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ABSTRACT

DIMENSIONAL STABILITY OF DESAMINOTYROSYL POLYARYLATES

by

Kalsank Vaishali Pai

Synthetic polymers have found widespread usage and acceptance in various areas of the medical device industry. The recognition that no polymeric biomaterials are truly biocompatible has led to the search for bioerodible materials with desirable biological and physical properties for use as tissue engineering scaffolds and to enable in-vivo devices. Several methodologies have been tried and tested to invent the “ideal” biopolymer. The ideal polymeric biomaterial would be one that offers a favorable response at both the cellular and the systemic level with minimum alteration to its mechanical properties and chemistry. The systematic investigation of process-structure-property space to determine the technical limits of the polymer performance, focusing on dimensional stability, has been studied in depth. The purpose of this study is to apply the material science paradigm to the Kohn polymers to:

- Assess the relationship of processing history to dimensional stability of polymers.
- Develop characterization protocols relevant to in-vivo use.
- Produce samples of known structure to investigate biological response

The results of this study shows the origin of the shrinkage of the Poly(2,2) to be caused by water plasticizing the Tg from 85°C to less than 37°C under aqueous test condition while the Poly(12,10) shows long range order unaffected by 37°C water.
DIMENSIONAL STUDY OF DESAMINOTYROSYL POLYARYLATES

by
Kalsank Vaishali Pai

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This thesis is dedicated to my beloved parents, my sister: Anjali and my best friends: Nikita and Darshana and my fiancé, Sudhir.
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CHAPTER 1
INTRODUCTION

1.1 Brief Background on Biodegradable Polymers

For the last several decades efforts have been made to develop of biologically inert materials that are stable under physiological conditions. Polymeric biomaterials are synthetically derived or modified biological polymers designed for use in close proximity with biological systems. These materials have been considered for long-term applications such as artificial heart valves, bone replacements etc. In recent years, research efforts have been shifted to bioresorbable polymers. Bioerodable or bioresorbable polymers are, by definition, materials that are converted under physiological conditions into water soluble materials without regard for the specific mechanism involved in the erosion process. Such materials experienced mass loss of polymer matrix as a result of biological, physical or chemical effects. Biodegradation is a part of bioerosion. In most cases the polymer degrades rapidly via a hydrolytic mechanism and may proceed homogeneously throughout the bulk or heterogeneously at the surface of the polymer [5]. These are valuable for short-term applications that only require temporary implant presence, do not require surgical removal and circumvents long-term toxicity and safety problems. The earliest (since the 1970’s) and most successful application of bioresorbable polymers were as sutures (made of PLA, PGA). They have also been used as orthopedics fixation devices in the form of plates and screws, as surgical clips and staples in fracture fixation and ligament reconstruction, as temporary grafts and stents and as scaffolds for repair of tissues and organs. The use of these synthetic materials in long term implants may result in unwanted and abnormal cellular responses which may in turn trigger various
pathological conditions. This necessitates the need for a collection of materials with specific end-use properties.

One approach to such materials has been pioneered by Prof. J. Kohn of Rutgers University, New Brunswick. He has explored a combinatorial library of polymers with desirable surface and mechanical properties. These polymers are A-B type and prepared by co-polymerizing, fourteen different tyrosine derived diphenols and eight different aliphatic diacids, resulting in 112 distinct polymers. The combinatorial approach not only increased the number of available candidate materials for medical applications, but also, facilitates the identification of correlations between polymer structure and glass transition temperature, air-water contact angle, mechanical properties and fibroblast proliferation [2].

Each of the 112 polymers contained a range of properties that would define their end-use utility as well as processibility. They are based upon varying main chain and side chain chemistry [1]. The backbone is comprised of diphatic diacids with varying carbon atoms (C2 to C10) and the pendant chain or side chain was systematically varied by varying the number of methylene groups, by substituting oxygen for the methylene groups or by introducing aromatic structures into the side chain. These materials are alternating A-B type copolymers, where the diacid allows for variation in polymer backbone whereas the diphenols contain a moiety for appending and varying a pendant chain (Figure 1.1). The diphenol components selected were the desaminotyrosyl-tyrosine alkyl esters and the diacids include succinic, adipic, suberic and sebacic acid that contain two, four, four, six and eight methylene groups and the pendant chain lengths were going to be alterable resulting in structural flexibility.
Figure 1.1 Illustration shows the chemical structure of the Kohn polyarylate library, where ‘Y’ represents the number of methylene groups of the alkyl side chain, diphenol component and ‘R’ represents the number of methylene units of the aliphatic diacid. These compositions are referred to as Poly(R, Y), with the relative amide content decreasing as either R or Y increases.

Each of the diphenols were derived from one of the tyrosine esters and either desaminotyrosine or hydroxyphenyl acetic acid. So for simple nomenclature purposes, the polymers were denoted by a three letter code for the diphenol followed by the name of the diacid eg. Poly(DTE Succinate) which tells us that the polymer was prepared from desaminotyrosyl tyrosine ethyl ester and succinic acid. Molecular weights for the entire library of 112 polyarylates were high - ranging from 50,000 to 150,000 g/mol [1]. These polymers have been characterized using DSC, GPC to determine the thermal behavior and mechanical properties of the polymers. It was determined that the glass transition temperature of the 112 polymers varied from 2°C to 91°C with increments of 1°C, where
as the air-water contact angle ranged from 64° to 101° and increased at intervals of about 0.5°C (Figure 1.2).

![Glass Transition Temperature as a Function of Polymer Structure](image)

**Figure 1.2** Display of the Tg, glass transition temperature, of the Kohn library of polyarylates, as a function of polymer structure. Note the increase in Tg(1°C) with increase in the number of methylene groups. The range of Tg, would vary from 23°C to 89°C over the 112 variations available.

Studies have brought out the correlations between Tg, contact angle variability and changing polymer structure chemistry such as increasing number of methylene groups and the presence of oxygen in the pendant and backbone respectively and its effect on polymer flexibility [3]. The presence of methylene groups in the main chain was found to bring about an exponential drop in Tg and in contrast, an increase in the contact
angle (Figure 1.2). Oxygen substitution results in reduced surface hydrophobicity and hence, the corresponding polymers will have air-water contact angles subsequently (5°C –10°C) less than their counterparts without the presence of oxygen. In general, the polyarylate library encompasses a wide variety of mechanical properties [4]. However, there seemed to be no obvious correlation between polymer strength and stiffness. The stiffest polymer had mechanical properties similar to Poly(D, L Lactic acid) and the most flexible polymer resembled polysiloxanes in its properties. Certain material properties remained constant throughout the entire library such as ready solubility in organic solvents, decomposition temperatures above 300°C and are easily processible by solvent casting, compression molding and extrusion.

The main purpose to the development of tyrosine based polymers was to provide a wider choice in the availability of biodegradable polymers. The Kohn polyarylates or “pseudo”-poly aminoacids, as they are known, support fibroblast proliferation and are compatible in-vivo. Rate of fibroblast proliferation was observed to a function of the chemical structure rather than surface chemistry. Cell proliferation decreased as the contact angle increased from 65° to 100°. These polymers degraded gradually, with mass loss occurring over a period of several months.

A comparative study of the histological response of tyrosine derived polyarylates, polycarbonates and PLLA was evaluated as a function of their molecular weight rather than a fixed time frame since they differ in their individual degradation rates [8]. Poly (DTE Adipate) was found to degrade the fastest (upto 5% of its initial Mw within 296 days of implantation) and the slowest degrading material was found to be Poly(DTE carbonate, requiring 366 days to degrade upto 50% of its initial Mw. PLLA showed a
mixed response, starting with a rapid degradation rate and then declining gradually, it degraded to 15% of its initial weight after 570 days. The histological observations showed that Poly(DTE Adipate) remained compatible with the surrounding tissue during the entire degradation process, whereas, PLLA exhibited the most significant inflammatory response along with mass loss [2, 8].

Combinatorial libraries permit the systematic study of material-dependent biological responses and provide the medical device designer with the option to choose a suitable material from a library of related polymers that encompasses a broad range of properties. For such a comparison to be meaningful, however, polymers must be compared at equivalent states of organization, that is as a function of phase composition and molecular chain orientation (Figure 1.3). This is best achieved by studying the process-structure-property relationships of selected chemistries within the combinatorial library matrix, that is applying the material science paradigm to compositions of interest.

The study involves the characterization of some of members Kohn library using thermal analysis techniques [5]. Over the past decade, thermal analysis, TA, has emerged as the most commonly used technique for the characterization of polymers. Thermal analysis methods are well established and aid the understanding of thermal and chemical stability, phase transition temperatures and kinetics, rheology and molecular relaxation times. Conventional thermal analysis involves the monitoring of a material characteristic of interest as a function of temperature [11].
The advantages of thermal analysis as a technique include the large amount of information that can be obtained from relatively simple and fast experiments, coupled with the low cost and availability of TA instrumentation. Extensive studies document the effects of heating rate, measurement atmosphere, additives and isothermal effects as a function of time. While the interface chemistry between biological systems and synthetic materials at the surface is of paramount importance in determining the nature of subsequent cell growth, bulk properties and bulk property stability determine the efficacy of an in-vivo device over its lifetime.

**Figure 1.3** Process-Structure- Property relationship: Materials have 2 kinds of properties—bulk and surface, which may be completely independent of each other and dependent highly on the processing techniques. Ideal performance and development of specially designed medical products require a complete understanding of structure dependent material properties. (MDC lab, Jaffé, M.)
Bulk properties of interest include shrinkage, mechanical properties in tension, compression and shear, creep, fatigue and environmental stability of both chemistry and microstructure [9]. And transport phenomena of small molecules. Except for expensive and complex in-vitro or in-vivo conditioning followed by conventional testing methods, test methodologies for assessing such performance are largely undeveloped.

Surface property differs from bulk but of equal importance in defining the in-vivo utility of polymeric biomaterials [6]. The study of these bulk properties is a far from easy task and requires a close monitoring of structure-sensitive properties such as bulk density, tensile strength, reactivity. These properties vary with synthesis and process history such as polymer spinning, drawing, heat setting, texturing, and result in “fingerprinting” of the material. Thus, the control of these processes can be used to predetermine the range of the thermal and mechanical properties realized therein.
1.2 Processing

1.2.1 Melt Spinning

Melt spinning of fibers from selected members of the desaminotyrosyl polyarylate library allows the regular variation of polymer structure – molecular orientation, phase nature and phase interconnectivity in a well defined manner [5]. There are two phases common to most polymers – amorphous regions and crystalline regions. Orientation refers to the number of covalent backbone bonds that are parallel to the fiber axis [11]. Synthetic polymers have a random coil conformation at equilibrium and orienting the polymers means deforming this coil to a non-equilibrium state. Crystalline and amorphous regions often are in series and acquisition of information such as degree of crystallinity, number of crystalline units, interconnection between the crystalline and amorphous units is pertinent to a complete understanding of these occurrences.

The crystalline phase or measurement of orientation is difficult to determine and often requires techniques like D.S.C. or X-ray spectroscopy to quantify it. The uniqueness of fibers and films often lies in their high molecular orientation. Orientation does not necessarily encourage crystallization. It may give rise to two conflicting phenomenon – an entropy driven shrinkage and an energy driven crystallization. Both these occurrences can result during processing.

High stress processing also enhances the conditions for higher orientation. The fibers spun at lower speeds develop some orientation, which can result in significant shrinkage at temperatures above Tg [10]. Crystallizable polymers will crystallize faster at higher molecular orientation, often shifting the onset of shrinkage from Tg to the melting point, Tm. If the polymer does not crystallize, higher orientations would lead to higher
shrinkage at Tg. Thus, increase in processing speeds would increase the orientation. The macromolecular nature of fibers rather than their exact chemistry determines most of the responses of the fibers to various testing conditions [3].

The presence of polar functional groups may increase the tendency to be crystalline whereas the introduction of bulky monomer units into the structure hinders the development of crystallinity. For example, the amorphous nature of branched polyethylene is due to the additional polymer units intruding between the polymer chains that form a solid solution that is disordered, while linear polyethylene is highly crystalline (Figure 1.4). Processing techniques such as melt spinning, drawing of fibers, melt processing or solution molded films result in orientation and may impart crystallinity to the material depending upon its inherent microstructure. Oriented by mechanical stress such as stretching etc the resulting polymer would be optically anisotropic and the
refractive index would be different along the direction of stress [16]. Process speed such as high speed spinning or stretching increase the level of stress in the structure and induce what is known as stress crystallization in the structure of the polymer. The higher the speed, the higher the stress induced.

1.2.2 Shrinkage

The origin of fiber shrinkage lies in the deformed amorphous regions. The shrinkage of the material depends upon the molecular orientation and the amorphous content present. Basically, there are two components in the amorphous phase – oriented and non-oriented component [12]. The greater the orientation and the amount of amorphous phase, the greater the predominance of the oriented phase is seen and hence, also the greater the shrinkage occurs in these structures. The shrinkage property can be defined by the simple relationship.

\[ St = (1-X) Fa \]  

(1.1)

where \( Fa \) is the crystal fraction or amount of orientation, \( X \) is the crystalline fraction and therefore, the stronger a material is, the more prone it is to shrink. This relationship is, thus, useful in providing an overview in process limitations.

Determination of the amount of shrinkage is extremely important in defining the limit the end-use potential of the polymeric fibers. The shrinkage pattern of a material is highly dependent upon its process history. Thermal Mechanical Analysis (TMA) experiments are beneficial in providing greater insight to the melting pattern and shrinkage behavior of the polymeric material. The typical shrinkage of a semicrystalline, drawn fiber under conditions of zero load seemed to follow four distinct phases. The initial phase from RT to \( T_g \) would be characterized by small amounts of mass loss due to
moisture, or solvents that are present in the fiber structure [5]. This is followed by the rapid shrinkage due to the relaxation of oriented amorphous chains. In the region between Tg and Tm, irreversible shrinkage occurs due to the chain folding, reorganization, and recrystallization taking place.

The final phase takes place prior to sample failure due to melting of the crystalline units in the structure. This typical behavior is not prominent in all fibers and is highly dependent upon process history. The influence of spinning speed on the shrinkage behavior of as-spun PET yarn was studied [12]. It was demonstrated that there was an initial increase in shrinkage as the spinning speed increased followed by a decrease in shrinkage after Tg. Therefore, higher shrinkage resulted with greater orientation and as the crystalline nature of the polymer increased, the shrinkage became more and more stabilized. The need to understand and quantify the shrinkage phenomenon of any polymeric biomaterial prior to its use in applications is of paramount importance to ensure its successful implementation. Synthetic polymers such as, Nylon fibers need to be heat set while being processed to prevent changes in its thermal properties while in use.

1.2.3 Effect of Plasticizers

Plasticizers are substances that are added during polymer processing to improve processibility and flexibility of the polymers. Usually, when substance behaving like a plasticizer is added to a polymer it results in lowering of the melt viscosity and glass transition of the polymer [5]. Plasticizers could be added to the material from the environment such as moisture and bring about unexpected change. It can be typically seen in the effects of water in commercial Nylon. Thus, preventing it from being brittle at
lower temperatures. These property enhancers create a variety of uses and increase the area of application of the existing polymeric material. A number of requirements however need to be met before a substance can be used as a plasticizer such as the amount of the substance that should be added, the resulting effect it would create on the thermal and mechanical properties.

With respect to the biodegradable polymers in view here, it could be said that water behaves as a plasticizer and results in a similar outcome of properties in some of the members of the polyarylate library [2, 9]. It has been discussed that the water uptake by the tyrosine derived polyarylates and polycarbonates implants was negligible (limit of detection ± w/w), along with < 5% mass loss when studied in-vivo over a period of 200 days [3]. On the other hand, the PLLA implants resulted in 20-30% water uptake within a short period of time. The members of the Kohn library particularly, the ones in lower hierarchy in terms of the length of main chain and side chain components, were found to display similar results when tested in the presence of an aqueous environment or biorelevant conditions. The glass transition temperature or Tg dropped to below 37°C, showing a dramatic drop in stiffness and tensile strength, even at RT, due to their impending transition from the glassy into the rubbery state. The water molecules would attach themselves to the hydrophilic components of the polymer backbone and the amount of moisture uptake can be quantified by thermal analysis procedures such as TGA.
CHAPTER 2
EXPERIMENTAL

2.1 Polymers and Sample Prep

The polymers that were used in this study were supplied by Prof. J. Kohn (Rutgers University, New Brunswick) and AMD, Inc. The polymer samples were received in batches as powders or as fine pellets of specified molecular weight in quantities between 20 and 500 grams. They were carefully stored and prepared for processing. The polymers were processed into films and melt spun into fibers. This would impart different levels of orientation into the polymer. A powdered form of the polymer was heated in an oven at 120°C under vacuum for about eight hours to remove any traces of moisture that it might have absorbed. The vacuum dried, powdered sample was weighed and molded into 0.1 mm thick film. Films were compression molded at 175°C in a Carver press and hand drawn to stimulate fiber processing. After extrusion, the film was then rapidly quenched to prevent the induction of crystallinity into the film that impart haze and impede drawability [5]. This would also help to prevent or minimize any irregularities that might result from variability in thickness. Circular sample sizes, weighing approximately 2 gm were punched out and placed in aluminum pans and sealed in aluminum pans.

Fiber spinning provides a convenient form for defining the process-structure-property relationships of polymers. The differences between polyethylene fiber used for ballistic protection and polyethylene film used in trash bags are almost totally a function of process history. The typical fiber forming process has three stages: spinning, drawing and annealing [5]. The fibers were then stretched or drawn to increase molecular orientation. Annealing is the final stage of the fiber forming process that is performed at
constant length to maintain orientation. For example, liquid crystalline polymers are highly oriented as spun and only require an annealing step to perfect maintain its morphology.

The spinning process requires the polymer to be in melt or solution form. The liquid polymer is then forced through the tiny holes of a spinneret to form the fiber filaments. The spinneret hole diameter is usually much larger than the final fiber diameter that is required. Here, the polymers were supplied in pellet form by (AMD). Fiber was spun with a James plunger fed micro melt spinner, fitted with a single hole 750 µ diameter spinneret. Polymer was dried for 24 hours at 125°C and the barrel of the spinner was filled with about 45 grams of polymer under flowing nitrogen conditions. Spinning temperatures were about 70°C above Tg with take-up speed (typically in the range of about 25 to 125 m/min) adjusted to meet target diameter. Typical drawdowns varied from about 25 to about 200. Since most of the stretching occurs near the melting temperature, during spinning, it is an inefficient way to bring about fiber orientation. As-spun synthetic fibers often possess low levels of orientation and little crystallinity that may be different from the final product. For the development of sufficient end-use properties, further processing is required. This is done by stretching the fibers under conditions where significant orientation is achieved. The principal conditions that influence the amount of orientation or drawing imparted to be the fiber would be draw ratio, temperature and strain rate [22]. The main goal of the drawing process would be to increase the specific strength and modulus of the fiber. The higher the draw ratio, the higher the molecular orientation of the fiber. The final step in the fiber spinning process is annealing. Drawn yarns are usually stabilized by annealing either under constant length
or relaxation conditions. Diameters were measured with a Nikon optical microscope fitted with a 5X micrometer eyepiece and a 10X objective. Diameter distribution histograms represent more than 20 independent measurements.

Formation of films also involves a similar process including polymer delivery, film formation, solidification, and orientation and annealing. The two major differences between fiber and film lie in the scale and dimensionality of the product. Accurate control of the key spinning variables of stress and temperature allows the manipulation of fiber morphology, hence detailed control of structure from the nanoscale through the mesoscale.

The polyarylate combinatorial library, produced by Professor J. Kohn has been spun to determine the range of mechanical properties and dimension stability as a function of spinning conditions and backbone chemistry [4]. In general, all of the library polymers show systematic changes tensile modulus, tensile strength and shrinkage at a glass transition with increasing molecular chain orientation as expected from a series of amorphous polymers with of varying Tg. These film or fiber samples were then analyzed using DSC (TA instruments Q100 DSC, run at 20°C/min under flowing N2 from -50°C to about 25°C above highest transition temperature, cooled at 20°C/min to -50°C and reheated thought the highest temperature transition). The prepared polymer samples were tested under different temperature and rate heat/cool/heat cycles. Two different heating rates are used between 10°C/min and 30°C/min. The cooling rate being used is different from the heating rate. A faster cooling rate is used at the rate of 10°C/min in liquid nitrogen environment. Liquid nitrogen can create cooling conditions to about -70°C. The TA instrumentation allows us to run MDSC experiments on the provided samples to
quantitatively determine the phase transitions, reaction temperatures and associated kinetics. Polymer samples were characterized for moisture content and thermal stability by TGA (TA instruments Q50 TGA, run at 10°C/min under flowing N2 from RT to 250°C).

Fiber tensile properties were measured in the laboratories of Prof. Michael Dunn using previously published methods. Dynamic mechanical properties of fiber and film samples were monitored with a Rheometrics RSA11 fitted with fiber jaws and run under flowing at 10°C/min [12]. Fiber shrinkage was measured dry in a TA Instruments 2940 TMA fitted with fiber jaws, run at 10°C/min. Fiber load was adjusted to be as close to zero as possible. Wide-angle X-ray scattering (WAXS) patterns were obtained using a Siemens Hi-Star X-ray area detector with Cu Kα radiation wavelength 1.54 Å. The sample to detector distance was 60mm. These were provided courtesy Professor Jeng Wu.
2.2 Characterization

2.2.1 Aqueous Shrinkage

All polymers absorb water from the environment in the form of moisture. Depending upon polymer chemistry, the water may hydrolyses the polymer resulting in degradation of its structure. It may also bring about plasticization in the polymer, in the absence of any polymer-water reaction by lowering its Tg and various changes in its thermal and mechanical properties. A brief understanding of the effects of an aqueous environment on the behavior and characteristics of the polymer is essential. Since the polymers being studied here would be used in the manufacture of medical applications, the structural changes and reactions that might take place in the polymer under biorelevant conditions was tested ie. saline conditions at 37°C.

Polymer fibers of a fixed length (10 cm.) were mounted on light fishing floats and immersed in a controlled water bath maintained at 37°C. The length of the dry fiber and weight of the samples were measured at RT. The test samples were then soaked in salt/water solution consisting of 0.9% NaCl (99.5% pure), dissolved in deionised water, resembling the aqueous environment created by the biofluids surrounding the cells in the body. Immersion time was approximately 48 hours and the fiber samples were measured for dimension change at set point of 5 min, 15 min and 30 min. A control or reference sample was placed in the dessicator for the same period of time to compare any change in length of the test sample.

The Poly (DTE Succinate) 2,2 fibers were observed to increase in weight by about 1.3% as compared to the initial weight of the dry fiber. The fibers did not seem to retain their color and were slightly turbid in appearance. The Poly(2,2) is amorphous in nature
with dry Tg at 60°C. When placed in an aqueous environment, there is a rapid drop in Tg to below 37°C. The fiber also exhibits decrease in stiffness and presence of brittleness. But the most significant observation was the decrease in length (>50%) of the wet fiber samples after the 48 hour incubation period. The unexpected behavior of Poly(DTE Succinate) 2,2 of the polyarylate limits its usefulness and implementation capabilities.
2.3 Thermal Analysis

2.3.1 Differential Scanning Calorimeter

The Differential Scanning Calorimeter (DSC) measures the temperatures and heat flows associated with transitions in materials as a function of time and temperature. The technique provides qualitative information about physical and chemical changes that involve endothermic or exothermic processes or changes in heat capacity using minimal amounts of sample. It has many advantages including fast analysis time, typically thirty minutes, easy sample preparation, applicability to both liquids and solids, a wide range of temperature applicability and excellent quantitative capability. Some measurements the DSC makes are glass transition, melting and boiling points, crystallization time and temperature, thermal stability etc. [20]. This technique has been used in the evaluation of small transitions such as multiple phase transitions in liquid crystals and those due to side chains in polymers which cannot be resolved by most other techniques. It allows accurate determination of temperatures associated with thermal events. Temperature can be calibrated with respect to one or more standards which allows highly accurate, precise and reproducible values.

The D.S.C. reveals the thermal history imparted to thermoplastics as a result of different processing conditions [5]. The information generated can be used to vary heating rates to deliver the required degree of crystallinity. Heat evolved during cure can be related to the degree of cure in thermosetting materials. Percent conversion with time at a given temperature or for the same time under varying temperatures can be determined. Experiments can be carried out isothermally at temperatures of interest. DSC finds application in the pharmaceutical and health care industry as a means to determine
purity of highly pure chemicals. Presence of an impurity leads to a decrease in melting point, which can be related to percent purity. Water in oil emulsions can cause a decrease in melting point, which can be related to percent purity which can be evaluated by following the depression in freezing point of water. DSC is used to evaluate metal alloys and provide data required to prepare phase diagrams. Greases and lubricants can be evaluated in terms if the transitions of interest, glass transition, wax dissolution, polyethylene melt, soap melt and decomposition in a single run allowing the determination of use window measuring the areas under the different peaks can make qualitative analysis of the different constituents. Modulated Differential Scanning Calorimeter (MDSC) results from a slight variation in the series of events incurring in the conventional DSC experiments. The MDSC allows the separation of reversible and non-reversible equilibrium effects directly. This experimental set-up provided a more complete understanding of the processes involved in the cause and effect analysis of these complex materials.

The analysis is carried out on the samples in film or fiber form. The issues associated with fibers is the length and then again, whether, it should be maintained at constant length or FTS [5]. Differences in the melting response and melting temperature of constrained and unconstrained samples have been observed. The fiber length is constrained by fixing either ends to a fixture or some kind of restraining device. Fixed length fibers seemed to melt at a higher temperature due to the slow relaxation in molecular orientation and crystallization. Other factors that would effect the results of these melt experiments include draw ratio of the fiber, rate of sample heating and cooling and sample size. Films on the other hand are the most straightforward and convenient
form for any thermal analysis technique. The resulting responses of films are a strong function of local microstructure, molecular chain orientation and hence, reflects its total process history [20]. Therefore, the sample should be carefully handled to prevent any kind of deformation during sample preparation, as it would add to its process history.

The trace from a melt experiment shows three basic responses- response due to cold crystallization, melting and then, recrystallization [19]. Melting experiment provide a “complete picture” of the fiber structure. The complexity of the stress and thermal history influencing fiber processing are reflected in the traces of the experiment. Other observations include Tg or glass transition temperature, which is the temperature at which the oriented molecular chains gain enough energy to move and perhaps, form thermally induced crystals, Tm or the peak melting temperature, Tc or peak crystallization temperature, heat of fusion, heat of decomposition. The melting temperature is important since it determines the ultimate use temperature of the fiber and also defines conditions for maintaining fiber stability. Thus these experiments define the conditions for safe fiber usage and improve its ultimate performance.

2.3.1 Dynamic Mechanical Analysis (DMA)

Dynamic Mechanical Analysis is a common relaxation technique that is used to measure the mechanical properties of materials such as stiffness, viscoelasticity and energy dissipation etc. as they are deformed under periodic stress [5, 20]. Detailed information on the polymer microstructure such as crystallinity and orientation can be obtained as a function of variables like frequency, humidity, environment (presence of gases) etc. Polymeric materials, which are viscoelastic in nature, are subject to time, frequency and temperature effects in mechanical properties, which can be analyzed by this method.
The DMA can be used to analyze a wide variety of materials in different forms. It finds application in the research and development for the investigation of material structure, their development, selection for specific end-uses, comparative evaluations and material lifetime predictions. It is also used in Quality Control for process stimulation and optimization, incoming and in process material certification and troubleshooting. The DMA allows a quick comparison of material properties between two dissimilar or two similar materials processed differently. Since the samples can be tested in the form of bars, films, fibers and viscous liquid samples, the technique comes closest to the actual application envisaged and results therefore reflect the actual application.

This analysis can be carried out on fibers as well as films as thin as five microns. The process involves applying a sinusoidal stress to one end of the sample and measurement of the resultant stress produced at the other end [6]. Thus the tensile modulus of the sample can be calculated along with its components. The DMA tests carried out on films differ from fibers since a greater static stress is required to prevent the sample from buckling under the compressive stress that is applied.

Four major transitions can be observed in the DMA trace [25]. First, the glass transition, which is usually known as the \( \alpha \) transition. \( T_g \), or the glass transition temperature measured will be higher when compared to that measured by DSC. This is because most DMA tests are run at a standard frequency of 1Hz. Fiber orientation may cause an increase in temperature of the \( \alpha \) relaxation. The next transition phase is observed between \( T_g \) and \( T_m \), since it is at this temperature that the molecular chains gain sufficient mobility. The subsequent relaxations depend upon the cold crystallization and
secondary transitions that occur. They are often referred to as \( \beta, \gamma, \delta \) transitions etc. in the order of decreasing temperature.

In addition to dimensional mechanical analysis, other measurements include determination of stress-strain curves, creep, and stress relaxation. Anisotropy is an inherent property of films. The DMA can be used to study the anisotropy of polymeric films by cutting the samples in the direction of the stress. It was observed that the temperature of the \( \alpha \) relaxation phase increases with increase in orientation. Dynamic Mechanical Analysis tests have been used in the study of dynamic modulus in Nylon-66, PET etc.

2.3.2 Thermogravimetric Analysis (TGA)

Thermogravimetric analysis is a type of degradation study that is used to determine the chemical constitution of the material rather than the physical microstructure. The principle involved here is the continuous measurement of mass as a function of time and temperature [21]. The analysis is independent of material orientation- fiber or film. A plot of mass as a function of time or temperature would display the final result. The process involves heating of samples weighing typically about two mg at a standard rate of 10\(^\circ\)C/min. Some of the applications include polymer degradation studies to determine the upper temperature limit of use of the material, measurement of moisture or solvent content, measurement of degradation kinetics, studies of the influence of additives of fiber bends on relative thermal stability.
2.3.3 X-ray Diffraction (XRD)

X-ray Diffraction is perhaps the most widely used technique for characterizing the material. The sample is usually in a powdery form, consisting of fine grains of single crystalline material to be studied [5]. The technique is used also widely for studying particles in liquid suspensions or polycrystalline solids (bulk or thin film materials). The crystalline domains are randomly oriented in the sample. Therefore, when the 2-D diffraction pattern is recorded, it shows concentric rings of scattering peaks corresponding to the various d spacings in the crystal lattice. The positions and the intensities of the peaks are used for identifying the underlying structure (or phase) of the material. For example, the diffraction lines of graphite would be different from diamond even though they both are made of carbon atoms. This phase identification is important because the material properties are highly dependent on structure similar to that seen in the contrasting structures of graphite and diamond.
CHAPTER 3
RESULTS & DISCUSSION

3.1 Parameters of Study

In general, all of the library polymers show systematic change in tensile strength, tensile modulus and shrinkage at glass transition with increasing molecular chain orientation as expected from a series of amorphous polymers with varying Tg. The two members of the Kohn polyarylate library being studied here extensively are Poly(2,2) and Poly(12,10), since their exhibited properties were the extreme of the spectrum of polymers produced within the combinatorial library matrix.

To determine the entire array of responses to the in-vivo environmental conditions, the samples were tested under several areas of variability – such as presence of moisture, under biorelevant conditions (in saline at 37°C), annealing over a range of temperatures from approximately 40°C above to 40°C below the glass transition temperature.

This group of polyarylates were designed for their application in the manufacture of medical devices. With the growing use of synthetic polymers and implantable devices in the body, it is of extreme importance to study the behavior of these materials when placed in-vitro. For this purpose, the polymers are tested in environments resembling the aqueous medium and biofluids surrounding the physiological systems in the body. All biomaterials must, therefore, function in a biorelevant environment i.e. in aqueous saline at 37°C, and in the presence of proteins, cell as and other biological molecules. While the interface chemistry between biological systems and synthetic materials at the surface is of paramount importance in determining the nature of subsequent cell growth, bulk
properties and its efficacy determine the efficacy of an in-vivo device over its lifetime. It has also been seen that the interaction of polymers with the bulk properties differs from their effects on the surface properties which makes it very important to understand the behavior of these polymers under biorelevant conditions.
3.1 Observations and Analysis of Poly(2,2)

The results of the shrinkage experiments performed in 37°C water on fibers of the Poly(2,2) as a function of time are shown in Figure 3.1.

![Graph showing water shrinkage as a function of time for Poly(2,2)](image)

**Figure 3.1** Wet shrinkage of Poly(2,2) as a function of time. The shrinkage or loss of dimensional stability increased steadily with time when placed in water at 37°C.

The effect of draw down ratio on the structural conformation and loss of weight in Poly(2,2) was experimented upon. It was noted that greater fiber orientation resulting from increasing draw down ratios during melt spinning only caused the polymer to shrink more under biorelevant conditions.
Figure 3.2 shows a plot of one day 37°C shrinkage as a function of draw down as seen in Poly(2,2).

Figure 3.2 Shrinkage of Poly(2,2) melt spun fibers as a function of draw down is seen here. Ratios >1.7 showed a sharp increase and almost linear shrinkage response (upto 50%).

Experiments were then performed to determine the level of water absorbed by the Poly(2,2) fibers as a function of time. Thermogravimetric analysis (TGA) experiments, as shown in Figure 3.3, shows a comparative study of the water content picked-up by the fibers when tested at RT and in 37°C water over a fixed time scale (32 hours), while using a sample of fiber in vacuum as control.
It was observed that the fibers picked up about 3.2 % water when placed in water, while sitting in air at room humidity leads to absorption of about 1 % water.

**Figure 3.3** Comparative plot of increasing water content as seen in Poly(2,2) when tested under vacuum, RT and biorelevant conditions.

**Figure 3.4** Displays the effect of water content on the glass transition temperature of Poly(2,2).
The effect of water absorption on the glass transition temperature of Poly(2,2) as measured by DSC is shown in Figure 3.4. The dry Tg for Poly(2,2) was calculated to be around 85°C approx. The drop in the glass transition temperature to below 37°C as a result of water pick-up at RT and when immersed in water can be clearly seen in the DSC layout. Similar experiments were performed at varying water content by placing samples for various times in a 37°C. Figure 3.5 shows the reduction of Tg for Poly(2,2) as a function of water content, reaching the critical value of in-vivo temperature of 37°C at 3.2 %, close to the maximum moisture regain already noted.

![Graph showing relationship between Tg and water content](image)

**Figure 3.5** A plot of change in the Tg of Poly(2,2) with absorbed water is shown.

These results show conclusively that Poly(2,2) and similar compositions of the Polyarylate combinatorial matrix are highly plasticized by water, with Tg lowering by about −14°C per % of water.
As expected, the relaxation evidenced by the shrinkage was also observed in mechanical measurements, as evidence in the DMA results shown in Figure 3.6.

![Figure 3.6](image)

**Figure 3.6** Results of tensile testing as shown by dynamic mechanical analysis (DMA) carried out on Poly(2,2) are shown here.

The tensile modulus can be seen to decrease in Poly(2,2) as a function of temperature. The loss in tensile strength can be correlated with the drop in Tg with increasing water content. Results, however seem to differ on similar tests conducted on long range compositions such as the Poly(12,10). It is known that annealing at constant length can allow relaxation of highly strained chains while essentially processing average orientation levels. Annealing of oriented Poly(2,2) at about 100°C allowed the wet shrinkage to be reduced to less than 10%, hence stabilizing the structure.
3.3 Analysis and Observations of Poly(12,10)

In addition to detailed study on the short chain composition and members of the combinatorial polyarylates, extensive testing was also carried out on some polymers with long main chain and side chain structure. To obtain comparative results, thermal analysis tests were carried out on the Poly(12,10) to observe the response to the test conditions. The results from experiments carried out using TGA under biorelevant conditions showed that surprisingly, even after four days of soaking in water at 37°C.

The Poly(12,10) fibers, oriented fibers showed no evidence of shrinkage. The glass transition temperature in the Poly(12,10) did not change when tested under dry and wet conditions [12]. It was also shown that orientation of Poly(12,10) imparted during processing is stable at room temperature as evidenced by the plot of modulus versus spinline draw down shown in Figure 3.7

![Figure 3.7](image)

**Figure 3.7** A DMA trace of the tensile modulus versus draw down as seen in the Poly(12,10) and other large members of the group of polyarylates.
To obtain a better insight and understanding of the polymer microstructure, X-ray diffraction studies were carried out on the Poly(12,10) and Poly(2,2). The Poly(2,4), another short chain composition which showed great similarity in its behavior and structure to the Poly(2,2), was studied using X-ray diffraction. The Wide Angle X-ray Diffraction patterns of oriented fibers of Poly(2,4) (similar to Poly(2,2)) and Poly(12,10) are shown in Figure 3.8. These results indicate that Poly(12,10) has unexpected long-range order (crystallinity) that apparently stabilize the structure at RT and at 37°C in water.

**Figure 3.8** The WAXS pattern of an oriented Poly(12,10) fiber, with two symmetrical equatorial arcs suggesting a spacing of about 4°Å, and a pair of intense meridional streaks corresponding to a spacing of about 29°Å, which is the length of the Poly(12,10) monomer unit.

This interpretation is confirmed by the DSC melting endotherms shown in Figure 3.9. When melt experiments were carried out on Poly(12,10) and it was heated to about 40°C above its glass transition temperature, it was seen to melt as seen by the melting
peak. After allowing it to cool and then on reheating it was observed to produce a crystalline peak (Tc) followed by several secondary transitions before the melting reoccurred. The glass transition temperature remained stable at about 15°C and did not shift.

![Figure 3.9](image_url)

**Figure 3.9** The effect of the melt DSC trace of Poly(12,10) under H-C-H conditions as a function of temperature.

Annealing studies show that the Poly(12,10) can be stabilized even further to elevated temperature changes as observed in Figure 3.10. It is observed that annealing produces a gradual shift in the Tp from 56.4°C to approximately 79.2°C when heating over a constant temperature range of 40°C to 70°C for one hour.
A histogram displaying the increasing trend in Tp is shown in Figure 3.11. Several pre-melt endotherms of varying sizes are also present and are influenced by process history and are independent of the temperature or heating rate of the experiment. Notice that the Tg remains stable and does not change.

Figure 3.10 The results of an annealing experiment carried out on the Poly(12,10) sample.
While not fully explaining all the stability of these polymers, it is clear that the stability is linked to the unexpected long-range order of the Poly(12,10) which is not seen in the compositions at the other end of the spectrum.

**Figure 3.11** A histogram displaying a plot of $T_p$ versus the Tanneal.

Further experiments and investigations are necessary to fully define the structure observed and understand the behavior and dimensional stability of Poly(2,2) and Poly(12,10).
CHAPTER 4
CONCLUSION

4.1 Structural Conformation

The diverse response of the compositions, although classified under the same polyarylate family, has not been completely understood. It is perceived to be a function of their microstructure and composition. A careful examination of the process-structure-property space of two unusual compositions desaminotyrosyl based polyarylate library The important findings are the strong plasticization effects noted for compositions with small values of R and Y and the long range order which stabilizes oriented structures in compositions with large values of R and Y. It is expected that many polymeric biomaterials with complex backbone geometries and stereochemical variations possible in the backbone will prove equally amenable to performance control through morphological manipulation.

These materials were found to exhibit process memory which influenced its microstructure, thus, depending upon spinning speed, annealing temperature, environmental condition either the polymer becomes more amorphous or more crystalline. The greater the crystallinity the greater the orientation and hence, the material exhibits more functionality. Most of the compositions with large structures, similar to the Poly(12,10), have been shown to have Tg’s below RT and relatively stable when tested under biorelevant conditions, rendering them useful for potential biomedical applications. The long range order and stability of the Poly(12,10) is characteristic of mesogenic liquid crystal polymers. All L.C.P.’s composed of stiff, highly aromatic molecules and are characterized by very high molecular orientation in the solid state. The WAXS pattern
when coupled with the low heat of fusion and low temperature transitions suggest that the Poly(12,10) possesses a highly layered mesogenic structure, with layering similar to that of a smectic or discotic crystal. The experiments and response of the Poly(2,2) under biorelevant conditions have proven them to be a less than ideal candidate for in-vivo applications unless their chemistry is altered making them more crystalline in nature. The effect of water plasticization is observed to be enhanced in members with fewer methylene groups in their structure presumably due to a backbone amide moiety and change in polymer flexibility. Both inter and intramolecular amide hydrogen bonds with water and differing bound water species were observed. Also, in the smaller compositions due to the short length of the backbone and pendant chain, the relative amide concentration/molecule increases as compared with the polyarylates with longer diacid-diphenol components and the effect of water on commercial polyester amides is well known. Thus, with increasing structural flexibility, the absolute value of the plasticization effect to bring Tg below 37°C is also reduced.

Processing techniques to bring about structural changes in the lower compositions or annealing methods to stabilize the glass transition temperature under biorelevant conditions and hence, increase they end-use applicability. Careful examination of the structure-process-property space of the desaminotyrosyl based polyarylate library has shown these polymers to be rich in process and performance options and significantly broader in potential than previously envisioned. Experiments to define the impact of these supramolecular features of histological responses such as cell attachment, tissue growth and drug delivery are currently underway.
4.2 Scope for the Future

Metals, various synthetic plastics such as Dacron, Teflon etc continue to be the most widely used raw materials for the design of medical devices. These biostable implant materials lack the molecular sequences and patterns crucial to normal cell function and often trigger aberrant cell responses upon long term implantation. The choice of synthetic degradation polymers is also very limited. The systematic study of material-dependent biological responded and the optimization of medical device performance necessitates a collection of materials exhibiting gradations in physicomechanical, chemical or biological properties.

These new found collection of polymeric biomaterials show promising responses to the characterization of specific materials to be used for the purpose of medical applications both in-vivo and in-vitro. The members of this family of polymers show distinct similarities in chemical structure and mechanical properties. Poly(DTE Carbonate) seemed to be the strongest among those investigated. Long term effects and degradation studies are hindered due to the longevity issue of the animal models.

The effect of various sterilization techniques such as ethylene oxide and gamma radiation on these polymers, its interaction with the existing mechanical properties and cell growth, is a matter the remains to be looked into. The polymer can either recombine into its original configuration, or if cross-scission occurs, a large three-dimensional matrix is formed and the polymer is strengthened. This post irradiation effects need to be studied because a polypropylene component may appear acceptable today, but may shatter in a couple of years due to the presence to trapped free radicals, gases etc.
A brief study of the physical degradation properties of these pseudo-poly(amino acids) was conducted. It was assumed that the length of the pendant side chain would greatly effect the ageing behavior of these materials. Comparative studies of the degradation behavior of three different types of polymeric biomaterials were studied, namely, poly(amino acids), poly(carbonates) and PLLA. Poly(DTE Adipate) consistently elicited the mildest tissue response, as judged by the lack of cellularity of the fibrous capsule formed around the implant. It also exhibited the fastest degradation rate, losing up to 5% of its initial molecular weight in less than 300 days.

Currently, bone fixation devices made of poly(glycolic acid) and polydioxanone are in clinical use. Poly(lactic acid) has also been widely investigated and has been found to be biocompatible in short-term applications. The main drawback in the polymeric biomaterials like PLA, PGA and other poly-hydroxy esters, being used is the release of degradation products that effect biocompatibility. Unlike these polymers, however, these polyarylates have favorable mechanical properties, are readily processible, and are based on natural metabolites. Bone biocompatibility studies have shown that the tissue proliferation and bone in growth into the PLA chambers decreased to less than half during a period of 24 weeks. Histological analysis of bone implant interface also revealed a fundamental difference in the response to PLA and polyarylates. By one month, a thick collarbone had formed around the implants and the evidence of fibrous tissue formation or a material mediated inflammatory response was largely absent. Studies have proved that the cellular response to a polymeric scaffold can be influenced by slight variations in the material substrate. The cellular response to incremental polymer structure variations was experimented upon. The increase in air-water contact angle with increase in the
length of the pendant chain from 73°C to 90°C. For example, pure polystyrene has an air-
water contact angle in the range of 40° – 60° and supports the attachment and growth of a
wide variety of cell types. Thus, this group of materials showed the ability to tailor
cellular responses with well-controlled structure alterations in the tyrosine-derived
polymer systems.

The combinatorial polyarylate library is a very attractive and promising group of
materials. With further detailed investigations into property and structures and controlled
processing techniques, the stage would be set for a new phase in the world of biomedical
applications.
REFERENCES


