Recent advances of basic materials to obtain electrospun polymeric nanofibers for medical applications

L R Manea\textsuperscript{1,2}, L Hristian\textsuperscript{1}, A L Leon\textsuperscript{1} and A Popa\textsuperscript{3}

\textsuperscript{1}“Gheorghe Asachi” Technical University of Iasi, Department of Knitting and Clothing, Faculty of Textiles, Leather and Industrial Management, Iasi, Romania
\textsuperscript{2}Romanian Inventors Forum, Str. Sf.P.Movila 3, L11, III/3, 700089, Iasi, Romania
\textsuperscript{3}“Aurel Vlaicu” University of Arad, Engineering Faculty, Textile Department, Romania

E-mail: eurotexmed@yahoo.com

Abstract. The most important applications of electrospun polymeric nanofibers are by far those from biomedical field. From the biological point of view, almost all the human tissues and organs consist of nanofibrous structures. The examples include the bone, dentine, cartilage, tendons and skin. All these are characterized through different fibrous structures, hierarchically organized at nanometer scale. Electrospinning represents one of the nanotechnologies that permit to obtain such structures for cell cultures, besides other technologies, such as self-assembling and phase separation technologies. The basic materials used to produce electrospun nanofibers can be natural or synthetic, having polymeric, ceramic or composite nature. These materials are selected depending of the nature and structure of the tissue meant to be regenerated, namely: for the regeneration of smooth tissues regeneration one needs to process through electrospinning polymeric basic materials, while in order to obtain the supports for the regeneration of hard tissues one must mainly use ceramic materials or composite structures that permit imbedding the bioactive substances in distinctive zones of the matrix. This work presents recent studies concerning basic materials used to obtain electrospun polymeric nanofibers, and real possibilities to produce and implement these nanofibers in medical bioengineering applications.

1. Introduction

The nanotechnologies and nanomaterials have known spectacular development recently. Electrospinning is one of the nanotechnologies with the largest diversity of applications, which permits the processing of a wide range of basic materials and the production of a diversity of electrospun nanofibers assembly organization, from 1D to 3D, and diversity of forms (mono-components, bi-components) with different arrangements (side by side, shell-core, pie-wedge, island in the sea etc.) [1-5]. The nanofibers obtained through electrospinning can be of polymeric (polymeric nanostructures), ceramic (ceramic nanostructures) or composite (composite nanostructures) nature. Each of these groups has a wide portfolio of applications (table 1) [6-8]. Biomedical applications of the polymeric nanofibers obtained through electrospinning are multiple (table 1) [9, 10].

Tissue industry brings together biological, medical and engineering disciplines, with a view to reshape, repair, restore or biologically regenerate some organs or tissues insufficiently developed, or those completely or partially degraded from functional or physiologic standpoint. The organs and tissues affected in this way are replaced with synthetic functional systems with three-dimensional structure, which will provide accommodation and support for the cellular charge taken from the same...
patient or from a donor [11]. These systems (extra-cellular proteic matrices- MPE) are porous nanostructures meant to support cell development, adhesion, migration and proliferation and, last but not least, they are meant to favor the development of a tissue-matrix specific interaction.

**Table 1. Applications of nanofibers obtained through electrospinning.**

| Nanostructures type | Implementation field |
|---------------------|----------------------|
| **Electrospun** nanostructures |                      |
| Polymeric           | Biomedical           |
|                    | Regenerative medicine (tooth, bone, blood vessel implants, neural tissue engineering, structural tissues, such as cartilages, muscles, ligaments) dressings, meshes, medial prostheses; |
|                    | Structures with controlled drug release, cosmetics, drug delivery, nanofibrous drug delivery system, polymer-drug blend fiber system, haemostatic devices; |
|                    | Indirect biotechnologies |
|                    | Filtering mediums, separating membranes, nanosensors |
|                     | Protective clothing |
| **Ceramics**       | Biomedical           |
|                    | Biomechanical devices, biosensors, medical implants (bone reconstruction) |
|                     | Industrial biotechnologies |
|                    | Catalysts, biosensors, membranes, storage batteries |
|                     | Other applications |
|                    | Aerospatiale applications, chemical finishing treatments, information storage devices |
| **Composites**     | Regenerative medicine |
|                    | Implants |

The cellular or intracellular interaction or communication between the host tissue and the proteic extracellular matrix (the kinetics of attachment/implementation subsequent to implant) depends on a series of characteristics, among which one can mention [12, 13]:

a. specific functional characteristics of the implanted MPE, determined by the specific characteristics of the native MPE corresponding to the tissue at the implant place;
b. degree of MPE fibrils spatial orientation;
c. structural, physical and mechanical characteristics of the MPE cells (cross section cell size, specific area, mechanical characteristics, corrosion etc.);
d. characteristics related to tissue-matrix interface (biostability, bio-compatibility, biodegradability, non-toxicity, immunogeneity etc.).

The modern tissue engineering implies the development of a 3D matrix with biologic and biomechanical properties, together with mimetic elements of the native extracellular matrix, thus promoting tissue regeneration. Electrospinning represents one of the methods used to obtain such structures for cell culture, besides other methods, such as self-assembly and phase separation methods. As compared to the last one, electrospinning offers efficiency, accessibility, possibility to obtain structures with an advanced control of their geometry, the formation of tissues with typology and functionality similar to those of the organs where the implant is to be performed. The other nanotechnologies present considerable shortcomings, such as: incomplete inter-connection of the pore systems, dimensional variations of pores inside the surface structures, reduced mechanical resilience to pressure, restrictions concerning some basic materials processing.
The basic materials used to produce electrospun nanofibers can be natural or synthetic, polymeric, ceramic or composite. These materials are chosen depending on the nature and structure of the tissue to be regenerated. Namely, for the regeneration of soft tissues, polymeric basic materials are processed through electrospinning, while for obtaining the supports for hard tissues regeneration one uses mainly ceramic materials or composite structures which permit the incorporation of bioactive substances into distinctive matrix areas. The main characteristics of polymers that compete in their selection for the realization of support matrices, for example, are elasticity, flexibility, resilience, presence of functional groups, dimensional flexibility etc. Most of the studies in this field are focused on the utilization of natural polymers in electrospinning process. Up to now, one could obtain supports for biological materials from materials resulted from electrospinning of biodegradable natural polymers, such as collagen, gelatin, fibrinogen, silk and elastin. Among the synthetic polymers electrospun until now for biomedical applications, we can mention biodegradable polymers: poly-lactic acid (PLA), poly-glycolic acid (PGA), poly-lactic-co-glycolic acid (PLGA), poly-ε-caprolactum (PCL), polypropylene (PP) and poly-tetra-fluoro-ethylene (PTFE) [14].

2. Basic materials used to obtain electrospun polymeric nanofibers for medical applications.

2.1. Natural polymers used to obtain nanofibers with medical applications

2.1.1. Collagen fibers are essential in tissue engineering, mainly from biophysical standpoint. Collagen enters the composition of bones, coetaneous tissues, tendons and cartilages, and it is the most abundant protein found with vertebrates. The molecule contains usually three very long polypeptide chains, each one consisting of about 1000 amino acids, which are twisted in triple helix regular shape, thus providing strength and elasticity to tendons and skin. Electrospinning has the potential to produce collagen fibers that manifest mimetic phenomena close to those of the native MPE and they can even reproduce the structural and biological properties of the natural fiber [15, 16].

The studies performed in vitro and in vivo prove that electrospun collagen matrices respond positively to their implantation into structures of cell engineering. The matrix obtained by electrospinning the collagen offers the possibility of cells adhesion, infiltration and proliferation for the synthesis of extracellular matrix. Given the material characteristics (resorbability, bio-degradability and non-inflammatory character ascribed to the constituent protein- collagen), this generates a tissue suitable as basic material for regenerative medicine. Fiber diameter and structural properties of the pure collagen nanofibers produced through electrospinning depend on the type of collagen, as well as tissues origin and concentration. Up to now, one has only reported for medical applications the electrospinning of the collagen types I, II and III [9, 10, 17] and of the collagen-based copolymers [18].

What concerns cartilage regeneration, until now there are reports on electrospinning of type II collagen from the chicken stern cartilage. The matrix fixed in glutaric aldehyde vapors favor the cell growth, such that the articular condrocytes can freely penetrate the matrix. Significant differences were identified between the structural characteristics of the non-cross-linked matrices and those of the cross-linked collagen matrices, namely:

- electrospun non-cross-linked matrices manifest stiffness and they do not reach the strength and elasticity of the native collagen;
- matrices cross-linked with glutaric aldehyde vapors and seeded with articular condrocytes are similar with the native cartilage from mechanical point of view [19]. Yet, the collagen fibers manifest reduced compression and shearing strength, characteristics imposed to cartilaginous tissues.

These defaults can be solved through structural modifications. Random orientation of fibers implies a smaller tension modulus than of ordered fibers, which significantly influences the mechanical properties of the native cartilage layers. At the same time, the proteo-glicans role is considered to be important for cartilage tissue compression properties, collagen involvement being no doubt important [20].
What concerns the dermis implants, the membrane made of collagen-coated polycaprolactone nanofibers obtained through electrospinning, have a good cell development, proliferation and migration inside human dermatic fibroblasts matrix [21]. Progresses have been made during the recent years in this field. For instance, nanofibers of collagen type I blended with polycaprolactone (PCL) were used to grow human dermal fibroblast cells. The matrices promoted cells adhesion, proliferation and spreading, having potential for healing the affected derm [22].

In the field of blood vessel tissue engineering, basic collagen constructions have a reduced applicability, due to the lack of structural integrity at intra-luminal physiologic pressures. Besides the imposed biomechanical properties, cell proliferation and adhesion parameters, the vascular grafts must possess an anticoagulant activity until the endothelial cell content is totally completed [23-26]. The electrospinning of the mixtures of collagen and elastin solutions determines the generation of nanostructures with advanced porosity, large specific area and fibers with outstanding mechanical properties. In addition, one can use separate electrospinning of the solutions to produce multilayered assemblies with controlled morphology and even to obtain superior mechanical properties.

2.1.2. At the same time, as a cheaper alternative to collagen, one has tested the electrospinning of the gelatin, an electrolyte polymer that possesses some ionizable groups, its strong hydrogen bonds resulting in 3D structures. Electospun gelatin nanostructures are widely used in medical clinics for various applications, such as artificial organs, dressings, controlled drug administration and adhesives [27].

2.1.3. Fibrinogen (blood plasma protein responsible for blood coagulation) is still another protein that was electrospun for biomedical applications. Through trombin catalytic action, fibrinogen is converted into insoluble molecules which get together to form protein agglomerations. Consequently, the fibrinogen-based electrospun materials are studied for applications in the field of regenerative medicine [28-30]. Until now, the performances of electrospun fibrinogen utilization are favorable for providing cells development in vitro and in vivo, with direct influence on cell adhesion to substrate, their phenotypical expression, as well as on the transport of oxygen and other nutritive substances to the cells [31].

2.1.4. The fibroin from silk has drawn more and more attention, due to its unique mechanical properties and perfect biocompatibility, thus being an interesting candidate for applications in biomedical field, where mechanical properties have priority (wound dressings, bone tissues regeneration), as well as in biotechnological applications (separating membranes) [32-34]. By electrospinning the natural silk, one has obtained nanofibres with diameters smaller than 500 nm, and a good surface/ volume ratio, which resulted in an excellent cellular adhesion and proliferation [9]. The electrospun fibrinoin has also promising applications in biotechnology (separating membranes) and biomedicine (bandages) [9, 35]. Electrospun nanofibers of natural silk have an excellent biocompatibility, increased permeability to water vapors and oxygen, biodegradability, minimum inflammatory reactions [10]. Electrospinning of some polysaccharides was also realized.

2.1.5. Cellulose represents a major constituent of almost all the forms of vegetal matter, which converts it into one of the most widely distributed available basic materials [9]. One can modify cellulose structure through reactions with a hydroxyl group or by degrading the cellulose chain. By electrospinning the cellulose, one can obtain nanofibers used to produce filtering materials or in biomedical applications (structures with controlled drug release). Cellulose acetate can be electprospun, and the ulterior fiber de-acetylation results in the production of pure cellulose filaments [9]. Electrospinning permits to obtain supports biocompatibles with living tissues from non-woven-type membranes, with geometric arrangements similar to those of natural extra-cellular matrices, with un increased surface/volume ratio, where their structure is considered to be much less ordered than in the native form or in that regenerated from cellulose. If the cellulose acetate fibers obtained through
Electrospinning are methacrylated, one obtains structures with unique properties (nanofibers with hydrophobic core and hydrophilic shell) [9, 10]. The frequent destinations of the nanofibers produced through electrospinning of cellulose acetate are semi-permeable membranes for dialysis, ultra-filtration, inverse osmosis. One has also produced cellulose acetate nanofibers having embedded silver particles with antiseptic role, used in wound cure.

2.1.6. Chitin is the natural polysaccharide the richest in nitrogen, insoluble in most of the organic solvents figure 1. Chitin is the basic product for producing dibutyryl chitin (DBC) figure 2. Chitin utilization in several applications was limited by its insolubility in organic solvents. Chitin is only soluble in specific solvents, such as N, N-dimethylacetamide (DMAC)-LiCl, hexafluoroacetone, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) ans saturated calcium. The nanofibers realized through this method have diameters smaller than 100 nm. Electrospinning of mixtures of chitin/PGA (polyglycolic acid) in HFIP, chitin/ silk fibroin (SF) in HFIP solvent has also been investigated, and nanofibers with mean diameters of about 140 nm and 340 nm (diameter decreases with increasing chitin concentration in the mixture content) respectively have been investigated in order to produce biodegradable and biomimetic scaffoldings.

2.1.7. Chitosan extracted from chitin, the second polysaccharid in terms of abundance after cellulose, is non-toxic, biodegradable, biocompatible and non-antigenic. Chitosan [9, 10], known for its antimicrobial and analgesic character, with the capability to reduce the inflammatory reactions, ensures through electrospinning the realization of nanofibers with random orientation of deposits for biomedical applications (bandages, drug administration systems). Chitosan electrospinning also permits to obtain hydrophilic surfaces of osteoconductive nature, with potential for applications in bone regeneration. A series of chitosan derivatives (carboxymethyl, carboxyethyl and hexanoil chitosan (excellent antitrombogenic) can also be electrospun to obtain biomedical materials [9, 10].

The hyaluronic acid (AH) is a versatile organic component, more exactly a natural polysaccharid that can be found concentrated in the synovial fluids, tissues fluids such as derma and cartilages, conjunctive (cornea, retina), epithelial and nervous tissues. As the result of mechanical, immuno-functional and biological function, the hyaluronic acid plays an important role among the interstitial proteins. Its chemical structure contains chains made of more than 3000 repetitive units of disaccharids consisting of D-glucoronic acid and N-acetylgulosamine [9]. Due to its unique rheological properties and its biocompatibility, AH is widely used in multiple ophthalmologic applications, in structures with controlled drug release. AH electrospinning leads to the production of AH membrane consisting of nanofibers with increased surface/volume ratio, used in solid tissue matrices, artificial blood vessels, bandages etc. [9].

2.2. Synthetic polymers to obtain nanofibers with medical applications
Polyvinil alcohol (PVA) is a water-soluble biocompatible, hydrophilic polymer with a good chemical and thermal stability, non-toxic, easy to process through electrospinning. These properties make possible the utilization of electrospun PVA for implants (bones implants [9, 36], artificial organs [9]). PVA processing through electrospinning using chitosan (as a thickening agent to improve the
The production of electrospun nanofibers with low diameters and the increase of polymer solution conductivity were realized by adding anionic and cationic electrolytes [9]. The electrospinning of polyethylene oxide (PEO) [9] with applications in regenerative medicine (implants of cartilaginous tissues [39], bandages [9] was also reported. Electrospinning was also used to process PEO mixed with chitosan, and the experiments proved that, in order to improve the processing conditions (conductivity, surface tension, viscosity of polymer solution etc.) the optimum mass ratios are 2/1 or 1/1 [9].

The polyglycolic acid (PGA) is a synthetic thermoplastic polymer with good biodegradability and resorbability which permits to obtain through electrospinning, support matrices utilisable in rebuilding the neuronal tissues or in producing structures with controlled drug release [40]. Poly-lactic acid (PLA) is a synthetic non-immunogenic and non-toxic polymer extracted from cornstarch, with excellent biodegradability, biocompatibility and resorbability; one can obtain through electrospinning polymeric extra-cellular matrices used in the regeneration of cardio-vascular tissues [41].

Polycaprolactone (PCL) is another synthetic thermoplastic polymer with good biodegradability and resorption capacity which, when electrospun, permits to obtain biomaterials used for cartilage implants, controlled drug release, suture etc. [9, 42]. There have also been tested electrospun nanofibers obtained from co-polymeric compounds such as:

a. poly-L-lactide-co-ε-caprolactone (PLLA-CL- muscle implants and endothelial cells regeneration, structures with controlled drug release and bio-absorbent membranes) [9];

b. poly-lactic-co-glycolid (PLGA- for bone and cartilage regeneration and controlled drug release);

c. polyethylene acetate (PEVA- to produce structures with controlled drug release);

d. polydioxanone, poly anhydrides, polyorthoesters, polytrimethylene carbonate. Still another biocompatible antibacterial electrospinnable polymer, with remarkable mechanical properties is polyethylene terephthalate (PET) that can be processed alone [9] or mixed with chitin or chitosan [43]. One can find the applications of these nanofibers also in cardio-vascular implants [9]. Electrospun nanofibers containing carbon nanotubes, with orthopedic, dental and neuronal implants have also been realized [9].

The possibility to produce electrospun nanofiber meshes is still another practical application from biomedical area (cardiac reconstructions, blood vessels, peripheral vascular reconstruction) [44]. Matrix nanofibers have a special porosity. The size of electrospun nanofibers inter-structural pores, much smaller than blood cell size, inhibits the cells migration. Despite this fact, experimental results indicate the capacity of electrospun nanofibers meshes to infiltrate the cells [10]. The cells that enter the matrix through amoebae movement migrate through the pores that push the surrounding fibers in several directions to expand the pore. The dynamics of fibers architecture permits cells adaptation to pores size, as well as the biological development inside the nanofiber matrices. Recent investigations have revealed the production of three-dimensional matrices for meshes of natural and synthetic polymers [9]. Even if the synthetic materials have a higher strength than the natural ones, they lack the cell recognition signal. The matrix built of natural proteins derived from extra-cellular matrix (ex. collagen) permits a better cell infiltration into the matrix. Co-electrospinning, multi-layering and utilization of bi-polymers or cross-linking, as well as surface modifications can improve the stability and biocompatibility of meshes from electrospun nanofibers [9].

One can apply surface treatments to modify the synthetic polymers and to bring the extra-cellular matrix components on the scaffolding surface. The collagen coated with poly(L-lactic) acid co-polymerized with poly-ε-capro lactone in nanofibrillar form, builds up meshes with mechanical properties adequate for vascular grafts, which intensifies endothelization, preserves the phenotype of the human endothelial cells or the coronary artery and which is manifested through increased spreading, intensified cell viability, good attachment capacity and phenotypical maintenance [45].
Electrospun nanofibers blends have potential for addition of various ingredients (ex growth factors) depending on the necessities of the cell type. The nanometer matrix prepared from collagen with condroitine sulphate presents after cross-linking excellent biocompatibility properties when sown with conjunctive fibroblasts. Combination of nanofiber-type collagen with the matrix of glucose aminoglucan prepared from natural components of extra-cellular matrix seems to mime the extra-cellular matrix and thus it presents a high potential for tissue engineering applications [9, 10]. In multilayered electrospinning, after having electrospun the first component, the second polymer is electrospun in sequences on the same target, thus producing multilayered meshes with hierarchically ordered layers (ex. mesh electrospun from three layers: collagen type I, gelatin styrene and segmented polyurethane [9]) or the mesh with electrospun polyurethane and polyethylene oxide obtained through simultaneous electrospinning of the two polymers from separate syringes. The resulted nanofibers are blended on the same collector, thus determining the formation of mixed fibers mesh [9]). The scaffoldings can mime the extra-cellular matrix, thus promoting tissue regeneration.

Still another application of electrospun polymeric nanofibers are the compression textiles (bandages, dressings etc.) [9]. The most frequent basic materials used up to now for dressing realization from electrospun polymeric nanofibers are:

a. natural polymers (collagen, collagen/chitosan, fibrinogen etc.);

b. synthetic polymers (polylactide, poli(lactide-co- glycolid), poly(ε-caprolactone) , poly(vinyl pyrrolidone)-iodine etc.);

c. silver nanoparticles embedded in electrospun nanofibers to provide antibacterial properties.

The dressings obtained from polymeric nanofibers made through electrospinning present, as compared to the classical ones, a series of notable performances [9], among which one can mention:

a. water absorption capacity of over 93% (usual dressing have a maximum water absorption capacity of 23%);

b. flexibility, elasticity, a better wound coverage and protection;

c. excellent cicatrisation capacity (reducing the time for wound curing from months/years to some days/weeks, without leaving severe scars);

d. high air and vapor permeability, excellent cell breathing, high epithelization rate, elasticity, non-adhesivity to wound surface [45];

e. confers self-repairing capacity to dermis cells. The very porous structure, small, well-interconnected pores (500 nm- 1μm), as well as large area of the specific surfaces (5- 100 m²/g), are important characteristics for wound fluid exudation. These characteristics of the electrospun membranes suppress the invasion of exogenous microorganisms, also providing a controlled fluid drainage.

The electrospun polymeric nanofibers can be loaded with a drug for its controlled release using the following methods: -pre-electrospinning drug incorporation, directly into the polymeric mass in coaxial electrospinning [46]; realize core-shell nanostructures, with post-electrospinning surface modifications of nanofibers. Core-shell electrospun nanostructures are recommended to obtain more efficient drug release, to increase drug release rate and to control better the drug release [46-48].

The basic characteristics that promote the electrospun nanofiber utilization in this medical applications are large surface area (which influences release efficiency and dissolution rate), porous structure, small, interconnected pores (which influences the amount of induced medicine), small mass on unit surface (0.05-5g/m²), excellent mechanical properties as related to the mass, biocompatibility, non-toxicity, high permeability, constant release rate during an adjustable time period. There are several factors that influence the performances of electrospun nanofibrous structures in providing a controlled drug release, namely polymer/solvent type, hydrophilic or hydrophobic character of the drug or polymer, solubility, drug-polymer-additive interaction. Until now electrospun nanofibers for controlled drug release systems were produced from the following biodegradable polymers [9, 10]: polylactic acid (PLA), poly-caprolactone (PCL), poly-D-lactide (PLDA), polylactic acid (PLLA), poly-lactide-co-glycolid (PLGA), and hydrophilic polymers, such as polyvinyl alcohol (PVA),
polyethylene glycol (PEG) and polyethylene oxide (PEO), as well non-biodegradable polymers, for example polyester urethane (PEU).

The selection of polymer and solvent type, as well as their compatibility, are very important for biomedical applications that impose drug embedding, given the following experimentally identified aspects: most of the medicamentary substances lose part of their bioactivity when mixed with organic solvents; it is difficult to completely remove the residual solvents (subsequent toxicity of the realized structures), to find the optimum combinations which permit also the realization of controlled drug release functionality. That is why the technological solution consists in electrospinning of medicamentary substances in water soluble solutions (avoiding the possibility to form aqueous dispersions). The electrospun nanofibers and nanofibrous networks permit controlled drug release directly in the internal tissues.

Among the medicament agents with small molecular mass which were embedded in electrospun polymeric fibers, one can mention [9, 10, 49-52]: ibuprophen, cephasoline, mephoxine, tetracycline hydroclorhydate etc. [9, 10]. Some controlled drug release systems based on electrospun nanofibers are being investigated for the release of anti-microbial, anti-cancer and anti-diabetes substances [9]. Until now, most of the studies performed in relation with embedding medicinal agents report the utilization of polyactic acid as polymeric base in the electrospinning process [9]. Yet, it was noticed that in this case the antibiotic release is not gradual, but sudden. Accordingly, recent studies are focused on finding new polymer-based solutions. From a structural point of view, the electrospun fibers used for this application (drug embedding) can have a normal (uniaxial) or coaxial structure.

Bone tissue engineering is a vast area for electrospun nanofibers implementation, requiring nanostructures with imposed characteristics (tensile strength, pores size 100-300nm, porosity higher than 90%, hardness and 3D architectures with imposed deposit density). One can increase the compatibility through combinations of natural and synthetic polymers (ex. PCL and gelatin 1:1; PLA with gelatin 1:2; 1:1; 1:3 etc.).

3. Conclusions
Electrospinning can be used to obtain spatially oriented ultra fine fibers, with large surface/volume ratio, nanofibers characterized by a quite high specific area, with small size interconnected pores, whose geometry can be easily controlled, and with big elasticity modulus. All these characteristics permit their implementation in various applicative fields. There are multiple biomedical applications of the polymeric nanofibers obtained through electrospinning, starting from applications in tissue engineering to meshes and controlled drug release systems, each of these applications imposing the characteristics of electrospun basic materials.

References
[1] Danu C M, Nechita E and Manea L R 2015 Studies and Scientific Researchs Economics Edition 21 p 14
[2] Manea L R, Nechita E, Danu M C and Agop M 2015 J. Comput. Theor. Nanosci. 12 (11) 4693
[3] Manea L R, Stanescu I, Nechita E and Agop M 2015 J. Comput. Theor. Nanosci. 12 (11) 4373
[4] Calin M A, Manea L R, Schacher L, Adolphe D, Leon A L, Potop G L and Agop M 2015 Journal of Nanomaterials 2015 Article 514501
[5] Leon A L, Manea L R 2008 ITC&DC 4th International Textile Clothing & Design Conference Magic World of Textiles ed Z Dragcevic (Dubrovnik, Croatia, 5-8 October 2008) Faculty f Textile technology, University of Zagreb sections E Book of Proceedings pp 803-806
[6] Scarlet R, Manea L R, Sandu I, Martinova L, Cramariuc O and Sandu I G 2012 Revista de Chimiie 63 (7) 688
[7] Scarlet R, Manea L R, Sandu I, Cramariuc B and Sandu A V 2012 Revista de Chimie 63 (8) 777
[8] Vasilica P, Liliana-Rozemarie M and Gabriel P 2009 ISC 2009 Industrial Simulation Conference 2009 ed Das D B, Nassehi V and Deka L (Loughborough, UK, 1-3 June 2009) Eurosis-ETI pp 352-355
[9] Manea L R and Scarlet R 2015 *Advanced fibers and yarns* vol 2 (Bacau Alma Mater)

[10] Nedjari S, Hebraud A and Schlatter G 2015 *Electrospinning. Principles practice and possibilities* (Cambridge, UK, The Royal Society of Chemistry) p 173

[11] Manea L R, Nejneru C, Mătăsaru D, Axinte C and Agop M 2013 *Journal of Modern Physics* 4 (7) 1013

[12] Susan M, Bujoreanu, L G Galusca, D G, Munteanu C and Mantu M 2005 *Journal of Optoelectronics and Advanced Materials* 7 (2) 637

[13] Popescu V, Manea L R, Curteza A and Vasluianu E 2011 *Tekstil* 60 (7) 306

[14] Diaconu M, Cretescu I, Luca F, Liliana M and Pohontu C 2010 *Environmental Engineering and Management Journal* 9 (1) 67

[15] Popescu V, Sandu I G, Vasluianu E, Sandu I, Campagne C and Manea L R 2014 *Revista de Chimie* 65 (12) 1439

[16] Cailean D, Barjoveanu G, Musteret C P, Sulitanu N, Manea L R and Teodosiu C 2009 *Environmental Engineering and Management Journal* 8 (3) 503

[17] Manea L R, Cramariuc B, Caunii V and Sandu I 2015 *Materiale Plastice* 52 (1) 82

[18] Verzea I, Luca G P, Manea L R and Lazarescu R P 2005 *Management of Technological Changes* ed Rusu C and Phillis Y (Chania, Greece, 19-20 August 2005) Technical University of Crete Book 2 pp 137-142

[19] Manea L, Lazarescu R P, Luca G P and Verzea I 2005 *Management of Technological Changes* ed Rusu C and Phillis Y (Chania, Greece, 19-20 August 2005) Technical University of Crete Book 1 pp 403-406

[20] Manea L, Lazarescu R P, Luca G P and Verzea I 2005 *Management of Technological Changes* ed Rusu C, Phillis Y, (Chania, Greece, 19-20 August 2005) Technical University of Crete Book 2 pp 71-74

[21] Popescu V, Manea L R and Popescu G 2009 *Management of Technological Changes* ed Rusu C (Alexandroupolis, Greece, 3-5 September 2009) Proceedings of the 6th International Conference on the Management of Technological Changes 2 pp 769-772

[22] Calin M A, Kheneussi N, Schacher L, Adolphe D, Manea L R, Gradinaru I, Zetu I and Stratulat S 2013 *Materiale Plastice* 50 (4) 257

[23] Manea L R and Sandu I 2015 *Revista de Chimie* 66 (12) 1968

[24] Vasilica P, Liliana-Rozenarie and Gabriel P 2009 *ISC’2009 Industrial Simulation Conference’ 2009* ed Das D B, Nassehi V and Deka L (Loughborough, UK, 1-3 June 2009) Eurosis-Eti pp 347-351

[25] Manea L R, Scarlet R, Leon A L and Sandu I 2015 *Revista de Chimie* 66 (5) 640

[26] Manea L R, Cramariuc B, Scarlet R, Cramariuc R, Sandu I and Popescu V 2015 *Materiale Plastice* 52 (2) 180

[27] Manea L R, Scarlet R and Sandu I 2015 *Revista de Chimie* 66 (10) 1622

[28] Popescu V, Manea L R, Sandu I G, Chirculescu A I and Sandu I 2013 *Revista de Chimie* 64 (3) 281

[29] Lazarescu R P, Duda-Daianu D C, Manea L 2009 *Management of Technological Changes* ed Rusu C. (Alexandroupolis, Greece, 3-5 September 2009) Proceedings of the 6th International Conference on the Management of Technological Changes 1 pp 377-379

[30] Gherasimescu C, Leva M, Butnaru R, Muresan A and Manea L R 2011 *Industria Textila* 62 (1) 19

[31] Popescu V, Radu C D and Manea L R 2010 *Industria Textila* 61 (1) 23

[32] Gribincea V, Chirita M and Manea L 1997 *Industria Textila* 48 (2) 79

[33] Gribincea V, Chirice M, Manea L and Sufitskii P 2002 *Izvestiya Vysshikh Uchebnykh Zavedenii, Seriya Teknologiya Tekstil’noi Promyshlennosti* 1 18

[34] Hristian L, Sandu A V, Manea L R, Tulbure E A and Earar K 2015 *Revista de Chimie* 66 (3) 342

[35] Manea L R, Curteza A and Sandu I 2015 *Materiale Plastice* 52 (4) 470
[36] Manea L R, Nechita E and Sandu I 2015 *Revista de Chimie* 66 (11) 1841
[37] Popescu V, Manea L R and Amariei N 2009 *Materiale Plastice* 46 (1) 95
[38] Lazarescu R P, Duda-Daianu D C and Manea L 2009 *Management of Technological Changes* ed C Rusu (Alexandroupolis, Greece, 03-05 September, 2009) Democritus University Thrace, University Campus Komotini 69100 Greece 1 pp 373-375
[39] Manea L R, Scarlet R, Amariei N, Nechita E and Sandu I G 2015 *Revista de Chimie* 66 (4) 542
[40] Asaftei I V, Sandu I G, Birsa L M, Manea L R and Earar K 2015 *Revista de Chimie* 66 (3) 336
[41] Verzea I, Luca G P, Manea L R and Benidir M 2009 *Management of Technological Changes* ed C Rusu (Alexandroupolis, Greece, 03-05 September, 2009) Democritus University Thrace, University Campus Komotini 69100 Greece 1 pp 757-760
[42] Maftei D, Asaftei I V, Sandu I, Manea L R, Birsa L M and Earar K 2015 *Revista de chimie* 65 (5) 673
[43] Manea L R, Curteza A and Sandu I 2015 *Materiale Plastice* 52 (3) 312
[44] Mareci D, Bolat G, Chelariu R, Sutiman D and Munteanu C 2013 *Materials Chemistry and Physics* 141 (1) 362
[45] Hristian L, Bordeianu, D L, Iurea P, Sandu I and Earar K 2014 *Materiale Plastice* 51 (4) 405
[46] Verzea I, Luca G P, Manea L R and Lazarescu R P 2005 *Management of Technological Changes* ed C Rusu and Y Phillis (Chania, Greece, 19-20 August 2005) Technical University of Crete 2 pp 143-148
[47] Luca G P, Verzea I and Manea L R 2009 *Management of Technological Changes* ed C Rusu (Alexandroupolis, Greece, 03-05 September, 2009) Democritus University Thrace, University Campus, Komotini, 69100, Greece pp 245-248
[48] Secula M S, Cretescu I, Cagnon B, Manea L R, Stan C S and Breaban I G 2013 *Materials* 6 (7) 2723
[49] Sarbu L G, Apostu M O, Sandu I G, Manea L R and Bahrin L G 2014 *Revista de chimie* 65 (11) 1327
[50] Manea L R, Danu M C and Sandu I 2015 *Revista de Chimie* 66 (6) 868
[51] Nejneru C, Nicuță A, Constantin B, Manea L R, Teodorescu M and Agop M 2013 *Journal of Applied Mathematics* 2013 137056
[52] Earar K, Matei M N, Sandu A V, Hristian L, Bejinariu C and Sandu I G 2015 *Revista de Materiale Plastice* 52 (1) 98