PREPARATION AND CHARACTERIZATION OF HYDROXYAPATITE (HA) FROM COW BONE AND ITS COMPOSITE WITH POLY(LACTIC ACID) FOR BONE REPLACEMENT

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SUPERVISOR'S DECLARATION

We hereby declare that we have checked this thesis and in our opinion, this thesis is adequate in terms of scope and quality for the award of the degree of Doctor of Philosophy in Chemical Engineering.

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I hereby declare that the work in this thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at Universiti Malaysia Pahang or any other institutions.

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ABSTRACT

The wide application of hydroxyapatite (HA) for medical applications such as bone tissue replacement sometimes constitutes environmental challenges as the conventional HA synthesis routes require the use of organic solvents. On the other hand, the current trend of research is to incorporate biomaterials such as HA into polymer matrices for some medical applications such as bone replacements. However, this often produces composites with inferior properties. This is due to poor HA dispersion within the composites as well as compatibility issues. In this study, natural HA was produced from cow bone through ultrasound and calcination processes at various temperatures. Composites then were produced from poly (lactic acid) (PLA) and hydroxyapatite (HA) through extrusion and injection molding. In order to foster good interaction between PLA and HA, and to impart antimicrobial properties onto the HA, surface of the HA was modified. On the other hand, impact properties of the PLA-HA composite was improved through the incorporation of impact modifier. Characterization of the produced HA was carried out through thermogravimetric (TGA) and field emission scanning electron microscope (FESEM) analysis. Spectrum obtained for the HA through Fourier Transform Infrared Spectroscopy was also compared with standard HA. Likewise, X-ray diffraction analysis of the HA in comparison with International Centre for Diffraction Data (ICDD) index for standard HA was conducted. On the other hand, Ca/P ratio of the produced HA was verified through Energy Dispersive X-ray analysis for elemental analysis. Likewise, different characterization techniques were used to characterize the composite produced. These include Fourier transforms infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), Differential Scanning Calorimetry (DSC), Dynamic Mechanical Analysis (DMA), tensile, flexural and impact analysis. Also microbial properties of the produced HA and its composite with PLA were assessed. In addition, in vitro biocompatibility study was used to assess the cell attachment and cell proliferation properties of the composites. Results showed that modification of HA led to increased HA dispersion within the PLA matrix, which resulted into significantly higher mechanical, thermal and dynamic mechanical properties of the resulting composite. Similarly, impact properties of the PLA-HA composite was remarkably improved after incorporation of biostrong impact modifier. In addition, in vitro study revealed that the PLA-HA composite exhibits good biocompatibility properties. In general, the results from this study shows that combination of the salient properties of HA with the good mechanical properties of PLA holds great potential for production of bone replacement composite materials with good load bearing ability. The composite produced herein can help to overcome the secondary operation procedures often associated with the conventional bone replacement procedures.

ABSTRAK

Hydroxyapatite (HA) mempamerkan beberapa sifat penting yang menjadikannya sangat diperlukan untuk pelbagai aplikasi perubatan termasuk penggantian tisu tulang. Walau bagaimanapun, terdapat satu cabaran untuk memenuhi permintaan yang meningkat setiap tahun untuk tulang seperti HA, tanpa memberikan kesan terhadap alam sekitar. Ini adalah disebabkan oleh peningkatan bilangan pesakit ortopedik. Dalam kajian ini, HA semula jadi dihasilkan daripada tulang lembu melalui proses ultrasound dan pengkalsinan pada pelbagai suhu. Perubahan struktur kekisi HA yang diperoleh melalui kaedah pengekstrakan berbanding kaedah lain telah dikaji. Pencirian HA yang telah dihasilkan ini dilakukan melalui analisis thermogravimetri (TGA) dan mikroskop elektron (FESEM). Spektrum yang diperolehi bagi sampel HA melalui Fourier transform infrared spektroskopi juga dibandingkan dengan HA piawai. Begitu juga pembandingan analisis pembelauan sinar-X HA dengan HA piawai telah dilakukan dengan International Center for Diffraction Data (ICCD) indeks. Selain itu, nisbah Ca/P bagi HA yang dihasilkan telah disahkan melalui analisa Energy Dispersive X-ray. Tambahan lagi, analisis unsur HA yang dihasilkan telah dijalankan. Hala tuju baru penyelidikan kini adalah dengan menggabungkan bahan-bio seperti HA ke dalam matriks polimer untuk beberapa aplikasi perubatan seperti penggantian tulang. Namun begitu, faktor-faktor seperti keberkesanan penyebaran bahan bioaktif dalam matriks polimer, sifat mekanik komposit dan kadar kemerosotan komposit adalah faktor utama dalam menentukan kesesuaian bahan polimer untuk aplikasi penggantian tulang. Dalam kajian ini, komposit telah dihasilkan daripada poli (asid laktik) (PLA) dan hydroxyapatite (HA) melalui kaedah penyemperitan dan pengacuan suntikan. Permukaan HA telah diubah untuk memperbaiki interaksi yang baik antara PLA dan HA, dan memberikan beberapa sifat antimikrob kepada HA. Tambahan pula, sifat impak komposit PLA-HA telah diperbaiki melalui kesan penggabungan pengubah. Teknik pencirian yang berbeza telah digunakan untuk mencirikan sifat komposit. Ini termasuk Fourier spektroskopi inframerah (FTIR), TGA, *differential scanning electron microscopy* (DSC), analisis mekanikal dinamik (DMA), analisis tegangan, lenturan dan impak. Sifat mikrob HA yang dihasilkan dan komposit dengan PLA juga dinilai. Di samping itu, kajian in vitro kesesuaian-bio digunakan untuk menilai susunan sel dan sifat-sifat percambahan sel komposit. Keputusan telah menunjukkan bahawa pengubahsuaian HA membawa kepada peningkatan penyebaran HA dalam matrik PLA, yang seterusnya mengakibatkan sifat termal mekanik dan dinamik mekanikal yang tinggi terhadap komposit yang terhasil. Begitu juga, sifat impak komposit PLA-HA telah meningkat selepas pertambahan pengubah impak *biostrong*. Tambahan lagi, kajian in vitro mendedahkan bahawa komposit PLA-HA mempamerkan sifat kesesuaian-bio yang baik. Secara umum, hasil dari kajian ini menunjukkan bahawa gabungan sifat-sifat penting HA dengan sifat mekanik yang baik PLA memberi potensi besar untuk menghasilkan bahan komposit penggantian tulang dengan keupayaan beban beban yang baik. Komposit PLA-HA yang dihasilkan ini dapat membantu mengatasi prosedur operasi sekunder yang sering dikaitkan dengan beberapa penggantian tulang dan proses regenerasi lain.

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LIST OF ABBREVIATIONS

ACP	Amorphous Calcium Phosphate
ATCC	American Type Culture Collection
ALP	Alkaline Phosphate
ASCs	Adipose Derived Stem Cells
BS	Biostrong
BMD	Bone Mineral Density
CDHA	Calcium-deficient Hydroxyapatite
CHNS	Carbon, Hydrogen, Nitrogen, Sulfur
DB	Database
DCPA	Dicalcium Phosphate Anhydrous
DCPD	Dicalcium Phosphate Dihydrate
DLPLGA	D,L- Poly(lacti acid-co-glycolic acid)
DMA	Dynamic Mechanical Analysis
DMEM	Dulbecco's modified Eagle's medium
DSC	Differential Scanning Calorimetry
DTG	Differential Thermal Gravimetry
EDX	Energy Dispersive X-ray
FA, FAp	Fluorapatite
FBR	Foreign Body Response
FDA	Food and Drug Administration
FESEM	Field Emission Scanning Electron Microscope
FM	Flexural Modulus
FS	Flexural Strength
FTIR	Fourier Transforms Infrared Spectroscopy
FWHM	Full Width at Half Maximum
HA	Hydroxyapatite
HA-PLGA	Hydroxyapatite, Poly(lacti acid-co-glycolic acid)
HDPE	High Density Polyethylene
GPa	Giga Pascal
ICDD	International Centre for Diffraction Data
IS	Impact Strength
LB	Luria Bertani
MPa	Mega Pascal
MSCs	Mesenchymal Stem Cells
MCPA	Monocalcium Phosphate Anhydrous
MCPM	Monocalcium Phosphate Monohydrate
PBS	Phosphate Buffered Saline
PBS	Poly(butylene succinate)
PCL	Poly(caprolactone)
PDLA	Poly(D- Lactide)
PEA	Poly(ester amides)
PEG	Poly(ethylene glycol)
PE	Polyethylene
PEO	Polyethylene Oxide
PET	Polyethylene Terephthalate
PGA	Poly(glycolic acid)
PHA	Poly(lactic acid), Modified Hydroxyapaptite

PHAB5	Poly(lactic acid), Modified Hydroxyapatite, 5 wt% Biostrong
PHAB10	Poly(lactic acid), Modified Hydroxyapatite, 10 wt% Biostrong
PHAB15	Poly(lactic acid), Modified Hydroxyapatite, 15 wt% Biostrong
PHB	Polyhydroxybutyrate
PLA	Poly(lactic acid)
PLA-HA	Poly(lactic acid), Hydroxyapatite
PLA-HA-BS	Poly(lactic acid), Hydroxyapatite, Biostrong
PLGA	Poly(lacti acid-co-glycolic acid)
PLLA	Poly(L- lactide)
PMHA	Poly(lactic acid), Modified Hydroxyapatite
PP	Polypropylene
PPG	Poly(propylene glycol)
PUHA	Poly(lactic acid), Unmodified Hydroxyapatite
OA, OAp	Oxyapatite
OCP	Octacalcium Phosphate
RAW	Raw Hydroxyapatite
RP	Rapid Prototyping
SEM	Scanning Electron Microscopy
TM	Tensile Modulus
TS	Tensile Strength
TCP	Tetracalcium Phosphate
TGA	Thermal Gravimetric Analysis
α-TCP	α-Tricalcium Phosphate
β-TCP	β-Tricalcium Phosphate
XRD	X-ray Diffraction
XPS	X-ray Photoelectron Spectroscopy
XRF	X-ray Fluorescence

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