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Polyurethane as a Biodegradable Polymer

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I. INTRODUCTION

Developments in science and technology, especially over the last two decades, have led to a significant increase in the global production of synthetic polymers. Annually, approximately 140 million tonnes of synthetic polymers are manufactured.[1]

In the United States, synthetic polymers make up an estimated 20% of municipal solid waste by volume. A similar situation is observed in Germany. In Australia, approximately 25% of the total household waste ends up in municipal landfill sites.[2]

Synthetic polymers are known to be significant contributors to solid waste pollution in the environment. Another issue is the disposal of plastic waste from agriculture. Since 1990, the plastic industry has invested $1 billion to support increased recycling and to educate communities. The recent inclusion of biological waste treatment (such as composting and gasification) in an integrated approach to solid waste management has led to a growing commercial interest in developing biodegradable materials for consumer products.[3]

Renewable resource feedstocks include microbial-grown polymers and those extracted from starch and its derivatives. These materials can be reinforced with natural fibers from plants such as flax, jute, hemp, and other cellulose. Biodegradable plastics are environmentally friendly because they can be produced from renewable feedstocks, thus reducing greenhouse gas emissions. For example, polyhydroxyalkanoates (PHA) and lactic acid (raw materials for PLA, polylactic acid) can be formed through fermentative biotechnological processes using agricultural products and microorganisms. Some petroleum-based plastics can also be degraded by biological processes. For example, aliphatic polyesters such as PCL and PBS can be degraded with enzymes and microorganisms.

Polymers like these are typically created by reacting a diisocyanate with a polyol. The polyols used are usually polyethers or polyesters. The resulting polymers are segmented block copolymers, with the polyol segment providing a soft segment with a low glass transition temperature (<25°C), and the diisocyanate component, often combined with a hydrocarbon chain extender, providing the hard segment. [8]

The understanding of how polyurethane breaks down and its reliance on the polyurethane's structure and composition has resulted in the creation of biodegradable polyurethanes for various tissueengineering purposes, including meniscal reconstruction, myocardial repair, and vascular tissues. Designing biodegradable polyurethanes involves using different diisocyanate compounds, as the traditional aromatic diisocyanates are considered to be potentially carcinogenic compounds. [9]

In the 1990s, tissue engineering emerged as a potential technique for repairing and regenerating damaged and diseased biological tissues. This led to a need for new biodegradable materials to advance the technology towards clinically useful products and therapies. Early investigations utilized biodegradable polymers such as poly(glycolide)s, poly(lactide)s, and their copolymers, which have a long history of clinical use, despite not being optimal for most tissue engineering applications [7].

POLYURETHANE CHEMISTRY

The chemical reaction between an isocyanate group and a hydroxyl or amine group generates urethane and urea groups, respectively. This reaction has been used to synthesize a range of thermoplastic polyurethanes (TPUs) and thermoset polyurethanes (TSPs). TPUs are prepared by reacting three compounds: a diisocyanate, a difunctional polyol (macrodiol), and a dihydroxy or diamine chain extender.[10]

The monomers combine to create linear, segmented copolymers with alternating "hard" and "soft" segment blocks, which are key structural

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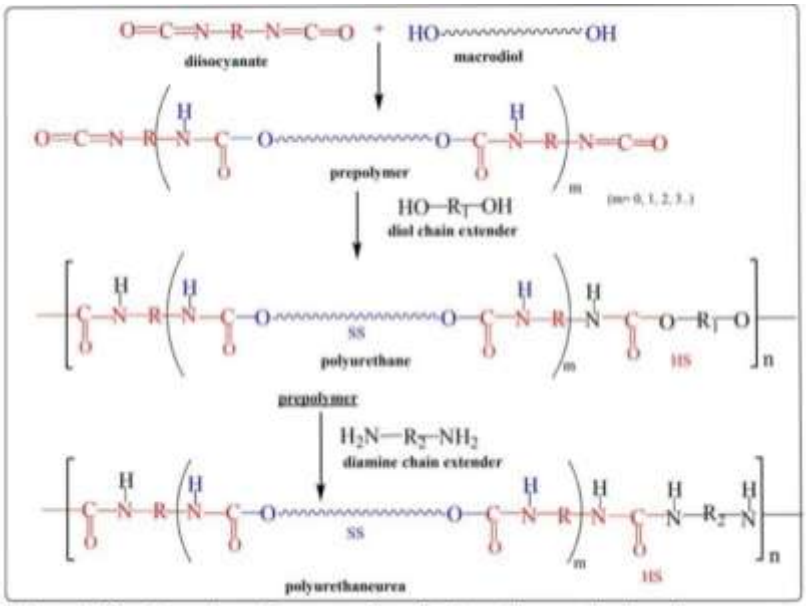
features of TPUs. The hard segment (HS) comes from the reaction of a diisocyanate with a chain extender, while the soft segment (SS) is derived from a longchain linear diol (macro diol or polyol). The general chemical structure of a TPU is shown in Scheme 1. Due to the thermodynamic incompatibility of soft and hard segments, polyurethanes display a twophase morphology, with the respective segments aggregating to form microdomains. HS domains form ordered structures, while the SS domains, with some exceptions, are generally amorphous. The relative compatibility of the two segments determines the morphology and thus the properties of polyurethanes; a highly phase-separated TPU generally exhibits poor mechanical properties [10, 11].



Scheme 1. Reaction scheme for preparation of polyurethane and polyurethane urea

The use of one or more tri- or higher-functional polyols, isocyanates, or chain extenders in a polyurethane formulation creates cross-linked TSPs, and this approach has been primarily used in the manufacturing of industrial PU foam.[12]

The reaction between the isocyanate and hydroxyl groups is exothermic. Catalysts such as organometallic compounds and tertiary amines increase the reaction rate. On the other hand, the reaction of the isocyanate group with a primary amine group is extremely fast, typically 1000 times faster than that with hydroxyl. Often, the reaction is carried out at low temperatures or in solvents to control the reaction exotherm. The polymerization proceeds via a step-growth polymerization mechanism, and many excellent textbooks and review articles provide detailed information on the steps to follow to synthesize high molecular-weight polyurethanes (10, 11).

The one-step batch synthesis of TPUs involves reacting a mixture of pre-dried macrodiol and the chain extender with the diisocyanate in the presence of a catalyst. Typically, the reaction is catalyzed with dibutyltin dilaurate, stannous octoate, or amine catalysts and is exothermic. The reagents are usually mixed between 70 and 80 degrees. This "one-step" reaction can also be conducted using special continuous mixing machines, reactive extruders, or continuous injection molding machines.

PROCESSING AND FABRICATION

Many of the papers on biodegradable polyurethanes reported in the literature have Described different techniques to fabricate porous scaffolds for implantation and Evaluation for tissue engineering applications. These techniques include salt Leaching/polymer coagulation. [14]

The TIPS method involves the dissolution of the polymer in a suitable solvent, Placing it in a mold and quenching to very low temperatures to phase separate and Freeze the solvent. Typically, liquid nitrogen or dry ice/acetone is Required for Quenching depending on the freezing point of the solvent. After removing the mold, The solid is placed in absolute alcohol at -20°C for an extended

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period to Extract the solvent. The type of solvent, the polymer concentration, and the rate of cooling Influence porosity, pore size, and geometry. Figure 1 shows electron micrographs of Scaffolds prepared by the TIPS method under different conditions. The PEUU in this case Was prepared from BDI, PEG-b-PCL- b-PEG polyol, and BDA. [15]

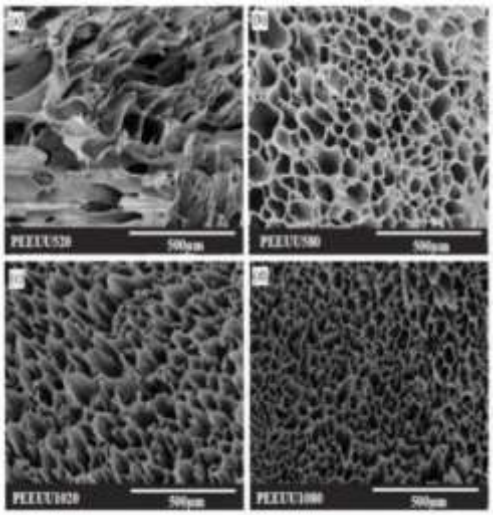

Fig. 1. Electron micrographs of PEUU scaffolds (longitudinal cross sections) prepared From different PEUU solution concentrations and quenching temperatures (a) 5%, -20°C (b) 5%, -80°C (c) 10%, -20°C (d) 10%, -80°C. (Reprinted from Biomaterials 2005, 26, 3961-3971; Guan, J.; Fujimoto, K. L.; Sacks, M. S.; Wagner, W. R.; with Permission from Elsevier)

Electrospinning is a well-established process used to create fibers with diameters in the nanoscale or submicron scale. This method has been utilized to produce nanofiber scaffolds from various synthetic polymers, such as poly(lactic acid), poly(glycolic acid), poly(ε-caprolactone), poly(hydroxybutyrate), and their blends [16].

The process utilizes the electrostatic attraction between a charged polymer and a grounded or oppositely charged collection plate within an electric field. The polymer droplets in the electric field will extend into a cone before elongating into a fine jet. In a typical laboratory process (Figure 2), the polymer, dissolved in a solvent or melted form, is pumped through a thin nozzle with an inner diameter on the order of 100 µm. The nozzle serves as an electrode, and a high electric field of 100-500 kV/m is applied to it with a counter electrode placed at a distance of 10 to 25 cm from the nozzle. Electrospun fibers are collected on a substrate to which the counter electrode is in contact. The shape and size of fibers formed in this process are governed by many parameters. The polymer molecular weight, polydispersity, glass transition temperature, solution viscosity, and concentrations are a few of those parameters.

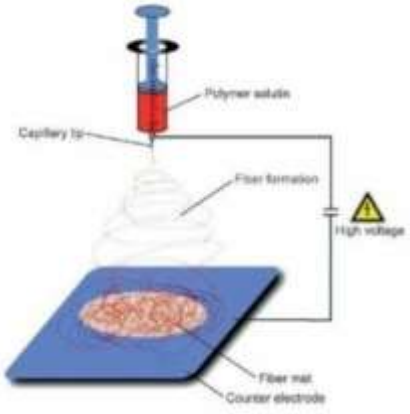

fig. 2. A laboratory set up for an electrospinning experiment with a perpendicular arrangement of electrodes. (greiner, a. and wendorff, j. h. electrospinning: a fascinating method for the preparation of ultrathin fibers. angew. Chem. int. ed. 2007, 46, 5670-5703. copyright wiley-vch verlag & co kgaa. reprinted with permission)

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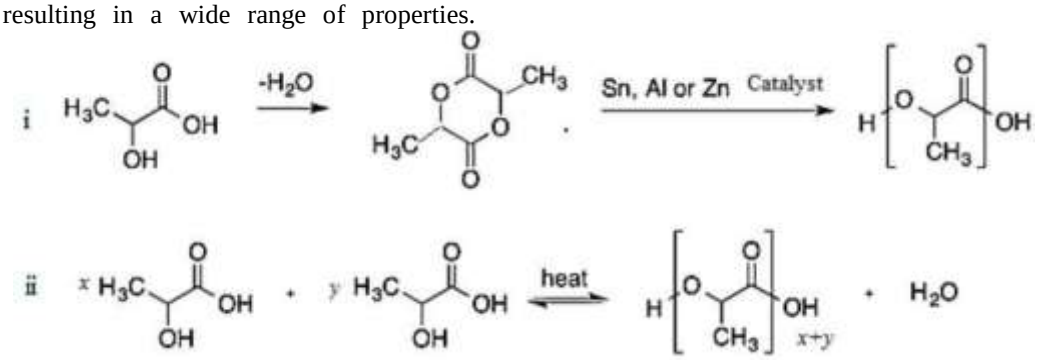
These studies not only demonstrate the application of electrospinning to create scaffolds with nanoscale fibers of varying pore size and porosity from biodegradable polyurethanes but also show techniques for incorporating various bioactive additives during fabrication.

SYNTHESIS

Biodegradable polymers called polyesters are widely studied and used. They can be made in several ways, including direct condensation of alcohols and acids, ring-opening polymerization (ROP), and metal-catalyzed polymerization reactions. A drawback of the step-wise condensation method is the need to constantly remove water to drive the reaction forward, which can lead to harsh conditions and long reaction times, resulting in a wide range of properties. Different starting materials can be used to make polyesters, and each type of monomer gives the final polymer unique characteristics and properties.ROP of cyclic dimeric glycolic or lactic acid forms α-hydroxy acids, which then polymerize to form poly-(α-esters). Organometallic initiators like tin, zinc, and aluminum complexes can be used to start the polymerization of polyesters. Tin (II) octanoate is a common initiator and has been accepted as a food additive by the U.S. FDA, but there are concerns about using tin catalysts in making biodegradable polymers for medical purposes. Poly (β-esters) and poly (γ-esters) can be made using ROP or condensation methods similar to poly (α-esters). Researchers are also looking into metal-free processes that use bacterial or enzymatic catalysis to make polyesters…..



Example of ways to formation of polyester using lactic acid.

a) condensation of lactic acid into dimeric lactide followed by ring-opening polymerization to form polylactic acid.
b) direct condensation of lactic acid, signifying the need to continuously remove water from the system to drive the reaction forward.

POLYURETHAN STRUCTURE-PROPERTY RELATIONSHIPS

The chemical structure of the diisocyanate, polyol, and chain extender, as well as the relative proportions of these components in the polyurethane, determine its mechanical properties, processability, and biodegradation. Only a limited number of suitable diisocyanates are commercially available for the formulation of biodegradable polyurethanes.

Many review articles and textbooks are available on the structure-property relationships of polyurethanes based on aromatic diisocyanates such as MDI and common polyether and polyester polyols. [9,10,18,19]

The studies have provided a good understanding of the relationship between the chemical structures of monomers forming hard and soft segments in polyurethanes, and their mechanical properties and morphology. This knowledge has been used in formulating biodegradable polyurethanes, with a focus on precursors that produce non-toxic degradation products. However, there have been only a few systematic investigations to understand the structure-property relationships of biodegradable polyurethanes [20,21].

1. Hard Segment

The chemical structure of the diisocyanate and the chain extender that forms the HS of PU have a significant influence on PU morphology and mechanical properties. HDI is the most widely chosen diisocyanate in formulating biodegradable polyurethanes. The commercial availability and relative non-toxic nature [22] of the corresponding diamine 1,6-hexane diamine, which is the by-product of polyurethane degradation, may be the main reasons for its choice. BDI is also another

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aliphatic diisocyanate used in the synthesis of biodegradable polyurethanes. The symmetrical molecular structures of these two diisocyanates lead to better ordering of the hard segment through intermolecular hydrogen bonding, resulting in high-strength elastomers. Elastomers with ultimate tensile strength up to 60 MPa and elongation up to 950% have been reported for HDI-based polyurethanes [23].

Diisocyanates with non-linear structures, such as CHDI and IPDI, have also been used in synthesizing biodegradable polyurethanes, although to a much lesser extent. Due to the less flexible backbone structure resulting from cyclohexane rings, these diisocyanates generally produce stiffer materials compared to their linear analogs. Polyurethanes based on aliphatic diisocyanates 1,3 and 1,4bis(isocyanatomethyl)cyclohexane exhibit excellent mechanical properties and dynamic viscoelastic properties compared to those based on other aliphatic diisocyanates, such as IPDI and HMDI, as reported by Xie et al. [24].

The polyurethanes prepared from 1,3 and 1,4-Bis(isocyanate methyl) cyclohexane, ε-PCL-diol, and BDO exhibited a tensile strength of 50 MPa at 35% hard segment. In contrast, the corresponding polyurethane prepared from H12MDI only showed a tensile strength of 16.8 MPa. Polyurethanes based on 1,3 and 1,4-Bis(isocyanate methyl) cyclohexane also demonstrated higher elongation, compression set, and Shore hardness compared to those based on H12MDI. Additionally, elastomers based on 1,3 and 1,4-bis(isocyanate methyl) cyclohexane displayed superior dynamic performance, characterized by constant modulus values over a wider working temperature range, lower than δ values, high softening temperature, and higher critical point temperature. The property difference was less significant for polyurethane ureas prepared from 1,3 and 1,4-bis(isocyanate methyl) cyclohexane, H12MDI, and IPDI with caprolactone and Ethacure 100 chain extender. At 20% hard segment, the tensile strength of PUU from all three diisocyanates was in the range of 36-37 MPa (Hettrich et al. [24]).

2. Soft Segment

The chemical structure of the polyol (macrodiol) that forms the SS influences the properties of polyurethanes, particularly the degradation rate. Many studies in the literature have exploited this aspect in designing polyurethanes for specific applications. Common polyols used in formulating biodegradable polyurethanes include poly(ε-caprolactone), poly(ethylene glycol), poly(propylene glycol), polyols based on hydroxy acids such as glycolic acid, lactic acid, and their copolymers, and poly(3-hydroxybutyrate)diols (see Table 2). Poly(caprolactone) diol is arguably the most widely investigated polyol in biodegradable polyurethanes and generally produces polyurethanes with good elastomeric properties due to its low glass transition temperature Tg (-60°C).

The impact of ε-PCL-diol molecular weight on polyurethane properties was studied by Heijkants et al. [25]. They achieved this by creating a series of polyurethanes with uniform-size hard segment lengths based on BDI and BDO. The ε-PCL-diol molecular weights ranged from 750 to 2800 Da, and the polyurethanes were synthesized using a two-step procedure without the use of a catalyst. The tensile strength gradually increased from 38.7 MPa for PCL-750 to 55 MPa for PCL-1900, while the elongation at break increased from 870% to 1173%. Polyurethanes based on PCL molecular weights of 1600 Da and lower exhibited crystalline urethane and amorphous PCL phases with some dispersed hard segments. In polyurethane with PCL molecular weights higher than 1600 Da, an additional crystalline phase was observed. This study illustrates that polyurethane with good mechanical properties can be prepared from ε-PCL-diol, and the choice of its molecular weight has an influence on the morphology [25,26].

DESIGNING BIODEGRADABLE POLYURETHANES FOR BIOMEDICAL APPLICATIONS

1. Cardiovascular applications

Biodegradable materials with good biocompatibility, elasticity, and high tensile strength are needed to create scaffolds for cardiovascular tissue engineering. Biodegradable polyurethanes with these properties have been developed using polyols such as poly(caprolactone), PEG, and their copolymers, along with diisocyanates ELDI, HDI, and BDI, and chain extenders BDO, 1,4-BDA, and 1,3-BDA. The low Tg of PCL (-60°C) gives elastomeric properties to the PUU, and adding PEG makes it more hydrophilic and affects the degradation rate. Gorna et al. [27] studied the synthesis and properties of a series of polyurethanes based on PCL/PEG, HDI/IPDI, and chain extenders BDO and 2-amino-1butanol to alter the hydrophilic-

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hydrophobic ratio. The tensile strength of the PU ranged from 4 to 60 MPa, while the elongation at break varied from 100 to 950%. Protein absorption was highest with PUs based on PCL, and no protein absorption was observed with those based on the PCL/PEG combination, regardless of the PEG molecular weight. Guan et al. [28]

An elastomeric, biodegradable porous (85%) cardiac patch was created using a biodegradable PUU made from BDI, BDA, and ε-PCL-diol 2000 through the thermally induced phase separation technique. Surgical defects in the right ventricular outflow tract of adult rats were implanted with PUU patches along with poly(tetrafluoroethylene) (PTFE) patches (control) and then removed after 4, 8, and 12 weeks. After 4 weeks, fibroblast in-growth into the PUU patch was observed, and cellular infiltration of the implant increased over time. The control PTFE patch exhibited no cellular in-growth and elicited a foreign body reaction. By 12 weeks, the PUU patch had completely degraded. The same authors studied the effectiveness of the PUU cardiac patch in promoting vascular remodeling and improving function by implanting the patch onto subacute infarcts in Lewis rats [29]. Additionally, the incorporation of growth factors to improve cell growth has been explored with biodegradable polyurethanes. A PUU based on BDI, ε-PCL-diol 2000, and an amino acid-based chain extender with H-Ala-Ala-Lys-OH was electrospun to form a fibrous scaffold with good mechanical strength (up to 11.1 MPa UTS) and elasticity (up to 88%). Insulin-like growth factor (IGF-1) encapsulated in PLGA microparticles was electrospray onto the scaffold. The growth of mesenchymal stem cells was significantly higher on scaffolds with IGF-1. In another study, basic fibroblast growth factor (bFGF) was incorporated into scaffolds prepared from polyurethanes based on BDI/PCL200/BDA. [30].

The ability to create biodegradable polyurethanes with mechanical properties that comply with cardiovascular tissues, and then fabricate them into porous scaffolds with good mechanical properties and high porosity, as well as incorporating biological agents to enhance cell growth and proliferation, makes this class of biodegradable polymers attractive for cardiovascular tissue engineering applications.

2. Musculoskeletal application

Biodegradable polyurethanes are a type of synthetic polymers used to create scaffolds for regenerating cartilage and bone. Many studies have been conducted to design, synthesize, and evaluate polyurethanes for these applications. Grad et al. [31] studied porous polyurethane scaffolds made from HDI, ε-PCL, and isosorbide diol to assess their suitability for supporting the attachment and proliferation of primary chondrocytes in vitro. The study showed that the scaffolds supported chondrocyte attachment and the production of extracellular matrix proteins, but one limitation was the diffusion of large amounts of matrix molecules into the culture medium. The scaffold's favorable mechanical properties may help provide mechanical stimulation to develop a functional cartilage-like extracellular matrix. Field et al. [32]

Polyurethane based on MDI, ε-PCL-diol (530 Da) and 1,3-PDA have been evaluated for use in fabricating yarns for anterior cruciate ligament (ACL) reconstruction. The fibers prepared using a wetspinning process, were found to be strong and stiff, retaining 50% of their original tensile strength for more than 9 months at body temperature. This material, trade-named Artelon, is commercialized by Artimplant AB in Gothenburg, Sweden, and has received CE Mark and FDA approval. Artelon films were observed to have an equal or lower ability to activate human mononuclear cells in vitro compared to titanium or polystyrene. In vivo studies with rabbits and mini pigs to test biocompatibility and safety have been reported [33].

Biodegradable scaffolds made from polyurethanes have been studied for use in knee-joint meniscus treatment. Early studies looked at MDI-based polyurethanes for healing meniscal lesions, but there were concerns about potential toxicity from the degradation product MDA. To address this issue, researchers have developed polyurethanes using aliphatic diisocyanate BDI, poly(ε-caprolactone-co-llactic acid) diol, and 1,4-BDA or 1,4-BDO for cartilage tissue regeneration. These polyurethane ureas were prepared using a salt leaching/freeze-drying technique, resulting in scaffolds with interconnected pores (150 to 300 microns) and a modulus of 200 kPa, which are suitable for fibrocartilage regeneration. [34]

Spaans et al. evaluated micro-porous polyurethane amide and polyurethane-urea scaffolds for repairing and replacing knee-joint meniscus. These polyurethanes used a 50/50 l-lactide/PCL polyol for the SS and BDI, adipic acid, and water for the HS. The reaction of water with BDI releases carbon dioxide to create a porous structure. By adding surfactant and exposing the

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mixture to ultrasonic waves, they were able to control the pore size and structure. Using this technique, they prepared scaffolds with 70 to 80% porosity. [35]

The study evaluated the impact of varying chemical composition and hydrophilic to hydrophobic ratio on bone growth. This was done by creating a range of polyurethanes using HDI, ε-PCl-diol, and pluronics. Porous scaffolds made from these polyurethanes were placed in monocortical defects in the iliac crest of healthy sheep for 6 months. The defect sites showed varying degrees of healing with cancellous bone, and the calcium-to-phosphate ratio was similar to that of healthy cancellous bone. It was observed that the more hydrophilic implants exhibited a higher mineral content in the new bone compared to the more hydrophobic implants. There was no cortex formation for any of the implants; instead, a soft tissue layer grew over the surface of the defect. In a separate study, scaffolds containing a calcium-complexing agent (citric acid) were implanted in estrogen-deficient sheep for 18-25 months, and they promoted the highest bone regeneration. [36]

3. Nerve regeneration

Scaffolds for nerve regeneration are tubular structures that guide regenerating axons to the distal nerve stump. Nerve guides based on biodegradable polymers with built-in systems to deliver growth factors or growth factor-producing cells are particularly attractive for peripheral nerve repair. Biodegradable polyurethane can offer attractive properties and processing options in fabricating scaffolds for nerve regeneration. [37]

Tubular structures made from polyurethanes were created using poly[glycolide-co-(ε-caprolactone)]diol and crystallizable blocks of poly[(R)-3-hydroxybutyric acid-co-(R)-3-hydroxyvaleric acid]-diol (PHB) with 2,2,4-trimethylhexamethylene diisocyanate (TMHDI) as the chain linker. These conduits, which were 10 mm long, were made from three different materials with varying PHB content (41%, 17%, or 8% PHB) and were implanted across an 8 mm gap in the sciatic nerve of rats for 4, 12, and 24 weeks. The regenerated tissue in the center of the guide lumen consisted of numerous myelinated axons and Schwann cells, and there was no significant difference in regeneration between the different materials. The inflammatory reaction associated with the polymer degradation did not interfere with the nerve regeneration process. By 24 weeks, the polymer with 8% PHB had degraded the most Yin et al. [38]

The study evaluated nerve guides made from biodegradable elastomeric PU prepared from HDI, εPCL-diol, and PEO-diol. These guides were used to repair a 12-mm femoral nerve gap in rabbits. The researchers observed myelinated axon regeneration starting from 4 weeks after implantation, and they also noted polymer degradation during the 12-week study.

4. **Injectable and in-situ cure polyurethane prepolymer systems**

Prepolymer systems with two components that react upon mixing under mild conditions have the advantage of being delivered to the implant site using minimally invasive procedures, such as arthroscopic delivery. These systems are particularly useful for applications in orthopedic fracture fixation, as bone cement or bone void fillers, and have the potential to deliver growth factors or other promoters to enhance cell growth. Since the urethane-forming reaction does not release any low molecular weight by-products, liquid two-part urethane systems can be formulated for these applications. Although two-part prepolymer systems are well known in the polyurethane industry, their potential applications in biomedical applications have only recently been explored.

The biodegradable polyurethanes mentioned earlier are mainly linear thermoplastic elastomers. They are used to create scaffolds for direct implantation or to support tissue regeneration by being seeded with cells and growth-promoting agents. Injectable prepolymer systems are designed to form crosslinked polymer networks when their components are mixed and the urethane/urea formation reaction is complete. Gunatillake et al. [39] have developed polyurethane prepolymers that can be cross-linked to create both rigid and elastomeric materials (NovoSorb™, PolyNovo Biomaterials, Melbourne, Australia) suitable for various biomedical applications, including tissue engineering scaffolds. The difference in reactivity of the two isocyanate functional groups in diisocyanates, such as ELDI or MLDI, is used to prepare prepolymers that are liquids at and above ambient temperature by reacting with multifunctional core molecules like pentaerythritol. Under controlled reaction conditions, star/hyperbranched prepolymers with isocyanate end-functional groups are formed. For example, the reaction of a diisocyanate with a core molecule

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such as pentaerythritol, glucose, or glycerol produces isocyanate end-functional prepolymers which are viscous liquids at ambient temperature. The second component (Prepolymer B) is usually a di-functional or multi-functional polyester polyol, with suitable examples including polycaprolactone, poly(orthoester)s, poly(glycolic acid), poly(lactic acid), and their copolymer polyols. The reaction of the two prepolymers, along with other appropriate additives, produces a cross-linked polymer network. By selecting the right precursors, materials with compressive strength of up to 260 MPa and compressive modulus over 2GPa have been produced [40].

Polyurethane prepared using this method has shown good compatibility with osteoblasts. The contact angles of polyurethane films produced through this approach were found to be between those of Thermonex (50°) and poly(D, L-lactic acid) (67°). The films supported the attachment of viable primary human osteoblasts, as shown by their healthy spindle-like morphology and >95% viability as determined by live/dead staining. The metabolic activity of the cells increased from day 1 to 7, indicating cell proliferation on these materials [41].

An experiment was conducted to assess the breakdown, safety, and appropriateness of an injectable prepolymer system used as a bone void filler in a study involving sheep implants. Prepolymer A was made from PE and ELDI, while prepolymer B was made from PE and DL-lactic acid (PEDLLA) or PE and glycolic acid (PEGA) with molecular weights of 456 and 453, respectively. The solidified polymers showed high compressive strength (100-190 MPa) and modulus (1600-2300 MPa). Before being implanted in the femurs of sheep, cylindrical test specimens (both porous and non-porous) were allowed to set for 8-10 minutes after being injected as a viscous liquid to fill 10mm diameter drill holes. The surgical site was then closed. Results from the sheep implant study indicated that the polymers, in both injectable and solidified forms, did not cause any surgical complications or adverse tissue reactions. Over up to 6 months, evidence of new bone growth and the gradual breakdown of the polymers were observed (see Fig 3).

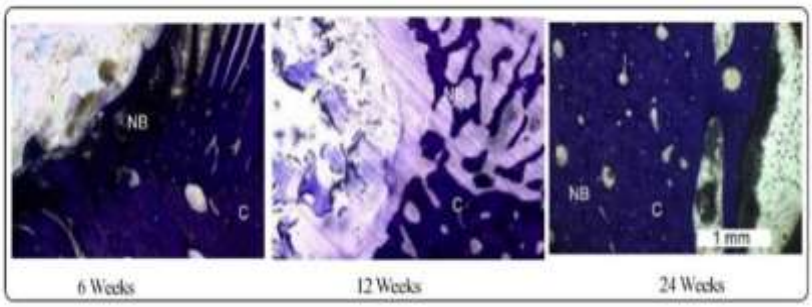

Fig. 3 Representative photomicrographs of histology sections of injectable porous polyurethane implants based on PE-ELDI (prepolymer A) and PEGA/PE-DLLA (Prepolymer B): Annotation: N= new bone, P = plug, FT or arrow = fibrous tissue, C = cortical bone

Guelcher et al used a quasi-prepolymer approach to address the miscibility and viscosity issues associated with two-part prepolymer systems. In this method, a large excess of polyisocyanate is reacted with a polyol (for example, NCO: OH equivalent ratio >5:1) to end-cap all the polyol hydroxyls. The excess diisocyanate helps maintain a low viscosity of the quasi-prepolymer. Biodegradable PUR networks were created by reacting the available isocyanate groups of the quasi-prepolymer with a polyester polyol. The modulus of the cast polymers ranged from 1200 to 1430 MPa, while the compressive strength ranged from 82 to 111 MPa. The materials degraded into non-toxic decomposition products and supported the attachment and proliferation of viable MC3T3 cells.

II. CONCLUSION

Over the past two decades, research groups worldwide have been investigating the potential of biodegradable polyurethanes for use in regenerative medicine and biomedical implants. These studies have confirmed that biodegradable polyurethanes have excellent biocompatibility, can be formulated to have a wide range of mechanical properties (from soft elastomers to rigid materials), and offer numerous processing options for creating scaffolds for tissue engineering. Among synthetic biodegradable polymers, polyurethanes stand out as

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one of the most versatile classes of polymers for fabricating scaffolds with a wide range of pore sizes, architectures, and mechanical properties. Polyurethane scaffolds have been created using various processing techniques such as electrospinning and thermally induced phase separation. These scaffolds provide a cell-friendly environment for the growth and proliferation of various cell types, including fibroblasts, osteoblasts, endothelial cells, chondrocytes, smooth muscle cells, and stem cells. Both in vitro and in vivo studies have shown that polyurethane scaffolds support cell and tissue ingrowth under controlled degradation conditions, producing non-cytotoxic degradation products. Long-term studies have also demonstrated the safety of polyurethane in various animal models, as well as examples of complete degradation.

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