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Suggesting A Full Two Level Experimental Factorial Model With Three Factors To Optimize Ti-HA Biocomposite Properties

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***Abstract*—A metal matrix composites (MMCs) is introduced to serve as synthetic bone grafts. The MMC was synthetized via powder metallurgical method after milling raw powder mixture of hydroxyapatite (HA) particles and pure titanium (Ti) powder. A full two level experimental factorial model with three factors (2^3) was developed to study the effect of three main parameters of synthetizing process on the hardness, density, and crystallite size of the composite. The synthetizing process parameters under consideration were the mechanical alloying time as well as the ceramic powder initial size and its mass fraction in the mixed powder. The results demonstrate that the composite's hardness is increasing with higher HA mass fraction (W/W) of the composite and longer milling time. The analysis of data also show that the initial HA particle size has insignificant influence on the composite's hardness, while higher HA content fraction in the MMC decreases the density of the composite.**

Keywords—Ti-HA, Nanocomposites, synthetic bone grafts, metal matrix composites (MMC), hydroxyapatite (HA)

1. Introduction

Many medical devices and implants are made of titanium and its alloys due to their mechanical and biocompatible attributes, such as bone ingrowths, modulus of elasticity, and corrosion resistance. However, pure titanium (Ti) is not suitable for application inside the human body because of its lack of desirable bioactive properties, particularly, bone-growth. Coating Ti with Hydroxyapatite (HA), $Ca_{10}(PO4)_6(OH)_2$ suggested an efficient method to enhance titanium's orthopedic implant fixation and surface bioactivity [1, 2]. HA exhibits biochemical activities close to human calcified hard tissues and thermodynamic stability in body fluids, and it thereon is used very often as bone substitute material. Nevertheless, the current coatings techniques are susceptible to wearing or delamination [3].

During the last decades, different metal matrix composites (MMCs) production methods have been implemented to improve the bioactivity and mechanical properties of Ti-HA composite (e.g. its hardness, corrosion resistance, density, strength) for medical applications [4-7]. However, these researchers have not suggested any analytical model based on the relationship among the synthetizing factors and the final composite's attributes to optimize the osteoconductivity of MMC materials.

In this paper, a 2^3 factorial model was developed to investigate the effect of particle size and mass percentage of HA in the mixed powder as well as the milling time on the hardness, density, and crystallite size of the Ti-HA composites. For this purpose, several Ti-HA composites were synthetized via ball milling method and powder metallurgy technology for synthetic bone grafts' applications.

2. Experimental procedure

HA particle size of 150 nm were synthesized by co-precipitation method, as described in literature [8]. Solution combustion method in literature [9] was adapted to prepare HA powder with 50 nm particle size. The Ti powder (<45 µm) from Merck KGaA was mixed with 10% and 30 % W/W HA-powders with 50 nm as well as 150 nm size to have four different Ti-HA mixture combinations. Then, half of four Ti-HA mixtures were milled for 20 hours, and the rest were milled for 50 hours, to have eight Ti-HA powder combinations, labelled as C1 to C8. The detail of mechanical milling alloying process was described in [10]. EDXA and SEM model LEO-1455VP were utilized to analyze the chemical compositions of the composite surface and its morphology, respectively.

The Vickers micro hardness of the bulk samples was carried out by holding 200 g load for 15 seconds on their polished surfaces using micro-hardness tester. Density of the samples were tested by Archimedes method according to ASTM D792 standards. The Ti crystallite size of the composite, L_c, was determined perpendicular to the (101) lattice by adopting Scherrer's equation for the X-ray diffraction through the milled pellet's thickness in 2θ of 40.17°direction as,

$$L_c = \frac{K\lambda}{\beta Cos\theta} \qquad \text{Eq : 1}$$

Where, β is half-width; λ is the X-ray wavelength; θ is the Bragg angle, and K is the Scherrer's constant of 0.9 related shape factor.

3. Factorial design analysis

The density (Y_1), the crystallite size (Y_2), and the hardness (Y_3) responses were determined by eight duplicate experiments executed in random order according to a 2^3 full factorial model. Eight duplicate experiments were related to synthetizing of the MMC using one of C1 to C8 powder mixtures. The experimental factors are HA content (X1), initial HA powder size (X2), and milling time (X3). The value of an effect was calculated by the following equation,

$$Effect = \frac{\sum Y+}{n+} - \frac{\sum Y-}{n-} \qquad \text{Eq}:2$$

n and Y in equation 2 refer to the number of data points collected at each level, and their associated responses. The results of the experimental design were analyzed with Minitab statistical software to evaluate the effects as well as the statistical parameters. The high and low levels of experimental factors are represented by +1 and −1, respectively. In this case, the low level (-1) for X1, X2 and X3 factors are 10 %W/W, 50 nm HA particle size, and 20 hours milling time, respectively. And, the high level (+1) for X1, X2 and X3 factors are 30 %W/W, 150 nm HA particle size, and 50 hours milling time, correspondingly. A1, A2 and A3 are designated for the main coefficients of HA content, initial HA powder size, and milling time, respectively. A4 to A7 are interaction coefficients of corresponding factors X1X2, X1X3, X2X3 and X1X2X3, in turn. The interaction between the levels (A1 to A7) are determined by algebra sign rules.

Table 1 shows the values of experimental factorial responses. The next expression is based on the 2^3 factorial analysis of the effect,

$$Y = A_0 + A_1X_1 + A_2X_2 + A_3X_3 + A_4X_1X_2 + A_5X_1X_3 + A_6X_2X_3 + A_7X_1X_2X_3 \qquad \text{Eq}:3$$

Where, A_0 represents the average of all actual responses and Ai (i=1 to 7) indicates associated regression coefficients.

Table 1: The results of the experimental factorial response for all powder mixture combinations.

Sample ID	Specifications of the sample	Hardness HV		Density gr/cm^3		Crystallite size (Nanometer)	
C1	Ti-HA particles with 30%(w/w) 150 nm milled for 50 hours.	385.8	385.0	3.07	3.10	21.7	22.4
C2	Ti-HA particles with 30%(w/w) 50 nm milled for 50 hours.	384.7	383.8	3.10	3.12	21.1	20.7
C3	Ti-HA particles with 10%(w/w) 150 nm milled for 20 hours.	286.0	287.2	3.43	3.47	22.3	21.0
C4	Ti-HA particles with 10%(w/w)- 50 nm milled for 20 hours.	287.5	286.2	3.48	3.41	21.4	22.6
C5	Ti-HA particles with 30%(w/w) 150 nm milled for 20 hours.	385.0	384.0	3.08	3.10	28.4	29.9
C6	Ti-HA particles with 30%(w/w) 50 nm milled for 20 hours.	383.0	384.6	3.12	3.03	28.7	29.8
C7	Ti-HA particles with 10%(w/w) 150 nm milled for 50 hours.	331.5	332.0	3.53	3.48	16.1	17.9
C8	Ti-HA particles with 10%(w/w) 50 nm milled for 50 hours.	333.4	333.7	3.45	3.48	16.7	17.0

Table 2: Calculated statistical parameters for hardness, density and grain size.

Response	Hardness (HV)			Density (gr/cm^3)			Crystallite size (Nano meter)		
Terms	Coefficient	Standard error	Effect	coefficient	Standard error	Effect	coefficient	Standard Error	effect
constant	347.087	0.1820	-	3.2780	0.00854	-	22.356	0.2032	-
X_1	37.4	0.1820	74.8	-0.1889	0.00854	-0.3779	2.981	0.2032	5.96
X_2	-0.025	0.1820	-0.05	0.0046	0.00854	0.0092	0.106	0.2032	0.21
X_3	11.65	0.1820	23.3	0.0122	0.00854	0.0244	-3.156	0.2032	-6.31
X_1X_2	0.487	0.1820	0.975	-0.0071	0.00854	-0.0143	0.156	0.2032	0.312
X_1X_3	-11.312	0.1820	-22.63	-0.0054	0.00854	-0.0108	-0.706	0.2032	-1.41
X_2X_3	-0.137	0.1820	-0.275	-0.0002	0.00854	-0.0004	0.2187	0.2032	0.437
$X_1X_2X_3$	0.25	0.1820	0.5	-0.0082	0.00854	-0.0164	0.0937	0.2032	0.187
R-square factor	**R-Sqr: 99.98%**			**R-Sqr: 98.41%**			**R-Sqr: 98.33%**		

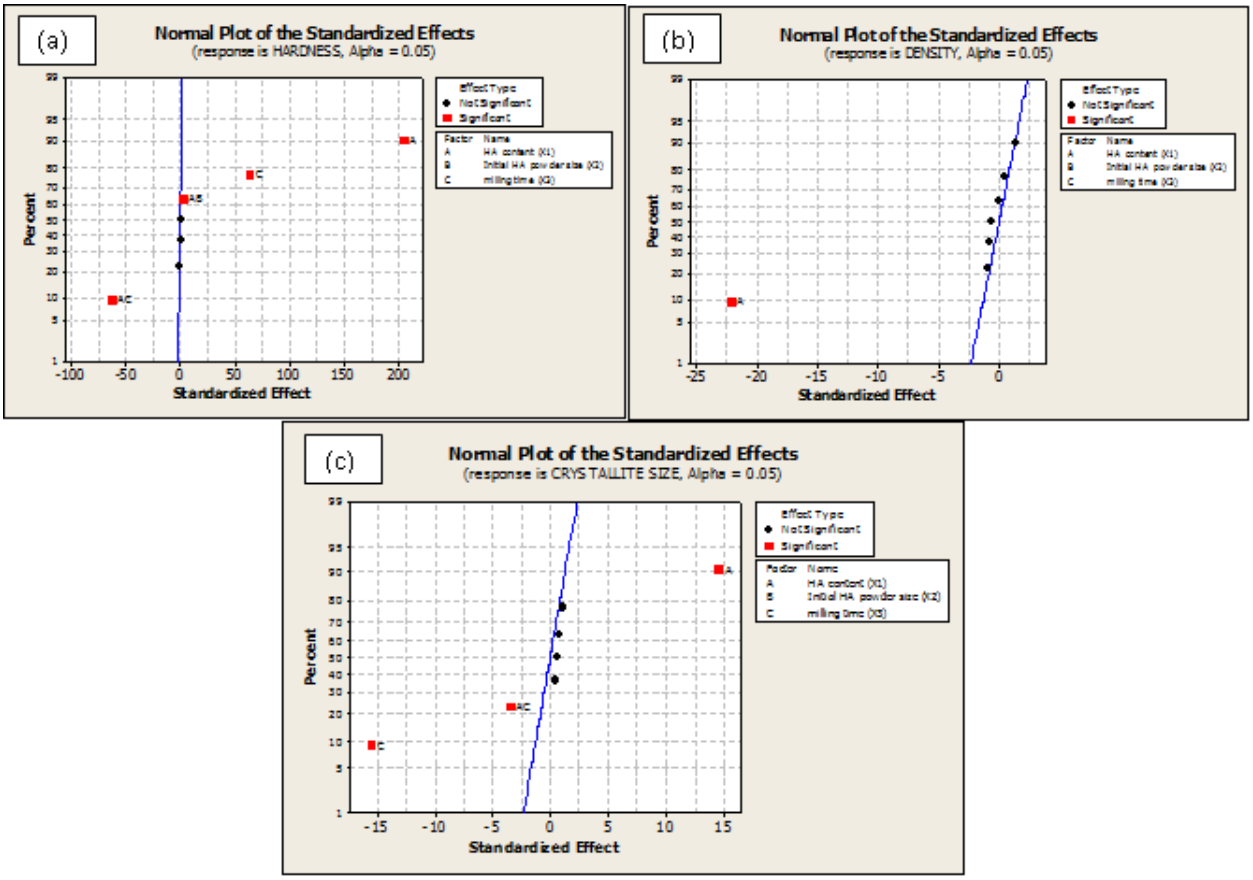

Fig 1 Normal probability plot of standardized effect for a) Hardness, b) density and c) crystallite size

Table 2 presents the regression coefficients standard errors and the effects of each factor. The equations for the responses can be obtained by substituting the value of the coefficients from Table 2 in equation 3. Equations 4, 5, and 6 give the correlations among the responses and HA content, milling time and initial HA powder size, correspondingly,

$$Y_1 = 3.2780 - 0.1889X_1 + 0.0046X_2 + 0.0122X_3 - 0.0071X_1X_2 - 0.0054X_1X_3 - 0.0002X_2X_3 - 0.0082X_1X_2X_3 \quad Eq:4$$

$$Y_2 = 22.356 + 2.981X_1 + 0.106X_2 - 3.156X_3 + 0.156X_1X_2 - 0.706X_1X_3 + 0.2187X_2X_3 + 0.0937X_1X_2X_3 \quad Eq:5$$

$$Y_3 = 347.087 + 37.4X_1 - 0.025X_2 + 11.65X_3 + 0.487X_1X_2 - 11.312X_1X_3 - 0.137X_2X_3 + 0.25X_1X_2X_3 \quad Eq:6$$

When the effect of a factor is positive, change of the factor from low to high can lead to an increase in the value of the associated responses. In contrary, associated responses are reducing when the negative factor increased from low to high.

The outcomes of the equations revealed that change in HA content (X_1) and milling time (X_3) from low to high-level result in upgrading hardness up to 74.8% and 23.3%, respectively. In addition, a variation from high to low level for initial HA powder size (X_2) results in increasing hardness by 0.05%. Moreover, lowering the HA content from high to low can increase density by 0.37 percentage. HA`s powder size and milling time impose their influences in their low levels by increasing density with 0.0092% and 0.0244%, respectively. HA content and milling time increase crystallite size at its high and low levels by 5.96% and 6.31%, respectively.

The accuracy of a regression model is determined with R-square factor. The hardness, density, and mean crystallite responses have R-square value of 99.86%, 98.44%, and 98.33% in Table 2, respectively. Thus, the regression model provides great degree of correlation between responses and factors.

The normal plot shown in Fig 1 is a common method for displaying significant effects in factorial designs. The significance of each factor on responses is studied through a normal probability plot of standardized effect with the significance level (denoted as □ or alpha) of 0.05, to consider only 5% for the excluded effects in the study. Important effects are larger and generally farther from the fitted line in the graphs, whereas non-influential effects tend to be smaller and approach to zero. Furthermore, Fig 1 suggests that all of the effects except X1X2 and X1X2X3 are significant for the hardness. The HA content has substantial effect since it is deviated the

most from the straight line in the graphs of Fig 1. Thereof, the significant factors for the composite's crystallite size are the milling time and the HA content, in turn. Similarly, HA content and milling time has the most contribution to the hardness and density. So, it can be concluded from Fig 1 that the order of significant in main factors is: HA content >milling time>initial HA powder size.

4. Results and discussion

It can be deduced from the factorial analysis that HA content influences the hardness of the Ti-HA composites in two ways. From one hand, higher HA content strengthens the hardness of the composition. The effect of the HA content in increasing the composite's hardness may be attributed to the fact that HA particles can act as barriers to dislocations. As a result, the hardness of the composites increases with the particle size reduction for constant volume fraction of HA particle due to the larger number of obstacles. From the other hand, the HA phase degrades the composition's hardness due to porosity induced into the matrix of the composition. The latter fact can be observed in low HA content composition, and it is more noticeable for the compositions for HA content lower than 30% W/W.

The degree of introduced strengthening by reinforcement phase particles depends on the distribution of particles in the ductile matrix. The reinforcement phase dispersion is a function of the phase particles` shape, the phase volume fractions, average particle diameter, and the mean inter particles spacing. These factors are all interrelated, and therefore, one factor cannot be changed without affecting the others. For instant, reducing the particle size decrease the average distances between particles for a given volume fraction of the reinforcement phase. Similarly, for a given size particle, the distance between particles decrease with an increase in volume fraction of the reinforcement phase.

Scherrer's equation claims that the Ti crystallite are crashed to the smaller size for longer milling time. It is due to the fact that the regular needle like shape of Ti powders particles break into the irregular morphology during the milling process as consequent of undergoing a severe plastic deformation (SPD). By other word, the composite is refined more for the longer milling time, and becomes more homogenized through SPD processes. Fig 1 indicates that HA content has greater effect on crystallite size than milling time, but the HA content has inverse effects on crystallite refining. According to the studies of morphologies in ductile – brittle powder systems, the fine brittle powders dispersed onto ductile powder surfaces during milling process [11]. Refining caused by milling process is lower in high content ratio of brittle phase than absence or lower brittle phase content [12]. As it can be seen in Table 1, Ti-HA composite powder with higher HA content has coarser crystallite for the same milling time.

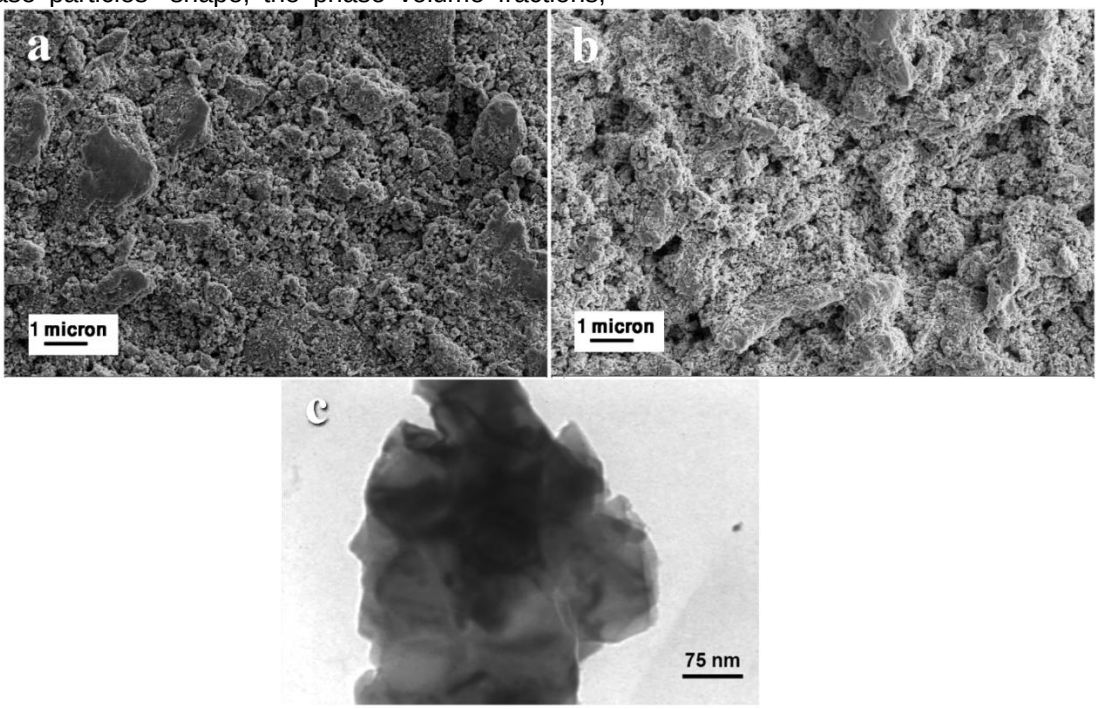

Fig 2 Scanning electron micrograph of a) C1 and b) C4 c) TEM micrograph of C1

Fig 2 exhibits the SEM micrograph of C1 and C4 samples. In Fig 2, 30% W/W HA content titanium composite has higher porosity in compare to 10% W/W HA content composite, which decreases the composite`s density for higher HA content. This could increase the wettability of the synthetized bone graft since hydrophilic attribute of ceramics is enhancing the surface wettability [13]. Higher HA content improves wetting properties by increasing the surface roughness induced by the ceramic structure and through larger amount of HA phase in Ti matrix. Apparently, the wettability of Ti-HA composite

increases by: a) ceramic phases which formed during sintering, and b) increase of the surface roughness induce by HA. Bright field microstructure in TEM images of C1 sample (Fig 2-c) are the blended Ti and HA particles during nanocomposite formation. Scherrer's equation suggests smaller crystallite size for the milled Ti powder than those of observed in TEM image. This can be as results of sintering process during the milling, which leads to some crystal growth. Fig 3 furnishes the X-ray diffraction analysis of Ti composites with Nano and micron size of HA powder after milling in different times. The X-ray diffraction pattern shows a line broadening with the increase in milling time because of crystallite size reduction. XRD analysis of Ti–HA nanocomposites in Fig 3 shows the presence of alpha-Ti (hexagonal-type structure) and absence of HA for all cases of composite reinforced with Nano size HA. In the composite reinforced with micron size HA powders, the elemental peaks of HA disappeared completely after 50 hours milling, while HA peaks can be observed for samples with 20 hours milling. Fig 3 registers no shift for the diffraction peaks of the (100), (002) and (101) crystal planes of titanium with respect to pure microcrystalline titanium. This suggests that most of the HA is incorporated into the Ti lattice without a significant change in lattice parameter.

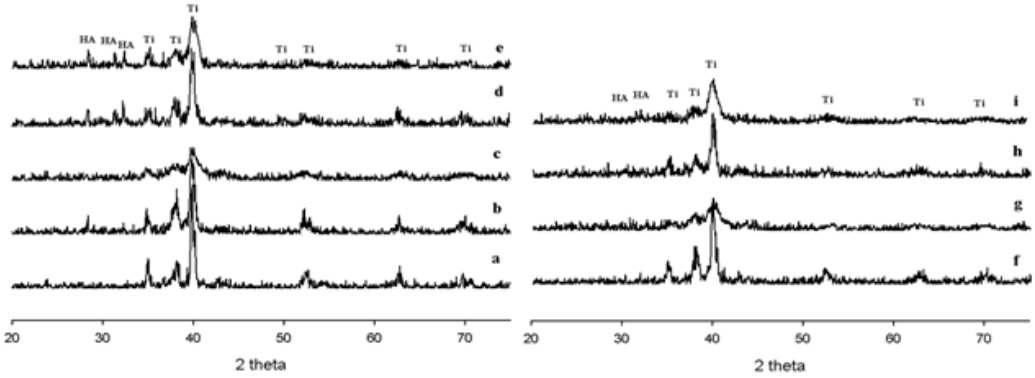

Fig 3 XRD spectra of (a) raw Ti powder for comparison purpose. (b) C8 (c) C2 (d) C4 (e) C6 (f) C7 (g) C5 (h) C3 and (i) C1

Table 3: ANOVA analysis of density

Factor	Sum of square	Degree of freedom	Mean square (MS)	F value	p-value
X1	0.571460	1	0.571460	489.25	0.000
X2	0.000339	1	0.000339	0.29	0.605
X3	0.002396	1	0.002396	2.05	0.190
X1X2	0.000818	1	0.000818	0.70	0.427
X1X3	0.000473	1	0.000473	0.41	0.542
X2X3	0.000001	1	0.000001	0.00	0.980
X1X2X3	0.001082	1	0.001082	0.93	0.364
Residual Error	0.009344	8	0.001168		
Total	0.585914	15			

Table 4: ANOVA analysis of crystallite size

Factor	Sum of Square	Degree of freedom	Mean square (MS)	F value	p-value
X_1	142.206	1	142.206	215.26	0.000
X_2	0.181	1	0.181	0.27	0.615
X_3	159.391	1	159.391	241.27	0.000
X_1X_2	0.391	1	0.391	0.59	0.464
X_1X_3	7.981	1	7.981	12.08	0.008
X_2X_3	0.766	1	0.766	1.16	0.313
$X_1X_2X_3$	0.141	1	0.141	0.21	0.657
Residual Error	5.285	8	0.661		
Total	316.339	15			

The analyses of variance (ANOVA) with mathematical statistics validate Eq. 3 in determining the significant factors affecting the responses. Tables 3, 4 and 5 present the ANOVA results. The F values were calculated by dividing the factor mean square with the error mean square. The null hypothesis should be rejected for the actual F value exceeding the critical F value at an acceptable risk value. Reference F value is equal to 5.32 for α equal to 0.5 and mean square factor with one and eight degrees of freedom. This indicates an effect is statistical significance if it presents actual F value higher than 5.32. In statically significant effect study method, p-value is used to assess whether the association between the response and each term in the model is statistically significant. If p-value ≤ α then the association is statistically significant, otherwise, the association is not statistically significant. Therefore, main effects or interaction effects with p-value less than 0.05 are statistically significant.

Table 3 hints that only two factors of X_1 and X_3 are statistically significant for the density. It can be concluded from table 4 that only X_1, X3, and their interaction have F value greater than 5.2, and therefore, have statically significant effect. Hence, a modified model was suggested for the density and the crystallite size by discarding insignificant terms, as next,

$$Y_1 = 3.2780 - 0.1889X_1 \qquad Eq:7$$

$$Y_2 = 22.356 + 2.981X_1 - 3.156X_3 - 0.706X_1X_3 \qquad Eq:8$$

Table 5 reveals that most of the terms in equation 6 are significant since the p-value associated with these terms are less than 0.05. The insignificant effects in equation 6 are X_2, X_1X_2, and $X_1X_2X_3$. Neglecting the contributions of insignificant terms in equation 6 simplifies the response equation as below:

$$Y_3 = 347.087 + 37.4X_1 + 11.65X_3 - 11.312X_1X_3 \qquad Eq:9$$

Table 5: ANOVA analysis of Hardness

Factor	Sum of Square	Degree of Freedom	Mean square (MS)	F value	P value
X_1	22380.2	1	22380.2	42226.72	0.000
X_2	0.0	1	0.0	0.02	0.894
X_3	2171.6	1	2171.6	4097.28	0.000
X_1X_2	3.8	1	3.8	7.17	0.028
X_1X_3	2047.6	1	2047.6	3863.33	0.000
X_2X_3	0.3	1	0.3	0.57	0.472
$X_1X_2X_3$	1.0	1	0.1	1.89	0.207
Residual Error	4.2	8	0.5		
Total	26608.6	15			

5. Conclusion

Powder metallurgy technology and milling process were employed to synthetize different Ti-HA bio-composite alloys to optimize the material properties of synthetic bone grafts. Correlative equations were optimized to compute the mechanical property responses of Ti-HA composite to alteration the synthetizing process parameters. The composite's hardness, density and crystallite size were estimated through eight duplicate experiments executed to a 2^3 full factorial design.

Results show that HA content plays major role in variation of density and hardness of the composite. Accordingly, higher HA content reduces the density and increases the hardness, whereas milling time is the important factor for the composite's crystallite size. The density and the hardness of the 30% w/w HA content composite could be optimized by 50 hours milling for both 50 and 150 Nanometer HA particles. Moreover, it was concluded that the initial HA size does not have significant effect on the composite's properties (i.e. crystallite size, density, and hardness), therefore, its effect could be ignored in factorial design analysis.

Further studies are necessary to examine the bioactivity and wettability of the proposed Ti-HA composites, and to verifying their osteogenesis mechanism for bone implant applications.

Compliance with Ethical Standards

The authors declare that:

- This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue.
- The authors have no affiliation, and no conflict of interest, with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript.

- This article does not contain any studies with human participants or animals performed by any of the authors.
- Informed consent was obtained from all individual participants included in the study.

References

[1]. K. Yamada, K. Imamura, H. Itoh, H. Iwata, and S. Maruno, Biomaterials, vol. 22, pp. 2207-2214, (2001)

[2]. W. Zhen-jun, H. Li-ping, and C. Zong-zhang, Transaction of Nonferrous Metals Society of China, no. 16, pp. 259-266, (2006).

[3]. J.-K. Chang, C.-H. Chen, K.-Y. Huang, and G.-J. Wang, Journal of Arthroplasty, vol. 21, (2006).

[4]. C. Ning and Y. Zhou, Acta Biomaterial, vol. 4, no. 6, p. 1944–1952, (2008).

[5]. S. Salman, et al., Ceramics International, vol. 35, p. 2965–2971, (2009).

[6]. K. Niespodziana, K. Jurczyk, J. Jakubowicz, and M. Jurczyk, Materials Chemistry and Physics, vol. 123, no. 1, pp. 160-165, (2010).

[7]. Changjun Han et. al., Titanium/hydroxyapatite (Ti/HA) gradient materials with quasi-continuous ratios fabricated by SLM: Material interface and fracture toughness, Materials & Design, Volume 141, Pages 256-266, (2018)

[8]. A. Sousa, K. Souza, and E. Souza, Acta Biomaterial, vol. 4, no. 3, pp. 671-679, (2008).

[9]. N. Bovand, S. Rasouli, M.-R. Mohammadi, D. Bovand, J Ceram Process Res, 13, pp 221-225, (2012).

[10]. Bovand, D., Allazadeh, M.R., Rasouli, S. et al. J Aust Ceram Soc (2018).

[11]. T. P. Yadav, R. M. Yadav, and D. P. Singh, Nanoscience and Nanotechnology, vol. 2, no. 3, pp. 22-48, (2012).

[12]. C. Suryanarayana, Progress in Materials Science, vol. 46, no. 1-2, p. 1–184, (2001).

[13]. J. J. Rosenberg AG, Rubash HE, eds. The adult hip. Philadelphia: Lippincott-Raven Publishers, 1998:217-229. (1998).