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Short communication

The drug incorporation affects the properties of hydrophilic nanofibers

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Introduction

Over the past three decades, nanofibers have gained significant attention in various fields such as tissue regeneration, wound healing, media filtration, and drug delivery (Kocbek, 2012). They are most frequently prepared by electrospinning since it enables the preparation of nanofibers with well-defined morphology in a single step and the continuous production of nanofibers at an industrial scale. The electrospinning process and the resulting nanofibers are affected by several parameters, including solution and process parameters as well as ambient conditions (Pelipenko et al., 2015). Until today the impact of the loaded drug on nanofiber properties has not been systematically investigated, since nanofiber formulation is usually developed for a specific drug. However, the drug substitution in nanofiber formulation may result in changes in drug loading and release kinetics as well as the overall properties of the nanofibers (Kajdič et al., 2019). Therefore, the objective of this study was to investigate the influence of different drugs (ibuprofen, carvedilol, paracetamol, and metformin hydrochloride) on the properties of hydrophilic nanofibers composed of polyethylene oxide (PEO) and poloxamer 188 (P188) in weight ratio 1:1.

Materials and methods

Ethanol-based polymer solutions were prepared using PEO (1.50%, w/w), poloxamer 188 (P188; 1.50%, w/w), and the selected drug (0.75%, w/w), namely ibuprofen (Formulation IBU), carvedilol (Formulation CAR), paracetamol (Formulation PAR), or metformin hydrochloride (Formulation MET). As a reference formulation, polymer nanofiber without drug were prepared (Formulation 0). The electrical conductivity and rheological properties of polymer solutions were determined and then the solutions were electrospun at room temperature for ~2 h using a Spinbox Systems® electrospinning device (Bioinicia; Valencia, Spain) at a high voltage of 15 kV, a needle-to-collector distance of 15 cm, a flow rate of 1.77 mL/h, and relative humidity < 45%. The obtained nanofibers were stored in a desiccator for at least 12 h before further analysis. The morphology (scanning electron microscopy, SEM), potential chemical interactions between components (Fourier transform infrared spectroscopy, FT-IR spectroscopy), surface hydrophobicity (contact angle measurement), residual moisture content, and moisture sorption ability (thermogravimetric analysis, TGA), dispersibility (visual inspection), drug content and *in-vitro* drug release from nanofibers were evaluated.

Results and discussion

All polymer solutions demonstrated typical viscoelastic Newtonian behavior, with dynamic viscosity independent of shear rate. The incorporation of carvedilol, paracetamol, or metformin hydrochloride into the polymer solution did not significantly alter its dynamic viscosity (Table 1).

However, the addition of ibuprofen resulted in a slight decrease in dynamic viscosity. The electrical conductivities of all investigated polymer solutions with the drug were low, except the polymer solution with metformin hydrochloride (Table 1).

The drug incorporation affected the morphology and diameter of the nanofibers (Fig. 1, Table 2). Additionally, the surface hydrophobicity of the nanofibers was influenced by the incorporated drug. The hydrophilic

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drugs, paracetamol, and metformin hydrochloride, resulted in decreased surface hydrophobicity compared to nanofibers without incorporated drug. In contrast, the more hydrophobic drugs, ibuprofen and carvedilol, did not significantly alter the surface hydrophobicity compared to the nanofibers without the incorporated drug.

Table 1. Dynamic viscosities and conductivities of polymer solutions for electrospinning at 25 °C.

	Dynamic viscosity [mPas]	Electrical conductivity [µS/cm]
Formulation 0	26.8 ± 0.6	2.45 ± 0.43
Formulation IBU	25.0 ± 0.2	1.53 ± 0.02
Formulation CAR	27.0 ± 0.2	2.66 ± 0.23
Formulation PAR	27.0 ± 0.2	1.66 ± 0.04
Formulation MET	26.1 ± 0.2	687.10 ± 12.60

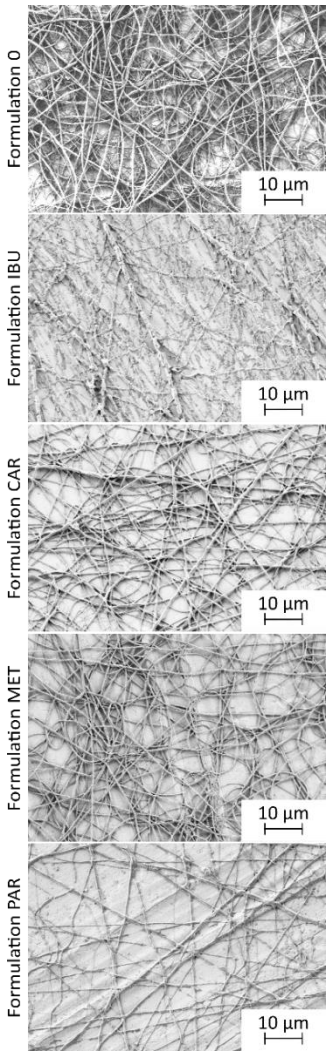

Fig. 1. Representative SEM images of nanofibers for all investigated formulations.

The residual moisture content in all electrospun nanofibers was below the limit of detection, indicating their dry state. FT-IR analysis revealed the formation of hydrogen bonds between the hydroxyl group of hydrogen bond donors (ibuprofen, carvedilol, and paracetamol) and the hydrogen bond acceptors (PEO and P188) in the nanofibers. However, no significant shifts of characteristic peaks were observed in the case of metformin hydrochloride-loaded nanofibers.

Table 2. The average nanofiber diameter, as determined from SEM images.

	Average nanofiber diameter [nm]
Formulation 0	252 ± 121
Formulation IBU	517 ± 180
Formulation CAR	290 ± 130
Formulation PAR	421 ± 195
Formulation MET	314 ± 86

The determined drug content in nanofibers was comparable to theoretical (20% (w/w)), indicating ~100% entrapment efficiency. *In-vitro* drug release studies demonstrated immediate drug release from all nanofibers, which is in line with the fast dispersibility of the prepared nanofibers. However, CAR was released slightly slower compared to other investigated drugs.

Conclusion

We showed that the drug importantly affects the properties of polymer solution for electrospinning as well as the properties of electrospun nanofibers. Thus, these findings underscore the importance of considering drug properties during the design of hydrophilic nanofibers for drug delivery.

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