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Thin films of polymer blends deposited by matrix-assisted pulsed laser evaporation: Effects of blending ratios

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ABSTRACT

In this work, we show successful use of matrix-assisted pulsed laser evaporation (MAPLE) for obtaining thin films of PEG:PLGA blends, in the view of their use for controlled drug delivery. In particular, we investigate the influence of the blending ratios on the characteristics of the films. We show that the roughness of the polymeric films is affected by the ratio of each polymer within the blend. In addition, we perform Fourier transformed infrared spectroscopy (FTIR) measurements and we find that the intensities ratios of the infrared absorption bands of the two polymers are consistent with the blending ratios. Finally, we assess the optical constants of the polymeric films by spectroscopic ellipsometry (SE). We point out that the blending ratios exert an influence on the optical characteristics of the films and we validate the SE results by atomic force microscopy and UV–vis spectrophotometry. In all, we stress that the ratios in which the two polymers are blended have significant impact on the morphology, chemical structure and optical characteristics of the polymeric films deposited by MAPLE.

1. Introduction

Within the last years, significant advances have been made in the controlled delivery of therapeutic agents/drugs, especially when traditional delivery methods (e.g. oral tablets or injectable doses) have shown poor therapeutic efficiency [1,2]. At first, reservoir-type implants, consisting of non-biodegradable polymer membranes surrounding a drug core, have shown good performances. However, a major drawback for these systems is that additional surgical procedures are required for removing the implants after the drug delivery is completed. To overcome this limitation, recent progresses have been made in the development of biodegradable implants capable to deliver drugs in a controlled manner [3 and references therein]. As a result, since the biodegradable polymers are easily absorbed within the body by natural metabolic processes, the subsequent removal of the implant is no longer required [4–7].

Furthermore, recent studies have shown that the performances of the polymers used for controlled drug delivery are much improved by blending [8,9]. A major advantage is that the characteristics of the polymeric matrix can be modified without altering the chemical structure of the component polymers. The most attractive feature for controlled drug delivery is that the polymer blends degrade differently and exhibit different drug release properties than single polymers, offering the possibility of a fine tuning of the drug release rates function of blend composition [9]. Due to this significant advantage, various polymer blends have been successfully used in controlled drug delivery [10,11].

Depending on the site of implantation and on the therapeutic purposes, the drug delivery devices have been developed in a variety of shapes (rods, pellets, nanoparticles). Particularly interesting are the devices in the shape of films. In this case, the drug delivery system usually consists of a drug core covered by a polymeric film that acts like a membrane and controls the drug delivery rates. For fabricating the films, various methods like molding, drop casting, spin coating, have been used [12,13]. For achieving full control over the properties of the films and for preserving the chemical structure of the polymers, novel fabrication procedures had to be developed. Lately, an attractive technique called matrix assisted pulsed laser evaporation (MAPLE) has been intensively used for obtaining thin polymer films [14]. It is generally accepted that MAPLE exhibits significant advantages compared to other fabrication techniques: it is inexpensive, easy-to-operate and, most importantly, preserves the chemical integrity and the functionality of the polymers. [15,16]. Although MAPLE has been extensively used for deposition of films of various polymeric materials, most studies have been dedicated to the case of individual polymers. We have recently shown the first successful use of MAPLE for obtaining films of polymer blends [17], with promising results for controlled drug delivery applications.

Besides obtaining the polymeric films by MAPLE, other prerequisites must be fulfilled for their safe utilization in real applications.

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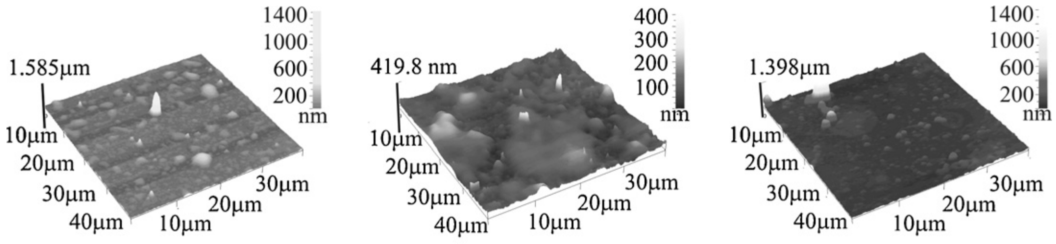

a) PEG:PLGA (1:1) b) PEG:PLGA (1:2) c) PEG:PLGA (2:1)

Fig. 1. AFM images (40 μm × 40 μm areas) of PEG:PLGA films, with the indicated blending ratios.

A critical requirement for efficient therapeutic procedures is a fine tuning of the drug delivery rates. As we mentioned earlier, a decisive factor for the dynamics of drugs release is represented by the blending ratio. Therefore, in this work we extend our initial study [17], reporting MAPLE deposition of polymer blends with various blending ratios.

On the other hand, in controlled drug delivery systems that contain polymers, the drug delivery rates are mainly determined by the dynamics of polymer degradation. Studies have shown that the degradation behavior of polymers is closely related to polymer structure and properties. For example, the pores and channels observed on the surfaces of certain polymeric films are considered to represent transport pathways of the drug through the polymer matrix. Therefore, the morphology of the polymeric films critically impacts their performances for controlled drug delivery applications. In addition, specific functional groups in polymers are known to be directly involved in polymer degradation, playing thus a significant role in the dynamics of drug release. In consequence, the chemical structure of the polymers strongly influences the drug release kinetics. Furthermore, in specific applications (e.g. for intraocular use) the optical constants of the polymeric films (refractive indices, extinction coefficients) directly affect the quality of the eyesight. Hence one can consider that the optical properties of the polymeric films are equally important for the quality of the drug delivery implants. In all, a complete elucidation of the properties of the polymeric films is essential for achieving the desired drug delivery rates, as well as for other specific requirements.

Based on the above considerations, in this work the influence of the blending ratios on the characteristics of MAPLE deposited films of polymer blends will be studied. To meet this objective, we will investigate the morphology of the films, the chemical structure of the polymers within the blends and we will assess the optical properties of the films. Based on these experimental results, we aim to establish a framework for the composition of the polymer blends, which will allow a refined tuning of the drug delivery rates, as well as of other functional implications.

2. Experimental

The polymers (polyethylene glycol PEG (1450 Da), poly (lactide-co-glycolide) PLGA ((40–75) kDa)) (Sigma–Aldrich) were individually dissolved in chloroform, in 1% wt polymer concentration. The two solutions were mixed together at room temperature in PEG:PLGA blending ratios of (1:1), (1:2) and (2:1), then stirred continuously for few hours. For MAPLE deposition, solutions of solvent/polymers were frozen in liquid nitrogen, placed in a vacuum chamber and submitted to laser irradiation. Film deposition was carried out with a Nd:YAG laser working at 266 nm and 10 Hz pulse repetition rate. For irradiating the target, 18000 pulses were used, the size of the laser spot reaching the target being ∼1 mm^2. We have previously shown [17] that the quality of the films is much reduced when MAPLE deposition is performed at fluences above 1 J/cm^2. Therefore, in the present study, MAPLE deposition of the polymeric films was performed at much lower fluence (200 mJ/cm^2). During laser irradiation, the polymer molecules were collected on a substrate in the form of a thin film, while the volatile solvent was pumped away. The substrates (glass slides, Si wafers and quartz plates) were placed at 4.5 cm, parallel with the target. The so-called "native" samples were prepared by drop casting and used as reference samples.

The morphology of the films was studied with an XE-100 atomic force microscopy (AFM) system. The chemical structure of the polymers within the blends was investigated by Fourier transformed infrared spectroscopy (FTIR). The optical characterization of the films was assessed with a Woollam variable angle spectroscopic ellipsometer system (WVASE).

3. Results and discussions

First, detailed morphological investigations of the MAPLE deposited films were performed. The AFM images of films of polymer blends with different blending ratios are illustrated in Fig. 1. For each film, several different areas of 40 μm × 40 μm were investigated, no dependence of surface roughness on the scanned area being observed. For all blending ratios, the films surfaces are continuous and reasonably smooth. In addition, the surface morphology depends on the blending ratios, smoother films being obtained for blends with higher content of PEG. Indeed, the root mean square roughness (RMS) for (2:1) PEG:PLGA blending ratio was found to be quite low (34.6 nm). In contrast, higher amount of PLGA ((1:2) PEG:PLGA blending ratio) results in increased surface structuring, with RMS up to 87.9 nm. For (1:1) PEG:PLGA blending ratio, RMS roughness was about 51 nm.

Furthermore, the changes at the level of chemical bonds were investigated by FTIR. For all blending ratios, all the spectral features are equally present in the MAPLE deposited films and in the native samples, with similar intensity ratios (Fig. 2a–c). This indicates that MAPLE did not damage the structural composition of the polymer blends. Assignments of the infrared absorption bands of PEG:PLGA blends specified in Table 1 are accordingly to [18–20]. We also found that, for all blending ratios, all absorption bands of the component polymers are well reproduced in the FTIR spectra of the blends, demonstrating that both polymers within the blends keep their chemical structure. Another interesting finding is that MAPLE does not seem to induce chemical interactions between the two polymers, since all infrared absorption bands of the polymer blends belong to one of the component polymers, no additional features being observed.

Next, the influence of the blending ratios on the infrared absorption bands of the polymer blends was investigated by FTIR measurements. To this end, we calculated the intensities ratios of two infrared absorption bands: the band at 1100 cm^{-1} (assigned to C–O–C stretching vibration in PEG [18] and the band at 1762 cm^{-1} (attributed to the C=O stretch in PLGA [19,20]). Fig. 2d shows