EVALUATING THE SURFACE PROPERTIES OF HA COATING ON Co-Cr BASED ALLOY SUBSTRATE

HIRBOD MALEKI KHEIMEH SARI

This project report submitted in partial fulfilment of
the requirements for the award of the degree of
Master of Engineering (Mechanical – Advanced Manufacturing Technology)

Faculty of Mechanical Engineering
Universiti Teknologi Malaysia

JANUARY 2014

Dedicated to…

My beloved parents, Mahdokht and Ardeshir

My cherished brother

And lastly my dear family and friends

Thanks for your endless support

ACKNOWLEDGEMENT

Apart from the efforts of mine, the success of any project largely depends on the inspiration and guidance comes from people around. I take this opportunity to declare my appreciation of the people who have been instrumental in accomplishing this project. I would like to extend my sincere thanks to all technical staffs at Production and Material Science Laboratories. I am deeply indebted to Assoc. Prof. Dr. Izman bin Sudin for his support and constant supervision as well as for providing necessary information and equipment regarding to my project.

I would like to express my gratitude towards my parents for their kind co-operation and encouragement which aided me in completion of my thesis. My thanks and appreciations also go to my colleagues in developing the project and people who have willingly helped me out with their abilities.

ABSTRACT

Hydroxyapatite (HA) is the main structural component of natural bone and due to its excellent biocompatibility and bioactivity it can be used in biomedical application as a coating layer for metallic implants to help formation of chemical bonding at HA/bone interface and work as a protective layer against ion release from a metallic prosthesis. In this study, HA bioactive coating was created using sol-gel method on the high carbon CoCrMo substrate. Although sol-gel is simple and cost effective method with capability to control chemical composition and able to coat on the complex-shape implants, massive cracks of HA sol-gel coated layer on implants are still the major issue. Cracks can be minimized by changing the viscosity, composition or variation in heat treatment procedure. In this study, Na_3PO_4 and $CaCl_2$ were used as the main precursors in sol-gel preparation. The sol-gel was centrifuged at three different speeds (1500, 1750 and 2000 rpm). Coated specimens were sintered at 500°C, 600°C and 700°C for 20 minutes and 1 hour respectively. HA coated samples were analyzed under FESEM, XRD, AFM and electrochemical corrosion tests. The initial FESEM test revealed that the best centrifuging speed that results in a crack free HA coated layer at room temperature is 1750 rpm with viscosity of 1798 CP. The FESEM and XRD results also revealed that the best surface morphology with semi-crystalline microstructure belong to the sample sintered at 600°C for 20 min. Also it is concluded that sintering temperature above 600°C for HA coating on Co-Cr based alloys results in cracks propagation. Moreover, in terms of surface roughness all coated and sintered samples except the one sintered at 500°C for 20 min, showed a good result as well. Finally, in terms of corrosion resistance the sample sintered at 600°C for 20 min showed the corrosion rate almost 3.5 times lesser than uncoated sample.

ABSTRAK

Hydroxyapatite (HA) adalah komponen utama struktur semula jadi tulang dan disebabkan sifat biokompatibiliti dan bioaktivitinya yang sangat baik, ia boleh digunakan dalam aplikasi bioperubatan sebagai lapisan salutan untuk implan logam bagi membantu pembentukan ikatan kimia pada antara muka HA/tulang dan bertindak sebagai lapisan perlindung terhadap pelepasan ion daripada prostesis logam. Dalam kajian ini, salutan bioaktif HA telah dihasilkan dengan kaedah sol-gel ke atas substrat CoCrMo berkarbon tinggi. Walaupun kaedah sol-gel adalah kaedah yang mudah dan kos efektif serta berupaya untuk mengawal komposisi kimia, dan mampu menyalut salutan ke atas implan yang kompleks, namun keretakan lapisan sol-gel HA pada implan masih menjadi isu utama. Keretakan boleh diminimumkan dengan menukar kelikatan, komposisi atau variasi dalam prosedur rawatan haba. Na_3PO_4 dan $CaCl_2$ telah digunakan sebagai prekursor utama dalam penyediaan sol-gel. Sol-gel telah diputar pada 1500, 1750 dan 2000 rpm. Spesimen yang tersalut, disinter pada 500°C, 600°C dan 700°C, selama 20 minit dan 1 jam. Sampel yang disaluti HA telah dianalisa dengan FESEM, XRD, AFM dan ujian kakisan elektrokimia. Ujian awal FESEM mendapati kelajuan putaran yang terbaik adalah 1750 rpm dengan kelikatan 1798 CP pada suhu bilik. Ia dapat menghasilkan lapisan salutan HA yang bebas dari keretakan. Keputusan FESEM dan XRD juga mendapati bahawa morfologi permukaan dan mikrostruktur semi-kristal terbaik ialah sampel yang dibakar pada 600°C selama 20 min. Kesimpulanya, suhu pembakaran melebihi 600°C untuk menyalut HA ke atas Co-Cr berasaskan aloi menyebabakan keretakan. Selain itu, dari segi kekasaran permukaan semua sampel tersalut dan tersinter kecuali yang disinter pada 500°C selama 20 min, menunjukkan hasil yang baik, akhir sekali dari segi ketahanan kakisan sampel disinter pada 600°C selama 20 min menunjukkan kadar kakisan hampir 3.5 kali lebih kecil daripada sampel yang tidak bersalut.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AFM	Atomic Force Microscopy
AISI	American Iron and Steel Institute
ASTM	American Society for Testing and Materials
CF	Carbon Fiber
CP	Centipoise
EDX/ EDS	Energy Dispersive X-Ray Spectrometer
FCC	Face-Centered Cubic
FESEM	Field Emission Scanning Electron Microscopy
g/ml	grams per milliliter
GPa	Giga Pascal
HA	Hydroxyapatite
HC	High Carbon
HCP	Hexagonal Close-Packed
HF	Hydrofluoric acid
HV	Vickers Hardness
J/m2	Joule per square meters
LC	Low Carbon
ml	milliliter
mmol l^{-1}	millimole per litter
mmpy	millimeter per year
MPa $m^{1/2}$	Mega Pascal per square meters
mv/s	millivolt per second
rpm	revolutions per minute
SP.rr	Setpoint ramp rate
TCP	Tricalcium Phosphate

TTCP	Tetracalcium Phosphate
V	Volt
XRD	X-Ray Diffraction Analysis
μA	micro ampere

LIST OF SYMBOLS

As	Arsenic
Br	Bromine
C	Carbon
Ca	Calcium
Cl	Chlorine
Co	Cobalt
Cr	Chromium
F	Fluorine
Fe	Iron
Ge	Germanium
K	Potassium
Klc	Plane strain fracture toughness
Mg	Magnesium
Mo	Molybdenum
Na	Sodium
Nb	Niobium
Ni	Nickel
O	Oxygen
P	Phosphorus
S	Sulfur
Si	Silicon
Ta	Tantalum
Ti	Titanium
V	Vanadium
W	Tungsten

Zr	Zirconium
μ	Dynamic viscosity

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

1.1 Introduction

Biomaterial refers to any substance (other than a drug) or combination of substances, synthetic or natural in origin, which can be used for any period of time, as a whole or as a part of a system which treats, augments, or replaces any tissue, organ, or function of the body [1]. Performance of biomaterials is controlled by two characteristics of biofunctionality and biocompatibility. Biofunctionality defines the ability of the device to perform the required function and refers to mechanical properties of the biomaterial, whereas biocompatibility determines the compatibility of the material with the body [2].

A wide range of materials encompassing all the classical materials such as Metals (gold, tantalum, Ti6-Al4-V, 316L stainless steel, Co-Cr Alloys, titanium alloys), Ceramics (alumina, zirconia, carbon, titania, bioglass, hydroxyapatite(HA)), Composite (Silica/SR, CF/UHMWPE, CF/PTFE, HA/PE, CF/epoxy, CF/PEEK, CF/C, Al_2O_3/PTFE), Polymers, Ultra high molecular weight polyethylene (UHMWPE), Polyethylene (PE), Polyurethane (PU), Polytetrafuoroethylene (PTFE), Polyacetal (PA), Polymethylmethacrylate (PMMA), Polyethylene Terepthalate

(PET), Silicone Rubber (SR), Polyetheretherketone (PEEK), Poly lactic acid (PLA), and Polysulfone (PS) have been investigated as biomaterials.

Researchers also classified materials into several types such as bioinert, bioactive, biostable, biodegradable and etc. In broad terms, inert (more strictly, nearly inert) materials prohibit or minimize tissue response. Active materials encourage bonding to surrounding tissue. Degradable or resorbable materials are incorporated into the surrounding tissue, or may even dissolve completely over a period of time. Metals are typically inert, ceramics may be inert, active or resorbable and polymers may be inert or resorbable [3]. Biomaterials must be nontoxic, noncarcinogenic, chemically inert, stable, and mechanically strong enough to withstand the repeated forces of a lifetime.

The physical properties of the materials, their potential to corrode in the tissue environment, their surface configuration, tissue induction and their potential for eliciting inflammation or rejection response are all important factors on this area. The biomaterial discipline has evolved significantly over the past decades. The goal of biomaterial researches has been continued to develop implant materials that induce predictable, control-guided and rapid healing of the interfacial tissues both hard and soft [4]. Very important requirement for any material used in the human body is biocompatibility which is defined as the ‘‘ability of a material to perform with an appropriate host response in a specific application”, because it should not cause any adverse reaction in the body [5].

Mostly metallic biomaterials used as orthopedic prostheses in biomedical applications. Metallic biomaterials used in bone plate are neither bioactive nor biodegradable. However, they are the most common biomaterials for manufacturing medical devices such as hip joints, bone plates and dental implants because they have good mechanical properties such as Modulus of elasticity, Tensile strength, Compressive strength, Elongation Metallurgical properties, low cost and also they are easy to fabrication. Indeed, among metallic biomaterials, stainless steel, cobalt alloys and titanium alloys have the most applications in orthopedic issues [6].

Among above-mentioned metallic biomaterials CoCrMo alloys are biocompatible materials and are widely used as orthopedic implant materials in clinical practice such as hip joint and knee replacement due to their superior mechanical properties, good wear- and corrosion-resistances. The biocompatibility of CoCrMo alloys are closely related to their good corrosion resistance due to the presence of an extremely thin passive oxide film that spontaneously forms on the alloy surface. XPS analysis reveals that its composition is predominantly Cr_2O_3 with some minor contribution from Co and Mo oxides. These films also form on the surfaces of other metallic biomaterials (stainless steels, titanium and its alloys) and serve as a barrier to corrosion processes in alloy systems [7].

In spite of the good corrosion resistance of CoCrMo alloys, there is still a concern about metal ion release from orthopedic implants into the body fluids (serum, urine, etc.). Metals from orthopedic implant materials are released into surrounding tissue by various processes, including corrosion, wear and mechanically accelerated processes such as stress corrosion, corrosion fatigue and fretting corrosion. Such metal ions and wear debris, concentrated at the implant-tissue interface, may migrate through the tissue. Research shows that the metal release is associated with clinical implant failure, osteolysis, cutaneous allergic reactions and remote site accumulations [8]. One effective approach for preventing and/or reducing the potentially harmful metal ion release from orthopedic implant materials is coating the surfaces of these materials.

A bioactive surface coating is capable to support bonding to surrounding bone. One of the best bioactive compounds which is suitable for coating metallic biomaterial implants is “Hydroxyapatite”. Hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH)_2$) is the main structural component of natural bone, and used as an important material for bone and tooth implants in the biomaterial field. In order to achieve bioactivity for metal implants (e.g. Co alloys, Ti alloys or stainless steel) as bone substitutes, HA coating is usually introduced onto their surfaces. Porous HA coating on these metal substrates can be adopted as bone cements in reconstruction. HA has many biological profits such as direct bonding to bone and enhancement of new bone formation around it due to its chemical similarity with hard tissues. HA as a coating also can reduce the amount of ion release from the metallic substrate. Because HA has poor mechanical properties and it is weak and brittle without any support, so it is applied as a coating on an inert metal with good bio-mechanical properties such as CoCrMo [9].

To date many essential techniques have been used in the preparation of HA coatings such as plasma spraying, magnetron sputtering, laser ablation, sol-gel, biomimetic, and electrochemical deposition [10]. Compared to other coating techniques, the sol-gel technique is one of the thin film methods provides some benefits over the others such as chemical homogeneity, fine grain structure, and low processing temperature. Moreover, compared to the other thin film methods, it is simple and cost efficient, as well as effective for the coating of complex-shaped implants.

1.2 Problem Statement

Massive cracks of HA sol-gel coated layer on implants are still a major issue due to releasing harmful ions from the body of implant which can result in adverse biological reactions in human body. Reduction of cracks can be done by controlling several parameters such as finding the most appropriate viscosity of sol-gel regarding to examine different range of centrifuging speed in the procedure of sol-gel preparation, obtaining the most suitable proportion of sol-gel precursors and finally applying different range of sintering time and temperature to get the best heat treatment procedure.

For Co-Cr based alloy as a metallic biomaterial there are some disadvantages that result in some restrictions in their usage in biomedical applications such as its corrosion behavior in vivo which made concerns about metal ion release in human body and its biocompatibility and cell growth on its surface which has not been reported as good as titanium alloys. Nonetheless, these problems would be solved by coating implants with biocompatible and corrosion resistant material like Hydroxyapatite (HA).

Furthermore, there are very limited extensive studies investigating the effect of coating method and heat treatments on Co-Cr based substrates as compared to Titanium alloy substrates

1.3 Objectives

Based on problem statement, the main aims of this study are:

1. To determine the feasible parameters for a crack free HA coating on Co-Cr based substrate.
2. To analyze the surface morphology of the HA coated layer on Co-Cr based substrate under different coating conditions.
3. To compare the corrosion behavior of Co-Cr based substrate before and after HA sol-gel coating.

1.4 Scopes of Study

The scopes of this project are narrowed as follow:

1. HC CoCrMo based alloy is used as the substrate material.
2. Sol-gel method is employed for coating HA on the substrate.
3. Na_3PO_4 and $CaCl_2$ are used as the main precursors of sol-gel preparation.

4. Centrifuging speed of sol-gel solution is varied in three levels (1500, 1750 and 2000 rpm).
5. Sintering temperature and soaking time of HA coated samples are 500ºC, 600ºC and 700ºC at 20 minutes and 1 hour, respectively.

REFERENCES

1. Dee, K.C., D.A. Puleo, and R. Bizios, *An introduction to tissue-biomaterial interactions*. 2003: Wiley. com.

2. Malekani, J., et al. *Biomaterials in orthopedic bone plates: a review*. in *Proceedings of the 2nd Annual International Conference on Materials Science, Metal & Manufacturing (M3 2011)*. 2011. Global Science and Technology Forum.

3. www.azom.com Biomaterials: An Overview.

4. Muddugangadhar, B., et al., B*iomaterials for dental implants: An overview.* International Journal of Oral Implantology and Clinical Research, 2011. 2**(**1): p. 13-24.

5. Gurappa, I., C*haracterization of different materials for corrosion resistance under simulated body fluid conditions.* Materials Characterization, 2002. 4**9(**1): p. 73-79.

6. Temenoff, J.S. and A.G. Mikos, Biomaterials: the intersection of biology and materials science2008: Pearson/Prentice Hall.

7. Contu, F., B. Elsener, and H. Böhni, Co*rrosion behaviour of CoCrMo implant alloy during fretting in bovine serum. C*orrosion science, 2005. 47**(8**): p. 1863-1875.

8. Okazaki, Y. and E. Gotoh, Co*mparison of metal release from various metallic biomaterials in vitro. B*iomaterials, 2005. 26**(1**): p. 11-21.

9. Ignjatovic, N. and D. Uskokovic, Sy*nthesis and application of hydroxyapatite/polylactide composite biomaterial. A*pplied surface science, 2004. 23**8(1**): p. 314-319.

10. Thian, E., et al., *Magnetron co-sputtered silicon-containing hydroxyapatite thin films—an in vitro study.* Biomaterials, 2005. 26**(1**6): p. 2947-2956.

11. Helmus, M.N., D.F. Gibbons, and D. Cebon, *Biocompatibility: meeting a key functional requirement of next-generation medical devices.* Toxicologic pathology, 2008. 36**(1**): p. 70-80.

12. Narayan, R., *Biomedical materials.* 2009: Springer.

13. Park, J.B. and J.D. Bronzino, *Biomaterials: principles and applications.* 2002: crc press.

14. NakaNo, T., *Mechanical properties of metallic biomaterials.* Metals for Biomedical Devices, 2010: p. 71.

15. Kokubo, T., H.-M. Kim, and M. Kawashita, *Novel bioactive materials with different mechanical properties.* Biomaterials, 2003. 24**(1**3): p. 2161-2175.

16. Rack, H. and J. Qazi, *Titanium alloys for biomedical applications.* Materials Science and Engineering: C, 2006. 26**(8**): p. 1269-1277.

17. Rodriguez-Gonzalez, F.A., *Biomaterials in orthopaedic surgery.* Corrosion Engineering, Science and Technology, 2010. 45**(2**).

18. Ratner, B., et al., *Biomaterials science: an introduction to materials in medicine.* San Diego, California, 2004: p. 162-164.

19. Rahaman, M.N., et al., *Ceramics for prosthetic hip and knee joint replacement.* Journal of the American Ceramic Society, 2007. 90**(7**): p. 1965-1988.

20. Marti, A., *Cobalt-base alloys used in bone surgery.* Injury, 2000. 31**:** p. D18-D21.

21. Fehring, T.K., J.H. Chaffin III, and R.L. Kennedy, *Enhanced biocompatible implants and alloys.* 2001, Google Patents.

22. Herrera, M., et al., *Effect of C content on the mechanical properties of solution treated as-cast ASTM F-75 alloys.* Journal of Materials Science: Materials in Medicine, 2005. 16**(7**): p. 607-611.

23. Niinomi, M., *Recent metallic materials for biomedical applications.* Metallurgical and materials transactions A, 2002. 33**(3**): p. 477-486.

24. Patel, B., et al., *Cobalt-based orthopaedic alloys: Relationship between forming route, microstructure and tribological performance.* Materials Science and Engineering: C, 2012. 32**(5)**: p. 1222-1229.

25. Hosoya, K., et al., *A novel covalently crosslinked gel of alginate and silane with the ability to form bone-like apatite.* Journal of Biomedical Materials Research Part A, 2004. 71**(4)**: p. 596-601.

26. Yan, Y., et al., *Biotribocorrosion of CoCrMo orthopaedic implant materials - Assessing the formation and effect of the biofilm.* Tribology international, 2007. 40**(1**0-12): p. 1728-1728.

27. Souza, J., et al., *Do oral biofilms influence the wear and corrosion behavior of titanium?* Biofouling, 2010. 26**(4)**: p. 471-478.

28. Lewis, A., et al., *Effect of synovial fluid, phosphate-buffered saline solution, and water on the dissolution and corrosion properties of CoCrMo alloys as used in orthopedic implants.* Journal of Biomedical Materials Research Part A, 2005. 73**(4)**: p. 456-467.

29. Sargeant, A. and T. Goswami, *Hip implants - Paper VI - Ion concentrations.* Materials & Design, 2007. 28**(1)**: p. 155-171.

30. Okazaki, Y., et al., *Comparison of metal concentrations in rat tibia tissues with various metallic implants.* Biomaterials, 2004. 25**(2**8): p. 5913-5920.

31. Davies, A.P., et al., *Metal-specific differences in levels of DNA damage caused by synovial fluid recovered at revision arthroplasty.* Journal of Bone and Joint Surgery-British Volume, 2005. 87**B(1**0): p. 1439-1444.

32. Jacobs, J.J., et al., *Can metal levels be used to monitor metal-on-metal hip arthroplasties?* Journal of Arthroplasty, 2004. 19**(8)**: p. 59-65.

33. MacDonald, S.J., *Can a safe level for metal ions in patients with metal-on-metal total hip arthroplasties be determined?* The Journal of Arthroplasty, 2004. 19**(8)**: p. 71-77.

34. Burstein, G.T., C. Liu, and R.M. Souto, *The effect of temperature on the nucleation of corrosion pits on titanium in Ringer's physiological solution.* Biomaterials, 2005. 26**(3)**: p. 245-256.

35. Keegan, G., I. Learmonth, and C. Case, Or*thopaedic metals and their potential toxicity in the arthroplasty patient A REVIEW OF CURRENT KNOWLEDGE AND FUTURE STRATEGIES.* Journal of Bone & Joint Surgery, British Volume, 2007. 89**(5**): p. 567-573.

36. Revie, R.W., Co*rrosion and corrosion control.* 2008: John Wiley & Sons.

37. Milosev, I., Th*e effect of biomolecules on the behaviour of CoCrMo alloy in various simulated physiological solutions. E*lectrochimica Acta, 2012. 78**:** p. 259-273.

38. Fathi, M.H., et al., In *vitro corrosion behavior of bioceramic, metallic, and bioceramic–metallic coated stainless steel dental implants. D*ental Materials, 2003. 19**(3**): p. 188-198.

39. Moreno, J.M.C., et al., Su*rface analysis and electrochemical behavior of Ti-20Zr alloy in simulated physiological fluids. M*aterials Science and Engineering B-Advanced Functional Solid-State Materials, 2013. 17**8(1**8): p. 1195-1204.

40. Lewis, G., Pr*operties of open-cell porous metals and alloys for orthopaedic applications. J*ournal of Materials Science-Materials in Medicine, 2013. 24**(1**0): p. 2293-2325.

41. Swiontkowski, M.F., et al., Cu*taneous metal sensitivity in patients with orthopaedic injuries. J*ournal of Orthopaedic Trauma, 2001. 15**(2**): p. 86-89.

42. Li, M., et al., Co*rrosion behavior of TiN coated type 316 stainless steel in simulated PEMFC environments. C*orrosion science, 2004. 46**(6**): p. 1369-1380.

43. Della Valle, A.G., et al., La*te fatigue fracture of a modern cemented forged cobalt chrome stem for total hip arthroplasty: a report of 10 cases. T*he Journal of Arthroplasty, 2005. 20**(8**): p. 1084-1088.

44. Reclaru, L., et al., Co*rrosion behaviour of cobalt–chromium dental alloys doped with precious metals. B*iomaterials, 2005. 26**(2**1): p. 4358-4365.

45. Liu, X., P.K. Chu, and C. Ding, Su*rface modification of titanium, titanium alloys, and related materials for biomedical applications. M*aterials Science and Engineering: R: Reports, 2004. 47**(3**): p. 49-121.

46. Boyan, B.D., et al., *Role of material surfaces in regulating bone and cartilage cell response.* Biomaterials, 1996. 17(**2**): p. 137-146.

47. Łaczka-Osyczka, A., et al., *Behavior of bone marrow cells cultured on three different coatings of gel-derived bioactive glass–ceramics at early stages of cell differentiation.* Journal of biomedical materials research, 1998. 42(**3**): p. 433-442.

48. Hayashi, K., et al., *Effect of surface roughness of hydroxyapatite—coated titanium on the bone-implant interface shear strength.* Biomaterials, 1994. 15(**14**): p. 1187-1191.

49. Deligianni, D.D., et al., *Effect of surface roughness of hydroxyapatite on human bone marrow cell adhesion, proliferation, differentiation and detachment strength.* Biomaterials, 2000. 22(**1**): p. 87-96.

50. Paital, S.R. and N.B. Dahotre, *Calcium phosphate coatings for bio-implant applications: Materials, performance factors, and methodologies.* Materials Science and Engineering: R: Reports, 2009. 66(**1**): p. 1-70.

51. Méndez-Vilas, A., J. Bruque, and M. González-Martín, *Sensitivity of surface roughness parameters to changes in the density of scanning points in multi-scale AFM studies. Application to a biomaterial surface.* Ultramicroscopy, 2007. 107(**8**): p. 617-625.

52. Jandt, K.D., *Atomic force microscopy of biomaterials surfaces and interfaces.* Surface Science, 2001. 491(**3**): p. 303-332.

53. Corbridge, D.E.C., *Phosphorus-an outline of its chemistry, biochemistry and technology.* 1985: Elsevier Science Publishers BV.

54. Hench, L.L. and J. Wilson, *An introduction to bioceramics.* Vol. 1. 1993: World Scientific.

55. Wolke, J., et al., *In vivo dissolution behavior of various RF magnetron-sputtered Ca-P coatings on roughened titanium implants.* Biomaterials, 2003. 24(**15**): p. 2623-2629.

56. Stephenson, P., et al., *The effect of hydroxyapatite coating on ingrowth of bone into cavities in an implant.* The journal of arthroplasty, 1991. 6(**1**): p. 51-58.

57. Thangamani, N., K. Chinnakali, and F. Gnanam, Th*e effect of powder processing on densification, microstructure and mechanical properties of hydroxyapatite. C*eramics international, 2002. 28**(4**): p. 355-362.

58. Rezwan, K., et al., Bi*odegradable and bioactive porous polymer/inorganic composite scaffolds for bone tissue engineering. B*iomaterials, 2006. 27**(1**8): p. 3413-3431.

59. Wang, C., et al., Ph*enotypic expression of bone-related genes in osteoblasts grown on calcium phosphate ceramics with different phase compositions. B*iomaterials, 2004. 25**(1**3): p. 2507-2514.

60. Zhang, S., et al., Ad*hesion strength of sol–gel derived fluoridated hydroxyapatite coatings. S*urface and Coatings Technology, 2006. 20**0(2**2): p. 6350-6354.

61. Wen, C., et al., Hy*droxyapatite/titania sol–gel coatings on titanium–zirconium alloy for biomedical applications. A*cta Biomaterialia, 2007. 3(**3**): p. 403-410.

62. Heimann, R.B., Pl*asma-spray coating.* 2008: Wiley. com.

63. Kim, H.-W., et al., Hy*droxyapatite coating on titanium substrate with titania buffer layer processed by sol–gel method. B*iomaterials, 2004. 25**(1**3): p. 2533-2538.

64. Liu, D.-M., T. Troczynski, and W.J. Tseng, Wa*ter-based sol–gel synthesis of hydroxyapatite: process development. B*iomaterials, 2001. 22**(1**3): p. 1721-1730.

65. Overgaard, S., et al., Th*e influence of crystallinity of the hydroxyapatite coating on the fixation of implants MECHANICAL AND HISTOMORPHOMETRIC RESULTS. J*ournal of Bone & Joint Surgery, British Volume, 1999. 81**(4**): p. 725-731.

66. Milella, E., et al., Pr*eparation and characterisation of titania/hydroxyapatite composite coatings obtained by sol–gel process. B*iomaterials, 2001. 22**(1**1): p. 1425-1431.

67. Fathi, M. and A. Hanifi, Ev*aluation and characterization of nanostructure hydroxyapatite powder prepared by simple sol–gel method. M*aterials letters, 2007. 61**(1**8): p. 3978-3983.

68. Raynaud, S., et al., Ca*lcium phosphate apatites with variable Ca/P atomic ratio I. Synthesis, characterisation and thermal stability of powders. B*iomaterials, 2002. 23**(4**): p. 1065-1072.

69. Gross, K., et al., Th*in hydroxyapatite coatings via sol–gel synthesis. J*ournal of Materials Science: Materials in Medicine, 1998. 9(**1**2): p. 839-843.

70. LeGeros, R., et al., Bi*phasic calcium phosphate bioceramics: preparation, properties and applications. J*ournal of materials science: Materials in Medicine, 2003. 14**(3**): p. 201-209.

71. Rodrıguez-Lorenzo, L., M. Vallet-Regı, and J. Ferreira, Fa*brication of hydroxyapatite bodies by uniaxial pressing from a precipitated powder. B*iomaterials, 2001. 22**(6**): p. 583-588.

72. Liu, J., et al., Th*e influence of pH and temperature on the morphology of hydroxyapatite synthesized by hydrothermal method. C*eramics international, 2003. 29**(6**): p. 629-633.

73. Yang, L., et al., De*scription of surface roughness of sol–gel films/coatings by X-ray reflectivity technique. A*pplied Surface Science, 2009. 25**5(1**9): p. 8226-8229.

74. Sonawane, R., S. Hegde, and M. Dongare, Pr*eparation of titanium (IV) oxide thin film photocatalyst by sol–gel dip coating. M*aterials Chemistry and Physics, 2003. 77**(3**): p. 744-750.

75. Gutoff, E.B. and E.D. Cohen, Co*ating and drying defects: troubleshooting operating problems.* 2006: Wiley-Interscience.

76. Kim, H.W., et al., So*l‐gel‐modified titanium with hydroxyapatite thin films and effect on osteoblast‐like cell responses. J*ournal of Biomedical Materials Research Part A, 2005. 74**(3**): p. 294-305.

77. Grandfield, K., et al., Fr*ee form fabricated features on CoCr implants with and without hydroxyapatite coating in vivo: a comparative study of bone*

contact and bone growth induction. Journal of Materials Science: Materials in Medicine, 2011. 22**(4)**: p. 899-906.

78. Harle, J., et al., *Initial responses of human osteoblasts to sol–gel modified titanium with hydroxyapatite and titania composition.* Acta Biomaterialia, 2006. 2(**5**): p. 547-556.

79. Yan, Y., A. Neville, and D. Dowson, *Biotribocorrosion of CoCrMo orthopaedic implant materials—assessing the formation and effect of the biofilm.* Tribology international, 2007. 40**(1**0): p. 1492-1499.

80. Vidal, C.V. and A.I. Muñoz, *Effect of thermal treatment and applied potential on the electrochemical behaviour of CoCrMo biomedical alloy.* Electrochimica Acta, 2009. 54**(6**): p. 1798-1809.