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Design and Manufacture of Polymeric Scaffolds

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Scaffolds are porous materials designed for organ replecement, which are manufactured with a shape and mechanical properties matched to that of original tissue. Such structures are sieved with cells, genes and proteins, that grow in the scaffold pores and after maturation may be implanted into the body. Scaffolds described in this paper are biodegradable and were fabricated from polylactide by three groups of technology: batch foaming and extrusion foaming, electrospinnig, moreover the microstucture was designed first with CAD technique, then fabricated by means of a rapid prototyping. Microstructure of scaffold was evaluated by the scanning electron microscopy.

Keywords Porosity; cell size; foaming; electrospinning; rapid prototyping

Introduction

Humankind uses different materials to a body repair for centuries. Surgery interventions result in the entire organ transplantations or replacements of natural body parts with natural or synthetic materials. Initially used metals have been replaced by polymers due to their lower density, high diversity of their physical, chemical and mechanical characteristics, and a reasonable price. Second generation of polymers constitute biodegradable ones, that are metabolized over time by the body. Typical applications of such polymers are sutures, stents, scaffolds, and drug delivery systems [1]. Among the requirements the biomaterials have to meet there are those related to medicine (biocompatibility) and engineering (selection of materials, function-related properties and shape, the life time, manufacturing technology, etc.). Recently a special attention attract biodegradable polymers that degrade in a body after performing their function and do not require a second surgical intervention [2].

In this paper scaffolds used in tissue engineering have been discussed. These medical devices represent sophisticated porous structures and may be manufactured by means of different technologies [3–5]. Biodegradable polymer polylactide (PLA) was used for formation of scaffolds. The scaffolds were fabricated by extrusion foaming and batch foaming, electrospinning, and by a rapid prototyping. Scaffold microstructures were evaluated by the scanning electron microscopy. Polymer foaming parameters have been correlated with the morphology details for their optimisation. Pore size as well as the connectivity of cells have been evaluated.

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Experimental

Materials

PLA used in this study was supplied by Natureworks(PLA 3052D). Polylactide was dried at 70°C for 4 h before processing. Chemical blowing agent Hydrocerol PLC742 (Clariant) was used in amount of 2.0 wt.% during extrusion. Nitrogen was used as the physical blowing agent during batch foaming.

Melt Rheology

Rheological measurements were carried out with Haake RheoStress 6000 rotational rheometer (Haake) usingh a plate-plate measuring system and a gap between the plates of 1 mm. The test temperature was 160°C.

Foaming Process

Extrusion foaming was performed using the single screw extruder Rheomex 252 (Haake, Germany) with 3 barrel zones and the extrusion die. The temperature profile was 150–160–180–145°C. The screw rotation was 15 rpm.

Saturation of PLA samples with gas (batch foaming technology) was performed in an autoclave (Parker Autoclave Engineers, USA) with a volume of 300 cm^3. Samples were then foamed in the glycerin bath at 160°C. The maximum working pressure was 10 MPa.

Electrospinning

Electrospinnning set consisted of a syringe and a needle of 0.8 mm inner diameter, syringe pump, high voltage supply, two electrodes and an aluminium collector. Electrospinning was performed using polymer solutions of different concentration prepared with chloroform, dimethyl formamide and dimethyl sulfoxide in variable proportions. The electrospinning voltage, needle-to-collector distance and solvent pumping were changed for optimization.

Rapid Prototyping

The scaffold design process was performed using SolidWorks® 2011 software. The files were then applied to 3D printing machine to manufacture the real structures in 1:1 scale. Scaffold structures were modeled regarding their shape, porosity factor and polymer stream thickness. Rapid prototyping process was carried out by means of a self – made 3D printer supplied with a polylacitide (PLA) wire, 3 mm in diameter. The process parameters (polymer melt pressure, temperature and flow speed) were optimized according to the final product geometry.

Cellular Morphology

Optical and scanning electron microscopy (SEM) were used to characterize the cellular morphology of foamed samples. Sputtering with gold was performed prior to SEM observations which were carried out with VEGA TESCAN microscope.

Results and Discussion

Poly (lactic acid) (PLA) 3052D exhibited a glass transition temperature (Tg) of 66°C, melting temperature (Tm) of 159°C (Fig. 1). PLA is of a semicrystalline structure, degree

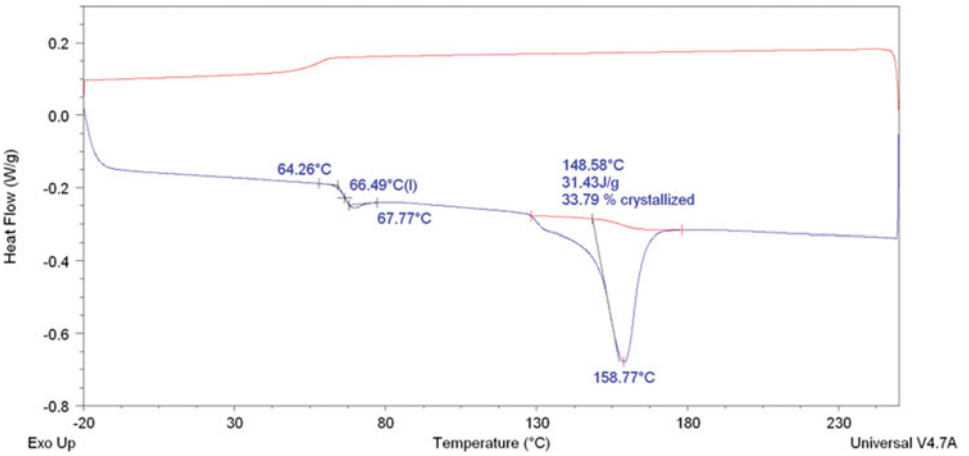

Figure 1. Thermal properties of PLA.

of crystallinity of about 33%, counted according to:

$$Percentage\,of\,crystallinity\,[\%] = [\Delta Hm - \Delta Hc]/\Delta Hm^{\circ} \times 100\%$$

where ΔHm (J/g) is the melting enthalpy, ΔHc (J/g) is the cold crystallization enthalpy and ΔHm° is the melting enthalpy of a 100% crystalline PLA reported to be equal to 93 J/g.

The rheological measurements revealed that polymer used is of pseudoplastic character typical for thermoplastic materials. The viscosity curve exhibited almost flat plateau up to ca. 1 Hz; above that frequency the viscosity decreased rapidly. Both moduli, related to the dissipative and absorption part, increased with frequency in the whole measured range (Fig. 2)

Selection of different process parameters brings about manufacturing of cellular materials with different morphology, estimated by the pore size and their distribution. Cellular structure obtained by extrusion foaming is dependent on the temperature profile along the extruder. The chemical blowing agent decomposed in a polymer melt at high temperature, the emitted gas was dissolved in a melt, then after rapid cooling while leaving the extruder head die the cells nuclei have arisen and grown until the polymer solidified. The cell size was dependend on the die temperature – at low die temperature a high number of small cells was generated (Fig. 3a). With increase of die temperature, the viscosity of the material decreased, which caused the cells may grow freely (Fig. 3b, 3c).

In the batch foaming technology the morphology of polylactide was related to the saturation time of a sample with gas. After the material was sufficiently saturated, its thermodynamic state was rapidly changed after the sample was removed from the autoclave (decrease of pressure) and its temperature increased in a glycerol bath. Such changes developed in a process resulted in the cells nucleation and growth. Short saturation time (24 h) contributed to creation of larger cell size of 300–400 μm (Fig. 4a). Longer gas saturation time (48 h) provided small cells (10–50 μm) (Fig. 4b).

Selected examples of structures manufactured by means of electrospinning have been presented in Fig. 5. Fiber thickness equals to approx. 800 nm whereas the cell size varied in a range of 5–20 μm. The results of this investigation showed that fibers diameter and morphology were very dependent on spinning solution. In both cases the concentration of PLA spinning solution was 10 wt%. Thus, continuous, bead free structures were obtained.

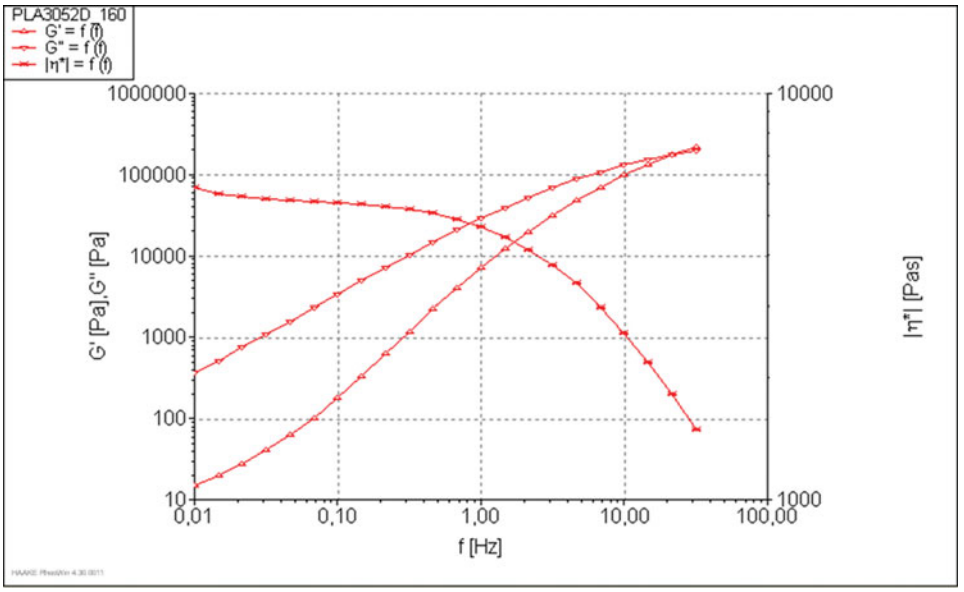

Figure 2. Rheological properties of PLA.

This was possible because of the appropriate amount of PLA chain entanglements, essential to maintain the continuity of the jet during the electrospinning process [6]. PLA fibers presented in this study were obtained from binary solvent systems. Fibers obtained from chloroform and DMSO (dimethyl sulfoxide) were much thinner when compared with the ones electrospun from chloroform and DMF (dimethyl formamide). Thin fibers (Fig. 5b) were fabricated, when the viscosity of the spinning solution, as well as the evaporation rate of the solvent were relatively low. Our results indicated that, by electrospinning of the PLA from chloroform and DMSO, it is possible to obtain homogeneous structures. Branched fibers were obtained by ejecting smaller jets from the surface of the primary jet when electrospinning the PLA from both chloroform/DMF and chloroform/DMSO binary solvent systems.

The most convenient way to design microstructures is a bottom-up approach. As a rule, when designing the scaffold structures one starts from a single unit cell (of a given geometry and sub-structure: the number and width of channels) and then multiplies it

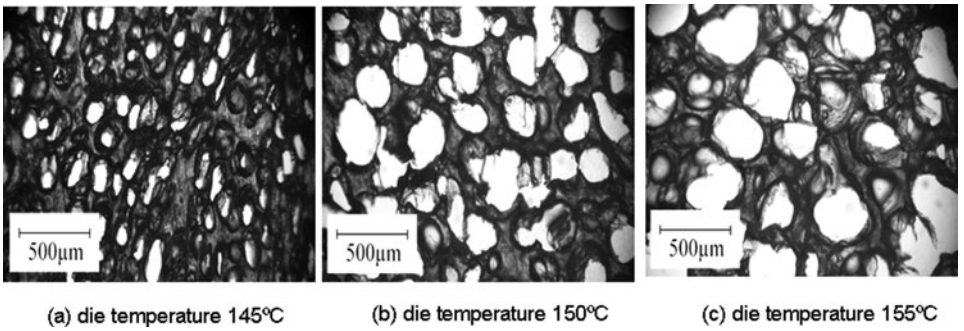

Figure 3. Cellular structure of foamed PLA obtained during extrusion.

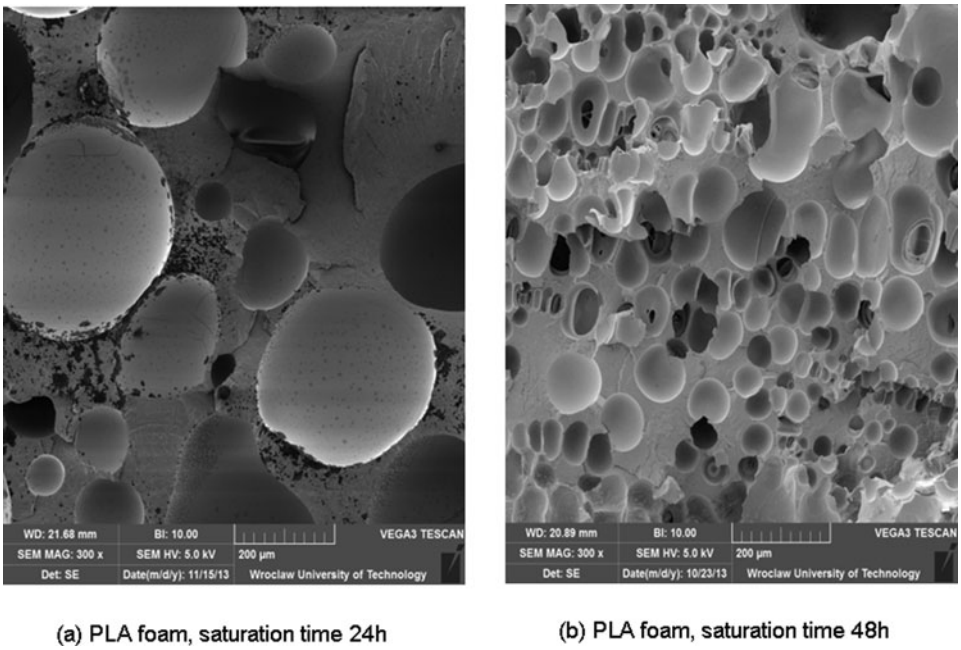

Figure 4. PLA foamed in batch process.

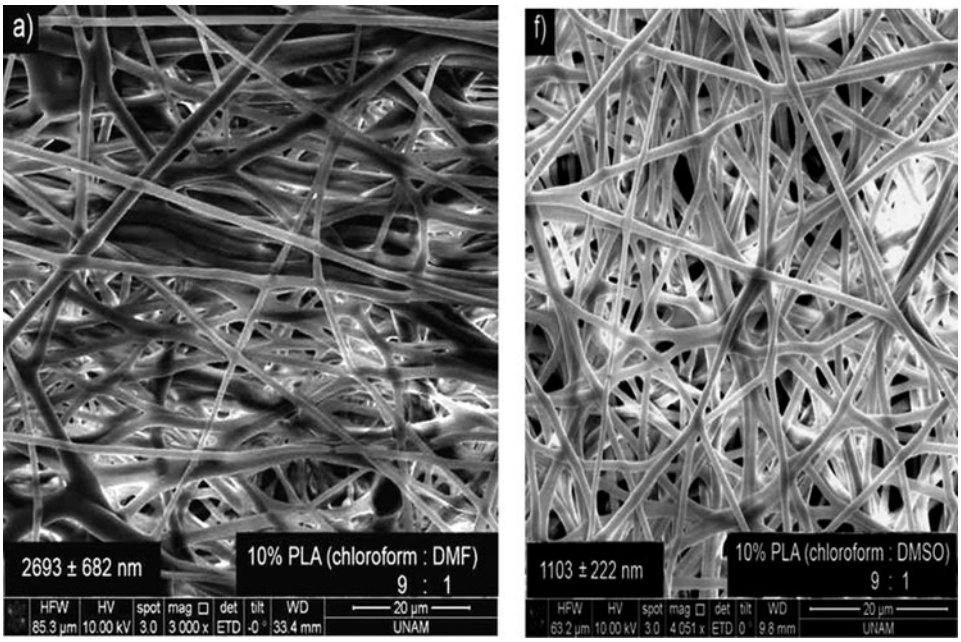

Figure 5. PLA structures manufactured by electrospinning from different solutions.

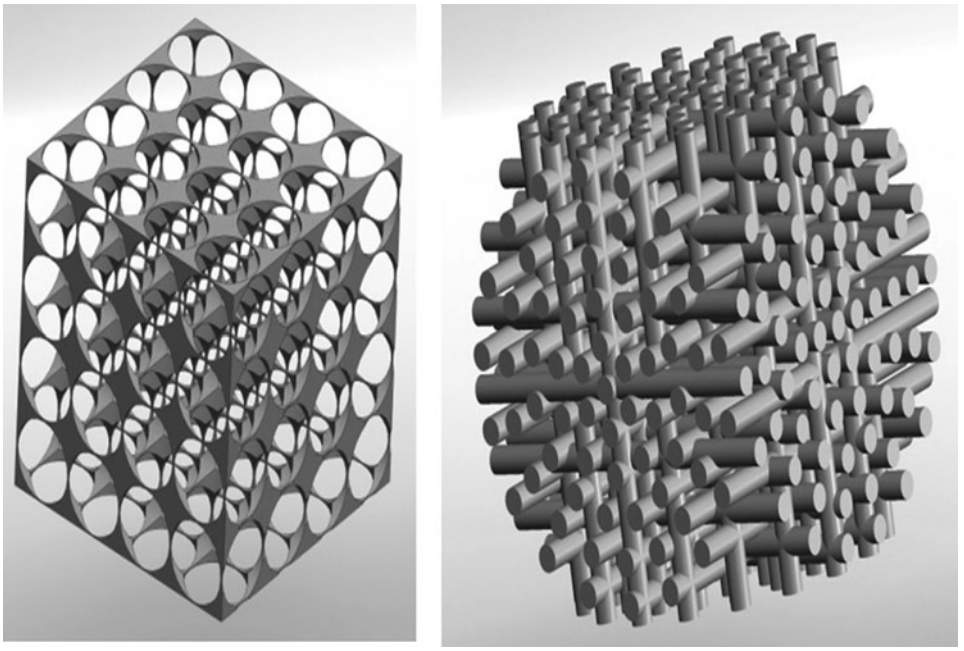

Figure 6. Single cuboidal unit cell length of 1 mm, hole diameter 0.98 (left). Examplary irregular structure (right).

in three directions to achieve finally a macroscopic element. This procedure allows to manipulate easily the whole scaffold geometry (thus, to control flow properties through the scaffold channels) and relatively easily to calculate its tensile properties, what is of a great importance.

It is well known that higher porosity favors transport phenomena in a biomaterial (and cell inoculation), however mechanical properties of the scaffold decrease. Therefore we have created irregular structures of different pore size. Figure 6 shows a scaffold designed

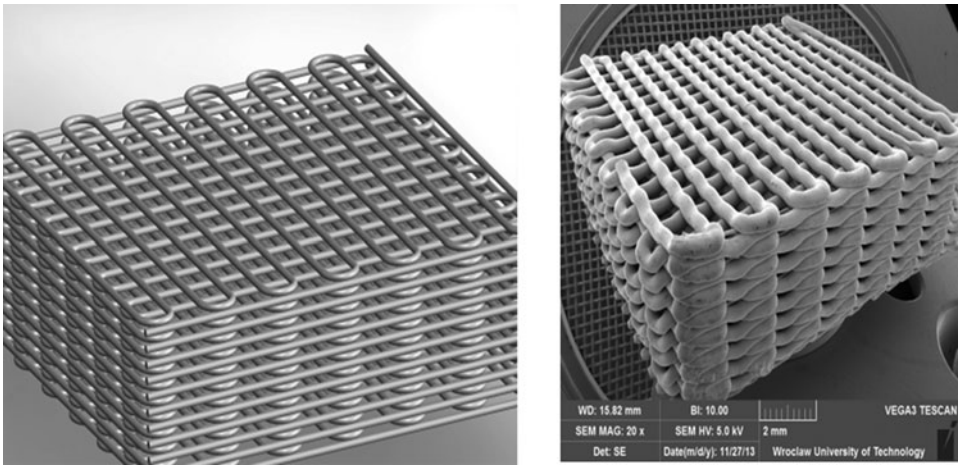

Figure 7. CAD model (left) and SEM photo of a real model (right).

using a bottom-up assumption (Fig. 6a) and an example of irregular structured scaffold (Fig. 6b).

Although the specific (respect to the tissue type) scaffold design needs a sophisticated computational work (tensile properties with finite element method, flow properties based on Stokes law), the details may be manufactured using a relatively simple equipment. The hardest technical task is to form a very thin polymer strand of even diameter within a whole processing time. Fig. 7 shows CAD model of a given porosity and a real scaffold which has been manufactured by means of rapid prototyping.

Conclusions

1. Cellular structure in polylactide was generated using foaming extrusion, batch process, electrospinning, and rapid prototyping.
2. Cells generated by means of extrusion foaming with a blowing agent were in the range of 300–400 μm.
3. Batch foaming with a direct gas saturation provided a material of 10–50 μm cell size.
4. Electrospinning allowed fabrication of materials with pore size of 10–20 μm and regular cell wall thickness of nanometer range.
5. Rapid prototyping provides products of highly regular structure.
6. Morphology of the materials allows their application as resorbable scaffolds in tissue engineering.

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