DESIGN OF EXPERIMENT (DOE) STUDY OF HYDROXYAPATITE (HA) FOR LOAD BEARING APPLICATION VIA 2^k FACTORIAL DESIGN

by

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DECLARATION

I hereby declare that I am the sole author of this dissertation. This is a through copy of the dissertation, including any required final revisions, as accepted by my examiners. It has not previously submitted for the basis of the award of any degree or diploma or other similar title of this for any other diploma/examining body or university. I understand that my dissertation may be made electronically available to the public.

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LIST OF ABREVIATIONS

2-D	2 Dimension
2^k	Two Level
3-D	3 Dimension
ACP	Amorphous Calcium Phosphate
Al_2O_3	Alumina
ANOVA	Analysis of Variance
Ca/P	Calcium to Phosphate Ratio
$Ca_{10}(PO_4)_6(OH)_2$	Hydroxyapatite
Ca^{2+}	Calcium
CaO	Calcium Oxide
CDA	Calcium Deficient Apetite
Cl^-	Chloride
ClA	Chlorapatite
CO_3^{2-}	Carbonate
DOE	Design of Experiment
EDX	Energy Dispersive X-ray Spectroscopy
F^-	Fluoride
FA	Fluorapatite
FESEM	Field Emission Scanning Electron Microscopy
GPa	Gigapascal
HA	Hydroxyapatite
HA/Al_2O_3	Hydroxyapatite Reinforced with Alumina
HIP	Hot Isostatic Pressing
ICSD	International Centre of Structural Data
K^+	Potassium
K_{IC}	Fracture Toughness
Mg^{2+}	Magnesium
MPa	Megapascal
Na^+	Sodium
P	Phosphate

PSZ	Partially stabilized zirconia
R^2	R-square
R^2_{adj}	R adjusted
R^2_{pred}	R predicted
S/N	Signal to Noise Ratio
SEM	Scanning Electron Microscopy
SiC	Silicon Carbide
TCP	Tricalcium Phosphate
TTCP	Tetracalcium Phosphate
XRD	X-ray Diffraction
Y_2O_3	Yttrium oxide
ZrO_2	Zirconia
α- TCP	Alpha- Tricalcium Phosphate
β-TCP	Beta- Tricalcium Phosphate
λ	Wavelength

KAJIAN REKABENTUK EKSPERIMEN (DOE) TERHADAP HIDROKSIAPATIT UNTUK APLIKASI PENGALAS BEBAN MENERUSI KAEDAH FAKTORAN 2^k

ABSTRAK

Tujuan kajian ini adalah untuk menghasilkan biokomposit hidroksiapatit (HA)/alumina (Al_2O_3) dengan menggunakan kaedah percampuran kering bagi mengkaji faktor eksperimen dan kesannya (kesan utama dan kesan interaksi) terhadap sifat akhir biokomposit (kekerasan, ketumpatan dan keliangan). Kesan-kesan ini diukur menggunakan rekabentuk eksperimen (DOE) bagi membentuk model matematik. Kajian ini merangkumi dua bahagian di mana bahagian I adalah berkaitan dengan cara-cara penyediaan sampel yang bermula dengan pencirian sifat fizikal, struktur (fasa) dan sifat kimia bagi bahan mentah. Prosedur ini diikuti dengan fabrikasi biokomposit HA/Al_2O_3 berdasarkan parameter yang berbeza (suhu pensinteran ;1100 ºC dan 1250 ºC, masa pencampuran ; 3 jam dan 9 jam dan komposisi Al_2O_3; 0wt% dan 30 wt%). Eksperimen ini dijalankan mengikut turutan yang dicadangkan oleh perisian DOE (Minitab 16) semasa proses perawakan. Setelah itu, sifat fizikal dicirikan melalui ujian ketumpatan dan keliangan manakala morfologi sampel dilihat dengan menggunakan mikroskop imbasan elektron (SEM). Bagi analisis fasa,sampel dicirikan menggunakan analisis pembelauan sinaran-X (XRD) dan ujian kekerasan Vickers digunakan untuk mengkaji kekerasan sampel. Dalam bahagian II, kaedah DOE faktoran dua aras (2^k) digunakan untuk mengkaji faktor-faktor yang memberi kesan dalam proses penghasilan biokomposit HA/Al_2O_3 berkekuatan tinggi. Faktor-faktor ini dianalisis dan faktor yang memberi kesan besar ditentukan menerusi model regresi dan analisis variasi (ANOVA). Model disahkan menerusi ANOVA bagi mengkaji kepadanan antara model

dan data yang diperoleh secara eksperimen. Seterusnya, ralat eksperimen dan interaksi antara parameter dikaji untuk mengenalpasti perbezaan antara nilai data ramalan dan data eksperimen. Keputusan menunjukkan komposisi Al_2O_3 dan suhu pensinteran telah memberi kesan yang besar ke atas respon manakala masa pencampuran tidak memberikan sebarang pengaruh. Untuk respon kekerasan, analisis telah menunjukkan bahawa untuk mendapatkan kekerasan yang tinggi, suhu pensinteran haruslah ditetapkan di atas suhu 1240 ^oC dan komposisi Al_2O_3 haruslah berada di bawah 3 wt%. Syarat yang sama juga diperlukan bagi respon keliangan di mana suhu pensinteran haruslah ditingkatkan melebihi 1188 ^oC dan komposisi Al_2O_3 haruslah berada di bawah 7 wt% untuk mendapatkan keliangan antara 5-10 %. Bagi respon ketumpatan, ketumpatan yang hampir menyamai ketumpatan tulang manusia (lelaki : 3.88 g/cm^3 ; wanita : 2.90 g/cm^3) boleh diperolehi dengan menetapkan suhu pensinteran masing-masing pada 1180 ^oC ke atas dan komposisi Al_2O_3 dibawah 30 wt% atau suhu pensinteran pada 1200 ^oC ke atas dan komposisi Al_2O_3 melebihi 10 wt%. . Secara keseluruhan, parameter yang memberi kesan besar terhadap respon-respon adalah komposisi Al_2O_3 dan suhu pensinteran.

DESIGN OF EXPERIMENT (DOE) STUDY OF HYDROXYAPATITE (HA) FOR LOAD BEARING APPLICATION VIA 2^k FACTORIAL DESIGN

ABSTRACT

The present study aims to fabricate hydroxyapatite (HA)/alumina (Al_2O_3) biocomposite via dry mixing process, in order to evaluate the experimental factors and their effects (main effects and interaction effects) on the response or final biocomposite characteristics (hardness, density, and porosity). These effects were quantified using Design of Experiments (DOE) to develop mathematical models. This study covered two parts where the part I deals with the sample preparation procedures which was started with the characterization of raw materials in term of physical, structural (phases) and chemical properties. This procedure was followed by the fabrication of HA/Al_2O_3 biocomposite with different parameter setting (sintering temperature; 1100 ºC and 1250 ºC, mixing time; 3 hours and 9 hours and Al_2O_3 composition; 0wt% and 30 wt%). The experiment was run by following the run order suggested by DOE software (Minitab 16) through randomization stage. Next, the physical properties was characterized using density and porosity testing while the morphology of the sample was studied using Scanning Electron Microscopy (SEM). For phase analysis, the sample was characterized through X-ray Diffraction analysis and Vickers hardness testing was employed to study its hardness. In part II, two-level (2^k) factorial method of DOE was employed to determine the suitable or significant factors in producing high strength HA/Al_2O_3 biocomposite. The experimental factors were analyzed and the significant factors were

determined through regression model and Analysis of Variance (ANOVA). The model was then validated through ANOVA in order to study how fit is the model with the experimentally obtained data. Experimental errors and interactions between factors were investigated to verify the significant between predicted and experimental data. Results shows that Al_2O_3 composition and sintering temperature has given a significant effects on the responses while mixing time has given no influence. For hardness response, it shows that, in order to obtained a high hardness, the sintering temperature must be set above 1240 ºC with Al_2O_3 composition lower than 3 wt%. The same requirement goes to porosity response where sintering temperature must be above 1188 ^{o}C with Al_2O_3 composition below 7 wt% in order to obtained 5-10 % porosity. For density response, acceptable density that mimicking the natural dense male and female bone density (3.88 g/cm^3 for male; 2.90 g/cm^3 for female) can be obtained by setting the sintering temperature above 1180 ^{o}C and Al_2O_3 composition below 30 wt% or sintering temperature above 1200 ^{o}C and Al_2O_3 composition above 10wt % respectively. The most significant parameters that effecting all the response are Al_2O_3 composition and sintering temperature.

CHAPTER 1

INTRODUCTION

1.1 Background

Medical world is in a transition where damaged organ is completely replaced with in vitro synthesized implants instead of curing it by lengthy surgical operations (Grained, 2011). However, only a few materials are known to satisfy the requirements of implantation in the human body. For example, materials such as vanadium steel, which was chosen for its good mechanical properties has corroded rapidly in the body and had caused infection or adverse effects on the healing process (Raynaud et al., 2002). However, these drawbacks regarding the infections and adverse effects tend to be solved by the application of biocompatible materials known as biomaterials (Mizuno, 2007).

Biomaterials can be simply defined as a synthetic materials used to replace part of a living system or to function in intimate contact with living tissue (Hench, 1991). It is considered clinically success when it has stable interface between implant and connective tissues, excellent resistance to corrosion, noncarcinogenic, acceptable to cyclic loading, high wear resistance and have a biocompatible chemical composition to avoid adverse tissue reaction (Best et al., 2008).

One of the attractive biomaterials is bioceramic where it can be classified into bioinert, bioactive and resorbable bioceramics (Hench, 1991). The selections of bioceramics are depends on its application. For instance, hard tissue and bone replacements are synthesized mainly from bioactive ceramics such as dense non-porous bioglass, ceravital and hydroxyapatite, (HA) (Best et al., 2008). However, in this application, HA has dominated any other material in quantity primarily because of its compositional and biological similarity to human bone, biocompatibility, bioactivity and osteoconduction characteristic (Jun et al., 2003).

Even though HA offers high biocompatibility, relatively low density, high compressive strength and high hardness, application of HA as a load bearing implant is limited because of its brittleness, relatively low-mechanical properties and a high-dissolution rate in body fluid. Hence, arise the need to reinforce the HA without hampering its biocompatibility (Balani et al., 2007)

Introduction of bioinert ceramics with better properties into HA ceramic is the effective way in producing a composite with acceptable strength in order to sustain the cylic loading (Mizuno, 2007). Bioinert ceramics are chosen to enhance the properties of bioactive HA because it can maintain their physical and mechanical properties while being implant in human body. Examples of bioinert ceramics are alumina, (Al_2O_3), zirconia, (ZrO_2), and carbons (Piconi and Maccauro, 1999).

1.2 Problem statement

Hydroxyapatite (HA) is a calcium phosphate bioactive material. It posses excellent biocompatibility, good osteoconduction properties (allow bone cells to grow on its surface) and identical chemical composition to the mineral phase of human bones (Shahriar, 2009). The benefits of HA as implants material have been widely acknowledged, but the occurrence of several poor performances such brittleness, relatively low-mechanical properties and high dissolution rate has generated concerns over the improvement of monolithic HA properties (Gergely et al., 2010).

The addition of zirconia, (ZrO_2) was proven to improve mechanical properties of HA such as fracture toughness and hardness (Piconi and Maccauro, 1999). However, the addition of ZrO_2 has led to a large volume change since it is not stable at high temperature. Thus, an adequate amount of dopant such as yttrium oxide (Y_2O_3) is used to stabilize the ZrO_2 properties at elevated temperature (Firmandika, 2008). ZrO_2 produced in this manner is referred as partially stabilized zirconia, (PSZ). Since the addition of ZrO_2 to HA involves multi steps preparation method, it requires a lot of time, thus making the process become even more costly (Piconi and Maccauro, 1999). Another attempt that has been done to enhanced the HA based composite properties is by adding silicon carbide, (SiC) (Hench 1991). Addition of SiC does not favor a high cost compared to PSZ but due to toxicity issues, the use of this material as biological implant has became restricted (Mizuno, 2007). Therefore, finding the suitable materials that are non toxic and cost effective is a must.

Alumina (Al_2O_3), being a bioinert material, has shown much promise. It posses high hardness, thus leads it to have the tribologic advantage (Jun et al., 2003). This properties is one of the focus in the fabrication of load-bearing implant in order to prevent wear-debris generation since it might cause adverse affect to the human body (Hench, 1991) . Since Al_2O_3 is a bioinert ceramic, it offers excellent degradation resistance and has biocompatible chemical composition which can avoid adverse tissue reaction (Grained, 2011). In addition, Al_2O_3 is insoluble in all ordinary chemical reagents which allow it to be planted in human body environment (Best et al., 2008). These qualities have make Al_2O_3 useful as a biomaterial.

Other than restriction in choosing a suitable reinforcement material, the complex procedures and high cost in HA based biocomposite fabrication has becoming another issue. HA based biocomposite are mainly produced by using heterogenous precipitation and wet mixing method (Grained, 2011). These methods are time consuming since it involved a lengthy homogenization, stirring and drying process. Moreover, the pH need to be monitored thoroughly during the precipitation process until it was done (Epure et al., 2007) . The usage of hot isostatic pressing (HIP) also can enhance the composite mechanical properties (Adolfsson et al., 2000). However, all these fabrication processes demand high cost and time which most researchers or manufacturers try to refrain.

With this background, it shows that the fabrication of biocomposite need to take account the biocompatibility, strength and cost. Conversely, the key of success of any implant, besides the correct surgical implantation, is the strict quality control during fabrication of the materials and the production of the implant (Hench, 1991). There are many factors affecting the quality and technical performances of the processing during the production, such as raw material selection, and process set up (N. Al et al., 1998). Trial and error method or conventional research methodology are frequently used to determine the optimal process parameters. This definitely involving a high cost and consuming a lot of time since a lot of experiment need to be done. Conventional methodolgy will generate a number of tests which do not always lead to conclusive and effective results (Kehoe and Eng, 2008). In order to reduce the frequency of experiment and determine factors influencing the characteristic of the product, Design of Experiment, (DOE) method can be adopted (Cabrelon and Zauberas 2008). In short, DOE mathematical models can be used to quantify the experimental output effectively and economically (Rajalingam et al., 2012).

The usage of DOE in determining the optimal process setting of HA/Al_2O_3 biocomposite fabrication has not been excessively done in the literature. Thus, the potential parameters or predictors (sintering temperature, mixing time and Al_2O_3 composition) that might influence the mechanical properties of the biocomposite will be studied by using this approach. The suitability of low cost conventional dry mixing process in HA/Al_2O_3 biocomposite fabrication also will be investigated based on the results obtained.

In this study, the DOE was carried out by using statistical tool known as two-level (2^k) factorial design which is widely used for experiment that involving several factors for a response. Factorial design is a combination of mathematical and statistical techniques which used in the modeling and analyzing of problems to get an improved response (Klimova et al., 2006). The interactions or relationships between inputs factors and one or more measured factors also can be quantified by using this tool. Since the levels involves in this study is only 2-levels, 2^k factorial design was chosen. In addition, another advantage of

2^k factorials are widely used in research work is because they are capable to form basis experimental design with considerable practical value.

1.3 Research Objectives

There are two main objectives for this research work:

1) To use Design of Experiment (DOE) method to determine the significant parameters among the predictors (sintering temperature, mixing time and Al_2O_3 composition) on the resultant mechanical properties of HA/Al_2O_3 biocomposite.

2) To study the usage reliability of dry mixing process whether it can improve the monolithic HA properties as those researches that used the complex and cost demanding process.

1.4 Research Approach

To achieve the mentioned objectives, research experimental investigations were divided into two main parts as follows:

Part I : This part deals with the preparation procedures which was started with the characterization of raw materials. Physical and chemical properties of commercial HA and Al_2O_3 powders were characterized. This procedure was followed by the fabrication of HA/Al_2O_3 biocomposite with different parameter setting (sintering temperature; 1100 ºC and 1250 ºC, mixing time; 3 hours and 9 hours and Al_2O_3 composition; 0wt% and 30 wt%). The experiment order was set by the Design of Experiment (DOE) through randomization stage. Physical, structural and hardness properties of this biocomposite were then characterized using X-ray Diffraction analysis (XRD), Scanning Electron Microscopy (SEM), density and porosity testing as well as Vickers hardness testing.

Part II: DOE via two-level factorial method was employed to determine the suitable or significant factors in producing high strength of HA/Al_2O_3 biocomposite. The experimental predictors or parameters (mixing time, sintering temperature and Al_2O_3 composition) were analyzed and the significant factors (factors that affecting the process and output) were determined through regression model. The model was then validated through mean square, (R^2) and mean square adjusted, (R^2 adjusted) observation in order to study how fit is the model with the obtained data. This approach was followed by the evaluation of experimental errors and interactions between parameters to study the correlations between each factors investigated. The characterization of the prepared samples based on the run order arrangements suggested by randomization process has been discussed to support the DOE results and useful in generating inference.

These two parts were studied, compared and evaluated to distinguish which parameter is giving significant effects to the hardness properties of HA/Al_2O_3 biocomposite.