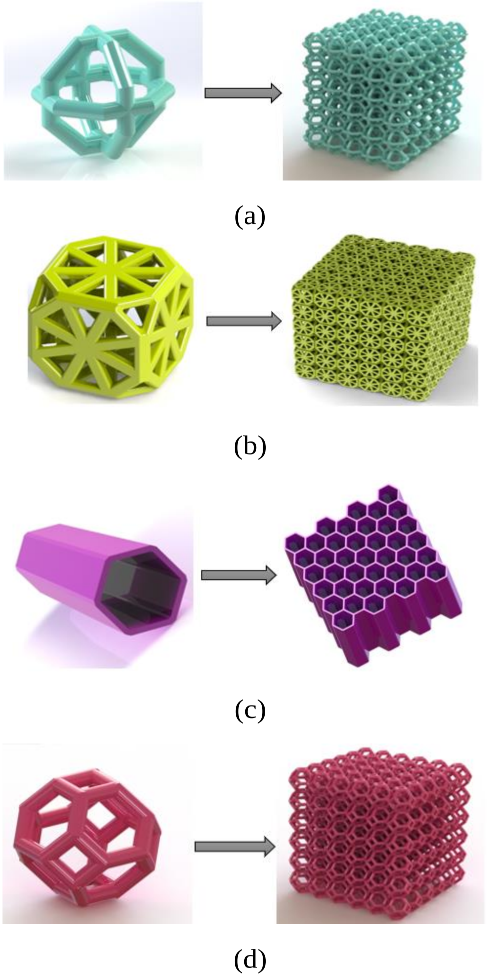
In this study, different designs of PLA/HA-based tscaffolds for use in bone tissue applications were obtained by modeling four different unit cell and lattice structures. The created models were defined in ANSYS Workbench software, static analyzes were carried out and the results were examined comparatively with similar studies.

2. MATERIAL AND METHODS

2.1. Three Dimensional (3D) Modeling

In this study, 3D modeling was performed using SolidWorks software to create four different unit cell models and lattice structures for bone tissue applications. Octagonal unit cell diameter is

0.813 mm, kelvin unit cell diameter is 0.748 mm, and honeycomb unit cell wall thickness is 0.362 mm [25]. The wall thickness of the unit cell in octagonal design was determined as 0.5 mm and the strut length was determined as 1.686 mm. The lattice structure models created by combining unit cells were then transferred to Ansys Workbench software. The appearance of the created models is shown in Figure 1.


(a)

(b)

(c)

(d)

Figure 1. 3D unit cell and lattice structures; (a) octagonal, (b) angular-octagonal, (c) honeycomb, (d) kelvin model.

2.2. Finite Element Model

To finite element analysis, PLA and PLA/HA combinations were determined as linear and isotropic, and are shown in Table 1. In order to see and compare the effect of the biomaterials, material definitions as 100 %, 75 % PLA and 25 % HA by weight, respectively, were defined separately on these models via ANSYS Workbench. After creating material properties for 3D design models, mesh assignment was carried out. To obtain the optimum design, first the stress and deformation values on the unit cells were evaluated. Optimization studies were carried out on the models to determine the most appropriate element sizes. As a result of the studies, the element size of the honeycomb and octagonal models was determined as 0.181 mm, while the element size of the octagonal model was determined as 0.4 mm. In addition, the results were examined by comparing them with finite element studies on similar models [26, 27].

Table 1. Mechanical properties of materials.

Properties	PLA	HA	PLA/HA
Density (g/cm^3)	1.24	3,16	1.72
Elastic Modulus (MPa)	1280	7000	2710
Poison Rate	0.36	0.27	0.34
Yield strength (MPa)	70	-	52.5
Shear Modulus (MPa)	470.59	2755.9	1031.1
Reference	[26]	[27]	

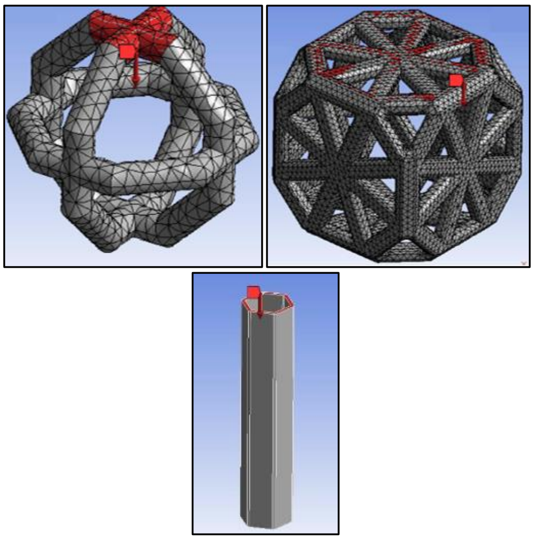


Figure 2. 20 N force applied on the mesh unit cells.

Boundary conditions are defined for 3D finite element models as shown in Figure 2. First of all, the optimum design was determined by analyzing unit cells with PLA and PLA/HA combinations to see the effect of the design. After applying 20 N as a preliminary force to force the unit cells in the compression direction, the force value to be applied on the optimum design was taken as 500 N. It was aimed to evaluate the stress values by applying axial load to the created bone models, considering that the average human weight is 80 kg. Unit cells are fixed by restricting their movements at the bottom and the compression force is defined from the top.

3. EXPERIMENTAL FINDINGS

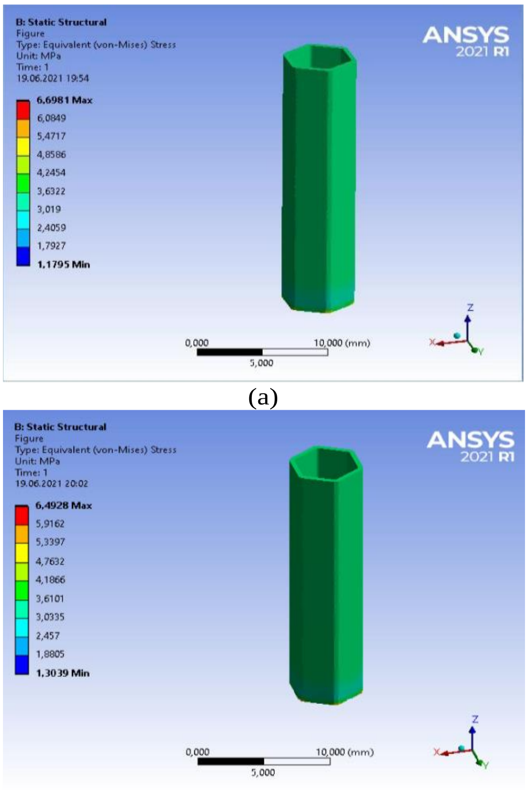
In the finite element analysis results, the Von Misses stress distribution was determined to evaluate the material strength as a criterion and the total deformation amount was determined to determine the rigidity. The obtained data are given in Table 2.

Table 2. Material strength values obtained from finite element analysis results.

Birim hücreler	Malzeme	Total deformasyon (mm)	Von-Mises (MPa)
Honeycomb	%100PLA	0.0679	6.69
	%75PLA %25HA	0.032	6.49
Octagonal	%100PLA	0.1958	53.02
	%75PLA %25HA	0.0927	53.13
Angular-octagonal	%100PLA	0.455	140.09
	%75PLA %25HA	0.2182	141.1

Among three different unit cells, the highest Von Mises stress value obtained when PLA material defined was calculated as 140.09 MPa in the angular-octagonal model. It is accepted that the probability of fracture increases with the maximum Von Mises stresses obtained by finite element analysis. Considering the finite element analysis unit cell results, the honeycomb unit cell has the lowest Von Mises stress value. The lowest stress value in the PLA honeycomb model is 6.69 MPa. In the PLA/HA honeycomb model, the lowest Von Mises stress value decreases to 6,493 MPa. It was observed that the Von Mises stress value increased to 53.02 MPa in the PLA octagonal model and 53.13 MPa in the PLA/HA octagonal model. While the Von Mises stress was 140.09 MPa in the PLA octagonal model, this value increased to 141.1 MPa in the PLA-HA octagonal model.

The geometry of bone tissues greatly affects their mechanical properties and behavior. For this reason, comparisons were made by looking at the total deformations on the models. While the total deformation was 0.1958 mm in the PLA octagonal model, the total deformation was reduced and calculated as 0.0927 mm in the PLA/HA octagonal model. The total deformation is 0.455 mm in the PLA angular-octagonal model and 0.2182 mm in the PLA/HA model. Finally, the total deformation was 0.0679 mm in the PLA honeycomb model and 0.032 mm in the PLA/HA model. Compared to other models, the lowest total deformation value was obtained in the honeycomb model. According to Von Mises criteria and total deformation results, the optimum and most critical model was determined to be the honeycomb model.

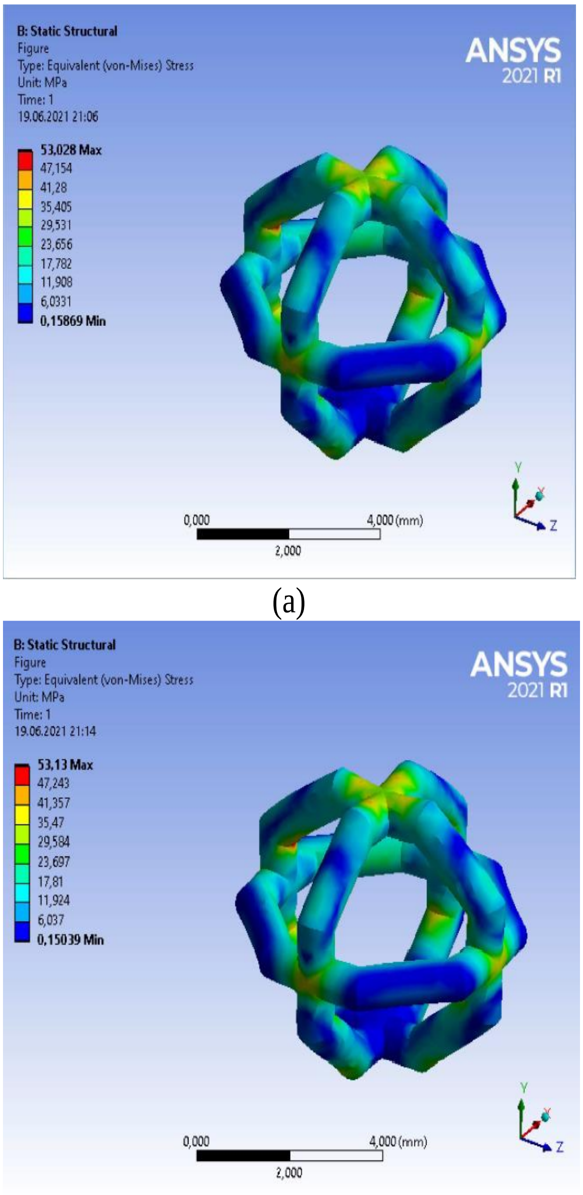


(a)

(b)

Figure 3. Honeycomb unit cell (a) %100 PLA (b) %75 PLA- %25 HA.

Based on this, 500 N force was applied on the honeycomb lattice structure. Figures 3, 4 and 5 show Von Mises stress distributions on the models. Figure 6 shows the total deformation values when 500 N force is applied (a) PLA honeycomb lattice structure (b) 75% PLA-25% HA added honeycomb lattice structure. In the PLA honeycomb lattice structure, the Von Mises stress value was found to be 3,543 MPa and the total deformation value was 0.043 mm. In the PLA/HA honeycomb lattice structure, the Von Mises stress value is 3.513 MPa and the total deformation value is 0.020 mm. When evaluated in terms of rigidity and strength, it was determined that the use of PLA alone was insufficient in all models.



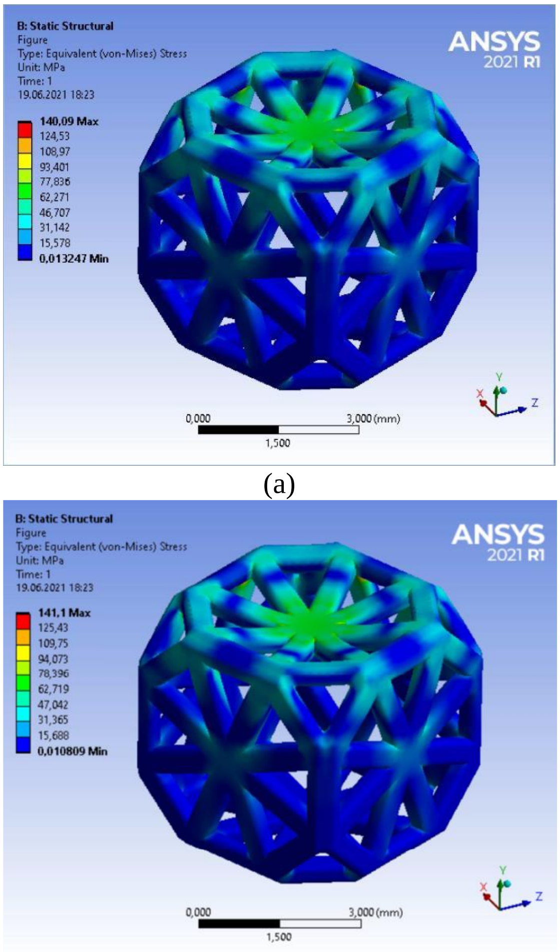
(a)

(b)

Figure 4. Octagonal unit cell (a) %100 PLA (b) %75 PLA- %25 HA.

4. DISCUSSION

Today, 3D printing method is one of the methods that attracts attention in bone tissue applications. Adapting computer-aided design to bone tissue engineering with 3D printing technology greatly increases production precision and repeatability compared to traditional methods. It is very advantageous that the 3D printing method provides precise modeling ability of bone tissue models and high efficiency production [29].

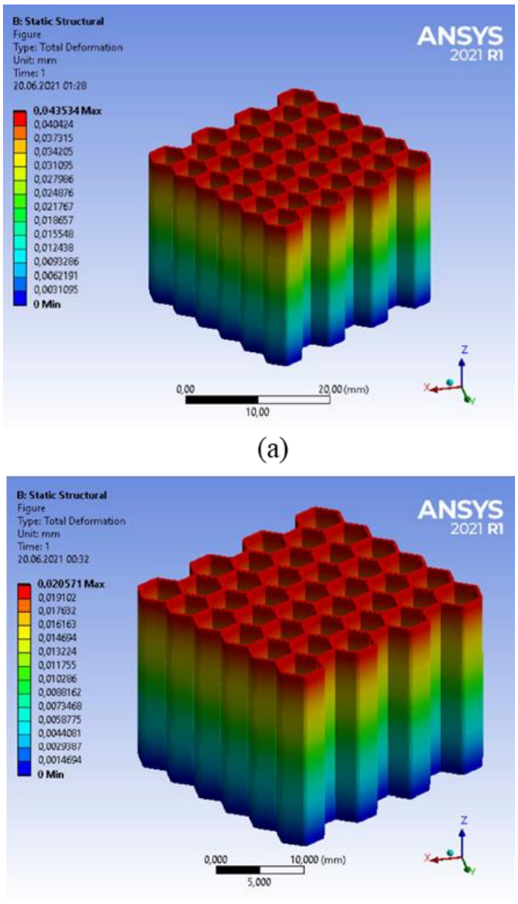


(a)

(b)

Figure 5. Angular-octagonal unit cell (a) %100 PLA (b) %75 PLA- %25 HA.

Within the scope of this study, the expansion of the usage areas of 3D printers and their suitability in bone tissue engineering applications were investigated. In this regard, modeling and analysis were carried out using the finite element analysis method. In the designed models, the effect of both the design and the biomaterials used on the design was evaluated by taking into account the total deformation and stress values obtained. 3D printing methods allow the manufactured scaffolds to imitate natural bone, thanks to the high controllability of the structures. Comparing and evaluating the results of analyzes designed in a simulation environment provides advantages in terms of cost and optimization. During bone design and fabrication, the selection of biomaterials, internal structure, pore diameter and porosity ratio, anatomical external geometry, permeability and selection of printing techniques appropriate to the design are very important. In addition, in order to obtain good results on models in 3D printing, layer thickness, extrusion speed, nozzle exit pressure, viscosity of the material to be used as bioink and table temperature are the parameters that need to be taken into consideration. Increasing printing speed or layer thickness may cause deterioration in surface quality. Similarly, if these parameters cannot be adjusted appropriately, negative situations such as premature cooling of the filament and weakening of the structure on the part may be observed [28].



(a)

(b)

Şekil 6. The total deformation values measured by applying a 500 N force to (a) the PLA honeycomb lattice structure and (b) the 75% PLA-25% HA added honeycomb lattice structure.

In the study by Adhikari et al. [30], it was reported that the optimum viscosity in 3D printed alginate/chitosan/HA scaffolds prevented the collapse of HA nanoparticles, the lateral pores of the scaffolds protected the integrity of the scaffold, and the produced scaffolds were suitable for 3D printing. Moreover, viscous inks are also suitable for maintaining the height of the scaffolds after printing [31], although it is known that extrusion becomes difficult and uninterrupted ink flow is disrupted with high viscosity bioinks. Since trouble-free extrusion is essential for production, the extrudability of the designed structure is extremely important. In the study, it can be said that the HA-containing design is more viscous than the 100% PLA-based design. This is because the increase in HA concentration increases the viscosity of the bioink. Therefore, for extrusion of high viscosity inks with HA loadings, the printing pressure should be higher than that of PLA-based design [30].

In addition to 3D design, determining the mechanical load range is very important. Bone tissue is constantly exposed to mechanical loads at varying intervals. As a result, a certain tension occurs both in the bone structure and in the tissue. For this reason, balancing the ductility of the polymer material and the brittleness of the ceramic material Ca-P-based HA is of great mechanical and biological importance [32]. On the other hand, some errors are encountered during production in the melt deposition modeling (FDM) method, which is another additive manufacturing method. One of these errors is that the parts with low thickness have low strength and the diameter of the nozzle through which the material flows also affects this. In general, ribs, which are support materials, break [33]. Feds break when removing material or during the initial assembly phase. As a solution to this situation, the thickness of the ribs should be made 1/3-1/2 thicker than the general wall thickness [34]. When rib thicknesses are made at these ratios, collapse on the outer surface of the rib area can be prevented while the part is produced in the injection machine.

It is known that there are two parameters for a cell-based bone implantation: the skeletal design and the cell assembly of this design [35]. In bone tissue engineering applications, PLA is a biomaterial with high biocompatibility and FDA approval for clinical applications. However, HA addition to PLA provides a dynamic 3D bone tissue by increasing the activation of osteoblast cells. In a study, it was reported that more surface roughness was obtained in HA-containing scaffolds compared to scaffolds designed with 100% PLA [32]. Increasing the surface roughness and expanding the surface area of the produced tissue scaffolds to adhere to living cells helps to increase the cell association rate. It has also been reported that FDM technology, which has low processing costs, can be successful in PLLA/HA hybrid scaffolds with up to a maximum of 30% ceramic contribution and causes relatively weak osteoblast activity [35]. Studies have shown that smaller macropores and higher fracture energies can be achieved by increasing the gelatin ratio in gelatin-containing tissue scaffolds when performing 3D printing [36-37]. At the same time, it has been determined that this method allows the designed model to be successfully obtained by providing the ability to print at appropriate viscosity values. In another investigation [38], it was found that a PLA scaffold with 15% HA by weight, created using an extrusion-based 3D printing method, could withstand a maximum stress of 3 MPa at 70°C. Research conducted by Ziminia et al. reported [39] that a PLA scaffold with a 15% weight additive exhibited a maximum strength of 2.47 ± 0.19 MPa, which decreased to 1.41 ± 0.37 MPa upon increasing the HA content to 20% by weight. Comparable compressive strength values were observed in chitosan/gelatin/HA 3D scaffolds, which demonstrated a strength of 4.16 MPa [40].

5. CONCLUSION

Finite Element Analysis is a well-respected method for biomechanical evaluations, offering significant advantages due to its capacity to produce predictive outcomes that closely align with experimental research findings. This study focuses the design and fabrication of tissue engineering scaffolds through the integration of computational strategies with 3D printing technologies. We conducted an extensive examination of various computational modeling and simulation techniques, especially for developing PLA-based tissue scaffolds. Computational approaches facilitate the prediction of scaffold characteristics and their behavior under various conditions. Scaffolds designed using computational methods are characterized by their reproducibility, precision, and adaptability, making them suitable for fabrication via 3D printing. The experimental validation of these computational designs showed a high degree of agreement between the simulated and actual results. Despite some challenges related to computational techniques and 3D printing technologies, the literatüre strongly supports the benefits of their combined use in the design and production of scaffolds. Our analysis of models specifically designed for 3D printing indicated that the PLA honeycomb structure, enhanced with 25% HA, yielded the best results. However, an increase in HA content was associated with a decrease in ultimate strength in the PLA constructs. Although the strength values of the produced bone tissue scaffolds are lower than that of natural bone, making them suitable for non-load-bearing areas of the body like the facial region, the achieved strength levels are consistent with those reported in similar studies. Variations in production parameters, as well as in the design and analysis stages, significantly affect the mechanical properties and overall quality of the final product. Precise adjustment of each parameter is essential in the 3D printing process. In conclusion, this study highlights the increasing importance and potential of PLA/HA-based composite scaffolds in future tissue engineering research.

REFERENCES

1. Shea, L.D., Wang, D., Franceschi, R.T., Mooney, D.J., “Engineered bone development from a pre-osteoblast cell line on three-dimensional scaffolds”, Tissue Engineering, Vol. 6, Pages 605-617, 2000.

2.Mondal, S., Nguyen, T.P., Hoang, G., Manivasagan, P., Kim, M.H., Nam, S.Y., & Oh, J., “Hydroxyapatite nano bioceramics optimized 3D prin-ted poly lactic acid scaffold for bone tissue engi-neering application”, Ceramics International, Vol. 46, Issue 3, Pages 3443-3455, 2020.

3.Burg, K.J.L., Porter, S., & Kellam, J.F., “Biomaterial developments for bone tissue engineering”, Biomaterials, Vol. 21, Pages 2347-2359, 2000.

4.Bulut, B. & Duman, Ş., “Evaluation of mechanical behavior, bioactivity, and cytotoxicity of chitosan/akermanite-TiO_2 3D-printed scaffolds for bone tissue applications”, Ceramics International, Vol. 48, Issue 15, Pages 21378-21388, 2022.

5.Persson, M., Lorite, G.S., Kokkonen, H.E., Cho, S.W., Lehenkari, P.P., Skrifvars, M., & Tuukkanen, J., “Effect of bioactive extruded PLA/HA composite films on focal adhesion formation of preosteoblastic cells”, Colloids and Surfaces B: Biointerfa-ces, Vol. 121, Pages 409-416, 2014.

6.Garlotta, D., “A literature review of poly (lactic acid)”, Journal of Polymers and the Environ-ment, Vol. 9, Issue 2, Pages 63-84, 2001.

7.Nampoothiri, K.M., Nair, N.R., & John, R.P., “An overview of the recent developments in poly-lactide (PLA) research”, Bioresource Techno-logy, Vol. 101, Issue 22, Pages 8493-8501, 2010.

8.Gentile, P., Chiono, V., Carmagnola, I., & Hat-ton, P.V., “An overview of poly (lactic-co-glycolic) acid (PLGA)-based biomaterials for bone tissue engineering”, International Journal of Mole-cular Sciences, Vol. 15, Issue 3, Pages 3640-3659, 2014.

9.Revati, R., Majid, M.A., Ridzuan, M.J.M., Normahira, M., Nasir, N.M., & Gibson, A.G., “Mechanical, thermal and morphological characterisation of 3D porous Pennisetum purpureum/PLA biocomposites scaffold”, Materials Science and Engineering: C, Vol. 75, Pages 752-759, 2017.

10.Sui, G., Yang, X., Mei, F., Hu, X., Chen, G., Deng, X., & Ryu, S., “Poly-L-lactic acid/hydroxyapatite hybrid membrane for bone tissue regeneration”, Journal of Biomedical Materials Research Part A: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials, Vol. 82, Issue 2, Pages 445-454, 2007.

11.Cui, Y., Liu, Y., Cui, Y., Jing, X., Zhang, P., & Chen, X., “The nanocomposite scaffold of poly (lactide-co-glycolide) and hydroxyapatite surface-grafted with L-lactic acid oligomer for bone re-pair”, Acta Biomaterialia, Vol. 5, Issue 7, Pages 2680-2692, 2009.

12.Hong, Z., Zhang, P., He, C., Qiu, X., Liu, A., Chen, L., Chen, X., & Jing, X., “Nano-composite of poly (L-lactide) and surface grafted hydroxya-patite: mechanical properties and biocompatibi-lity”, Biomaterials, Vol. 26, Issue 32, Pages 6296-6304, 2005.

13.Zhou, H., & Lee, J., “Nanoscale hydroxyapati-te particles for bone tissue engineering”, Acta biomaterialia, Vol. 7, Issue 7, Pages 2769-2781, 2011.

14.Zhang, X.Z., Leary, M., Tang, H.P., Song, T., Qian, M., “Selective electron beam manufactured Ti-6Al-4V lattice structures for orthopedic implant applications: Current status and outstanding challenges”, Current Opinion in Solid State and Material Science, Vol. 22, Issue 3, Pages 75-99, 2018.

15.Maconachie, T., Leary, M., Lozanovski, B., Zhang, X., Qian, M., Faruque, O., Brandt, M., “SLM lattice structures: Properties, performance, applications and challenges”, Materials and De-sign, Vol. 183, Pages 108-137, 2019.

16.Yuan, L., Ding, S., & Wen, C., “Additive manufacturing technology for porous metal implant applications and triple minimal surface structures: A review”, Bioactive Materials, Vol. 4, Pages 56-70, 2019.

17.Helou, M. & Kara, S., “Design, analysis and manufacturing of lattice structures: an overview”, International Journal of Computer Integrated Manufacturing, Vol. 31, Issue 3, Pages 243-261, 2018.

18.Fousová, M., Vojtěch, D., Kubásek, J., Jablonská, E., Fojt, J., “Promising characteristics of gradient porosity Ti-6Al-4V alloy prepared by SLM process”, Journal of the Mechanical Behavior of Biomedical Materials, Vol. 69, Pages 368-376, 2017.

19.Li, X., Wang, C., Zhang, W., Li, Y., “Fabrica-tion and characterization of porous Ti6Al-4Vparts for biomedical applications using electron beam melting process”, Materials Letters, Vol. 63, Pages 403-405, 2009.

20.Chethan, K.N., Zuber, M., Shenoy, S., Kini, C.R., “Static structural analysis of different stem designs used in total hip arthroplasty using finite element method”, Heliyon, Vol. 5, Issue 6, Pages e01767, 2019.

21.Studart, A.R., Gonzenbach, U.T., Tervoort, E., Gauckler, L.J., “Processing routes to macroporous ceramics: a review”, Journal of the American Ceramic Society, Vol. 89, Issue 6, Pages 1771-1789, 2006.

22.Mutlu, B., Çaylak, S., & Duman, Ş. “Incorporation of cerium oxide into hydroxyapatite/chitosan composite scaffolds for bone repair”, Processing and Application of Ceramics, Vol. 16, Issue 3, Pages 207-217, 2022.

23.Singh, D., Babbar, A., Jain, V., Gupta, D., Saxena, S., & Dwibedi, V., “Synthesis, characterization, and bioactivity investigation of biomimetic biodegradable PLA scaffold fabricated by fused filament fabrication process”, Journal of the Brazilian Society of Mechanical Sciences and Engineering, Vol. 41, Issue 3, Pages 1-13, 2019.

24.Duman, Ş. & Bulut, B., “Effect of akermanite powders on mechanical properties and bioactivity of chitosan-based scaffolds produced by 3D-bioprinting”, Ceramics International, Vol. 47, Issue 10, Pages 13912-13921, 2021.

25.Habib, F., Iovenitti, P., Masood, S., Nikzad, M., & Ruan, D., “Design and evaluation of 3D printed polymeric cellular materials for dynamic energy absorption”, International Journal of Ad-vanced

Manufacturing Technology, Vol. 103, Issue 5, Pages 2347–2361, 2019.

26.Torres, J., Cotelo, J., Karl, J., & Gordon, A.P., “Mechanical property optimization of FDM PLA in shear with multiple objectives”, JOM: The Jour-nal of the Minerals, Metals & Materials Soci-ety, Vol. 67 Issue 5, Pages 1183-1193, 2015.

27.The Biomedical Engineering Handbook, Jo-seph D. Bronzino, Ed. CRC Press in Cooperation with IEEE Press, Boca Raton, FL, 1995.

28.Gurkan, U.A., El Assal, R., Yildiz, S.E., Sung, Y., Trachtenberg, A.J., Kuo, W.P., & Demirci, U., “Engineering anisotropic biomimetic fibrocartila-ge microenvironment by bioprinting mesenchymal stem cells in nanoliter gel droplets”, Molecular Pharmaceutics, Vol. 11, Issue 7, Pages 2151-2159, 2014.

29.Evlen, H., Özdemir, M.A., & Çalışkan, A., “Doluluk oranlarının PLA ve PET malzemelerin mekanik özellikleri üzerine etkileri”, PoliTeknik Dergisi, Vol. 22, Issue 4, Pages 1031-1037, 2019.

30.Adhikari, J., Perwez, M. S., Das, A., & Saha, P., “Development of hydroxyapatite reinforced alginate–chitosan based printable biomaterial-ink”, Nano-Structures & Nano-Objects, Vol. 25, Pages 100630, 2021.

31.Liu, Q., Li, Q., Xu, S., Zheng, Q., & Cao, X., “Preparation and properties of 3D printed alginate–chitosan polyion complex hydrogels for tissue engineering”, Polymers, Vol. 10, Issue 6, Pages 664, 2018.

32.Russias, J., Saiz, E., Nalla, R.K., Gryn, K., Ritchie, R.O., & Tomsia, A.P., “Fabrication and mechanical properties of PLA/HA composites: A study of in vitro degradation”, Materials science & engineering. C, Biomimetic and SupraMolecular Systems, Vol. 26, Issue 8, Pages 1289-1295, 2006.

33.Maden, H. & Kamber, Ö.Ş., “FDM teknoloji ile üretilen prototip parçalarinin hatalari ve hatala-rin önlenmesi”, International Journal of 3D Prin-ting Technologies and Digital Industry, Vol. 2, Issue 1, Pages 40-51, 2018.

34.Sun, L. & Liu, X., “Control analysis of production and apparent quality of automobile large plastic parts”, Procedia Engineering, Vol. 16, Pa-ges 438-443, 2011.

35.Guduric, V., Metz, C., Siadous, R., Bareille, R., Levato, R., Engel, E., Fricain, J.-C., Devillard, R., Luzanin, O., & Catros, S., “Layer-by-layer bioassembly of cellularized polylactic acid porous membranes for bone tissue engineering”, Journal of Materials Science: Materials in Medicine, Vol. 28, Issue 5, Pages 1-11, 2017.

36.Azami, M., Rabiee, M., & Moztarzadeh, F., “Glutaraldehyde crosslinked gela-tin/hydroxyapatite nanocomposite scaffold, engi-neered via compound techniques”, Polymer Com-posites, Vol. 31, Issue 12, Pages 2112-2120, 2010.

37. Ko, C.C., Oyen, M., Fallgatter, A.M., & Hu, W.S., “Effects of gelatin on mechanical properties of hydroxyapatite-gelatin nanocomposites”, MRS Online Proceedings Library (OPL), Symposium L – Mechanical Behavior of Biological and Biomi-metic Materials, Vol. 898, 2005.

38.Senatov, F.S., Niaza, K.V., Zadorozhnyy, M.Y., Maksimkin, A.V., Kaloshkin, S.D., & Estrin, Y.Z., “Mechanical properties and shape memory effect of 3D-printed PLA-based porous scaf-folds”, Journal of the Mechanical Behavior of Biomedical Materials, Vol. 57, Pages 139-148, 2016.

39.Zimina, A., Senatov, F., Choudhary, R., Kolesnikov, E., Anisimova, N., Kiselevskiy, M., Orlova, P., Strukova, N., Generalova, M., Manskikh, V., Gromov, A., & Karyagina, A., “Biocompatibility and physico-chemical properties of highly porous PLA/HA scaffolds for bone reconstruc-tion”, Polymers, Vol. 12, Issue 12, Pages 2938, 2020.

40.Hu, X., Man, Y., Li, W., Li, L., Xu, J., Parun-gao, R., Wang, Y., Zheng, S., Nie, Y., Liu, T., & Song, K., “3D bio-printing of CS/Gel/HA/Gr hyb-rid osteochondral scaffolds”, Polymers (Basel), Vol. 11, Issue 10, Pages 1601, 2019.