

# Designing biopolymer scaffolds and oral mucoadhesive films for controlled drug delivery

Petar Uskoković<sup>1</sup>, Anđela Radisavljević<sup>2</sup>, Marija Jovanović<sup>1</sup>, Dušica Stojanović<sup>1,\*</sup> and Vesna Radojević<sup>1</sup>

<sup>1</sup>University of Belgrade, Faculty of Technology and Metallurgy, Karnegijeva 4, 11120 Belgrade, Serbia University of Belgrade

<sup>2</sup>University of Belgrade, Innovation Centre of the Faculty of Technology and Metallurgy, Karnegijeva 4, 11120 Belgrade, Serbia

Keywords: Electrospinning; 3D-printing; buccal films; tissue engineering

Hem. Ind. 78(15) 24 (2024)

Available on-line at the Journal web address: <http://www.ache.org.rs/HI/>

**INTRODUCTION:** There is a great potential to use electrospun nanofibers and 3D-printed structures as drug carriers for biomedical applications, due to the possibility of delivering drugs at a controlled rate over some time at the site of action.

**EXPERIMENTAL:** Poly( $\epsilon$ -caprolactone) (PCL), polyvinylpyrrolidone (PVP), gelatin (GE), and organic solvents were supplied by Sigma-Aldrich. The antibiotic Cefazolin and the waste yarrow were received from Pharmanova and the Institute of Medicinal Plant Research "Dr Josif Pančić," Belgrade, Serbia, respectively. Propranolol hydrochloride (PRH) and Ibuprofen (IBU) were obtained from Galenika a.d., Belgrade, Serbia while alendronate sodium trihydrate (ALN) was provided from Hemofarm. A.D. Vrsac, Belgrade. Cefazolin or yarrow-loaded PCL nanofiber mats (PCL/CEF and PCL/YAR, respectively) were produced from PCL solutions by using the blend electrospinning method (vertical electrospinning setup CH-01, Linari Engineering, Italy) [1,2]. Commercially available silicone and rubber urinary catheters were coated with the nanofiber mats by using adhesive n-butyl-2-cyanoacrylate. Semi-solid extrusion 3D printer (Ultimaker 2+ (Ultimaker B.V., Utrecht, Netherlands) was used to obtain gelatin-based mucoadhesive films and scaffolds using PRH, ALN, and IBU as model drugs [3,4].

**RESULTS AND DISCUSSION:** Under the conditions that simulate catheterization *in-vitro*, it has been shown that coated catheters can prevent bacterial growth and the formation of biofilm, which is a source of infection in real conditions. Yarrow powder and cefazolin retained their biological activity during the fabrication process, as confirmed by the antioxidant and antibacterial activity of these nanofiber scaffolds. Both in vitro release studies and in silico simulations indicated that processed oral films could provide effective drug transport through the buccal mucosa. Gelatin-based scaffold with IBU, enabling a synergic effect of tissue regeneration and controlled drug delivery.

**CONCLUSIONS:** The newly developed biomaterials show high potential for further practical utilization in biomedicine. PCL nanofiber mats with CEF or YAR could be used as a relevant drug scaffold with pronounced antibacterial activity, while 3D-printed gelatin-based films and scaffolds could be used for buccal applications and osteoporosis treatments.

**Acknowledgements:** This work was supported by the ExcellMater project (European Union's Horizon 2020 No. 952033).

## REFERENCES

- [1] Radisavljevic A, Stojanovic DB, Perisic S, Djokic V, Radojevic V, Rajilic-Stojanovic M, Uskokovic PS. Cefazolin-loaded polycaprolactone fibers produced via different electrospinning methods: characterization, drug release and antibacterial effect. Eur. J. Pharm. Sci. 2018;124:26-36. <http://dx.doi.org/10.1016/j.ejps.2018.08.023>
- [2] Radisavljevic A, Stojanovic DB, Petrovic M, Radojevic V, Uskokovic P, Rajilic-Stojanovic M. Electrospun polycaprolactone nanofibers functionalized with Achillea millefolium extract yield biomaterial with antibacterial, antioxidant and improved mechanical properties. J. Biomed. Mater. Res. A 2023;111:962-974. <http://dx.doi.org/10.1002/jbm.a.37481>
- [3] Jovanović, M.; Petrović, M.; Cvijić, S.; Tomić, N.; Stojanović, D.; Ibrić, S.; Uskoković, P. 3D printed buccal films for prolonged-release of propranolol hydrochloride: development, characterization and bioavailability prediction. *Pharmaceutics* 2021, 13, 2143. <https://doi.org/10.3390/pharmaceutics13122143>
- [4] Bojana Obradović, Jasmina Stojkovska, Ivana Banićević, Anđela Radisavljević, Marija Jovanović, Miloš Petrović, Mirjana Rajilić-Stojanović, Petar Uskoković, Dušica Stojanović, Vesna Radojević, The ExcellMater project for advancements in biomaterials and 3D in vitro culture systems for applications in pharmacy and biomedicine. *Maced. Pharm. Bull.*, 69 (Suppl 1) 5 - 6 (2023). doi: 10.33320/maced.pharm.bull.2023.69.03.002.

\*Corresponding author E-mail: [duca@tmf.bg.ac.rs](mailto:duca@tmf.bg.ac.rs)

