

**PREPARATION AND CHARACTERIZATIONS OF  
POLY(L-LACTIC ACID) (PLLA) BLENDS AND PLLA  
SCAFFOLD**

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**UNIVERSITI SAINS MALAYSIA**

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**PREPARATION AND CHARACTERIZATION OF POLY(L-LACTIC ACID)**

**(PLLA) BLENDS AND PLLA SCAFFOLD**

**by**

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## LIST OF SYMBOLS

$a$	The initial crack length
$A$	Cross-section area of scaffold
$b$	Width of bending specimen
$B$	Specimen thickness of mode I fracture specimen
$d$	The interplanar spacing in a crystal
$D_a$	Density of complete amorphous PLLA
$D_c$	Density of complete crystalline PLLA
$D_s$	Density of PLLA scaffold
$D_p$	Density of PLLA skeletal
$E_c$	Compressive modulus
$E'$	storage Modulus
$E$	Bending modulus
$F_{\max}$	The maximum load
$J_{\text{in}}$	The J-integral at crack initiation
$J_f$	The average mode I fracture energy
$h$	thickness of bending specimen
$L$	The span length of bending specimen
$\eta$	The geometrical correction factor
$\eta_s$	Porosity
$2\theta$	The angle between the diffracted beams and transmitted beams
$P$	The maximum load of bending
$S$	The slop of the initial linear portion of bend load-displacement curve

$T_c$	Crystallization temperature
$T_{c, PLLA}$	Crystallization temperature of PLLA
$T_g$	Glass Transition Temperature
$T_m$	melting temperature
$\sigma_f$	Bending Strength
$U_{in}$	Critical energy at crack initiation
$U_f$	Total fracture energy
$W$	Width of mode I fracture specimen
$X_c$	Percentage of crystallinity
$X_{c, PLLA}$	Percentage of crystallinity of PLLA
$\Delta H_m^o$	Melting enthalpy of 100% crystalline polymer
$\Delta H_m$	Melting enthalpy of the testes specimens
$\Delta H_c^o$	Crystallization enthalpy of 100% crystalline polymer
$\Delta H_c$	Crystallization enthalpy of the testes specimens
$\varepsilon$	Strain
$\lambda$	The wavelength of the incident X-ray beam
$\sigma_c$	Compressive strength
$\sigma_{yo}$	yield stresses of the polymer matrix

## LIST OF ABBREVIATIONS

ASTM	:	American Society of Testing and Materials
ABS	:	Acrylonitrile-butadiene-styrene
CDCl <sub>3</sub>	:	Acronym (Deuterated Chloroform)
DMA	:	Dynamic mechanical analysis
DSC	:	Differential scanning calorimeter
ECM	:	Extracellular matrix
FT-IR	:	Fourier-transform infrared spectroscopy
GPC	:	Gel permeation chromatography
HA	:	Hydroxyapatite
ISO	:	International Organization for Standardization
IDT	:	Initial decomposition temperature
MDI	:	Methylenediphenyl diisocyanate
MFI	:	Melt Flow Index
$M_n$	:	Number average molecular weight
$M_w$	:	Weight average molecular weight
NBR	:	Acrylonitrile rubber
NMR	:	Nuclear magnetic resonance
<sup>1</sup> H NMR	:	Proton nuclear magnetic resonance
LTI	:	Lysine Triisocyanate
SENB	:	Single-edge-notch bend
PAMP	:	Poly( <i>N</i> -acryloyl- <i>N</i> '-methylpiperazine)
PCL	:	Poly (ε-caprolactone)
PBS	:	Poly(butylenes succinate)
PBSC	:	Poly(butylenes succinate-co-ε-caprolactone)
PBSL	:	Poly(butylenes succinate-co-L-lactate)
PBSA	:	Poly(butylenes succinate adipate)
PBAT	:	Polybutylene adipate terephthalate
PBT	:	Polybutylene terephthalate
PBST	:	Polybutylene succinate terephthalate
PET	:	Polyethylene terephthalate

PEO-PPO-PEO	:	Poly ethylene oxide-polypropylene oxide-poly ethylene oxide
PTMAT	:	Polytetramethylene adipate terephthalate
PDO	:	Polydioxanone
PGA	:	Polyglycolic acid
PLGA	:	Poly(lactic- <i>co</i> -glycolic acid)
PHH	:	Polyhydroxyhexanoate
PHA	:	Polyhydroxyalkanoate
PVA	:	Polyvinylalcohols
PVAC	:	Polyvinylacetate
PVPh	:	Poly(4-vinyl phenol)
PHB	:	Polyhydroxybutyrate
PVC	:	Poly(vinyl chloride)
PHV	:	Polyhydroxyvalerate
PLA	:	Poly(lactide)
PLLA	:	Poly (L-lactide acid)
PDLA	:	Poly(D-lactic acid)
PLDA	:	Poly (ld- lactide)
PLGA	:	Poly (lactic- <i>co</i> -glycolic acid)
PDI	:	polydispersity index
PP	:	Polypropylene
PS	:	Polystyrene
FE-SEM	:	Field emission scanning electron microscope
SFF	:	Solid freeform fabrication
$T_c$	:	Cold crystallization temperature
TGA	:	Thermogravimetric analysis
$T_g$	:	Glass transition temperature
$T_m$	:	Melting temperature
XRD	:	X-ray diffraction
$\mu\text{m}$	:	Micrometer

## LIST OF PUBLICATIONS

### Publication A: International Journals

1. V. Vilay, M. Mariatti, Zulkifli Ahmad, K. Pasomsouk, Mitsugu Todo. Characterization of the Mechanical and Thermal Properties and Morphological Behavior of Biodegradable Poly(L-lactide)/Poly( $\epsilon$ -caprolactone) and Poly(L-lactide)/ Poly(butylene succinate-co-L-lactate) Polymeric Blends. *Journal of Applied Polymer Science*, Vol. 114, 1784–1792 (2009)
2. Vilay Vannaladsaysy, Mitsugu Todo, Tetsuo Takayama, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk. Effects of lysine triisocyanate on the mode I fracture behaviour of polymer blend of poly (L-lactic acid) and poly (butylenes succinate-co-L-lactate). *Journal of Materials Science* (2009) 44:3006–3009.
3. Vilay Vannaladsaysy, Mitsugu Todo, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk. Characterization of Microstructure and Mechanical Properties of Biodegradable Polymer Blends of Poly(L-lactic acid) and Poly(butylene succinate-co-e-caprolactone) With Lysine triisocyanate. *Polymer Engineering & Science*, Volume 50, Issue 7, pages 1485–1491, July 2010
4. V. Vilay, M. Mariatti, Zulkifli Ahmad, K. Pasomsouk and Mitsugu Todo. Effect of PEO-PPO-PEO copolymer on the mechanical and thermal

properties and morphological behavior of biodegradable poly (L-lactic acid) (PLLA) and poly (butylenes succinate-co-L-lactate) (PBSL) blends. *Polymers Advanced Technologies*, (www.interscience.wiley.com) DOI: 10.1002/pat.1672

5. V. Vilay, M. Mariatti, Zulkifli Ahmad, K. Pasomsouk, Mitsugu Todo. Improvement of microstructures and properties of biodegradable PLLA and PCL blends compatibilized with a triblock copolymer. *Materials Science and Engineering A*, 527 (2010) 6930–6937.
6. V. Vilay, M. Mariatti, Z. Ahmad, K. Pasomsouk, M. Todo. Improvement of Microstructure and Fractured Property of Poly(L-lactic acid) and Poly(butylene succinate-co-e-caprolactone) Blend Compatibilized with Lysine Triisocyanate. *Engineering Letters*, Volume 18, Issue 3, Pages 303-307.
7. V. Vilay, M. Mariatti, Z. Ahmad, K. Pasomsouk, M. Todo. Characterization of Microstructure and mode I Fracture property of Biodegradable Poly(L-lactic acid) and Poly( $\epsilon$ -caprolactone) Polymer Blends with the Additive Lysine Triisocyanate. Submitted to *Journal of Materials Science: Materials in Medicine*.

#### **Publication B: National Journals**

1. V. Vilay, M. Mariatti, Z. Ahmad, K. Pasomsouk, M. Todo. Fabrication and characterization of macroporous poly(L-lactic acid) scaffolds by solid-liquid phased separation and freeze-drying techniques. *Malaysian Journal of Microscopy*, December 2010, Pag. 64-68, Vol.6 ISSN 1823-7010.

### **Publication C: Proceeding Conferences**

1. Vilay Vannaladsaysy, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk, Mitsugu Todo,. Characterization of biodegradable PLLA/PCL polymeric blends. International Conference and Exhibition on Composite Materials & Nano-Structure (iC2MS'08). August 5-7<sup>th</sup>, 2008 Legacy Hotel, Melaka, Malaysia.
2. Vilay Vannaladsaysy, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk, Mitsugu Todo. Characterization of biodegradable PLLA/PCL and PLLA/PBSL polymeric blends. The 6<sup>th</sup> Asia-Australasian Conference on Composite Materials (ACCM-6), September 23-26<sup>th</sup>, 2008. Kumamoto, Kyushu, Japan.
3. Vilay Vannaladsaysy, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk, Mitsugu Todo. Improvement of fracture properties of biodegradable PLLA/PBSL and PLLA/PBSC blends due to LTI addition. Japan Society for Composite Materials-38 (JCOM-38), 10-11<sup>th</sup> March 2009, Doshisha University Imadegawa (Kanbaikan), Kyoto, Japan.
4. Vilay Vannaladsaysy, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk, Mitsugu Todo,. Improvement of fracture properties of biodegradable PLLA/PBSL and PLLA/PBSC polymer blends with LTI addition. M&M 2009, 24-26, July, 2009. International Conference Center, Hokkaido, Japan.
5. Vilay Vannaladsaysy, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk, Mitsugu Todo,. Characterization of microstructure and mechanical properties

- of biodegradable PLLA polymer blends with LTI addition. International Symposium on Nano/Amorphous Materials and Interface, August 7-8<sup>th</sup>, 2009, Sansa-tei (Tohgatta, Miyagi-Zao), sendai, Japan.
6. Vilay Vannaladsaysy, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk, Mitsugu Todo,. Effect of the blend ratio and copolymer on mechanical behavior of biodegradable polymeric blends. The 2nd AUN/SEED-Net Regional Conference on Materials Engineering: Material for Changing World. 19-20<sup>th</sup> November, 2009. Bangsaen Beach, Chonburi, Thailand.
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  9. Vilay Vannaladsaysy, Mariatti Jaafar, Zulkifli Ahmad, Korakanh Pasomsouk, Mitsugu Todo,. Effect of Lysine triisocyanate on the microstructure and mechanical properties of biodegradable poly(L-lactic acid) (PLLA) and poly( $\epsilon$ -capprolactone) (PCL) blends. PRIM Golden Jubilee International



Polymer Conference 2010 (PRIM 2010) Sunway Resort Hotel & Spa, 16-17<sup>th</sup> March, 2010. Kuala Lumpur, Malaysia.

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## PERSEDIAAN DAN PENCIRIAN POLI(L-LAKTIK ASID) (PLLA) PERANCAH DAN GAULAN PLLA

### ABSTRAK

Pengoptimuman gaulan poli(L-laktik asid) (PLLA) telah dihasilkan melalui pengaulan polimer bio liat seperti poli(kaprolakton) (PCL), poli(butil suksinat-ko-L-laktad) (PBSL) dan poli(butilena suksinat-ko-e-kaprolakton) (PBSC) dan penambahan agen perserasian seperti lysine triisosianat (LTI) dan tiga blok kopolimer polietilena oksida - polipropilena oksida - polietilena oksida (PEO-PPO-PEO). Penyediaan perancah berasaskan PLLA juga dipertimbangkan dalam kajian ini. Dalam siri pertama, kesan komposisi campuran (100/0, 90/10, 80/20, 70/30, 50/50, 25/75 dan 0/100 % berat) ke atas sifat morfologi, mekanikal dan haba bagi campuran PLLA/PCL, PLLA/PBSL, dan PLLA/PBSC telah dilakukan. Didapati sifat kelenturan menurun dengan peningkatan kandungan PCL atau PBSL atau PBSC. Ini telah dikesan menerusi pelekatkan antara muka yang tidak baik di antara PLLA dan PCL atau PBSL atau PBSC seperti yang diperhatikan dalam morfologi fasa pemisahan. Siri kedua adalah melibatkan kesan kandungan LTI ke atas sifat gaulan PLLA/PCL. Sifat mekanikal bagi gaulan PLLA/PCL telah didapati meningkat dengan kehadiran LTI dengan sifat optimum ditunjukkan pada penambahan 5 phr LTI. Ini adalah disebabkan oleh tindak balas antara kumpulan isosianat LTI dan kumpulan OH pada kedua-dua PLLA dan PCL. Kesan penserasian kandungan LTI ke atas gaulan PLLA/PCL telah terbukti melalui peningkatan sederhana dalam keliatan pecah dan disahkan melalui morfologi keliatan yang diperhatikan melalui FE-SEM. Nilai tenaga pecah gaulan PLLA/PCL meningkat dengan peningkatan kandungan LTI. Kesan keliatan optimum telah diperhatikan dalam gaulan PLLA/PCL (50/50) terserasi dengan 5phr LTI. Dalam siri ketiga, kesan penambahan kandungan tiga blok kopolimer PEO-PPO-PEO (0.5, 1 dan 2phr) ke atas PLLA/PCL (70/30 % berat) telah dijalankan. Penambahan kopolimer ke dalam PLLA/PCL meningkatkan keliatan pecah. Suhu peralihan kaca ( $T_g$ ) dan suhu peleburan ( $T_m$ ) PLLA dan PCL beralih berdekatan sedikit, ini menunjukkan keserasian gaulan meningkat dan seterusnya meningkatkan mod sifat pecah. Sebagai tambahan, pemisahan fasa pepejal-cecair dan teknik beku-kering (SPS-FD) boleh digunakan dalam penyediaan bahan perancah dengan keliangan yang tinggi dengan sifat mampatan yang tinggi. Dengan teknik fabrikasi ini perancah PLLA yang berkeliangan tinggi dan bersambung telah di fabrikasi dengan jayanya, didapati PLLA dengan kepekatan di bawah 10% mempamerkan potensi yang bagus untuk aplikasi kejuruteraan tisu.

## PREPARATION AND CHARACTERIZATIONS OF POLY(L-LACTIC ACID) (PLLA) BLENDS AND PLLA SCAFFOLD

### ABSTRACT

Optimization of poly(L-lactic acid) (PLLA) blends was carried out by blending with ductile biopolymers such as poly( $\epsilon$ -caprolactone) (PCL), poly(butylene succinate-co-L-lactate) (PBSL) and poly(butylene succinate-co- $\epsilon$ -caprolactone) (PBSC) and addition of compatibilizer such as lysine triisocyanate (LTI) and polyethylene oxide-polypropylene oxide-polyethylene oxide (PEO-PPO-PEO) triblock copolymer. Preparation of PLLA based scaffold was also been considered in the present study. In the first series, the effects of blend composition (100/0, 90/10, 80/20, 70/30, 50/50, 25/75 and 0/100 wt%) on the morphological, mechanical and thermal properties of PLLA/PCL, PLLA/PBSL, and PLLA/PBSC blends were carried out. It is found that the bending properties decreased with increasing PCL or PBSL or PBSC contents. This was traced by the poor interfacial adhesion between PLLA and PCL or PBSL or PBSC as observed in the phase separation morphology. The second series were on the effects of LTI content on the properties of PLLA/PCL blends. The mechanical properties of the PLLA/PCL blends were observed to increase with the presence of LTI with optimum properties shown at LTI loading of 5phr. This was attributed to the interaction between isocyanate group of LTI and OH group of both PLLA and PCL. The compatibilizing effects of LTI content on the PLLA/PCL blends were proven by moderate improvement in the fracture toughness and confirmed by the ductile morphology as observed by the FE-SEM. The fractured energy values of the PLLA/PCL blends increased with the increasing of LTI contents. The optimum toughening effect was observed in PLLA/PCL (50/50) blend compatibilized with LTI at 5phr. In the third series, the effects of addition of PEO-PPO-PEO triblock copolymer contents (0.5, 1 and 2phr) into PLLA/PCL (70/30 wt%) were carried out. The addition of the copolymer into the PLLA/PCL improved its fracture toughness. The glass transition temperature ( $T_g$ ) and melting temperature ( $T_m$ ) of PLLA and PCL shifted slightly closer together, indicating that the blend miscibility slightly increased and hence increased mode I fracture properties. In addition, solid-liquid phase separation and freeze-drying techniques (SPS-FD) is able to be used in preparing highly porous scaffolds with higher compression property. With this fabrication technique, highly porous and interconnected PLLA scaffolds were successfully fabricated, suggesting that PLLA concentration below 10 wt% exhibits great potential for tissue engineering applications.

# CHAPTER 1

## INTRODUCTION

### 1.1 Background

The last two decades of the twentieth century saw a paradigm shift from biostable biomaterials to biodegradable (hydrolytically and enzymatically degradable) biomaterials for medical and related applications (Shalaby and Burg, 2003; Domb and Wiseman, 1998; Piskin, 1995). In the current trend, many of the permanent prosthetic devices used for temporary therapeutic applications will be replaced by biodegradable devices that could help the body to repair and regenerate the damaged tissues. There are several reasons for the favorable consideration of biodegradable over biostable materials for biomedical applications. The major driving force being the long-term biocompatibility issues with many of the existing permanent implants and many levels of ethical and technical issues associated with revision surgeries. A biomaterial can be defined as a material intended to interface with biological systems to evaluate, treat, augment or replace any tissue, organ or function of the body (Williams, 1999).

Biodegradable polymeric materials are being investigated in developing therapeutic devices such as temporary prostheses, three-dimensional porous structures as scaffolds for tissue engineering and for pharmacological applications, such as drug delivery (both localized and targeting systems). Some of the current biomedical applications of biodegradable polymeric materials include: (1) large implants, such as bone screws, bone plates and contraceptive reservoirs, (2) small implants, such as staples, sutures and nano- or micro-sized drug delivery vehicles, (3) plain membranes for guided tissue regeneration and (4) multifilament meshes or porous structures for tissue

engineering (Vert, 2005). A tissue engineering approach uses a biodegradable construct to assemble cells in three-dimensions to ultimately develop into functioning tissue. Polymeric materials with a wide range of mechanical and degradation properties are required to mimic the properties of various tissues. In controlled drug delivery, bioactive agents are entrapped within a biodegradable polymer matrix from which they are released in an erosion- or diffusion-controlled fashion or a combination of both. The release characteristics of the bioactive agents can be effectively modulated by suitably engineering the matrix parameters.

Due to the versatility of polymeric materials, they are rapidly replacing other material classes, such as metals, alloys and ceramics for use as biomaterials. In 2003, the sales of polymeric biomaterials exceeded \$7 billion, accounting for almost 88% of the total biomaterial market for that year (Medical Device and Diagnostic Industry, 2005). Nair *et al.*, (2007) predicted huge market for polymeric biomaterials in the coming decades.

Polyester such as polyglycolide (PGA) and polylactide (PLA) has been studied and were used as biodegradable suture since 1970 (Park *et al.*, 2003). PGA was first selected as a biodegradable material due to its good biodegradability and biocompatibility (Velde and Kiekens, 2002). However, rapid hydrolytic degradation and poor mechanical properties associated with PGA has limited its applications as porous scaffold material. Since then, PLA was developed as a promising alternative due to its good mechanical properties, good biodegradability and biocompatibility. However, despite the high modulus, PLA is low in toughness which consequently limits its processibility and commercialization (Jamiołkowski and Dormier, 2006). Therefore, copolymerization technique has been introduced to optimize the properties of various

biodegradable polymers. Copolymers of lactide and glycolide have been most extensively studied and commercialized for several medical applications such as suture, skin, cartilage, and bone regeneration (Bertoldi, 2008).

## 1.2 Problem Statements

Poly(L-lactic acid) (PLLA) is a promising synthetic biopolymer derived from biomass through bioconversion and polymerization (Sodergard *et al.*, 2002). PLLA has great potential of applications as bioabsorbable medical devices (Bhattarai *et al.*, 2004). The disadvantage of PLLA is that it is too soft above its glass transition temperature (60 °C) and has low toughness, which limits its applications. Its brittleness is also a disadvantage for its application in various commercial items.

Blending PLLA with others ductile biodegradable have been investigated by many researchers (Shibata *et al.*, 2006a; Harada *et al.*, 2007; Todo *et al.*, 2007b). It is known that in general these PLLA polymer blends exhibit phase-separation if directly blended without any additives (Todo *et al.*, 2007a). Copolymerization of PLA/PCL is reported to decrease the brittleness of PLLA (Hiljanen-Vainio *et al.*, 1996; Grijpma *et al.*, 1991). Various compatibilizers have been used to increase the miscibility of the blend composites (Aslan *et al.*, 2000).

In the present study, LTI and triblock PEO-PPO-PEO copolymer have been utilized as compatibilizers in PLLA blends. It is expected that the addition of these compatibilizers will increase the chance of reaction at the PLLA blend interface and hence increase its physical properties.

### **1.3 Research objective**

This study is focused on the preparation and characterization of PLLA blends and scaffolds. The primary objectives of these studies are divided into the following categories:

- (i) To determine the effect of blend compositions on the mechanical, thermal and morphological properties of PLLA/PCL, PLLA/PBSL and PLLA/PBSC blends.
- (ii) To study the effects of LTI as a reactive processing agent and triblock PEO-PPO-PEO copolymer as a compatibilizer on the best composition of PLLA blend (PLLA/PCL system).
- (iii) To fabricate and characterize porous PLLA scaffold produced with different parameters such as solid-liquid phase separation and freeze-drying techniques.

### **1.4 Dissertation Overview**

This thesis deals with incompatible pairs of polymer, compatibilization and the morphology of the PLLA blends.

Chapter one starts with a brief introduction on biodegradable polymer based biomaterials for medical applications. Issues concerned that generated the ideas and energies to this work are also stated. The primary objectives and the general flow of the whole research program are also carefully outlined.

Chapter two is a literature survey pertaining to recent progress in the biodegradable polymers. Their definition, classifications, blends, characterizations of the blends and applications are discussed in this chapter.

Chapter three focuses on the explanation of the raw materials used in the present study, i.e. PLLA, PCL, PBSL, PBSC, additives LTI and PEO-PPO-PEO copolymer. Fabrication methods of the PLLA blends and characterization of the samples are explained in this chapter.

Chapter four discusses on the properties of various PLLA blends, effect of additions of LTI and copolymer in PLLA/PCL blend and production of PLLA porous scaffold using solid-liquid phase separation and freeze-drying techniques. The influence of PLLA solution concentration, polymer molar mass and relative humidity on pore dimensions in producing is discussed.

Chapter five presents some conclusive remarks on the present works as well as some suggestion for future works.



## CHAPTER 2

### LITERATURE REVIEW

#### 2.1 Introduction to Biodegradable Polymers

Biodegradable polymer is an emerging area of science crucial in the current situation with depleting fossil residues and increasing environmental burden caused by non degradable polymers. These polymers are set to solve both problems by providing a renewable resource for degradable green polymers with minimal environmental repercussions. In addition, due to their biodegradability and biocompatibility, some of these polymers are also useful for new emerging medical applications. Type and properties of the polymers have been discussed in the recent works (Akaraonye *et al.*, 2010; Grabow *et al.*, 2010; Hay *et al.*, 2010; Thompson *et al.*, 2010; Yunos *et al.*, 2010; Wang *et al.*, 2010; Sato *et al.*, 2010).

The definition of the words biodegradable, bioerodable, bioresorbable and bioabsorbable are described as follow (Hutmacher, 2000):

- (i) **Biodegradable** are solid polymeric materials and devices which break down due to macromolecular degradation with dispersion *in vivo* but no proof for the elimination from the body (this definition excludes environmental, fungi or bacterial degradation).
- (ii) **Bioresorbable** are solid polymeric materials and devices which show bulk degradation and further resorb *in vivo*; *i.e.* polymers which are eliminated through natural pathways either because of simple filtration of degradation by-products or after their metabolization.

- (iii) **Bioresorption** is thus a concept which reflects total elimination of the initial foreign material and of bulk degradation by-products (low molecular weight compounds) with no residual side effects. The use of the word “bioresorbable” assumes that elimination is shown conclusively.
- (iv) **Bioerodible** are solid polymeric materials or devices, which show surface degradation and further, resorb in vivo.
- (v) **Bioerosion** is thus a concept, too, which reflects total elimination of the initial foreign material and of surface degradation by-products (low molecular weight compounds) with no residual side effects.
- (vi) **Bioabsorbable** are solid polymeric materials or devices, which can dissolve in body fluids without any polymer chain cleavage or molecular mass decrease. For example, it is the case of slow dissolution of water-soluble implants in body fluids. A bioabsorbable polymer can be bioresorbable if the dispersed macromolecules are excreted.

A number of standards authorities have sought to produce definitions for biodegradable plastics. In ISO 472 (1999), plastic is designed to undergo a significant change in its chemical structure under specific environmental conditions resulting in a loss of some properties that may vary as measured by standard test methods appropriate to the plastics and application in a period of time that determines its classification. A committee on “Environmentally Degradable Plastics and Bio-based products” defined degradable plastics as materials that undergo bond scission in the backbone of a polymer through chemical, biological and/or physical forces in the environment at a rate which leads to fragmentation or disintegration of the plastics. Moreover, Japanese

Biodegradable Plastic Society (Fukada, 1992) defined biodegradable plastics as polymeric materials that are changed into lower molecular weight compounds where at least one step in the degradation process is through metabolism in the presence of naturally occurring organisms.

## **2.2 Classification of Biodegradable Polymers**

Biodegradable polymers (hereafter called biopolymers) are classified according to their origin; natural polymers, polymers coming from natural resources and synthetic polymers based on polymers synthesized from crude oil. Biopolymers from natural origins used on chemical point of view induces, six sub-groups: polysaccharides, proteins, lipids, polyesters produced by micro-organism or by plants, polyester synthesized from bio-derived monomers and a final group of miscellaneous polymers (Ray Smith, 2005). Biopolymers from natural resources include four sub-groups: aliphatic polyesters, aromatic polyesters or blends of the two types, polyvinylalcohols, and modified polyolefins (polyethylene or polypropylene with specific agents sensitive to temperature or light). Here, modified polyolefins are referred to the polyolefins which are produced from sugarcane. Biopolymers based on natural resources will be discussed in the following sections since the materials are used in the present study.

## **2.3 Biopolymer from Mineral Resources**

The polymers are divided into four groups: aliphatic polyesters; aromatic polyesters, polyvinylalcohols and modified polyolefins. Polyesters represent a large family of polymers having in their structure the potentially hydrolysable ester bond (Figure 2.1). The polyesters can be classified following the composition of their main

chain. They are aliphatic and aromatic polyesters (Table 2.1). In the family of aliphatic polyesters there are polymers of natural resources such as polyhydroxyalkanoate (PHA), polyhydroxybutyrate (PHB), poly(hydroxybutyrate-hydroxyvalerate) (PBH/HV) PHV, polyhydroxyhexanoate (PHH), mineral origin such as Poly(butylenes succinate) (PBS), poly(butylenes succinate adipate (PBSA), poly( $\epsilon$ -caprolactone) (PCL) or those which originate from both polylactic acid (PLA) and polyglycolic acid (PGA). In the family of aromatic polyesters, those coming from polyethylene terephthalate (PET) or from polybutylene terephthalate (PBT), polybutylene adipate terephthalate (PBAT), polybutylene succinate terephthalate (PBST), polytetramethylene adipate terephthalate (PTMAT) and copolymers are separately classified.

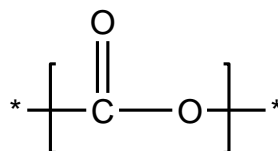


Figure 2.1: Structure of ester bond (Clarinval and Halleux, 2005).

Table 2.1 Biodegradable polyesters (Clarinval and Halleux, 2005).

Group		Type	Derivate	Origin	Production
Polyesters	aliphatic	PHA	PHB	Natural	Natural
			PHV	Natural	Natural
			PHH	Natural	Natural
		PGA		Double	Synthetic
		PLA		Double	Synthetic
		PBS	PBSA	Mineral	Synthetic
		PCL		Mineral	Synthetic
	aromatic	PBT	PBAT	Mineral	Synthetic
			PBST	Mineral	Synthetic
			PTMAT	Mineral	Synthetic

### 2.3.1 Aliphatic Polyesters

Aliphatic polyesters are generally sensitive to hydrolysis and are biodegradable (Gross and Bhanu, 2002). They are formed by polycondensation reaction of an aliphatic glycol with an aliphatic dicarboxylic acid. Among the aliphatic polyesters there is family of polymers, the poly( $\alpha$ -hydroxy acids) such as polyglycolic acid (PGA), polylactic acid (PLA), and some of their copolymers, which have been used in a number of clinical applications; sutures, plates and fixtures for fracture fixation devices and scaffolds for cell transplantation.

PGA is a rigid thermoplastic material with high crystallinity (45-50%) produced by ring opening of glycolide, a diester of glycolic acid. The structure of PGA is shown in Figure 2.2. The glass transition is 36 °C and the melting temperature is 225 °C. PGA is not soluble in most organic solvents but has high sensitivity to hydrolysis. It can be processed by extrusion, injection and compression molding. The attractiveness of PGA as a biopolymer in medical applications is the fact that its degradation product (glycolic acid) is a natural metabolite.

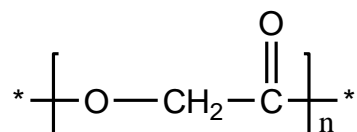


Figure 2.2: Structure of polyglycolic acid.

Polylactic acid (PLA) (Figure 2.3) can be synthesized from lactic acid or by ring-opening polymerization of lactide (a cyclic dimer of lactic acid). The lactide exists as two optical isomers, *l*-isomers, both polymerizations give semi-crystalline polymers, in addition, its stereochemical structure can be easily modified by polymerizing a

controlled mixture of both isomers to yield amorphous or semi-crystalline polymers (Nair and Laurencin, 2007; Garlotta, 2001). PLA can be found in two forms as poly(L-lactic acid) (PLLA) and poly(D-lactic acid) (PDLA) synthesized from L-lactic acid (natural occurring) and D-lactic acid. PLLA is a semi-crystalline polymer while PDLA is an amorphous polymer. The preferred route for producing high molecular weight PLA is the catalytic ring-opening bulk polymerization of lactide (dilactone of lactic acid). The chemistry of PLA involves the processing and polymerization of lactic acid monomer. Lactic acid  $\text{COCH}_3\text{CHCOOH}$  is a simple chiral molecule which exists as two enantiomers, L- and D-lactic acid (Figure 2.4), different in their effect on polarized light. The L isomer rotate the plane of polarized light clockwise, the D isomer rotates it counterclockwise. The optically inactive D, L or meso form is an equimolar (racemic) mixture of D and L isomes (Lunt, 1998a; Lunt *et al.*, 2000b). Lactic acid is produced in mammalian muscles during glycogenolysis and it involved in the Krebs's cycle through pyruvic acid and acetcyL-CoA (Fambri *et al.*, 1997). Lactic acid is easily prepared in high yield by fermentation of molasses or potato starch or of dextrose from corn (Gupta *et al.*, 2007; Eling *et al.*, 1982).

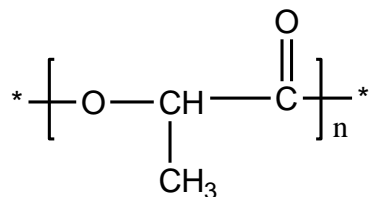


Figure 2.3: Structure of polylactic acid.

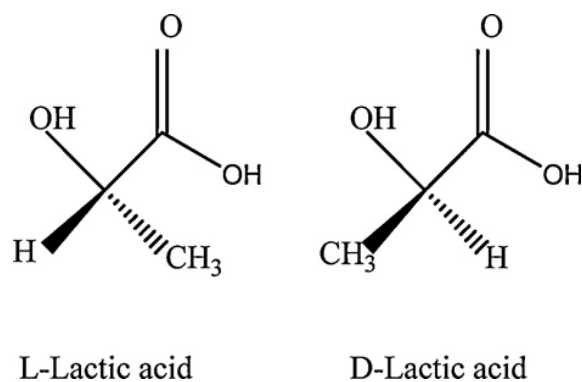


Figure 2.4: Optical isomers of lactic acid.

Poly(L-lactide) (PLLA), which is derived from pure L-lactide, has a high melting temperature (175 °C), poor processability, and crazes easily because of its high crystallinity. The D, L-PLA is an amorphous polymer with 60 °C, which is low for many packaging uses. Properties, such as melting point, mechanical strength, and crystallinity, are determined by the polymer architecture (determined by different proportion of L, D) and the molecular mass. Similarly, the time for degradation is also affected by the crystallinity and molecular mass of the polymer; higher values require longer time for degradation. On the contrary, poly(D-lactide) (PDLA) is an amorphous polymer due to the random distribution of l- and d-lactide units and has a  $T_g$  of 55–60 °C (Garlotta, 2001). In this review we used PLA as a general term indicating either amorphous or crystalline polymers, whenever necessary, the specific structure is indicated as PLLA, PDLA or PLDA.

Poly(L-lactide) (PLLA) has gained clinical attention in recent years due to its biocompatibility and biodegradability, therefore, it has been used extensively for biomedical applications including orthopedic fixation devices, three dimensional scaffolds, sutures, and drug delivery matrix materials. During metabolization by the

human body, PLLA can be degraded by hydrolysis into lactic acid, which under aerobic conditions can be further metabolized into water and carbon dioxide and finally excreted by the organism. However, the *in vivo* degradation of PLLA occurs predominantly by a cellular process, as a result of local inflammatory reactions. One drawback of PLLA is its brittleness and stiffness, these mechanical properties could be improved by blending or by copolymerization with more flexible polymer components (Nair and Laurencin, 2007; Mothé *et al.*, 1999; Garlotta, 2001).

Poly(butylenes succinate) (PBS) has properties similar to PET. It has a crystallinity of 35 - 45%, a glass transition temperature of -32 °C and a melting temperature of 114-115 °C. PBS is generally blended with other compounds, such as starch and adipate copolymers (to form PBSA). PBSA has a crystallinity of 20-35%, a  $T_g$  of -45°C and a  $T_m$  of 93-95 °C. Its properties are closed to those of LDPE (linear low density polyethylene). These polymers can be processed via conventional melt processing techniques (blow moulding, extrusion, injection) and application include mulch film, packaging film, bags and ‘flushable’ hygiene products. Bionolle’s (Showa Denko) are a family of aliphatic polyesters synthesized by polycondensation of glycols and dicarboxylic acids. There are two series: the 1000 series with PBS obtained from 1,4 butane diol and succinic acid and the 3000 series consisting of PBSA copolymer from 1,4 butane diol and a mix of succinic acid and adipic acid (Figure 2.5). The structure of PBSA is linear or branched (Showa High Polymer Ltd, 1998; Kettle Belinda, 1998).

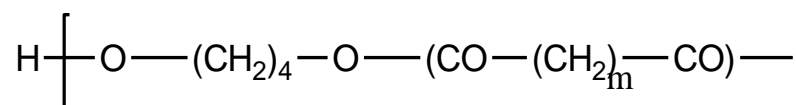


Figure 2.5: Structure of poly(butylenes succinate).



Polycaprolactone (PCL) is a semi-crystalline polymer with a glass transition temperature of about  $-60\text{ }^{\circ}\text{C}$  and a melting temperature of  $59\text{-}64\text{ }^{\circ}\text{C}$ . The structure of PCL is shown in Figure 2.6 (Gunatillake *et al.*, 2003). PCL degrades at a much lower rate than PLA and is used as a base polymer for developing long-term, implantable drug delivery systems. PCL is prepared by ring-opening polymerization of  $\epsilon$ -caprolactone with catalysts such as stannous octoate and initiators such as low molecular weight alcohol to control the molecular weight of the polymer. PCL can be slowly degraded (2–3 years) by hydrolysis of its ester linkages in physiological conditions (such as in the human body) and has therefore received a great deal of attention for use as an implantable biomaterial in drug delivery devices, bioresorbable sutures, adhesion barriers, and scaffolds for injury repair via tissue engineering (Castillo and Muller, 2009). Compared to other biodegradable aliphatic polyesters, PCL has several advantageous properties, including: high permeability to small drug molecules; maintenance of a neutral pH environment upon degradation; facility in forming blends with other polymers; and suitability for long-term delivery afforded by slow erosion kinetics as compared to polylactide (PLA), polyglycolide (PGA), and polylactic-co-glycolic acid (PLGA) (Nair and Laurencin, 2007; Ghoroghchian *et al.*, 2006; Zhou *et al.*, 2003). However, the rather high crystallinity of PCL decreases its compatibility with soft tissues and lowers its biodegradability. These drawbacks may obstruct its application in drug-controlled release systems. This problem can be overcome by the copolymerization of  $\epsilon$ -caprolactone ( $\epsilon$ -CL) with other monomers (Zhou *et al.*, 2003).

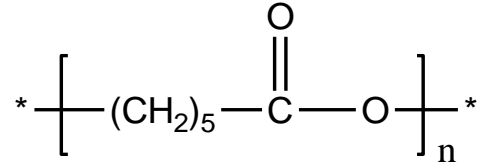


Figure 2.6: Structure of polycaprolactone.

### 2.3.2 Aromatic Polyester

Aromatic polyesters are formed by the polycondensation of aliphatic diols and aromatic dicarboxylic acids. The aromatic ring gives the polymer an excellent resistance to hydrolysis and chemical agents. They are difficult to hydrolyse and therefore not renewable. For example, polyethylene terephthalate (PET) and polybutylene terephthalate (PBT) are well-known polyesters obtained by polycondensation of aliphatic glycols and terephthalic acid. They can be modified by addition of hydrolysis sensitive monomers (ether, amide or aliphatic groups) giving a family of biodegradable polyesters.

### 2.3.3 Polyvinylalcohols (PVA)

The structure of PVA is shown in Figure 2.7. PVA is produced by polymerization of vinylacetate to polyvinylacetate (PVAC), followed by the hydrolysis of PVAC in PVA. The degree of polymerization determines the molecular weight and viscosity of PVA in solution. The degree of hydrolysis (saponification) signifies the extent of conversion of the PVAC to PVA. Partially hydrolysed PVA has a  $T_g$  of 58 °C and a  $T_m$  of 180 °C. Totally hydrolysed PVA has a  $T_g$  of 85 °C and a  $T_m$  of 230 °C. PVA can be used in the production of paper, clothes, glues, paints, pharmaceutical products, building materials, ceramics, etc.

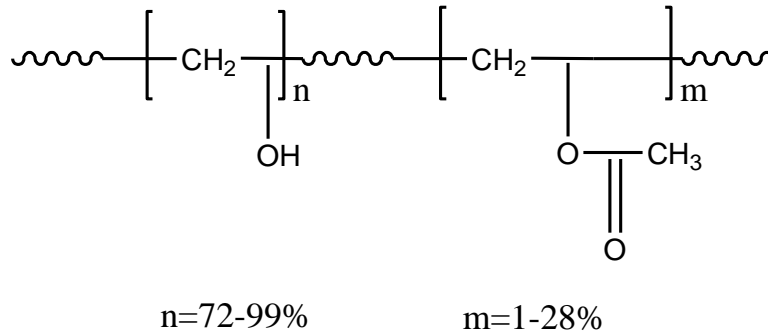


Figure 2.7: Structure of polyvinylalcohol.

### 2.3.4 Modified Polyolefins

Polyolefins like polypropylene (PP) and polyethylene (PE) are very resistant to hydrolysis and are totally non-renewable. It is possible to alter their structure by the addition of an agent that will, by an oxidative radical mechanism, degrade the carbon chain of the polymer. Heat or light can be initiating the mechanism. The agent containing transition metal ions transform the polymer into low molecular mass carboxylic acids and alcohols. Bacteria, fungi and enzymes of the milieu then degrade the residues into biomass and CO<sub>2</sub>. Used photosensitisers include diketones, ferrocene derivatives (aminoalkylferrocene) and carbonyl-containing species (Nolan-ITU Pty Ltd, 2002).

## 2.4 Polymer Blends

A polymer blend is a mixture of at least two polymers or two copolymers (Utracki 1990). Synthetic polymers, including polymer blends, are useful in designing tailor made materials with good properties, processability and price/ performance ratio (Seidenstucker and Fritz, 1998). Currently, many engineered biodegradable polymers have excellent product properties and performance, however, their widespread use is limited by high cost. There are many commercially available polymer blends and

common ones include blend of poly(vinyl chloride) (PVC) and acrylonitrile rubber (NBR), acrylonitrile-butadiene-styrene copolymer (ABS) and starch/polyethylene. According to Utracki, (1990), the most sought after properties for engineering blends are high impact strength, processability and tensile strength. Quite notably, biodegradability is not listed under any of the categories. Blending to achieve biodegradability is only a relatively new concept and is largely still in the developmental phase. However, starch-based materials are now industrial products and are leading the still small market of biodegradable products (Bastioli, 1998).

The blends of biopolymers and additives became the first class of biodegradable materials, as classified by Huang *et al.*, (1990). To date, most research on biodegradable blends has concentrated on blends containing a non-biodegradable component, making them not 100% biodegradable. There are many examples of starch in these types of blends including starch and polyethylene (St-Pierre *et al.*, 1997). However, little research has been undertaken into the blending of 100% biodegradable blends.

## **2.5 Aliphatic Polyester Blends**

As been mentioned in Section 2.4, aliphatic polyesters have been recognized for their biodegradability and susceptibility to hydrolytic degradation. Examples of this group are PLAs, which also have the advantage of controllable crystallinity and hydrophilicity, and therefore overall degradation rate (Tsuji *et al.*, 2000a; Albertsson, 2002; Tsuji *et al.*, 2002b; Yu *et al.*, 2006). Another family of polyesters being studied widely are poly(hydroxyalkanoate)s (PHAs) that occur in nature. They are produced by a wide variety of micro-organisms as an internal carbon and energy storage, as part of their survival mechanism (Yu *et al.*, 2006; Scholz and Gross, 2000). Bacterially

synthesized PHAs have attracted attention because they can be produced from a variety of renewable resources and are truly biodegradable and highly biocompatible thermoplastic materials. Biosynthesis and characterization of various copolymers, including copolymers of hydroxybutyrate (HB) with 3-hydroxyvalerate (3HV) (Holmes, 1985; Doi *et al.*, 1998a), 3-hydroxypropionate (3HP) (Nakamura *et al.*, 1991), 3-hydroxyhexanoate (3HH) (Doi *et al.*, 1995b) and 4-hydroxybutyrate (4HB) (Kunioka *et al.*, 1988) have been developed. Over 90 different types of PHA consisting of various monomers have been reported and the number is still increasing (Yang *et al.*, 2002).

Among the family of biodegradable polyesters, polylactides (i.e. PLA) have been the focus of much attention because they are produced from renewable resources such as starch and they have very low or no toxicity and high mechanical performance, comparable to those of commercial polymers. However, the thermal stability of PLAs is generally not sufficiently high enough for them to be used as an alternative in many commercial polymers applications (Tsuji and Fukui, 2003c). Ikada *et al.*, (1987), studied various PLA blends to improve their thermal properties. A stereocomplex is formed from enantiomeric PLAs, poly(L-lactic acid) (PLLA) and poly(D-lactic acid) (PDLA) due to the strong interaction between PLLA and PDLA chains (Ikada *et al.*, 1987). The stereocomplexed PLLA/PDLA blend has a melting temperature ( $T_m$ ) (220–230 °C) approximately 50 °C higher than those of pure PLLA and PDLA (170–180 °C), and can retain a non-zero strength in the temperature range up to  $T_m$  (Tsuji and Ikada, 1999d).

On the basis of these findings, enantiomeric polymer blend is expected to enhance the thermal stability of the PLLA/PDLA blend in the melt compared with those of the pure PLLA and PDLA. An enantiomer is one of two stereoisomers that are mirror images of each other that are "non-superposable". Tsuji and Fukui, (2003c) studied the

films of poly(L-lactide) (i.e. PLLA) and poly(D-lactide) (PDLA), and their equimolar enantiomeric blend (PLLA/PDLA). The films were prepared and the effects of enantiomeric polymer blending on the thermal stability and degradation of the films were investigated isothermally and non-isothermally under nitrogen gas using thermogravimetry. The enantiomeric polymer blending was found to successfully enhance the thermal stability of the PLLA/PDLA films compared with those of the pure PLLA and PDLA films (Yu *et al.*, 2006).

To achieve a similar outcome, Urayama *et al.*, (2002), developed blends of polylactides with high and low L-isomeric ratios of the lactate units (PLA 99.0 and 77.0, where the numbers correspond to the L-ratios). The crystallinity of the blends was similar to that of the blends of PLLA and PDLA. The glass transition behavior was indicative of the compatible nature of both polymers. The tensile modulus of the blends was almost identical irrespective of the blend ratio, while their tensile strength decreased with decreasing composition of PLA 99.0. Above the  $T_g$ , the storage modulus of the blends dropped from  $2 - 3 \times 10^9$  to  $1 - 3 \times 10^6$  Pa and then increased to a different level depending on the crystalline nature of the blends. The biodegradability of the blends increased with decreasing composition of PLA 99.0. This difference in degradability can be explained by a random packing model of local helices of the L-sequenced chains for the L-rich PLA samples (Urayama *et al.*, 2002).

## **2.5.1 Blends of Hydrophobic and Hydrophilic Polymers**

### **2.5.1.1 Starch/PLA Blends**

PLA and starch are both biodegradable polymers derived from renewable sources. Starch, a hydrophilic renewable polymer, has been used as a filler for

environmentally friendly plastics for about two decades. PLA is a biodegradable polymer, but its applications are limited by its high cost. Blending starch with PLA is one of the most promising efforts, because starch is an abundant and cheap biopolymer and PLA is biodegradable with good mechanical properties. Starch granules become swollen and gelatinized when water is added or when they are heated, and water is often used as a plasticizer to obtain desirable product properties. Ke and Sun, (2001a), characterized blends of starch and PLA in the presence of various water contents. It was found that the initial moisture content of the starch had no significant effect on its mechanical properties, but it had a significant effect on the water absorption of the blends. The thermal and crystallization properties of PLA in the blend were not affected by moisture content. The blends prepared by compression molding had higher crystallinities than those prepared by injection molding. However, the blends prepared by injection molding had higher tensile strengths and elongations and lower water absorption values than those made by compression molding. The crystallinities of the blends increased greatly with annealing treatment at the PLA second crystallization temperature (155 °C). The decomposition of PLA indicated that PLA degraded slightly in the presence of water under the processing temperatures used.

Relationship of microstructure and mechanical and thermal properties of the starch/PLA blends have been studied by previous works (Ke and sun, 2003b; Park and Im, 2000; Willett and Shgren, 2002; Raghavan and Emekalam, 2001). Studies on the thermal behavior of starch/PLA blends were carried out by Ke and Sun, (2003c), the experimental data was evaluated using the well-known Avrami kinetic model. Talc, a nucleating agent, was also blended with PLA at 1% by volume (v/v) as a comparison. Starch effectively increased the crystallization rate of PLA, even at a 1% content, but the

effect was less than that of talc. The crystallization rate of PLA increased slightly as the starch content in the blend was increased from 1 to 40%. An additional crystallization of PLA was observed, and it affected the melting point and degree of crystallinity of PLA.

Ke *et al.*, (2003d), studied on the effect of amylase content in starches on the mechanical properties of starch/PLA. Four dry corn starches with different amylase content were blended at 185 °C with PLA at various starch:PLA ratios using a lab-scale twin-screw extruder. Starch with 30% moisture content was also blended with PLA at a 1:1 ratio. Each extrudate was ground and dried. The powder was mixed with about 7.5% plasticizer and injection molded (175 °C) into tensile test bars. These were characterized for morphology, mechanical properties and water absorption. Starch performed as filler in the PLA continuous matrix phase, but the PLA phase became discontinuous as starch content increased beyond 60%. Tensile strength and elongation of the blends decreased as starch content increased, but no significant difference was observed among the four starches at the same ratio of starch:PLA. The rate and extent of water absorption of starch/PLA blends increased with increasing starch content. Blends made with high-amylase starches had lower water absorption than the blends with normal and waxy corn starches.

### **2.5.1.2 Compatibilizers used for Starch/PLA Blends**

PLA and starch are reported as two promising candidates for biodegradable polymer blends (Wang *et al.*, 2001a, 2002b, 2002c, 2003d; Zhang and sun, 2004; Ke and sun, 2003c; Shogren *et al.*, 2003). However, hydrophobic PLA and hydrophilic starch are thermodynamically immiscible, leading to poor adhesion between the two components, and hence poor and irreproducible performance. Wang *et al.*, (2001a) used



methylenediphenyl diisocyanate (MDI) to improve the interface and studied a blend of 55/45 (w/w) mixture of PLA and dried wheat starch in an intensive mixer with or without MDI. Blends with MDI had enhanced mechanical properties that could be explained by the *in situ* formation of a block copolymer acting as a compatibilizer. Morphology observed by SEM showed reduced interfacial tension between the two phases. The presence of MDI also enhanced the mechanical properties of the blend at temperatures above  $T_g$  (Wang *et al.*, 2002c). Pure PLA had a tensile strength of 62.7 MPa and elongation of 6.5%. The blend with 45% wheat starch and 0.5 wt% MDI gave the highest tensile strength of about 68 MPa with about 5.1% elongation. The blend with 20% starch and 0.5 wt% MDI had the lowest tensile strength of about 58 MPa with about 5.6% elongation. Dynamic mechanical analysis showed that storage modulus increased and  $\tan \delta$  decreased as starch level increased, but almost leveled off when the starch level reached 45% or higher. Water absorption of the blends increased significantly with starch content. Yet the blend, if waterproofed on its surface, has potential for short-term disposable applications.

### **2.5.2 Chitosan/PLA Blends**

Chitosan is a natural polymer, non-toxic, edible, biodegradable, derived by deacetylation of chitin and is the second most abundant biopolymer in nature after cellulose. Chitosan has been used in edible coatings or films to extend the shelf life of foodstuffs, e.g. fruit, meat, and fish and seafood. However, its high sensitivity to moisture limits its applications for packaging. One strategy to overcome this drawback is the blending of chitosan with moisture-resistant polymers, while maintaining the overall biodegradability of the products. Suyatma *et al.*, (2004) reported on biodegradable film