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Poly(lactic–co-glycolic acid): Carbon nanofiber composites for myocardial tissue engineering applications

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ABSTRACT

The objective of the present in vitro research was to investigate cardiac tissue cell functions (specifically cardiomyocytes and neurons) on poly(lactic–co-glycolic acid) (PLGA) (50:50 wt.%)–carbon nanofiber (CNF) composites to ascertain their potential for myocardial tissue engineering applications. CNF were added to biodegradable PLGA to increase the conductivity and cytocompatibility of pure PLGA. For this reason, different PLGA:CNF ratios (100:0, 75:25, 50:50, 25:75, and 0:100 wt.%) were used and the conductivity as well as cytocompatibility of cardiomyocytes and neurons were assessed. Scanning electron microscopy, X-ray diffraction and Raman spectroscopy analysis characterized the microstructure, chemistry, and crystallinity of the materials of interest to this study. The results show that PLGA:CNF materials are conductive and that the conductivity increases as greater amounts of CNF are added to PLGA, from 0 S m^{-1} for pure PLGA (100:0 wt.%) to 5.5 $\times$ 10^{-3} S m^{-1} for pure CNF (0:100 wt.%). The results also indicate that cardiomyocyte density increases with greater amounts of CNF in PLGA (up to 25:75 wt.% PLGA:CNF) for up to 5 days. For neurons a similar trend to cardiomyocytes was observed, indicating that these conductive materials promoted the adhesion and proliferation of two cell types important for myocardial tissue engineering applications. This study thus provides, for the first time, an alternative conductive scaffold using nanotechnology which should be further explored for cardiovascular applications.

1. Introduction

Cardiomyocytes (specialized contractile muscle cells that form part of the myocardium tissue of the heart) and neurons (electrically excitable cells that process and transmit certain information by electrical and chemical signaling in the heart [1,2]) depend on continuous conductivity to function [3,4]. However, such conductivity may break down during heart disease or malfunction. For instance, a myocardial infarction, also known as a heart attack, usually occurs because a major blood vessel supplying the heart's left ventricle is suddenly blocked by an obstruction, such as a blood clot [5–7]. During myocardial infarction, part of the cardiac muscle, or myocardium, is deprived of blood and, therefore, oxygen, which destroys cardiomyocytes and neurons, leaving dead tissue [5–7], as well as denervation of the myocardium [1,8,9]. In particular, nerve damage to cardiac tissue can result in nerve sprouting in the left ventricle [8,10] and development of arrhythmia [11]. Scarred cardiac muscle results in heart failure for millions of heart attack survivors worldwide. In 2009, an estimated 785,000 Americans had another coronary attack and about 470,000 had recurrent heart attacks leading to coronary events [12].

In recent years various techniques have been developed to promote cardiomyocyte and neuron growth around dead tissue after a myocardial infarction. Such techniques include ex vivo culture of cardiomyocytes on cardiac patches for eventual implantation [13–22], direct cell injection [23–28], scaffolds made from collagen, poly(lactic acid) (PLA), or polycaprolactone (PCL) [29–35], three-dimensional (3D) printing using thermal inkjet printing technology [36–38], and injectable scaffolds using materials ranging from fibrin to carbon nanofibers (CNF) [39–41]. Each approach has its own advantages [42], as well as disadvantages [42], but in general all of the above can be divided into two groups: (a) conductive cardiovascular patches (using scaffolds and 3D printing techniques, usually with polypyrrole) and (b) non-conductive cardiovascular patches (mostly involving direct cell injection, scaffolds, and injectable scaffolds). Cardiovascular biomaterials can be based on either biodegradable or on non-biodegradable materials. Within this matrix of conductive vs. non-conductive and biodegradable vs. non-biodegradable materials lie the most commonly studied materials and techniques used to promote heart health.

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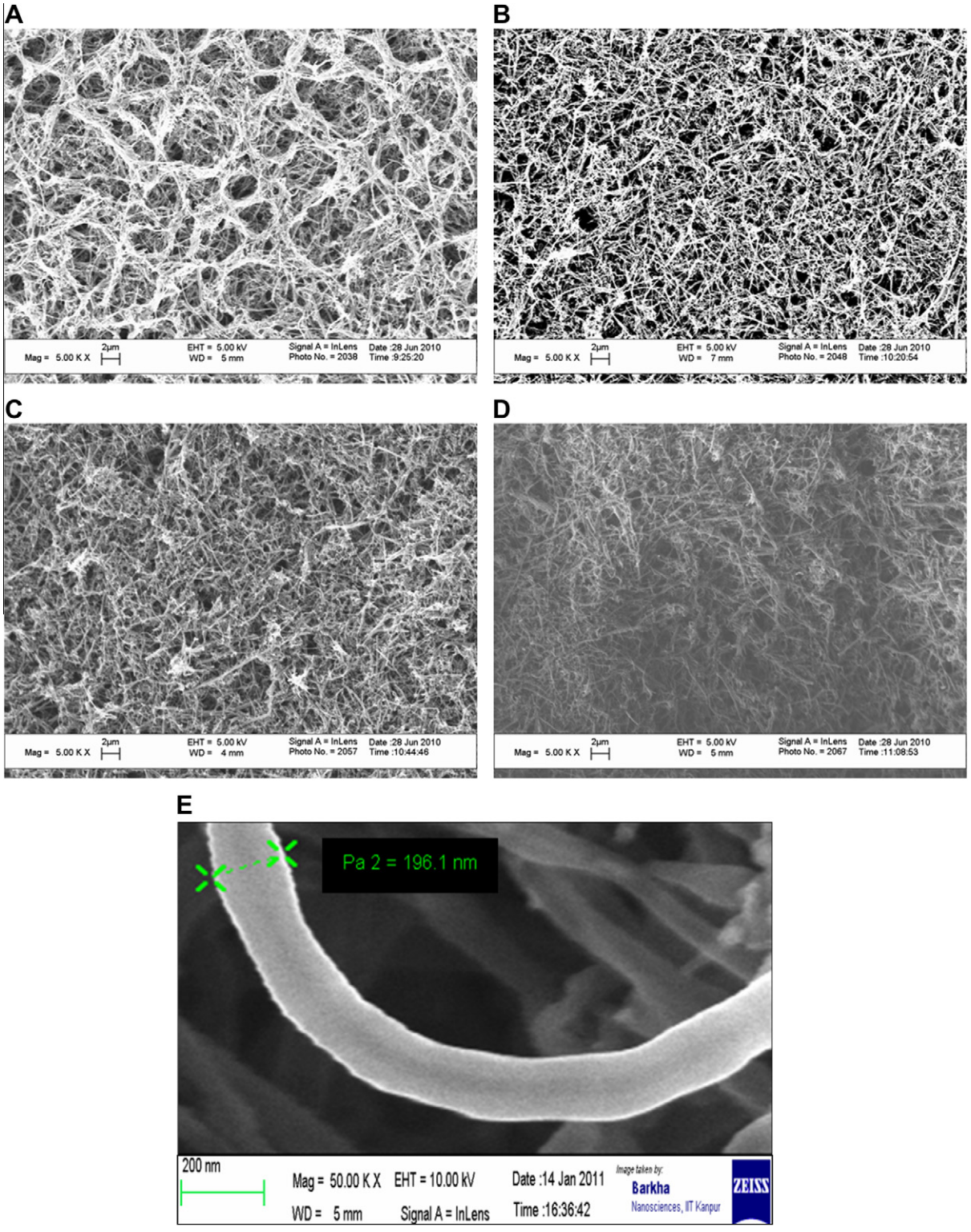

Fig. 1. SEM images at 5000× magnification showing the distribution of CNF fibers in the PLGA matrix at different PLGA:CNF (wt.%) material ratios for the (A) 75:25, (B) 50:50, (C) 25:75, and (D) 0:100 composites. (E) A typical high resolution image revealing one CNF diameter is also shown.

However, one area that has been largely omitted to date is the exploration of nanotechnology (materials with one dimension in the nanometer regime) in cardiovascular applications.

Numerous articles have suggested that using nanotechnology can specifically promote cell functions on a variety of materials, ranging from titanium to silicon [43–45] due to optimization of surface chemistry and wettability, which control protein adsorption onto the surface. While some degree of nanostructuring may promote tissue growth, it is also known that certain topographies can hinder cell activity [46–48]. For example, when comparing nano with micron diamond features, Yang et al. showed that osteoblast (bone forming cell) adhesion and proliferation increased on the nano-rough topography [46]. In contrast, using a 1718 gene microarray, Dalby et al. suggested that nano-rough topographies

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