Biodegradable Polymer Scaffold for Tissue Engineering

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Tissue engineering and regenerative medicines are an exciting research area that aims at regenerative alternatives to harvested tissues for transplantation. Cell, Scaffold and growth factors are the three key materials for tissue engineering. Biomaterials play a pivotal role as scaffolds to provide three dimensional templates and synthetic extracellular matrix environment for tissue regeneration. With the advance processing techniques, the long awaited and much anticipated construction of a truly [biomimicking] or ideal tissue engineered environment or scaffold, for a variety of tissues is now highly feasible. This article gives the brief overview on the fundamentals of tissue engineering, novel processing technology for scaffold synthesis, biodegradable polymers properties and application.

Introduction

Tissue engineering represents an emerging interdisciplinary field that applies the principles of biological, chemical, and engineering sciences towards the goal of tissue regeneration [1]. A distinctive feature of tissue engineering is to regenerate patient's own tissue and organs that are entirely free of poor biocompatibility and low biofunctionality as well as severe immune rejection. Cell, scaffold and growth factors are the three key materials for tissue engineering [2]. Cells are often implanted or 'seeded' into an artificial structure capable of supporting three-dimensional tissue formation. These structures are typically called as scaffolds.

Scaffolds usually serve at least one of the following purposes

1. Allow cell attachment and migration
2. Deliver and retain cells and biochemical factors
3. Enable diffusion of vital cell nutrients and expressed products
4. Exert certain mechanical and biological influences to modify the behavior of the cell phase [3].

Prerequisites of scaffolds include

1. Acceptable biocompatibility and toxicity profiles and having ability to support cell growth and proliferation [4].
2. Should have mechanical properties matching those of the tissue at the implantation site or mechanical properties that are sufficient to shield cells from damaging compressive or tensile forces without inhibiting appropriate biomechanical cues [3].
3. The absorption kinetics of scaffold should depend on tissue to be regenerated. For eg if scaffold is used for tissue engineering of skeletal system, degradation of scaffold biomaterial should be relatively slow, as it has to maintain the mechanical strength until tissue regeneration is almost completed [2].
4. It should have process ability to form complicated shapes with appropriate porosity. A high porosity and an adequate pore size are necessary to facilitate cell seeding and diffusion throughout the whole structure of both cells and nutrients. An optimum pore size is in the range between 100 and 500 µm [2].
5. Biodegradability is often an essential factor since scaffolds should preferably be absorbed by the surrounding tissues without the necessity of a surgical removal [5].
6. Mimic the native extracellular matrix (ECM), an endogenous substance that surrounds cells, bind them into tissues and provide signals that aid cellular development and morphogenesis.
7. Ideally an injectable prepolymer composition should be in liquid/paste form, sterilisable without causing any chemical change, and have the capacity to incorporate biological matrix requirements to be useful in tissue engineering applications. Upon injection the prepolymer mixture should bond to biological surface and cures to a solid and porous structure with appropriate mechanical properties to suit the application. The curing should be with minimal heat generation and the chemical reactions involved in curing should not damage the cells or adjacent tissues [4].
Synthesis of tissue engineering scaffolds

A number of different methods have been described in literature for preparing porous structures to be employed as tissue engineering scaffolds. Each of these techniques presents its own advantages, but none is devoid of drawbacks.

Nanofiber Self–Assembly

Currently, there are three techniques available for the synthesis of nanofiber: electrospinning, self-assembly, and phase separation (Table 1), in which electrospinning is the most widely studied technique [1]. The development of Nanofiber has enhanced the scope for fabricating scaffolds that can potentially mimic the architecture of natural human tissue at the nanometer scale. The high surface area to volume ratio of the Nanofiber combined with their microporous structure favours cell adhesion, proliferation, migration, and differentiation, all of which are highly desired properties for tissue engineering applications [6]. In the electrospinning process, fibers ranging from 50 nm to 1000 nm or greater [7, 8, 9] can be produced by applying an electric potential to a polymeric solution [10, 11]. The solution is held at the tip of a capillary tube and electrical potential applied provides a charge to the polymer solution. Mutual charge repulsion in the polymer solution induces a force that is directly opposite to the surface tension of the polymer solution [12, 13]. An increase in the electrical potential causes the electric potential to reach a critical value, at which it overcomes the surface tension forces to cause the formation of a jet that is ejected from the tip. The charged jet undergoes instabilities and gradually thins in air primarily due to elongation and solvent evaporation [8, 14, 15, 16, and 17].

Solvent casting/particulate leaching method

The solvent casting/particulate leaching method uses particulate porogen to form sponge/foam–like scaffolds. This method involves dispersing the porogen (e.g. sodium chloride, sodium citrate) into a polymer solution (e.g. PLLA/chloroform), casting the solution, evaporating off the solvent and finally leaching out the salt [19, 20]. The resulting scaffold’s porosity can be controlled by the amount of salt added, while the pore size is dependent on the size of the salt crystals. In an alternate form of the particulate leaching method, Shastri et al [21] recently reported the fabrication of PLLA and PLGA scaffolds with up to 87% porosity and pores well over 100 mm in diameter using waxy hydrocarbons as porogens. After mixing the porogen and polymer (dissolved in methylene chloride or chloroform) into a paste, the composite is packed in a Teflon mold which is immersed in a hydrocarbon solvent (pentane or hexane) to remove the wax without dissolving the PLLA/PLGA. The remaining foam is vacuum–dried for several days to extract any solvents. When blended with polyethylene glycol (PEG) and seeded with bovine chondrocytes for four weeks, formation of cartilage–like tissue is seen in these foams, demonstrating their biocompatibility [21]. Disadvantages include the time–consuming leaching step, which can significantly increase scaffold preparation time [22].

Phase separation/emulsification

They include emulsification/freeze–drying [23] liquid–liquid phase separation [24, 25, and 26]. Emulsion freeze–drying technique is used for the fabrication of highly porous PLGA scaffolds [23, 27]. The processing method consists of creating an emulsion by homogenization of a polymer solution (in an organic solvent) and water mixture, rapidly cooling the emulsion to lock in the liquid state structure, and removing the solvent and water by freeze–drying. Scaffolds with porosity greater than 90% and a pore size ranging from 20 to 200 µm can be fabricated with this method [23]. One disadvantage of this technique is the closed pore structure in the resulting matrix [27].

Both PLLA and PLGA scaffolds have been formulated using liquid–liquid phase separation [24, 25, 26, 27, 28]. The polymers are dissolved in a solvent with a low melting point and that is easy to sublime, such as naphthalene, phenol or 1, 4 dioxane. In some cases, small amounts of water are added as a non–solvent to induce phase separation [26, 27, and 28]. The polymer solution is cooled below the melting point of the solvent (polymer poor phase) and then vacuum dried for several days to ensure complete solvent sublimation. The cooling parameters for the solution play an important role in determining the morphology of the resultant scaffold. At temperatures just below the critical temperature the phase separation occurs via a nucleation and growth mechanism. At lower temperatures, the separation occurs via spinodal decomposition. While the nucleation and growth mechanism results in spheroidal domains, spinodal decomposition causes the formation of interconnected cylinders. Annealing can cause enlargement of domains formed by either mechanism [29].

Gas–Foaming Process

In order to eliminate the need for organic solvents in the pore–making process, a new technique involving gas as a porogen has been introduced [30, 31, 32]. Solid polymer disks are exposed to high pressure carbon dioxide to allow saturation of carbon dioxide in the polymer leads to thermodynamic instability by rapidly releasing carbon dioxide gas from the polymer system. Polymer sponges

<table>
<thead>
<tr>
<th>Process</th>
<th>Lab/industrial application</th>
<th>Ease of processing</th>
<th>Advantages</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Self assembly</td>
<td>Lab</td>
<td>Difficult</td>
<td>Achieves fibre diameter on lowest ECM scale (5-6 nm)</td>
<td>Creation of only Short fibre (&lt;1µm) and low yield</td>
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<tr>
<td>Phase separation</td>
<td>Lab</td>
<td>Easy</td>
<td>Mechanical properties and pore size can be tailored and batch to batch consistency is achieved.</td>
<td>Low yield</td>
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<tr>
<td>Electrospinning</td>
<td>Lab/Industrial</td>
<td></td>
<td>Cost effective, Mechanical property and pore size can be tailored and long continuous fibre production</td>
<td>Large nanometre to micro scale fibres</td>
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with a pore size of 100 μm and a porosity up to 93% can be fabricated using this technique. The disadvantage of this method is that it yields mostly a nonporous surface and closed-pore structure, with only 10–30% of interconnected pores [30, 32]. The porosity and interpore connectivity can be significantly improved by combining particulate leaching technique with the gas-foaming process although completely eliminating closed pores remains challenging [21, 30, 33, 34].

Rapid-Prototyping Techniques

Rapid prototyping is a technology based on the advanced development of computer science and manufacturing industry [35, 20]. The main advantage of these techniques is their ability to produce complex products rapidly from a computer-aided design (CAD) model. This process generates components by ink-jet printing a binder on to sequential powder layers. The operation parameters such as the speed, flow rate, and drop position can be computer controlled to produce complex 3D polymer scaffolds. Biological agents, such as growth factors, can also be incorporated into the scaffolds in the printing process. However, the limitation of this method is that the resolution is determined by the jet size, which makes it difficult to design and fabricate scaffolds with fine microstructures. The porosity of the scaffold fabricated with this method is low, and the mechanical properties of the scaffolds have to be significantly improved [36].

Researchers have shown it is possible to form three-dimensional scaffolds, printing bars of PLLA powder then adding a solvent, namely chloroform, delivered from the ink-jet printer. Disadvantages include the low milling yield (30%) of the PLLA granules and manual positioning of the polymer powder bed, a time-consuming action [35].

Thermally Induced Phase Separation

In this process the polymer is first dissolved in a solvent at a high temperature; liquid–liquid or solid–liquid phase separation is induced by lowering the solution temperature. Subsequent removal of the solidified solvent–rich phase by sublimation leaves a porous polymer scaffold [37, 38, 26, 39]. The factors governing pore size are polymer, solvent, concentration of the polymer solution and phase separation temperature. This method usually generates scaffolds with a pore size of 10–100 μm. One advantage of this method is that the fabricated scaffolds have good mechanical properties [40].

Surface Modification

Nowadays, a variety of synthetic biodegradable polymers have been used as tissue engineering scaffolding materials. The disadvantage of these scaffolds is their lack of biological recognition on the material surface. Hydrophobic polymers do not provide the ideal environment for cell–material interactions [41]. Therefore, surface modification of polymeric scaffolds is an active research area [42, 43]. Various techniques are being utilized to improve surface such as SBF concentration, incubation time, pH value, pre-treatment using aqueous solution [44].

Figure 1: Flow chart for the classification of biodegradable polymers
Advantages of biodegradable polymer scaffold over others

1. Metals are a choice as scaffold due to their superior mechanical properties [7], but they are disadvantageous for scaffold applications because of the lack of degradability in a biological environment [5].

2. Inorganic/ceramic materials such as hydroxypatite (HAP) or calcium phosphates, having good osteoconductivity and being studied for mineralized tissue engineering, are also limited due to poor processability into highly porous structures and brittleness.

3. A natural ECM or its derivatives may actually not be the ideal scaffold for tissue engineering applications because tissue engineering should be an accelerated regeneration process compared to the natural development program. Mature tissue matrix often does not possess the highly interconnected macro–or micro–pore structures to allow for quick and uniform cell population throughout, which is essential for a tissue engineering/repair process. Therefore certain artificially designed scaffold features (such as porosity, pore size, interpore connectivity, etc.) are necessary for optimal tissue engineering applications (accelerated tissue regeneration). In addition, there are always concerns over the possible immune rejection and pathogen transmission when a natural ECM is used [45]. Classification of biodegradable polymer used in scaffolds is mentioned figure 1.

Polymer properties and application

Collagen

Collagen can be isolated from animal tissues and it can also be produced by recombinant technology [46]. It is defined by high mechanical strength, good biocompatibility, low antigenicity and ability of being crosslinked, and tailored for its mechanical, degradation and water–uptake properties [47, 48]. Disadvantages of collagen include difficulty in processing and sterilization and also hard to control extent and rate of degradability [49]. Scaffold properties can be varied by using different concentrations of collagen [50]. Collagen is the major protein component of the extracellular matrix, providing support to connective tissues such as skin, tendons, bones, cartilage, blood vessels and ligaments [51, 52, 53, 54, 55]. For example, bilayered collagen gels seeded with human fibroblasts in the lower part and human keratinocytes in the upper layer have been used as the ‘dermal’ matrix of an artificial skin product, which is essential for a tissue engineering/repair process. Therefore certain artificially designed scaffold features (such as porosity, pore size, interpore connectivity, etc.) are necessary for optimal tissue engineering applications (accelerated tissue regeneration). In addition, there are always concerns over the possible immune rejection and pathogen transmission when a natural ECM is used [45]. Classification of biodegradable polymer used in scaffolds is mentioned figure 1.

Gelatin

Gelatin is a natural polymer that is derived from collagen [67]. Under specific conditions, such as temperature, solvent or pH, gelatin macromolecules present sufficient flexibility to realize a variety of conformations. This makes it possible to vary also all the gelatin characteristics dependent on its molecular structure [68]. Due to presence of both acidic and basic function at groups in gelatin macromolecules, it shows large number of structural diversity than other synthetic polymers [69]. Li et al. has compared gelatin with collagen, elastin, and recombinant human tropoelastin in an experiment where human embryonic palatal mesenchymal cells (HEPM) were seeded on each of the four scaffolds, and allowed to culture for 6 days. Gelatin behaved in much the same manner as the other proteins and in that it supported cell attachment, migration, and proliferation for the duration of the trial [70]. Huang et al. developed a bilayered gelatin–chondroitin 6 sulfate–hyaluronic acid membrane with a different pore size. Chondroitin–6-sulfate and hyaluronic acid were incorporated within the gelatin membrane to
mimic skin composition and create an appropriate microenvironment for cell proliferation, differentiation, and migration [71].

Elastin

Elastin is the most linearly elastic biosolid known. It is a highly insoluble, hydrophobic protein that the body utilizes extensively in organs where shape and energy recovery are critical parameters. Sell et al. formed electropores 6 mm ID seamless tubes for the testing of graft compliance. Dynamic compliance measurements produced values that ranged from 1.2 to 5.6%/100 mmHg for a set of three different mean arterial pressures, with the 50:50 ratios closely mimicking the compliance of native femoral artery [72].

Agarose

Agar is a gelatinous substance derived from seaweed. Chemically, agar is a polymer made up of subunits of the sugar galactose. Agarose hydrogel scaffolds were engineered to stimulate and guide neuronal process extension in three dimensions in vitro. The extracellular matrix (ECM) protein laminin (LN) was covalently coupled to agarose hydrogel using the bifunctional cross-linking reagent 1, 1’-carbonyldiimidazole (CDI). Compared to unmodified agarose gels, LN–modified agarose gels signifi cantly enhanced neurite extension from three-dimensionally (3D) cultured embryonic day 9 (E9) chick dorsal root ganglia (DRGs), and PC 12 cells [73]. Alaminos et al. cultured corneal cells from rabbits and used them to develop an organotypic substitute of the rabbit cornea by tissue engineering. They have shown agarose is less commonly used in tissue engineering of the cornea due to the reduced growth rate and have less biomechanical properties but, they had designed a scaffold made of a mixture of fibrin and agarose with good biomechanical strength and used it as a stromal substitute [74]. Agarose gel is widely used in the application of tissue engineering concepts to cartilage repair because it supports the cartilage phenotype [75]. Shinji Sakai synthesized a conjugate in which gelatin was covalently crosslinked to agarose that showed a sol–gel transition around body temperature. Since the conjugate used in this study did not result in mechanical instability compared to that of an unmodified agarose gel, agarose–gelatin conjugate is a good candidate material for tissue engineering [76].

Dextran

Dextran, a complex polysaccharide derived from bacteria, consists of glucose subunits and possesses anti-thrombotic properties. Scaffolds made from dextran are resistant to protein and cell adhesion and have been investigated for use as coatings for neural implants. Dextran can be chemically modified to add selective cell adhesion sites and growth factors [77, 78]. Recent fabrication techniques have made it possible to create macroporous dextran scaffolds that can allow for cellular infiltration [79].

Chitosan

Chitosan is the most abundant polysaccharide found in nature, particularly in the shell of crustacean, cuticles of insects and cell walls of fungi. Chitosan molecule has amino and hydroxyl groups which can be modified chemically providing a high chemical versatility and is metabolized by certain human enzymes [80]. Concerning cartilage engineering, chitosan is structurally similar to glycosaminoglycans (GAGs) which is native to articular cartilage and are very important in playing a key role in modulating chondrocytes morphology, differentiation and function. It can act as an ideal wound dressing as it exhibits a positive charge, film-forming capacity, mild gelation characteristics and a strong tissue-adhesive property with enhanced blood coagulation [81]. It accelerates wound healing by enhancing the functions of inflammatory cells such as polymorph nuclear leukocytes, macrophages and fibroblasts [82, 83, 84].

Polypyrrole

One major advantage of polypyrrole is its conductivity to allow signal transduction in nerve cells and ability to be easily doped so that properties such as wettability and charge density can be varied to best mimic neural structure. George et al. performed in vivo studies where doped polypyrrole was inserted into the cerebral cortex of a rat. After 6 weeks, the level of gliosis (inflammatory response) was found to be low as well as neural and glial cell adhesion was seen. The authors hypothesised that these scaffolds could be beneficial in diseased states where neuronal replacement is required, such as in stroke or in Parkinson’s disease [85]. Richardson and co–worker have developed the polypyrrole scaffolds further, where they attempted to seed the doped scaffold with auditory neuron explant cells and neurotrophin–3; a nerve growth factor. They found that neurite outgrowth was enhanced [30].

Polyporphazenes

Due to the flexible P–N backbone of polyphosphazenes, researchers have assessed the scope of this polymer with regards to both hard and soft tissue engineering [86]. Owing to their synthetic flexibility, wide range of physico–chemical properties, non-toxic and neutral degradation products and excellent biocompatibility polyphosphazenes are suitable candidates for biomedical applications [87]. Properties of these polymers are controllable by addition of variety of substitution to the phosphorous atoms. They undergo hydrolytic surface degradation into phosphate and ammonium salts by products but rate of degradation is slow [88]. Ambrosio and co–workers reported that Polysphazenes showed the mixed surface erosion and bulk–erosion properties and support osteoblast adhesion and proliferation which make them suitable for bone tissue engineering [89]. Poly (organ) phosphazenes has been studied as scaffolds for synthetic nerve grafts in peripheral nerve regeneration [86]. Other derivatives tried for tissue regeneration includes Poly [bis(ethyl alanto)phosphazene] and poly[(ethyl alanto)(imidazole) phosphazene] for nerve generation and poly[(80% phenyl alanine ethyl ester) (20% imidazole)phosphazene] for tissue regeneration in the periodontal cavity[90].

Polyanhydrides

Polyanhydrides are a class of hydrophobic polymers containing anhydride bonds, which are highly water
reactive and degrade by predictable surface degradation mechanism [91]. Aromatic polyanhydrides have slow degradation times and produces relatively insoluble degradation products. Degradation rate can be altered through changes in the hydrophobicity of the diacid building blocks like addition of hydrophilic monomer, such as sebacic acid [92].

Anhydrides are useful as polymer scaffolds for use as functional soft tissue substitutes [93]. Polyanhydrides may have an orthopaedic application but Modest Young's Modulius for entangled polyanhydrides network has limited application in weight-bearing environment. This limitation can be improved by formation of cross-linked networks with incorporated imides, which has significant mechanical properties, such as compressive strength which are in the intermediate range of cortical and trabecular human bone [91]. The degradation products may be therapeutically useful since they have shown anti-thrombogenic qualities [92].

Poly (glycerol sebacate)

This polymer class can form elastomeric and tough biomaterials that are scaffolds can support the growth of a variety of cells, including fibroblasts, hepatocytes, and endothelial, smooth muscle, cardiac muscle, [2] and Schwann cells [95].

Polynuoroester

Polynuoroester (POE) can be created by reacting ketene acetics with diols. The hydrophobic nature of PEO'surfaces allows this polymer to undergo surface degradation and bulk of material remains structurally intact. Hence act as sustained mechanical support for surrounding tissue. Rate of degradation can be controlled by incorporating short acid groups, such as glycolic acid or lactic acid. Hydrolysis of the polyester linkages in POE is more sensitive to acids. It was tried as scaffold for hepatocytes proliferation and also for bone reconstitution [96]. Poly(hydroxyxtho esters) such as polyglycolic acid (PGA), polylactic acid (PLA), and their copolymers have been used for three dimensional culture and transplantation of articular, auricular, nasal, costochondral, tracheal, and intervertebral disk, chondrocytes. This is in large part due to the availability, biocompatibility, and processibility of these materials [97]. The rapid degradation of this polymer can often hinder processing of this material after exposure to aqueous media. To overcome these problems, the use of PLA/PGA composites has been documented. Blending of poly-4-hydroxybutyrate with PLA and its copolymers has been found to improve toughness and lower stiffness than polylactic acid polymers or copolymers alone [98].

Junchuan et al have fabricated scaffold of hydrophobic biodegradable and bioreosorbable poly (D, L-lactic–co–glycolic acid) (PDLLA) and poly (D, L-lactic–co–glycolic acid) (PLGA) by combining modified compression molding and conventional particulate leaching method. Scaffolds produced by this method have various anatomical shapes eg that of the auricles, 90% porosity, interconnected and uniformly distributed pores, good viability of seeded cells and satisfactory mechanical properties [99]. Cortizo et al have proved that polyester polymers like poly–propiolactone (PBPL), poly–caprolactone (PCPL) show more porous and rougher surfaces than polyfumarates and hence significant increase in proliferation on polyester–derived scaffold [100].

A very important amorphous biodegradable polyester, poly (D, L–lactic–co–glycolic acid) (PLGA) has been employed as the skeletal material [101] as it has similar properties to those of normal tissue [91]. But it undergoes plastic deformation and failure when exposed to long–term cyclic strain, limiting their use in engineering elastomeric tissue. Webb et al showed this polymer as scaffolds to engineer tissues, such as heart valves and blood vessels [102]. Nagura et al. developed a new porous scaffold made from a synthetic polymer, poly (DL–lactic–co–glycolide) (PLG), and evaluated its use in the repair of cartilage in rabbits and found that the new porous PLG scaffold is effective for repairing full–thickness osteochondral defects without cultured cells and growth factors [103].

Pluronic

Chemically pluronic is co–polymer of poly (ethylene oxide–co–propylene oxide–co–polyethylene oxide) (PEO–PPO–PEO). Thermosensitive Pluronic change their structure and physical property in response to the surrounding environments, including temperature, pH, and electrical potential [104]. Among all classes of pluronic only F68 (molecular weight: 8,700) and F127 (molecular weight: 12,600) were approved by the U.S. FDA have been used as materials for a living body. Pluronic F127 is a non–toxic copolymer (molecular weight: 12,600) of polyethylene oxide (PEO)–propylene oxide (PPO)–polyethylene oxide (PEO) in a molar ratio of 98:68:98, and has a temperature–dependent sol–gel conversion properties. It can be converted to a gel at around the body temperature that are similar to tissues of a living body while maintained as a sol at room temperature, and have an affinity to cells so that the cells can generate tissues having a three–dimensional structure within the scaffold, and also function as a barrier between transplanted cells and host cells [105]. Jeong et al developed a new method of cartilage tissue engineering comprising chondrocyte mixed Pluronic F–127 and cultured chondrocyte cell sheet which entirely cover the cell–Pluronic complex which is an effective method for providing higher cartilage tissue gain and reliable success rate for cartilage tissue engineering[106].

Polyurethanes

After over 40 years of use in biomedical applications, polyurethanes remain a popular choice due to their exceptional biocompatibility, mechanical properties and versatility [107]. Biodegradable polyurethanes have been shown to support the ingrowth of cells and undergo controlled degradation to non–cytotoxic decomposition. This combined with the tuneable biological, mechanical, and physicochemical properties make these new materials excellent candidates for tissue engineering scaffolds. Polyurethanes are a class of polymers that contain the urethane (–NH–CO–O–) linkage that is typically generated through the addition of an isocyanate to a hydroxy group. Segmented polyurethanes most often used in biomedical applications are block copolymers consisting of relatively high molecular weight polyol soft segments linked together by urethane containing hard segments [108,109].
Ramrattam et al. studied two biodegradable polyurethane scaffolds (Estane and poly(ε-caprolactone)-polyurethane [PCLPU]) out of which PCLPU scaffolds showed significantly higher tissue ingrowth rates than Estane scaffolds [110].

Polycaprolactone (PCL)

PCL is relatively inexpensive, highly elastic polyester that demonstrates a lack of toxicity with good mechanical properties and a slow degradation time (1-2 years) [2, 111, 112]. Yoshimoto et al. and Shin et al. have formed electrospun PCL for a tissue engineered cardiac graft [36]. After pre-coating with soluble collagen, the material was also found to exhibit acceptable cellular interaction. Li et al. were able to successfully demonstrate the potential of PCL as a scaffolding material for cell based, multiphasic tissue engineering by seeding the Human mesenchymal stem cells (hMSCs) on scaffold made from polycaprolactone and induced to differentiate along adipogenic, chondrogenic, and osteogenic lineages [113].

Concluding Remark and Future Aspects

For the clinical success of the tissue engineering numerous areas of research are critical. Precise understanding of cell biology with emphasis on cellular differentiation, cell to cell interaction and extracellular matrix formation will be of paramount importance. Tissue engineering is a technology with profound benefits and an enormous potential that offers future promise in the treatment of loss of tissue or organ function as well as for genetic disorders with metabolic disorders. Without intimate collaboration among different fields it would be unlikely for tissue engineering to gain success. It seems probable that a major reason for delay in clinical trials of tissue engineering be ascribed to insufficient responses of biomaterial group to the requirements of medical groups, apart from recent excessive regulations and stringent assessment levels of review board on tissue engineering product.

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