PREPARATION AND CHRACTERIZATION OF PLA AND PLGA SCAFFOLD AND FILM

Thesis submitted to
National Institute of Technology, Rourkela
For the partial fulfilment of the Master degree in
Life science

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CERTIFICATE

This is to certify that the thesis entitled "PREPARATION AND CHARACTERIZATION OF PLA AND PLGA SCAFFOLD AND FILM" submitted to National Institute of Technology; Rourkela for the partial fulfilment of the Master degree in Life science is a faithful record of bonafide and original research work carried out by Gouri Shankar Haripal under my supervision and guidance.

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DECLARATION

I hereby declare that the thesis entitled "Preparation and characterization of PLA and PLGA scaffold and film", submitted to the Department of Life Science, National Institute of Technology, Rourkela for the partial fulfilment of the Master Degree in Life Science is a faithful record of bona fide and original research work carried out by me under the guidance and supervision of Dr. Bismita Nayak, Assistant Professor, Department of Life Science, National Institute of Technology, Rourkela. No part of this thesis has been submitted by any other research persons or any students.

Date: GOURI SHANKAR HARIPAL

Place:

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Date: Gouri Shankar Haripal

Place:

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ABSTRACT

In this research, the PLA/PLGA scaffolds and films were prepared successfully from PLA/PLGA blank microparticles. The morphology of the PLA/PLGA scaffolds and films are characterized by means of SEM. Biodegradable and biocompatible scaffolds having a highly open porous structure and good mechanical strength are needed for cell proliferation, migration, and differentiation, and guidance for cellular in-growth. Biodegradable porous scaffolds can be surface engineered to provide an optical microenvironment for better cell adhesion and tissue in-growth. According to scanning electron microscopy (SEM), a 3-dimensional porous structure of films could be observed on the surface. As the morphology of PLA/PLGA scaffolds and films could not be stabilized, we investigated the effect of temperature and concentration of polymer on the properties of microporous scaffolds and films. The degradation of polymeric porous films occurs through a homogeneous hydrolytic chain cleavage mechanism and this process is altered by factors such as molecular weight and molecular weight distribution. So, the biocompatible film plays an important role in development of fully biodegradable, tissue compatible active wound dressing material.

Keywords: scaffold; microporous film; PLA; PLGA

1. INTRODUCTION

Scaffolds are key components in the tissue engineering paradigm, in which they can function as templates to allow new tissue growth and provide temporary structural support. The development of novel scaffolds is very challenging and critical to achieve the appropriate function for tissue regeneration (Kretlow, 2007). Biodegradable and biocompatible nanocomposite micro particles are developed as cell scaffolds.

Scaffolds play a critical role in tissue engineering. The regulation of the growth of cells either cultivated within the porous structure of the scaffold or migrating from surrounding tissue is one of the major functions of the scaffold. Generally mammalian cells are anchorage-dependent. So, the scaffold gives a suitable substrate for cell attachment, cell proliferation, differentiated function and cell migration. The physicochemical properties of scaffolds are: to support and deliver cells; induce, differentiate, and channel tissue growth; target cell-adhesion substrates; stimulate cellular response. These are biocompatible and biodegradable; highly porous with a large surface/volume ratio; possess mechanical strength and dimensional stability; and have sterilisability. Generally, three-dimensional porous scaffolds can be fabricated from natural and synthetic polymers.

To achieve the goal of tissue reformation, scaffolds must face some specific requirements. A high porosity and an appropriate pore size are necessary to facilitate cell seeding and diffusion throughout the whole structure of both cells and nutrients. The degree of biodegradability is an essential factor, since scaffolds should preferably be absorbed by the surrounding tissues without the necessity of a surgical removal. The rate at which degradation occurs has to coincide as much as possible with the rate of tissue formation: this means that while cells are fabricating their own natural matrix structure around themselves, the scaffold must provide the structural integrity within the body and eventually it will break down leaving the new tissue, newly formed tissue which will take over the mechanical load.

Tissue engineering has emerged as a promising alternative approach to treat the loss or malfunction of a tissue or organ without the limitations of current therapies (Langer et al., 1993) Tissue engineering involves the expansion of cells, followed by the culturing of the cells in temporary three-dimensional scaffolds to form the new organ or tissue.

Therefore, porous three-dimensional temporary scaffolds play an important role in manipulating cell function and regulation of new organ formation (Peter et al., 1995). Isolated

and expanded cells adhere to the temporary scaffold in all three dimensions, generally proliferate, and secrete their own extracellular matrices, replacing the biodegrading scaffold. Significant challenges to this approach include the design and manufacture of the scaffolds. Ideally, scaffolds for tissue engineering should meet several design criteria: (1) the surface should permit cell adhesion, promote cell growth, and allow the retention of differentiated cell functions; (2) the scaffolds should be biocompatible; (3) the scaffold should be biodegradable and eventually eliminated; (4) the porosity should be high enough to provide sufficient space for cell adhesion, extracellular matrix regeneration and the porous structure of scaffold must allow even spatial cell distribution throughout the scaffold to facilitate homogeneous tissue formation; (5) the material should be reproducibly able to process into three-dimensional structure, and should be mechanically strong.

Many processing techniques have been developed to fabricate natural and synthetic polymeric scaffolds. Although naturally derived materials are more versatile in providing various biological functions, synthetic polymeric scaffolds are favoured because they can be fabricated from a wide range of biodegradable polymers with easy process ability, controlled degradation, and susceptibility to modification (Peter et al., 1998). While natural polymeric scaffolds are generally fabricated by freeze drying/cross linking in aqueous solution, synthetic polymeric scaffolds have been prepared by various methods including solvent casting, particulate leaching, phase separation, (Mikos et al., 1993). The surfaces of a scaffold promote cell adhesion by specific cell– matrix interactions (Hubbell et al., 1995). Furthermore, growth factors can be encapsulated or imbedded within the porous matrices and delivered in a sustained manner to enhance cell growth and morphogenesis.

Studies on scaffolds releasing DNA encoding the growth factor have also been suggested as an alternative approach to bypass limitations of protein delivery (Park et al., 2001). Recently, 3-D matrices based on different structural characteristics or minimally invasive surgical methods have drawn attention for potential tissue engineering applications in the next generation. A nanofibrous matrix prepared by electro spinning or self-assembly would provide a better resemblance of the physiological environment (Fig. 1-B) (Boyan et al., 1999). Hydrogels (Fig. 1-C) and micro-spheres (Fig. 1-D), which are already widely utilized as sustained protein release formulations, have also been applied in tissue engineering for its potential use as a cell delivery carrier or supportive matrix (Hutmacher et al., 2001). This review will introduce previous techniques for fabricating biodegradable scaffolds, followed by surface engineered and drug releasing scaffolds for directing a series of tissue regeneration processes in a more active manner.

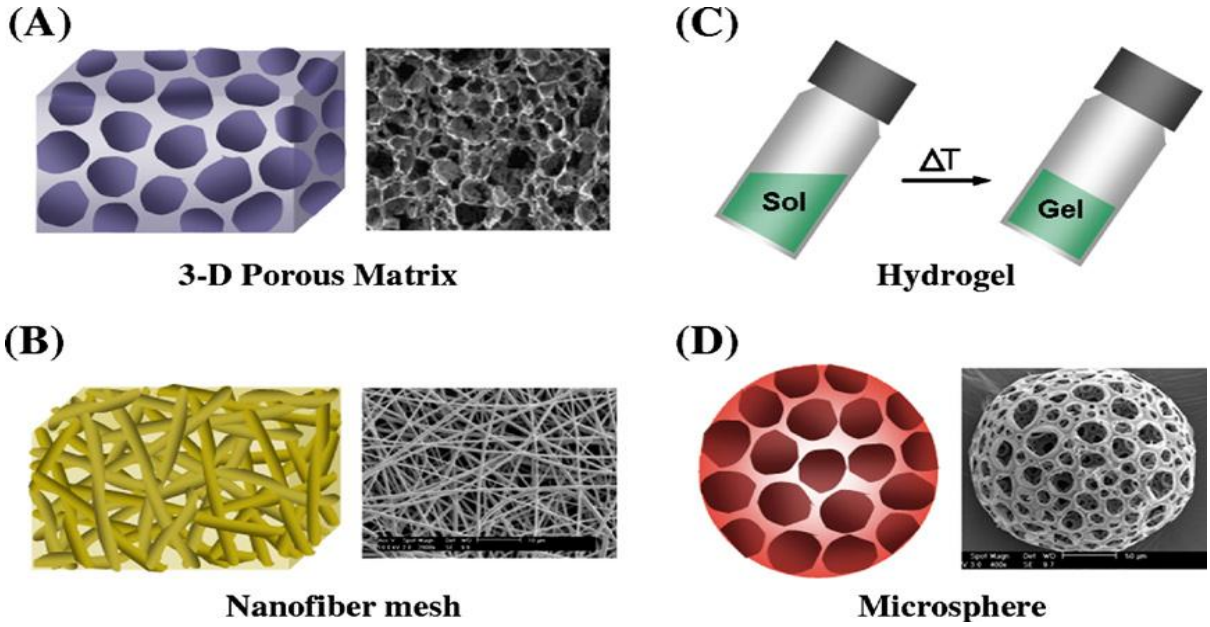


Fig. 1 Different forms of polymeric scaffolds for tissue engineering: (A) a typical 3-D porous matrix in the form of a solid foam, (B) a nanofibrousmatrix, (C) a thermo sensitive Sol–gel transition hydro gel and (D) porous microsphere.

Many biodegradable types of polymers, such as PLA and PLGA, often used in clinical applications for a very long time. There are several methods for the preparation of porous, biodegradable film has been developed in the past few years. The method of solvent–nonsolvent (SNS) phase separation is one of the most convenient route to prepare multiporous films with micro pores on the surface, and these structures enhance the hydrophilicity of the films.

Polymers, which are manufactured or processed to be suitable for use in or as a medical device. Recently, a variety of polymers, biopolymers have been developed specifically for medical applications.

Polymeric wound dressings that are capable of maintaining a controlled environment at the wound site have been shown to promote healing (Winter, et al; 1962). Active wound dressings have been developed to promote healing that enable the controlled, local delivery of therapeutic agents (Higa et al., 1999).

Ideally, the active wound dressing would deliver a nearly instantaneous initial dosage of the drug at the optimum therapeutic concentration, followed by a sustained constant delivery rate of the drug that maintains the local concentration at the optimum dosage level for as many days as necessary to achieve complete and effective wound healing.

In this study, to obtain a novel film structure for wound healing, we investigated the factors that could affect the micro forming of PLA and PLGA film with micro porous structure.

2. REVIEW OF LITERATURE

Polymer materials have received increasing attention and been widely used for tissue engineering because of easy control over biodegradability and process ability. There are two kinds of polymer materials: synthetic polymer, and naturally derived polymers (Thomson, et al; 1995). The main biodegradable synthetic polymers include polyesters, such as poly (glycolic acid) (PGA), poly (lactic acid) (PLA), and their copolymer of poly [lactic-co-(glycolic acid)] (PLGA) are most commonly used for tissue engineering. PLA undergoes hydrolytic scission to its monomeric form, lactic acid, which is eliminated from the body by incorporation into TCA cycle. The major elimination path for lactic acid is respiration, and it is primarily excreted by lungs as CO_2. PGA can be broken down by hydrolysis, nonspecific esterases and carboxypeptidases.

PLA (poly lactic acid) and PLGA (poly lactic acid/glycolic acid) are superior in biocompatibility and biodegradability, and also act as base material for sustained-release formulation.

2.1 PLA

The name "polylactic acid" is to be used with caution, not complying to standard nomenclatures (such as IUPAC) and potentially leading to ambiguity (PLA is not a poly acid (polyelectrolyte), but rather a polyester.

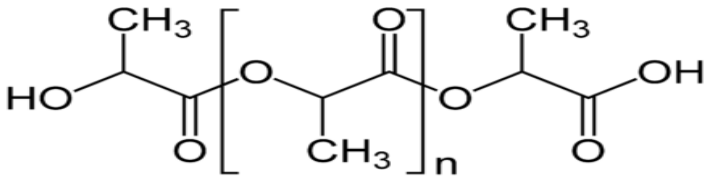


Fig. 2 Chemical structure of PLA

Poly (lactide) (PLA) has been widely used in various biomedical applications due to its biodegradability, biocompatibility, and good mechanical properties. The processing of this material by conventional means (such as film casting and foaming) often imposes several limitations in the optimization of their final properties.

Synthesis

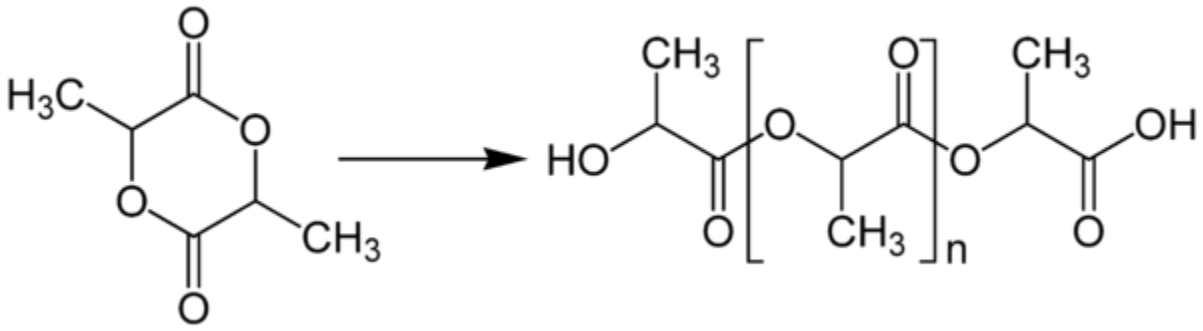


Fig. 3 Catalytic and thermolytic ring-opening polymerization of lactide (left) to polylactide (right)

Bacterial fermentation is used to produce lactic acid from corn starch or cane sugar.But lactic acid cannot be directly polymerized to a useful product, because each polymerization reaction produces one molecule of water, which accelerates the degradation of the forming polymer chain. Dimerization also generates water; which can be separated prior to polymerization due to a wide variation in polarity. High molecular weight PLA is generated from the delectate ester by ring-opening polymerization , but for laboratory demonstrations tin (II) chloride is often used.

Chemical and physical properties

Due to the chiral nature of lactic acid, several unique forms of poly lactide exist: poly-L-lactide (**PLLA**) is the product resulting from polymerization of L,L-lactide (also known as L-lactide). The degree of crystallinity of PLLA is around 37%, having a glass transition temperature between 60-65 °C, a melting temperature between 173-178 °C and a tensile modulus between 2.7-16 GPa (John et al., 2000). However, heat resistant PLA can withstand temperatures of 110C (230F).

PLA has similar mechanical properties to polymer PETE, but has a significantly lower maximum continuous use temperature.

Polylactic acid can be processed like most thermoplastics into fibre (for example using conventional melt spinning processes) and film. The melting temperature of PLLA can

be increased 40-50 °C and its heat deflection temperature can be increased from approximately 60°C to up to 190 °C by physically blending the polymer with PDLA (poly-D-lactide). A highly regular stereo complex with increased crystallinity is produced by PDLA and PLLA. The temperature stability is maximised when a 50:50 blend is used, but even at lower concentrations of PDLA, there is still a substantial improvement. In the latter case, PDLA acts as a nucleating agent, as a result the crystallization rate is increasing. Biodegradation of PDLA is slower than for PLA due to the higher crystallinity of PDLA. PDLA has the useful property of being optically transparent. There is also poly (L-lactide-co-D,L-lactide) (PLDLLA) – used as PLDLLA/TCP scaffolds for bone engineering.

2.2. PLA SCAFFOLD

Bioresorbable scaffolds of polylactic acid (PLA) offer several benefits. They require only a single surgery and leave native tissue behind. They gradually transfer load to tissue during the degradation period, useful for bone remodelling and reducing the risk of re-fracture. They can be also used to drugs delivery, growth factors or other substances conducive to the healing of bone locally to the implant site (Middleton, 2000).

The acidic products from the degradation of PLA act to catalyse further degradation which can cause an accumulation of acidic products at the healing site and elicit an inflammatory response. Hydroxyapatite (HA) is known to buffer the acidic degradation products of polylactic acid. Addition of HA to scaffolds results in controlled rate of degradation and reduced risk of inflammation. Exposure of osteogenic cells to bioactive ceramics such as HA is known to increase osteoblast differentiation and growth (Jung et al., 2005).

Biodegradable synthetic polymers including poly (lactic acid) (PLA) are suitable for biocompatible scaffold constructs but are known to undergo *in vitro* degradation. This may limit their potential for use in long-term cultures or loading regimes. This investigation determines whether it is advantageous to culture cells on scaffolds prior to mechanical compression

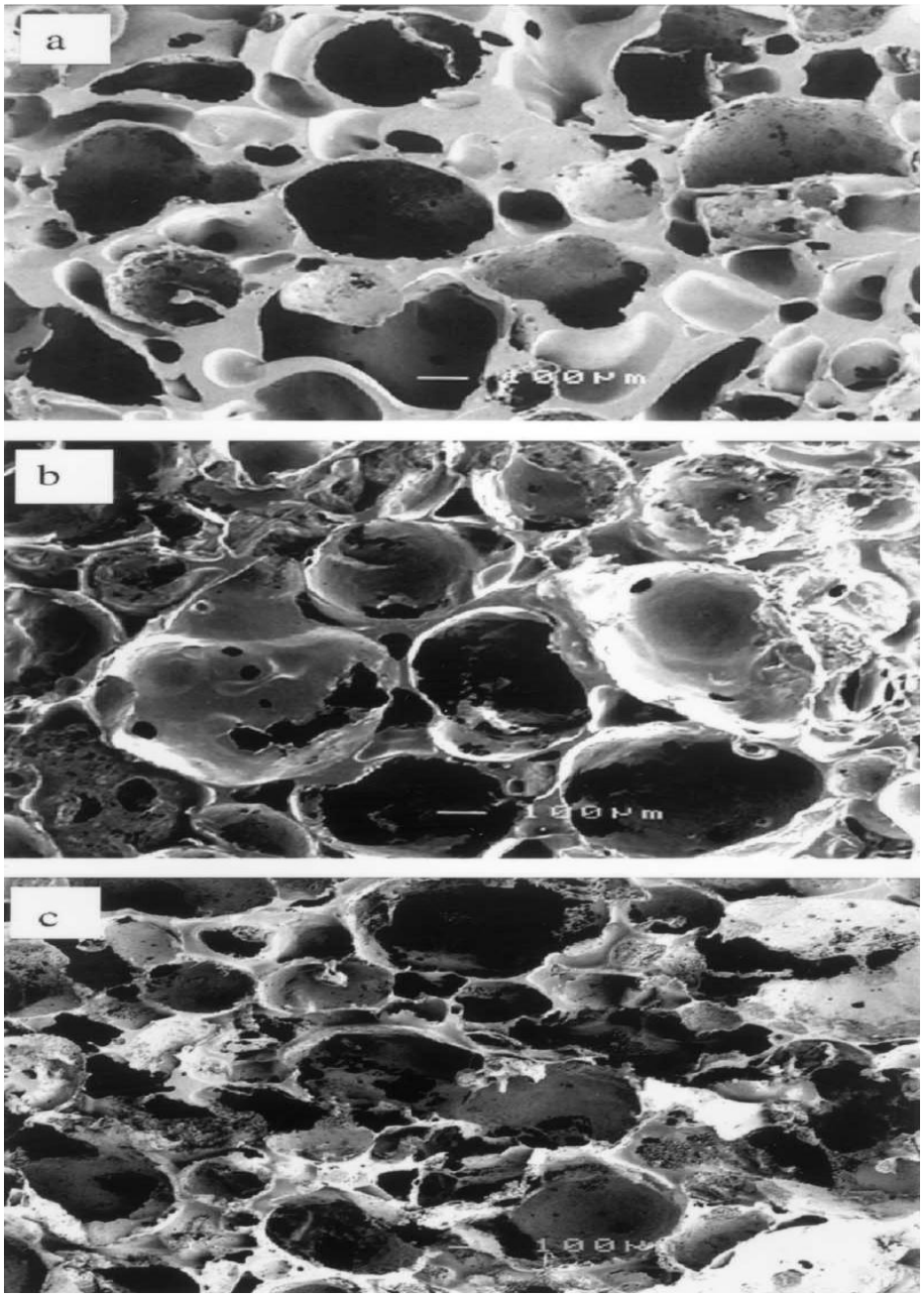


Figure.4 SEM photomicrographs of cross sections of PLA scaffolds prepared with the weight fractions of ice particulates of 70% (a), 80% (b), and 90% (c).

PLA is biodegradable thermoplastic polyester that can be produced through ring-opening polymerization of lactic acid. Since lactic acid is a chiral molecule, it exists in two forms, D-PLA and LPLA. PLLA is the result of L-PLA polymerization. While PLLA is semi-crystalline and it shows a high mechanical strength, poly (D,L-lactic acid) (PLA) is essentially amorphous, or, at most with a low crystallinity.

The methylated version of PGA is PLA ,but is less hydrophilic and, therefore, it degrades slowly.Poly (lactic acid) PLLA degrades to form lactic acid which is normally present in the body. This acid then enters TCA cycle and is excreted as water and carbon dioxide.

2.3 PLGA

PLGA or **poly(lactic-*co*-glycolic acid)** is a copolymer which is used in a host of Food and Drug Administration (FDA) approved therapeutic devices, due to its biodegradability and biocompatibility.

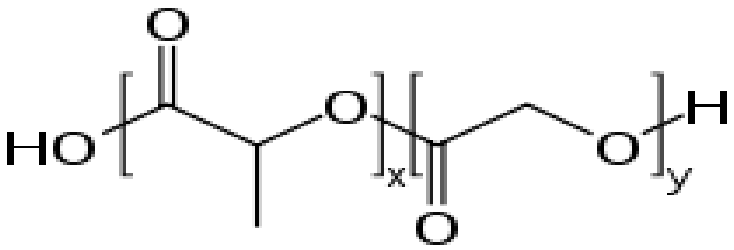


Fig.5 Chemical structure of PLGA

PLGA is synthesized by means of random ring-opening co-polymerization of two different monomers, the cyclic dimers (1, 4-dioxane-2,5-diones) of glycolic acid and lactic acid. In the preparation of this polymer common catalysts used are tin(II) 2-ethylhexanoate, tin(II) alkoxides, or aluminium isopropoxide. Monomeric units (of glycolic or lactic acid) are linked together in PLGA by ester linkages during polymerization, thus yielding a linear aliphatic polyester as a product.

PLGA is soluble in wide range of common solvents including chlorinated solvents, tetrahydofuran, acetone or ethyl acetate. Degradation of PLGA occurs in water by hydrolysis of its ester linkages. Presence of methyl side groups in PLA makes it more hydrophobic than PGA and hence lactide rich PLGA copolymers have low degree of hydrophilicity, absorb less water and more slowly degraded. Due to the hydrolysis of PLGA, parameters that are typically considered invariant descriptions of a solid formulation change with time, such as moisture content, molecular weight and the glass transition temperature (Tg).

The change in PLGA properties during polymer biodegradation influences the release and degradation rates of incorporated drug molecules. PLGA physical properties themselves

have been shown to depend upon multiple factors, including the initial molecular weight, the size of the device, exposure to water and storage temperature.

Different forms of PLGA can be obtained depending on the ratio of lactide to glycolide used for the polymerization. These are usually identified in regard to the monomers' ratio used (e.g. PLGA 75:25 identifies a copolymer whose composition is 75% lactic acid and 25% glycolic acid). All PLGAs are amorphous rather than crystalline and show a glass transition temperature in the range of 40-60 °C. PLGA can be dissolved by a wide range of common solvents, including chlorinated solvents, tetrahydrofuran, acetone or ethyl acetate.

PLGA degrades by hydrolysis of its ester linkages in water. It has been observed that the time required for degradation of PLGA is related to the monomers' ratio used in production: the higher the content of glycolide units, less time required for degradation. An exception to this rule is the copolymer with 50:50 monomers' ratio which exhibits the faster degradation. The end-capped polymers with esters (as opposed to the free carboxylic acid) demonstrate longer degradation half-lives.

PLGA has been successful as a biodegradable polymer because it undergoes hydrolysis in the body as a result of which original monomers are produced, lactic acid and glycolic acid. Under normal physiological conditions these two monomers are by-products of various metabolic pathways in the body. As the body effectively deals with the two monomers, there is minimal toxicity associated with using PLGA for drug delivery or biomaterial applications. Also, the possibility to tailor the polymer degradation time by altering the ratio of the monomers used during synthesis has made PLGA a common choice in the production of a variety of biomedical devices like implants, prosthetic devices, micro and nanoparticles, grafts and sutures.

2.4. PLGA SCAFFOLD

PLGA and its copolymers are the most extensively used for biodegradable and biocompatible scaffolds. These polymers which are biocompatible, biodegradable are approved by the Food and Drug Administration (FDA), and are easily processed into various 3-D matrices like structures.

Especially, biodegradable devices made of poly (lactide-co-glycolide) (PLGA) copolymers are advantageous due to their controlled degradation behaviour and tunable mechanical properties. The rate of polymer degradation should be carefully controlled to synchronize with the rate of tissue formation and in-growth to achieve successful regeneration or repair within a desired time frame.

A variety of techniques have been used for processing biodegradable polymers into 3-D porous scaffolds. The conventional methods include fibre felts, fibre bonding, melt moulding, solvent casting/particulate leaching, phase separation method, and processing of high pressure. A number of 3-D porous scaffolds fabricated from various kinds of biodegradable materials have been developed and used for tissue engineering of liver (Kneser et al.,1999), bladder (Oberpenning et al.,1999), nerve (Hadlock et al., 2000), skin (Hansbroughbone et al., 1993), cartilage (Cao et al.,1997) and ligament(Freed et al., 1994) etc.

The fabrication of three-dimensional (3D) scaffolds that mimic the cellular microenvironment is of fundamental importance to the success of tissue engineered constructs. Both scaffold chemistry and architecture can influence the fate and function of engrafted cells (Bhatia et al., 1999).

Material microstructure, in contrast, is often controlled by process parameters such as the choice of solvent in phase separation, gas foaming, woven fibres, and controlled ice crystal formation and subsequent freeze-drying to create pores (Lo H et al., 1995) however, these scaffolds lack a well-defined organization that is found in most tissues.

Modification of the bulk properties of the porous poly (lactide-*co*-glycolide) (PLGA) scaffold was performed by irradiation with a high energy cyclotron proton ion beam. The PLGA scaffolds were formulated in advance by the gas-foaming method by employing ammonium bicarbonate particles as porogens.

Irradiation with ion beams was performed with 40 MeV for 3, 6 and 9 min on the scaffolds at a distance of 30 cm from the beam exit to the scaffold surface. The bulky ion beam-treated PLGA scaffold apparently demonstrated no color changes. The chemical structures of the untreated samples seemed to be kept well when analyzed by both Fourier transformed infrared but a subtle change was observed in its x-ray photoelectron spectroscopy.

The results of *in vitro* tissue culture with smooth muscle cells for up to 4 weeks also demonstrated no significant difference in terms of its handling stability during cell culture

and cellular behaviour between the untreated PLGA scaffolds and the ion beam-treated PLGA scaffolds. However, significant changes were observed in its molecular weight as measured by gel permeation chromatography, indicating a significant molecular weight reduction. These results of *in vitro* tests and GPC measurements indicated that while bulk modification of the scaffold was processed (Woo *et al.*, 2009).

Scaffolding plays an important role in tissue engineering. In this work, a novel processing technique has been developed to create three-dimensional biodegradable polymer scaffolds with well-controlled interconnected pores which are spherical in nature. Paraffin spheres were fabricated with a dispersion method, and were bonded together strongly through a heat treatment to form a three-dimensional mold structure. Biodegradable polymers such as PLLA and PLGA were dissolved in a solvent and cast onto the paraffin sphere assembly. After dissolving the paraffin, a porous polymer scaffold was formed. The fabrication parameters have importance in relation to the pore shape, interpore connectivity, pore wall morphology, and mechanical properties of the polymer scaffolds. The modulus of the scaffolds decreased with increasing porosity. More time for heat treatment of the paraffin spheres resulted in larger openings between the pores of the scaffolds. Foams of smaller pore size (100-200 micron) resulted in significantly lower compressive modulus than that of larger pore sizes (250-350 or 420-500 micron). The PLLGA foams had a skeletal structure consisting of small platelets, whereas homogeneous skeletal structures were found in PLGA foams. The new processing technique can make the polymer scaffolds for a variety of potential tissue engineering applications because of the well-controlled architecture, interpore connectivity, and mechanical properties (Ma PX et al., 2001)

Solvent-evaporation method was modified using sucrose as an additive to form large porous microparticle of poly (d,l-lactic-*co*-glycolic) (PLGA) polymer. Micro particles containing hydrophilic polymers (poly vinyl alcohol) incorporated in their internal matrix structure were also formulated. Different formulations of micro particles were evaluated for physical properties, cell adhesion, and cell growth in culture. PLGA micro particles containing poly(vinyl alcohol) (PVA) in the matrix structure (PLGA-PVA) and treated with serum prior to cell seeding demonstrated better cell adhesion and cell growth than other formulations of micro particles. (Labhasetwar et al., 2005).

3. OBJECTIVES

1. Preparation of blank PLA and PLGA micro particles

2. Preparation of PLA and PLGA Scaffolds

3. Preparation of PLA and PLGA Films

4. Characterization of PLA and PLGA Scaffolds and Films by SEM

4. MATERIALS AND METHODS

4.1. Preparation of PLA and PLGA micro particles

4.1.1.: Equipments

- Stratos low-temperature high-speed centrifuge(Thermo, Germany)
- Cooling centrifuge (REMI)
- Magnetic stirrer
- Sonicator
- Scanning electron microscope (Jeol Jsm-6480 LV)

4.1.2. Materials required:

- Sucrose
- PLA(Sigma- Aldrich)
- DCM
- PVA(Sigma- Aldrich)

4.1.3. Procedure:

PLA and PLGA dummy particles were prepared using double solvent evaporation method.

Method is as follows:

1) Internal aqueous phase (200 micro litres):10% sucrose (w/v)

2) Organic phase (4 ml) : PLA 200mg/4 ml DCM

: PLGA 200mg/4 ml DCM

3) External aqueous phase (16 ml) :1% PVA (w/v)

: 10% Sucrose (w/v)

4.1.4. Preparation:

- Polymer dissolved in organic phase (4 ml) was associated with 200 micro litre of internal aq.phase was added to make primary emulsion.
- For the formation of the secondary emulsion 16ml of external aq.phase was taken in a beaker and the primary emulsion was added drop wise while sonicating the primary emulsion. This led to the formation of the secondary emulsion.
- This was kept on a magnetic stirrer for overnight for excess DCM to evaporate. Particles formed were separated by centrifugation at 15000 RPM which was performed for a period of 20 minutes.
- Separated particles were washed twice with ice cold MQ water. After washing the particles were lyophilized for 24 hrs to obtain dry particles.

4.2 Preparation of PLA /PLGA Scaffold

For PLA and PLGA

Chemicals required:

- Chloroform
- Ethanol
- Ammonium bicarbonate
- Aqueous citric acid

Procedure:

For both PLA and PLGA micro particle

- 100 mg of PLA /PLGA micro particle dissolved in chloroform was precipitated in ethanol.
- A gel slurry was obtained, 50 mg of ammonium bicarbonate salt particles mixed with this gel paste were cast in a mold, semi solidified at room temperature and immersed into 5 ml of aqueous citric acid solution.
- Finally macro porous PLA/PLGA scaffolds with a porosity of over 90% were obtained.

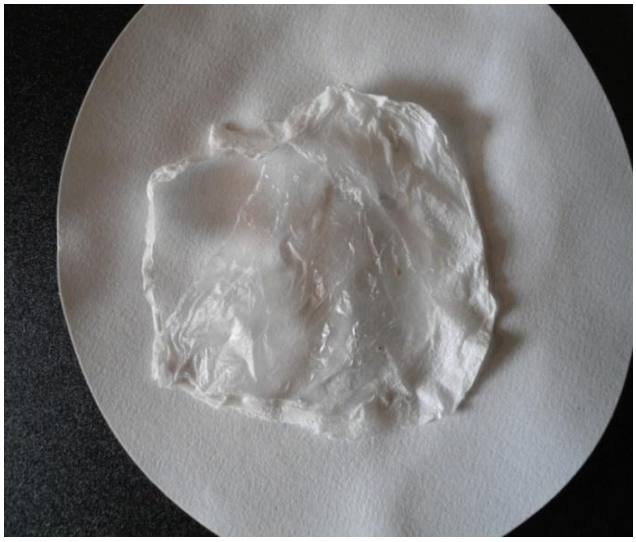


Fig.6: PLA scaffold

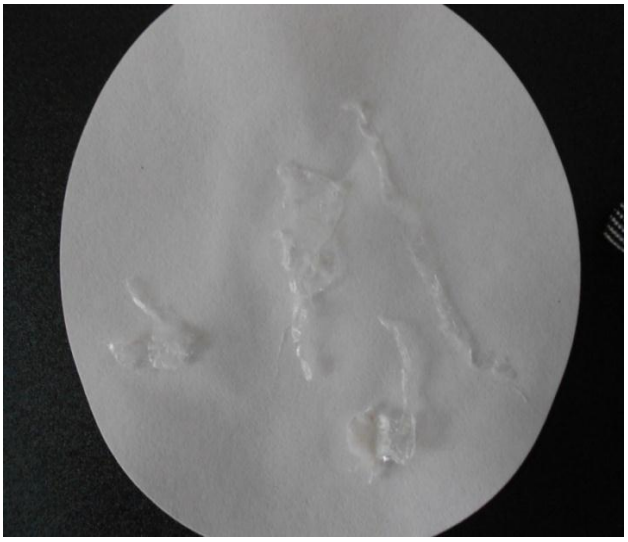


Fig7: PLGA scaffold

4.3. Preparation of PLA and PLGA films

For PLA and PLGA

Chemicals required:

- Dichloro methane(DCM)
- Tetrahydrofuran (THF)
- Ethylene glycol(EG)
- Glycerol

Procedure:

For both PLA and PLGA micro particle

- 100 mg of PLA/PLGA microparticle was first dissolved in 5 ml of DCM at room temperature.
- After PLA/PLGA microparticle was completely dissolved in 10 ml of THF was then added into the mixed solution at 55^0C to ablate DCM by volatilization.
- Since PLA/PLGA was uniformly dissolved in THF the solution was added dropwise onto the surface of EG/glycerol mixed solution.
- Finally the system was left for volatilization overnight and was microporous PLA/PLGA film was obtained.

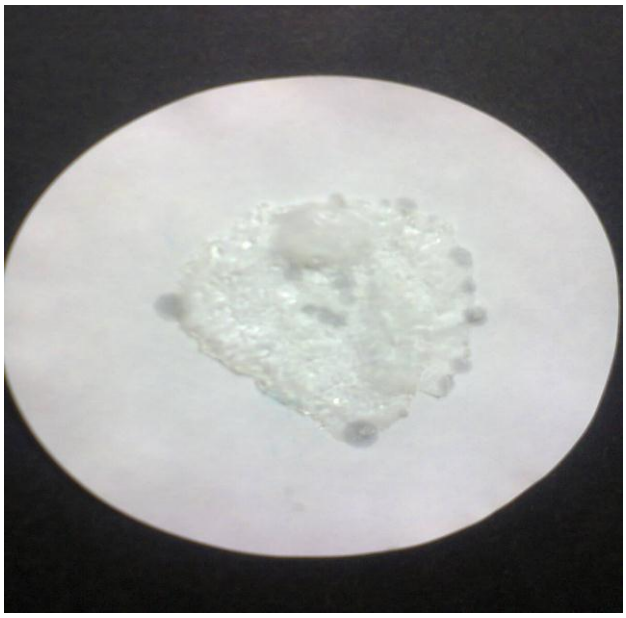


Fig 8: PLA Film

Fig 9: PLGA Film

5. RESULTS

Characterization of PLA and PLGA scaffolds and films by SEM

The PLA scaffold prepared by this method was highly porous with evenly distributed and interconnected pore structures. The pore shapes were almost the same as those of the ice particulates. The degree of interconnection increased as the weight fraction of the ice particulates increased.

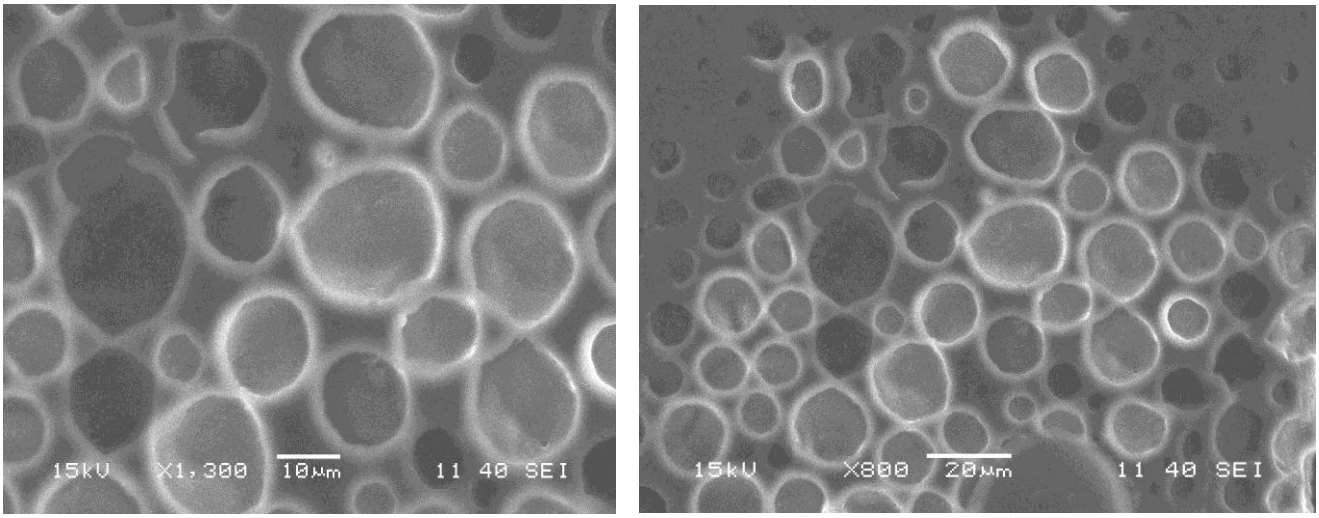


Fig.10 SEM images of PLA scaffolds

The polymer concentration also had some effect on the pore wall structure, i. e., lower polymer concentration resulted in more porous pore wall structures. The porosity and surface area/weight ratio increased with the increase of the weight fraction of the ice particulates. Therefore, the pore structure of the porous temporary scaffolds could be manipulated by varying the shape, weight fraction, size of the ice particulates, and the polymer concentration.

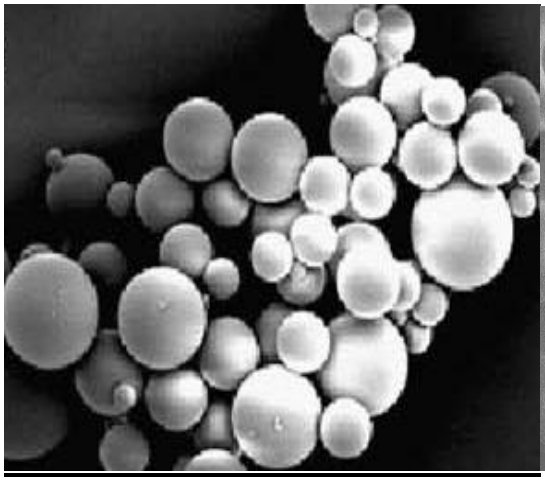


Fig. 11 PLGA microspheres

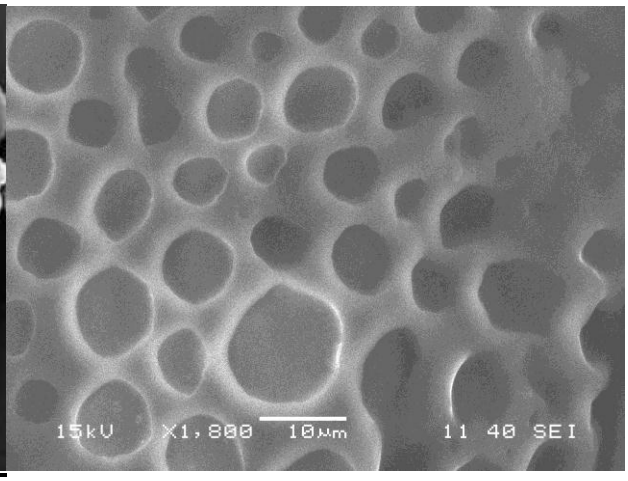
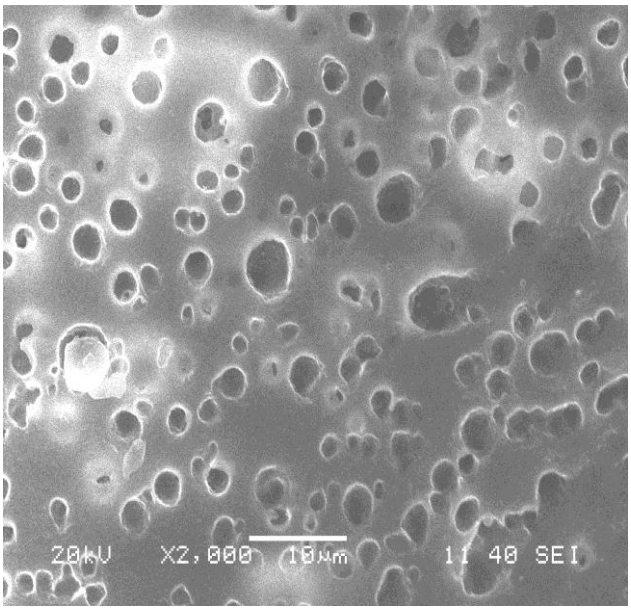


Fig .12 PLGA scaffold with pores

The wettability of a polymer scaffold is considered very important for homogeneous structure. Under the fabrication conditions used here, the PLGA microspheres have a spherical morphology with a smooth surface.



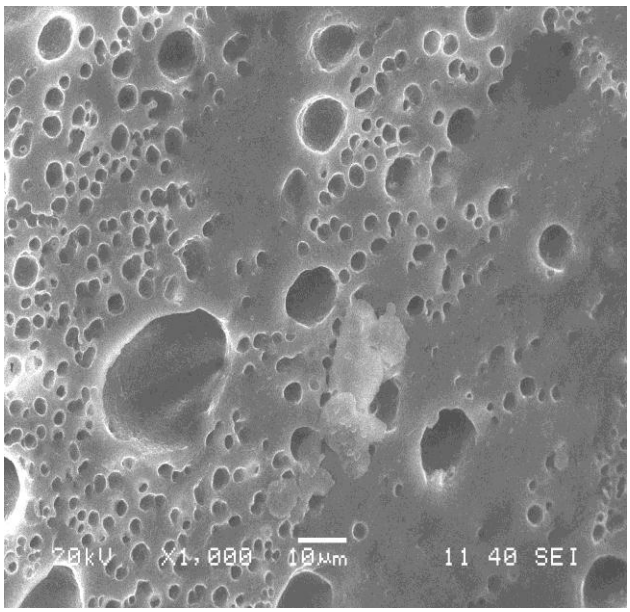


Fig .13 SEM morphology of various types of PLA porous films at different temperatures

The morphology observation shown in above indicates that the pore appearances in different films are conspicuously different and that the films had a smoother surface .The pores are evenly distributed throughout the film.

The volatility of THF at different temperatures was not concordant, and for this reason, we obtained various PLA films with disparate morphology. We observed the scaffold prepared at 4°C, 25°C and 50°C, the film had unique micro pores on its surface. This experiment showed an ambient temperature is beneficial for shaping the surface of the scaffold with multipores and the obtained films were smoother at a low speed of phase separation. That is to say, a moderate rate of evaporation is beneficial for formation of droplets of the solvent, and after these droplets volatilized, spherical holes appeared and occupied the interface.

6. CONCLUSION

In this study, the morphology of PLA/PLGA scaffolds and films prepared from PLA/PLGA blank microparticle are observed. The results showed that PLA /PLGA scaffolds possessed higher degree of porosity with evenly distributed and interconnected pore structures. The pore shapes were almost the same as those of the ice particulates. The polymer concentration also had some effect on the pore wall structure, i.e., lower polymer concentration resulted in more porous pore wall structures. These porous scaffolds prepared by solvent casting/particulate leaching have been intensively studied to provide implantable devices for tissue regeneration. These polymeric devices are usually surface modified by immobilizing cell adhesive or growth factor binding moieties to improve its cell adhesive characteristics or actively induce cell migration, proliferation and differentiation. According to SEM films had a smoother surface and the pores are evenly distributed throughout the film. The degradation of PLA and PLGA microfilms occurs through a homogeneous hydrolytic chain cleavage mechanism where the rates of polymer degradation are similar for both the surface and the bulk of the microfilms. Factors such as molecular weight and molecular weight distribution as well as sterilization may also alter the degradation rate of the biodegradable polyesters in microfilms. In these way biocompatible films represents an important advance in the development of fully biodegradable, tissue compatible active wound dressing material capable of delivering a broad range of therapeutic agents.

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