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Effects of Compression Processing Parameters and Antioxidants on Molecular Degradation of Biodegradable Poly-L-Lactide (PLLA)

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ABSTRACT

The purpose of this research was to find a combination of poly (L-lactic acid), also known as poly-L-lactide or (PLLA) and antioxidants that would, together, produce a product whose degradation rate would be advantageous for use in biodegradable medical implants. Intrinsic viscosity tests were conducted on compression molded samples of PLLA that were molded at various processing parameters in order to find optimal parameters. The optimal processing parameters were found to be time 10 minutes, temperature 220°C, and pressure 1000 psi.

The molecular weight of PLLA sample was taken while pressure, time, and temperature were varied. As pressure increased, no significant change in molecular weight was noticed. When the time was increased, the molecular weight decreased. Then when temperature increased, the molecular weight of PLLA also decreased.

Compression molded samples were also made with a mixture of PLLA and antioxidants. At 0.6% of concentration, antioxidants in this study did not prove any benefits for PLLA to reduce the molecular degradation. All samples with 0.6% antioxidants showed lower molecular weight than pure PLLA.

Outcomes of this research provide a better understanding of biodegradable polymers and the factors that contribute to a successful mold. This research develops the best possible poly-L-lactic acid compression sample for further studies in the industry, including medical applications.

DEDICATION

To the memory of my father, Thomas J. Hannan, Sr., who was always a true parent and teacher…

His dreams, support, sacrifice, answers to my never ending questions, love, and encouragement over the years has made a true and real impact on my life.

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I would like to take this occasion to express my sincerest appreciation and gratitude to Dr. Ping Liu for the opportunity to conduct this research and for his constant support, continuous guidance, and patient assistance throughout graduate school, this research, and the thesis writing process. Dr. Ping Liu will always be one of my true mentors in my life. I would also like to thank Dr. Larry Helsel and Dr. Wafeek Wahby for their advisement, consultation, and willingness to serve as my thesis committee members. It has been an honor to work with all three professors.

I also would like to acknowledge with sincere thanks the encouragement, strength and support of my entire family and friends provided for me. I would especially like to express my heartfelt appreciation to my future wife Jodi, for her time, patience, and understanding inside and outside the laboratory throughout the entire research process. They have all made a very noticeable difference in my life and were essential to the success of this research.

Lastly, I would like to thank and acknowledge the School of Technology and the Graduate School Office at Eastern Illinois University for the assistance they provided during this work.

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CHAPTER I

INTRODUCTION

Biomaterials have long been used by physicians in the medical field to repair, assist, or replace living tissue or organs in the human body that are functioning below an acceptable level (Kroshchwitz, 1998). Poly-L-lactide (PLLA) is a polymer that degrades in the human body. The biodegradability of PLLA is attractive for many implant applications where ceramics, metals, or other polymers are ineffective.

During the early days of medicine, surgeons used stainless steel and metallic devices as staples, sutures, pins, rods, screws, and tacks in the human body. While their use was and continues to be important, implanting stainless steel provides a permanent fixture in the body. Just as the first surgical wound begins to heal, it is time for a surgeon to perform a second operation to physically remove the temporary implant from the body because it is no longer needed. Implants cannot be left in the body because all metallic materials corrode (Black, 1988). The second operation is inconvenient and unpleasant for the patient because they must wait even longer to fully heal. After removal of the device, the area of the body in which the device was implanted has the potential of becoming damaged again because it bears the stress and weight of the body all at once, rather than easing into it gradually.

Ceramics are among the oldest materials. Their use in the world of medicine is quite new. Inertness and chemical resistance makes ceramics an excellent biomaterial because the chemical structure of ceramics does not noticeably change after implantation.

Currently, aluminum oxides, hydroxyapatite, and glass-ceramics are the three most prominent ceramics used in medical implants (Middleton & Tipton, 1998).

Scientists studying polymers during the first half of the 20th century concluded that polymers synthesized from glycolic acid and other alpha-hydroxy acids were too unstable for long-term use. Alpha-hydroxy acids started to degrade as they were processed. However, the instability of these polymers has become very relevant for use with medical devices in society today. The fact that these polymers do degrade has rendered them much more useful today in specialized fields that rely on controlled degrading over a short period of time (Birmingham Polymers Applications, 2000).

Biodegradable sutures were approved in the 1960s by the Federal Drug Administration (FDA). The significance of biodegradable implants is that they do not need to be retrieved from the body. Biodegradable materials decompose through the body's natural metabolic processes, allowing the tissue cells to re-form as the device degrades and permits the stress of the body to be slowly transformed. The FDA's approval of biodegradable sutures has led to the development of other biodegradable implants.

Poly (L-lactic acid), also known as poly-L-lactide or PLLA, is manufactured or synthesized by combining of many lactic acid monomers that occur naturally and degrade slowly over time. PLLA has a high tensile strength and low elongation, which makes it more suitable for load-bearing applications, i.e., orthopedic fixations and sutures (Middleton & Tipton, 1998). PLLA is used as a biomaterial for sutures, clips, nets, and bandages (Boehringer Ingelheim, 1999a). It reacts with water and aqueous acids or bases to form lactic acid (Purac Product Data, 1996). According to Boehringer Ingelheim (1999a), other applications of PLLA include wound closures such as staples, meshes, and

dressings; prosthetic devices such as bone screws, pins, rods, plates, tendons, ligaments, skin substitutions, vascular grafts, stints, nerve guides; and drug delivery systems, such as microspheres, rods, needles, hollow fibers, peptides, proteins, vaccins, hormones, and cytostatics.

1.1 Statement of the Research

The purpose of this research was to experiment with processing parameters and to identify effective antioxidants to minimize degradation of PLLA during processing. The experiment involved identifying the optimal balance of processing parameters, i.e., temperature, time, and pressure. After the optimum parameters were found for PLLA, antioxidants were introduced to reduce oxidative degradation during processing. The effects of pressure, time, temperature, and antioxidants on molecular degradation of PLLA were investigated. The molecular degradation was evaluated using the intrinsic viscosity method.

1.2 Significance of the Research

The problem with degradable materials, including PLLA, is that they degrade during the manufacturing process. Although degradation is exactly what scientists look for in biomaterials, the degradation that takes place during manufacturing needs to be minimized or eliminated altogether.

A typical manufacturing process for biodegradable polymer products involves heating the polymer and forming the product under pressure. Thus, pressure, temperature, and process time are important parameters for processing biodegradable polymers. These parameters are also critical for controlling the polymer degradation

during processing. Therefore, an optimal combination of processing parameters needs to be identified to reduce degradation of biodegradable polymers during the molding process.

During processing, the major degradation event is oxidation of the polymer, due to high temperature. Antioxidants can be introduced into the polymer as additives to reduce degradation of the polymer during processing. In order to retard oxidation, effective types and amounts of antioxidants need to be identified to provide optimal protection for the polymer.

1.3 Hypotheses

1. Incorporating a variety of antioxidants into compression molded PLLA specimens decreases the amount of degradation as measured by its molecular weight.
2. Degradation is slowed by employing optimal processing parameters.

1.4 Definition of Terms

3-hydroxyanthranilic acid:	HAA is a new antioxidant that was isolated from the methanol extract of tempeh (Esaki, 1996).
Antioxidant:	A substance that inhibits reactions with oxygen or peroxides.
BHT:	Butylated hydroxytolune, a low molecular weight food grade synthetic antioxidant.
Compression molding:	A process used to form a finished component from raw resin by applying pressure on the molds while heating.
Fraxetin:	The trade name for 7,8-dihydroxy-6-methoxycoumarin, 98%.
Free Radical:	An unstable molecule that contains an unpaired electron (Strong, 1996).

Isophorone diisocyanate, 98%:	IPDI or 3,5-di-tert-butyl-4-hydroxyl benzyl hexamethylene dicarbamate with a molecular weight (MW) of 640. A hindered phenol group with higher MW synthesized by direct addition reaction of 2,6-di-tert-butyl-4-hydroxyl methyl phenol (DBHMP) and isocyanates.
Molecular weight:	The average mass of a molecule of a compound compared to 1/12 the mass of carbon 12; the sum of the atomic weights of the constituent atoms.
Oxidation:	The process of reaction with oxygen (Strong, 1996).
PLLA:	Poly (L-lactic acid), also known as poly-L-lactide is a biodegradable polymer with about 37 % crystalline, a melting point of 175-178 °C and a glass-transition temperature of 60-65 °C (Middleton & Tipton, 1998).
Polymer:	A chemical compound or mixture of compounds formed by polymerization and consisting essentially of repeating structural units called monomers.
Quercetin:	A natural flavonoid antioxidant that has been isolated from many plants.
TBHQ:	Tertiary butylhydroquinone, a synthetic phenolic antioxidant.
Vitamin E:	Tocopherol, fat-soluble phenolic compound with varying degrees of antioxidant vitamin E activity obtained from germ oils or by synthesis.
Viscosity:	The resistance to flow in a fluid or semi-fluid.

1.5 Assumptions

In this research the following will be assumed:

1. The antioxidants used in this research were close to their original condition and in compliance with industry standards.
2. PLLA is consistent and uniform throughout.
3. Antioxidants are evenly distributed throughout the polymer matrix.
4. Viscosity is an accurate predictor of molecular weight.

1.6 Limitations

The findings in this research have the following limitations:

1. Human error and accuracy of the testing equipment can affect the accuracy of the test results.
2. The quality of the PLLA and antioxidants is controlled by the suppliers.
3. Changes in ambient temperature and the associated rate of cooling between the compression molded specimens can affect research results.
4. Characteristics of PLLA and antioxidant combinations can affect the compression molding process.
5. Changes can occur in humidity after drying and before compression molding.

1.7 Delimitations

The research is bound to the following parameters:

1. The type of PLLA used in this research is limited to Purac biochem, a family of homopolymers of PURASORB.
2. Molecular weight is determined using intrinsic viscosity. The evaluation of all polymer specimens was performed using an intrinsic viscosity constant temperature bath.
3. Compression pressure was applied using a press by Buehler.
4. Temperature in the compression molding of PLLA was maintained by an Athena XT16 temperature controller.
5. The amount of time the sample was held was measured using a stopwatch.
6. Antioxidants used in this research included the following: Quercetin, TBHQ (tertiary butylhydroquinoe), IPDI (isophorone diisocyanate), HAA (3-hydroxyanthranilic acid), and Fraxetin.

CHAPTER II

LITERATURE REVIEW

This review of literature includes sources related to the significance of and problems associated with biodegradable polymers, antioxidants, and processing parameters. The past and current use of implantable polymers is discussed. Past research describing the benefits of antioxidants will be discussed.

2.1 Polymers

Polymers are chemical compounds or mixtures of compounds formed by polymerization, essentially consisting of repeated structural units called monomers. Polymers are used by various industries, including food and beverage, foundry, lumber, bulk materials handling, transportation, mining, mineral processing, paper, recreational equipment, textiles, and medical implants.

2.2 Processing

Thermoplastic polymers can be melted and processed by conventional means such as extrusion, injection molding, and compression molding. Each process is different and has its advantages and disadvantages.

Extrusion begins when polymer resin from a hopper is fed into a chamber. After the resin is in the chamber, an oscillating ram arm forces the resin material into a die. Heat is applied to the material, making the polymer expand and causing resistance to the ram. It is a continuous process that produces bar stock of varying cross-sections (Biomet, 1996). Other typical extruded products include profiles, bars, rods, and pipes.

Injection molding is a key process in the polymer processing industry. The process is economical and efficient. An injection molding machine consists of an injection unit, a mold clamping unit, a hydraulic unit, and a control unit. Shearing and heating the injection unit melts resin material. The melted material is injected with pressure into a mold that is held by the clamping unit. As the polymer cools, it solidifies into the shape of the mold. Figure 1 shows a basic injection molding machine (Gao and Tian, 1999). Injection molding provides excellent product consistency.

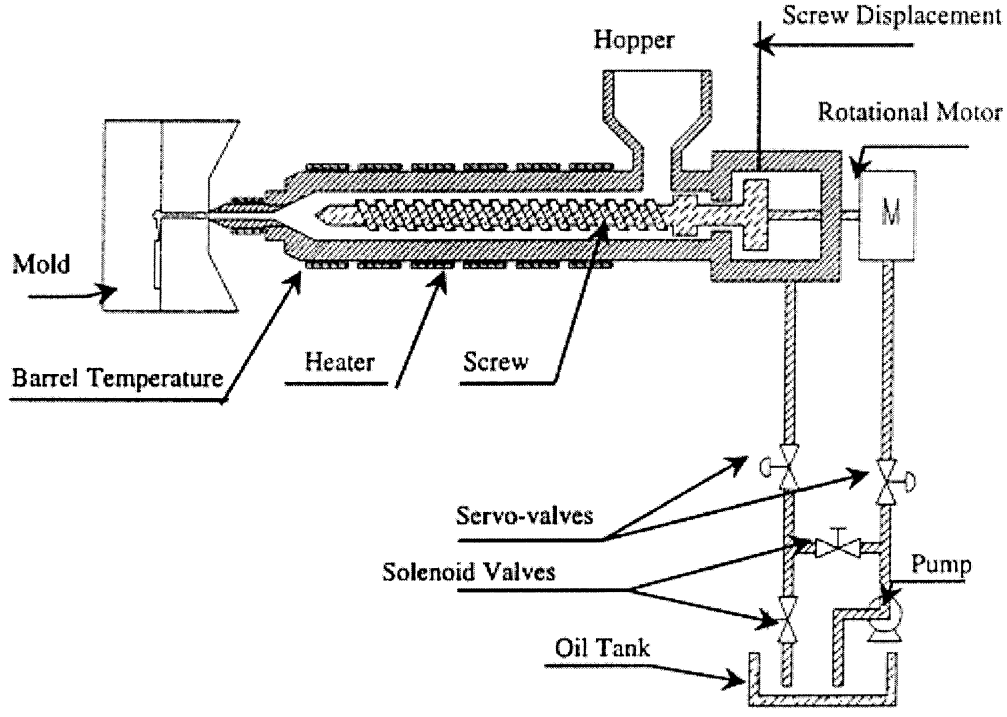

Figure 1 Illustration of basic injection molding process.

Compression molding is used to form complete pieces from raw material resin by compressing molds being heated. Figure 2 is a typical compression molding process. The outer rod diameter and inner sleeve diameter are the same. To mold a material, the bottom rod is placed into the sleeve and a known amount

of material resin is placed into the mold. The mold is capped with a rod with the same diameter, then pressed and cycled through specific temperatures, times, and pressures. The compression mold is allowed to cool before de-molded and trimmed. Compression molding wastes the least amount of material by leaving little unused material out of the mold, thus is better for large parts. Resin quality and surface roughness can be controlled during processing (Ramani and Parasnis, 1998). The disadvantages of compression molding are material inconsistency and low production rate (Compression Molding, 2001).

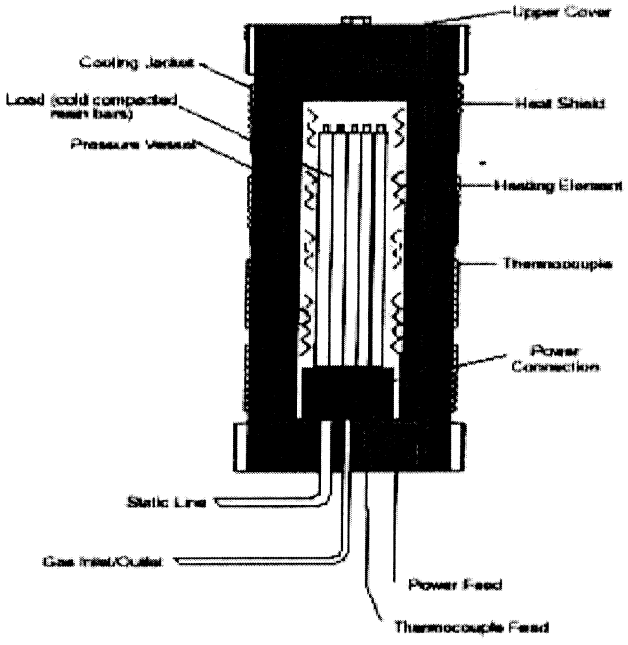

Figure 2 Illustration of a typical compression molding process.

2.3 Biodegradable Polymers

Biodegradable polymers have a wide range of mechanical properties and degradation rates. All polymers degrade and consequently material properties deteriorate. During degradation, the chain length of polymer molecules decreases. This process is known as molecular degradation. Because of their ability to degrade, biodegradable polymers are used in the human body as temporary devices. The significance of biodegradable polymer implants in humans is that a second operation is not needed for removal, allowing an individual more freedom to heal without reintrusion.

Middleton and Tipton (1998) stated that orthopedic fixation devices made from synthetic biodegradable polymers have advantages over metal implants because they transfer stress over time to the damaged area. This allows healing of the tissues and eliminates the need for a subsequent operation for implant removal. Current materials have not exhibited sufficient stiffness to be used as bone plates for support of long bones, such as the femur. Rather, they have found applications where lower-strength materials are sufficient. For example, they are being used as interference screws in ankle, knee, and hand areas; as tacks and pins for ligament attachment and minuscule repair; as suture anchors, rods, and pins for fracture fixation.

2.4 Physiological Compatibility of Biodegradable Polymers

Boehringer Ingelheim (1999a) stated that various types of polymers are nontoxic and are well tolerated by organisms. A number of animal tests and clinical trials have verified this with lactic and glycolic acid. PLLA is easily metabolized and excreted by the human body or by animals (Boeinger Ingelheim, 1999a).

2.5 Failure of Polymers

Most polymers begin to degrade as soon as they are made. Moisture, temperature, and gamma-radiation increase the degrading process. Boehringer Ingelheim (1999b) suggest that contact with moister cause PLLA to degrade quickly. This includes improper drying of the polymer. The second way to cause failure of polymers is to subject them to higher temperatures than needed for drying purposes. Processing polymers requires a very accurate temperature control since the material degrades considerably even in the pellet form. Processing temperatures have to be as low as possible, as thermal damage is significant. When not in use polymers should be stored in a freezer at a temperature below 10 °C. Costa, Luda, Trossarelli, Brach del Prever, Crova & Gallinaro (1998) stated that the last significant cause of failure of polymers is the sterilization method used by medical device manufacturers. Gamma-radiation breaks polymer molecular chains, resulting in generation of free radicals, which leads to oxidation and accelerated wear.

2.6 Biodegradation

Biodegradation is the process in which a material is broken down from its original state. Hydrolysis is one form of degradation for glycolide, ε-caprolactone, and lactide polymers. After water or moisture is introduced to the material, random hydrolysis begins, and fragments of the material are split from one another causing phagocytosis. Phagocytosis is a process of diffusion and metabolism. Hydrolysis is affected by the size, the crystallinity, pH, and temperature of the environment (Birmingham Polymers Applications, 2000).

The degradation rate depends on the molecular weight, surface quality, composition of the polymers, and environmental conditions. The hydrolytic degradation of polymers leads first to a decrease in molecular weight. Only at the end of the degradation time can a loss in mass be observed, which leads to the complete decomposition of the polymer (Boehringer Ingelheim, 1999a).

2.7 Evaluation of Molecular Degradation

Polymeric degradation causes deterioration in material properties. The degradation in the molecular structure of polymers is of critical importance for many applications. One of the important measures for polymer structure is molecular weight, which is decreased as a result of polymer chain scission. The molecular weight of a polymer is related to its intrinsic viscosity (limiting viscosity number) according to the following Mark-Houwink-Sakurada equation (Kumar & Gupta, 1998):

$$Mv=(n/k)^{1/a}$$

Where n is intrinsic viscosity. Mv is known as viscosity-average molecular weight and k and a are empirical constants that are determined by polymer type and experimental conditions. For biodegradable poly(L-lactide), k and are 5.45 x $10A^{-4}$ dL/g and 0.73, respectively. A viscometer can be used to measure the viscosity, or molecular weight, of a polymer (Ciesielska & Liu, 1998).

Ciesielska and Liu (1998) stated: $N_{red} = (t_c - t_o) / (t_oC)$ where N_{red} is reduced viscosity, t_c is efflux time for polymer solution at concentration C, and t_o is efflux time for solvent. The reduced viscosity N_{red} can be calculated for each solution in order to measure the intrinsic viscosity of plastic. A graph of reduced viscosity vs. polymer concentration can be plotted. Intrinsic viscosity can be extrapolated as the reduced viscosity at zero concentration. Thus, molecular chain length or molecular weight can be measured in terms of intrinsic viscosity.

2.8 Processing Parameters and Equipment

PLLA is the family of homopolymers of L, L(-)-lactide. According to PURAC's product data sheet, PLLA is supplied in the standard form of white granules suitable for conventional processing methods. PLLA can be essentially stable when stored at low temperatures, e.g., freezer in an inert atmosphere. The sealed bag needs to be warmed up to room temperature before opening. PLLA reacts with water and aqueous acids or bases to form lactic acid (Purac Product Data, 1996).

2.9 Drying

PLLA homopolymer resin must be dried before processing in order to avoid unnecessary degradation during molding. The drying is performed in a vacuum oven at 120° C for five hours. Boehringer concluded that when using the drying temperature of 140° C, no significant molecular weight decrease was observed after a period of 24 hours. However, it has been proven that increasing the drying temperature has detrimental effects on the material. Effects of drying depends more on the drying temperature than on the drying time. Drying values approach an asymptotic limit depending on the temperature applied. Drying can be done in a vacuum oven or in an absorption-circulating drier (Boehringer Ingelheim, 1999b).

2.10 Compression Molding

The processing parameters for polymers are pressure, time, and temperature. Ramani and Parasnis (1998) state that compression molding involves the application of pressure and temperature in a proper sequence to provide parts of highest quality. Heat is applied to start melting the sample, and as the sample starts to melt and pressure is applied, voids are eliminated. The plastic powder mixture turns into a well-consolidated sample. During compression molding, the mixture is placed into the mold, heated above melting point, and allowed to cool to an ambient temperature.

2.11 Antioxidants

Antioxidants are used to improve the thermal stability of various polymers, however, are yet to be used consistently in biodegradable polymers. Oxygen reacts with free radicals in the material, thus repelling the oxygen away from the biodegradable material. In order to function well, an antioxidant molecule must react with oxygen more rapidly than the oxygen can react with the biodegradable material. The products of the reaction with free radicals must not be pro-oxidant (Aim, 2000).

The most widely used antioxidants in foods include: butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate (PG), and tert-butylhydroquinone (TBHQ) (Shahidi, 2000). Henry, et al. (1998) demonstrated butylated hydroxytoluene (BHT) to be effective in the suppression of oxidation in safflower oil during heat-catalyzed oxidation. They compared BHT with β-carotene, and found that BHT prolonged the onset of oxidation significantly more than β-carotene. Papas (1999) stated that α-tocopherol, or vitamin E, is an effective antioxidant for neutralizing free radicals that are generated within the human body. Dougherty (1993) showed high temperature data, which indicated stability of α-tocopherol. Research by Tomita, et al. (1999) pointed out that the addition of vitamin E to gamma irradiated UHMWPE molds stopped the development of surface cracking and particulate debris generation in vitro testing. Gamma irradiation resulted in hardening of the grain boundary in the polymer that was subjected to sliding fatigue.

2.11.1 Natural and Synthetic Antioxidants

Cadenas and Packer (1996) acknowledged that β-carotene may be a very effective antioxidant or protective compound for human photosensitivity disorders. Shahidi (2000) stated that naturally occurring inhibitors of oxidation in foods generally originate from plant-based ingredients. These may be produced as a result of process-induced chemical changes in foods or are extracted from non-food ingredients. The use of synthetic antioxidants in foods dates back to the 1940's, when butylated hydroxyanisole (BHA) was found to retard oxidation and the effectiveness of several alkyl esters of gallic acid. Bagchi, Garg, Krohn, & Bagchi (1997) studied Grape Seed Proanthocyanidin Extract (GSPE), vitamin C, and vitamin E succinate (VES). Chemiluminescence and cytochrome reduction determined the oxygen free radical scavenging abilities. GSPE was superior for scavenging oxygen free radicals over both vitamins C and E.

In the article "Antioxidative Effects of Some Natural Antioxidants in Sunflower Oil" by Marinova and Yanishlieva (1996), antioxidant effectiveness was measured. Antioxidants fraxetin, caffeic acid, and esculetin or 3,4-dihydroxycinnamic acid were compared. Fraxetin was shown to have the greatest oxidative stability of the group. Fraxetin is two and a half times more effective than butylated hydroxytoluene (BHT) in sunflower oil at 25 and 100 °C. Fraxetin has a melting point of 230 –231 °C and a molecular weight of 208.17.

Lau, Pan, and Liu investigated antioxidants octadecyl isocyanate (OI), hexamethyl diisocyanate (HMDI), toluene-2,4-diisocyanate (TDI), isophorone diisocyanate (IPDI), and methylene diphenylene diisocyanate (MDI). All five antioxidants were new hindered phenol antioxidants which were synthesized by

direct addition reaction of 2,6-di-tert-butyl 4-hydroxyl methyl phenol (DBHMP) and isocyanates. The five antioxidants have high molecular weights and are more effective than butylated hydroxytoluene (BHT) at 140 °C. Table 1 shows the chemical name, melting temperature (T_m) and molecular weight (Mv) of each antioxidant.

TABLE 1
Selected Physical Properties of Antioxidants

Chemical Name	Abbreviation	T_m	Mv
octadecyl isocyanate	OI	54.5 - 55.5	531
Hexamethyl liisocyanate	HMDI	105-106	640
toluene-2,4-diisocyanate	TDI	135-136	646
Isophorone diisocyanate	IPDI	82	694
Methylene diphnylene diisocyanate	MDI	>270	722
Butylated hydroxytoluene	BHT	69-70	220

Esaki, Onozaki, Kawakishi, & Osawa compared the antioxidant 3-hydroxyanthranilic acid (HAA) with 6,7,4'-trihydroxyisoflavone and butylated hydroxytoluene (BHT). HAA is an extract of Tempeh that exhibits strong antioxidative activity in water/ethanol, rabbit erythrocyte membrane ghost systems, and soybean oil and soybean powder. The researchers indicated that HAA was tested at room temperature. The induction period for HAA was less than BHT in the water/ethanol system, but (100 and 200 μg) HAA was better in the soybean oil test. HAA has a melting temperature of 240 °C and a molecular weight of 153.14.

In "Flavonoids Quercetin, Myricetin, Kaemferol and (+)-Catechin as Antioxidants in Methyl Linoleate" (Heinonen, Hopia, and Pekkarinen, 1999),

antioxidant effectiveness was measured on flavonoids. Flavonoids are a group from the plant kingdom and occur most often as glycosides. The antioxidants myricetin, Quercetin, α-tocopherol, (+)-catechin, kaemferol, and rutin were compared. Oxidation was measured by conjugated diene and by determining the formation of hydroperoxide isomers by HPLC. Myricetin and Quercetin showed the greatest amount of hydroperoxide formation. The article concluded that myricetin and Quercetin were the most effective antioxidants for inhibiting the hydroperoxide formation for methyl linoleate. Quercetin dihydrate has a molecular weight of 338.3 and myricetin has a molecular weight of 318.24, both having a melting temperature of >300 °C.

Gordon and Roedig-Penman (1998) compared the antioxidant activities of myricetin 10^{-3} M, BHT at .02 %, myricetin 10^{-4} M, Quercetin 10^{-4} on sunflower oil. Myricetin 10^{-3} M was determined to be the strongest free radical scavenger of the chemicals at 60 °C during Peroxide Value (PV) in (meq/kg) changes, with a strength almost 3 times that of BHT.

CHAPTER III

RESEARCH METHODS

3.1 Materials

For this research, poly-L-lactic acid (PLLA) Purac biochem was provided by Gorinchem (Holland) in solid white granules. Purac's specifications are: intrinsic viscosity 3.8-4.2 (dl/g, $CHCL_3$, 25 °C), melting rage 170-195 (°C), heat of fusion min. 30 (J/g), specific rotation (-155)-(-160) (degree, CHCL*3*, 20 °C, Molecular weight of approx. 200.000 (g/Mole), residual solvent max. 0.01 (%) and residual monomer max. 0.10 (%). The molecular formula is [O-$CH(CH_3)$-CO]n. The PLLA received was of high crystallinity, T_m = 170 °C, T_g = 56 °C , T_{dc} = 240 °C, modulus (Gpa) 8.5, and elongation of 25% (Purac Product Data, 2000). Normal packaging of PLLA consisted of an inner bag of PE-PA laminate, an intermediate bag of aluminum coated polyester-polyethylene laminate, and an outer bag of polyethylene (PE). The bags are shipped in PE-containers for added protection. Figure 3 is a photograph of the antioxidants and PLLA samples used in compression molding process. Antioxidants used in this research were purchased from the Sigma/Aldrich Chemical Company, St. Louis, MO. They include the following: Quercetin, tertiary butylhydroquinoe (TBHQ), octadecyl isocyanate (OI), isophorone diisocyanate (IPDI), 3-hydroxyanthranilic acid (HAA), and Fraxetin.

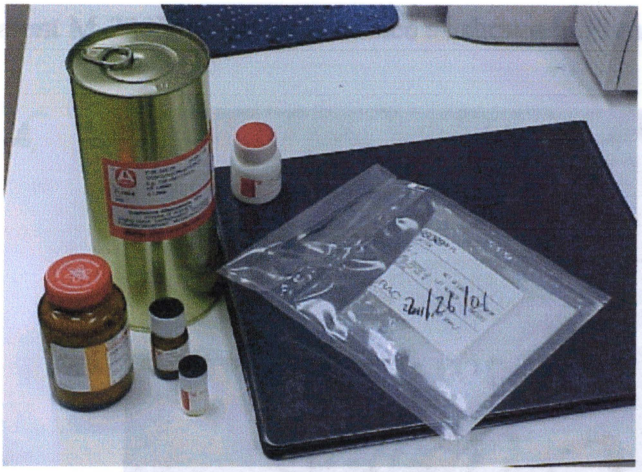

Figure 3 A photograph of the antioxidants and PLLA samples used in compression molding.

3.2 Test Specimens

Test specimens were produced by compression molding samples of PLLA at different processing parameters. After the optimal processing parameters were found, PLLA was mixed with various antioxidants according to the following processes: Storage, Weighing, Drying, Mixing, Vacuum, and Compressing.

3.3.1 Storage. Remove PLLA from the freezer where it is stored at –10 C° and allow the bag to reach room temperature before opening. All samples and materials that are stored are encased in plastic bags with nitrogen gas.

3.3.2 Weighing. The PLLA and antioxidant sample is weighed using a Denver Instrument M-220D electronic balance as shown in Figure 4.

Figure 4 Denver Instrument M-220D electronic balance.

3.3.3 Drying. The mixture of PLLA sample is placed into a flask. Figure 5 is a photograph of the glass flask inside an oven connected to a vacuum pump. The inside lip of the beaker is coated with a thin coat of grease. The grease creates an air tight seal between the beaker and the vacuum line. The beaker is then placed inside the environmental chamber and is connected to a vacuum hose. The vacuum hose leads outside the environmental chamber to a vacuum pump. The vacuum pump is turned on pulling a vacuum on the beaker. The environmental chamber is preheated to 120 °C. After the vacuum is pulled, the valve on the vacuum line is opened, creating a vacuum in the beaker. The vacuum is maintained during the entire drying process. The sample of PLLA is dried for five hours. The vacuum valve is shut off, releasing the pressure, and the beaker is twisted off the vacuum line.

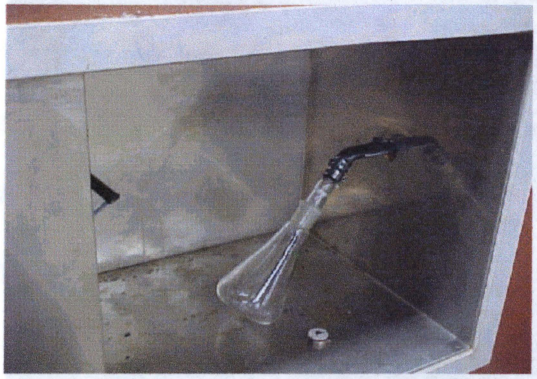

Figure 5 Photograph of a glass flask inside oven connected to a vacuum pump.

3.3.4 Mixing Antioxidants with Ethonol. Figure 6 represents the mixing equipment used to prepare compression molding samples. Ethanol alcohol was utilized as a solvent to enhance the incorporation of antioxidants into PLLA. The first step in making a uniformly mixed sample was to place an antioxidant into a 2-cup container with 20mL of ethanol alcohol and agitate it until the antioxidant was dissolved. PLLA was added into this solution and mixed using a stir rod for seven to ten minutes, scraping the sides of the container to ensure a homogenous mixing of ingredients. The mixture was then placed in a vacuum and heated to 70°C in order to remove all solvent and moisture.

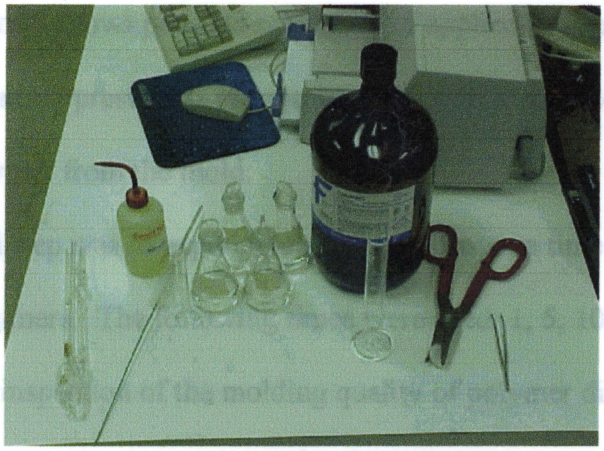

Figure 6 Supplies used to prepare compression molding samples.

3.3.5 Vacuum. A vacuum oven was used to pull all solvent and moisture out of the PLLA and antioxidant mixture. The mixture was placed in a flask connected to a vacuum. The vacuum was pulled for an hour at 70 °C.

3.3.6 Compressing. Figure 7 represents a basic compression molding process with a temperature controller. After the 1.5 gram sample of PLLA/antioxidant mixture was dried in a vacuum, the sample was compression molded. The sample was then poured out of the beaker into a compression mold.

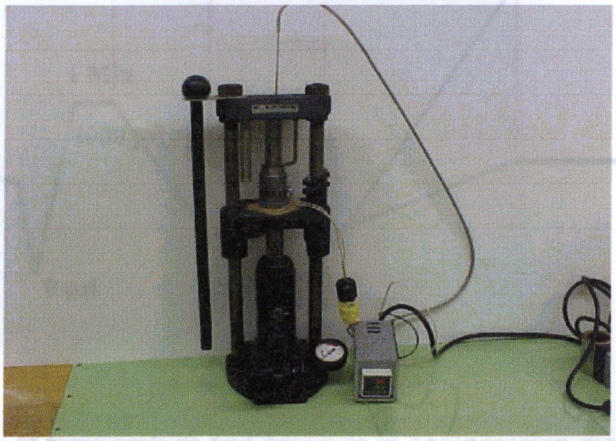

Figure 7 Basic compression molding process with temperature controller.

The first step in the compression molding process was to experiment with the pressure. Figure 8 shows possible schematic of applied pressure as a function of time. Proper starting pressure was experimented with to avoid excessive leakage of the polymer from the mold.

The second step was to experiment with compression time on molecular degradation of polymers. The following times were used: 1, 5, 10, 30, and 60 minutes. A visual inspection of the molding quality of polymer disks was performed. Then, an evaluation of the molecular weight via intrinsic viscosity was performed.

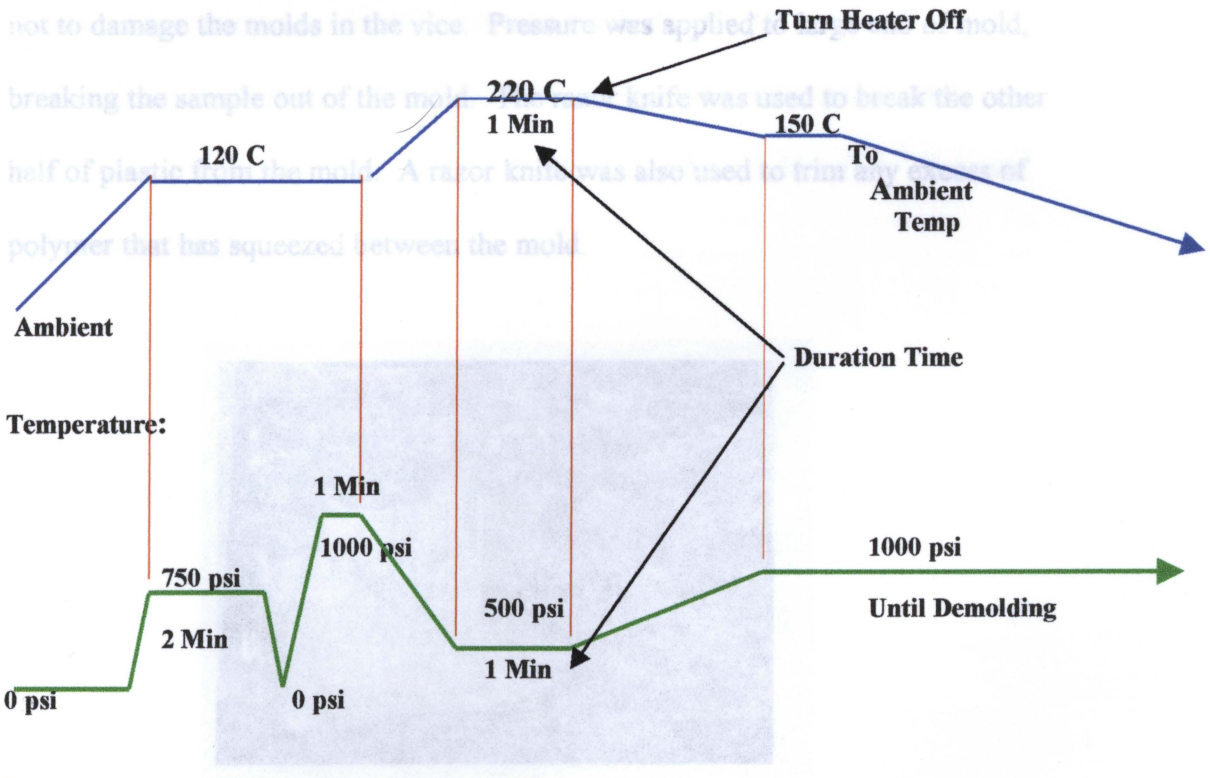

Figure 8 Schematic of temperature and pressure in compression molding.

The third step was to study the effect of compression temperature on molecular degradation of polymers. Molding plastic at various temperatures (190, 200, 210, 220, and 230 °C) caused different degradation on the polymer.

3.3.7 Demolding. Figure 9 represents both PLLA powder in a package and a processed PLLA sample. After molding, the core was extracted from the mold by a ram arm on the press. The molded sample was connected to the two pieces of the inner core, which needed to be separated. The mold was then scored with a razor knife along the boundary with the sample. The small end of the core was placed in the vice between two copper plates. Copper plates were used so as not to damage the molds in the vice. Pressure was applied to large end of mold, breaking the sample out of the mold. The razor knife was used to break the other half of plastic from the mold. A razor knife was also used to trim any excess of polymer that has squeezed between the mold.

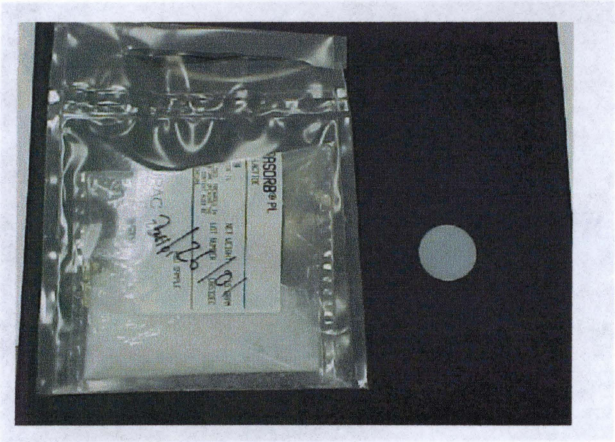

Figure 9 PLLA powder in package and compression molded sample.

3.3.8 Preparation for Intrinsic Viscosity Evaluation. Figure 10 shows a processing jogger used to mix the prepared compression molded sample with chloroform. Intrinsic viscosity was measured on diluted solutions of PLLA polymer in chloroform. The molecular weight of a polymer was related to its intrinsic viscosity (limiting viscosity number) according to the following Mark-Houwink-Sakurada equation (Kumar & Gupta, 1998):

$$Mv = (n/k)^{1/a}$$

Where n was intrinsic viscosity, which was also referred to as limiting viscosity number. Mv is known as viscosity-average molecular weight and k and a are empirical constants that are determined by polymer type and experimental conditions. For biodegradable poly(L-dactide), k and are 5.45 x $10A^{-4}$ dL/g and 0.73, respectively.

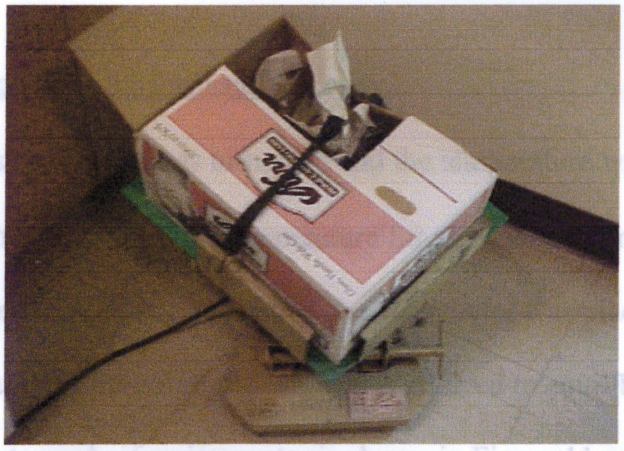

Figure 10 Processing jogger used to mix the prepared compression molding sample with chloroform.

Table 2 shows the solution concentration, amount of PLLA, and the volume of chloroform used in the tests. Diluted solutions were prepared by adding the polymer into the solvent. Five different solution concentrations were made: 0, 0.04, 0.1, 0.16 and 0.20 grams per deciliter. Chloroform (99.9%, ACS HPLC grade) was used to dissolve each sample. Separate flasks of the concentration were closed with a glass stopper. The flasks were then shaken for two hours. After the polymer was dissolved into the solvent completely, the solution was loaded into the glass viscometer, which was then placed in the constant temperature bath equilibrated at 25 °C.

Table 2
PLLA Concentration Plan for Intrinsic Viscosity Measurement

Solution Concentration (g/dL)	Amount of PLLA (g)	Volume of Chloroform (ml)
0.00	0.00	20
0.04	0.02	50
0.10	0.05	50
0.16	0.08	50
0.20	0.10	50

3.3 Testing Procedure for Intrinsic Viscosity

The viscosity bath was turned on and the temperature was set for 25°C. The bath was maintained at this temperature for at least thirty minutes before the viscometers were placed into the bath. The viscometer was placed in the constant temperature bath and the solution sample was allowed to equilibrate for 15 minutes. A photograph of a viscometer is shown in Figure 11.

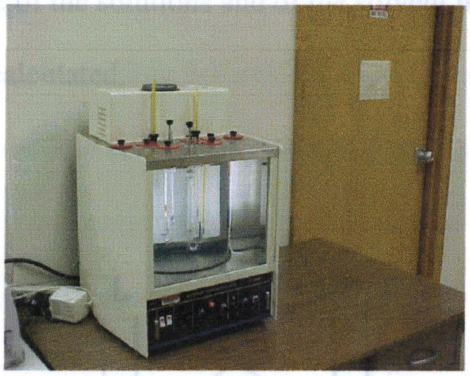

Figure 11 Constant temperature bath used in measuring intrinsic viscosity.

Using a pipette, each solution was loaded from the flask into the viscometer, Figure 12 is a schematic of a glass viscometer used in measuring intrinsic viscosity. The solution level must be between the upper and lower marks (A & B). A finger was placed on an opening (N), closing the main exit of the solution. A rubber bulb was inserted in the entrance of the viscometer and pressure was applied (L). The solution was raised to fill the bulb (C). Then, the finger was removed, which created an atmospheric pressure in the bottom end of the capillary.

Efflux time was taken by simultaneously opening the hole the finger was covering (N) and releasing the pressure from the bulb (B). A stopwatch was started when the liquid level was at the top of the viscometer bulb (F). The stopwatch was stopped after all the solution was out of the viscometer bulb (E). The time taken for the liquid level to move from the top of the viscometer bulb (F) to the bottom of the bulb (E) was efflux time in seconds. This procedure was duplicated five times for each solution and the average efflux time was calculated.

The average efflux time of the solutions and of the solvent was recorded and the reduced viscosity was calculated.

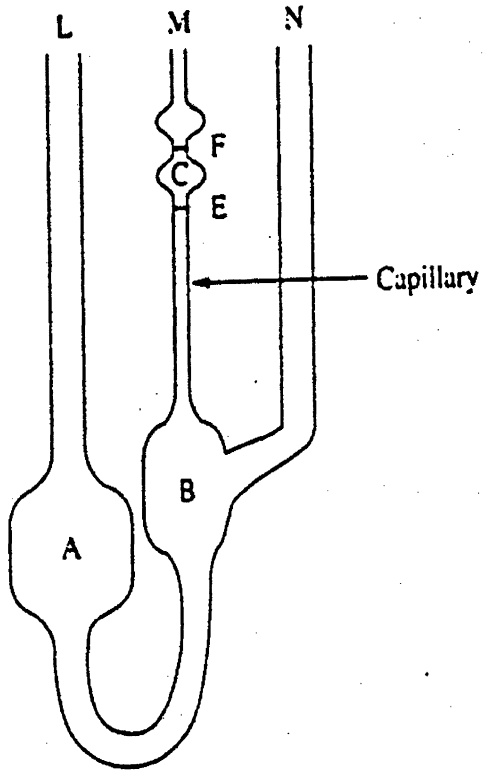

Figure 12. Schematic of a glass viscometer used in measuring intrinsic viscosity.

A graph of reduced viscosity versus solution concentration was plotted using the recorded data. The line of best fit was found using the least squares method. An extrapolation was used to obtain intrinsic viscosity. The viscosity-average molecular weight of the polymer was calculated using the relative viscosity equation.

The optimal pressure, time, temperature, antioxidant, and concentration of antioxidant for compression molding process of PLLA was identified by limiting the change of degradation. The effect of pressure in the compression molding process was evaluated by keeping the temperature and time constant with no antioxidant. Then, time or temperature was varied by keeping the other parameters constant. Changing only one variable at a time permitted the effect of each parameter to be fully understood. Keeping all other variables constant, the optimal processing parameters for compression molding PLLA sample was found. No antioxidants were used in finding the optimal pressure, time, and temperature in the compression molding process until each variable was set. After the optimal processing parameters were found for compression molding, antioxidants were added to determine if they have any effect on the change in molecular degradation. Antioxidant concentrations were evaluated to determine if the amount of antioxidant effects the molecular weight of the polymer.

3.4 Analysis

The analysis of the results for each PLLA compression mold sample was based on the change in molecular degradation during processing. The decrease in molecular weight was an indication of molecular degradation. The molecular weight of each sample was determined by intrinsic viscosity. A decrease in molecular weight will decrease intrinsic viscosity. Figure 13 shows the relationship between intrinsic viscosity and molecular weight.

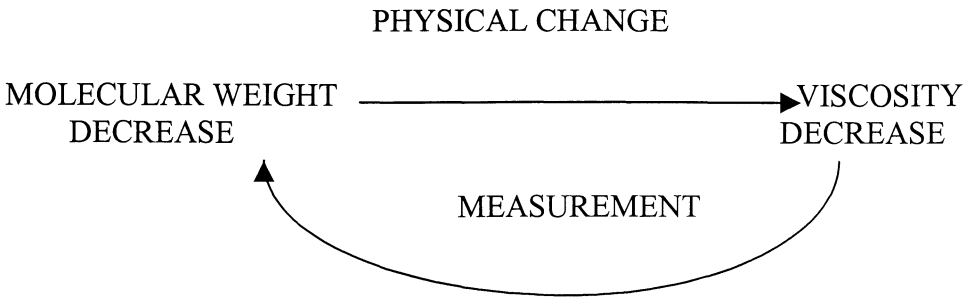

Figure 13. Relationship between physical change in viscosity and molecular weight.

3.5 Data Analysis

The following questions were addressed during the analysis process:

1. Will degradation decrease when the optimal temperature, time, and pressure for processing PLLA is found?
2. With the optimal parameters will the antioxidants Quercetin, Tertiary Butylhydroquinoe, isophorone diisocyanate, 3-hydroxyanthranilic acid, and Fraxetin at in compression molded samples decrease molecular degradation measured by molecular weight?
3. Will the concentration of the best antioxidant affect molecular degradation measured by molecular weight?

CHAPTER IV

PRESENTATION AND INTERPRETATION OF THE DATA

4.1 Effect of Pressure on Molecular Weight and Degradation

4.1.1 Quality of Sample with Varying Pressure

Pressure was experimented with to prevent significant leakage of the polymer melt from the mold. In order to accomplish this task, three samples with no antioxidants were made. Pressure was varied between 500 and 1,500 psi and the temperature and compression time were kept constant. Figure 14 was a 50X magnification picture of a PLLA sample compression molded under 500 psi of pressure at 220°C for 10 minutes.

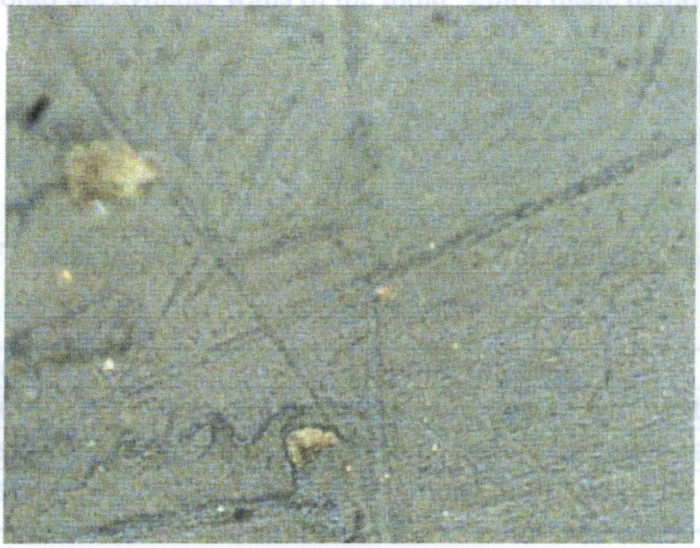

Figure 14 PLLA compression molded sample under 500 psi, at 220°C for 10 minuets under a magnification of 50X.

Each sample was visually inspected and observations were recorded in a notebook. Table 3 shows results from visual inspections of PLLA compression molded samples under different pressures. The 500 psi sample was clear, with small cracks and one or two white spots of unmelted PLLA. The sample did not come out of the compression mold onto the cylinder walls. The sample molded at compression of 1,000 psi was even clearer, with no cracks, and only had one or two white spots, and the sample was not cloudy. Some of the material did, however, start to come out of the compression mold onto the cylinder walls. The sample was stuck to the mold even after a vise was used to pull the two ends of the mold apart. The last sample, compressed at 1,500 psi., was also clear with no cracks, but more than two white spots were present. The sample also started to come out onto the cylinder walls of the mold, which made demolding the sample harder.

TABLE 3
Results of Visual Inspections of PLLA Samples Compression Molded at Different Pressures.

Pressure	Characteristics
500 psi	Clear, small cracks, and one or two white spots
1,000 psi	very clear, no cracks, one or two white spots, and not cloudy
1,500 psi	Clear, no cracks, more than two white spots

4.1.2 Differences in Molecular Weight of Samples with Varying Pressure

Figure 15 demonstrates the variation of molecular weight and degradation due to the effect of pressure on different samples of compression molded PLLA while being processed. This graph shows that pressure may not be a significant

cause in the increase or decrease in molecular weight of PLLA. Although the molecular weight was clearly higher at 1,000 psi, it was not significant enough to rule out other causes.

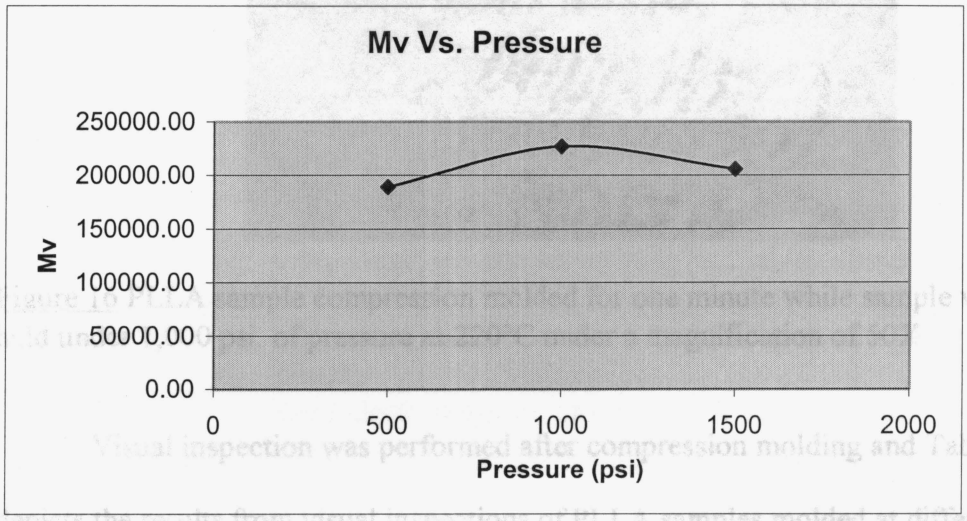

Figure 15. Variation of molecular weight and degradation due to the effect of pressure on different samples of compression molded PLLA.

4.2 Effect of Holding Time on Molecular Weight and Degradation

4.2.1 Quality of Samples Varying the Duration of Hold Time

The quality of the PLLA sample was directly affected by hold time during compression molding process when the temperature and pressure with no antioxidants were held constant. Five molds were prepared using the following times: 1, 5, 10, 30, and 60 minutes. Figure 16 shows a 50X magnified photograph of a PLLA sample compression molded for one minute while the sample was held at 200°C and under 1,000 psi of pressure. The small spots in this photograph were unmelted PLLA surrounded by uniformly melted PLLA.

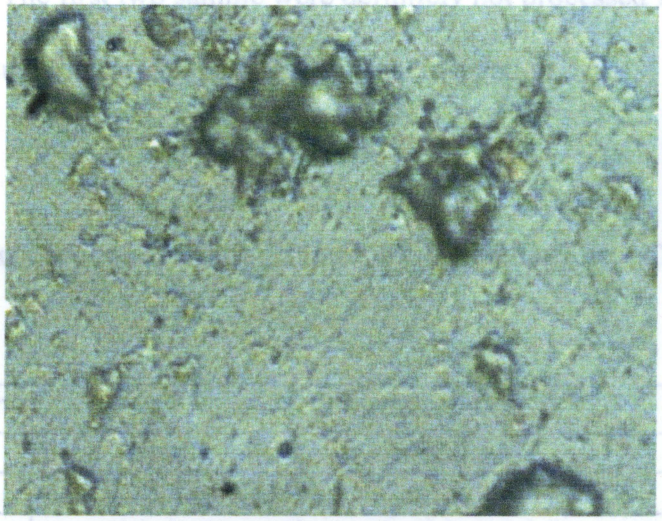

Figure 16 PLLA sample compression molded for one minute while sample was held under 1,000 psi. of pressure at 220°C under a magnification of 50X.

Visual inspection was performed after compression molding and Table 4 depicts the results from visual inspections of PLLA samples molded at different compression times. The first sample was held for one minute and can be described as clear, with more than two small white spots, and the sample was cloudy. At five minutes the mold was still not clear, and a lot of bigger white spots made the sample even cloudier. This sample clearly was not processed completely. The third sample held for ten minutes was very clear with no cracks. Only one or two white spots were seen, and the mold was not cloudy. This sample did look like it was completely processed. Sample number four at thirty minutes was also very clear, small cracks were present and there were no white spots. The sample was not cloudy and looked like it was fully processed. The last mold, at sixty minutes, turned out very clear, containing cracks. With no white spots and not appearing cloudy, it appears as though the 60 minute compression was fully melted if not

overly processed. The first two sample were definitely not processed fully. The 10, 30, and 60 minute samples all passed the visual inspection.

TABLE 4
Results of Visual Inspections of PLLA Samples Molded at Different Compression Times

Compression Time	Characteristics
1 min	clear, small white spots, and cloudy
5 min	not clear, big white spots, and cloudy
10 min	very clear, no cracks, one or two white spots, and not cloudy
30 min	very clear, small cracks, no white spots and not cloudy
60 min	very clear, medium cracks, no white spots and not cloudy

4.2.2 Differences in Molecular Weight of Samples with Varying Hold Time

Figure 17 shows the relationship between the duration of compression molding and the molecular weight of PLLA. As the duration increased, the molecular weight of PLLA decreased.

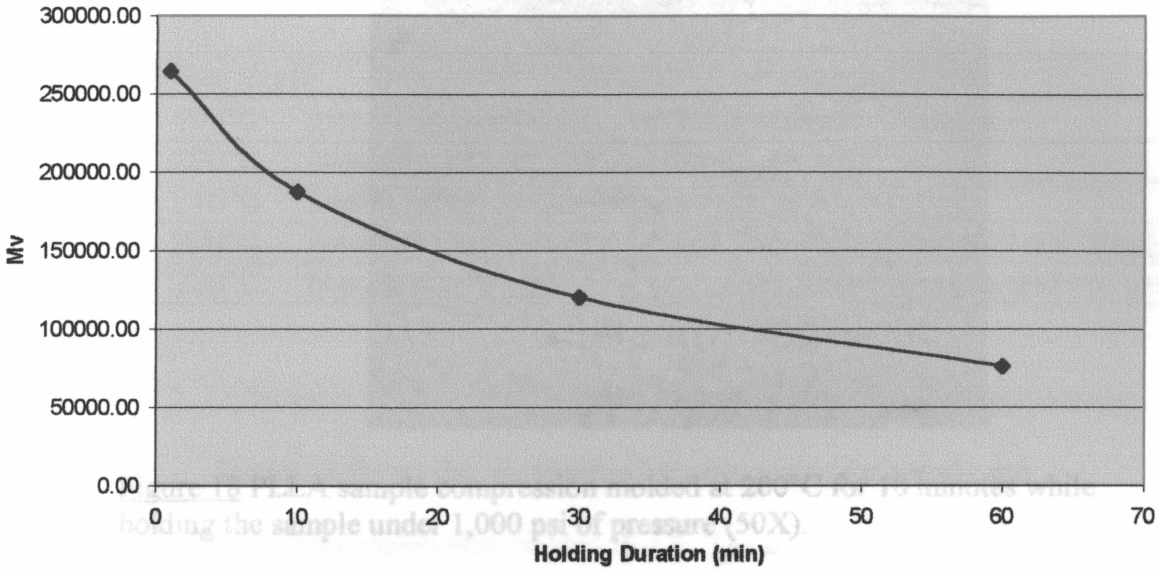

Figure 17 Variation of molecular weight with different holding times during compression molding process.

4.3 Effect of Temperature on Molecular Weight

4.3.1 Quality of Samples at Varying Temperatures

To provide a basic understanding of the effect of the proper temperature on compression molded PLLA, five samples were prepared at different temperatures from 190 to 230 °C, while holding pressure and compression time constant, with no antioxidants. Figure 18 shows how a typical PLLA sample appears under at 50X magnification. Although the sample was not shown as white in color, unmelted specks of PLLA are visible under the 50X magnification.

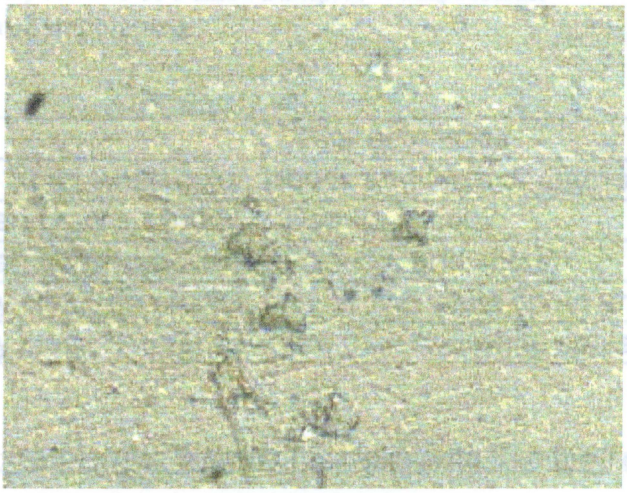

Figure 18 PLLA sample compression molded at 200°C for 10 minutes while holding the sample under 1,000 psi of pressure (50X).

A visual inspection was done after each sample was made. In Table 5 the characteristics of each sample was reported for easy referencing. The 190°C sample can be described as non-transparent, white in color, cloudy, which had lines or cracks. The 200°C mold had cracks, cloudiness, and was white in color. The 210°C sample was clearer, had cracks, was less cloudy, and had white spots. At 220°C, the sample was very clear, which had no cracks and had one or two white spots. The last sample melted at 230°C, was very clear, had no cracks, and contained more than two white spots. The 220°C sample, which remained at constant pressure, compression time, with no antioxidants, was the best in sample quality.

TABLE 5
Results of Visual Inspections of PLLA Samples Compression Molded at Different Temperatures

Temperature	Characteristics
190°C	not clear, white color, cloudy and lines or cracks
200°C	clear, cracks, cloudy and white in color
210°C	clear, some cracks, less cloudy, and spots
220°C	very clear, no cracks, one or two white spots and not cloudy
230°C	very clear, no cracks, more then two white spots and not cloudy

4.3.2 Differences in Molecular Weight of Samples with Varying Temperature

Figure 19 shows the relationship between molecular weight and temperatures for compression molded PLLA The graph shows the molecular weight decreases as the temperature of the process increases.

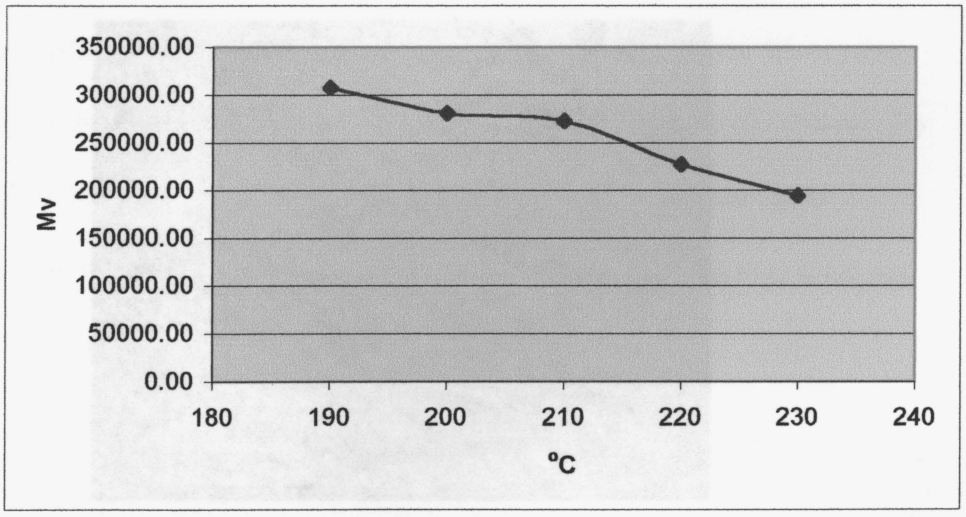

Figure 19. Variation of molecular weight with processing temperatures for compression molded PLLA samples.

4.4 Effect of Antioxidants on Molecular Weight and Degradation

4.4.1 Quality of Sample with Different Antioxidants at 0.6%

The effect of antioxidants on molecular weight degradation was experimented under 1,000 psi, at 220°C for 10 minutes. A 0.6 % concentration of antioxidants was chosen for the first round of experimentation. Figure 20 is a 50X magnification photograph of PLLA with 0.6 % of isophorone diisocyanate, which was compression molded at 220°C for 10 minutes at 1,000 psi of pressure. This figure shows a thoroughly uniform sample of PLLA with the antioxidant. Only one piece of PLLA was not melted, thus this sample shows a good combination of melting temperature, time, and pressure.

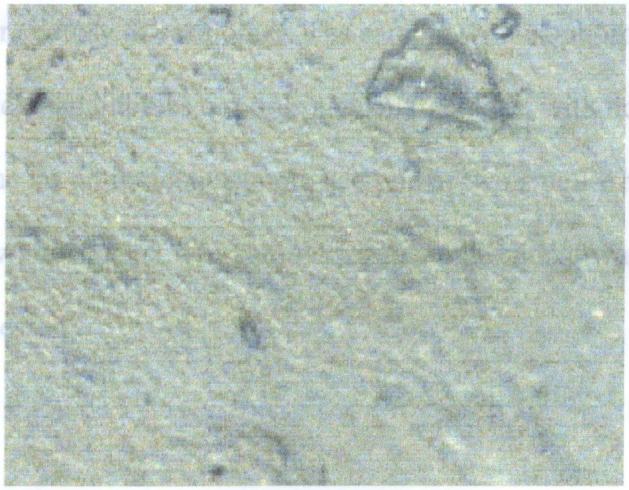

Figure 20 PLLA with 0.6 % of isophorone diisocyanate compression molded at 220°C for 10 minutes under 1,000 psi of pressure.

A visual inspection was also conducted on all six samples. The results of the visual inspections of PLLA samples compression molded with different antioxidants mixed are shown in Table 6. The first sample with 3-hydroxyanthranilic, was clear with a yellow tint. Only one or two white spots were present, and small cracks were present. The sample with Quercetin was yellow in color, clear, and with no cloudiness. Only one or two yellow spots or white cracks can be seen. The third sample with the antioxidant 7,8-dihydroxy-6-methoxy-coumarin, (98%) was clear, with small cracks, still no cloudiness, and no white spots. The tert-butylhydroquinone mold was translucent, very cloudy, and a lot of cracks and spots could be seen. The sample was clear but also had spots that made the mold cloudy. The sample had a couple of different phases that were contradictory to each other. The sample with isophorone diisocyanate was clear, which had bubbles or pools and small cracks, with no cloudiness. By comparison, the no-antioxidant sample had one or two small white spots connected by white cracks. The sample without antioxidant was very clear and very well processed.

TABLE 6
Results of Visual Inspections of PLLA Sample with Different Antioxidants

0.6% Antioxidant	Characteristics
3-hydroxyanthranilic	Clear, yellow tint, one or two white spots, no cloudiness, and small cracks
Quercetin	Yellow in color, clear, no cloudiness, and one or two yellow spots with white spots
7,8-dihydroxy-6-methoxy-coumarin, 98%	Small cracks, no cloudiness, and no white spots
Tert-butylhydroquinone	Clear, very cloudy, a lot of cracks, and spots
Isophorone diisocyanate	Clear in color, bubbles or pools are seen, small cracks, and no cloudiness
No Antioxidants (PURE PLLA)	Very clear, no cracks, one or two white spots, and not cloudy

4.4.2 Differences in Molecular Weight of Samples with Varying Antioxidants

Figure 21 shows molecular weight of PLLA samples with different types of antioxidant at 0.6%. All samples had lower molecular weight than pure PLLA sample.

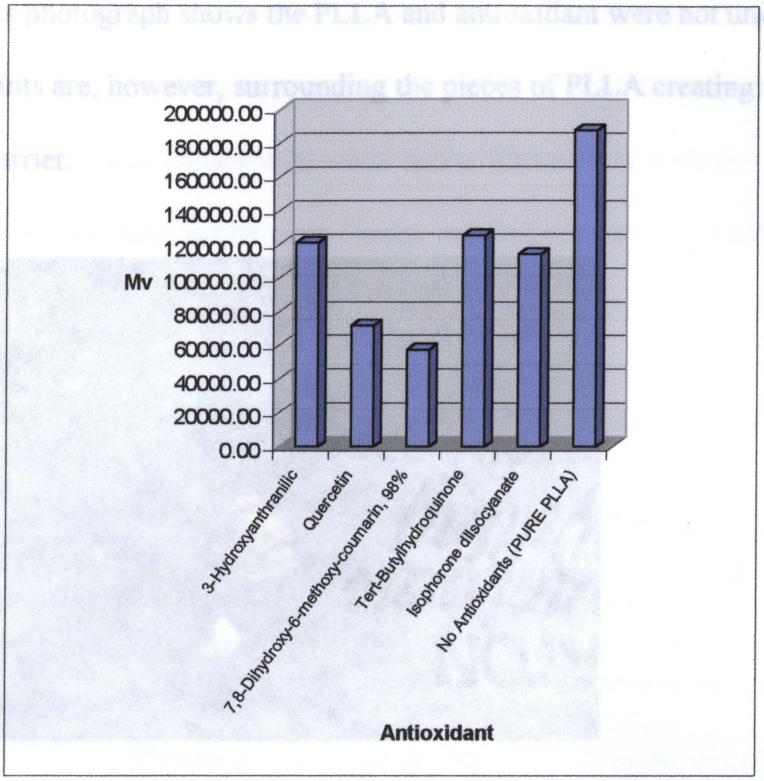

Figure 21 Molecular weight of samples with different types of antioxidants at 0.6% concentration.

4.5 Effect of Ethanol on Molecular Weight

4.5.1 Quality of Samples with Ethanol and Different Antioxidants at 0.6%

Each sample used ethanol in order to mix the antioxidant into the PLLA uniformly. The effect of ethanol on molecular weight was investigated. Comparing the mixture of antioxidants and PLLA with ethanol to different samples with the same concentrations without the ethanol would show any relationship, if present. Samples were made without ethanol using the same parameters of the samples with ethanol. Figure 22 is a 50X magnification photograph of PLLA, 0.6 % of isophorone diisocyanate that has not been mixed

with ethanol. The mold was compressed for 10 minutes at 220°C at 1,000 psi., of pressure. This photograph shows the PLLA and antioxidant were not uniform. The antioxidants are, however, surrounding the pieces of PLLA creating an antioxidant barrier.

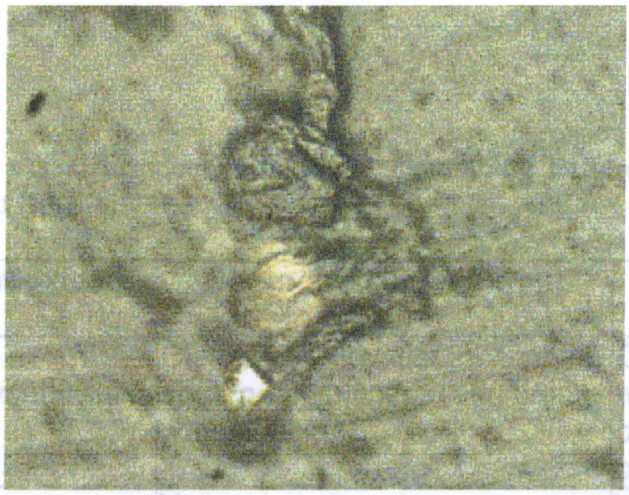

Figure 22 PLLA, with 0.6 % of isophorone diisocyanate that has not been mixed with ethanol.

A visual inspection was also done on all six samples with ethanol, including the control mold that had no mixed antioxidants. Table 7 shows results of visual inspections of PLLA samples with different antioxidants without and with ethanol. The sample 3-hydroxyanthranilic mold is clear, with no yellow tint, has one white spot, shows no cloudiness, and contains small white cracks. Quercetin was transparent yellow in color with no cloudiness or yellow spots. This sample mold does have pools or voids with white cracks. Sample 7,8-dihydroxy-6-methoxy-coumarin, (98%) was not processed fully. Antioxidants are still very visible, like specks of pepper. The mold has a transparent yellow tint, small cracks and pools, no cloudiness, and has spots. The tert-butylhydroquinone

mold was clear with cloudy spots, and has a lot of cracks and pools. The isophorone diisocyanate mold is not clear, and pools of PLLA are seen suggesting the antioxidant fully coated every piece. There are small cracks between each pool, and the sample was cloudy with white spots. The sample with no antioxidant was very clear, contains no cracks, and had one or two white spots.

TABLE 7
Results of Visual Inspections of PLLA Containing Different Antioxidants with and without Ethanol.

0.6% Antioxidant	Characteristics Without Ethanol	Characteristics With Ethanol
3-hydroxyanthranilic	Clear, no yellow tint, one white spot, no cloudiness, and small white cracks	Clear, yellow tint, one or two white spots, no cloudiness, and small cracks
Quercetin	Yellow in color, clear, no cloudiness, and no white or yellow spots	Yellow in color, clear, no cloudiness, and one or two yellow spots with white spots
7,8-dihydroxy-6-methoxy-coumarin, 98%	Antioxidant was visible, yellow tint, clear, small cracks and pools, no cloudiness, and has spots	Small cracks, no cloudiness, and no white spots
Tert-butylhydroquinone	Clear, cloudy, a lot of cracks, pools, and a lot of spots	Clear, very cloudy, a lot of cracks, and spots
Isophorone diisocyanate	Not clear, no cracks, one or two white spots, and not cloudy	Clear in color, bubbles or pools are seen, small cracks, and no cloudiness
No Antioxidants (PURE PLLA)	Very clear, no cracks, one or two white spots, and not cloudy	Very clear, no cracks, one or two white spots, and not cloudy

4.5.2 Differences in Molecular Weight of Samples with and without Ethanol.

Figure 23 shows molecular weight of PLLA samples with and without ethanol and different types of antioxidant at 0.6% concentration. All samples have lower molecular weight than pure PLLA sample. All samples without ethanol have higher Molecular Weights except tert-butylhydroquinone, which had a lower Molecular Weight.

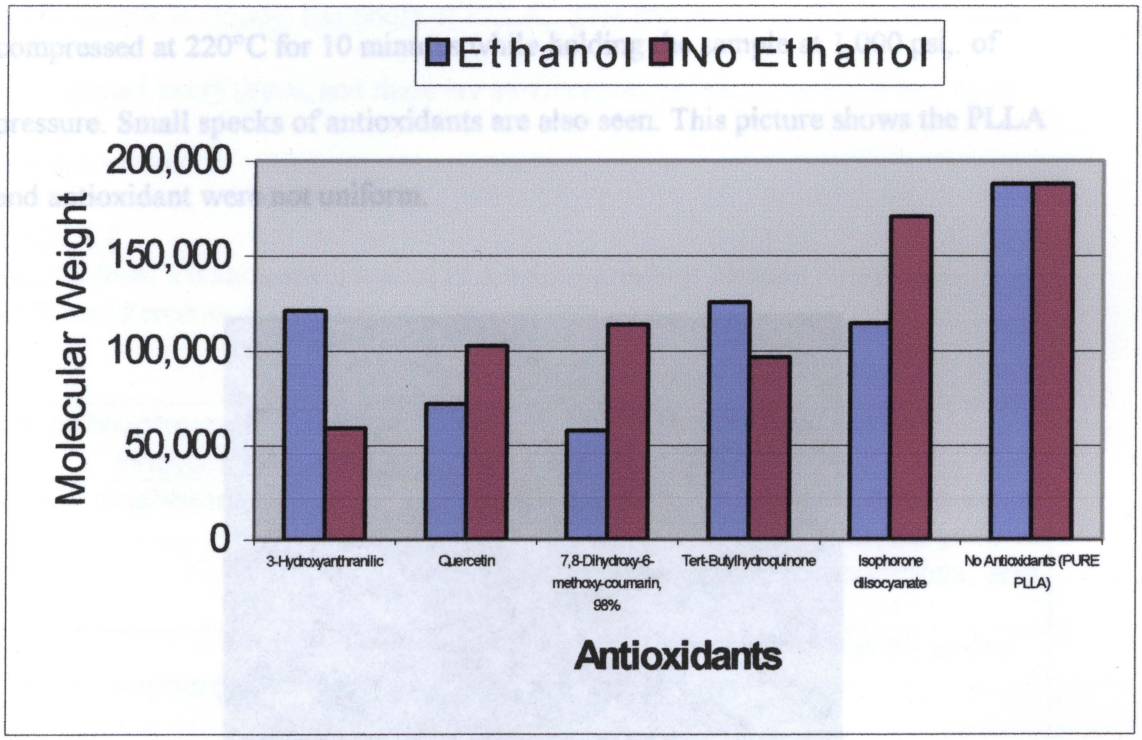

Figure 23. Molecular weight of PLLA samples with and without ethanol and different types of antioxidant at 0.6% concentration.

4.6 Effect of Different Concentrations of Antioxidants on Molecular Weight.

The effect of concentration of isophorone diisocyanate on molecular weight was investigated. Concentrations of 0, 0.1, 0.2, 0.4, and 0.6 percent were tested with the pure form of PLLA.

4.6.1 Quality of Sample with Different Concentrations of Isophone Diisocyanate

Figure 24 was a 50X magnification photo of PLLA having, 0.4 % of isophorone diisocyanate that has not been mixed with ethanol. The mold was compressed at 220°C for 10 minutes while holding the sample at 1,000 psi,. of pressure. Small specks of antioxidants are also seen. This picture shows the PLLA and antioxidant were not uniform.

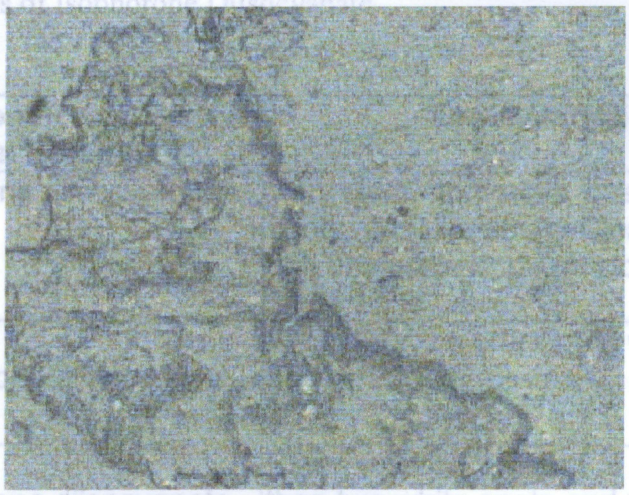

Figure 24 PLLA, sample with 0.4 % of isophorone diisocyanate that has not been mixed with ethanol. The mold was compressed at 220°C for 10 minutes while holding the sample under a pressure of 1,000 psi.

A visual inspection was also performed on all five samples with no ethanol, including the control mold that had no antioxidants. Table 8 shows results from visual inspections of PLLA compression molded samples at different percentages of isophorone diisocyanate. The pure PLLA sample is very clear, has no cracks, and has one or two white spots. The 0.1% sample is very clear, has no cracks, and no white spots. The .02% mold was clear, minimal amount of cracks, more than two white spots, and has cloudy spots. The 0.4% mold is clear, minimal amount of cracks, one or two white spots, and was not very cloudy. The 0.6% sample is cloudy, has pools of PLLA. This fact suggests that antioxidants fully coated every piece, and there are small cracks between pools. White spots are also present.

TABLE 8

Results from Visual Inspections of PLLA Compression Molded Samples at Different Percents of Isophorone Diisocyanate.

% of Isophorone Diisocyanate Without Ethanol	Characteristics
0% isophorone diisocyanate	Very clear, no cracks, one or two white spots, and not cloudy Clear, no yellow tint, one white spot, no cloudiness, and small white cracks
0.1% isophorone diisocyanate	Very clear, no cracks, no white spots and not cloudy
0.2% isophorone diisocyanate	Clear, minimal amount of cracks, more then two white spots and was cloudy.
0.4% isophorone diisocyanate	Clear, minimal amount of cracks, one or two white spots and was not very cloudy
0.6% isophorone diisocyanate	Not clear, no cracks, one or two white spots and not cloudy

4.6.2 Differences in Molecular Weight of Samples with Varying Concentrations of Isophorone Diisocyanate

Figure 25 shows molecular weight of PLLA as a function of isophorone diisocyanate concentration. The graph shows the concentration of the antioxidant isophorone diisocyanate was not a significant factor in changing the molecular weight. As the concentrations increase from 0% to 0.6% on the left of the graph, the molecular weight fluctuates by approximately 170,000 g/Mole.

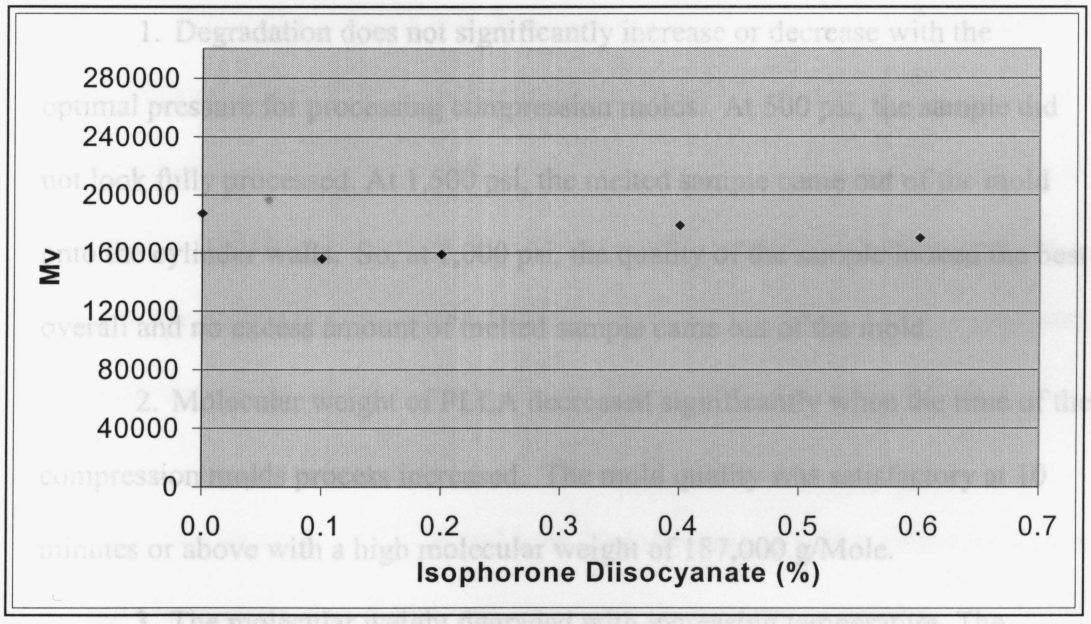

Figure 25. Variation of molecular weight of PLLA with percentage of isophorone diisocyanate.

CHAPTER V

CONCLUSIONS AND RECOMMENDATIONS FOR FURTHER STUDY

5.1 Conclusions

A study of effects of compression processing parameters and antioxidants on molecular degradation of biodegradable poly-L-lactide (PLLA) was performed. The following conclusions were found:

1. Degradation does not significantly increase or decrease with the optimal pressure for processing compression molds. At 500 psi, the sample did not look fully processed. At 1,500 psi, the melted sample came out of the mold onto the cylinder walls. So, at 1,000 psi, the quality of the sample looked the best overall and no excess amount of melted sample came out of the mold.

2. Molecular weight of PLLA decreased significantly when the time of the compression molds process increased. The mold quality was satisfactory at 10 minutes or above with a high molecular weight of 187,000 g/Mole.

3. The molecular weight degraded with increasing temperature. The compression molded PLLA sample at 190°C had a molecular weight above 300,000 g/Mole and went below 200,000 at 230 °C. The best quality sample was produced at 220 °C.

4. At 0.6% of concentration, antioxidants, 3-hydroxyanthranilic acid, Quercetin, 7,8-dihydroxy-6-methoxy-coumarin, (98%), tert-butylhydroquinone, isophorone diisocyanate, did not provide any benefits for PLLA in reducing

molecular degradation. (All samples with antioxidants showed lower molecular weight than pure PLLA.)

5. Ethanol used as a solvent helped even distribution of antioxidants in PLLA polymer. Their effects on molecular degradation of PLLA are not very significant, which may vary depending on the types of antioxidants used.

6. The effect of isophorone diisocyanate concentration on the molecular weight of PLLA did not prove to be significant.

5.2 Recommendations for Further Study

While this research was thoroughly planned, prepared, and executed, the conclusions show there is room for future research in this area. Samples that were created by adding PLLA and antioxidants together before processing should be tested to find the combination that will provide an acceptable mixture for the purpose of creating biodegradable medical implants. The chemistry, composition, and statistics of this mixture should also be further studied in such manners:

1. The basic structure of PLLA and how the molecular weight is found for a pure sample has been discovered with this research; however, a greater understanding of the chemistry of the PLLA, antioxidants, and ethanol needs to be understood. Free radicals that repel oxygen from PLLA and act as an antioxidant for biomaterials should be studied. How does ethanol affect the structure of PLLA or the antioxidants used?

2. Composition and interface of PLLA and antioxidants needs to be further investigated. Two distinct phases were seen in samples of PLLA and antioxidants. Does the composition of the samples effect the molecular weight? Are the samples being uniformly mixed and in turn combining all phases of the sample.
3. The research data needs to be further analyzed to provide statistical significance.

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