CHARACTERIZATION AND DEVELOPMENT OF POLYCAPROLACTONE (PCL)/MONTMORILLONITE (MMT)/HYDROXAPAPTITE (HA) NANO-COMPOSITES FOR FUSED DEPOSITION MODELLING (FDM) PROCESS

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ABSTRACT

In this study, characterization and development of polymer nanocomposites filament wire for Fused Deposition Modelling (FDM) was investigated. The polycaprolactone (PCL) filled montmorillonite (MMT) and Hydroxyapaptite (HA) composites were prepared by melting and compounding using a single screw extruder. The mechanical properties were assessed by tensile, flexural and charpy impact tests while the thermal properties were studied via differential scanning calorimetry (DSC) and thermogravimetry analyzer (TGA). Simulated body fluid (SBF) test was used to assess the bioactivity properties of the composites. The filament wire with the diameter of 1.75+0.05 were fabricated using a single screw extruder with die hole 1.6 mm in diameter. Design of experiment (DOE) software was used to find the optimum setting for the screw speed, roller speed and die temperature in order to achieve the specific diameter of the filament wire. The flexural strength, elastic modulus and flexural modulus of PCL/MMT blends increased with the decrement of tensile strength and impact strength. Apparently, the inclusion of HA upon PCL/ MMT composite shows a slight improvement in elastic modulus, flexural modulus and flexural strength with reduction of impact strength. Addition of MMT and HA enhanced the thermal stability and the decomposition temperature of the composites. Formation of apatite crystals on the PCL/MMT/HA composites surfaces confirmed the occurrence of bioactive properties. Composites with 3 wt.% of MMT and 10 wt.% of HA were chosen as optimum composition in terms of strength and bioactive properties to be fabricated as filament wire for FDM process. The optimum parameter setting to produce 1.75+0.05 of filament wire was successfully found at screw speed of 7.30 Hz, roller speed of 4.3 rpm and die temperature of 90°C. The characteristic of the FDM process shows that the samples with optimum dimensional accuracy and relative density was found at room temperature and 80°C of platform and nozzle temperature respectively. The composites with 3 wt.% of MMT and 10 wt.% of HA samples produced from the FDM process show an improvement in elastic modulus and impact strength compared to samples prepared by injection molding process.

ABSTRAK

Dalam kajian ini, pencirian dan penghasilan polimer nanokomposit wayar filamen untuk pemodelan pemendapan bersatu (FDM) telah dikaji. Polimer polycaprolactone (PCL) diisi montmorilonit (MMT) dan hydroxyapaptite (HA) komposit telah disediakan dengan penyebatian leburan menggunakan pemyemperit skru tunggal. Sifat-sifat mekanik dikaji melalui ujian regangan, lenturan dan hentaman manakala sifat terma dianalisa menggunakan kalorimeter pengimbasan perbezaan (DSC) dan penganalisis termogravimetri (TGA). Ciri- ciri bioaktiviti PCL/MMT/HA komposit dikaji melalui ujian secara rendaman ke dalam cecair badan simulasi (SBF). Wayar filamen berdiameter 1.75 + 0.05 telah dihasilkan menggunakan penyemperit skru tunggal dengan lubang acuan berdiamater 1.6 mm. Perisian reka bentuk eksperimen (DOE) digunakan untuk mencari tetapan yang optima bagi kelajuan penggelek, kelajuan skru dan suhu acuan untuk mencapai diameter yang tepat bagi wayar filamen. Kekuatan lenturan, modulus elastik dan modulus lenturan PCL/MMT meningkat dengan susutnya kekuatan tegangan dan kekuatan hentaman. Penambahan HA di dalam PCL/MMT komposit menunjukkan sedikit peningkatan pada modulus elastik, modulus lenturan dan kekuatan lenturan dengan pengurangan kekuatan hentaman. Penambahan MMT dan HA juga meningkatkan kestabilan terma dan suhu penguraian bagi komposit. Pembentukan kristal apatit pada permukaan komposit PCL/MMT/HA mengesahkan berlakunya sifat bioaktif. Komposit dengan campuran 3 wt.% MMT an 10 wt.% HA dipilih sebagai komposisi yang optima dari segi kekuatan dan sifat bioaktif yang akan direka sebagai wayar filamen bagi proses FDM. Parameter optima untuk menghasilkan 1.75 + 0.05 wayar filamen daripada komposit PCL/MMT/HA adalah dengan kelajuan skru 7.30 Hz, kelajuan penggelek pada 4.3 rpm dan suhu acuan pada 90°C. Ciri-ciri ketumpatan relative dan ketepatan dimensi yang optima bagi sampel yang dihasilkan daripada proses FDM adalah pada suhu landasan dan muncung pada 0°C dan 80°C masing-masing. Sampel 3 wt.% MMT an 10 wt.% HA yang dihasilkan dengan proses FDM menunjukkan peningkatan pada modulus elastic dan kekuatan hentaman berbanding dengan sampel yang dihasilkan dengan proses pengacuan suntikan.

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cm^2	-	Centimeter square
cm^3	-	Centimeter cubic
d	-	Spacing between diffractional lattice plane (interspacing)
g	-	Gram
H_f	-	Heat of Fusion
ΔH_{100}	-	Heat of Fusion of theoretically 100% crystalline polymer
mg	-	Milligram
T_g	-	Glass transition temperature
T_m	-	Melting temperature
T_c	-	Crystallization temperature
wt%	-	Weight percent
X_c	-	Crystallinity content
^oC/min	-	Degree celsius per minute
θ	-	Diffraction angle
λ	-	Wave length
α	-	Alpha
μm	-	Micron
nm	-	Nanometer
ASTM	-	American Standards Test Method
DSC	-	Differential scanning calorimetry
MPa	-	Mega pascal
GPa	-	Giga pascal
PCL	-	Polycaprolactone
HA	-	Hydroxyapatite
MMT	-	Montmorillonite
b-TCP	-	Beta tricalcium phosphate
Ca/P	-	Calcium to phosphate ratio
XRD	-	X-ray diffraction

EDX	-	Energy dispersive X-ray
SBF	-	Simulated body fluid
BET	-	Brunauer-Emmet-Teller
TEM	-	Transmission electron microscopy
TGA	-	Thermogravimetric analysis
3-ATMS	-	3-aminopropyltrimethoxysilane
EDX	-	Energy dispersive X-ray

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CHAPTER 1

INTRODUCTION

1.1 Background

Additive Manufacturing (AM) is a technique of manufacturing in which a solid physical model of a part is made directly from a three-dimensional computer-aided design (CAD) file. AM techniques such as selective laser sintering (SLS), stereolithography (SLA), three-dimensional printing (3DP), laminated object manufacturing (LOM), and fused deposition modeling (FDM) were first developed to create prototypes for purposes of designing a new product. Later, with the progress of material and enabling technology, these AM techniques emerged out and have been applied in the fields such as rapid tooling and molding, direct formed usable part, and bio-manufacturing (Chua, 2003)

Fused deposition modelling (FDM) has become a widely used additive manufacturing technology for various applications in engineering. The uniqueness of FDM technique is more economical for small to medium size parts in the shortest lead time, it is because SLA and SLS use resin to build models and it deteriorates over time and also it uses a laser which depreciates over time making it difficult to ensure repeatability. Apart from that, with the recent introduction of portable 3D printer, it makes it more popular as it is easy to use and user friendly compared to

other type of the AM process. But typically the part produce is not strong enough, or some other material property is not suitable for the application.

Now, FDM has progressed one step further from fabricating a prototype to a fully functional product. One of the key industries that shows a huge impact in emerging of this technology are medical industries (Espalin *et al.*, 2010). The strongest reason is because of the ease in which 3D medical imaging data can be converted into solid objects. In this way the objects or product can be customized to suit the needs of an individual patient. This eventually led to a reduction in cost of production of an implant and other medical instruments which significantly reduce the cost that have to be charged over most of the patients. Presently most of the research work is directed toward developing new materials or processes which target on mechanical properties improvement of parts produced from FDM and biocompatible polymers are one of the material that have been top choices for most researchers. (Masood, 1996; Woodruff & Hutmacher, 2010).

There are a lot of different types of biocompatible polymers nowadays that have been investigated by most of the researcher associate with FDM and one of the most famous biopolymer is Polycaprolactone (PCL). Polycaprolactone (PCL) is a semicrystal-line polyester and highly processible as it is soluble in a wide range of organic solvents. It has a relatively low melting point (55 - 60°C) and glass transition temperature -60°C and the more important that it has the ability to form miscible blends with a wide range of polymers has stimulated extensive research into its potential application in the biomedical field (Nair & Laurencin, 2007). PCL have been major acceptance in the tissue engineering field. The properties of PCL which possesses superior viscoelastic and rheological properties over other bioploymer make it easy to be manufactured and manipulate into a large range of scaffolds.

Scaffolds for tissue engineering have become a large focus of research attention and can be fabricated in a wide variety of ways and a biomaterial which lends itself very well to scaffold fabrication is PCL. PCL is an incredibly versatile bioresorbable polymer and by way of its superior rheological properties it can be used by almost any polymer processing technology to produce an enormous array of scaffolds.

As the material development effort progresses by time, composites approaches comes into action to continue to improve the properties whilst maintaining material characteristics required for producing products. The key

development for direct manufacturing of parts from FDM has been the incorporation of additives to polymer matrix material to enhance the mechanical properties of the resulting parts. There are many efforts underway to develop high-performance, rapid prototyping materials with promise for engineering applications, including enhanced mechanical properties (Zhang *et al*., 2004; Wang *et al*., 2005; and Koo *et al*., 2006) by using polymer nanocomposites (PNCs) material. PNCs are based on controlling microstructure by incorporating nanometer-size as second-phase dispersions into polymer matrixes (Vollath & Szabo, 2004). PNCs have emerged as materials which can show significantly enhanced mechanical properties over those of the base polymer through the addition of relatively small amounts of nano-scale additives. Improvements in strength and modulus of 40-70% have been reported to have arisen as a result of the addition of 2-5wt% of nano clay (Pavlidou & Papaspyrides, 2008).

A part of improving the mechanical properties of polymers by the addition of nanoclay, the current filament wire used in FDM is also not bioactive. The filament wires currently available and being investigated by researchers for FDM is only biocompatible, which can only adapt in the human body without regenerating the tissues. Much attention has been paid towards the development of polymer composites with hydroxyaptite (HA) as bioactive material in bone tissue engineering (Wang *et al*., 1997; Fang *et al*., 2006). Applying of HA filler particles to form composites has been shown to enhance bone-bonding rates. The emerging interest of using HA is due to its chemical and structural similarity with natural bone mineral. Due to its bioactive traits, HA has the ability to integrate into bone structures and support bone growth. The addition of Ca-P ceramic to the polymer makes a composite bone analogue and improves the bone bonding behavior of unfilled polymers (Gomes & Reis, 2004). Calcium phosphate increases the osteoconductivity of the biocomposite (Murphy *et al*., 1999). It has been found that the right amount of HA is required to enhance the bioactivity of polymers without making the composites fragile. This can promise a positive result in producing a bioactive filament wire for FDM process.

At present, most of the research on FDM has focused on producing a medical device and great attention of studies has been paid in material development for FDM process. So far there is no work has been done on producing composites by incorporation of both MMT and HA with biopolymer.

Therefore, this work introduces MMT and HA as a filler in PCL to improve the properties of filament wire composites for FDM. With reinforcement of MMT, which will enhance the mechanical properties of the filament wire composite meanwhile the incorporation of HA, offers special properties as a particulate bioactive phase in biomedical composites. Thus, this research focuses on the preparation of PCL/MMT/HA filament wire nanocomposites for FDM with both mechanical and bioactive properties.

1.2 Problem statement

Most of medical parts today are still made by conventional method such as machining and injection molding. There are a lot of disadvantages using this method as it is not economical because it involves in fabricating a mold to produces a parts. Secondly, it is time consuming as the whole process from manufacturing until producing the parts takes a lot of time and finally, each molds only specific for each person, where different patient needs a different mold. However, using AM technique all these problems can be overcome as there no needs of mold fabrication and more towards customize medical parts. But, there are certain limitation using AM techniques, where current AM technique produces prototypes from pure polymer materials resulting in limited uses especially in medical industries.

A good combination of mechanical properties, processability and bioactivity properties with absence of toxic together with manufacturing techniques is an important aspect in the development of biomaterials for biomedical applications using FDM technique. In terms of mechanical properties, composite with high modulus (elastic as well as flexural modulus) and strength is expected to produce for medical applications.

Introduction of polymer nanocomposites for the FDM process may be one of the best options that could overcome this problem. The incorporation of MMT provides an alternative choice to improved the PCL/MMT composite mechanical properties as it has been proven that by the addition of small amounts of MMT led to an improvement of the mechanical properties of a composite (Pavlidou & Papaspyrides, 2008).

Besides that, bioactive implant is one of the greatest interest in the medical field nowadays and reinforcing ceramic is one of the popular choices. Among ceramic materials, HA is widely used in implant material as it can favor the cell proliferation and support bone in growth. So far there is no such polymer nanocomposites material develops by incorporating MMT and HA into PCL for FDM process which seems to promise an interesting finding.

1.3 Objectives of the study

This study embarks on the following objectives:

a. To investigate the effect of MMT content on the mechanical and thermal properties of PCL blends.
b. To evaluate the effect of HA concentration on the mechanical, thermal and bioactivity properties of PCL/MMT composites blends.
c. To optimize parameters setting for fabrication of the filament wire for the FDM process from PCL/MMT/HA composite using Response Surface Methodology (RSM).
d. To develop PCL/MMT/HA filament wire nanocomposites for FDM process.
e. To investigate the effect of FDM processing temperature (nozzle and platform) on the quality of product produce from PCL/MMT/HA using FDM process.

1.4 Scope of the study

This study will focus on:-

a. Preparing samples through:
    i. Dry blending.
    ii. Extrusion of composites using single screw extruder nanomixer.
b. The PCL, MMT and HA are mixed and tried in a different composition.
c. Flexural test, tensile test and impact test will be carried out to determine the mechanical properties of the composites.
d. SEM (Scanning Electron Microscopy) and TEM (Transmission Electron Microscopy) will be carried out to correlate the mechanical properties of the nano sized MMT reinforced PCL composites with the morphology (structure-property relationship).
e. Determination of thermal properties by using:
    i. Differential Scanning Calorimetry (DSC).
    ii. Thermogravimetry Analysis (TGA).
f. Evaluating the bioactivity properties of PCL/MMT/HA composites through immersion in simulated body fluid (SBF).
g. Fabrication of PCL/MMT/HA filament wire through an extrusion process with the aid of roller puller and water bath.
h. Optimize the parameter for fabricating PCL/MMT/HA composite filament wire using Design of Experiment (DOE).
i. Analyzing the nozzle and platform temperature of FDM process through the dimensional error and relative density of bending sample.
j. Produce the tensile, bending and impact test samples from 3D printer and compare with injection molding samples.

1.5 Novelty and significance of the study

From this research, development of a new PCL/MMT/HA polymer nanocomposites for FDM process that have potential in producing biomedical implant application. The utilize of PCL/MMT/HA polymer nanocomposites for FDM process is expected to increase with the improvement of its mechanical and bioactivite properties by incorporation of MMT and HA.

CHAPTER 2

LITERATURE REVIEW

2.1 Additive Manufacturing

Additive Manufacuring (AM) techniques were developed to create prototypes for purposes of designing a new product. Traditional prototyping methods involve laborious mold making and casting steps (Pham and Gault., 1998), whereas the ability to create an object within hours from a computer design by rapid prototyping (RP) significantly speeds up the development of products. Currently, AM techniques is common practice in the automotive industry, for jewelry making and for designing end-user devices and appliances (Wendel *et al*., 2008). Also in designing surgical tools, implants and other biomedical devices, these additive fabrication methods have been used. Some other advantages of AM technology compared to conventional technologies are:

a. Formation of objects with whatever point of geometrical complexity without the demand for any tooling or computer programming
b. Fabrication of objects potentially from a mixture of materials and any composites, and the ability to even vary feed materials in a controlled way at any position in an object

c. Enhancing the scope of product growth with reduced cost and time in specific areas such as biomedical engineering, tooling development, and consumer products.

As AM fabrication technologies are continuously evolving, fabrication costs are decreasing and the properties of the manufactured parts are becoming better. Therefore, these techniques are more and more being used for the rapid manufacturing of products in small series. The time gain in product development, freedom of design and tool-free fabrication can outweigh the increased fabrication costs per item (Wendel *et al*., 2008).

There are many types of different AM processes recognized today, which are divided into three categories of liquid-based, powder-based, and solid-based systems, based on the raw materials used in the process (Chua *et al*., 2003; Hopkinson *et al*., 2006). From all these, the most widely used AM processes include Stereolithography (SLA), Fused Deposition Modelling (FDM), Selective Laser Sintering (SLS), 3D Printing (3DP), and Laminated Object Manufacturing (LOM) (Grenda, 2006; Liou, 2008; Wohlers, 2008).

2.1.1 Fused deposition modelling (FDM)

In recent years, fused deposition modelling (FDM) has become a widely used AM technology for various applications in engineering. FDM systems, developed by Stratasys Inc., can fabricate parts in a range of materials including elastomers, acrylonitrile butadiene-styrene (ABS) and investment casting wax with the layer by layer deposition of extruded material through a nozzle using feedstock filaments from a spool (Stratasys Inc, 1991). Most of the parts fabricated in these materials can be used for design verification, form and fit checking and patterns for casting processes and medical application.

The basic principle of operation of the FDM process offers great potential for a range of other materials, including metals, ceramics, and composites to be developed and used in the FDM process as long as the new material can be produced in the feedstock filament form of required size, strength, and properties.

In FDM, the prototyping process begins with unwinding the feedstock filament from a reel and feeding it through the liquefier located inside the system working envelope, as shown in Figure 2.1, where it gets gradually heated by temperature gradient provided by a number of coils wrapped helically about the axis of the liquefier. The heated liquefier melts the plastic filament and deposits the melt through a nozzle attached at the exit controlling the diameter of the final extrudate. Two step motors at the entrance of liquefier make sure a continuous supply of material during the model build-up. The nozzle and liquefied assembly are mounted onto a mechanical stage numerically controlled in X-Y plane.

Upon receipt of precise tool paths prepared by the software, the nozzle moves over the platform depositing a thin bead of thermoplastic model material along with any necessary support structure. Deposition of fine extruded filaments onto the substrate produces a layer corresponding to a slice of the CAD model of the object. Once a layer is built the substrate moves down in z direction in order to prepare the stage for the deposition of the next layer. The deposited filaments cool down, immediately below the glass transition temperature of the polymer and get hardened. The entire build system is contained within a temperature-controlled environment with temperatures just below the glass-transition temperature of the polymer to provide an efficient intra-layer bonding.

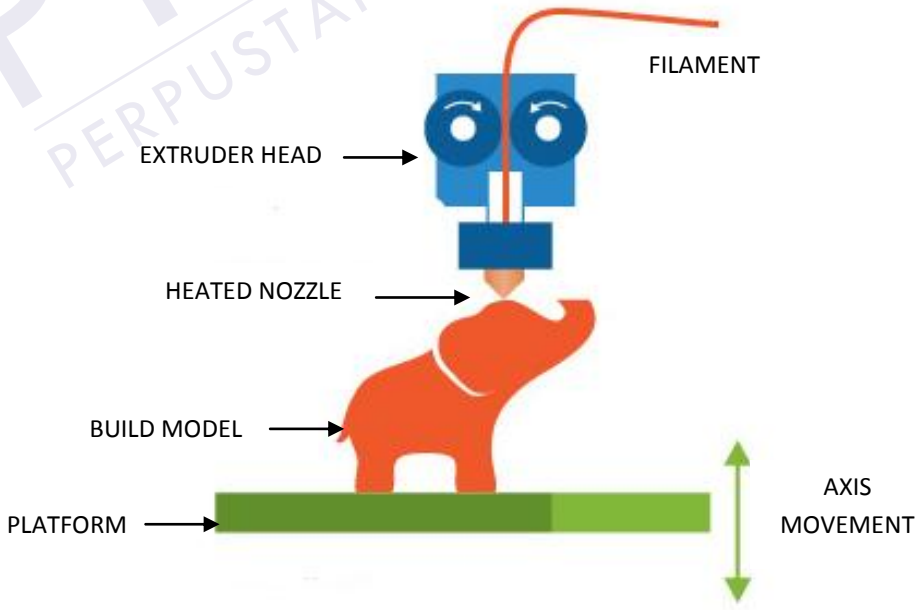


Figure 2.1: Schematic of FDM process, (Levy *et al*., 2003)

Materials used in FDM are non-toxic and inert, synthesized from commercially available thermoplastics and waxes. They all vary in strength, rigidity and surface finish, providing a wide range of testable models (Stratasys retrieved 2009). Currently, it can build durable, accurate and strong models from Acrylonitrile Butadiene Styrene (ABS), Polycarbonate (PC), and Polyphenylsulfones (PSSF). Among these, ABS is the most commonly used material for part fabrication on the FDM because of its superior engineering properties. Due to non-toxicity of the feedstock materials the process is office-friendly. The material can be easily changed, and the waste is negligible. The feedstock material is fed in the form of filament with diameters of 1.75± 0.05 mm. Since the size of strands produced as building elements of the prototypes is limited to the nozzle tip size, the process can have limited accuracy compared to the liquid-based processes such as SLA. Limited materials, limited size, and unpredictable shrinkage are the disadvantages of FDM technology.

One of the most demanding areas that gain a lot of interest from the researcher is in the biomedical area (Wiria *et al*., 2007; Tan *et al*., 2003; Hao *et al*., 2006). The increasing trend to incorporate artificial devices into the human body has sharply focused attention onto the compatibility of the materials from which such devices are made with human physiology. Given that it is widely predicted that more and more functions will be taken over by artificial devices, not only for repairing damaged function, but also for enhancing function, the need to solve the problem of how to design and manufacture such materials to make them maximally compatible with living tissue (including biofluids such as blood) has become a major priority of the medical device industry.

2.2 Biomaterial

A biomaterial can be defined as any material used to make devices to replace a part or a function of the body in a safe, reliable, economic and physiologically acceptable manner. A variety of devices and materials are used in the treatment of disease and

injury. A biomaterial also recognized as a synthetic material used to replace part of a living system or to function in inmate contact with living tissue.

Biomaterials in the form of implant are widely used to replace and/or restore the function of traumatized tissues or organs, to assist in healing, to improve function, and to correct abnormalities. Researchers have used the words 'biomaterial' and 'biocompatibility' to indicate the biological performances of materials (Ramakrishna *et al*., 2004). In order to improve the quality life of patients, the design, material selection, and biocompatibility remain as the paramount issues of biomaterials for medical applications. Until recently, most of medical devices are still made from single phase homogeneous and isotropic materials such as metals, ceramics and polymer (Ramakrishna *et al*., 2004).

Metallic implants have been used either as permanent prostheses such as the hip prosthesis, dental implants, etc., or as temporary implants such as plates, pins, screws and rods for the fixation of bone fractures. Metals are known for high strength, ductility, and resistance to wear. Cobalt-chromium alloys, stainless steel and titanium alloy are common metals that have been extensively used in to fabricate the implants due to its strength and toughness that are required in load-bearing parts of the body (Long & Rack, 1998). However, many metals are known for its low biocompatibility, corrosive, and high density, which may cause allergic tissue reaction. Other disadvantages of using metallic implants include the need for the second operation to remove temporary implants and these implants are usually not integrated by the bone tissue or only after extended implantation periods.

Bioceramics material with its advantage of being compatible with the human body environment has been chosen for tissue substitution since the last 30 years. However, the brittleness of ceramics, which are much stiffer than human cortical bone lead to mechanical mismatch problems between the existing implant and bone. This mismatch of stiffness between the bone and the metallic or ceramic implants may lead to lower bone density, and altered bone architecture (Ramakrishna *et al*., 2004). The drawback of ceramics also includes low fracture toughness that hinders clinical use in load bearing implants (Eniwumide *et al*., 2004).

Thus, polymer with its advantages such as available in a wide variety of compositions, properties and forms (solids, fiber, and films) can be fabricated readily into complex shapes and structures seem to be a promising choice, in particular for bone tissue engineering and provide alternative choices to overcome many

shortcomings of metals and ceramic material. The main advantages of the polymeric biomaterials compared to metal or ceramic, materials are ease of manufacturability to produce various shapes, ease of secondary processability, reasonable cost, and availability with desired mechanical and physical properties (Lee *et al*., 2007). Table 2.1 shows the classifications of biomaterial used in the human body with their advantages and disadvantages.

Table 2.1: Classifications of biomaterial as an implant used in the body

Materials	Advantages	Disadvantages	Examples
Polymers (Nylon, silicone rubber, polytetrafuoroethylene, etc.)	• Resilient • Easy to fabricate	• Not strong • Deforms with time • May degrade	Sutures, blood vessels, hip socket, ear, nose other soft tissues.
Metals (Ti and its alloys, Co–Cr alloys, stainless steels, Au, Ag, Pt, etc.)	• Strong • Tough • Ductile	• May corrode • Dense • Difficult to make	Joint replacements, bone plates and screws, dental root implants, pacer and suture wires.
Ceramics (Aluminum oxide, calcium phosphates including hydroxyapatite, carbon)	• Very biocompatible • Inert • Strong in compression	• Brittle • Not resilient • Difficult to make	Dental and orthopedic implants
Composites (Carbon–carbon, wire or fiber reinforced bone cement)	• Strong • Tailor-made	• Difficult to make	Bone cement, dental resin

2.3 Polymeric biomaterial

Polymers are long chain molecules that consist of small repeating units. There are variety of polymers including natural materials and synthetic polymers. Medical use of synthetic polymers has a long history. The great number of currently available synthetic polymers makes the selection of a suitable polymer for a particular biomedical application a difficult task. However, among all properties required for an application, the biocompatibility of the polymer with tissues and biological fluids is always the foremost consideration for all candidate materials.

Many types of polymers are widely used in biomedical devices that include orthopedic, dental, soft tissue, and cardiovascular implants. Polymers represent the

largest class of biomaterials. Polymers may be derived from natural sources, or from synthetic organic processes. Synthetic polymeric biomaterials range from hydrophobic, non-water-absorbing materials such as silicone rubber (SR), polyethylene (PE), polypropylene (PP), poly(ethylene terephthalate) (PET), polytetrafluoroethylene (PTFE), and poly(methyl methacrylate) (PMMA) to somewhat more polar materials such as poly(vinyl chloride) (PVC), copoly(lactic–glycolic acid) (PLGA), and nylons, to waterswelling materials such as poly(hydroxyethyl methacrylate) (PHEMA) and beyond, to water-soluble materials such as poly(ethylene glycol) (PEG or PEO). Some are hydrolytically unstable and degrade in the body while others may remain essentially unchanged for the lifetime of the patient.

2.3.1 Polycaprolactone

Polycaprolactone (PCL) is a bioresorbable polymer with potential applications for bone and cartilage repair. PCL has certain advantages relative to other polymers such as PLA (poly lactic acid). PCL is more stable in ambient conditions; it is significantly less expensive and is readily available in large quantities. Much research currently focused on the use of PCL biocomposites and co-polymers of PCL with both natural and synthetic polymers (Azevedo *et al.*, 2003; Washburn *et al*., 2002)

Polycaprolactone (PCL) is also used for drug delivery; drug compounds are mixed in the polymer matrix and gradually become released as the polymer is dissolved in the tissue (Landers *et al*., 2002; Sachlos & Czernuszka, 2003). In the emerging field of tissue engineering, biodegradable polymers are used for realizing polymer scaffolds to assist tissue and cell growth during formation of artificial organs (Taboas *et al*., 2003). In such applications, biodegradable polymers have been shown to allow successful cell attachment, proliferation, and functioning.

PCL, an aliphatic polyester that has been intensively investigated as a biomedical material (Zhong *et al*., 2001), demonstrates a low melting point (57°C) and a low glass-transition temperature (-62°C). PCL can be degraded by micro-organisms as well as by a hydrolytic mechanism under physiological conditions (Pitt

et al., 1981). Under certain circumstances, it is possible to enzymatically degrade crosslinked PCL (termed enzymatic surface erosion). Low molecular-weight fragments of PCL are also reportedly absorbed by macrophages intercellularly (Woodward *et al*., 1985). PCL material has a significantly slower biodegradation rate than other BDP materials, making it suitable for design of long- term implantable systems such as apronor, a US FDA- approved contraceptive device (Pitt *et al.*, 1981). Another interesting property of PCL is its propensity to form compatible blends with a wide variety of polymers (Koleske, 1978). The toxicology of PCL has been extensively studied as part of the evaluation of Capronor (Pitt *et al*., 1981); and it is currently regarded as non- toxic and tissue compatible.

Polycaprolactone has been used in extensively in the field of tissue engineering. Also, PCL fibers have been proven effective for cell proliferation, especially under the cultures of MCF-7 mammary carcinoma (Khil *et al*., 2005). The cultures of the mammary cells had a slow growth during the first few days, however, when compared to the control groups, the PCL does improve the cell growth kinetic rates over time.

PCL has become very beneficial in the development of tissue structures for bone growth. Previously, poly (DL-lactide-co-glycolide) (PLGA) has been used for developing scaffolds for bone cell growth. In particular, bone marrow was harvested from rats and used in this study (Yoshimoto *et al*., 2003). Mesenchymal stem cells, from the bone marrow, were used upon PCL electrospun scaffolds. The PLGA used previously had only shown limited topical growth and 40% shrinkage in length (Yoshimoto *et al*., 2003). The usefulness of the PCL can be attributed to the higher glass transition temperature (-70°C to -60°C) (Cruz *et al*., 2005).

The following section will explain the use of PCL scaffold in varied areas of tissue engineering.

2.3.1.1 Bone tissue scaffold

The potential used of PCL in bone tissues engineering have been investigated by a lot of researchers. Lam *et al*., (2009) who have investigated a bioactive and bioresorable scafoold fabricated from PCL incorporating 20% beta-tricalcium phosphate. This studies was further develop for regeneration at load bearing by Abbah *et al*., (2009). From their research, they have found that the PCL-TCP scaffold could act as bone graft substitutes by providing act as bone graft substitutes by providing a suitable environment for bone regeneration in a dynamic load bearing setting such as in a porcinemodel of interbody spine fusion.

Choi *et al*., (2008) carried a work on an electrospun PCL/collagen nanofibers of different orientations.which focus on producing functional muscle tissue for restoring large skeletal muscle tissue defects. They have fabricated PCL cylindrical scaffold to investigate the pore size effect on cell and tissue interactions by centrifugation method. In their findings, they have concluded that the pore size gradient scaffolds fabricated by this centrifugation method might be considered a good tool for the systematic studies of interactions between cells or tissues and scaffolds with different pore sizes.

There are also work have been done by the National University of Singapore on bone research based on medical grade PCL both in vitro and in vivo and have been commerciallized after clinical approval in 2008 (Lam *et al*., 2008).

2.3.1.2 Cartilage engineering

Huang *et al*., (2004) has developed a biphasic implant comprising PCL with TGF-β1-loaded fibrin glue to determine whether the implant could recruit mesenchymal cells and induce the process of cartilage formation when implanted in ectopic sites. PCL scaffolds loaded with various doses of TGF-β1 in fibrin glue were implanted subcutaneously, intramuscularly, and subperiosteally and assessed histologically 2, 4, and 6 weeks postoperatively. The entire pore spaces of the scaffolds were filled with various tissues in each group. The entire volume of the

scaffolds in the groups loaded with TGF-β1 and implanted intramuscularly and subcutaneously was populated with mesenchymal cells surrounded with an abundant extracellular matrix and blood vessels. The scaffold loaded with TGF-β1 and implanted subperiosteally was found to be richly populated with chondrocytes at 2 and 4 weeks and immature bone formation was identified at 6 weeks. The study concluded that scaffolds loaded with TGF-β1 could successfully recruit mesenchymal cells and that chondrogenesis occurred when this construct was implanted subperiosteally.

Wise *et al*., (2009) in his research of electrospun oriented PCL scaffolds onto which they seeded human mesenchymal stem cells. Cell viability, morphology, and orientation on the fibrous scaffolds were quantitatively determined as a function of time. While the fiber-guided initial cell orientation was maintained even after 5 weeks, cells cultured in the chondrogenic media proliferated and differentiated into the chondrogenic lineage, suggesting that cell orientation is controlled by the physical cues and minimally influenced by the soluble factors. Based on assessment by chondrogenicmarkers, they concluded that the use of the nanofibrous scaffold enhanced chondrogenic differentiation and indicate that hMSCs seeded on a controllable PCL scaffold may lead to an alternate methodology to mimic the cell and ECM organization.

Shao *et al*., (2006) fabricated a hybrid scaffold system which comprised 3D porous PCL scaffold for the cartilage component and tricalcium phosphate-reinforced PCL scaffold for the bone portion.They have found a superior repair results as compared to the control group using gross examination, qualitative and quantitative histology, and biomechanical assessment. The hybrid scaffolds provided sufficient support to the new osteochondral tissue formation and the bone regeneration were consistently good from 3 to 6 months, with firmintegration to the host tissue.

2.3.1.3 Cardiovascular engineering

Van *et al*., (2006) have developed two types of scaffolds for tissue engineering of the aortic valve; an electrospun valvular scaffold and a knitted valvular scaffold. These scaffolds were compared in a physiologic flow system and in a tissue-engineering process. In fibrin gel enclosed human myofibroblasts were seeded onto both types of scaffolds and cultured for 23 days under continuous medium perfusion. Tissue formation was evaluated by confocal laser scanning microscopy, histology and DNA quantification. They concluded that an optimal scaffold seems to be a combination of the strength of the knitted structure and the cell-filtering ability of the spun structure.

Ajili *et al*., (2009) have used a polyurethane/PCL blend as a proposed material for shape memory stents. Polyurethane copolymer based on PCL diol was melt blended with PCL in four different ratios of 20, 30, 40 and 50wt.% and their shape memory behaviors were examine. They have found that the blend supported cell adhesion and proliferation, which indicated good biocompatibility in addition to shape memory properties, providing potential use as a stent implant. Wang *et al*., (2004) have studied a gene therapy system to treat hypertension and congestive heart failure based on the release of atrial natriuretic peptide (ANP) from ANP-cDNA-transfected Chinese Hamster Ovary cells which had been encapsulated within PCL tubes. The encapsulated cells remained viable during culture and ANP secretion was maintained for at least 6 months.

2.3.1.4 Skin engineering

Powell & Boyce, (2009) blended PCL with collagen before electrospinning the composite to formsubmicron fibers. Tensile testing indicated that the inclusion of PCL from 10% to 100% significantly improved the strength and stiffness of the acellular scaffold. They have also reported that, the epidermal formation and reduced cell viability was evident at when the PCL content was increased beyond 10% and there was an associated loss of engineered skin construct strength indicating that high

cell viability and proper development of the epidermis and important factors for developing engineered skin with high strength.

A studied by Dai *et al*., (2004) who produced PCL/collagen composites for tissue-engineered skin substitutes an demonstrated good cell attachment and proliferation of fibroblasts and keratinocytes. They utilize PCL/collagen blends as skin substitutes through seeding human single-donor keratinocytes and fibroblasts alone on both sides of the 1:20 biocomposite to allow for separation of two cell types and preserving cell signals transmission via micro-pores with a porosity of 28.8 ± 16.μm. They have also reported that the bi-layered skin substitute exhibite both differentiated epidermis and fibrous dermis in vitro. Moreover, fast wound closure epidermal differentiation, and abundant dermal collagen deposition were observed in composite skin in vivo.

Reed *et al*., (2009) have studied on several cell types (human foreskin fibroblasts, murine keratinocytes and periosteal cells) cultured together on PCL nanofibers. His work was to produce trilaminar constructs, to reflect a compound tissue, although clear obstacles exist in maintaining an appropriate interface between the tissue types and neo vascularizaion of the composite structure. Chen *et al*., (2009) have used a vacuum seeding technique on PCL electrospun scaffoldswhile using NIH 3T3 fibroblasts as themodel cell system. Vacuum seeding was used in this study to enhance fibroblasts seeding and proliferation at different depths. Results showed that the kinetics of cell attachment and proliferation were a function of varying vacuum pressure as well as fiber diameter.

2.3.1.5 Nerve engineering

Dendunnen *et al*., (1993) in his work began evaluating PCL as a composite, combined with PLLA in guided nerve regeneration. Cytotoxicity tests, subcutaneous biodegradation and an in situ implantation studies in the sciatic nerve of the rat were undertaken. The nerve guide copolymer was found to be non-toxic, according to ISO/EN standards, and it showed a mild foreign body reaction and complete fibrous encapsulation after implantation.

Kim *et al*., (2008) looked at the role of aligned polymer fiber-based constructs in the bridging of long peripheral nerve gaps, demonstrating a significant role of submicron scale topographical cues in stimulating endogenous nerve repair mechanisms. Nisbet *et al*., (2009) assessed axonal infiltration and guidance within neural tissue-engineering scaffolds, made from PCL, and characterized of the inflammatory response. The extent of microglial and astrocytic response was measured following implantation of electrospun PCL scaffolds into the caudate putamen of the adult rat brain. They have found no evidence of microglial encapsulation and neurites infiltrated the implants, evidence of scaffold neural integration.

PCL/collagen blends were investigated by Schnell *et al*., (2007) as a conduit for axonal nerve regeneration after peripheral nerve injury. Aligned PCL and collagen/PCL nanofibers designed as guidance structures were produced by electrospinning and tested in cell culture assays. Both types of eletrospun fibers gave good cell migration, neurite orientation and process outgrowth, however the collagen/PCL fibers gives a better result compared to pure PCL fibers. They have concluded that electrospun fibers comprising a collagen and PCL blend represents a suitable substrate for supporting cell proliferation, process outgrowth and migration and as such would be a good material for artificial nerve implants.

Overall, PCL has been proven effective for the use in tissue engineering settings. The biocompatibility with the body has been proven. The fact the polymer is bioresorbable helps with numerous tissue engineering factors. With bioresorbable polymers, the fibers provide a back support for the cell growth. Over time in the body, the fibers, essentially dissolve and leave the cell growth (sometimes in tissue form) in a pure form within the body.

2.4 Polymer nanocomposites (PNCs)

Reinforcement of polymers with a second organic or inorganic phase to produce a polymer composite is common in the production of modern plastics. Material such as metals and fiber were the earliest materials added to thermoplastics and thermosets to form polymer composites (Krishnamoorti, 2001).

One of the primary reasons for adding fillers to polymers is to improve their mechanical performance. In traditional composites (refer to micro size filler), unfortunately, this often comes at the cost of a substantial reduction in ductility, and sometimes in impact strength, because of stress concentrations caused by the fillers (Kornmann, 2002). Well-dispersed nano fillers, on the other hand, can improve the modulus and strength and maintain or even improve ductility because their small size does not create large stress concentrations. In addition, the large interfacial area of nanocomposites provides an opportunity for altering the matrix properties in unique ways (Kornmann, 2002).

Advances in synthetic techniques and the ability to readily characterize materials on an atomic scale has lead to an interest in reinforcement of polymers with nanometer-size materials to create a new class of composites called polymer nanocomposites (PNCs) (Brauer, 2000). This new class of materials, exhibits superior properties in comparison with pure polymer or conventionally filled polymers and the properties can be achieved at a much lower volume fraction of reinforcement, normally less than 5% by weight (Vaia, 2002). As reported by NPL (2004), PNCs in general, with 2 vol% addition, can increase properties in tensile strength (>40%), tensile modulus (>70%), flexural strength (>60%), flexural modulus (>125%), heat distortion temperature (65º-150ºC), lower water sensitivity and permeability to gas, excellent flame retardancy, UV resistance, and barrier properties.

PNCs are commonly defined as particle-filled polymers for which at least one dimension (i.e. length, width, or thickness) of the dispersed particles is in the nanometer size range, generally at less than 100nm (Vollath & Szabo, 2004). They were developed in the late 1980s in both commercial research organizations and academic laboratories. The first company to commercialize these nanocomposites was Toyota (Richard *et al.*, 2002), which used them for timing belts in their car engine components. Since then, the number of commercial applications for nanocomposites has grown at a rapid rate. Several potential applications have been identified in the following industrial sectors. More detail on specific applications can be found in Fischer (2003):

a. Automobile (gasoline tanks, bumpers, interior and exterior panels, etc)
b. Construction (shaped extrusions, panels)

c. Electronics and electrical (printed circuits, electric components)
d. Food packaging (containers, films) and
e. Aerospace (flame retardant panels and high performance components)

Most commercial interest in PNCs has focused on thermoplastics. Thermoplastics can be broken down into two groups: less expensive and more expensive (higher performance) commodity resins. Hence, one of the goals of PNCs was to allow the substitution of more expensive engineering resins with a less expensive commodity resin nanocomposite (Vaia, 2002). Substituting a nanocomposite commodity resin with equivalent performance for a more expensive engineering resin should yield overall cost saving. Another goal for PNCs is providing lighter weight alternatives to conventionally-filled polymer (Manias, 2004).

2.4.1 Layered silicates

The layered silicates or clay commonly used in nanocomposites belong to the structural family known as the 2:1 phyllosilicates and the most commonly used layered silicates are montmorillonite (MMT). It was discovered in 1847 in Montmorillon in the Vienne, France. Clays have been extensively used in the polymer industry as fillers to reduce the amount of the polymers used in shaped structures, thereby lowering the high cost of the polymer systems.f The efficiency of the clay as a reinforcing agent to modify the physicomechanical properties of the polymer is determined by the degree of its dispersion in the polymer matrix, which in turn depends on its particle size (Akelah et al., 1995). Natural clays may contain divalent cations such as calcium and require expensive exchange procedures with sodium prior to further treatment with onium salts (Zanetti *et al*., 2000).

Pristine layered silicates usually contain hydrated Na+ or K+ ions. Obviously, in this pristine state, layered silicates are only miscible with hydrophilic polymers, such as poly (ethylene oxide) (PEO), or poly (vinyl alcohol) (PVA). To render layered silicates miscible with other polymer matrices, one must convert the normally hydrophilic silicate surface to an organophilic one, making the intercalation

of many engineering polymers possible. Generally, this can be done by ion-exchange reactions with cationic surfactants including primary, secondary, tertiary, and quaternary alkylammonium or alkylphosphonium cations. alkyl-ammonium or alkylphosphonium cations in the organosilicates lower the surface energy of the inorganic host and improve the wetting characteristics of the polymer matrix, and result in a larger interlayer spacing. Additionally, the alkylammonium or alkylphosphonium cations can provide functional groups that can react with the polymer matrix, or in some cases initiate the polymerization of monomers to improve the strength of the interface between the inorganic and the polymer matrix (Sinha & Okamoto, 2003).

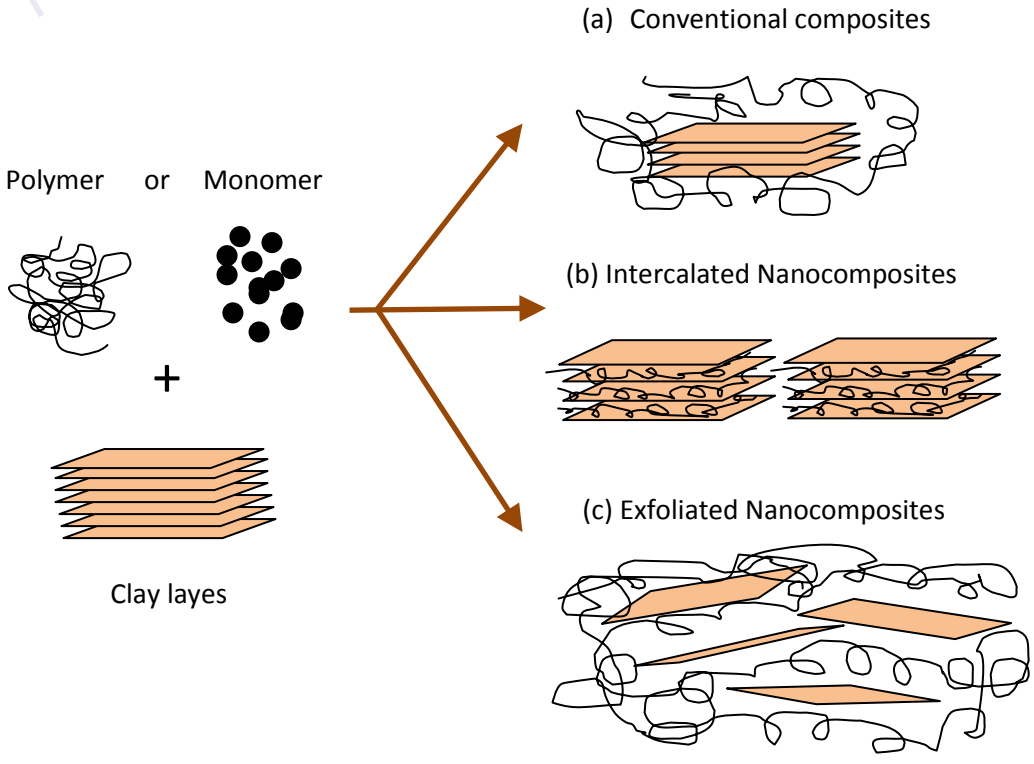
2.4.1.1 Dispersion state of layered silicates

The dispersion state of PNC's is depending on how many dimensions of the dispersed phase are in the nanometer range, one can distinguish three different nanocomposites can be reinforced by isodimensional phases, which have three dimensions in the nanometer range such as precipitated silica, silica-titania oxides synthesized by the sol gel process, silica beads but also colloidal dispersion of rigid polymers, and many others. They can also be reinforced by a phase which has only two dimensions at the nanometer scale. It is the case of polymer matrices reinforced by cellulose whisker or nanotubes. The third type of nanocomposites corresponds to the case where the reinforcing phase, in the shape of platelets, has only one dimension on a nano level. Polymer-layered silicate nanocomposites belong to this third class (Alexandre & Dubois, 2000).

Conventional composite or microcomposite where the layered silicate acts as a conventional filler, intercalated nanocomposites consisting of a regular insertion of the polymer in between the silicate layers and exfoliated or delaminated nanocomposites where 1 nm-thick layers are dispersed in the matrix forming a monolithic structure on the micro scale. Because thermoset-layered silicate nanocomposites are synthesized by in-situ polymerization, silicate layers separated by 5 to 10 nanometers remain parallel if the extent of intragallery polymerization is uniform. Nanocomposites presenting such structure with long-range order have also

been considered as exfoliated. The exfoliated configuration is of particular interest because it maximizes the polymer-layered silicate interactions, making the entire surface of the layers available for interactions with the polymer. This should lead to more dramatic changes in mechanical and physical properties (Alexandre & Dubois, 2000).

Depending on the nature of the components used (layered silicate, organic cation and polymer matrix) and the method of preparation, three main types of composites may be obtained when layered clay is associated with a polymer as shown in Figure 2.2 (Alexandre & Dubois, 2000). Conventional composite is obtained if the polymer cannot intercalate into the galleries of clay minerals. The properties of such composite are similar to that of polymer composites reinforced by micro particles. There are two extreme nanostructures resulting from the mixing of clay minerals and a polymer providing a favor conditions. One is intercalated nanocomposite (Figure 2.2a), in which monolayer of extended polymer chains is inserted into the gallery of clay minerals resulting in a well ordered multilayer morphology stacking alternately polymer layers and clay platelets and a repeating distance of a few nanometers. The other is exfoliated or delaminated nanocomposite (Figure 2.2b), in which the clay platelets are completely and uniformly dispersed in a continuous polymer matrix. However, it should be noted that in most cases the cluster (so-called partially exfoliated) nanocomposite (Figure 2.2c) is common in polymer nanocomposites (Zeng et al., 2005).



REFERENCES

Abbah, S. A., Lam, C. X. L., Hutmacher, D. W., Goh, J. C. H. & Wong, H.K. (2009). Biological performance of a polycaprolactone-based scaffold used as fusion cage device in a large animal model of spinal reconstructive surgery. *Biomaterials, 30(28),* pp. 5086-5093.

Ahmed, J., Auras, R., Kijchavengkul, T. & Varshney, S. K. (2012). Rheological, thermal and structural behavior of poly(ε-caprolactone) and nanoclay blended films. *Journal of Food Engineering, 111(4),* pp. 580-589.

Ajili, S. H., Ebrahimi, N. G. & Soleimani, M. (2009). Polyurethane/ polycaprolactane blend with shape memory effect as a proposed material for cardiovascular implants. *Acta Biomaterialia, 5(5),* pp. 1519-1530.

Akelah, A., El-Deen, N. S., Hiltner, A., Baer, E. & Moet, A. (1995). Organophilic rubber-montmorillonite nanocomposites. *Materials Letters, 22(1),* pp. 97-102.

Albano, C., Perera, R., Cataño, L., Alvarez, S., Karam, A. & González, G. (2010). Compatibilization of Polyolefin/Hydroxyapatite Composites Using Grafted Polymers. *Polymer-Plastics Technology and Engineering, 49(4),* pp. 341-346.

Alexandre, M. & Dubois, P. (2000). Polymer-layered silicate nanocomposites: Preparation, properties and uses of a new class of materials. *Materials Science and Engineering R: Reports, 28(1),* pp. 1–63.

Athreya, S. R., Kalaitzidou, K. & Das, S. (2011). Mechanical and microstructural properties of Nylon-12 /carbon black composites: Selective laser sintering versus melt compounding and injection molding. *Composites Science and Technology, 71 (4),* pp. 506-510.

Azevedo, M., Reis, R., Claase, M., Grijpma, D. & Feijen, J. (2003). Development of polycaprolactone/hydroxyapatite composite bio-materials. *Journal of material science: material in medicine, 14*, pp. 103-107.

Bonfield W., Grynpas M. D., Tully A. E., Bowman J. & Abram J. (1981). Hydroxyapatite reinforced polyethylene--a mechanically compatible implant material for bone replacement. *Journal of Biometerial, 2(3)*, pp. 185-186.

Bonfield, W. (1988). Composites for bone replacement. *Journal of Biomedical Engineering, 10(6)*, pp. 522-526.

Bryk, M. T. (1991). *Degradation of Filled Polymers: High Temperature and Thermal-Oxidative Process*. 1st ed. PTR Prentice Hall.

Bose, S. & Tarafder, S. (2012). Calcium phosphate ceramic systems in growth factor and drug delivery for bone tissue engineering: A review. *Acta Biomaterialia, 8(4)*, pp. 1401-1421.

Boyce, S. T & Powell., H. M. (2009). Engineered Human Skin Fabricated Using Electrospun Collagen–PCL Blends: Morphogenesis and Mechanical Properties. *Tissue Engineering Part A, 15(8)*, pp. 2177-2187.

Brauer, S. (2000). Polymer nanocomposites, Market report, Business Communications Company, USA.

Chen, D. Z., Tang, C. Y., Chan, K. C., Tsui, C. P., Yu, P. H. F., Leung, M. C. P. & Uskokovic, P. S. (2007). Dynamic mechanical properties and in vitro bioactivity of PHBHV/HA nanocomposite. *Composites Science and Technology, 67*, pp. 1617-1626.

Chen, M., Michaud H. & Bhowmick. S. (2009). Controlled vacuum seeding as a means of generating uniform cellular distribution in electrospun polycaprolactone (PCL) scaffolds. *Journal of Biomechanical Engineering 131(7)*, pp. 1-8.

Chua, C. K., Leong, K. & Lim, C. S. (2003). *Rapid Prototyping: Principles and Applications*. 2nd ed. Singapore: World Scientific Publishing Co. Pte. Ltd.

Cho, J. W. & Paul, D. R. (2000). Nylon 6 nanocomposites by melt compounding. *Polymer*, *42*, pp. 1083-1094.

Choi, J. S., Lee, S. J., Christ, G. J., Atala, A. & Yoo, J. J. (2008). The influence of electrospun aligned poly(ε-caprolactone)/collagen nanofiber meshes on the formation of self-aligned skeletal muscle myotubes. *Biomaterials*, *29(19)*, pp. 2899-2906.

Chow, W. S., Ishak, Z. A. M., Ishiaku, U. S., Karger-Kocsis, J. & Apostolov, A. A. (2004). The effect of organoclay on the mechanical properties and morphology of injection-molded polyamide 6/polypropylene nanocomposites. *Journal of Applied Polymer Science*, *91(1)*, pp. 175-189.

Chrissafis, K., Paraskevopoulos, K. M., Tsiaoussis, I. & Bikiaris, D. (2009). Comparative study of the effect of different nanoparticles on the mechanical properties, permeability, and thermal degradation mechanism of HDPE. *Journal of Applied Polymer Science*, *114(3)*, pp. 1606–1618.

Cotterell, B., Chia, J. Y. H., & Hbaieb, K. (2007). Fracture mechanisms and fracture toughness in semicrystalline polymer nanocomposites. *Engineering Fracture Mechanics*, *74(7)*, pp. 1054–1078.

Cruz, F., Simões, J., Coole, T. & Bocking, C. (2005). Direct manufacture of hydroxyapatite based bone implants by selective laser sintering. *In Virtual Modelling and Rapid Manufacturing - Advanced Research in Virtual and Rapid Prototyping*, pp. 119-125.

Dai, N. T., Williamson, M. R., Khammo, N., Adams, E. F. & Coombes, A. G. A. (2004). Composite cell support membranes based on collagen and polycaprolactone for tissue engineering of skin. *Biomaterials*, *25(18)*, pp. 4263-4271.

Di, Y., Iannace, S., Di Maio, E., & Nicolais, L. (2003). Nanocomposites by melt intercalation based on polycaprolactone and organoclay. *Journal of Polymer Science, Part B: Polymer Physics*, *41(7)*, pp. 670–678.

Diamond, W. J. (2001). *Practical experiment design for engineers and scientists*. 3rd ed. New York: John Wiley & Sons, Inc.

Den Dunnen, W. F. A., Schakenraad, J. M., Zondervan, G. J., Pennings, A. J., Ven De Lei, B. & Robinson, P. H. (1993). A new PLLA/PCL copolymer for nerve regeneration. *Journal of Materials Science-Materials in Medicine*, *4(5)*, pp. 521-525.

Dutta, S., Bhowmick, A. K., Mukunda. P. G. & Chaki, T. K. (1995). Thermal degradation studies of electron beam cured ethylene-vinyl acetate copolymer. *Polymer Degradation and Stability, 50(1)*, pp. 75-82.

Eniwumide, J. O., Joseph, R. & Tanner, K. E. (2004). Effect of Particle Morphology and Polyethylene Molecular Weight on the Fracture Toughness of Hydroxyapatite Reinforced Polyethylene Composites. *Journal of Materials Science-Materials in Medicine, 15(10)*, pp. 1147-1152.

Espalin, D., Arcaute, K., Rodriguez, D., Medina, F., Posner, M. & Wicker, R. B. (2010). Fused Deposition Modeling of Patient-Specific Polymethylmethacrylate Implants. *Rapid Prototyping Journal*, *16(3)*, pp. 164-173.

Eyers, D. & Dotchev, K. (2010). Technology review for mass customisation using rapid manufacturing. *Assembly Automation, 30(1)*, pp. 39-46.

Fang, L., Leng, Y. & Gao, P. (2005). Processing of hydroxyapatite reinforced ultrahigh molecular weight polyethylene for biomedical applications. *Biomaterials*, *26(17)*, pp. 3471-3478.

Fang, L., Gao P. & Leng, Y. (2006). Processing and Mechanical Properties of HA/UHMWPE Nanocomposites. *Biomaterials, 27*, pp. 3701-3707.

Fischer, H. (2003). Polymer Nanocomposites: From Fundamental Research to Specific Applications. *Materials Science and Engineering*, 23, pp. 763-772.

Fornes, T. D. & Paul, D. R. (2003). Crystallization behavior of nylon 6 nanocomposites. *Polymer*, *44*(14), pp. 3945-3961.

Gain, O., Espuche, E., Pollet, E., Alexandre, M. & Dubois, Ph. (2005). Gas barrier properties of poly(e-caprolactone)/clay nanocomposites: influence of the morphology and polymer/clay interactions. *Journal of Polymer Science, Part B: Polymer Physics, 43*, pp. 205-214.

Gomes, M. E. & Reis, R. L. (2004). Biodegradable polymers and composites in biomedical applications: from catgut to tissue engineering - Part 2 - systems for temporary replacement and advanced tissue regeneration. *Biomaterials, 49(5)*, pp. 274-285.

Gorrasi, G., Tortora, M., Vittoria, V., Kaempfer, D. & Mulhaupt, R. (2003). Transport properties of organic vapors in nanocomposites of organophilic layered silicate and syndiotactic polypropylene. *Polymer, 44(13)*, pp. 3679-3685.

Gorrasi, G., Tortora, M., Vittoria, V., Pollet, E., Lepoittevin, B., Alexandre, M. & Dubois, P. (2003). Vapor barrier properties of polycaprolactone montmorillonite nanocomposites: effect of clay dispersion. *Polymer, 44(8)*, pp. 2271-2279.

Grenda, E 2006, *Printing the future: The 3D priniting and rapid prototyping source book*, Castle Island Co., Arlington, MA.

Guo, C.Y., Ke, Y., Liu, Y., Mi, X., Zhang, M. & Hu, Y. (2009). Preparation and properties of polyethylene/montmorillonite nanocomposites formed via ethylene copolymerization. *Polymer International, 58(11)*, pp. 1319-1325.

Han, G., Lei, Y., Wu, Q., Kojima, Y. & Suzuki, S. (2008). Bamboo-fiber filled high density polyethylene composites: Effect of coupling treatment and nanoclay. *Journal of Polymers and the Environment*, *16*(2), pp. 123-130.

Hao, L., Savalani, M. M. & Zhang, Y. (2006). Effect of material morphology and processing conditions on the characteristics of hydroxyapatite and high-density polyethylene biocomposite by selective laser sintering. *Journal of Materials: Design and Application, 220(L3)*, pp. 125-137.

Herliansyah, M. K., Toque, J. A., Hamdi, M., Ide-Ektessabi, A. & Wildan, M. W. (2006). Fabrication of Bovine Bone Hydroxyapatite: Effect of The Material Shapes and Calcination Temperature. *ISTECS Journal, 8,* pp. 25-33.

Hing, K. A., Best, S. M. & Bonfield, W. (1999). Characterization of porous hydroxyapatite. *Journal of Materials Science: Materials in Medicine, 10*(3), pp. 135-145.

Hing, K. A., Best, S. M., Tanner, K. E., Bonfield, W. & Revell, P. A. (1997). Biomechanical assessment of bone ingrowth in porous hydroxyapatite. *Journal of Materials Science: Materials in Medicine*, 8, pp. 731-736.

Huang, Q., Goh, J. C. H., Hutmacher, D. W. & Lee, E. H. (2004). In Vivo Mesenchymal Cell Recruitment by a Scaffold Loaded with Transforming Growth Factor β1 and the Potential for in Situ Chondrogenesis. *Tissue Engineering*, *8(3),* pp. 469–482.

Hunter, D. L., Kamena, K. W., Paul D. R. (2007). Processing and Properties of polymers modified by clays. *MRS Bulletin, 32(4),* pp. 323.

Joseph, R., McGregor, W. J., Martyn, M. T., Tanner, K. E. & Coates, P. D. (2002). Effect of hydroxyapatite morphology/surface area on the rheology and processability of hydroxyapatite filled polyethylene composites. *Biomaterials, 23(21),* pp. 4295-4302.

Kang, Y., Xu, X., Yin, G., Chen, A., Yao, Y., Huang, Z. & Liao, X. (2007). A comparative study of the in vitro degradation of poly(L-lactic acid)/B-tricalcium phosphate scaffold in static and dynamic simulated body fluid. *European Polymer Journal*, 43, pp. 1768-1778.

Kim, Y., Haftel, V. K., Kumar, S., & Bellamkonda, R. V. (2008). The role of aligned polymer fiber-based constructs in the bridging of long peripheral nerve gaps. *Biomaterials, 29(21),* pp. 3117-3127.

Kim, Y. H., Cho, C. S., Kang, I. K., Kim, S. Y. & Kwon, O. H. (2007). A Novel polycaprolactone/Hydroxyapatite Scaffold for Bone Tissue Engineering. *Engineering Materials*, *342*, pp. 265-268.

Kokubo, T. & Takadama. H. (2006). How Useful is SBF in Predicting in Vivo bone bioactivity. *Biomaterials*, *27*, pp. 2907-2915.

Koleske, J. V. (1978). *Polymer Blends*, *Academic Press*, *2*, pp. 369–389.

Kong, L. B., Ma, J. & Boey, F. (2002). Nanosized Hydroxyapatite Powders Derived From Coprecipitation Process. *Journal of Materials Science, 37,* pp. 1131-1134.

Kornmann. (2002). Polymer-layered silicate nanocomposites. Switzerland: EMPA.

Koo, J. H., Lao, S., Ho, W., Ngyuen, K., Cheng, J. & Pilato, L. (2006). Flammability, mechanical, and thermal properties of polyamide nanocomposites. Dallas, TX, United States.

Krishnamoorti, R. (2001). Polymer nanocomposites : synthesis, characterization, and modeling. Editor, Richard A. Vaia, Washington, D.C., Cambridge, American Chemical Society, Royal Society of Chemistry.

Kurtz, S. (1999). Advances in the processing, sterilization, and crosslinking of ultra-high molecular weight polyethylene for total joint arthroplasty. *Biomaterials*, *20(18)*, pp. 1659-1688.

Labidi, S., Azema, N., Perrin, D. & Lopez-Cuesta, J. M. (2010). Organo-modified montmorillonite/poly(e-caprolactone) nanocomposites prepared by melt intercalation in a twin-screw extruder. *Polymer Degradation and Stability*, *95(3)*, pp. 382–388.

Lam, C. X. F., Hutmacher, D. W., Schantz, J. T., Woodruff, M. A. & Teoh, S. H. (2009). Evaluation of polycaprolactone scaffold degradation for 6 months in vitro and in vivo. *Journal of Biomedical Materials Research Part A, 90A(3),* pp. 906–919.

Lam, C. X. F., Savalani, M. M., Teoh, S. H. & Hutmacher, D. W. (2008). Dynamics of in vitro polymer degradation of polycaprolactone-based scaffolds: accelerated versus simulated physiological conditions. *Biomedical Materials*, *3(3)*, pp. 1-15.

Landers, R., Pfister, A., Hubner, U., John, H., Schmelzeisen, R. & Mulhaupt, R. (2002). Fabrication of soft tissue engineering scaffolds by means of rapid prototyping techniques. *Journal of Materials Science*, *37(15)*, pp. 3107–3116.

Lee, B. H., Abdullah, J. & Khan, Z. A. (2005). Optimization of rapid prototyping parameters for production of flexible ABS object. *Journal of Materials Processing Technology*, *169(1)*, pp. 54–61.

Lee, Y. H., Park, C. B., Sain, M., Kontopoulou, M. & Zheng, W. (2007). Effects of clay dispersion and content on the rheological, mechanical properties, and flame retardance of HDPE/clay nanocomposites. *Journal of Applied Polymer Science*, *105(4)*, pp. 1993–1999.

Leong, Y. W., Abu Bakar, M. B., Ishak, Z. A. M., Ariffin, A. & Pukanszky, B. (2004). Comparison of the mechanical properties and interfacial interactions between talc, kaolin, and calcium carbonate filled polypropylene composites. *Journal of Applied Polymer Science*, *91*(*5)*, pp. 3315–3326.

Leonora, I. B., Itob, A., Onumab, K., Kanzakib, N. & Reis R. L. (2003). In vitro bioactivity of starch thermoplastic/hydroxyapatite composite biomaterials: an in situ study using atomic force microscopy. *Biomaterials*, *24*, pp. 579–585

Levy, G., Schindel, R. & Kruth, J. P. (2003). Rapid manufacturing and rapid tooling with layer manufacturing technologies: State of the art and future perspectives. *Ann CIRP, 52(2)*, pp. 589-609.

Le Geros, R. Z. (2008). Calcium Phosphate Based Osteoinductive Materials. *Chemical Review, 10*, pp. 4742-4753.

Lieshout, M. V. A. N., Peter, G., Rutten, M. & Baaijens, F. (2006). A Knitted, Fibrin-Covered Polycaprolactone Scaffold for Tissue Engineering of the Aortic Valve, *Tissue Engineering, 12*(3), pp. 481-487.

Lim, K. L. K., Ishak, Z. A. M., Ishiaku, U. S., Fuad, A. M. Y., Yusof, A. H., Czigany, T. & Ogunniyi, D. S. (2006). High density polyethylene/ultra high molecular weight polyethylene blend. II. Effect of hydroxyapatite on processing, thermal, and mechanical properties. *Journal of Applied Polymer Science, 100(5)*, pp. 3931–3942.

Liou, F. W. (2008). *Rapid prototyping and engineering applications: a toolbox for prototype development*. CRC Press.

Liu, Y. & Wang, M. (2007). Fabrication and characteristics of hydroxyapatite reinforced polypropylene as a bone analogue biomaterial. *Journal of Applied Polymer Science, 106(4)*, pp. 2780–2790.

Long, M. & Rack, H. J. (1998). Review: Titanium alloys in total joint replacement-A Materials Science Perspective. *Biomaterials, 19*, pp. 1621-1639.

Luduena, L. N., Kenny, J. M., Vazquez, A. & Alvarez, V. A. (2011a). Effect of clay organic modifier on the final performance of PCL/clay nanocomposites. *Materials Science and Engineering: A, 529*, pp. 215-223.

Luduena, L. N., Kenny, J. M., Vazquez, A., & Alvarez, V. A. (2011b). Effect of clay organic modifier on the final performance of PCL/clay nanocomposites. *Materials Science and Engineering: A, 529*, pp. 215-223.

Manias, E. (2004). Origins of the Material Properties Enhancements in Polymer/Clay nanocomposites. Pennsylvania: The Pennsylvania State University.

Masood, S. (1996). Intelligent rapid prototyping with fused deposition modelling. *Rapid Prototyping Journal, 2(1)*, pp. 24-33.

Middleton, J. C. & Tipton, A. J. (2000). Synthetic Biodegradable Polymers As Orthopaedic Devices. *Biomaterials, 21*, pp. 2335-2346.

Min, K. D., Kim, M. Y., Choi, K. Y., Lee, J. H. & Lee, S. G. (2006). Effect of Layered Silicates on the Crystallinity and Mechanical Properties of HDPE/MMT Nanocomposite Blown Films. *Polymer Bulletin. 57(1),* pp. 101-108.

Miyagawa, H., Jurek, R. J., Mohanty, A. K., Misra, M. & Drzal, L. T. (2006). Biobased epoxy/clay nanocomposites as a new matrix for CFRP. *Composites Part A: Applied Science and Manufacturing, 37(1),* pp. 54–62.

Mizutani, Y., Hattori, M., Kasuga, T. & Nogami, M. (2005). Large-sized Hydroxyapatite Whiskers Derived From Calcium Tripolyphosphate Gel. *Journal European Ceramic, 25,* pp. 3181–3185.

Khil, M. S., Bhattarai, S. R., Kim, H. Y., Kim, S. Z. & Lee, K. H. (2005). Novel fabricated matrix via electrospinning for tissue engineering. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 72B(1),* pp. 117-124.

Montgomery, D. (2001). *Design and Analysis of Experiments.* 5th ed. New York: John Wiley & Sons, Inc.

Moussaif, N., Crespo, C., Meier, J. G. & Jimenez, M. A. (2012). Synergistic reinforcement of nanoclay and mesoporous silicate fillers in polycaprolactone: The effect of nanoclay on the compatibility of the components. *Polymer (United Kingdom), 53(17),* pp. 3741-3748.

Murphy, W. L., Kohn, D. H. & Mooney, D. J. (1999). Growth of continuous bonelike mineral within porous poly (lactide- co -glycolide) scaffolds in vitro. *Biomaterials, 21,* pp. 2521-2527.

Murugan, R. & Ramakrishna, S. (2005). Development of nanocomposites for bone grafting. *Composites Science and Technology, 65(15),* pp. 2385-2406.

Nair, L. S. & Laurencin, C. T. (2007). Biodegradable polymers as biomaterials. *Progress in Polymer Science, 32(8),* pp. 762-798.

Nisbet, D. R., Rodda, A. E., Horne, M. K., Forsythe, J. S. & Finkelstein, D. I. (2009). Neurite infiltration and cellular response to electrospun polycaprolactone scaffolds implanted into the brain. *Biomaterials*, *30(27)*, pp. 4573-4580.

Ojijo, V. & Ray, S. S. (2014). Nano-biocomposites based on synthetic aliphatic polyesters and nanoclay. *Progress in Materials Science*, *62*, pp. 1-57.

Olley, R. H., Hosier, I. L., Bassett, D.C. & Smith, N. G. (1999). On Morphology of Consolidated UHMWPE Resin in Hip Cups. *Biomaterials*, *20*, pp. 2037–2046.

Panda, S. K., Padhee, S., Sood, A. K. & Mahapatra, S. S. (2011). Optimization of Fused Deposition Modelling (FDM) Process Parameters Using Bacterial Foraging Technique. *Intelligent Information Management, 1,* pp. 89-97.

Parija, S., Nayak, S. K., Verma, S. K. & Tripathy, S. S. (2004). Studies on physico-mechanical properties and thermal characteristics of polypropylene/layered silicate nanocomposites. *Polymer Composites*, *25(6)*, pp. 646-652.

Paul, D. R. & Robeson, L. M. (2008). Polymer Nanotechnology: Nanocomposites. *Polymer*, *49(15)*, pp. 3187-3204.

Pavlidou, S. & Papaspyrides, C. D. (2008). A review on polymer–layered silicate nanocomposites. *Progress in Polymer Science*, *33(12)*, pp. 1119–1198.

Petersson, L. & Oksman, K. (2006). Biopolymer Based Nanocomposites: Comparing Layered Silicates and Microcrystalline Cellulose as Nanoreinforcement. *Composites Science and Technology*, *66*, pp. 2187-2196.

Pham, D. T. & Gault, R. S. (1998). A comparison of rapid prototyping technologies. *International Journal of Machine Tools and Manufacture*, *38(10-11)*, pp. 1257-1287.

Pitt, C. G., Chasalow, F. I., Hibionada, Y. M., Klimas, D. M. & Schindler, A. (1981). Aliphatic polyesters. I. The degradation of poly(ϵ-caprolactone) in vivo. *Journal of Applied Polymer Science*, *26(11)*, pp. 3779-3787.

Pitt, C. G., Gratzl, M. M., Kimmel, G. L., Surles, J. & Schindler, A. (1981). Aliphatic polyesters II. The degradation of poly (DL-lactide), poly (epsilon-caprolactone), and their copolymers in vivo. *Biomaterials, 2(4),* pp. 215-220.

Pradnya, N. C., Manjushri, M. B., Ravindra, U. M., Megha, P. M. & Rajendra, S. K. (2010) Study of nanobiomaterial hydroxyapatite in simulated body fluid: Formation and growth of apatite. *Materials Science and Engineering, B 168,* pp. 224-230.

Pramoda, K. P., Liu, T., Liu, Z., He, C. & Sue, H.J. (2003). Thermal degradation behavior of polyamide 6/clay nanocomposites. *Polymer Degradation and Stability, 81(1),* pp. 47-56.

Priya, L. & Jog, J. P. (2003). Intercalated poly(vinylidene fluoride)/clay nanocomposites: structure and properties. *Journal of Polymer Science Part B: Polymer Physics, 41,* pp. 31–38.

Qiu, Z., Wang, H. & Xu, C. (2011). Crystallization, mechanical properties, and controlled enzymatic degradation of biodegradable poly(epsilon-caprolactone)/multi-walled carbon nanotubes nanocomposites. *Journal of Nanoscience and Nanotechnology, 11 (9),* pp. 7884-93.

Ramakrishna, S., Mayer, J., Wintermantel, E. & Leong, K. W. (2001). Biomedical applications of polymer-composite materials: a review. *Composites Science and Technology, 61(9),* pp. 1189-1224.

Ramakrishna, S., Huang, Z. M., Kumar, G. V., Batchelor, A. W. & Mayer, J. (2004). An Introduction to Biocomposites. London: *Imperial College Press. Series on Biomaterials & Bioengineering, (1),* pp. 1-33.

Ramirez, C., Albano, C., Karam, A., Dominguez, N., Sanchez, Y. & Gonzalez, G. (2005). Mechanical, thermal, rheological and morphological behaviour of irradiated PP/HA composites. *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms, 236(1-4),* pp. 531-535.

Rea, S. M., Best, S. M. & Bonfield, W. (2004). Bioactivity of Ceramic-Polymer Composites With Varied Composition and Surface Topography. *Journal of Materials Science: Materials in Medicin,. 15*, pp. 997-1005.

Reed, C. R., Han, L., Andrady, A., Caballero, M., Jack, M. C., Collins, J. B., Saba, S. C, L. & Cairns, B. A. (2009). Composite tissue engineering on polycaprolactone nanofiber scaffolds. *Annals of Plastic Surgery, 62(5),* pp. 505-512.

Reis, R. L., Cunha, A. M., Oliveira, M. J., Campos, A. R. & Bevis, M. J. (2001). Relationship between processing and mechanical properties of injection molded high molecular mass polyethylene/hydroxyapatite composites. *Materials Research Innovations, 4(5-6),* pp. 263-272.

Rezwan, K., Chen, Q. Z., Blaker, J. J. & Boccaccini, A. R. (2006). Biodegradable and bioactive porous polymer/inorganic composite scaffolds for bone tissue engineering. *Biomaterials, 27(18),* pp. 3413-3431.

Richard, A. V. & Krishnamoorti, R. (2002). Polymer Nanocomposites: Introduction. American Chemical Society.

Sachlos, E. & Czernuszka, J. T. (2003). Making tissue engineering scaffolds work. Review: the application of solid freeform fabrication technology to the production of tissue engineering scaffolds. *European Cells & Materials, 5,* pp. 39-40.

Scaffolds, C. & Responses, T. C. (2009). Processing of Polycaprolactone and Polycaprolactone-Based Copolymers into 3D Scaffolds, and Their Cellular Responses. *Tissue Engineering, 15(10),* pp. 3023-3024..

Schnell, E., Klinkhammer, K., Balzer, S., Brook, G., Klee, D., Dalton, P. & Mey, J. (2007). Guidance of glial cell migration and axonal growth on electrospun nanofibers of poly-ε-caprolactone and a collagen/poly-ε-caprolactone blend. *Biomaterials, 28(19),* pp. 3012–3025.

Shao, X., Goh, J. C., Hutmacher, D. W., Lee, E. H. & Zigang, G. (2006). Repair of large articular osteochondral defects using hybrid scaffolds and bone marrow-

derived mesenchymal stem cells in a rabbit model. *Tissue Engineering Part A: Tissue Engineering*, *12(6)*, pp. 1539–1551.

Shi, D., & Jiang, G. (2005a). Introduction to Bioceramics. *In Introduction to Biomaterials,* pp. 3-12. Co-Published with Tsinghua University Press.

Shi, D., & Jiang, G. (2005b). Properties and Characterization of Biomaterials. *In Introduction to Biomaterials*, pp. 61-73. Co-Published with Tsinghua University Press.

Shia, D., Hui, C. Y., Burnside, S. D. & Giannelis, E. P. (1998). An interface model for the prediction of Young's modulus of layered silicate-elastomer nanocomposites. *Polymer Composites, 19(5),* pp. 608–617.

Schadler L.S, Ajayan P.M, Braun P.V (2003) Nanocomposite science and technology, Weinheim, Cambridge, Wiley-VCH.

Sinha Ray, S., & Okamoto, M. (2003). Polymer/layered silicate nanocomposites: a review from preparation to processing. *Progress in Polymer Science*, 28(11), pp. 1539-1641.

Sousa, R. A., Reis, R. L., Cunha, A. M., & Bevis, M. J. (2003). Processing and properties of bone-analogue biodegradable and bioinert polymeric composites. *Composites Science and Technology, 63(3-4),* pp. 389-402.

Spencer, M. W., Cui, L., Yoo, Y., & Paul, D. R. (2010). Morphology and properties of nanocomposites based on HDPE/HDPE-g-MA blends. *Polymer*, *51(5)*, 1056-1070.

Stratasys. (2001). FDM3000 Operation Manual, Eden Prairie, Minnesota

Stratasys Retrieved (2009). Thermoplastic Model Materials, viewed <http://www.stratasys.com/default.aspx

Strong A. B. (2000). *Plastics: Materials and Processing*. 2nd ed. Prentice Hall, Inc.; Upper Saddle, NJ.

Taboas, J. M., Maddox, R. D., Krebsbach, P. H. & Hollister, S. J. (2003). Indirect solid free form fabrication of local and global porous, biomimetic and composite 3D polymer-ceramic scaffolds. *Biomaterials*, *24(1)*, pp. 181-194.

Tan, K. H., Chua, C. K., Leong. K. F., Cheah, C. M., Cheang, P. & Abu Bakar M. S. (2003). Scaffold development using selective laser sintering of polyetheretherketone- hydroxyapatite biocomposite blends. *Biomaterials, 24*, pp. 3115-3123.

Tanniru, M., Yuan, Q. & Misra, R. D. K. (2006). On Significant Retention of Impact Strength in Clay-Reinforced High-Density Polyethylene (HDPE) Nanocomposites. *Polymer, 7(6),* pp. 2133-2146.

Tortora, M., Gorrasi, G., Vittoria, V., Galli, G., Ritrovati, S. & Chiellini, E. (2002). Structural characterization and transport properties of organically modified montmorillonite/polyurethane nanocomposites. *Polymer*, *43(23)*, pp. 6147-6157.

Vaia, R. A. (2002). Polymer Nanocomposites Open a New Dimension for Plastics and composites. New York: AMPTIAC.

Vollath, D. & Szabo, D. V. (2004). Synthesis and Properties of Nanocomposites. *Advanced Engineering Materials*, *6(3)*, pp.117-127.

Vyazovkin, S., Dranca, I., Fan, X. & Advincula, R. (2004). Kinetics of the thermal and thermo-oxidative degradation of a polystyrene-clay nanocomposite. *Macromolecular Rapid Communications*, *25(3)*, pp. 498–503.

Wang, K. (2010). Description of Extrudate Swell for Polymer Nanocomposites. *Materials*, *3*, pp. 386-400.

Wang, M., Porter, D. & Bonfield, W. (1994). Processing, characterization, and evaluation of hydroxyapatite reinforced polyethylene composites. *British Ceramic Transactions*, *93(3)*, pp. 91–95.

Wang, M., Ward, I. M. & Bonfield. W. (1997). Hydroxyapatite-Polyethylene Composites for Bone Substitution: Effects of Hydrostatic Extrusion. In

Proceedings of the 11th International Conference on Composite Materials (ICCM-11) Gold Coast, Australia, pp. 488-495.

Wang, M. (1998). Hydroxyapatite-polyethylene composites for bone substitution: effects of ceramic particle size and morphology. *Biomaterials, 19(24),* 2357-2366.

Wang, M. (2003). Developing bioactive composite materials for tissue replacement. *Biomaterials*, *24(13),* pp. 2133–2151.

Wang, Y., Shi, Y. & Huang, S. (2005). Selective laser sintering of polyamiderectorite composite. *Part L: Journal of Materials: Design and Applications*, *219(1),* pp. 11–16.

Wang, Z., Chen, L., Wan, C., Qu, Y., Cornelissen, G., & Halberg, F. (2004). In vitro circadian ANP secretion by gene transferring cells encapsulated in polycaprolactone tubes: gene chronotherapy. *Peptides, 25(8),* pp. 1259–67.

Washburn, N. R., Simon, C. G., Tona, A., Elgendy, H. M., Karim, A. & Amis, E. J. (2002). Co-extrusion of biocompatible polymers for scaffolds with co-continuous morphology. *Journal of Biomedical Materials Research*, *60(1),* pp. 20-29.

Way, J. L., Atkinson, J. R. & Nutting, J. (1974) The effect of spherulite size on the fracture morphology of polypropylene. *Journal of Materials Science*. *9(2),* pp. 293-299.

Wendel, B., Rietzel, D., Kuhnlein, F., Feulner, R., Hulder, G. & Schmachtenberg, E. (2008). Additive processing of polymers. *Macromolecular Materials and Engineering, 293 (10),* pp. 99-809.

Wiria, F. E, Leong, K. F, Chua, C. K, & Liu, Y. (2007). Poly-e-capralactone/hydroxyapatite for tissue engineering scaffold fabrication by selective laser sintering. *Acta Biomaterials, 3(1),* pp. 1-12.

Wise, J. K., Yarin, A. L., Megaridis, C. M., & Cho, M. (2009). Chondrogenic differentiation of human mesenchymal stem cells on oriented nanofibrous

scaffolds: engineering the superficial zone of articular cartilage. *Tissue Engineering. Part A, 15(4),* pp. 913–921.

Wohlers, T. T (2008). 'State of the industry,' Proceedings of the 3rd International Conference on Advanced Research in Virtual and Rapid Prototyping: *Virtual and Rapid Manufacturing Advanced Research Virtual and Rapid Prototyping*, pp. 3-6.

Woodruff, M. A. & Hutmacher, D. W. (2010). The return of a forgotten polymer-Polycaprolactone in the 21st century. *Progress in Polymer Science*, *35(10),* pp. 1217-1256.

Woodward, C. S., Brewer, S. P., Moatamed, F., Schindler, A. & Pitt G. C. (1985). The intracellular degradation of poly(e-caprolactone). *Journal of Biomedical Materials Research, 19(4),* pp. 437-444.

Xu, Y., Brittain, W. J., Xue, C. & Eby, R. K. (2004). Effect of clay type on morphology and thermal stability of PMMA-clay nanocomposites prepared by heterocoagulation method. *Polymer*, *45(11),* pp. 3735-3746.

Yoshimoto, H., Shin, Y. M., Terai, H., & Vacanti, J. P. (2003). A biodegradable nanofiber scaffold by electrospinning and its potential for bone tissue engineering. *Biomaterials, 24(12),* pp. 2077-2082.

Younesi, M. & Bahrololoom, M. E. (2009). Producing toughened PP/HA-LLDPE ternary bio-composite using a two-step blending method. *Materials & Design*, *30(10)*, pp. 4253-4259.

Yourdkhani, M., Mousavand, T., Chapleau, N., & Hubert, P. (2013). Thermal, oxygen barrier and mechanical properties of polylactide–organoclay nanocomposites. *Composites Science and Technology*, *82*, pp. 47-53.

Yu, S., Hariram, K. P., Kumar, R., Cheang, P., & Aik, K. K. (2005). In vitro apatite formation and its growth kinetics on hydroxyapatite/polyetheretherketone biocomposites. *Biomaterials, 26*, pp. 2343-2352.

Zanetti, M., Lomakin, S., and Camino, G. (2000). Polymer layered silicate nanocomposites. *Macromolecular Materials and Engineering*, *279(1)*, pp. 1-9.

Zeng, Q., Yu, A., & Lu, G. (2005). Interfacial interactions and structure of polyurethane intercalated nanocomposite. *Nanotechnology*, *16(12)*, pp. 2757.

Zeng, Q. H., Wang, D, Z., Yu, A. B. & Lu, G. Q. (2002). Synthesis of polymer–montmorillonite nanocomposites by in situ intercalative polymerization. *Journal of Nanotechnology*, *13(5)*, pp. 549.

Zhang, J., Xu, Z. F., Zheng, H. Z. & Huang, Y. H. (2004). Preparation of polymer/A1uminium Oxide nano-composites by selective laser sintering. *Journal of Materials Engineering*, *(5)*, pp. 36-39.

Zhang, X., Li, Y., Lv, G., Zuo, Y. & Mu, Y. (2006). Thermal and crystallization studies of nano-hydroxyapatite reinforced polyamide 66 biocomposites. *Polymer Degradation and Stability*, *91(5)*, pp. 1202-1207.

Zhao, J., Guo, L. Y., Yang, X. B. & Weng, J. (2008). Preparation of bioactive porous HA/PCL composite scaffolds. *Applied Surface Science*, *255(5)*, pp. 2942-2946.

Zhong, W., Li, F., Zhang, Z., Song, L. & Li, Z. (2001). Short fiber reinforced composites for fused deposition modeling. *Materials Science and Engineering A*, *301(2)*, pp. 125–130.

Zhong, Y. & De Kee, D. (2005). Morphology and properties of layered silicate-polyethylene nanocomposite blown films. *Polymer Engineering & Science*, *45(4)*, pp. 469–477.