

Non-woven Electrospun Microfibers Inserts for Sustained Topical Ocular Drug Delivery



Wenrui Zhang, Wafa Al-Jamal, Thakur R.R. S.

School of Pharmacy, Queens University Belfast, 97 Lisburn Road, Belfast, BT9 7BL, Northern Ireland, United Kingdom.

E-mail: wzhang08@qub.ac.uk

Introduction

Ocular inserts are a promising strategy to achieve sustained drug delivery to the anterior segment of the eye. Common challenges with ocular inserts include corneal abrasion, accidental loss or sticking out due to poor muco-adhesiveness, allergic reaction and inflammation. However, electrospun (ES) patches have a high potential to overcome some of these issues due to their softness, strong mucoadhesiveness and improved biocompatibility. Moreover, their ability to achieve high drug loading and tailored thickness make them versatile in both the engineering and medical field. The aim of this research is to develop a small and effective ocular insert in the cul-de-sac which can achieve sustained drug delivery for one week in treating anterior segment ocular diseases.

Aims & Objectives

The present study aimed to investigate, as fundamental research, the possibility of PCL-based non-woven ES mats to be applied as inserts in cul-de-sac for sustained drug delivery.

In this study, Triamcinolone acetonide (TA) loaded PCL inserts were prepared, where the influence of different solvent systems and thermal properties of the inserts was investigated. The mucoadhesive properties of inserts were compared with traditional PCL casting films to illustrate if non-woven structures stick on the mucosa better than casting films.

Methods

Briefly, PCL and TA blended solution was prepared at different concentration in different solvent system. Residual solvent, fibres morphology and crystalline were then investigated for the optimizing of processing parameters via thermogravimetry analysis (TGA), scanning electron microscope (SEM) and differential scanning calorimeter (DSC).

Two solvent system (dichloromethane, acetone and DMSO mixture and 2,2,2-Trifluoroethanol alone) were used to spin PCL fibers loaded with 10% to 30% w/w of TA. The formation of PCL fibers was investigated with change in several factors such as spinning height, the voltage, the collector and spinning rate.

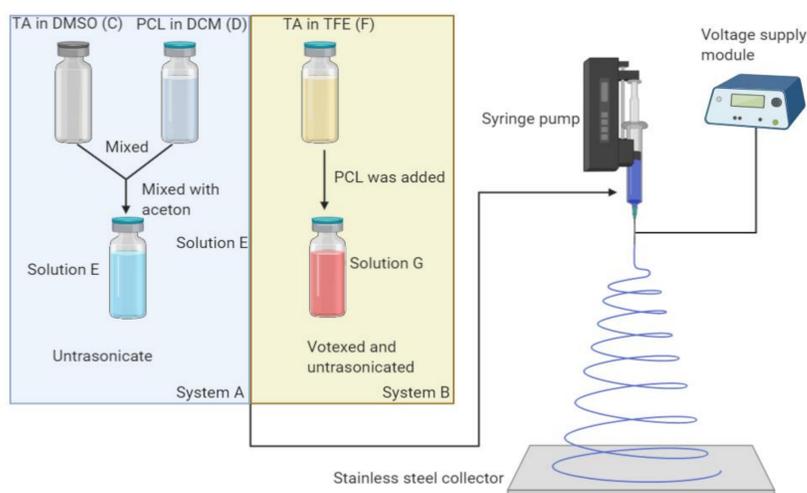


Figure 1. Electrospinning apparatus setup

Table 1. Formulations selected for characterisation

Formulation code	PCL concentration (w/w%)	Theoretical drug loading(w/w%)	Solvent
S1	13	10	Solvent system A
S2	13	20	Solvent system A
S3	13	30	Solvent system A
NS1	10	10	TFE
NS2	10	20	TFE
NS3	10	30	TFE

Results & Discussions

- The result of swelling studies is shown in Table 2. It could be found that the ES mats have a significantly higher % swollen weight and % thickness compared with casted films.
- All the ES groups witnessed a thickness increase around 50% after swelling. The thickness increase was mainly caused by the swelling of fibers after the media entered the space left behind by TA released.
- ES mats showed good wettability due to the highly porous structure.

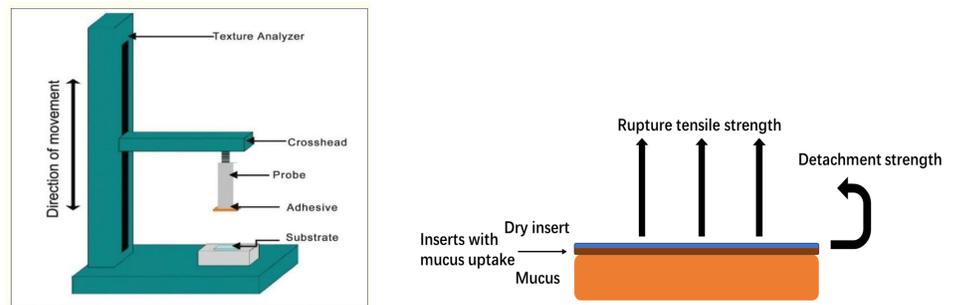


Figure 2. Muco-adhesiveness test apparatus setup

- The results of muco-adhesive studies is shown in Figure 5. As non-adhesive materials with smooth surface, similar rupture tensile strength was observed for the probe, the casting film and the PE film. However, for detachment strength, since the probe has a rigid structure, it can not be investigated. The ES mats showed a significantly higher (55%) rupture tensile strength and higher (86%) detachment strength than the casting films ($p < 0.0001$). This illustrated that the micro-structure of the inserts itself improved muco-adhesive properties. The inserts would be less likely to move or fall out compared with casting films.
- SEM images of selected ES patches are as shown in Figure 3. All selected formulations could generate homogeneous microfibers which would improve comfort while application.
- *In-vitro* release profiles are shown in Figure 4. TA release from all inserts was >90% by day 7. It could be found that drug loading % has a significant influence on both burst release ($p = 0.0213$ or less between S1 and S2; S1 and S3; NS1 and NS2; NS1 and NS3) and the drug release pattern ($p < 0.0001$ among all groups). With the same% drug loading, solvents affected the drug burst release significantly as well ($p = 0.01779$ between S1 and NS1, 0.0092 between S2 and NS2). Formulations with higher % drug loading and TFE showed a more controlled release pattern.

Table 2. 7-day swelling study of Inserts with different drug loading. C1 is a TA loaded PCL casting film as controlled group.

Sample Code	% weight after swelling for seven days (N=3)	% thickness after swelling for seven days (N=3)	Fiber diameter (μm , N=18)
C1	104 \pm 2	102 \pm 2	-
S1	240 \pm 13	163 \pm 6	2.23 \pm 0.97
S2	234 \pm 11	156 \pm 5	2.82 \pm 1.32
S3	226 \pm 15	162 \pm 6	3.32 \pm 1.09
NS1	279 \pm 6	149 \pm 7	1.86 \pm 0.48
NS2	293 \pm 3	155 \pm 2	2.15 \pm 0.42
NS3	289 \pm 13	148 \pm 5	3.01 \pm 0.73

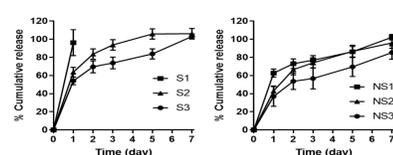


Figure 4. *In-Vitro* release study data of E29,30,31 and NE 11,12,13

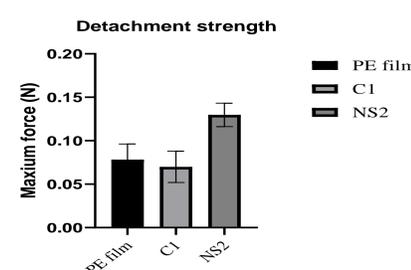
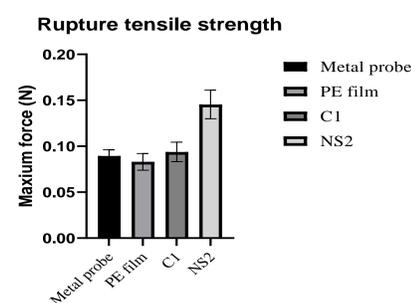


Figure 5. Muco-adhesive mechanism of ES micro/nano fibre patches

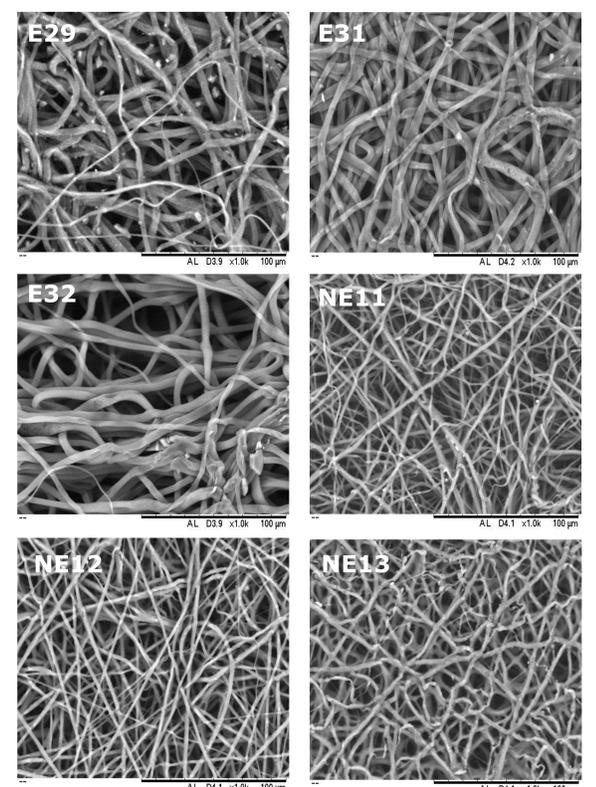


Figure 3. SEM image of ES patch, $\times 1000$ magnification

Conclusion

In conclusion, PCL-based ES microfibres could achieve sustained release for TA up to 7 days. TFE as solvent could disperse TA better within PCL fibres during ES process. TGA analysis proved that only trace of solvent remained and this will be further confirmed by GC analysis.

The ES patches showed the possibility of strong muco-adhesiveness which would prevent the accidental movement or loss compared with the tradition ocular patches. Other potential properties including permeability, porosity, irritation and comfortless will be further investigated.