Materials Science and Engineering C 42 (2014) 102–110

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

A novel bio-safe phase separation process for preparing open-pore biodegradable polycaprolactone microparticles

Aurelio Salerno *, Concepción Domingo

Institute of Materials Science of Barcelona (ICMAB-CSIC), Campus de la UAB s/n, Bellaterra, 08193, Spain

ARTICLE INFO

Article history:
Received 12 February 2014
Received in revised form 22 April 2014
Accepted 7 May 2014
Available online 22 May 2014

Keywords:
Biodegradable particles
Ethyl lactate
Phase separation
Polycaprolactone
Porosity

ABSTRACT

Open-pore biodegradable microparticles are object of considerable interest for biomedical applications, particularly as cell and drug delivery carriers in tissue engineering and health care treatments. Furthermore, the engineering of microparticles with well definite size distribution and pore architecture by bio-safe fabrication routes is crucial to avoid the use of toxic compounds potentially harmful to cells and biological tissues. To achieve this important issue, in the present study a straightforward and bio-safe approach for fabricating porous biodegradable microparticles with controlled morphological and structural features down to the nanometer scale is developed. In particular, ethyl lactate is used as a non-toxic solvent for polycaprolactone particles fabrication via a thermal induced phase separation technique. The used approach allows achieving open-pore particles with mean particle size in the 150–250 μm range and a 3.5–7.9 m^2/g specific surface area. Finally, the combination of thermal induced phase separation and porogen leaching techniques is employed for the first time to obtain multi-scaled porous microparticles with large external and internal pore sizes and potential improved characteristics for cell culture and tissue engineering. Samples were characterized to assess their thermal properties, morphology and crystalline structure features and textural properties.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

During the last decade biocompatible and biodegradable microparticles have received considerable attention from the scientific community as potential devices for drug and cell delivery and tissue engineering applications [1–3].

Microparticles for drug delivery are a powerful tool in applications where either low or high molecular weight molecules, such as growth factors and proteins, must be long-lastingly released in a specific area at programmed rates. This is because the microparticles can guarantee the adequate protection of these molecules from inactivation occurring in biological environments, as well as the preservation of their bioactivity during the whole release process [4]. Concomitantly, drug release kinetics can be easily modulated, according to the requirements of the specific application, by appropriately tuning microparticles composition, biodegradation, size distribution and pore structure [4,5].

Biocompatible and biodegradable microparticles are also used as platforms for cell seeding, expansion and culture [2,3]. Depending on the required application, cells can be encapsulated inside the microparticles or seeded onto their surface. Cell microencapsulation is carried out by using semi-permeable polymers enabling the transport of nutrients and therapeutic agents, while isolating the encapsulated cells from the host immune system avoiding the need of immunosuppressive agents that could have a undesired toxic effects [2,6]. Microparticles are also widely used as scaffolds for cell delivery and bottom up tissue engineering [7–9]. Indeed, cell-seeded microparticles offer a range of unique advantages, such as the delivery of cells and active agents with minimally invasive procedures, the capacity to facilitate diffusion of nutrient/oxygen to the cells, the possibility to fit complex anatomical defects and, finally, the option to obtain large three-dimensional constructs with homogeneous distribution of cells [2].

Besides the properties of the constituent biomaterial, several studies highlighted the importance of the structural properties of microparticles on their potential application. Parameters such as particle size and shape, surface topography, porosity and pore size have a profound impact on both drug release and cell behavior [2,3,8,10,11]. For instance, several works have demonstrated that an open porosity on both surface and interior of microparticles is necessary to provide a suitable substrate for the transplanted cell adhesion and proliferation and, ultimately, for the delivery of a high cell number [3,8].

Microparticles composition, size, shape, microstructure and drug release capability can be controlled by selecting appropriately the fabrication technique and processing conditions. From the fabrication point of view, microparticles are mainly obtained starting from polymeric

* Corresponding author.
E-mail address: asalerno@icmab.es (A. Salerno).

http://dx.doi.org/10.1016/j.msec.2014.05.037
0928-4931/© 2014 Elsevier B.V. All rights reserved.

solutions and by means of techniques such as emulsification, spray drying and coacervation [9,11]. Furthermore, the recent development of microfluidic techniques holds great promise in both the fields of drug delivery and tissue engineering, as it allows a fine tuning over the biophysical and biochemical properties of microparticles [12]. Currently, a great challenge is the development of completely bio-safe products by using non-toxic chemicals and fabrication processes, as chemicals used during the preparation process are often present in the final product as a residue.

Ethyl lactate (EL) is a green and economically viable alternative to some traditional organic toxic solvents. This solvent received the FDA approval for its use as additive in food products and in perfumery as a flavor [13]. Recently, our group has combined EL and supercritical CO_2 for fabricating porous scaffolds [14] and for enhancing foaming of biodegradable polymers [15–17]. In this work we reported a bio-safe and highly valuable approach for the design and fabrication of porous polycaprolactone (PCL) microparticles. The developed approach is based on the thermally induced phase separation (TIPS) process of PCL/EL solutions, followed by polymer coagulation and particles setting in water. The effect of polymer concentration in the initial solution and cooling temperature on the morphology and pore structure features of PCL particles was investigated. Finally, a combined approach using TIPS and gelatin particles as a solid porogen agent was developed in order to fabricate multi-scaled porous PCL microparticles with potential application as cell carries for tissue engineering.

2. Materials and methods

2.1. Materials

PCL (molecular weight = 45 kDa), EL (photoresist grade; purity ≥ 99.0 wt.%) and paraffin oil were provided by Sigma-Alldrich (Madrid, Spain). Ethanol (96% v/v) was provided by Panreac (Barcelona, Spain). Bovine gelatin (Merck, Darmstadt, Germany) was used for the preparation of the porogen particles. All reagents were used without further purification.

2.2. Methods

The porous PCL microparticles were prepared in the four steps shown in Fig. 1. First, PCL/EL solutions with a polymer concentration in the 5–30 wt.% range were prepared at 70 °C maintaining magnetic stirring for 4 h. The solutions were then cooled down to a gelation temperature of either 6 or −15 °C to induce the TIPS process. Gelled samples were further soaked in excess of water to extract the EL and to induce PCL microparticles coagulation and setting at the bottom of the mold. The supernatant was then removed and the particles were washed three times with water allowing the complete removal of EL and the setting of the pore structure. Microparticles were finally dehydrated in ethanol and further dried at room temperature and ambient pressure.

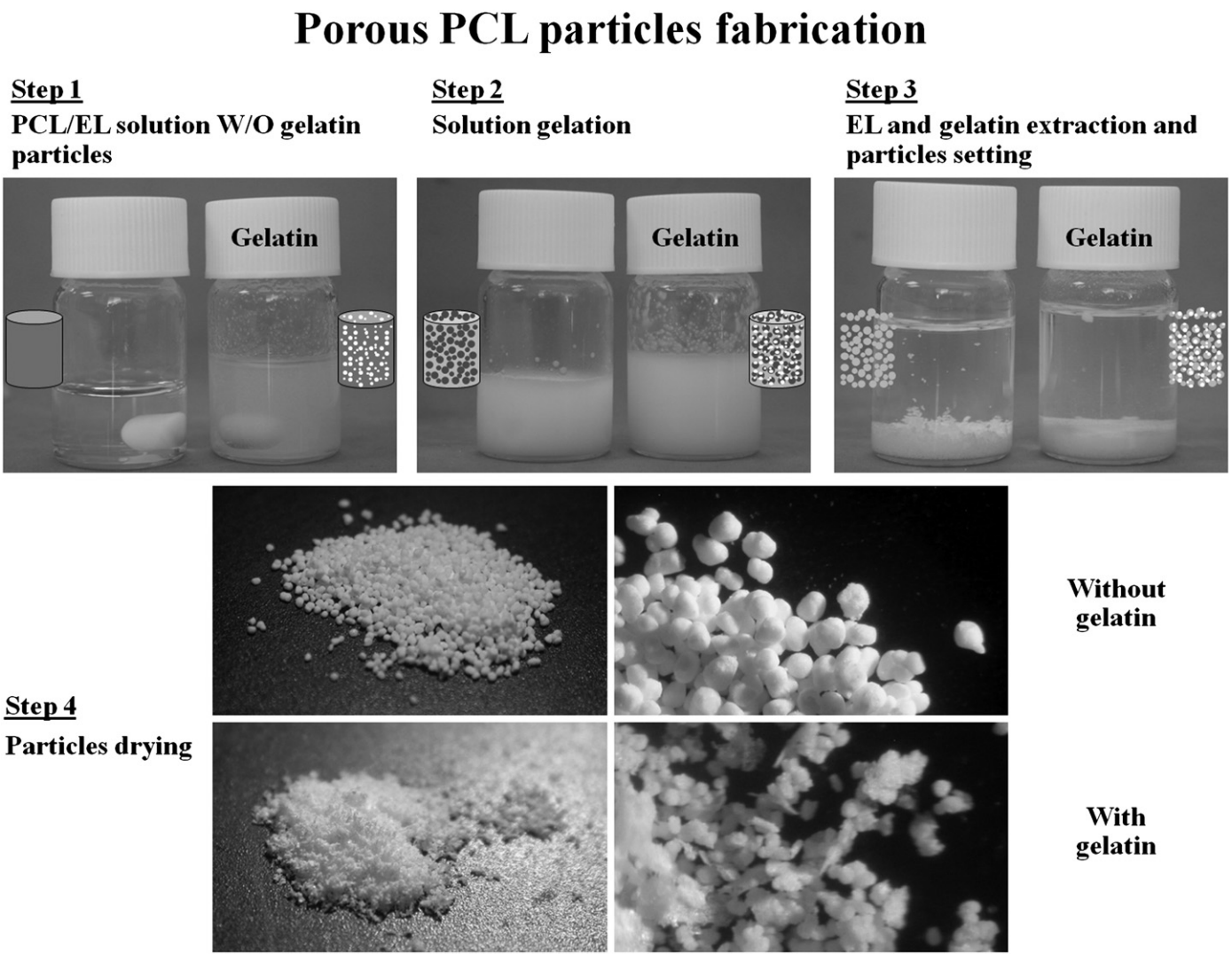

Fig. 1. Scheme of the preparation of porous PCL particles by TIPS process and TIPS combined with a porogen leaching technique.

Download English Version:

https://daneshyari.com/en/article/1428616

Download Persian Version:

https://daneshyari.com/article/1428616

Daneshyari.com