

# Electrospun Polycaprolactone Nanofibers for Sustained Release of Naringin

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## ABSTRACT

Electrospun nanofibers have enormous potential to deliver bioactive molecules in a sustained manner for various drug delivery applications. In this study, naringin loaded polycaprolactone nanofibers were fabricated using electrospinning technique. The scanning electron microscopy results showed an increased fiber diameter in naringin loaded polycaprolactone nanofibers compared with control. Further, an X-ray diffraction analysis showed amorphization of naringin in nanofibers during the encapsulation process. Furthermore, sustained release of naringin was observed for 12 days. These results suggested that naringin loaded polycaprolactone nanofibers helps to deliver encapsulated naringin in a sustained manner and also it can be advantageous in various drug delivery and tissue engineering applications.

**Keywords:** Electrospinning, Polycaprolactone Nanofibers, Naringin, Drug Delivery

## I. INTRODUCTION

The recent development of nano based drug delivery systems has ability to overcome the limitations to a drug and also improves the therapeutic potential by delivering the encapsulated bioactive molecules to the targeted site in a sustained manner [1–3]. Several forms of nanoscale materials (nanofibers, nanoparticles, nanogels, nanotubes, nanocapsules, nanospheres *etc*) have reported earlier, which have been synthesized from several natural and synthetic polymers [4,5]. Among them, nanofibers fabricated by electrospinning technique have enormous potential in various drug delivery and tissue engineering applications due to its high surface-area-to-volume ratio, high loading capacity, complex porous structure, cost-effectiveness, multi-drug delivery *etc* [1,6].

Polycaprolactone is Food and Drug Administration approved biodegradable semi-crystalline polymer. It has been widely used in long-term implants for sustained delivery of therapeutic molecules due to an excellent properties such as biodegradability, biocompatibility and slower degradation rate [7–9]. Many studies have reported on polycaprolactone as carrier for delivery of various drugs for drug delivery applications [7]. Naringin, flavanone glycoside found in grapefruit and

related citrus species, has various therapeutic potential such as osteogenic differentiation, anti-cancer, anti-inflammatory, anti-ulcer, anti-oxidant *etc* [10–12].

In this study, naringin loaded polycaprolactone nanofibers were electrospun and characterized. In addition, the naringin release profile was observed from naringin loaded polycaprolactone nanofibers.

## II. METHODS AND MATERIAL

### A. Electrospinning

The nanofibers were fabricated by an electrospinning process (ESPIN – NANO (PECO – Chennai, India)). Polycaprolactone (average Mn 80,000, Sigma-Aldrich) (1g) was dissolved in 10ml of dichloromethane:dimethylformamide (1:1) solution [13]. Further, naringin (Sigma-Aldrich) (2mg/ml) was added to the prepared polycaprolactone solution and transferred to a syringe fitted with a needle (0.55 x 25 mm). The prepared solution was electrospun with a high-voltage of 15kV, 1ml/hr flow rate, collector drum speed of 1500 rpm and 15cm distance from the needle tip to collector. Similarly, polycaprolactone nanofibers were prepared without naringin were considered as control.

## B. Characterization of the Fabricated Nanofibers

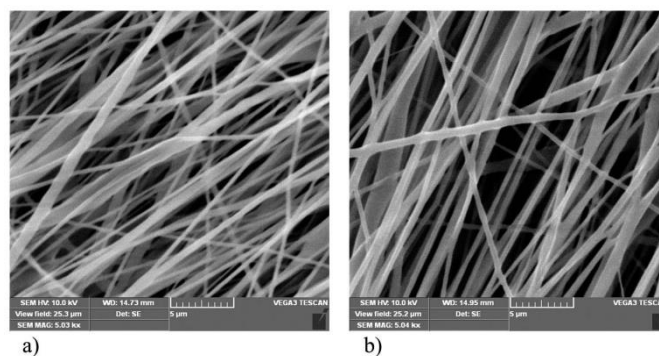
1) *Scanning electron microscopy (SEM)*: The prepared nanofibers were sputtered with gold and the morphological analysis was evaluated by using SEM (TESCAN VEGA3 SBU) with an applied voltage of 10 kV and 5000x magnifications. From each SEM image, 20 fibers were selected randomly and the average fiber diameter was calculated manually by using ImageJ software (ImageJ 1.51j8, National Institutes of Health, USA) and the results were expressed as mean  $\pm$  standard deviation.

2) *X-ray diffraction*: Further, the crystallinity of the polycaprolactone nanofibers, naringin and naringin loaded polycaprolactone nanofibers were evaluated by an X-ray diffraction studies using PANalytical X'Pert PRO Powder instrument with the  $2\theta$  scan ranging from  $5^\circ$ – $70^\circ$  with a step size of 0.05.

3) *Naringin release from naringin loaded polycaprolactone nanofibers*: The naringin loaded polycaprolactone nanofibers were cut into  $1\text{cm} \times 1\text{cm}$  and incubated in 2ml of Dulbecco's Phosphate Buffered Saline (DPBS) under static condition. From this, 700 $\mu\text{l}$  was taken out and replaced with equal volume of DPBS at a fixed time interval; the collected samples were read at 284nm using UV-Vis spectrophotometer. Further, the released naringin concentrations were calculated from the standard curve of naringin.

## III. RESULTS AND DISCUSSION

The morphology of the fabricated nanofibers was observed using SEM and it showed the considerable effects on the fiber diameter. The SEM results (Fig. 1) showed the average fiber diameters were found as  $427.28 \pm 193.14\text{nm}$  for polycaprolactone nanofibers and  $464.01 \pm 160.44\text{nm}$  for naringin loaded polycaprolactone nanofibers. Several studies have reported that increased fiber diameter was observed in drug loaded nanofibers compared with control [14–17]. Hence, the SEM results concluded that an increasing average fiber diameter was observed in naringin loaded polycaprolactone nanofibers compared with polycaprolactone nanofibers.

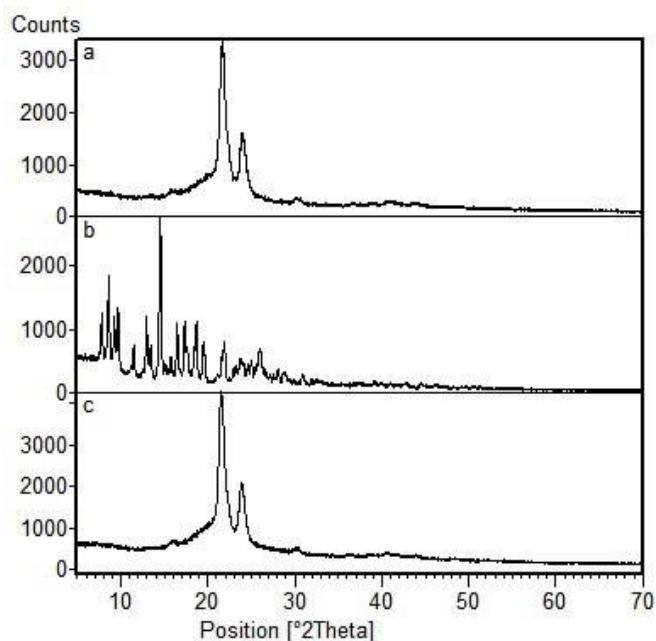


**Figure 1:** SEM Images showing morphology of the fabricated nanofibers. Where, a – Polycaprolactone nanofibers; b - Naringin loaded polycaprolactone nanofibers

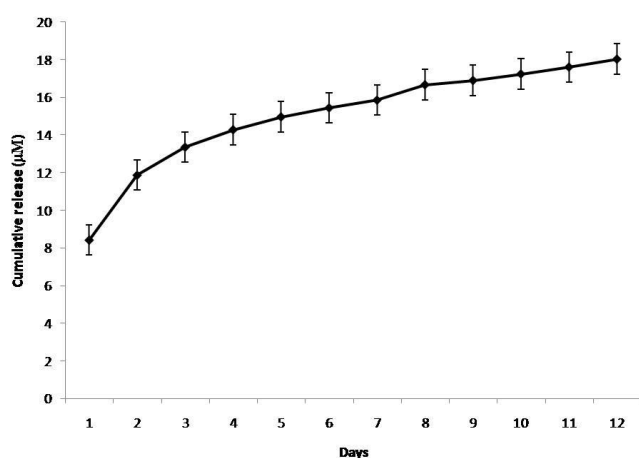
Further, the crystallinity of polycaprolactone nanofibers, naringin and naringin loaded polycaprolactone nanofibers were analyzed by an X-ray diffraction analysis (Fig. 2). Multiple intense diffraction peaks were observed in naringin spectra as previously reported [18]. Also, two semicrystalline peaks were observed in both polycaprolactone nanofibers (at  $2\theta$  of  $21.73^\circ$  and  $24.07^\circ$ ) and naringin loaded polycaprolactone nanofibers (at  $2\theta$  of  $21.44^\circ$  and  $23.90^\circ$ ). And, no naringin diffraction peaks were observed in naringin loaded polycaprolactone nanofibers which imply that naringin was amorphized during fabrication process. Previous studies have reported that encapsulated drugs are underwent amorphous state during the electrospinning process [14,19]. Thus, this X-ray diffraction results suggested that naringin was entrapped in amorphous form which is suitable for drug delivery applications.

Subsequently, naringin release profile was observed from naringin loaded polycaprolactone nanofibers and the cumulative release was found as  $18.03\mu\text{M}$  on day 12 (Fig. 3). Many studies have reported that controlled release of encapsulated drugs and therapeutic molecules were observed from drug loaded nanofibers [15,20–23]. The high surface area to volume ratio of the electrospun nanofibers supports to enhance the dissolution of the insoluble drugs by encapsulating into nanofibers [24]. In 2006, sustained release profile of water insoluble and water soluble drugs were observed from polyvinyl alcohol nanofibers [25]. In addition, the electrospinning technique could not affect the chemical integrity of the drugs during the encapsulation process [25,26]. Hence, this naringin release profile imply naringin loaded polycaprolactone nanofibers was successfully releases

the encapsulated naringin in sustained manner which could help to enhance the therapeutic potential.



**Figure 2:** X-ray diffraction spectra. Where, a - Polycaprolactone nanofibers; b - Naringin; c - Naringin loaded polycaprolactone nanofibers



**Figure 3:** Cumulative release of naringin from naringin loaded polycaprolactone nanofibers

#### IV. CONCLUSION

Naringin loaded polycaprolactone nanofibers were fabricated and the SEM analysis showed an increased fiber diameter in naringin loaded polycaprolactone nanofibers compared with polycaprolactone nanofibers. The X-ray diffraction results suggested that naringin was in amorphous form after encapsulation into the

polycaprolactone nanofibers. Further, sustained naringin release profile was observed from naringin loaded polycaprolactone nanofibers for 12 days. From this study, we conclude that naringin was successfully entrapped into the polycaprolactone nanofibers and it has ability to deliver the encapsulated naringin in sustained manner. Furthermore, the effect of solution, processing and ambient parameters on fiber morphology and naringin release need to evaluate extensively to determine the suitable naringin release profile for drug delivery and tissue engineering applications.

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