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ELECTROSPUN-BASED FIBROUS SCAFFOLD FOR CARDIOVASCULAR ENGINEERING APPLICATIONS: A REVIEW

Nur Syazana[1] and Irza Sukmana[2]
[1]MediTeg Research Group, Faculty of Biosciences and Biomedical Engineering, Universiti Teknologi Malaysia, Johor, Malaysia
[2]Department of Mechanical Engineering, Faculty of Engineering, University of Lampung, Bandar Lampung, Indonesia
E-Mail: irza.sukmana@eng.unila.ac.id

ABSTRACT

Heart failure is a major cause of mortality and morbidity occurring in human population all over the world. Heart transplantation following heart failure is difficult to achieve due to limited availability of organ donor supply. Transplantation of a complete engineering tissue of heart and artificial blood vessel remains a dream. However, tissue engineering research field provides opportunity to fabricate bioactive scaffold to support the function of defective tissue or organ, through the development of bio-composite scaffolds construct. The construct that match the chemical, mechanical, biological properties and extracellular matrix morphology of native tissue could be suitable for supporting heart recovery after the failure. This study aims to report current development and future potential on using electrospun-based scaffold. The challenge and opportunity on developing and using electrospun bio-composite scaffolds will also highlight.

Keywords: electrospun fibres, tissue engineering, cardiovascular, scaffolds, bio-composite.

INTRODUCTION

Cardiovascular diseases have becoming the number one global killer. The diseases are including heart failure, stroke, coronary disease, hypertension, heart infraction and inflammatory also rheumatic heart disease [1]. There are about 17 million people was died every year related to this diseases. Factors leads to cardiovascular disease are smoking, physical inactivity, an unhealthy diet and harmful use of alcohol [2]. In the case of these chronic illness, tissue engineering look very useful as method of healing when it may not be able to meet the needs of patients because of organ donor shorten.

Tissue engineering (TE) research offer hopes to replace, repair or regenerate tissues or organs which offer a potential option for patient due to the shorten of donor of organ supply [3]. TE concept includes the development of engineering scaffold construct to seed or encapsulate cells for further formation of functionalize cell-tissue structures [4]. In order to achieve that application, the scaffolds have to be implementing in both biomechanical and biophysical. Performance in biomechanical include the excellent of material selection and designing the three-dimensional (3D) structure of scaffold construct, while biophysical aspect relates to the bioactive clues for the interaction between the material, cells, and their extracellular matrix (ECM) [5].

Electrospinning is one of the current technologies used to produce polymer fibre materials for engineering scaffold construct. The process is based on electrostatic force applied to polymer solution for producing nano/micro scale fibrous scaffolds, mimicking the environment of extracellular matrix in vivo [6]. The potential on fabricating different fibrous scaffold from a broad range of purely natural or synthetic polymers or mixing both polymer types as well as producing a composite structure by introducing ECM-based protein have increased the interest on using electrospun fibres in tissue engineering research exponentially. The electrospinning technology also can precisely control over the polymer composition, fibre diameter, pore size, fibre alignment and distribution for the possibility of tunable scaffold architecture with specific mechanical and biophysical properties. Therefore, successful results that using natural and or synthetic polymer fibre scaffold have been reported elsewhere [7, 8]. This review aims to highlight the current status and future challenge on developing and using electrospun-based fibrous scaffold for cardiovascular and tissue engineering applications.

ELECTROSPINNING TECHNOLOGY

Electrospinning technology was initially patented in the US in 1902 [9]. Due to the limited application it was almost forgotten until in 1934, Formhals patented the production of polymer string using electrostatic force which called electrospinning [9, 10]. Since the development of nanoscience and nanotechnology, electrospinning has been used for producing and investigating nano-scale fibers [11].

Fibers production using an electrospinning technique is started when the polymer solution is carrying through a needle and a high voltage is applied to induce charges in the fluid. This will affect in producing a fluid jet and the development of a Taylor cone from the droplet at the tip of the needle. The generated electrospinning jet is projected toward a lower potential region known as grounded collector. Between the needle tip and the collector, the jet is highly stretched, dried and deposited as a nonwoven fiber structure onto the collector [11, 12].

This process is influenced by the type of polymer and their solution, process parameter, collector conditions and other ambient parameters. By alter those parameters it is possible to obtain electrospun fibers and structures with various morphologies and properties. This possibility opens for further potential application of electrospinning technology for biomedical and tissue engineering fields by producing scaffold and engineering tissue constructs [12].

ENGINEERED TISSUE AND SCAFFOLDS FOR CARDIOVASCULAR APPLICATIONS

In cardiovascular research, there are some potential applications of engineering tissues constructs, they are including: artificial heart valve, vascular graft, and cardiac patches. Chosen the right materials with the right properties are an important subject to be focus. For example, in application of cardiovascular tissue engineering, synthetic biodegradable polymers such as: polyglycolic acid (PGA), polylactic acid (PLA), and co-polymer of PGA and PLA have been widely used because of possibility on tailoring those polymer properties [13]. Also, Polyurethane (PU) and polycarbonate have been used in cardiovascular engineering application as cardiac tissues replacement due to their resistance on stress which is suitable for cardiovascular application [9, 14].

Recent inventions have been also done in order to solve the limitations of today's heart valve replacements with different tissue engineering concepts using various scaffold materials [13]. For example: Hoerstrup and colleagues have been proposed the production of functional TEHV from human MSC was possible employ a biomimetic in vitro environment. The human MSC established characteristics of myofibroblast differentiation [15]. There is also invention that involves a tendency from mechanical valve prostheses to biological valves sources from homo- and xenografts that are safe for encapsulation of fibroblasts or endothelial cells from the patient [13, 16].

Other tissue engineering studies have been also dedicated to engineering the vascular graft using electrospun fibres. For example: He et al. studied the tubular nanofiber scaffolds based on PLLA- PCL blend of 70:30 (v/v) and coated with collagen to fabricate a blood-vessel-like structure that incorporate endothelial cells to perform lumen formation with a solid cell-cell interconnection within 10 days of culture [17]. Also, Sell et al. have been designed and fabricated electrospun fibres scaffold composed of polydioxanone (PDO) and elastin with mechanical properties closely match to human native arterial tissues [18]. Those developments open more potential application of bioresorbable vascular grafts in the future.

Further research in cardiovascular engineering involves in producing cardiac grafts that resist pulsation, high pressure and flow rate of blood stream. The scaffold must support strong cellular attachment and being compliance matched to the surrounding tissue and able to maintain the heart after myocardial infarction diseases [19].

Cell survival is a critical issue in cardiac patch since cells are dense in the outer regions of the graft meaning that the transportation of nutrients and waste in and out of the scaffold is restricted [20, 21]. This result is considerably less cells in the inner regions of the scaffold producing an undesired core effect [21]. Consequently, design criterion is of important for the promotion of rapid vascularization of the scaffold [22]. Good electrospun-based scaffolds architecture should have suitable mechanical properties to support cell growth, proliferation, differentiation, and motility. Furthermore, to apply specific structural formation of engineering tissue construct for their targeted cell type in respect to the cell–biomaterial interactions, contact guidance and cell differentiation, manufacturing of bio-composite scaffold is our current concern in tissue engineering and regenerative medicine research [11, 22].

BIO-COMPOSITE SCAFFOLDS

The native cardiovascular and blood vessels in the human body are complex in structures and functions. For example, human native blood vessels have composed with three different tissue layers, they are: (i) intima, where the endothelial cells are lined, (ii) media, which consist of smooth muscle cells to support microvascular structure of endothelial cell in the intima layer, and (iii) adventia that mainly comprises fibroblast cells and other perivascular nerve cells [23]. Therefore, the need of creating a unique electrospun fibre scaffold and strategy allowing the guidance of different cell types is of important.

One possible strategy is to create a thick engineered bio-composite scaffold that able to promote the microvessel development in a directional fashion in order to vascularize the construct, as proposed elsewhere [22, 23]. Three-dimensional bio-composite electrospun fibre scaffold that composed of self-assembled polycaprlolactone (PCL) sandwiched in human-resources hudrogel (i.e., gelatin, chitosan, and fibrinogen) also shows a potential used for surgical reconstruction of congential heart defect [24]. Multi-layer bio-composite fibre scaffold has sufficient tensile strength for use as a cardiac path, allowing migration of cardiac cells in an environment mimicking the cardiovascular native tissues. Challenges and opportunity on the application of electrospun-based bio-composite scaffold is presented in the Table-1.

CONCLUSIONS

Over the past years, significant advances in tissue engineering have given substantial contribution to the commercial utility of electrospun-based fibre scaffold materials. Some simple engineered fibre scaffolds (e.g., vascular graft and cardiac patches) have been successfully applied and implanted for a short time period, while for the more complex cardiovascular tissue applications and for long term application, some problem still remain. Consequently, bioactive electrospun fibers scaffold construct as well as strategy on enhancing vascularization inside the engineered tissue become of important. Therefore to overcome the complex interplay between various factors influencing the cardiac tissue vascularization, the use of bioactive and bio-composite electrospun fibre scaffold is necessary.

Table-1. Resume of challenge and opportunities on electrospun-based bio-composite scaffold applications.

No.	Bio-composite materials	Challenge	Opportunities	References
1.	Poly(DL-lactide-co-glycolide)/gelatin (PLGA/Gel)	Build up TE that matches the chemical, mechanical, biological properties and extracellular matrix morphology of native tissue use for cardiac patch .	PLGA/Gel nanofibers possible bringing on of an endogenous cardiomyocyte proliferation and will reducing the cardiac dysfunction and also improving cardiac remodelling and bio-mechanical support for injured myocardium.	[5, 24, 25]
2.	Poly(L-lactic acid)-co-poly(3-capro- lactone), gelatin and hydroxyapatite (HA)	Bone replacement therapy using a nano-structured materials	Using electrospraying techniques in electrospinning process may create more appropriate bio-composite nanofibrous scaffolds for bone tissue regeneration	[17, 26]
3.	Type I collagen and nanohydroxyapatite (nanoHA)	Surface modification of electrospun nano fibrous structure to facilitate cells-integrin binding.	Nanoscale features of nano-fibrous collagen and nano-HA able to mimic bone extra cellular matrix and has a potential application as scaffolds for hard tissue regeneration in a low or non-load bearing organs.	[9, 27]
4.	PCL/gelatin bio-composite	Electrospun fibrous construct for nerve tissue regeneration	PCL/gelatin nanofibrous scaffold shows a suitable bio-composite material for nerve tissue restoration and regeneration.	[10, 28, 29]
5.	Poly(L-lactic acid)-co-poly(ε-caprolactone) (PLACL) /gelatine	Extracellular matrix (ECM) -like configuration for skin tissues applications.	Electrospun nanofibres have the opportunity to be implemented as skin regeneration.	[6, 30]

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