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Suitable forming condition of hydroxyapatite and bioactive glass composites for a bone fixation plate using Taguchi experimental design

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Abstract

Biomaterials have been recently implemented in medical applications such as devices for orthopedic and dental surgery. Biomaterials, such as Hydroxyapatite (HA) and Bioactive glasses (BG) have common chemical components which are similar to those found in a human bone. These biomaterials can be synthesized from natural resources with the calcium as the main component. Therefore, this paper emphasizes on investigating in suitable forming conditions of the mentioned biomaterials for fabricating a new proposed biocompatible bone plate for damaged bone treatment. In this study, HA powder was synthesized from bovine bones, while BG (45S5) was prepared from mollusk shell through chemical reactions. The materials were grounded and mixed using high speed ball milling machine in order to reduce and to thoroughly mix those composites prior to forming of the proposed materials. In addition, the formed composites were compressed by a hydraulic pressing machine. Design of experiment based on Taguchi method was implemented for evaluating the effect of forming conditions, including of mixing ratio, compression force, holding time for pressing and sintering temperature. Consequently, the formed compacts were compressed into a specimen with a diameter of 10 mm, height of 20 mm for compressive strength testing. Then, an appropriate condition was evaluated based on compressive strength as the response. The results showed that the optimal condition was found from the specimen with the ratio of BG:HA equal to 30:70 wt%, compacting pressure of 30 MPa, sintered at 1,500 ˚C and holding time has no significant effect to the compressive strength. At this appropriate condition, the compressive strength of HA-BG composite was 249.46 MPa.

Keywords: Hydroxyapatite, Bioactive glass (45S5), Taguchi methods, Compressive strength

1. Introduction

Locking compression plate (LCP) is widely used as bone fixation plate for surgical bone fracture treatment. LCP is usually made from alloy materials such as stainless steel (i.e. stainless steel grade 316L) and titanium alloys. However, the plate which is made from these alloys can be corroded by human internal body fluids. It is found that the most corrosion of the plate is caused by the chemical reaction around the surrounding tissue that sometimes leads to the infection, inflammation, pain, and swell. Besides, it can be risky for osteoarthritis. Therefore, this plate is not appropriate for a long term use inside human body. Patient who uses the plate has to be operated to take it out in order to protect the inflection and other problems [1]. Furthermore, the expense of bone fracture treatment using metal alloyed LCP is very high because the LCP plates have to be imported from manufacturers oversea. The cost of locking compression plate (LCP) which is made from 316L stainless steel which is about 7,000 Baht per piece [2] contributes greatly to patient treatment cost. From the above problems, bone fixation plate made from local biomaterials can help with both the biocompatibility and the treatment cost problems. Development of biomaterials for medical applications places an importance on the compatibility with human body. Bioactive ceramics have been developed and implemented in medical application as a bone substitute material for fractures. Calcium phosphate ceramics, particularly hydroxyapatite (HA:$Ca_{10}(PO_4)_6(OH)_2$) and bioactive glass (BG: 45S5), were widely implemented as implant materials due to their biocompatibility and close resemblance to the mineralized phase of human bone structures [3], which can stimulate the formation of new bone with the surrounding tissues[4]. Furthermore, HA and BG can be synthesized from natural sources with calcium-based structures such as bovine bone, mollusk shell or corals [5-6]. Therefore, these materials may be regarded as cost-effective biomaterials bone tissue engineering for bone graft applications. For this reason, researchers have previously attempted to combine HA with BG to develop composite biomaterials structure with better mechanical and biological properties [7]. This combination could be achieved through sintering, though sintering above 597 ˚C will cause crystallization of amorphous BG [8]. The $Na_2Ca_2Si_3O_9$

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crystalline phase formed improves the mechanical property [9] and bioactive response [10]. Besides, the materials for producing the bioactive ceramics bone plates can be found in the country which is cheaper than the alloy bone plates that have to be imported from the foreign source of production. The cost of bone plates which are made from biomaterials is about 500 Baht per piece. To compare with the metal alloyed LCP, the biomaterial bone plates can be up to 14 folds cheaper than the LCP.

Therefore, this work aims to investigate and identify appropriate forming conditions for a HA-BG compact specimen using the experimental design based on the Taguchi method. The optimal condition was evaluated based on compressive strength. Finally, the actual mechanical properties of the compact specimen were used to apply to the forming LCP for the future.

2. Methodology

2.1 Preparation and biomaterial characterization

Hydroxyapatite (HA) was synthesized from bovine bones. First of all, the bovine bone was cut into small pieces and soaked in hydrogen peroxide (H_2O_2) solution in order to remove the ligaments and tissues. Then, the small pieces of bones were boiled in water to eliminate organic substances and collagen. Next, these bones were kept in the hot air oven to reduce their moisture content. The dried bones were calcined at 900 °C for 3 hours, before being grinded into powder by a high speed ball milling machine until the average particle size is less than 20 μm. The Bioactive glass (BG) composes of 45 wt% SiO_2, 24.5 wt% Na_2O, 24.5 wt% CaO and 6 wt% P_2O_5 is also known as Bioglass® 45S5 [11]. In the present study, the BG was synthesized from both chemical and natural substances: silicon oxide (Merck), sodium oxide (Merck), calcium oxide (synthesized using mollusk shell) [12] and phosphorus pentaoxide. An appropriate ratio of reagents was thoroughly mixed using a magnetic stirrer and poured into a ceramics crucible. It was then heated at 1,100 °C for 2.5 hours using a furnace, as BG is known to start melting at 1,100 °C [13]. In this experiment, an agate mortar was used to reduce the particle size of material down to less than 20 μm. To characterize the crystal phase in sintered BG, a small sample of pulverized BG was heated at 770 °C with 2 hour holding time to ensure formation of crystals. The synthesized biomaterial was evaluated using X-Ray diffraction analysis (XRD) for phase identification.

2.2 Fabrication of HA/BG compact specimen

Binder was prepared by mixing DI water and polyvinyl alcohol at 97 per 3 by weight percent, then it was stirred and heated until the solution were homogenous. Hydroxyapatite powders (HA) were mixed with a proper amount of Bioglass®45S5 (BG) in 250 ml polyethylene bottles, and ball milled for 23 hours with ethanol media. Binder was added and the ball milling process was continued for 1 hour. After that, the powders were dried in the oven at 110 °C for 24 hours. The powders were sieved at polyester screen no. 77 (67 micron), and then added binder into powders for granule. The specimens were fabricated by uniaxial pressing with compression at 25 MPa and 30 MPa shown in Figure 1(a). HA-BG composite specimens were sintered at 1,400 and 1,500ºC

2.3 Experimental design

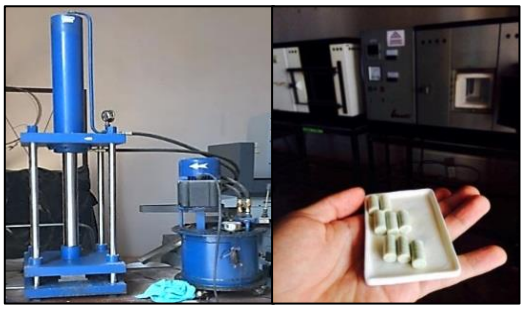
The effect of pressing conditions was investigated by using a design of experimental technique: Taguchi method. Table 1 describes the experimental design of factors including the mixing ratio, pressure, holding time for pressing and sintering temperature. A total of 8 specimens were fabricated for the experiments, in order to identify an appropriate pressing condition which would form a compact specimen with optimal compressive strength.

Table 1 Experimental Design of relevant factors and its levels

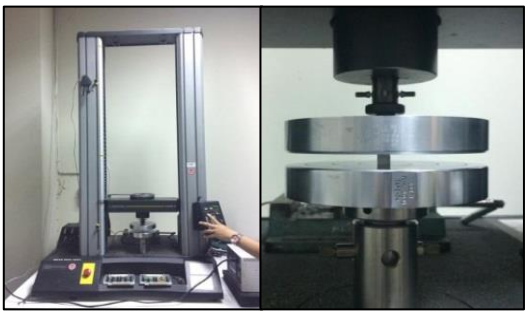
Factors	Level		Unit
	Low (-)	High (+)	
1. Bioactive glass (BG) mixing ratio (Ratio)	4.53	30.0	wt%
2. Compacting Pressure (Pressure)	25	30	MPa
3. Holding Time for Pressing (Time)	60	120	second
4. Sintering Temperature (Temp)	1,400	1,500	ºC

2.4 Characterization of mechanical property

The compressive strength of sintered materials was measured using a universal testing machine (Instron 5566) at crosshead speed 0.5 mm/min [14], with 10 kN load cell. Eight different HA-BG cylindrical bio-ceramic samples were prepared according to ASTM C773-88 (2006).The formed compacts were compressed into a specimen with Diameter of 10 mm, high 20 mm. The compressive strength testing is shown in Figure 1(b).



(a)



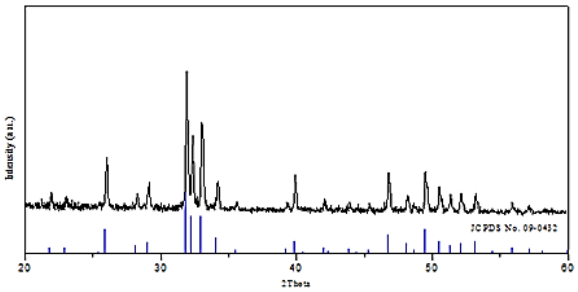
(b)

Figure 1 Equipment for fabrication of HA-BG composite, Hydraulic pressing machine, the sample specimens (a), Compression test using universal testing machine (b)

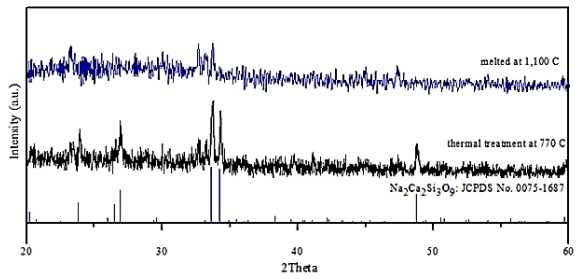
3. Results

3.1 Characteristics of hydroxyapatite and bioactive glass

The X-ray diffraction spectra of HA from bovine bone and BG were compared with JCPDS-ICDD No.09-0432 and JCPDS-ICDD No.0075-1687, respectively. According to the comparison, the dominant peaks of both synthesized materials significantly resembled the JCPDS standards. The diffraction peaks of the HA sample matched neatly with the standard peaks, as seen in Figure 2(a). This shows that the synthesized powder is indeed hydroxyapatite.



(a)



(b)

Figure 2 X-ray pattern of as-received HA powder (a) and BG 45S5 powder (b)

X-ray diffraction of the synthesized BG is shown in Figure 2(b). The diffraction spectra before sintering proved that the synthesized BG was largely amorphous, while the spectra of the powder after thermal treatment at 770 °C and thermal treatment at 1,100 °C for 1 hour [15] revealed intense peaks, which correlated to $Na_2Ca_2Si_3O_9$.

3.2 Compressive strength results

The experimental results of the HA-BG specimen based on compressive strength at each forming conditions is illustrated in Table 2.

The results in Table 2 shows that the HA–BG bio-ceramic contains with 4.53 and 30.0 wt% of BG displays the lowest and highest compressive strength, respectively. These results show that the amount of added BG can improve the compressive strength of HA–BG bio-ceramic. In addition, the mechanical strength in all condition is close to of the cortical bone's (100–230 MPa) [16]. However, in this study only compressive strength values achieved for condition#8: 30.0 wt.% BG added HA bio-ceramic specimen with a crystalline $Na_3Ca_6(PO_4)_5$ phase in a glassy silicate matrix was slightly higher than the required compressive strength of the human cortical bone.

4. Discussion

Taguchi experimental design technique in MINITAB software has been used in determining significant factors in various kinds of applications. In this research, experimental design Taguchi L8 orthogonal array of the 2 level consisted of the low and high, four factors shown in Table 1. The Taguchi method analyzed the signal to noise ratio (S/N), selected as the larger is the better (the larger means the larger compressive strength is better). The L8 orthogonal array of four factors: Ratio (A), Pressure (B), Time (C), Temp (D) and the response was the compressive strength, shown in Table 2. Results showed that all four factors were statistically significant as Figure 3 showed that the factors affecting the compressive strength of the composite specimen were the mixing ratio, pressure and sintering temperature while the holding time has no significant effect. Results from Table 3 showed that sintering temperature (temp) was the most significant factor (rank1) followed by mixing ratio, and pressure.

Table 2 Taguchi L8 orthogonal array design response values and S/N ratio

Run	A Ratio (wt%)	B Pressure (MPa)	C Time (sec)	D Temp (°C)	diameter (mm)	Length (mm)	Area (mm^2)	Compressive Strength (MPa)	S/N ratio
1	4.53	25	60	1,400	9.65	19.60	73.10	135.92	42.6657
2	4.53	25	120	1,500	8.34	17.54	54.60	146.87	43.3387
3	4.53	30	60	1,500	8.19	17.15	52.65	162.53	44.2187
4	4.53	30	120	1,400	9.48	19.49	70.54	142.07	43.0500
5	30.00	25	60	1,500	8.55	17.25	57.38	214.72	46.6374
6	30.00	25	120	1,400	9.51	19.24	71.00	139.62	42.8990
7	30.00	30	60	1,400	9.21	19.29	66.58	147.72	43.3888
8	30.00	30	120	1,500	8.03	17.01	50.61	249.46	47.9400

Table 3 Compressive strength Taguchi S/N ratio

Response Table for S/N ratio					**Response Table for Means**				
Level	Ratio	Pressure	Time	Temp	Level	Ratio	Pressure	Time	Temp
1	43.32	43.89	44.23	43.00	1	146.8	159.3	165.2	141.3
2	45.22	44.65	44.31	45.53	2	187.9	175.4	169.5	193.4
Delta	1.90	0.76	0.08	2.53	Delta	41.0	16.2	4.3	52.1
Rank	2	3	4	1	Rank	2	3	4	1

The HA–BG bio-ceramic can be improved their mechanical properties by increasing the pressure and sintering temperature, which increase the dense green body compaction and pores reduced, respectively. The amount of BG can be acted like dispersion in HA matrix and to be glassy phase during sintering that cause an increase in compressive strength.

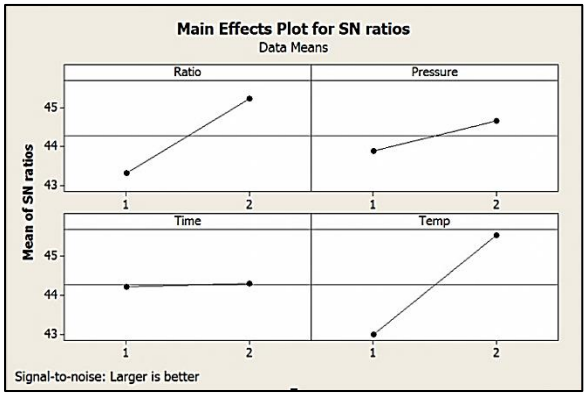


Figure 3 Taguchi results of compressive strength and the S/N ratio

5. Conclusions

In this study, the effects of forming conditions on specimen compressive strength was investigated based on Taguchi statistically experimental design. The optimal condition was found from the specimen with the ratio of Bioactive glasss:HA equal to 30:70 wt%, with the compacting pressure of 30 MPa, sintered at 1,500 ˚C and holding time has no significant effect to the compressive strength. At this condition, the compressive strength of HA-BG composite was 249.46 MPa. Further investigation on biological properties of the HA-BG compact specimen is on-going to develop LCP prototypes for clinical use in the near future.

6. Acknowledgements

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