 DOI: 10.33892/aph.2021.91.260-261

P-48

Application of Automated Ultrasound Signal Generator in the Development of Electrospun Multi-Layered Polymeric Nanofibrous Structures

ARLE KÕRKJAS[1]; IVO LAIDMÄE[1]; KARIN KOGERMANN[1]; ARI. SALMI[3]; HEIKKI. J. NIEMINEN[4]; EDWARD HÆGGSTRÖM[3]; JYRKI HEINÄMÄKI[1]

[1]*Institute of Pharmacy, Faculty of Medicine, University of Tartu, Nooruse 1, EE-50411, Tartu, Estonia*
[2]*Institute of Biomedicine and Translational Medicine, University of Tartu, Estonia*
[3]*Electronics Research Laboratory, Department of Physics, University of Helsinki, Finland*
[4]*Medical Ultrasonics Laboratory, Department of Neuroscience and Biomedical Engineering, Aalto University, Espoo, Finland*

Correspondence: arle.korkjas@ut.ee

Keywords: *USES, ultrasound-enhanced, electrospinning, nanofibers, multi-layered*

1. Introduction

Multi-layered polymeric nano- and micro-fibrous structures have found uses in tissue engineering and drug delivery applications [1]. Ultrasound-enhanced electrospinning (USES) is a new nozzle-free continuous manufacturing technology to fabricate polymeric nanofibers [2]. In the USES, controlled high-intensity focused US bursts generate a liquid protrusion from the surface of a polymer solution, and the fibers are collected on a grounded plate (***Figure 1***). The aims of the present work were (1) to further develop the USES process in fabricating nanofibrous mats, and (2) to develop the multi-layered polymeric nanofibrous structures of a water-soluble polymer using an automated ultrasound signal generator (Image 1).

2. Materials and methods

An in-house USES method was used for fabricating the polymeric nanofibrous structures. A focusing 2.16 MHz ultrasonic transducer generates an ultrasonic fountain on top of a bath of polyethylene oxide (PEO, Mw 900 kDa, 4 wt-% dissolved in ion exchanged water). This fountain acts as the base for the electric field induced Taylor cone, from where the nanofiber is spun (***Figure 1***). An arbitrary waveform generator (Agilent 33120A) drove a power amplifier (Kalmus Model 121C) that transmitted the signal to the transducer. The humidity of the climate chamber, encasing the setup, was kept at 4-5% with dehumidifier. A waveform generator integrated in the USES system was programmed by using NI Labview NXG 4.0 software. Scanning electron microscopy (SEM) was used for investigating the fiber size and the separate fibrous layers of the nanomats.

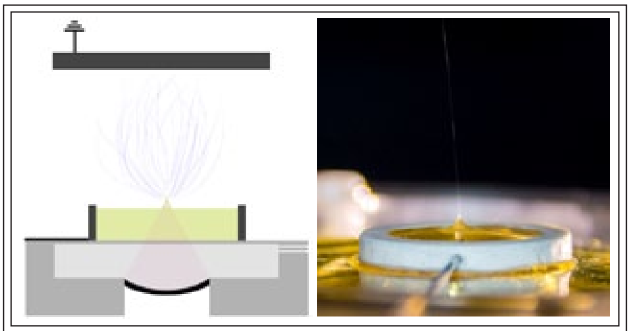
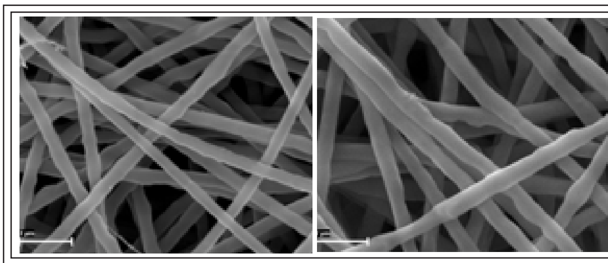


Figure 1 *Needleless ultrasound-enhanced electrospinning (USES): (A) Schematic and (B) ultrasonic fountain and nanofiber formation.*

3. Results

We were able to continuously adjust the US settings in a signal generator by using an automated program (NI Labview NXG 4.0 software, and consequently, to generate nanofibrous mats with a nanofiber thickness gradient. The USES system ena-



Scale bars in SEM images are 2 µm.
Figure 2 *SEM images (A – At the start of the process, B – final layer on the nanofibrous mat) of USES layered continuous nanofibrous mat.*

Table 1 *Ultrasonic parameters of the signal generator at the time of taking a fiber sample and respective nanofiber diameters*

	Process parameters		Nanofiber properties		
Sample testing phase (layer)	**Amplitude (mV_{p-p})**	**Burst count (cycles)**	**Average diameter (±SD) (nm)**	**Minimum (nm)**	**Maximum (nm)**
Base-layer of the nano-fibrous mat	200	950	493.8 (± 44.4)	397.0	681.6
Middle-layer of the nano-fibrous mat	443	516	573.2 (± 61.7)	461.2	788.8
Top-layer of the nano-fibrous mat	600	100	603.5 (± 66.5)	420.2	796.7

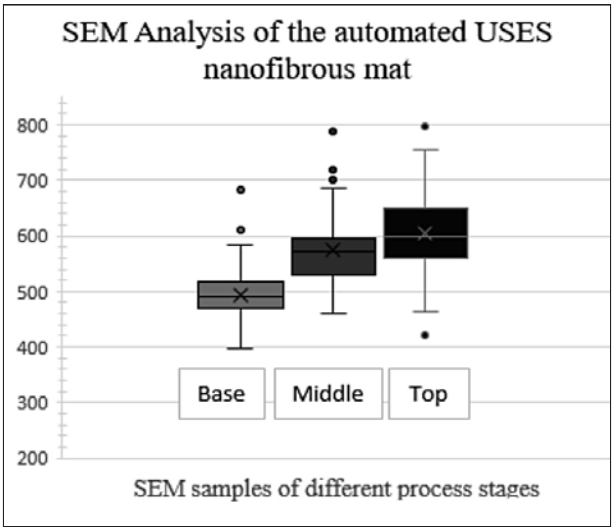


Figure 3 *The gradient change in the fiber size on the course of the USES process obtained by using an automated continuos adjustment of US settings. The SEM fiber size was measured in three different sampling layers (base, middle and top)*

bled to form such nanofibrous gradient layers in a continuous manner. The SEM micrographs on the nanofibrous layers showed the difference of approximately 100 nm on average size of the fibers on the course of an USES process (***Figure 2***). To our best knowledge, this the first time ever to successfully generate a gradient structure of the nanofibers in a nozzle-free ES process.

Table 1 summarizes the US parameters of a signal generator used in fabricating the multi-layered nanofibrous gradient structures and the average fiber size (diameter) of the nanofibers in the three different layers tested. ***Figure 4*** illustrates the increasing trend of the fiber diameters in three different layers studied (base, middle and top). The samples of the nanofibers were taken for the SEM analysis during the entire process.

As seen in ***Figure 3***, the size of the nanofibers was gradually increased from the base layer to the top layer. The nanofibrous layer in the middle of the nanomat consisted of the nanofibers, which were larger in size (diameter) compared to those in a base layer but smaller in diameter compared to those generated in a top layer (***Figure 3***). When generating the US signal, the signal amplitude (peak to peak) was increased after every 1 second over a 5-hour period and burst count (cycles) was decreased over the same time period.

4. Conclusions

In this study, we further developed an ultrasound-enhanced electrospinning (USES) system for generating novel polymeric nanofibrous structures for pharmaceutical and biomedical applications. Automation of the continuous change of US signal parameter in an USES process is possible with the aid of a NI Labview NXG 4.0 software. Automated programming assisted USES allows us to fabricate advanced nanofibrous structures with gradually growing nanofiber thickness (i.e., gradient structures) through a nanofibrous mat.

5. Acknowledgements

This study is funded by the Estonian national research projects IUT34-18 and PUT 1088, and by the Business Finland, L`ORÉAL Baltic “For Women in Science” 2018 (K. Kogermann).

References

1. *A. Repanas, S. Andriopoulou, B. Glasmacher, J. Drug Delivery Sci. Technol. 31, 137 (2016).*
2. *H. Nieminen, I. Laidmäe, A. Salmi, T. Rauhala, T. Paulin, J. Heinämäki, E. Hæggström, A Nature Res. Journal, Scientific Reports 8, Article 4437 (2018).*