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Twin Screw Extrusion Based Technologies Offer Novelty, Versatility, Reproducibility and Industrial Scalability for Fabrication of Tissue Engineering Scaffolds

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Introduction

Porous, biodegradable and bioresorbable polymeric scaffolds are utilized in various tissue engineering applications and are shaped typically via 3-D printing, solvent casting, particulate leaching, phase separation, gas foaming, freeze drying, electrospinning and solid-form fabrication. However, significant issues and limitations remain in the polymers and additives that can be used, cost, reproducibility of the microstructure and properties of the fabricated scaffolds, and scalability of the fabrication processes to realistic manufacturing rates. These remaining major challenges require the development of alternative materials processing methods. Recently, a number of novel fabrication methods based on the twin screw extrusion process have been developed and were used in the fabrication of different types of scaffolds for tissue engineering, especially focusing on bone and cartilage applications. These new processes integrate twin screw extrusion with spiral winding, co-extrusion and electrospinning and provide significant advantages over conventional methods of scaffold fabrication. These advantages include versatility, reproducibility and industrial scalability.

Challenges in Fabrication of Scaffolds for Tissue Engineering

Tissue engineering relies on the utilization of porous, biodegradable and bioresorbable polymeric scaffolds to promote cell proliferation, differentiation, migration and extracellular matrix generation [1,2]. Important criteria that need to be considered for scaffold development include suitability of the surface properties and biocompatibility, kinetics of biodegradation, and micro structural requirements which include porosity, pore size, and pore interconnectivity. The conventional methods that are used to fabricate tissue engineering and mechanical properties scaffolds include 3-D printing, solvent casting, particulate leaching, phase separation, gas foaming, freeze drying, electrospinning and solid-form fabrication [1-4]. In spite of the significant advances made during the last decade significant issues and limitations remain in the polymers and additives that can be used, cost, reproducibility of the microstructure and properties of the fabricated scaffolds, and scalability of the fabrication processes to realistic manufacturing rates. These remaining major challenges require the development of alternative materials and materials processing methods for scaffold fabrication. Recently, a number of novel fabrication methods based on the twin screw extrusion process have been developed and were used in the fabrication of different types of scaffolds for tissue engineering applications [5-20]. These new processes integrate twin screw extrusion with spiral winding, co-extrusion and electrospinning and provide significant advantages over conventional methods of scaffold fabrication. These advantages include versatility, reproducibility and industrial scalability.

Advantages Offered by Twin Screw Extrusion for Fabrication of Scaffolds

Twin screw extrusion processes (two screws rotating in the opposite, i.e., counter-rotating or same, i.e., co-rotating directions), which can be fully-intermeshing, or non-intermeshing, are highly versatile and scalable continuous processing operations that generate reproducible mixtures and extrudates within strict dimensional and structural tolerances [5-8]. Twin screw extrusion allows multiple unit operations, including solids conveying, melting, distributive, and dispersive mixing of particles and nanoparticles, deaeration, and shaping of the scaffolds, to take place within the confines of a single process. The screws generally have modular designs, which allow the concomitant use of multiple screw elements with different functionalities, i.e., regular-flighted conveying screws (both right-handed and left-handed) and lenticular elements, i.e., the kneading disks. The kneading disks can be staggered at different stagger angles and stagger directions to provide a dispersive mixing capability, which enables the break-up of particle clusters, i.e., a capability not found in conventional scaffold fabrication methods. A die which is designed to extrude the desired scaffold shape is attached to the front-end of the twin screw extruder.

Twin Screw Extrusion Based Technologies for Fabrication of Tissue Engineering Scaffolds

The twin screw extrusion based technologies which are recently developed for the fabrication of tissue engineering scaffolds principally consist of five different fabrication methods [9-20]. These are:

1. Twin screw extrusion and die combination [9]
2. Twin screw extrusion and co-extrusion [10-13]
3. Twin screw extrusion and spiral winding [14, 15]
4. Twin screw extrusion and electrospinning [16-19]
5. Twin screw extrusion, electrospinning and spiral winding [20]

All five methods are amenable to industrial scale-up and generate scaffolds which are reproducible in geometry and properties. All of these five methods can also be used with and without solvents (dry versus wet extrusion methods). All five methods have been applied in the area of interface tissue engineering, targeting regenerative medicine for bone and cartilage repair and regeneration [9-20].

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For processes #1-3, various polymeric resins including Poly(Glycolic Acid) (PGA), Poly(Lactic Acid) (PLA), and Poly(Caprolactone) (PCL) are compounded in the twin screw extruder with one or more porogens involving dissolvable salts and polymers, physical (typically supercritical CO_2) or chemical blowing agents to facilitate the development of a porous structure [21]. Various bioactives including nanoparticles, drugs, and proteins can also be incorporated. A die with a geometry that is designed to enable the conversion of the mixture found in the twin screw extruder into a desired shape is connected to the twin screw extruder. A co-extrusion die can also be used to allow multiple layers involving differences in materials of construction, porosity, composition to be shaped into scaffolds [9-13]. For example, a co-extrudable cage/core structure has been targeted for use in spinal arthrodesis [12,13]. The twin screw extrusion and spiral winding process integrates the twin screw extrusion process with a modified filament winding method (designated here as "spiral winding") [14,15]. The extrudate emerging from the die is wound around a mandrel that concomitantly rotates and translates sideways creating a helical and spiral trajectory for the fabrication of cylindrical extrudates [14,15]. Scaffolds with a wide range of sizes and thicknesses, and radial and axial distributions of pore size and porosity can be developed using the twin screw extrusion and spiral winding method, especially addressing the needs for relatively large critical bone defects [15].

In processes #4 and #5, the twin-screw extruder is integrated with the electrospinning process [16-20]. The electrospun mesh is porous and the porosity can be controlled via the manipulation of the voltage (typically 10-30 kV), the spinning distance between the spinneret and the conductive surface, the use of a rotating mandrel with a conductive surface, the flow rate, temperature, and the solution concentration, when a wet spinning method is used. The spinneret die can have multi-channels for flow to enable the increase of the production rate. The twin screw extrusion and electrospinning process generates nanofibrous meshes which can be incorporated with various types of bioactives to target the generation of especially interface tissues, for example the bone and cartilage interface fabrication of especially interface tissues, [18,19]. The electrospinning process can also be married to the spiral winding process for the fabrication of multi-featured scaffolds which consist of a spiral wound shell around an electrospun core [20]. Such hybrid processes are suitable for fabricating multiscale scaffolds to engineer vascularized osteon-like structures [20].

Use of Twin Screw Extrusion Based Scaffold Fabrication Methods for Functional Grading

Finally, it should be noted that all of these methods (#1-5) possess the ability to introduce various ingredients of the formulation/s in a time-dependent fashion into the twin screw extruder for the manufacture of spatially (radially and axially) graded, i.e., functionally-graded scaffolds with heterogeneous structure and properties [13, 15,17,19]. The availability of such graded scaffolds further allows the control of the spatial distributions of bioactives, porosity, pore sizes, mechanical properties and provides the tissue engineering practitioners with additional capabilities for mimicking the complex elegance of native tissues.

References

1. Castro NJ, Hacking SA, Zhang LG (2012) "Recent progress in interfacial tissue engineering approaches for osteochondral defects". Ann Biomed Eng 40: 1628-1640.

2. Lu HH, Subramony SD, Boushell MK, Zhang (2010) "Tissue engineering strategies for the regeneration of orthopedic interfaces". Ann Biomed Eng 38: 2142-2154.

3. Puppi D, Chiellini F, Piras AM, Chiellini E (2010) "Polymeric materials for bone and cartilage repair". Prog Polym Sci 35: 403-440.

4. Seidi A, Ramalinga M, Elloumi-Hannachi I, Ostrovidov S, Khademhosseini A (2011) "Gradient biomaterials for soft-to-hard interface tissue engineering", Acta Biomater 7: 1441-1451.

5. Gotsis D, Kalyon DM (1989) "Simulation of mixing in co-rotating twin screw extruders". Society of Plastics Engineers ANTEC Technical Papers 35: 44-48.

6. Gotsis D, Ji A, Kalyon DM (1990) "3-D Analysis of the Flow in Co-rotating Twin Screw Extruders". SPE ANTEC Technical Papers 36: 139-142.

7. Kalyon DM, Jacob C, Yaras P (1991) "An Experimental Study of the Degree of Fill and Melt Densification in Fully-intermeshing, Co-rotating Twin Screw Extruders," Plastics, Rubber and Composites Processing and Applications 16: 193-200.

8. Kalyon DM, Malik M (2007) "An integrated approach for numerical analysis of coupled flow and heat transfer in co-rotating twin screw extruders" International Polymer Processing 22: 293-302.

9. Ergun A, Kalyon D, Valdevit A, Ritter A, Yu X (2011) "Twin screw extrusion and co-extrusion based fabrication of uniform and multilayered scaffolds for bone tissue engineering". Orthopedic Research Society, Transactions 36: 0285.

10. Ergun A, Yu X, Valdevit A, Ritter A, Kalyon DM (2011) "In vitro analysis and mechanical properties of twin screw extruded single-layered and co-extruded multi-layered poly(caprolactone) scaffolds seeded with human fetal osteoblasts for bone tissue engineering". J Biomedical Mater Res A 99: 354-66.

11. Ergun A, Kalyon D, Valdevit A, Ritter A (2011) "Compressive fatigue behavior of osteoblast seeded tissue constructs of poly(caprolactone) multilayered scaffolds for bone graft substitute applications". Orthopaedic Research Society Transactions 36: 1850.

12. Ergun A, Chung R, Ward D, Valdevit A, Ritter A, et al. (2012) "Unitary bioresorbable cage/core bone graft substitutes for spinal arthrodesis coextruded from polycaprolactone biocomposites". Ann Biomed Eng 40: 1073-1087.

13. Ergun A, Yu X, Valdevit A, Ritter A, Kalyon DM (2012) "Radially and axially-graded multi-zonal scaffolds targeting critical-sized bone defects from polycaprolactone/hydroxyapatite/tricalcium phosphate", Tissue Eng Part A 18: 2426-2436.

14. Ozkan S, Kalyon DM, Yu X, McKelvey C, Lowinger M (2009) "Multifunctional protein-encapsulated polycaprolactone scaffolds: Fabrication and in vitro assessment for tissue engineering". Biomaterials 30: 4336-4347.

15. Ozkan S, Kalyon D, Yu X (2010) "Functionally graded beta-TCP/PCL nanocomposite scaffolds for bone tissue engineering: In vitro evaluation with human fetal osteoblast cells". J Biomed Mater Res A 92: 1007-1018.

16. Erisken C, Kalyon D, Wang H (2008) "A hybrid twin screw extrusion/electrospinning method to process nanoparticle-incorporated electrospun nanofibers". Nanotechnology 19: 165302.

17. Erisken C, Kalyon DM, Wang H (2008) "Functionally and continuously graded electrospun polycaprolactone and β-tricalcium phosphate nanocomposites for interface tissue engineering applications". Biomaterials 29: 4065-4073.

18. Erisken C, Kalyon D, Wang H (2010) "Viscoelastic and biomechanical properties of tissue engineered constructs for osteochondral tissue regeneration". J Biomech Eng 132: 091013.

19. Erisken C, Kalyon D, Ornek-Ballanco C, Wang H, Xu J (2011) "Osteochondral tissue formation through adipose-derived stem cell differentiation using biomimetic tissue scaffolds with graded stimulator concentrations". Tissue Eng Part A 17: 1239-1252.

20. Chen X, Ergun A, Gevgilili H, Ozkan S, Kalyon DM, et al. (2013) "Shell-core bi-layered scaffolds for engineering of vascularized osteon-like structures". Biomaterials 34: 8203-8312.

21. Aktas S, Gevgilili H, Kucuk I, Sunol A, Kalyon DM (2013) "Extrusion of poly(ether imide) foams using pressurized CO_2: Effects of imposition of supercritical conditions and nanosilica modifiers". Polymer Engineering and Science DOI: 10.1002/pen.23753.