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Research Article

Biodegradable Pla/Ha Composite Material Production and Mechanical Characterization for Temporary Implant Applications

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ABSTRACT

Hard tissues in the human body are damaged due to age, trauma, and bone diseases. Metal implants/prostheses are traditionally preferred to repair and treat these damaged tissues. Today, metals and their alloys meet the mechanical requirements of the musculoskeletal system well. However, the need to develop alternative composite materials has increased since metals are very stiff materials compared to bone. Problems such as stress shielding, and aseptic loosening can arise due to their high modulus of elasticity, and the need for secondary revision operations for such reasons. Also, the metal implant/prostheses should be removed after the healing that causes the undesirable secondary operation. In this study, polylactic acid (PLA) and hydroxyapatite (HA)-based composite materials were produced and their mechanical characteristics evaluated for possible implant applications. In addition, the PLA/HA composite materials stayed in Artificial Body Fluid (ABF) at different times, and the change in the mechanical properties were determined. PLA granules and HA powders were mixed in different ratios of weight (weight ratio 1:0, 9:1, 7:3, and 1:1) to produce 80 samples using the solvent casting technique. PLA was dissolved with chloroform in a magnetic stirrer at 200 rpm and room temperature, and then nano HA was added and mixed until homogeneity was achieved. After casting and drying, the samples were cut into appropriate standard sizes. The samples were subjected to biodegradability in-vitro test. In the results of this study, the modulus of elasticity increased with the increase of HA in the samples; however, the yield strength, ultimate strength, and yield strain of the samples decreased. In addition, it was observed that the existence of HA decreases the rate of degradation; therefore, the percentage of weakening in mechanical strength decreased in the measurements made at the end of the 15th day. According to these results, it was concluded that PLA/HA biodegradable composites can be developed to use as implant/prosthesis material.

1. Introduction

Bone tissue can be damaged over time due to age, genetic factors, trauma, and disease. Surgical treatment methods using biomaterials in short-term or continuous contact with the human body are applied for fractures that cannot be controlled by conservative treatment methods such as bandages, plasters, and orthoses. Implant and prosthesis placement is a surgical treatment method that is frequently used for this purpose today. Metal and metal alloy materials are commonly preferred for the fixation of bones, as they are the type of material that meets the mechanical limits of the skeletal system quite well. In general, metals are applied permanently for the treatment of bone fractures requiring the removal of the implants [1]. Corrosion is also another problem in addition to stay in the body permanently with metal implants. Biocompatible metal alloys are frequently used in joint and bone implants due to their good physical properties such as high strength, toughness, and ductility [2]. However, the stress transfer problem caused by the high modulus of elasticity of metal alloy biomaterials [3, 4] leading to osteoporosis [5] and the need for a secondary operation for removal are among the disadvantages. So, there is a need to develop a biodegradable and non-toxic material for removable implants. Magnesium (Mg)-based biomaterials are biodegradable, and these types of materials have been studied . recently [6]. However, the corrosion rate of Mg is very high, and as a result of Mg corrosion, hydrogen gas is released, which can prevent the healing process [7, 8]. This property of the Mg limits its use as an implant material. Polymer-based biomaterials might solve these problems. Lactic and glycolic acid polymers are widely used in biodegradable supports for orthopedic applications. However, due to their mechanical properties, their use is limited to non-load-bearing applications [9]. Since polymers in the medical field are generally not osteoconductive, a composite structure is formed by supporting a secondary phase [10]. The addition of HA to the polymer matrix can improve osteoconductive and bone-bonding potentials. In addition, HA improves the mechanical properties of PLA by playing the role of reinforcing material [11].

Composite materials are composed of at least two dissimilar materials that are bonded together without dissolving in order to achieve the desired properties. The greatest benefit of composite materials is their suitability for developing or enhancing desired properties. In terms of structure, composition, and mechanical compatibility, PLA/HA composite scaffolds are more similar to natural bone tissue than ceramic or polymer materials alone [12]. Polylactic acid (PLA) and hydroxyapatite (HA) are prominent implant and prosthesis materials due to their high biocompatibility, biodegradability (PLA), and rapid bone integration (HA) [11]. Due to its lack of sufficient mechanical

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properties, like PLA, and brittleness, like HA, each material cannot be used alone in implants and prostheses requiring high strength [9]. However, the desired properties can be achieved by combining these two materials into a composite material. In this study, mechanical characterizations of composite (PLA or HA) materials formed by combining these two distinct biomaterials were performed. In addition, degradation of the PLA/HA composite material occurs during the repair of biological tissues. Thus, the problems associated with the use of metal implants, such as stress shielding and aseptic loosening, etc., can be reduced, and the issue of the implants' permanence can be eliminated.

2. Materials and Methods

2.1. PLA/HA Composite Material Preparation

The production of composite materials was accomplished through the use of the solvent casting method. In a solvent composed of chloroform (CHCl3), PLA granules were stirred together using a magnetic stirrer until they were completely dissolved. In order to prevent the loss of substance, PLA was dissolved in jars that were sealed with the assistance of a magnetic stirrer at room temperature (Figure 1). To ensure that the PLA was completely dissolved, a solution of chloroform and PLA was made according to the proportions stated in Table 1 and allowed to mix at a speed of 200 revolutions per minute for approximately 18 hours. The following day, nano-hydroxyapatite particles were added to the PLA that had been entirely dissolved, and the process of magnetic stirring was continued until a homogeneous mixture was created, which took about two hours.

Fig 1. Magnetic stirrer and PLA/HA solution

Table 1. The amount of material that composes the solution and the composite

The ratio of the matrix (%)	Chloroform (mL)	PLA (gr)	HA (gr)
%100 PLA	100	20	0
%90 PLA- %10 HA	90	18	2
%70 PLA- %30 HA	70	14	6
%50 PLA- %50 HA	50	10	10

PLA/HA mixtures were poured into Petri dishes to dry as a thin film as shown in Figure 2. The solutions poured into Petri dishes were left to dry in a fume hood at room temperature. It was observed that the chloroform solvent was removed in approximately 36 – 120 hours. The longest drying time was observed in the samples with pure PLA, and the drying time of the casting was considerably shortened due to the increase in the amount of HA in the solution. At the end of this period, the castings come out of the mold easily. The samples were cut within the size limits specified in the ASTM D638-02 standard. The samples were cut to have dimensions of 60 mm in length, 20 mm in width, and 5 mm in thickness. The cut samples were lettered as A (100% PLA), B (90% PLA-10% HA), C (70% PLA-30% HA), and D (50% PLA-50% HA). All the cut samples were kept in an oven at 50°C for 24 hours, and the solvent was completely removed from the composites [13].

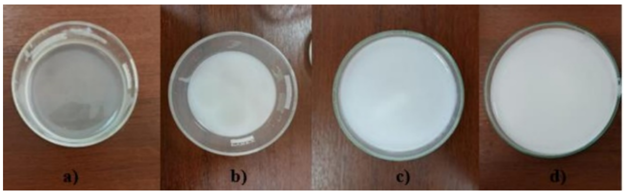

Fig.2. Pouring PLA/HA mixtures into petri dishes a) 100% PLA, b) 90%-10% PLA/HA, c) 70%-30% PLA/HA, d) 50%/50%

Table 2. Volume, height and post-drying wall thickness of the samples obtained

Composite Matrix Ratio (%)	Solution Volume (mL)	Solution Height (mm)	Sample Wall Thickness (mm)
%100 PLA	116±1.6	14.7±0.5	2±0.08
%90 PLA- %10 HA	105±1.3	13.4±0.35	1.9±0.07
%70 PLA- %30 HA	83±1.1	10.6±0.22	1.75±0.05
%50 PLA- %50 HA	62±0.9	7.9±0.21	1.43±0.045

2.2. In-Vitro Biodegradability Tests

The initial mechanical properties of the produced samples, as well as the change in mechanical properties during in vitro biodegradability experiments conducted over a period of 0-15 days, were investigated. The solution given in Table 3 and developed by Kokubo [14] was used to create artificial body fluid (ABF). The compounds listed in Table 3 were added to the ABF solution, and the pH was adjusted to 7.4, which was close to the blood value, using 1 M HCl. The solution was carefully prepared to be transparent, homogeneous, and free of precipitation. The prepared ABF solution could be stored at 5°C for one month without spoiling, or it could be used right away [15].

Table 3. Compounds used in ABF and their amounts [14]

Order	Compound	Amount
1	NaCl	8.035 gr
2	NaHCO3-	0.355 gr
3	KCl	0.225 gr
4	$K2HPO4.3H2O$	0.231 gr
5	$MgCl2.6H2O$	0,311 gr
6	1 M-HCl	39 ml
7	$CaCl2$	0,292 gr
8	$Na2SO4$	0.072 gr
9	Tris (Hydroxymethyl)	6,118 gr
10	1 M HCl	0-5 ml

ABF solution was used after fresh preparation. The samples were immersed in a tightly closed jar as shown in Figure 3. The temperature of the solution was set to 37 °C and each A, B, C, D samples were kept in ABF for 5-10-15 days, and each sample was taken from the solution and its mechanical test was performed. In order to examine the weight losses as a result of the samples waiting in the ABF, each sample was measured on a precision balance, before and after. A total of 80 samples, 5 from each sample, were produced from the A, B, C, and D samples, which were never kept in ABF and were kept for 5-10-15 days. In order to monitor the weight loss of the samples, the weights of each sample were measured on the 2nd, 5th, 8th, 10th, 12th, and 15th days before being left to the ABF and subjected to mechanical testing.

Fig. 3. Waiting of samples in ABF

2.3. Tensile Tests and Determination of Mechanical Properties

Figure 4 depicts the results of a tensile test that was carried out on samples that had been prepared in line with the ASTM D638-02 standard. The tensile test was performed in the Kocaeli University Biomechanics Laboratory at room temperature using a universal testing machine with a capacity of 20 kN and a preload of 3 N. Seven samples were subjected to the tensile test for each group. Tensile force was applied at a rate of 3 mm/min, until the rupture-breakage point was reached. Sandpaper was applied to the areas where the samples would come into contact with the jaws to keep them from moving around while the load is applied.

Fig. 4. Placement of the sample in the universal test machine (left picture) and failure of the sample as a result of the tensile test (middle and right picture)

3. Results

Tensile tests were carried out to determine the mechanical properties of the produced samples. The samples were kept in ABF for 5, 10, and 15 days and the samples were subjected to tensile testing at the end of each period. The elastic modulus, tensile strength, and yield strength values of the materials were obtained from the stress-strain graphs obtained as a result of the tensile test. In Figure 5, average stress-strain graphs obtained from samples not kept in ABF are given. Accordingly, pure PLA material has a high toughness value. The toughness value decreased as HA was added to PLA. In addition, as can be seen in Table 4, weakening is observed in the yield strength values. While the yield strength value of pure PLA is 11.07±0.93 MPa, this value decreases to 8.43±0.47 MPa in composite material with 50% PLA. This reduced its strength by approximately 24%. Similarly, the maximum tensile strength value decreases from 16.07 MPa to 9.6 MPa. In other words, the tensile strength has decreased by about 40%. In addition, the elastic modulus values of the samples increase as the HA ratio increases. In other words, the elastic modulus values increase from 398.25 MPa to 640 MPa. An increase in elastic modulus of approximately 38.5% was observed.

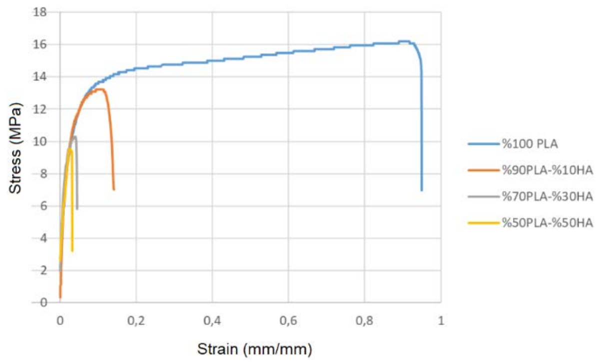

Fig. 5. Average stress-strain plot of samples tested without waiting in ABF

Table 4. Determined mechanical properties of the produced composite materials before being kept in ABF

Samples	Yield Strength (MPa)	Modulus of Elasticity (MPa)	Tensile Strength (MPa)	Density (g/cm3)	Yield Strain (%)
A	11.07±0.93	398.25±18	16.07±0.63	1.24±0.08	2.777±0.052
B	9.59±0.7	437.24±25	13.2±0.74	1.32±0.1	2.193±0.048
C	8.7±0.82	498.88±16	10.25±0.9	1.52±0.12	1.744±0.097
D	8.43±0.47	640.84±25	9.6±0.51	1.78±0.11	1.132±0.083

Another important feature of the obtained composite material is that it is biodegradable. For this reason, in order to be used as an implant or prosthesis of the material, the bone must show sufficient strength and provide fracture healing without decomposition during the healing process. In addition, deterioration of the implant/prosthesis after healing will also eliminate future implant/prosthesis problems. For this reason, in this study, the response of PLA/HA composite material kept in ABF within the first 15 days was also examined. The first weeks are crucial for fracture healing success [16]. In Figure 6, the change in elastic modulus values obtained from the samples after being kept in ABF is given. Accordingly, the 50-50% PLA/HA material could not maintain its high elastic modulus compared to other samples at the beginning, and a high (50%) decrease in the elastic modulus value was observed. In other sample groups, a high (66%) decrease in elastic modulus values was observed at the end of 15 days. On the other hand, the strain values of the samples in yield strength also decrease as the amount of HA in the composite material increases. A decrease of approximately 50% was observed in this value.

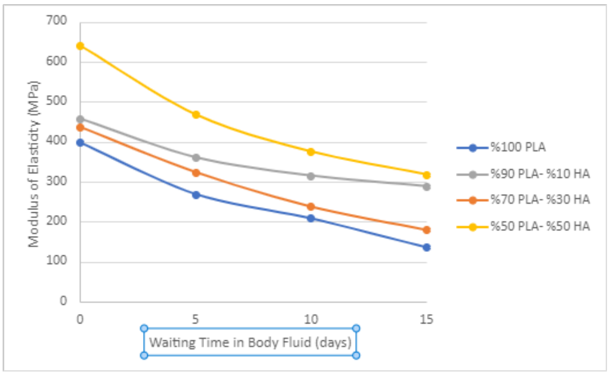

Fig. 6. Elastic modulus changes of the samples according to the waiting time in ABF

Weight losses in the samples are observed as a result of decomposition. The weight losses experienced in the samples are shown in Figure 7 in proportion. After the samples were placed in the ABF, weight measurements were taken every two days. The weight loss was related to the PLA content, and at the end of 15 days, up to 4% weight loss was experienced in the samples containing high PLA content. The weight loss ratio in the samples decreased to 3% as the PLA ratio decreased.

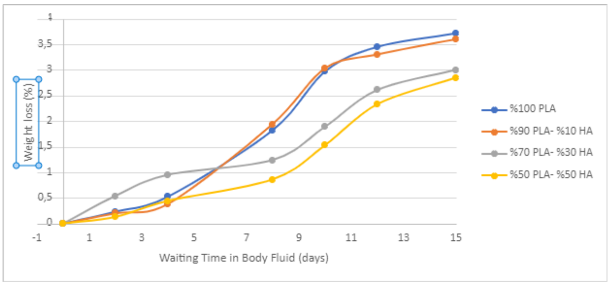

Fig. 7. Weight loss changes of the samples according to the waiting time in ABF

4. Conclusion

The field of biomedical technology is getting better every day, especially when it comes to implant and prosthetic technologies. However, the problems experienced with implants and prostheses have not completely disappeared. One of the main reasons for this is the high level of elastic modulus difference between metals and bone tissue [3,4]. Because the elastic modulus is the most effective factor in the stress transfer between bone and metal prostheses and implants. Depending on the elastic modulus difference, stress differences occur between the bone and the implant/prosthesis interface. Bone stimulation occurs in areas of high stress levels, while it does not occur in areas of low stress levels. According to Wolf's law, sufficient bone cells must be stretched for bone stimulation [17]. Regional bone development cannot occur due to these stress differences between the prosthesis and the bone, and bone and implant/prosthesis integration cannot take place in the future (no osseointegration occurs). This situation is called stress shielding [18]. As a result of the stress shielding, aseptic (germ-free) loosening arises, and implant/prosthesis failure occurs. The materials closest to the bone's elastic modulus should be preferred to solve these problems, However, the elastic modulus of titanium alloys, which is the most preferred metal, is 110 GPa. For this reason, studies are carried out on composite materials [9, 19, 20]. Within the scope of this study, the mechanical examination of composite materials formed from PLA material, which is popular today with the development of 3D printers and suitable in terms of biocompatibility, manufacturability, and biodegradability, and HA materials, which are the basis of bone tissue, was carried out. It has been observed that these materials are difficult to use in the first place, as they do not have sufficient yield strength in areas requiring high strength (hip replacement, knee replacement, etc.). However, it can be said that it is suitable for plate production for fracture fixation in small bone fractures (clavicle, finger, and toe fractures, etc.) that require lower strength. In addition, the elastic modulus of PLA/HA composite materials is very close to that of the cancellous bones [11, 21]. Although the values of concentric bone strength have different values in different parts of the body, they are around 100–2000 MPa on average [22]. By adding different third- and fourth-generation materials to this, new materials can be produced that can also be used in implants/prostheses that require high strength due to the production of functionally graded materials.

Leaving the samples in SBF is an excellent way to determine how the body reacts to sample materials [14]. SBF can also be used to investigate the bonding mechanism of the bone-implant surface and the biodegradable's material capability. The decay time for the biodegradable material, which is an important parameter, can be determined using the SBF method. In this study, the developed PLA/HA materials were exposed to different time periods in SBF to determine their degradation capability and decay time. The elastic modulus of the PLA/HA composites was dramatically reduced over a 15-day period. This result shows that the PLA/HA composite deteriorated. HA is a bioactive material that has the ability to bond between bone and implant. It is not biodegradable. Hence, the reason why reduces the elastic modulus of PLA/HA material is PLA polymer that is a biodegradable material. According to the current study, the elastic modulus of PLA/HA composites decreased by almost 66% on the 15th day. The maximum degradation ratio was observed for which sample had 100% PLA. According to the study, the degradation was determined to be dependent on the PLA/HA ratios.

The solvent casting method was generally preferred in the production of PLA/HA composite material, as described in the literature [23, 24]. Initially, dichloromethane was used as the solvent, but closed and open bubbles were observed in the fast-drying samples due to its low boiling point (approximately 40°C). As a result, chloroform was used as a solvent to achieve controlled drying through slower evaporation. In this way, the formation of bubbles was prevented. In addition, since cracks and breaks occur in composite materials with an increased ceramic weight ratio, composite materials with a ceramic weight above 50% could not be tried as seen in Figure 8. The amount of solution prepared depends on the amount of PLA in the composites, the amount of solvent required to dissolve PLA, and the mass/volume relationship resulting from the density of HA. According to the research in the literature, the easy processability, and biodegradability of PLA, which forms the composite structure; the high biocompatibility, and the improvement of mechanical properties of HA support its use in medicine [9, 14, 17, 21]. Suitable biodegradable materials for the non-highly load-bearing regions of the maxillary and upper extremity bones can be developed by experimenting with narrower spacings and different reinforcement phase percentages.

Fig. 8. Cracks on the sample with a HA ratio of 60% (a) and 70% (b).

PLA/HA composite materials can be obtained by different production methods. Foremost among these is 3D printing technology. On the other hand, the casting method used in this study can also be used in the production of composite materials. The production of such composite materials by plastic injection has been studied recently [25]. Among the most important factors affecting the mechanical properties of PLA/HA composite materials is the production method. While the maximum strength value from the mechanical properties of the PLA material produced with a 3D printer is at the level of 16 MPa [21], the strength of the PLA part produced by the plastic injection method can increase up to 59 MPa [11]. In this study, the maximum strength value of the PLA part obtained by pouring the mixture into the container was 16.07 MPa. This value coincides with the part value obtained from the 3D printer printouts [21]. However, the maximum strength of the PLA/HA composite part has dropped to 9.6 MPa. Since PLA is hydrophobic and HA is hydrophilic, adequate bonding has not been formed as the HA ratio in the mixture increased [26]. As a result, as the HA ratio increased, so did the elastic modulus of the obtained samples. This circumstance is an important obstacle to the use of PLA/HA composite material for implants and prostheses. For this reason, new production methods or strength-enhancing methods should be developed for PLA/HA composite materials.

Declaration of conflicting interests

The authors declare no competing interests.

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