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Porogen Effect of Solvents on Pore Size Distribution of Solvent-Casted Polycaprolactone Thin Films

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ABSTRACT

In this study, the effect of porogenic solvents on pore size distribution of the polycaprolactone (PCL) thin films was investigated. Five thin PCL films were prepared using the solvent-casting method. Chloroform, Methylene Chloride (MC) and three different compositions of MC/ Dimethylformamide (DMF) (80/20, 50/50 and 20/80) were used as solvents. Scanning Electron Microscopy (SEM) investigations were employed to study morphology and consequently the pore size distribution of the prepared films. The PCL films made by chloroform and MC as a solvent were completely non-porous. Whereas the other films (made by a combination of MC and DMF) showed both uni-modal and bi-modal pore size distributions.

Keywords: Porous Films; Polycaprolactone; Porogen; Solvent Casting

1. Introduction

Polycaprolactone (PCL) is a linear aliphatic polyester which is interested in tissue engineering scaffolds due to its biodegradability, excellent thermomechanical properties, processability, and comparatively low-cost[1-4]. PCL based scaffolds are prepared using different fabrication techniques including electrospinning[5], solvent casting and particle leaching (SCPL)[6,7], melt molding[8], gas foaming[9] and membrane lamination[10].

Among different approaches, electrospinning has been commonly more utilized and investigated[11]. However, the electrospun scaffolds have two important limitations; (i) the pore size of these scaffolds are not large enough for cell penetration[12-14], and (ii) the thickness of these scaffolds is less than one millimeter in many cases[15]. In order to overcome these limitations, the SCPL technique with high processability and fewer complications can be applied[16]. Fabrication of porous scaffold with acceptable thickness is possible by polymer casting method followed by particle leaching, a simple technique which is most widely used. Different porogens such as salt, sugar and entrapped CO_2 gas bubbles were used for producing required pore density in the porous scaffold[17]. Recently, using solvent self-proliferating process has been considered to improve the SCPL method. The prepared scaffolds showed 3D porous networks, in which homogenously distributed cavities in the size of 300 to 400 μm were interconnected by some smaller holes in a size of 100–200 μm[18].

Two routes of the solvent-casting method are applicable to form porous scaffolds[16]. The first approach is dipping a mold into a polymeric solution and remove it after solvent evaporation which makes a layer of polymeric membrane. The second way which is easier, simpler and inexpensive without the need for specific equipment is the casting of polymeric solution into a designed mold and obtaining a layer of the membrane after solvent evaporation. Different methods of drying including air drying, vacuum drying, and freeze-drying can be employed to remove highly toxic solvents from scaffolds which can denature biomolecules.

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In the current research, five PCL thin films were prepared by the solvent-casting method with solvating (SOL) andnon-solvating (NON-SOL) porogens. While the evaporation method is air drying, the effect of porogenic solvents properties such as boiling point, polarity and solubility parameter on pore size distribution of thin films was discussed.

2. Experimental

2.1. Sample Preparation

PCL, purchased from Merck Co. was used as the polymer in this study. Chloroform, MC, and DMF as porogens were all purchased from Merck Co. and used as received, without any further purification. Five PCL solutions with a total concentration of 10 wt.% were prepared in chloroform, MC, and three different compositions of MC/DMF (**Table 1**). The solutions were prepared in cylindrical glassy Petri-dishes at room temperature (25 °C ± 2) for 24 hours by magnetic heater-stirrer. Subsequently, the Petri-dishes were kept in room temperature for 2 weeks in order to remove the solvent.

Solvents	**Boiling point (˚C)**	**Polarity (D)**	**Solubility parameter [$cal^{1/2}cm^{-3/2}$]**	**$\|\Delta\delta\|$ [$cal^{1/2}cm^{-3/2}$]**	**Porogenic type**
Chloroform	61.2	1.15	9.21	0.59	-
MC	40.0	1.60	12.10	2.30	-
MC 80/ DMF 20	62.6	2.05	11.64	1.84	NON-SOL
MC 50/ DMF50	96.5	2.73	10.95	1.15	NON-SOL
MC 20/ DMF 80	130.4	3.41	10.26	0.49	SOL

Table 1. The physical properties of the applied solvents

2.2. Sample Characterizations

The morphology of the prepared PCL films was investigated by scanning electron microscopy (SEM, Philips, XL 30). Micrographs with two magnifications were obtained to get a comprehensive understanding of the surface morphology of the films. The Pores diameters were measured using the Image J software (Image J, National Institutes of Health, USA) using 120 measurements for each porous film.

3. Results and Discussions

In the current work, chloroform, MC, and different compositions of MC and DMF were employed as porogenic and non-porogenic solvents. The physical properties of the solvents are summarized in Table1. The boiling point, polarity and the solubility parameter of the MC/DMF compositions were calculated from mixture rule (equation 1) and reported in Table 1.

$$\Sigma(x_n \times y_n) = y_t \quad (1)$$

The x_n is the weight percentage of the solvents and y_n is the solvent characteristic and y_t is the characteristic of the solvent mixtures. The differences of the solubility parameter $|\Delta\delta|$ between PCL and the solvents are also reported in Table 1.

Figure 1 shows the SEM micrographs of the samples at two magnifications (×30 and ×1000). As can be seen, the prepared films from chloroform and MC are not porous, while the three different combinations of MC and DMF resulted in porous structures. It can be discerned that using a binary mixture of porogens is more successful in fabricating of porous structures.

An organic solvent must have some special properties such as high boiling point and inertness to be considered as a porogen. Furthermore, the differences of polarity and solubility parameters between the polymer and solvent the are other factors which determine a solvent acts as a porogen and makes it be SOL or NON-SOL. A solvating porogen has miscibility in both monomer and polymer with low solubility parameter differences $|\Delta\delta|$. Whereas, the non-solvating porogen shows poor miscibility with a polymer and has high solubility parameter differences[19].

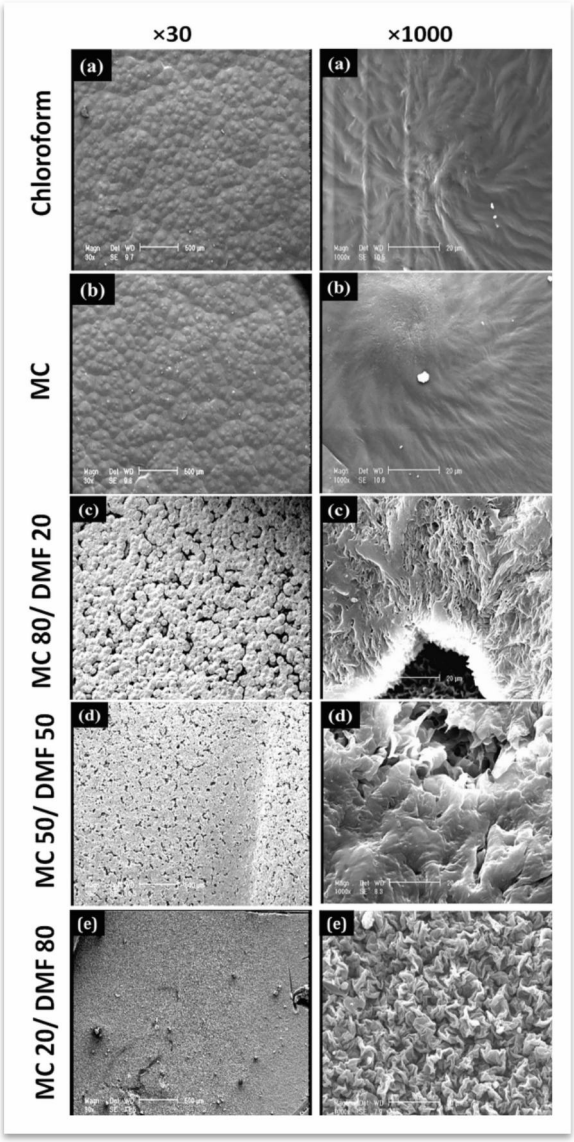
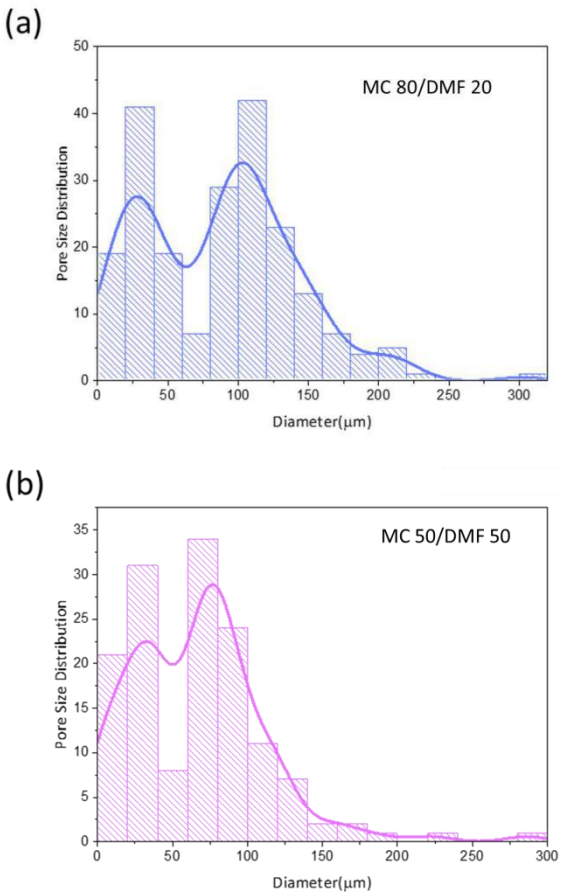


Figure 2; SEM micrographs of the prepared films using (a) Chloroform, (b) MC, (c) MC 80/ DMF 20, (d) MC 50/ DMF 50, and (e) MC 20/ DMF 80 solvents at two magnifications (×30 and ×1000)**.**

Compared to MC 80/DMF 20, chloroform has a similar boiling point, but it's nonpolar and the solubility parameter difference is lower. Therefore, chloroform has good miscibility with PCL, and can't act as a porogen and make a porous PCL film. The immiscible MC solvent also results in a non-porous structure due to its low boiling point. Therefore, these solvents can't be classified as porogens.

All the three compositions of MC/DMF were succeeded in the fabrication of the porous structures. The presence of DMF, with higher boiling point and higher polarity compared to MC made thin films to be porous. Increasing the DMF proportion in MC/ DMF mixture decreased the solubility parameter difference from 1.84 to 0.49. So the porogenic type of the solvent changed from non-solvating in MC 80/ DMF 20 to solvating in MC 20/ DMF 80.

The pore size distributions of the porous PCL films are illustrated in **Figure 2.** The non-solvating porogens (MC 80/ DMF 20 and MC 50/ DMF 50) result in an early-stage phase separation because of high solubility parameter differences and lead to a bi-modal pore size distribution (Figure 2. a and b). The pore sizes ranged in 10 to 300 µm and two peaks were observed at 30 and 110 µm, and 30 and 75 µm, respectively. While the solvating porogen (MC 20/ DMF 80) makes a late-stage phase separation and forms micro-pores ranging from 0.1 to 30 µm with uni-modal pore size distribution with a peak at 4 µm (Figure 2.c).



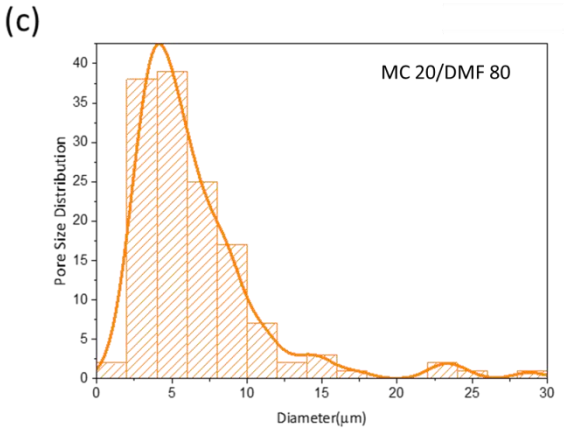


Figure 2; Pore size distribution of the PCL films prepared using (a) MC 80/ DMF 20, (b) MC 50/ DMF 50, and (c) MC 20/ DMF 80 solvents**.**

5. Conclusions

In this study, a simple solvent casting method was employed to produce porous thin films with controllable pore size. The principal of this method is based on the physical properties of solvent or solvent mixtures such as boiling point, polarity, and solubility parameter. The non-porous, uni-modal and bi-modal pore structures were fabricated using SOL and NONSOL porogens. The PCL films made by 80/20 and 50/50 ratio of MC/DMF showed bi-modal pore size distribution, whereas the prepared film with 20/80 ratio of MC/DMF has uni-modal pore structure due to low solubility difference and late-stage separation leading to more uniform pore structure. Porous thin films have critical applications such as tissue engineering scaffolds.

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