International Journal of Emerging Engineering Research and Technology
Volume 2, Issue 4, July 2014, PP 30-34
ISSN 2349-4395 (Print) & ISSN 2349-4409 (Online)

Studies on Scaffolds for Skin Tissue Engineering with Electro Spun Technology

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Abstract: *Tissue-engineering skin is a significant advance in the field of wound healing.Scaffold has mainly been developed because of limitations associated with the use of autografts and allografts where donor suffer from pains,Infection, and scarring. Recently, tissue engineering skin replacement have been finding widespread application in the case of burns ,where the major limiting factor is the availability of autologus skin. The development of 3 dimensional bioartificial, biocompatible and biodegradable skin facilitates the treatment of patients with deep burns and various skin related disorders. The present review gives a comprehensive overview of the development and future prospects of of scaffolds as skin substitutes for tissue repair and renegeneration.*

Keyword: *Scaffold, skin tissue engg., polymer material, electro spinning.*

1. INTRODUCTION

Tissue engineering has emerged as an alternative treatment to traditional autografts and allografts for excessive skin loss. Such an approach involves scaffolds, cells and biological factors alone or in combination. In biomedical applications, nanofibers mat have been used as carriers for drug/therapeutic agent delivery, wound dressing materials and as porous three dimensional scaffolds for engineering various tissues such as skin, bone, Blood vessels, nerve and cartilage. Such scaffolds are bio-degradable and biocompatible & helps supporting media for original cells. Through scaffolds medicines & proteins are transfered towards original cells for fast growth. Nanofibers due to their extremely high surface to mass ratio possess several novel properties such as low density, high pore volume, variable pore size and exceptional mechanical properties. These remarkable properties of nanofibers have led to the development of several non-woven applications. A current research emphasis is to develop scaffolds using nanofibers from a wide range of polymers and characterize them for skin tissue applications.

Unique biocompatible scaffolds were produced by electrospinning process of Polymers like PLA (Poly lactic Acid), PGA (Poly Glycolic Acid) PLGA(Poly lactic co Glycolic Acid), PCS (Polycarbosilanes). Nonwoven mats of PEI fibers in the range of 1600–687 nm were evaluated as interaction scaffolds form normal human fibroblast (NHF) cells. The electrospun scaffolds were characterized by Fourier transform infrared spectroscopy and ultraviolet–visible spectroscopy. The growth of the NHF cells was followed by scanning electron microscopy as well as optical microscope. Cell viability was evaluated by staining with propidium iodide for dead cells and fluorescein diacetate for live cells. Fluorescence studies confirmed that NHF cells attached and spread throughout the cross-linked linear polyethylene scaffold. The attachment and spreading of cells suggests that electro-spun linear polyethyleneimine scaffolds support growth of normal human fibroblasts cells. Thus, these biomaterial scaffolds may be useful in skin tissue engineering. Polymeric nanofiber matrices can also act as carriers for a variety of bioactive agents including antibiotics, antifungal, antimicrobial, proteins (enzymes, DNA, etc), anticancer and other valued drugs. Core-shell nanofibers have been successfully designed to release the desired bioactive agents at therapeutic concentrations in both a spatial and temporal pattern. These microfiber matrices obtained by electrospinning showed significant numbers of viable cells over long periods of time.. In this research, electrospun scaffolds (Bioscaffolds) are prepared to regenerate ,repair & replace soft tissues for skin which is used for human skin deases like Victims of third-degree burns, Traumatic injuries endure Pains, disfigurement, Invasive surgery, wound. Such Bioscafold helps to avoid Infection , reduce patients discomfort & healing time & Increase growth rate of skin cells.

2. ELECTRO SPUN SCAFFOLDS

2.1. Skin grafts

A common problem in the design of tissue engineered scaffolds is the poor cellular infiltration into the structure. To tackle this issue, electrospinning approaches to scaffold design were investigated.

Electrospun nanofiber scaffolds due to their high surface area-to-volume ratio provide more surface for cell attachment compared to other structures from the same material. Using nanofibers, it is now possible to produce biomimetic scaffolds that can mimic the extracellular matrix for tissue engineering. Interestingly, nanofibers can guide cell growth along their direction. Combining factors like fiber diameter, alignment and chemicals offers new ways to control tissue engineering. In vivo evaluation of nanomats included their degradation, tissue reactions and engineering of specific tissues. In addition, nanofiber scaffolds are extensively used as wound dressings since they protect the wound area from the loss of fluid and proteins, aid in removal of exudates, inhibit exogenous microorganism invasion, improve appearance and have excellent anti-adhesion properties. Polymer nanofiber matrices used as wound dressing materials in skin defect model showed increased rate of epithelialization with well-organized dermis which provided good support for wound healing. PLAGA nanofiber matrices showed an excellent anti-adhesion effect and prevented complete cell adhesions. Several polymers of both natural and synthetic origins, alone or in combination, were successfully electrospun into nanofiber scaffolds, and evaluated as dermal substitutes with cells. Nanofiber matrices as tissue engineering scaffolds need to have interconnected highly porous structures to facilitate cellular migration and transport of nutrients, and metabolic wastes to allow the formation of new tissue. The surface-modified polyamide nanofibers coated with ECM proteins namely fibronectin, collagen I and laminin-1 supported primary mouse embryonic fibroblasts adhesion and proliferation better than tissue culture polystyrene (TCPS) protein-coated surfaces .Polymeric nanofiber matrices alone or in combination with other materials and structures have been successfully used as implants or prosthetic devices. Polymeric nanofiber matrices can also act as **carriers** for a variety of bioactive agents including antibiotics, antifungal, antimicrobial, proteins (enzymes, DNA, etc), anticancer and other valued drugs. Core-shell nanofibers have been successfully designed to release the desired bioactive agents at therapeutic concentrations in both a spatial and temporal pattern . Recently. These microfiber matrices obtained via cell electrospinning showed significant numbers of viable cells over long periods of time. Thus, nanofiber matrices encapsulated with suitable growth factors, cells or bioactive agents have a great potential for use in tissue regeneration by providing cells with necessary physical and chemical cues

2.2. Methodology

Electrospinning is a process used to manufacture nano-sized fibers from various polymer materials. Electrospinning has emerged to be a simple, elegant and scalable technique to fabricate polymeric nanofibers. Pure polymers as well as composites of both natural and synthetics have been successfully electrospun into nano fibermatrices. Physiochemical properties of nanofiber matrices can be controlled by manipulating electrospinning process parameters such as of polymer material electrical field, Pressure, polymer concentration, Distance between anode & Cathode and temperature to meet the requirements of a specific application. Electrospinning involves four basic steps that are given below.

1) Emulsification of core materials in a solvent;
2) Dissolution of fiber-forming polymers in the continuous phase;
3) Eelectrospinning process of the resulted system;
4) Harvesting the composite fibers on the receptor (Collector).

In the electrospinning process a high voltage i.e. 2Kv to 40 Kv is used to create an electrically charged jet of polymer solution, which dries or solidifies to leave a polymer fiber. One electrode is placed into the spinning solution/melt and the other attached to a collector. Electric field is subjected to the end of a capillary tube that contains the polymer fluid held by its surface tension. This induces a charge on the surface of the liquid. Mutual charge repulsion causes a force directly opposite to the surface tension. As the intensity of the electric field is increased, the hemispherical surface of the fluid at the tip of the capillary tube elongates to form a conical shape known as the Taylor cone. With increasing field, a critical value is attained when the repulsive electrostatic force overcomes the surface tension

and a charged jet of fluid is ejected from the tip of the Taylor cone. The discharged polymer solution jet undergoes a whipping process. wherein the solvent evaporates, leaving behind a charged polymer nanofiber, which lays itself randomly on a grounded collecting metal screen at collector. In the case of the solution the discharged jet solidifies when it travels in the air and is collected on the grounded metal screen as collector.

Electrospinning is shown in figure 1. A Polymer jet is ejected from the surface of a charged polymer solution when the applied electric potential overcomes the surface tension. The ejected jet under the influence of applied electrical field travels rapidly to the collector and collects in the form of non-woven fibers as the jet dries. With low viscosity polymer solutions, the ejected jet may break down into droplets and result in electrospray. Therefore, a suitable polymer concentration is essential to fabricate nanofibers without any beads. For instance, increase in viscosity or polymer concentration and electrical voltage, results in fiber diameter increase. By changing polymer concentration alone it is possible to fabricate the fiber diameters in the range of few nm to several micrometers while keeping other electrospinning parameters at a constant.

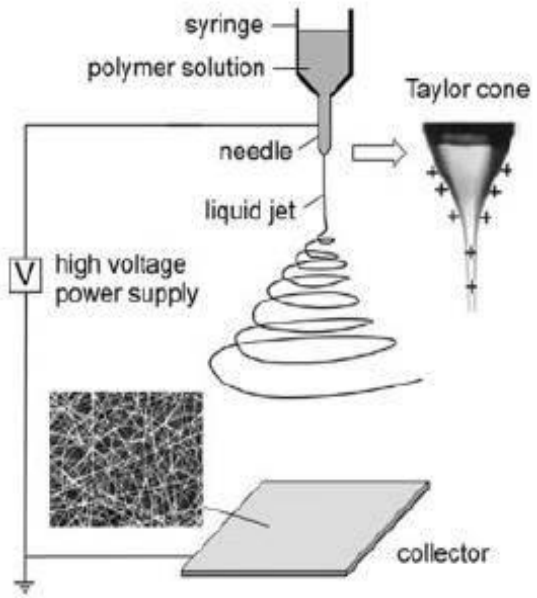

Fig1. *Basic Electrospinning Process*

Various polymers are used for the fabrication of bioscaffold like PCS,PLA,PLGA with molecular weight of 120 kDa and density of 1.25 g/cc. PLGA was chosen to be used due to its biocompatibility, biodegradability and its wide use in drug delivery & skin repair.The solvent used to obtain the polymer solution was acetone of grade ACS reagent. Polymer solution is injected through a needle, which is maintained at a critical voltage (to create charge imbalance) and placed in proximity to a grounded target. At critical voltage, charge imbalance begins to overcome the surface tension of the polymer fibers, forming an electrically charged jet. Grounded target is a collector which collects polymeric fibers with unique diameter. The above description of the process suggests that the following parameters affect the process**:**

2.3. Process Parameters

- Electric potential
- Flow rate & Concentration
- Distance between the capillary and collector screen
- Ambient parameters (temperature, humidity and air velocity in the chamber)
- Polymer concentration
- Type of polymer material

2.4. System Parameters

- Molecular Weight

- Molecular-Weight Distribution and Architecture (branched, linear etc.) of the polymer
- Solution properties (viscosity, conductivity & and surface tension)

2.5. Outcomes

Electro spun nano fiber matrices show morphological similarities to the natural extra-cellular matrix (ECM), characterized by ultra fine continuous fibers, high surface-to-volume ratio, high porosity and variable pore-size distribution. The results obtained from the qualitative and quantitative analyses of the SEMs (scanning Electron Microscope) were divided in to two categories, the effect of processing parameters and the effects of concentration of the polymer solution. Each of these sections present the results obtained of the effect of the parameter of the study on the fibre diameter as well as the bead density. To investigate the effects of some of the key process parameters, we conducted electro spinning at different conditions. The parameters study are concentration, capillary-screen distance (C-SD), electric potential at the tip and flow rate. Different concentrations (15-25 wt %) of PLGA were prepared in DMAc (N, N-dimethylene acetamide) that were electrospun at different voltages (2 - 40kV), capillary-screen distances (12-27 cms) and flow rates (3-7 ml/h). The electrospun samples were collected on a stainless steel mesh (count 20x20) and later sputtered-coated with a 5 nm Pt layer. FESEM (Field Emission Scanning Electron Microscopy) was performed on these samples. Fig. 2 shows the effect of capillary-screen distance (C-SD) on 15-wt % Estane (in DMAc) that were electro spun at 10kV and 3ml/h.

3. CONCLUSION

The overall goal of this research is to evaluate biocompatible & biodegradable electrospun scaffolds as supports for skin tissue engineering. To accomplish this, PLA and PLGA polymers will synthesized with target molecular weights of 42,000 g/mol. Next these two polymers and commercially available PLLA and PDLLA will electrospun to form scaffolds with fibers of diameters 0.14 to 2.1 µm. Finally, cell culture studies were performed to characterize cell morphology, proliferation, and osteoblastic differentiation.

4. FIGURES & TABLES

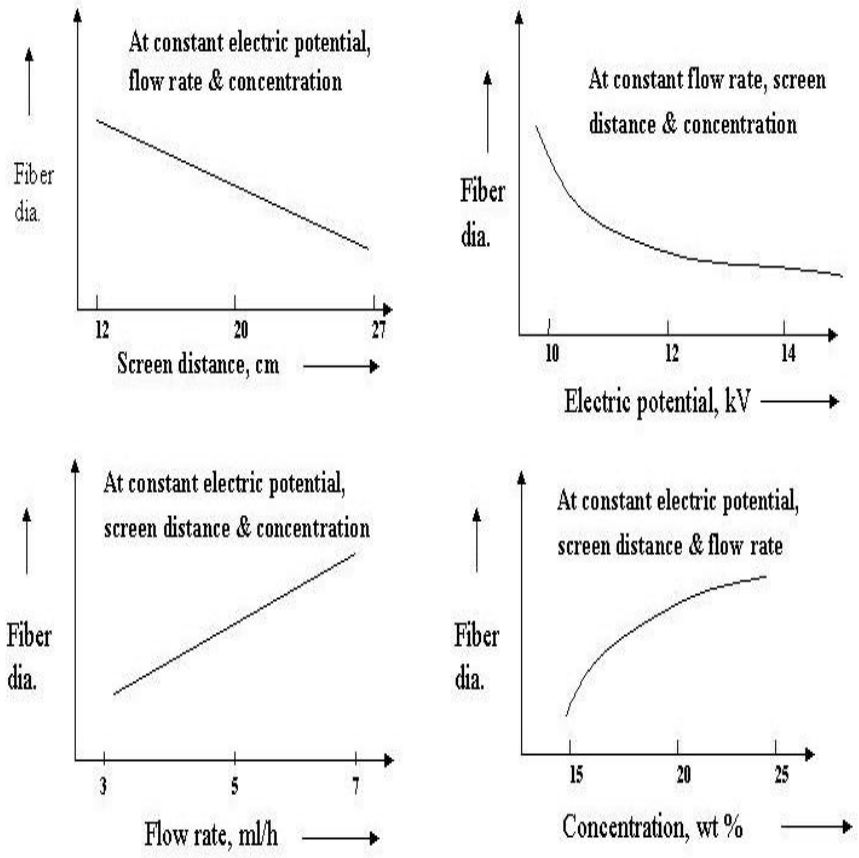

Figure 6. Effect of process parameters on fiber diameter, produced by Electrospinning

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