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Effect of Flow Rate on Fiber Morphology and Naringin Release of Electrospun Naringin Loaded Polycaprolactone Nanofibers

R. Ranjith, S. Balraj, J. Ganesh, M. C. John Milton*

P.G. and Research Department of Advanced Zoology and Biotechnology, Loyola College, Chennai, Tamil Nadu, India

ABSTRACT

Electrospun nanofibers can be used as carriers in various drug delivery applications for controlled delivery of several bioactive molecules. In this study, effect of flow rate on fiber morphology and naringin release of naringin loaded polycaprolactone nanofibers was evaluated. The scanning electron microscopy results showed increased average fiber diameters in naringin loaded polycaprolactone nanofibers compared to polycaprolactone nanofibers as well as with increasing flow rates. Further, Fourier transform infrared spectroscopy analysis implies that encapsulated naringin was not chemically changed during the encapsulation process. Furthermore, increased cumulative naringin release profiles were observed with increasing flow rates for 12 days. These results suggest that, naringin release rate can be manipulated by varying the flow rates which could help to obtain desired naringin release rate for various therapeutic applications.

Keywords: Electrospinning, Flow Rate Effect, Polycaprolactone Nanofibers, Naringin, Drug Delivery

I. INTRODUCTION

Drug delivery systems are capable to deliver the encapsulated drugs to the targeted site which could enhances the therapeutic potential and also reduces the drug toxicity [1,2]. In general, the polymeric drug carriers are classified into four types such as nano/micro spheres, micelles, hydrogels and nanofibers [1]. Among them, nanofibers fabricated by electrospinning technique have gathered more attention in various biomedical applications which could help to overcome the limitations of nano/micro spheres, micelles and hydrogels [3,4]. Several studies have used the biodegradable polymeric electrospun nanofibers as carrier to deliver various hydrophobic and hydrophilic bioactive molecules in a sustained manner [4–6]. Further, the fiber diameter can be manipulate by altering the electrospinning parameters such as solution, processing and ambient parameters which could help to attain the drug release rate with desired concentration [6]. Flow rate is one of the important processing parameter which determines fiber diameter and its continuity [7]. Also, increasing flow rates could result in increased fiber diameter up to certain point beyond which droplets and beaded structure are formed [7].

Polycaprolactone is a biodegradable semi-crystalline polymer have been used as carrier for delivery of several bioactive molecules in a sustained manner [8]. It has several advantages such as biocompatibility, biodegradability, chemical stability, slower degradation rate *etc* [2]. Naringin is a flavanone glycoside, has numerous therapeutic potential such as anticancer, osteogenic differentiation, anti-inflammatory, antioxidant *etc* [9–11]. Hence, naringin release rate can be manipulated by varying the flow rate to obtain the desired concentration ranges for various therapeutic applications.

In this study, we fabricated naringin loaded polycaprolactone nanofibers by using electrospinning process with two different flow rates and characterized using scanning electron microscopy and Fourier transform infrared spectroscopy analysis. Further, naringin release profiles were observed from fabricated nanofibers for 12 days.

II. MATERIALS AND METHODS

A. Fabrication of Naringin Loaded Polycaprolactone Nanofibers

The nanofibers were fabricated using ESPIN – NANO (PECO – Chennai, India) [12]. Naringin (4 mg/ml) (Sigma-Aldrich) was added to the prepared 10% (w/v) polycaprolactone solution (polycaprolactone (average Mn 80,000, Sigma-Aldrich) in 1:1 of dichloromethane:dimethylformamide) and mixed well. The prepared solution was transferred to a syringe fitted with a needle (0.55 x 25 mm). Further the solution was electrospun by applying a high-voltage of 15 kV, 15 cm distance from the needle tip to collector and collector drum speed of 1500 rpm. Moreover, electrospinning of naringin loaded polycaprolactone nanofibers was done under two different flow rates namely 1 ml/hr (N-PCLNF-1) and 2 ml/hr (N-PCLNF-2). Similarly, polycaprolactone nanofibers was prepared without naringin were considered as control under two different flow rates namely 1 ml/hr (PCLNF-1) and 2 ml/hr (PCLNF-2).

B. Characterization of the Fabricated Nanofibers

1) Scanning electron microscopy (SEM): The morphological analysis of the prepared nanofibers was evaluated by using SEM (TESCAN VEGA3 SBU). The nanofibers were sputtered with gold and evaluated under 10 kV applied voltage and 5000x magnifications. The average fiber diameter of prepared nanofibers was evaluated manually by using ImageJ software (ImageJ 1.51j8, National Institutes of Health, USA). Twenty fibers were selected randomly from each SEM image and calculated the average fiber diameters, the results were expressed as mean ± standard deviation.

2) Fourier transform infrared spectroscopy (FTIR): Naringin, polycaprolactone nanofibers and naringin loaded polycaprolactone nanofibers were examined by FTIR spectrophotometer (Perkin Elmer). Potassium bromide was mixed with samples and the pellets were made; analysed at 4,000–400 cm^{-1} with the resolution of 1 cm^{-1}.

3) Naringin release studies: Nanofibers (1 cm x 1 cm) were incubated in Dulbecco's phosphate buffered saline (2ml); 700µl was collected at fixed time interval and replaced with fresh Dulbecco's phosphate buffered saline. The collected aliquots were read at 284nm by UV-Vis spectrophotometer and the amount of naringin released was calculated using naringin standard curve.

III. RESULTS AND DISCUSSION

The morphology of the nanofibers was evaluated using SEM analysis and the results were shown in Fig. 1. The average fiber diameters were found as 424.79±124.29nm for PCLNF-1 and 487.48±122.41nm for PCLNF-2. Similarly, the average fiber diameters were found as 508.64±243.41nm and 576.86±221.19nm for N-PCLNF-1 and N-PCLNF-2 respectively. Numerous studies have reported that, an increased fiber diameter in bioactive molecules loaded polymeric nanofibers compared to control [1,2,13,14]. Overall, the SEM results indicated that an increased average fiber diameters were observed in naringin loaded polycaprolactone nanofibers compared to control as well as with increasing flow rates.

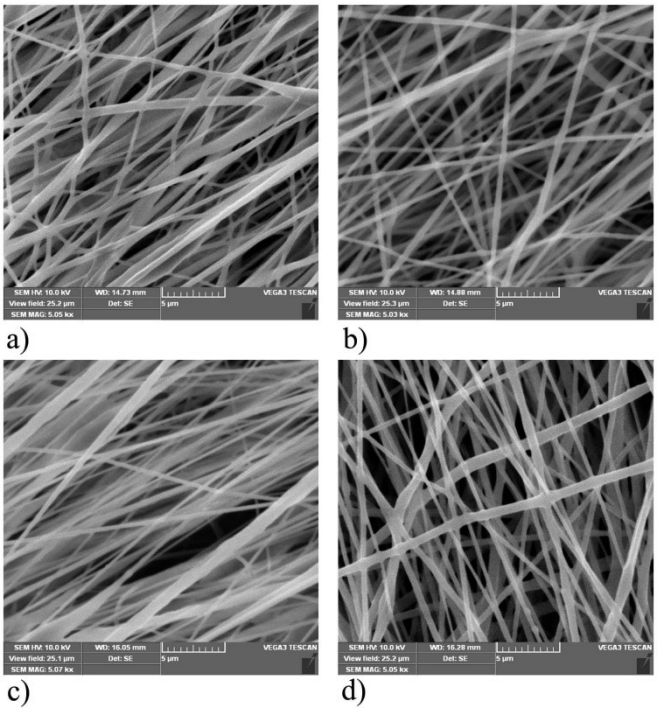

Figure 1: SEM Images. Where, a) Polycaprolactone nanofibers (1 ml/hr flow rate); b) Polycaprolactone nanofibers (2 ml/hr flow rate); c) Naringin loaded polycaprolactone nanofibers (1 ml/hr flow rate); d) Naringin loaded polycaprolactone nanofibers (2 ml/hr flow rate)

FTIR spectra (Fig. 2) showed the characteristic peaks of naringin, polycaprolactone nanofibers and naringin loaded polycaprolactone nanofibers. The naringin characteristic peaks (Fig. 2a) were observed at 1643 cm^{-1}, 1518 cm^{-1}, 1452 cm^{-1}, 1176 cm^{-1} and 1135 cm^{-1} [15]. Further, polycaprolactone nanofibers (Fig. 2b) showed the peaks at 2944 cm^{-1} (symmetric CH2- stretching), 2867 cm^{-1} (asymmetric CH2- stretching) and 1239 cm^{-1}

which corresponds to polycaprolactone [11,16]. Furthermore, the spectra of naringin loaded polycaprolactone nanofibers (Fig. 2c) showed the peaks at 1642 cm^{-1}, 1365 cm^{-1} and 1168 cm^{-1} representing the characteristic peaks of naringin [15] along with the characteristic peaks of polycaprolactone. Thus, this FTIR results suggested that the chemical nature of the naringin was not modified after encapsulation into the polycaprolactone nanofibers.

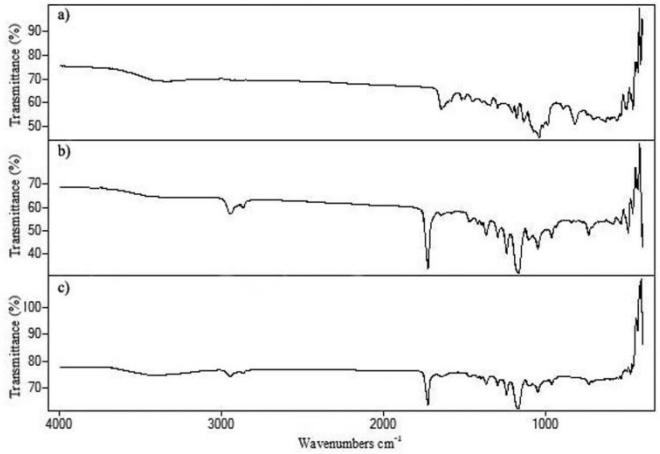

Figure 2: Fourier transform infrared spectra. Where, a – Naringin; b – Polycaprolactone nanofibers; c – Naringin loaded polycaprolactone nanofibers

The cumulative naringin release profiles were observed from the fabricated naringin loaded polycaprolactone nanofibers (Fig. 3). On day 12, the cumulative naringin release were found as 42.98 micromolar (µM) and 67.57 µM for N-PCLNF-1 and N-PCLNF-2 respectively. Previous studies have reported on delivery of several drugs and bioactive molecules from various polymeric nanofibers for various drug delivery applications [12,17–19]. The encapsulation of drugs into polymeric nanofibers helps to enhance the dissolution of the water insoluble drugs due to nanofibers high surface area to volume ratio properties [17]. Hence, this cumulative naringin release profiles suggest that increasing flow rates results increased average fiber diameters, consequently increased cumulative naringin release profiles.

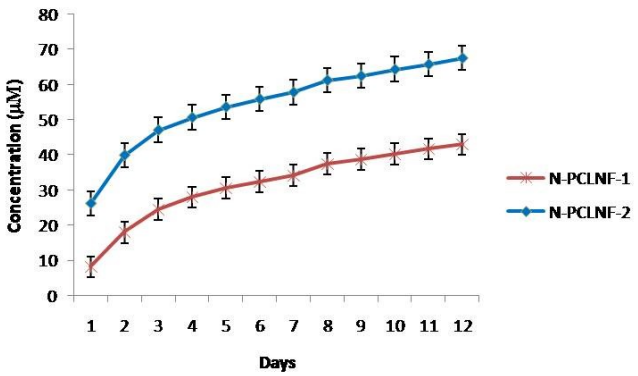

Figure 3: Cumulative naringin release profiles. Where, N-PCLNF-1 - Naringin loaded polycaprolactone nanofibers (1 ml/hr flow rate); N-PCLNF-2 - Naringin loaded polycaprolactone nanofibers (2 ml/hr flow rate)

IV. CONCLUSION

Naringin loaded polycaprolactone nanofibers were fabricated with two different flow rates. The SEM results suggest that, naringin loaded polycaprolactone nanofibers has showed increased average fiber diameters compared to polycaprolactone nanofibers. Further, increasing flow rates substantially increased average fiber diameters in both polycaprolactone nanofibers and naringin loaded polycaprolactone nanofibers. In addition, the FTIR analysis indicated that encapsulated naringin was not altered during the encapsulation process. Furthermore, naringin release study showed that, increased cumulative release profiles were observed with increasing flow rates. From these results, we conclude that flow rate is one of the important parameter in electrospinning process to obtain the appropriate naringin release rate which is suitable for various therapeutic applications.

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