GREEN CHEMISTRY AND GREEN ENGINEERING

Processing, Technologies, Properties,
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and Applications

Edited by

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Contents

<i>Contributors</i>	<i>ix</i>
<i>Abbreviations</i>	<i>xi</i>
<i>Preface</i>	<i>xvii</i>
1. Electrospinning of Bio-Based Polymeric Nanofibers for Biomedical and Healthcare Applications	1
Rinky Ghosh, Veereshgouda Shekharagouda Naragund, and Neha Kanwar Rawat	
2. Solar Energy for Green Engineering Using a Multicomponent Absorption Power Cycle	23
Satchidanand R. Satpute, Nilesh A. Mali, and Sunil S. Bhagwat	
3. Characterization Techniques for Bio-Nanocomposites	49
Shrikaant Kulkarni	
4. Chemistry Matrices of Biotransformation	83
Shrikaant Kulkarni	
5. Sustainable Chemistry and Pharmacy	109
Hitesh V. Shahare and Shweta S. Gedam	
6. Magnetism, Polyoxometalates, Layered Materials, and Graphene	123
Francisco Torrens and Gloria Castellano	
7. Plasma, Photo/Radiochemical Reactions, and Relativity Theories	135
Francisco Torrens and Gloria Castellano	
8. Mesoporous, Graphene Composite, Li-Battery, Topology, and Periodicity	149
Francisco Torrens and Gloria Castellano	
9. Boom for Circular Economy and Creativity: Chemistry to Improve Life	163
Francisco Torrens and Gloria Castellano	
10. Application of Engineered Nanomaterials in Environmental Protection and the Visionary Future	189
Sukanchan Palit	

11. Chemistry and Sustainable Development.....	211
Francisco Torrens and Gloria Castellano	
12. Manganese Porphyrins as Pro-Oxidants in High-Molar-Mass Hyaluronan Oxidative Degradation.....	223
Katarína Valachová, Peter Rapta, Ines Batinic-Haberle, and Ladislav Šoltés	
13. Modified Magnetic Metal-Carbon Mesoscopic Composites with Bioactive Substances	243
V. I. Kodolov, I. N. Shabanova, V. V. Kodolova-Chukhonzeva, N. S. Terebova, Yu. V. Pershin, R. V. Mustakimov, and N. M. Pogudina	
14. Pre-Treatment of Rusted Steel Surfaces with Phosphoric Acid Solutions.....	255
Victor M. M. Lobo and Artur J. M. Valente	
15. Transport Phenomena of Electrolytes in Aqueous Solutions: Concepts, Approaches, and Techniques	269
Ana C. F. Ribeiro, Eduarda F. G. Azevedo, Ana Paula Couceiro Figueira, and Victor M. M. Lobo	
<i>Index.....</i>	285

EPA	Environmental Protection Agency
EPR	electron paramagnetic resonance
ESI	electrospray ionization
ETH	Zürich Eidgenössische Technische Hochschule Zürich
FCT	Fundação para a Ciência e a Tecnologia
FLU	fluorescence
FM	ferromagnetic
FPF	fine particle fraction
FRs	free radicals
FTIR	Fourier transform infrared spectrometry
G	gaseous
GDH	glucose dehydrogenase
GPS	global positioning system
GR	graphene
GSK	Glaxo Smith Kline
GTR	general theory of relativity
GW	gravitational-wave
H	hypotheses
H ₃ PO ₄	phosphoric acid
HA	hyaluronan
HA	hydroxyapatite
HCs	hydrocarbons
HF	Hartree-Fock
HF	high-frequency
HHDH	halohydrin dehalogenase
HILIC	hydrophilic interaction liquid chromatography
HN	hydroxynitrile product
HTs	high temperatures
ICP	inductively coupled plasma
ICP-AES	inductively coupled plasma-atomic emission spectroscopy
ICP-MS	inductively coupled plasma-mass spectroscopy
IG	ideal gas
IR	infrared
IS	interstellar space
ITC	isothermal titration calorimetry
JWST	James Webb space telescope
KQs	key questions
KRED	ketoreductase
L and RCPL	left and right-handed circularly polarized light

L	liquid
LCA	life cycle analysis
LDHs	layered double hydroxides
LP	low pressure
LTs	low temperatures
MA	magnetic anisotropy
MAE	magnetic anisotropy effect
MCM	Mobil composition material
MDGC	multidimensional gas chromatography
MF	magnetic field
MFLs	MF force lines
MHD	magnetohydrodynamic
MI	mass intensity
MnPs	manganese porphyrins
MnSOD	manganese superoxide dismutase
MOFs	metal-organic frameworks
MP	mass productivity
MP	medium pressure
MS	mass spectrometry
MS-FTIR	mass spectrometry-Fourier-transform infrared spectroscopy
MSs	magnetic susceptibilities
MT	MF trap
MWs	microwaves
NAC	<i>N</i> -acetylcysteine
NAP	near ambient pressure
NCs	nanocomposites
NG	natural gas
NMR	nuclear magnetic resonance
NMs	nanomaterials
NS	nanoscale
ORC	organic Rankine cycles
OSs	oxidation states
P	plasma
PCS	photon correlation spectroscopy
PEO	poly(ethylene oxide)
PGA	polyglycolide
PLA	poly-lactic acid
PLGA	poly lactic-co-glycolic acid
PM	paramagnetism

PMs	porous materials
PMT	photomultiplier tube
POM	polyoxometalate
PPO	poly(propylene oxide)
Pt	platine
PTE	periodic table of the elements
PTs	phase transitions
PV	photovoltaic
QM	quantum mechanics
RCL	rust conversion layers
RE	renewable energy
Red-Ox	reduction-oxidation
RME	reaction mass efficiency
ROS/RNS	reactive oxygen and nitrogen species
RPES	x-ray photoelectron spectroscopy
RT	room temperature
S	solid
SBA	<i>Santa Barbara Amorphous</i>
SCF	self-consistent field
SCs	superconductors
SEM	scanning electron microscopy
SEs	side effects
SF	silk fibroin
SMs	standard models
SPM	scanning probe microscopy
SPR	surface plasmon resonance
SPRs	structure-property relationships
SQUID	superconducting quantum interference device
SSA	specific surface area
STEM	scanning transmission electron microscopy
STM	scanning tunneling microscopy
SVR	surface to volume ratio
SWNHs	single-wall nature of nanohorns
SWNTs	single-wall carbon nanotubes
TBG	twisted bilayer GR
TCD	tip-to-collector
TEM HP	transition electron microscopy with high permission
TEM	transmission electron microscopy
TEOS	tetraethylorthosilicate

TFs	thin films
TIP	thermodynamics of irreversible processes
TLC	thin-layer chromatography
TNT	trinitrotoluene
TP	transport properties
TQC	topological quantum chemistry
TTM	tris(triazolyl)methane
UHCs	unsaturated hydrocarbons
UV	ultraviolet
VIS	visible
VSM	vibrating sample magnetometer
WDXRF	wavelength dispersive X-ray fluorescence spectrometry
WWI	World War I
XPS	x-ray photoelectron spectroscopy
XRF	x-ray fluorescence spectrometry
ZnO	zinc oxide

CHAPTER 1

Electrospinning of Bio-Based Polymeric Nanofibers for Biomedical and Healthcare Applications

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ABSTRACT

The interest in the electrospinning process for the medicinal chemistry and nanotechnology field has escalated recently. This is because of simplicity in its design, cost-effectiveness, and interconnected porosity, better encapsulation of therapeutic agents, thermal consistency, higher loading capacity, and controlled release of drugs/gene carriers. Electrospun scaffolds recently have high behest for successful fabrications of scaffolds due to its significant endocytosis interactions with the cells and suitable degradation profile, tremendously exposed in the implants surgery and tissue regenerations.

Scaffolds of biocompatible nanofibers offer an efficient sustainable route for easy production of and facilitate the tailoring of surface properties by grafting and functionalization with bioactive agents. The biological studies have shown high potential in applications of biocompatible and biodegradable nanofiber scaffolds for wound dressing patches and drug delivery.

This chapter briefly discusses the electrospinning fundamental approaches to produced nanofibers scaffolds, biocompatible properties, drug-releasing rate kinetics, and its various applications in the interdisciplinary field of medicinal science.

1.1 INTRODUCTION

Innovative and scientific technologies focused around bio-based materials have gained considerable attention recently. They are currently at a peak of exigency to decline the usage of petroleum products and to raise the demands for bioplastics. The petrochemical products are now an integral and substantial part of society. The fossil fuel-based products can also be termed as never-ending life cycle [1] products causing a devastating effect to the natural habitat leading to climate changes, which create an environment pressure are now escalating day-by-day and the crude oil reserve prevalent currently coming to an end. The overall growth in the petrochemicals products is underpinning due to difficulty in finding an alternative for various structural applications. With consistent rise in demand of plastics on the per capita basis has lead to some major consequences around the globe creating permanent environmental pollution which needs to be addressed immediately. This has forced governments to curb the single-use plastics and focus more value chain of production activities to minimized effluents, wastage, and emissions rate during conversion of crude oil to the desired plastics products. The need for imposing a strict rule for waste management and recycling process is an urgent need that will not only maintain ecological balance but also helps in sustainable growth [1]. Today bio-based polymers are of pivotal importance and a popular choice for number of applications due to its sustainable benefits. High-performance properties of the bioplastics can be achieved by significant use of the nanofibers or biofibers [2] as composite materials or filler particles or as an additive. Before the starting of this new era, nanofibers are of vital importance and have gained growing scientific recognition, technological importance in the field of aviation, automobile, biomedical, etc. Electrospinning has been successfully used in the past few decades to produce nanofibers ranging from few micrometers to nanometers. It provides an opportunity for blending, incorporation of nanofillers into electrospun nanofibers; tune the surface properties and making fabrication more economically feasible and cheaper.

1.2 HISTORICAL EVIDENCE

It was unfamiliar for most of the researchers around the world during the beginning of this new era that electrospinning can enable to us produce nanofibers in the form of continuous filaments with diameter ranges from submicron to nanometers. The word ‘electrospinning’ has been derived from the term ‘electrostatic spinning’ and this process was first patented by Anton Formhals in the year 1934. He disclosed complete setup to produce polymeric filaments from the polymeric solution of cellulose acetate using a phenomenon of opposite polarity effects that generates an electrostatic effect.

1.3 A BRIEF ABOUT ELECTROSPINNING FUNDAMENTALS AND ITS VARIOUS PARAMETERS

The electrospinning set up mainly consists of two electrodes: one dipped into the polymeric solution and the other connected to the collector/rotatory plate. With the application of high voltage ranging from 10–25 kV to the polymeric solution, the electrical charges flow through the spinneret to the tip of the capillary tube. As the electric current encounters the solution at the tip end, this induced separation of charges on the surface of the droplet leads to the deformation of the hemispherical surface to the conical shaped (Taylor Cone). Once it exceeded the cohesive force or surface tension of the liquid, a thin jet emerges out and subdivides collecting on the moving rotatory drum which is kept at some suitable distance. Based on the reported articles, spinneret has been considered as an essential part of nanofibers production. Nanofibers with various diameters and multiple configurations can be obtained by slight variations in the processing parameters and core-shell implementation of the spinneret part. The salient features of electrospun nanofibers are dependent on various parameters-viscosity, voltage, surface tension, flow-rate, tip-to-collector (TCD) distance, temperature, and relative humidity. These essential parameters have a major impact on the diameter and morphology as well as the mechanical properties of the produced nanofibers. Through carefully conducted experiments and optimizations of the experimental set up allow hindering the possible contamination of produced nanofibers useful in wound healing treatment and its effective interconnected porous feature promotes cell adhesion-vital important phenomenon to improve biological functions and improved wound healing rate [12–16]. Figure 1.1 illustrates the application of electrospun nanofibers in various fields.

FIGURE 1.1 Various properties and applications of electrospun polymeric nanofibers.

The unoriented fibrous structure and high SVR mimicking the morphological 3D characteristics of the skin's extracellular matrix [17, 18] is useful for muscles and nervous tissue regeneration and nourishes wound segments thereby provide a moist environment for collagen resynthesis and enhancement of angiogenesis.

1.3.1 ELECTROSPINNING PROCESS

A schematic of an electrospinning setup is shown in Figure 1.2. In an electrospinning process, a high voltage electric field (EF) is applied between a polymer solution and a metallic collector. When the voltage crosses a limiting value, the charges in the polymer solution overcome the surface tension forces and a jet is ejected. The jet due to its hydrodynamic instabilities subdivides into millions of nanofibers as it travels towards the collector. The solvent evaporates quickly due to the large surface area of nanofibers and fibers are collected on the collector. With increasing time, the membrane thickness increases and can be peeled off from the collector.

The parameters affecting the electrospinning process are of great interest because, with the understanding of these parameters, it is possible obtaining nanofibers with different morphology and diameters. It is also possible to

optimize setups to yield fibrous structures of various forms and arrangements. If one observes the electrospinning the three things that stand apart are: (i) the solution used, (ii) the capability of the electrospinning equipment, and (iii) the environmental conditions at which electrospinning is occurring. Thus, the parameters affecting the process can be categorized into two classes:

FIGURE 1.2 A schematic diagram of electrospinning equipment using a rotating drum collector to obtain aligned nanofibers.

1. The material system parameters:
 - i. The polymer parameter:
 - The molecular weight of the polymer granules;
 - The weight distribution and architecture of the polymer (branched, linear, etc.).
 - ii. The solution parameters:
 - Viscosity: High enough to maintain continuity within fibers and low enough to come through the capillary;

- The conductivity of solution;
 - The dielectric constant of the solvent;
 - Surface tension;
 - The charge carried by the spinning jet.
2. The processing parameters: These pertain to the electrospinning processing conditions that can be controlled by the operators. Some electrospinning equipment support precise control over environments within the enclosure:
- i. The electric potential applied;
 - ii. The flow-rate of solution;
 - iii. Distance between capillary tips to a collector;
 - iv. Ambient parameters (temperature and pressure);
 - v. The motion of the target screen.

Therefore, in electrospinning, the above conditions can be varied to produce nanofibers with different morphologies/diameters and then optimize the parameters to produce highly aligned nanofibers.

1.3.2 METHODS TO OBTAIN ALIGNED NANOFIBERS VIA ELECTROSPINNING

Aligned nanofibers are obtained by many researchers using different techniques applying modifications to the conventional electrospinning equipment. These can be classified into three categories: (i) mechanical, (ii) electrical, and (iii) magnetic. All of these may involve one or more of (i) modified nanofibers collector system, and (ii) use of additional electrodes to direct electrical or magnetic fields (MFs). Some of the techniques used are:

1. High speed rotating drum collector;
2. Disc type collector with sharp edge;
3. Wire drum collector;
4. Dual vertical collector;
5. Collection between flat magnetic bars/strips;
6. Secondary Wedge electrodes;
7. Post-processing operation such as stretching;
8. Patterned insulating gaps on quartz electrodes;
9. Use of auxiliary electrodes to manipulate EFs;

10. Ring electrodes and EFs using the principle of right-hand thumb rule to align magnetic fibers;
11. Use of AC voltages.

Sarkar et al. [35] reported the use of combination of DC and AC potentials for minimizing the inherent fiber instability in the electrospinning process, calling it as “biased AC electrospinning,” and obtained highly-aligned mats of polymer or composite polymer fibers. The applied AC voltage introduces alternating positively and negatively charged regions in the fiber, resulting in a decrease in electrostatic repulsion and an increase in fiber stability found that a very high degree of fiber uniformity and alignment could be achieved for each polymer/solvent system investigated in this study as long as the following two general process requirements were followed: (i) The magnitude of the DC bias must be less than half the total amplitude of the AC potential; (ii) The AC frequency should be between 500 and 1000 Hz for optimum fiber stability.

Matthews [36] noted that collagen fibrils electrospun onto a mandrel rotating at a rate of less than 500 rpm produced random fibers. On increasing the velocity of the mandrel to 4500 rpm (1.4 ms^{-1}), finally resulted in the deposition of fibrils along the axis of rotation.

Ashish Aphale et al. [38] investigated a new configuration of axial rotating disc collector setup that yielded a good amount of alignment in PVA nanofibers of around 200 nm in diameter embedded with CNT over the surface of rotating disc.

Another interesting report by Ajao et al. [37], they demonstrated the use of MFs to align PEO nanofibers. Their modified electrospinning setup consisted of cylindrical magnet covered with silicon wafers on all sides kept between the ground electrode and spinneret. The aligned nanofibers were only observed over the top portion of the silicon wafer.

Li et al. [39] obtained aligned nanofibers in insulating gaps of various shape such as triangular, rectangular, circular holes cut between quartz electrodes (Figure 1.3).

Katta et al. [43] fabricated Cu wire drum ($d = 12.7 \text{ cm}$, $l = 30 \text{ cm}$) rotating collector at 1 rpm to obtain macro alignment of 20% nylon nanofiber for shorter duration of times. The possible reason might be the charge deposition over the nanofibers. It is possibly due to an accumulation of charge in the fiber mat, but the jet was not observed to stray away from the grounded wires as is often the case with low conductivity polymers. It is also possible that the nylon mat acts as a conductor; the thickened mat on the wire drum fills in the gaps between the wires with a grounded surface

and the electrospinning jet effectively experiences the grounded field of a solid drum.

FIGURE 1.3 Aligned nanofibers obtained by nanofibers obtained by dual vertical stainless-steel wire technique.

Source: Reprinted with permission from [43]. © 2004 American Chemical Society.

1.4 PROPERTIES AND VERSATILE BIOMEDICAL APPLICATIONS OF ELECTROSPUN BIODEGRADABLE NANOFIBERS

With the advent of nanotechnology and nanoscience, it has gained significant popularity and commercial interests with global productive benefits. Among various versatile techniques available scientists around the globe focuses more on electrospinning process to fabricate nanofibers, its remarkable properties have been intensively investigated due to its unique morphology and enhanced flexibility. Several publications of inexpensive electrospinning process for biomedical applications has grown exponentially due to its outstanding porous sizes or interconnected pore structure, ease of fabrication and large surface to volume ratio (SVR) facilitate the active loadings of biomolecules which helps in possible transportation of nutrients and other bioactive agents. The successful *in-vitro* and *in-vivo* studies suggested that biodegradable and biocompatible polymers for example Collagen, chitosan-chitin, poly-lactic acid (PLA), elastin, alginate, poly(ϵ -caprolactone), polyglycolide (PGA), fibrinogen, and polyesters, etc., have wide range of future aspects due to its significant endocytosis

interactions with the cells and suitable degradation profile, tremendously acknowledged in the implants surgery and tissue regenerations. As they metabolize, at the same pace and also its degradation time are tunable with the tissue regrows time range. Literature, reported the overwhelming and garnering performance of electrospinning process although several others advanced technologies are available to fabricate nanofibers/nanofibrous mats some of them includes, template synthesis, drawing process, solvent-casting, stretching method, inland spinning and phase separation. But more importantly with the increased knowledge of nanostructures, nanoparticles, and nanofibers, highlighted research conclusions pointed-out in numerous articles suggested the issues regarding fabrications using other techniques but in spite of all electrospinning pave the way for advancements in many bioengineering areas due to its easy, cost-effective, and versatile processing techniques with scant drawbacks that can be tunable (Figure 1.4). Scaffold fabrications have been developed with the help of the electrospinning process as it also provides an efficient sustainable route for easy production of biocompatible scaffolds and its properties can be preferably tailored with suitable grafting or functionalization. Haider et al. have reported the intriguing performance and important characteristics of hybrid scaffolds successful in providing similar environment to the cells for better adhesion; attachment ultimately results in proliferation [30]. More efforts are still performed to widespread the electrospinning techniques and to scale up the process as it enables the processing of biodegradable polymeric solution of several liters in a single run, therefore has gained noteworthy interests and profitable business to be used for industrial applications.

From the biological viewpoint, human tissues and organs possessing hierarchical fibrous structures, therefore progressive researches focused more on the biopolymers based nanofibrous for bioengineering applications [4]. Electrospinning is the most reliable, versatile, ease of processing technology to develop highly efficient uniform surface area non-woven nanofibrous mats with small porous size are of physiochemical and biological importance competent in the field of tissue prosthesis, organ implantation, drug delivery, and wound dressings. To ideally design the scaffolds for tissue engineering applications is one of the greatest challenges, as such fibrous based matrix effectively fabricated that can imitate the native biological functions and provides a template for cell proliferation which helps in the regeneration of tissues/organs [4] (Figure 1.5). Therefore, it has been reported and surges in the number of reports depicting the effective utilization of biodegradable polymeric nanofibrous in the field of

biomedical science by imparting a favorable cellular environment that can mimic the extracellular matrix [8] and provide a platform for the development of biomaterials scaffolds [5–7].

FIGURE 1.4 Schematic representation of various biomedical applications of electrospun biodegradable nanofibers.

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The modern technology relies most on the fibrous hemostatic bandages for wound healing applications with desired pore size essential for the wound healing treatment [9]. It effectively declines the penetration of bacteria's and prevents the wound from its further attack because of its desirable pore diameter. With specific choice of biopolymers based fibrous bandages are new subject of interests to many researchers around the world as it provides several requisite promising properties in one single foundation such as antibacterial, antimicrobial, and it helps in remedying the pain by imparting anti-inflammatory conditions which enhance the rate of healing.

In the competitive market for cosmetics and skincare products polymeric nanofibers find greater recognition widely used for skin cleansing agent and facial mask having both therapeutic and medicinal effects [10]. As the nanofibers have very small interstices and pore diameter which are effective for rapid transfer of additives into the skin pores, penetrate painlessly and cover the topography of the skin-is well known for increasing the rate of skin healing and helps in the skincare treatment.

FIGURE 1.5 Schematic representation of tissue regeneration with the help of electrospun nanofibrous scaffolds.

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The traditional and outrageous methods to stop bleeding and promote rapid hemostasis is by applying hand pressure or using chemical spray technique on the wounded topography that promotes vasoconstriction but change in clotting activity or secondary damaged to the wounds has been observed [11]. The clotting cloth available for rapid hemostasis have some drawbacks associated with it, for example, poor adhesion, less soothing effect, and a possible chance for bacteria's penetration.

In contradiction, electrospun nanofibrous mats developed is of crucial importance and have attracted much attention for the rapid hemostasis. They facilitate the blending of hemostasis components with polymeric solution resulting in mats formations have a large surface area and high porosity which promotes good adhesion. They inhibit the breeding of bacteria and further provide a favorable condition for the regrowth of cells by absorbing all the extracellular fluids [3], as shown in Figure 1.6.

Electrospinning of nanofibers involves the preparation of a suitable polymer solution using a particular compatible solvent of various viscosities. This technique of producing nanofibers increases the SVR ensures large porosity facilitates the growth of cells attachment and proliferation.

FIGURE 1.6 (a) Showing electrospinning technique to produce nanofibrous mats. (b) to (h) Schematic diagram of rapid hemostasis and rapid healing effect using nanofibrous mats.

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1.5 HEALTHCARE APPLICATIONS OF BIO-BASED POLYMERIC ELECTROSPUN NANOFIBERS

1.5.1 TISSUE ENGINEERING/SKIN REGENERATION AND WOUND HEALING

Since a decade, the main tissue engineering application lies in the healing of physiological disorders which have a devastating effect on the nervous, bone, and spinal tissues, etc., to seek repair and replace tissues by appropriate incorporation of biologically active molecules. Transplantations of organ/tissue are a major health issue as firstly it is not economical, secondly

limited accessibility of donor matching. Skin burns/wounds have its own fundamental aspects to self-heals or having significant self-regenerating ability by maintaining the bodies homeostasis conditions unless the consequence of chronic wounds is severe or unpleasantly extensive lesions [19]. Since many of the effective treatments are currently available sometimes failed to treat the wounds completely causing trans epidermal water loss and microbial growth and as a result infection spreads swiftly have a major impact which leads to patient's death. The other important factor to be considered is bio-degradability, as old tissue scaffolds must be replaced with new ones with a passage of time. Thus, to make them skilled in expediting this novel cell-biomaterial interfaces. Scaffolds are the most essential part and are highly suitable for tissue regeneration as the morphological structure contains microscale interconnected pores topographically similar features to that of ECM presents in our body which possessed 3D porous structure and exclusively made up of collagen and others biocomponents. Several authors have recently reported the incorporations of proteins to the interconnected pores of the electrospun nanofibrous mats. Proteins are known to be produced crucial biological signals beneficial for tissue regenerations particularly helpful in the regrowth of nervous tissue. PCL nanofibers are amenable for incorporation of protein molecules due to its large topographical network are promisingly attractive with improved depositions efficiency because of its physiological, biocompatible features and degradation rate which is closely matched with the rate of regeneration of new tissues obliging for scaffolds preparation and drug-delivery applications. The fundamental goal is to develop neotissues/neoorgans with similar biomimetic geometries as native one. One drawback of using PCL is its poor hydrophilic nature leads to reduction of cell migration, cell attachment, proliferation, and differentiation [22, 23]. The need for arterials prostheses is now in urgent demand due to failure of vascular system its main cause lies in cardiovascular disease which leads to stroke, coronary, inflammatory, and infraction. The blood vessels are primary source of transfer of nutrients and maintaining temperature in human body. Fabrication of vascular tissues is the most fundamental challenges faces through the decade, but with advent growth of electrospinning process and use of composite biodegradable polymers have reduced the chances of deaths. Valence et al. has successfully reported the electrospun scaffolds composed of PCL and cross-linked with acrylate L-lactide-co-trimethylene carbonated elastomer depicted burst pressure, suture retention strength and negligible formation of aneurysm show striking resemblance with human veins confirmed through *in-vivo* studies [24, 25].

Jayakumar et al. were reported the electrospun fibrous materials-chitosan/chitin based used for posttraumatic wound healing applications, tissue engineering scaffolds, and drug delivery [20, 21]. Chitosan/chitin possessed certain properties such as biocompatibility, low cytotoxicity, high durability, microfluids absorption, biodegradability, and antimicrobial-antifungal activity, causing an accelerating effect on the wound healing rate. But major drawbacks associated with it using neat chitosan lies in its poor mechanical properties and loss of integrity in aqueous media restricted their applications in biomedical fields. To overcome these disadvantages of single-use electrospun polymer, researchers across the globe are more interested in the composite scaffolds to avoid fishnet effects and to promote cell proliferation and cell adhesion.

Fibrous nanocomposites (NCs) composed of hydroxyapatite (HA) and silk fibroin (SF) owing to its flexibility, low inflammatory responses, biocompatibility, and show better permeability towards oxygen and water vapor. Thus emulating the basic building blocks structure of collagen nanofibers present in the orthopedic area specifically used as a substitute for bone replacement and dental implantation due to its weak osteogenic capacity. SF is a fibrous protein obtained from the silk-worm in the filamentary form. Bone formation required the requisite mesenchymal stem cells derived from bone marrow and was a cell cultured in osteogenic media for 30 days at ambient conditions. The novel biomimetic SF composite scaffolds prepared by electrospinning, aid the growth of mesenchymal stem cells demonstrated the significant bone formation as shown in Figure 1.7.

1.5.2 WOUND DRESSING

Various biodegradable natural and synthetic polymers electrospun into nanofibers facilitates the cell proliferation of fibroblasts and cell attachment with the additional benefit of tunable mechanical properties which prevent the wound contraction during implantation and has significantly accelerated the fabrication of scaffolds for wound healing applications.

Kumber et al. have reported the efficacy for dermal regrowth, improvement in cell proliferation and effective propagation of human skin fibroblasts through scaffold fabrication using polylactic acid (PLA) and poly lactic-co-glycolic acid (PLGA) [26]. The entire outcome of the process was investigated through *in-vivo* studies and has demonstrated the biodegradable scaffolds made of PLA/PLGA are best till date for wound healing treatment, as it supported the growth of keratinocyte, fibroblast, and endothelial cell. The *in-vivo* studies revealed that the slight variations in the mole fractions of

nanofibers of lactide/glycolide (85:15, 75:25, and 50:50) would significantly result in better up-gradation in the expression of collagen and fibroblasts growth [27]. He has shown the mole fraction ratio of nanofibers 85:15 and 75:25 remained stable after 1 year of implantation and therefore considered it as a favorable scaffold for wound treatment whose degradation rate closely matches with the healing rate in defected tissue as shown in Figure 1.8.

FIGURE 1.7 (a–e) Represents the SEM micrograph of nanocomposite scaffolds composed of Silk fibroin (SF) and hydroxyapatite particles which are well exposed to the surface of the scaffolds.

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FIGURE 1.8 Implanted scaffolds composed of electrospun PLA and PLGA of varying molar ratios into the Wistar rats and the tests conducted from 2 weeks to 2 years to see the fibroblasts growth.

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1.5.3 DRUG DELIVERY

Many therapeutic compounds are incorporated into synthetic or natural bio-based electrospun scaffolds as a drug carrier for preferable delivery of antibiotics and anticancer drugs in the preferred sections of our body. Electrospun nanofibers have shown inevitably controlled at the release of

drug at the definite period of time and hence a suitable prospect for drug delivery applications. The rate of release of drug profile can be tunable by controlled modulation of morphology, interconnected pore size, short diffusion length, and drug-binding sites which ensure better therapeutic effects. The various attractive features of electrospinning nanofibers such as mechanical modulus, hydrophilicity, higher drug loading capacity, higher encapsulation efficiency, cost-effectiveness, and drug-releasing kinetics can easily be determined by the drug diffusion analysis and weightage average of distribution of drug particles on the surface of the nanofibers. Nanofibers scaffolds used as a tool for drug delivery and postoperative chemotherapy due to its excellent barrier properties and biocompatibility.

To design the proper drug release system, blending of drugs into polymeric solutions is a primary requirement before performing the electrospinning process to obtain ultrafine drug-loaded scaffolds. The drug loaded-scaffolds exhibited burst release at the initial stage of the installations to eliminating the effect of bacterial attacks before proliferation [28].

Huang et al. have successfully demonstrated the importance of Gelatin nanofibers for drug delivery applications [29]. Gelatin is a natural-based biodegradable polymer derived from collagens a potential candidate for controlled release of drugs has several advantages compared to conventional pharmaceutical dosage materials available in the market such as desired therapeutic effect, low cytotoxicity, enhanced biocompatibility, etc.

Yuan et al. have demonstrated a pH-sensitive polylactide nanofibers comprised of sodium hydrogen bicarbonate (NaHCO_3) used for controlled release of drug carrier ibuprofen, resulted in faster rate of skin wound healing. The pH-sensitive stimuli-responsive behavior of electrospun nanofibers are well justified and shown rate kinetics of drugs can be enhanced by using smart electrospun nanofibers in terms of drug release [31] (Figure 1.9).

1.6 CONCLUSION

Electrospinning is the most versatile technique for making of continuous nanofibers and showed great potential in the emerging field of biomedical applications. With the advent of new technological advancement to produce ultrafine nanofibers, electrospinning has manifested new route for exploring both synthetic and natural biodegradable polymers for the fabrications of peerless scaffolds. Tremendous researches are going on this ancient known technology to develop nanofibrous scaffolds and

with proper selection of polymeric materials as its play key role in the fabrication process broadly applied as the therapeutic agents and tissue regenerations. The more reliable, realistic, and judiciary pathway facilitates the incorporation of drug loadings and mimics the native ECM due to microstructures and morphological similarities and promisingly useful for future biomedical applications such as tissue engineering, asymmetric dressing and controlled release of drug carriers (genes). Furthermore, effective modifications of scaffolds with the functional agents fine-tune the surface properties of scaffolds offer the versatility and unique nanostructures potential for biomedical applications.

FIGURE 1.9 Wistar rat model and schematic representation of stimuli-responsive electrospun nanofibers.

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However, despite many achievements and numerous studies which have successfully demonstrated the promising characteristics of electrospun nanofibers *in-vitro* studies, but few articles reported the *in-vivo* studies of nanofibers scaffolds which reveals the further need for nanofibers meshes for

drug delivery and healing applications. In other words, this exciting research area needs new avenues and further requirement of more complicated and sophisticated design to meet the demands for diagnostic and therapeutic applications.

KEYWORDS

- **biomedical applications**
- **drug-delivery applications**
- **electrospinning**
- **grafting**
- **nanofibers**
- **nanotechnology**
- **scaffolds**
- **sustainable route**
- **therapeutic agents**
- **tissue regenerations**
- **wound dressings**

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