SCHOOL OF MATERIALS AND MINERAL RESOURCES ENGINEERING

UNIVERSITI SAINS MALAYSIA

BIOACTIVE GLASS REINFORCED POLYURETHANE SCAFFOLDS: EFFECT OF PU SOLUTION CONCENTRATION

By

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Dissertation submitted in partial fulfillment

of the requirements for the Degree of Bachelor of Engineering with Honours

(Materials Engineering)

Universiti Sains Malaysia

JULY 2017

DECLARATION

I hereby declare that I have conducted, completed the research work and written the dissertation entitles "**Bioactive Glass Reinforced Polyurethane Scaffolds : Effects of PU Solution Concentration**". I also declare that it has not been previously submitted for the award of any degree or diploma or other similar title of this for any other examining body or university.

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Date : 4 July 2017

ACKNOWLEDGEMENTS

First and foremost, all praises to ALLAH S.W.T, for the strength given to complete the final year project throughout the academic session of 2016/2017. I would like to express my sincere gratitude to my lovely supervisor, Dr. Syazana bt Ahmad Zubir for her continuous support during my degree study and related research, for her patience, motivation, and immense knowledge. Her guidance helped me in through the project and writing of this thesis. I could not have imagined having a better advisor and mentor throughout my degree journey.

In addition, I would like to thank to Dr. Tuti Katrina Bt. Abdullah, who has helped me in giving ideas and suggestion as well as support throughout my final year project. I also owe my graduate to the technicians who had given me helping hands during the period of the project. I express my gratitude for their kind co-operation, guidance, patient, encouragement and support they have provided. Without them, I could not make this far.

I would also like to take this opportunity to thank all the lecturers involved during my project for the precious guidance and opinions valuable in my study. Furthermore, special thanks to all my friends who helped me a lot during this project. They have always been supportive in helping me with thesis writing and moral support.

My sincere indebtedness and gratitude goes to my parents for their love, dream and sacrifice throughout my life. Their sacrifice had inspired me from the day I learned how to read and write until what I have become now. There are no words to describe my appreciation for their devotion, support and faith in my ability to achieve my dreams.

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LIST OF ABBREVIATIONS

Bioactive glass	**-**	**BG**
Extracellular matrix	**-**	**ECM**
X-ray diffraction	**-**	**XRD**
X-ray Fluorescence	**-**	**XRF**
Fourier Transform Infrared Spectroscopy	**-**	**FTIR**
Dynamic Mechanical analysis	**-**	**DMA**
Thermogravimetric analysis	**-**	**TGA**
Differential Scanning Calorimetry	**-**	**DSC**
Amine bonding	**-**	**-NH**
Hydrogen oxide bonding	**-**	**-OH**
Hydrogen bonded Carbonyl group	**-**	**H-CO**
Free Carbonyl group	**-**	**F-CO**

LIST OF CHEMICAL FORMULA

Polyurethane	**-**	**PU**
Polycaprolactone	**-**	**PCL**
Silicon dioxide	**-**	**SiO_2**
Sodium oxide	**-**	**Na_2O**
Calcium oxide	**-**	**CaO**
Phosphorous pentoxide	**-**	**P_2O_5**
Tetrahydrofuran	**-**	**THF**
Aluminum Oxide	**-**	**Al_2O_3**

LIST OF SYMBOLS

millimetre	**-**	**Mm**
mentimetre	**-**	**Cm**
micrometre	**-**	**µm**
milligram	**-**	**Mg**
weight percent	**-**	**wt. %**
degree Celsius	**-**	**^{o}C**
Glass transition temperature	**-**	**T_g**
Melting temperature	**-**	**T_m**

PERANCAH POLIURETANA DIPERKUAT KACA BIOAKTIF: KESAN TERHADAP NISBAH PU – THF

ABSTRAK

Dalam kajian ini, perancah berliang komposit poliuretana (PU) diperkuat kaca bioaktif telah difabrikasi dengan berat PU yang berbeza. Dalam kajian ini, perancah poliuretana (PU) -kacabioaktif (BG) telah disediakan menggunakan teknik garam larut-lesap. Sifat kimia dan fizikal perancah komposit yang telah dinilai menggunakan teknik yang berbeza iaitu Analisis Termogravimetri (TGA), Analisis Infra-merah (FTIR), Mikroskopi Imbasan Elektron (SEM), Ujian Keliangan dan Simpanan Mampatan. SEM analisis dijalankan untuk menganalisa mikrostruktur keratan rentas perancah berliang yang disediakan dimana pengagihan liang struktur perancah dan partikel kaca pada matrik PU telah dianalisa. Kesan bagi penambahan kepekatan PU terhadap sifat perancah PU-BG seperti keliangan, simpanan mampatan dan modulus simpanan mampatan telah dinilai. Keliangan menunjukkan peningkatan sekiranya perancah poliuretana tinggi. Keputusan untuk simpanan mampatan juga menunjukkan peningkatan dengan meningkatnya perancah komposit poliuretena. 12. wt% mempunyai nilai simpanan mampatan paling tinggi iaitu 0.13 Mpa berbanding nilai yang terendah iaitu 0.04 Mpa. Secara keseluruhan, berdasarkan keputusan modulus simpanan mampatan yang diperoleh, perancah komposit poliuretana yang tinggi mempunyai modulus simpanan mampatan yang lebih tinggi berbanding dengan perancah poliuretana yang rendah kepekatannya.

BIOACVTIVE GLASS REINFORCED POLYURETHANE SCAFFOLD: EFFECT OF PU SOLUTION CONCENTRATION

ABSTRACT

In this research, porous bioactive glass (BG) reinforced polyurethane (PU) composite scaffolds with different PU mass was fabricated by using salt leaching technique. There are a number of characterization techniques applicable for determining the chemical and physical properties of the fabricated porous scaffolds. SEM analysis is performed to observe the microstructure at the cross-sectional area of porous scaffolds. The porous scaffolds prepared exhibit the closed pore as concentration of PU increase. The porosity showed the increasing trend as increasing the PU solution concentration from 8. wt% to 12. wt%. For the result of compressive strength, it also showed an increasing trend in compressive strength as increasing in PU concentration. 12. wt % has the highest value of compressive strength which is (0.13 Mpa) compare to the lowest one which is 0.04 Mpa. The result also showed that the composite scaffolds prepared with more PU concentration (0.28 Mpa) has higher compressive modulus than the scaffolds with lower amount of PU (0.12 Mpa.

CHAPTER 1

INTRODUCTION

1.1 RESEARCH BACKGROUND

Nowadays, tissue engineering has been highly demand due to limitation of transplantation, transfusion or grafts technologies. Tissue engineering has become an option for repairing or replacing damaged tissues or organs by implanting the synthetic construct into patients (Harrison, 2007). The main target of bone tissue engineering is to restore and maintain functionality of damaged or diseased bone tissue by means of a synergic combination of cell biology, materials and engineering. With this aim, in order to promote bone regeneration, a proper scaffold can be used as a template for cell interaction and new tissue in-growth. Bone has the unique healing ability for self-repair after an injury. This self-healing ability can be improved and required a platform to regenerate the fracture region (Poh et al., 2013). The concept of bone regeneration is to use a scaffold that can act as a three-dimensional (3D) temporary template to guide bone repair and stimulate the natural regenerative mechanism of human body (Huang et al., 2009)

The main goal of scaffold is to provide appropriate base for tissue growth and cell proliferation. Scaffold also acts as the substrate that allows cells to attach, proliferate, differentiate which transform from a non-specific or primitive state into cells exhibiting the bone specific functions, and organizes into normal, healthy bone as the scaffold degrades (Chen et al., 2008). Ideally the scaffold will stimulate the natural regenerative mechanisms of the human body.

There are many designs criteria for bone tissue engineering scaffolds. Firstly, the scaffold must be able to deliver cells. Scaffold must also be osteoconductivity and it would be best if the material encourage osteoconduction with host bone. Osteoconductivity does not only eliminate the formation of fibrous tissue encapsulation but it also brings about a strong bond between the scaffold and host bone (Chen et al., 2008).

The mechanical properties of the scaffold are important where it should be compatible with the natural human tissue. Scaffold must be in porous structure and containing interconnected porous structure with porosity > 90% and diameters between 100-400 μm for cell penetration, tissue in growth and vascularisation, and nutrient delivery (Cannillo et al. 2010) Other than that, the pores need to be large enough to allow cells to migrate into the structure, where they eventually become bound to the ligands within the scaffold, but small enough to establish a sufficiently high specific surface, leading to a minimal ligand density to allow efficient binding of a critical number of cells to the scaffold.

For the bioactive glass, many of the best inventions have been made. The first bioactive glass was invented by Larry Hench at the University of Florida in 1969. Professor Hench began his work on finding material that could bond to bone with US Army colonel. The colonel asked him if materials could be developed that could survive the aggressive environment in human body. The problem was that all implant materials available at that time like metals and polymers that were designed to be bioinert, triggered fibrous encapsulation after implantation rather than forming a stable interface or bond with tissues. Hence, Professor Hench decided to make a degradable glass in the Na_2O-CaO-SiO_2- P_2O_5 system which is high in calcium content and with a composition

close to a ternary eutectic in the Na_2O-CaO-SiO_2 diagram (Hench, 2006). The main discovery was that a glass of the composition 45 mol.% SiO_2, 24.5 mol.% Na_2O and CaO and 6 mol.% P_2O_5, formed a bond with bone so strong that it could not be removed without breaking the bone.

Among the advantages of bioactive glass include the high bioactivity index and the ability to stimulate more bone regeneration than other bioactive ceramics. It also has excellent osteoconductivity and bioactivity, controllable biodegradability and ability to induce osteogenesis and angiogenesis (Jones, 2010). Besides, bioactive glass also reinforce with polyurethanes as a potential candidate for synthetic bone graft. However, bioactive glass has poor mechanical properties. It limits their usage in medical applications where the fracture toughness is low (0.6 MPa). Numerous reports show that the crystallinity, while decreasing bioactivity, increases mechanical properties.

Polyurethanes are attractive candidates for biomedical applications. Different amount of polyurethane will affect the mechanical properties of scaffold. It is often associated with properties of durability, elasticity, elastomer-like character, fatigue resistance, compliance and acceptance or tolerance in the body during the healing. Polyurethanes also have the hydrophobic group of alkyl and chain extenders. The speciality of polyurethanes is the present of this special group that is non-toxic and can control degradation rate (Huang et al., 2009). Polyurethanes have been used for fabricating biomedical devices such as cardiovascular catheters, diaphragms of blood pumps, coating materials for implantable pacemakers and other biomedical products (Ryszkowska et al., 2010).

The combination of bioactive glass and polyurethanes improves the properties of the scaffold. This combination will improve the bioactivity and the mechanical

properties of the polyurethanes, forming polyurethanes/bioglass composites. It also combines polyurethanes and bioactive glass biocompatibility, mechanical and physical properties to produce good properties of scaffold (de Oliveira et al., 2012).

1.2 PROBLEM STATEMENT

Our body is generally made of bone which is about 15% of our overall body mass and it is a really important part in our body. This is because the bone provides support and structure to the body. Any damages to the bone would limit our body movement. Hence, causing unhealthy body.

Any fracture or cracks in the bone would have to be repaired immediately. Even though bones contain high regeneration potential, appropriate platform is needed for large bone fracture by internal and external fixation technique. Furthermore, cells are incapable to regenerate new tissue by itself because of its restricted degree of restoration capacity in forming a new tissue. So, the best way for stabilising bone restoration process after a treatment is by the internal fixation treatments.

Among the applicable internal fixation treatments for bone fracture is bone grafting. However, bone grafting is complex because it can only be acquired via autograft (from patient's own body) or allograft (obtained from bone bank or other donors). Hence, the bones obtained through this method are fully dependent on the donor itself. To overcome this problem, engineered tissues are used as a proper platform for bone regeneration. Engineered tissues are distinct from bone grafting because it is made from biomaterial, which has better response. The characteristic of biomaterials used as artificial ECM materials is low stiffness for the purpose of avoiding large stiffness mismatch gap.

Nowadays, biodegradable synthetic extracellular matrix (ECM) biomaterials is widely used and there are a number of researches which developed these biomaterials for the usage of bone tissue engineering application. Poly(L-lactic acid) (PLLA), polycaprolactone (PCL), polyurethane (PU) and polyethylene (PE) are examples of polymers that have been developed for orthopaedic application.

PU is selected as tissue engineering composite matrix for bone tissue engineering in this experiment due to its capability of excellent performance in various medical implants application. Many researchers have investigated the biocompatible and biodegradability of PU for almost thirty years to ensure that it can be used as scaffolds for tissue engineering applications. PU are also favourable due to the flexibility associated with their versatile chemistry (Tetteh et al., 2014). Furthermore, PU helps in customizing scaffolds in obtaining desirable chemical, physical and mechanical properties such as durability, elasticity and fatigue resistance.

Notwithstanding the many advantages of PU, some disadvantages have also been identified, such as the bioactivity of PU. Its bioactivity is relatively low towards bone tissues due to the characteristic of fully reacted PU, which is chemically inert polymer. To overcome this problem, 45S5 bioglass has been introduced and added in order to improve the PU characteristics. In order to achieve desired properties, 45S5 bioactive glass filler is introduced to improve strength and bioactivity of polyurethane scaffolds.

1.3 RESEARCH OBJECTIVES

The objectives of this experiment includes:

1. To fabricate the PU-BG scaffold using salt leaching technique.

2. To study the effect of different PU solution concentration on the mechanical strength and porosity distribution of PU-BG scaffold.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

Daily, thousands of surgical procedures are performed to replace or repair tissue that has been damaged by diseases or trauma. There are four main factors for tissue engineering which are living cells, control over growth factors, culturing and scaffold. The scaffold has been developed to regenerate the tissue damaged by combining cells from the body with highly porous scaffold biomaterials which helps in the growth of a new tissue. Scaffold extracellular matrix is the basis of tissue engineering with the triad of signal for tissue induction responding to stem cells. Figure 2.1shows the schematic diagram of a latest functional tissue growth method.

The main function of bone tissue engineering is to restore and maintain human bone tissue by combining cells biology, materials science and engineering principles. Harvested cells, recombining signal molecules and 3D matrices are the key ingredients for tissue engineering. Signal molecules can be seeded into porous biodegradable scaffold by coated onto the scaffold or directly incorporated into them. It also can be cultured in vitro, and subsequently, the scaffold are implanted into bone defect (Saltzman, 2004).

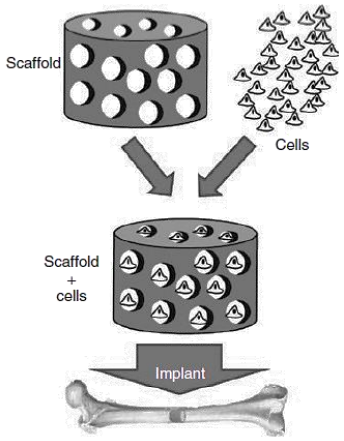


Figure 2.1 Growth process for a functional neo-tissue (Vallet-Regí, 2014).

2.2 Characteristic of scaffold

The most important part in designing scaffold is the requirement needed for scaffold and its materials selection. The choice of material is highly important in designing scaffolds (Smith et al., 2009). Biocompatibility, biodegradability and mechanical properties are the main requirements of a good scaffold.

It should also be biodegradable to allow cells to produce their own extracellular matrix (Babensee et al., 1998). Modulus of the bone and materials should also be similar or less in order to limit the occurrence of shield stress phenomena between the implant and the host bone (Ikada, 2006).

The mechanical properties of the scaffold must be strong enough for implantation and also to ensure that the surgical handling is easy. Designing scaffolds with a good mechanical property is a big challenge for cardiovascular and orthopaedic applications because the implanted scaffold must have sufficient mechanical integrity to function from the beginning of implantation until remodelling process. The modulus should be low but has high strength for orthopedic application in order to make the implantation easy.

2.3 Types of scaffold

There are many types of scaffolds that have been widely used for many applications especially in biomedical applications such as naturally derived scaffolds, inorganic scaffolds, composite scaffolds and etc. Different types of scaffold have different properties that have been used in bone tissue engineering. These scaffold also an alternative ways in supporting organs systems that may damage by injuries.

Composite scaffolds always become one of the main selection for many applications because of the properties that have sufficient mechanical strength, adequate elastic modulus close to the bone tissue modulus and controlled in vivo degradation rate (Verrier *et al.*, 2011) They also have properties that can be controlled to fulfill desired application.

2.3.1 Natural Scaffold

Scaffold is not only specifying to one type of scaffold, but there are many types of scaffolds that can be used as a tissue for biomedical application. Natural scaffold is one of the examples of scaffold that applied to this application.

However, polymer also involves in producing natural scaffold. Chitosan, collagen and alginate are the examples of the polymers used in producing natural scaffolds. These scaffolds must have characteristics like a good toughness, flexible and does not undergo pore creation process (Ikada, 2006). At scaffold surface can occur proliferation of cells because of the polymer that can provide good adhesion on the scaffolds surface, this enabled the proliferation of cells to occur on the scaffolds surface.

2.3.2 Inorganic scaffolds

Inorganic scaffolds or ceramic scaffolds are one of the bioceramic materials. There are many types of these scaffolds applied as bone tissue engineering application such as hydroxyapatite (HA), bioactive glass, β-Tricalcium phosphate (TCP) and other bioceramic materials.

HA ceramics has the characteristics which are osteoconductive and biocompatible. It is also widely used in dental, craniofacial and many more in the form of granules. But, this type of ceramic has some disadvantages which are brittle and quite difficult to process (Kokubo,1991).

For the 45S5 bioactive glass, the speciality of this glass is the ability to bond with soft and hard tissues. Furthermore, the bone bonding ability of this glass contributes to capability to form a surface layer of hydroxycarbonate apatite (HCA) (Kokubo, 1991). According to Hench et al (1971), this bioactive behaviour in this group of glass goes to SiO_2-Na_2O-CaO-P_2O_5 system. This bioactive glass is also used in dental orthopaedic, maxillofacial and many more.

β-TCP supplies excellent biocompatibility, osteoconductivity and also being used in dental and orthopaedic application. Despite of many advantages of β-TCP, it also has some disadvantages which are uncontrolled rate of degradation and poor mechanical properties.

2.3.3 Composite scaffold

Composite scaffolds are porous scaffolds that are generally highly porous with interconnected pore networks to facilitate nutrient and oxygen diffusion and waste removal with the combination of two or more distinct constituent materials, which are separated by an interface (Sultana et al., 2015b). Scaffolds with graded porosity have ability to better represent the actual in vivo situation where cells are exposed to layers of different tissues with varying properties. The dispersed phase presence in scaffolds is considered as a reinforcement component as they are stiffer than the matrix phase

Composite scaffold can be produce by using biodegradable polymers because of the nature of biodegradable polymers. However, biodegradable polymers are inadequate in providing desired properties needed for bone tissue engineering applications due to low compressive strength and high modulus properties.

While for the bioactive glass, it has bone excellent bonding properties and excellent bone grafting material (Niemelä and Kellomäki, 2011). Bioactive glass also has opposite properties with biodegradable polymers because it is high compression strength but low fracture toughness properties due to their ceramic nature which are rigid but brittle. Furthermore, it has non-crystalline glass structural properties that made it limited for clinical applications (Heikkilä, 2011).

To overcome these problems, composite is created by combining of bioactive glass and polymers. Combination of both materials (biodegradable polymers with bioactive glass) is expected to strengthen the strength of polymeric matrix due to the inclusion of bioactive glass in the polymeric matrix (Ikada, 2006). The characteristic of bioglass which stiffer than polymer cause an action of bioglass to act as disperse phase

to reinforcement in scaffold applications. The schematic diagram of composite scaffold fabrication process is shown below in Figure 2.2 shows the schematic diagram of composite scaffolds fabrication process.

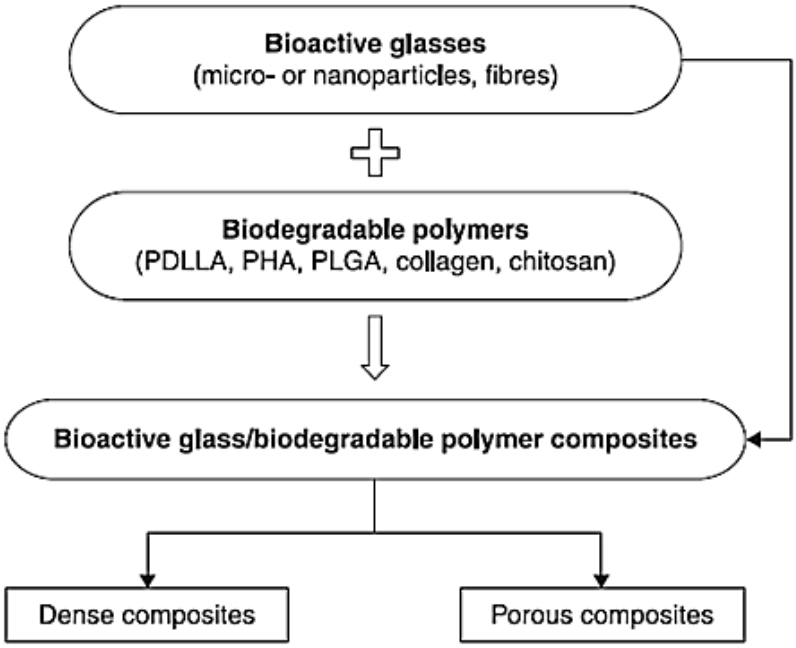


Figure 2.2 Schematic diagram of bioactive glass/polymer composite scaffolds fabrication process (Verrier et al., 2011).

2.4 Biomaterials for Bone Tissue Engineering Scaffold

2.4.1 Polymer

Polymers have been widely used as biomaterials for the fabrication of medical device and tissue-engineering scaffolds. The composition, structure, and arrangement of their constituent macromolecules determine the properties of the polymer. There are a few types of classification in terms of their structural, chemical, and biological characteristics which natural polymer and synthetic polymer are the famous polymer for biomedical application (Yannas, 2004).

Table 2.1 Some of the polymers that used in tissue engineering and biomedical devices (Saltzman, 2004).

Purpose	Materials
Artificial skin	Collagen
Dialysis membranes Sutures	Polyamides
Vascular grafts Artificial hearts	Poly(ethylene terephthalate) (PET)
Drug delivery vehicles	Poly(L-lactic acid), Poly(glycolic acid) and Poly(lactide-co-glycolide) (PLA, PGA and PLGA)

Typical Applications	Materials
Bone cement for fracture fixation Dentures	Poly(methyl methacrylate) (PMMA)
Heart valves Vascular grafts Membrane oxygenators	Poly(tetrafluoroethylene) (PTFE)

Catheters and sutures	
Hip prostheses	Polyethylene (PE)
Catheters Pacemaker leads Artificial hearts and ventricular assists devices	Polyurethanes (PU)
Drug delivery vehicles Hearts valves Catheters	Polydimethylsiloxane (PDMS)

2.4.1.1 Natural polymer

Natural polymers can be classified as proteins (silk, collagen, gelatin, fibrinogen, elastin, keratin, actin, and myosin), polysaccharides (cellulose, amylose, dextran, chitin, and glycosaminoglycans), or polynucleotides (DNA, RNA) (Yannas, 2004). Natural polymers are also the first biodegradable biomaterials that have been used clinically. They also provide natural substrate for cellular attachment, proliferation and differentiation and are considered favourite substrates for tissue engineering (Seal et al., 2001).

Natural polymers make up most of the body's native extracellular matrix (ECM). The function of ECM is to provide structure and mechanical integrity to tissues. Besides, it also supports to help facilitate and regulate daily cellular processes and

wound healing. Natural polymers are also studied for biomaterials like collagen, chitosan and alginate. The classification of natural polymer is shown in Figure 2.3.

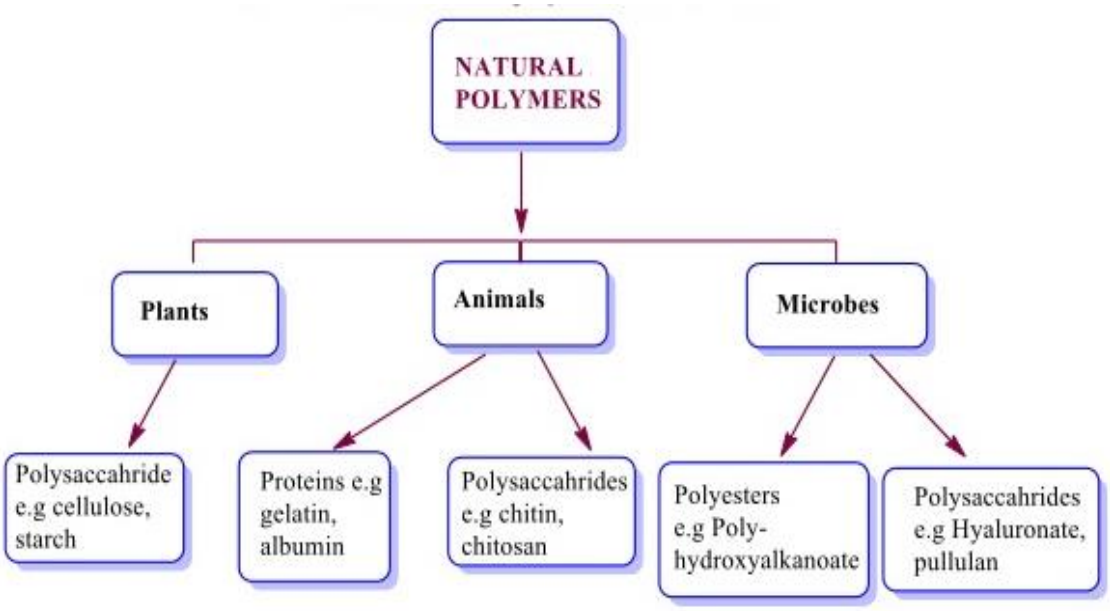


Figure 2.3 The classifications of natural polymers.

Collagen is the main provider of strength in tissue engineering. It can be dissolved into the body as it is non-toxic which functions as minimal immune response and good for attachment and biological interaction with cells. Many types of foam like porous sponges, gels and sheets and have the ability to crosslink with chemical that can be processed from collagen (Harrison, 2007)

Despite the advantages, there are also a few downsides of collagen. It can cause alteration of cell behaviour, unsuitable mechanical properties and can be easily shrink. Collagen can also cause scaffold to lose their shape because it can easily interact with cells. (Boccacini et al, 20015)

According to Du and his co-workers (1998) and (1999), hydroxyapatite p0-(HAp)/collagen composite scaffolds was studied because it was seen to be interested as

the scaffolds to replicate the composition of bone tissue. Based on Wang and his co-workers (1995) method, the scaffolds was fabricated where type I collagen matrix was extracted from bovine Achilles tendon and ultra-sonicated with nano-sized HAp to obtain a homogeneously mixed slurry. The scaffolds was prepared by using centrifugation methods and followed by freeze-dried. With this method, the scaffolds obtained not only have similar composition but also microstructure of bone tissue.

Chitosan is a type of polysaccharide which is one of the most abundant polysaccharides that present in the hard exoskeleton of shellfish. It can be easily obtained and also inexpensive product. It is one of the most favourable in tissue engineering due to the properties of chitosan which are minimal foreign body reaction and it is controllable mechanical/biodegradation properties (such as scaffold porosity or polymer length). Thus, it makes chitosan as one of the most interest tissue engineering (Saltzman, 2004).

Eventhough there are many advantages of chitosan, it also has some disadvantages like low strength and inconsistent behaviour with seeded cell. Chitosan is a semi-crystalline polymer and it is biosynthetic linear polysaccharides that derived from chitin that can be obtained in fungal fermentation processes (Harrison, 2007). Degree of crystallinity can control the degradation rate of chitosan. When high degree of crystallinity, the rate of degradation of chitosan will decrease (Harrison, 2007).

Alginate is also a polysaccharide that can be easily processed in water. It is also a biodegradable and can control porosity that can be used as entrapping cells into beads when forms a solid gel under mild processing conditions. In biomedical, it is used in many parts of human body like liver, nerve, heart and cartilage. However, it has low mechanical properties and poor cell adhesion. To overcome these, it has to be mix with

other materials (Boccacini et al., 2005).

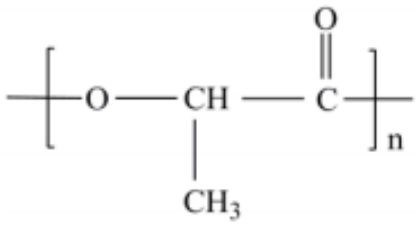
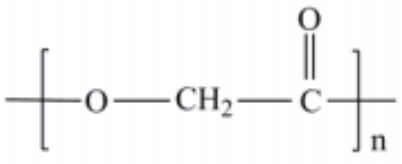
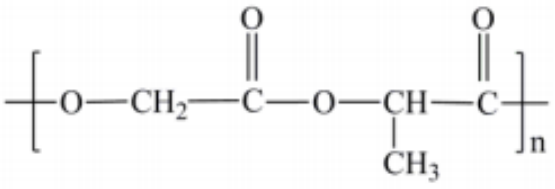
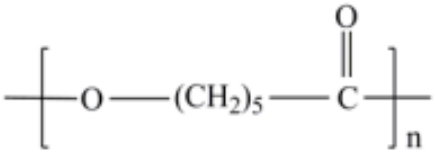
2.4.1.2 Synthetic polymers

Synthetic polymers are widely used because of its properties that can be tailored for specific applications and it is cheaper than biologic scaffolds. The ability of a long shelf time and can be produced in a large quantities make it be as the main reason for synthetic polymers to be used in biomedical application. Synthetic polymers have numerous advantages, such as excellent processing characteristics, which can ensure the off-the-shelf availability as well as being biocompatible and biodegradable at rates that can be tailored for the intended application (Boccaccini et al., 2005).

Synthetic polymer represents the largest group of biodegradable polymer. The most commonly used synthetic polymers in tissue engineering are polycaprolactone (PCL), poly(glycolic) acid (PGA), poly(lactide) acid (PLA) and poly (lactide-co-glycolic acid) (PLGA) as shown in table 2.2. These biodegradable polymers are the family member of poly (α-hydroxyl) acid (Harrison, 2007).

Poly ($_{L}$-lactide) acid (PLLA), poly ($_{D, L}$-lactide) acid (PDLLA) and polyurethanes (PU) are the examples of the polymeric materials that can be used as biodegradable scaffolds. These polymers also have the ability in their constituent units that provide them a favourable toxicological profile (Sawhney and Drumheller, 1998).

Table 2.2 Synthetic biodegradable materials.

Synthetic biodegradable polymers	Chemical structure
PLA	
PGA	
PLGA	
PCL	

2.4.1.3 Composites

Composites materials refer to the combination of many materials which has different composition or morphology which influence the chemical, physical and mechanical properties. They are continuous and have a bulk phase, called as matrix and one or more discontinuous phases called reinforced. The bulk phase functions as transferring the load accepted by large surface area and transfer it to the reinforce phase which will change the mechanical properties in terms of strength, stiffness, toughness, or fatigue resistance. One important group of composite scaffolds reported in literature comprises tailored combinations of Bioglass® particles and biodegradable polymers (e.g. PLGA, PDLLA, PHB) (Ambrosio et al., 2001), which have shown high application potential.The characteristic of these composite are well-defined porous structure, at the same time their mechanical properties are close to those of cancellous bone (Schwartzalder et al., 1963). The combination of many materials in composite also may show better properties than single constituents.

While new tissue is formed, composite scaffolds may gradually degrade. The suitable materials for composite scaffolds are the materials that have ability to degrade in vivo like polymer and ceramics. Because of the characteristic of reinforced which is stiffer than matrix, the composite is more stiffer than bulk polymer and resulting in a reduction in bulk strain on deformation, as seen in Figure 2.4.

The research in composite materials started since the mid-1960s. Nowadays, composites have been used as the main materials for many applications like an aerospace structure, a boat, or a motor because they meet the performance requirement. The advantages are mostly in weight and cost, measured in terms of ratios such as stiffness/weight, strength/weight, etc. In biomedical, composites have been widely used

in dental and orthopedic implants especially for structural application.

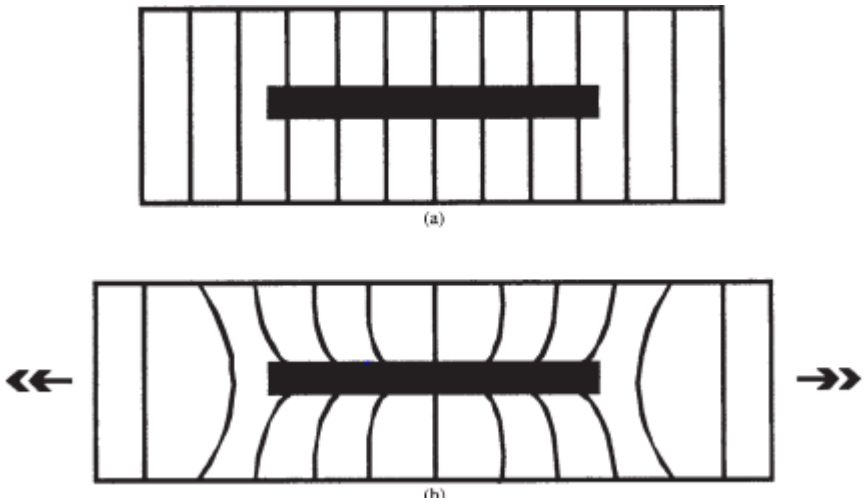


Figure 2.4 High-modulus fiber opposes strain around it in a low-modulus matrix, (a) Before deformation; (b) after deformation. Arrows indicate force direction.

2.4.2 Bioactive glass

In the 1970s, Professor Larry Hench was the first person who found the era of glass used in medical field on the ability of glass to form interfacial bond with the bone (Hupa, 2011). Bioactive glass is one of the biomaterials that usually applied in bone tissue engineering, other than biopolymers (Chatzistavrou *et al.*, 2011). 'Bioactive' is the termed for this group of glasses that being "a material that elicits a specific biological response at the material surface which results in the formation of a bond between the tissues and the materials" (Hench et al, 2006).

Traditional melting methods and sol-gel techniques are the fabrication technique used for bioactive glasses (Guarion et al, 2007). Bioactive glasses which are being melt or sol-gel derived, should have the ability to interact with living tissue, in particular forming strong bonds to bone. Establishing bond with bone, such a biologically active

apatite surface layer must form at the material/bone interface. Sol gel process also is a versatile process which can made bioactive glasses as nanoporous powder or monoliths or nanoparticles by changing the PH of the process (Hupa, 2011). Tetraethyl orthosilicate (TEOS), $Si(0C_2H^5)$ that reacts with water is the typical silicate precursor under acidic or basic conditions to form a solutions (sol) as shown in Figure 2.5.

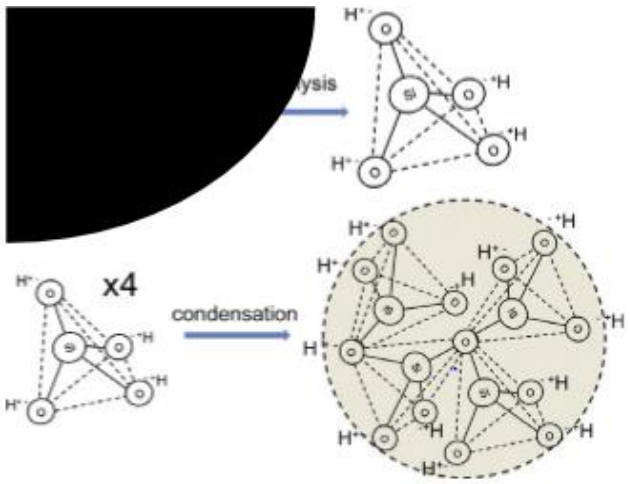


Figure 2.5 Schematic of reactions in the sol-gel process: Formation of silica tetrahedra and nanoparticles at room temperature (Julian, 2013)

Basically, glass is the material that is stiff but brittle. Without undergo plastic deformation, glass tends to fail. So, bioactive glass shows excellent compressive strength and; yet very low tensile strength on their mechanical behaviour (Vallet-Regí, 2014). However, the mechanical behaviour of bioactive glass is more likely to depend on the glass surface condition rather than composition (Hupa, 2011).

Today, the bioactive glass was used as composite components in medical application by composite the materials between glass particulate and organic polymer in order to improve the structural properties (Hupa, 2011). Bioactive glass improves its

function in clinical application especially in increasing structural strength that has limited application for tissue engineering. The factor that make composite increases the structural strength is the bond formed between bioactive glass and bone are relatively strong and almost impossible to break the bond without fracturing the bone (Jones, 2013).Silicate-based (conventional types), borate-based and phosphate-based glasses are the examples of bioactive glass available today. These bioactive glasses have different properties that can be used in certain specific area (Guarion et al, 2007).

2.4.2.1 Silicate bioactive glass

Silicate bioactive glass is an amorphous silica-based glass with SiO_2 3D-network structure with other components (Rahaman *et al.*, 2011). It is widely used in many applications especially for medical applications such as bone tissue engineering, dentistry and regenerative medicine.

Silica, SiO_2 and phosphorus, PO_4 are the network glass formers of silicate bioactive glass. The network structure for the silicate bioactive glass is in tetrahedral environment (Brauer, 2012). This structure is formed because phosphorus and silica have similar coordination numbers which are four that formed tetrahedral (Cormack, 2012).

45S5 bioactive glass, 13-93; S53P4 are the types of silicate bioactive glass that has been used in tissue engineering. All the silicate bioactive glass, 45S5, 13-93 and S53P4 components are superimposed in the Na_2O-CaO-SiO_2 ternary system shows in Figure 2.6.

A = Bone Bonding

B = Non-bonding (low reactivity)

C = Non-bonding (high reactivity)

S = Soft tissue bonding

E = 45S5 bioactive glass composition

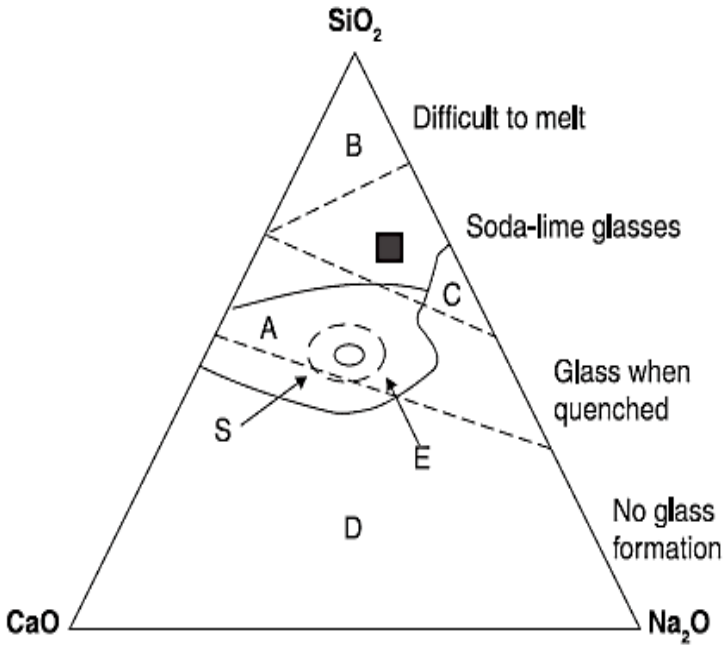


Figure 2.6 Bioactive response region shown in bioactivity composition map of SiO_2–Na_2O–CaO system (Hupa, 2011; O'Donnell, 2012)

Figure above shows that all silicate glasses fall in region A. Region A means that these silicate will able to form bond with surrounding bone tissue without elicit occurs. If the compositions move towards the centre of the SiO_2–Na_2O–CaO ternary system, the bioactivity of the glass level will increase. The composition of 45S5 bioactive glass is placed into region E that means it has a good bioactivity towards bone tissue since it is on the centre of SiO_2–Na_2O–CaO system. However, for region S that has silica-based glasses is only relevant for soft tissue bonding applications due to insufficient mechanical strength and modulus. Region B, C and D indicate that glasses in that region are not suitable for bone tissue engineering application because it can be degrade too

rapidly or inert towards degradation process. No glass formation is seen in region D.

2.4.2.2 45S5 Bioactive Glass

45S5 bioactive glass, also known as Bioglass® or BG with the composition 45 wt% SiO_2, 24.5 wt% Na_2O, 24.5 wt%, CaO and 6 wt% P_2O_5. Hench is the first person found this glass composition and it is still widely used in clinical application until today (Heikkilä, 2011). Besides, US Food and Drug Administration (FDA) approved this composition for the in vivo clinical applications (Verrier et al., 2011).

Melt-derived method, sol-gel method, and other techniques are the techniques used in preparing bioactive glass (Gerhardt and Boccaccini, 2010). Melt-derived is the main technique that always use for preparing BG and also for laboratory purpose.

In biomedical application, bond was formed between the implanted glass and rat femur when one of the first compositions for 45S5 glass was tested (Hupa, 2011). The BG composition are considered ideal due to the low SiO_2 content, high Na_2O and CaO content and high CaO:P_2O_5 ratio (Jones, 2013). The bond that formed between silica influence the bioactivity of BG (O'Donnell, 2012).

2.5 Polyurethane-bioactive glass scaffold

Polyurethanes can be classified as one of the most versatile plastic materials which can solve challenging problems and can be molded into unusual shape. Prof. Dr. Otto Bayer (1902-1982) said, 'no matter how polyurethane is transformed, the underlying chemistry is the result of one man's genius'. Prof. Dr. Otto Bayeri is called as "father" of the polyurethanes industry because of his invention of the basic diisocyanate polyaddition process (Saltzman, 2004).