IECP 2020
The 1st International Electronic Conference on Pharmaceutics
01–15 DECEMBER 2020 | ONLINE
Chaired by DR. ANDREA ERXLEBEN and PROF. DR. ELISABETTA GAVINI
pharmaceutics
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High-throughput electrospinning of bioactive scaffolds for bone regeneration

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Abstract: Among the most promising technologies for sustained drug delivery systems are core-shell nanofibres prepared by electrospinning. However, the most common method for production of those, coaxial electrospinning, suffers from extremely low flow-rates limiting the practical applications of such fibres. Emulsion electrospinning, on the other hand, enables the use of the high-throughput needle-less electrospinning devices for the production of the core-shell nanofibres with active pharmaceutical ingredients embedded and protected in their core. Development of such drug delivery systems for the applications in bone regeneration are further challenged by the need of the inorganic additives meant to stimulate the regeneration of the bone. The main objective of this work is to develop a high-throughput electrospinning method for production of hybrid (organic-inorganic) and bioactive scaffolds needed for bone regeneration. We demonstrate the importance of the formulation, e.g. presence of surfactants, on the stability of the emulsion and thus electrospinning. Our work is an important step forward towards high-throughput production of complex multi-material scaffolds for sustained drug delivery.

Keywords: High-throughput electrospinning; bioactive scaffolds; emulsion stability, emulsion electrosinning; core-shell nanofibres, drug release.

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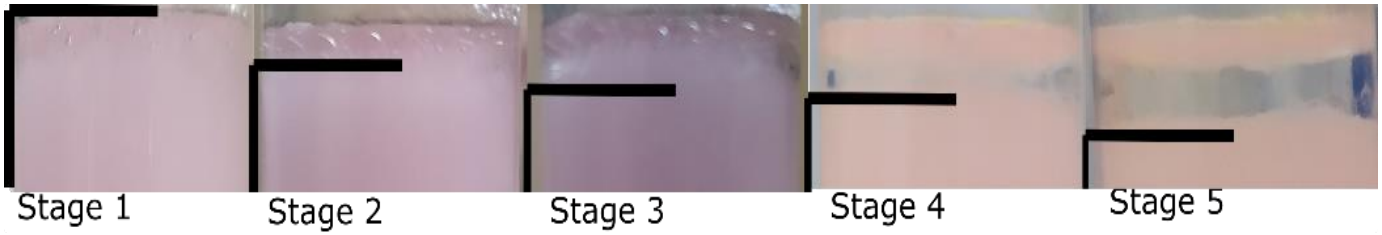
Methods

Preparation sequence of the emulsions

- 5ml of water phase (mixture of PF68, PVA, and protein or fluorophores)
- 10.5 ml of chloroform (+P31R1 when needed).
- premixed by hand.
- 5 ml PCL stock solution
- homogenization for 2 min at 6600 rpm using IKA T-18 Digital ULTRA TURRAX.
- remaining amount of PCL stock
- 5 ml of ethanol with manual mixing for approximately 2 minutes.

Evaluation of the stability of the emulsions



1. Completely stable emulsion, no signs of separation;
2. First slightly distinguishable changes/ water phase-related bubbles start to appear;
3. Start of visible separation/big-sized bubbles;
4. Circumferential separation with still slightly stable central part;
5. Completely separated into two clearly distinguishable water, oil phase layers.

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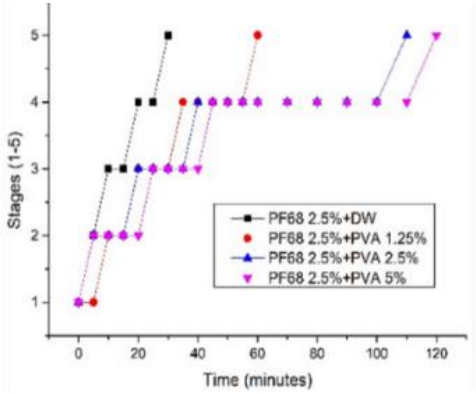
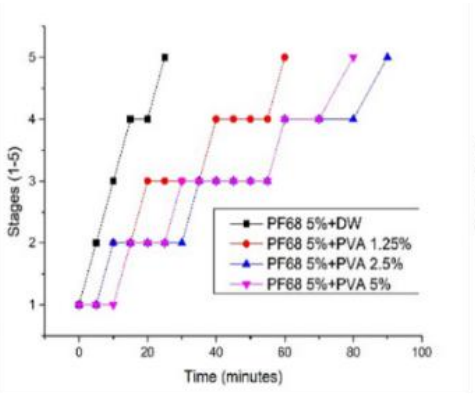
Results

Recordings of the stability of the emulsions

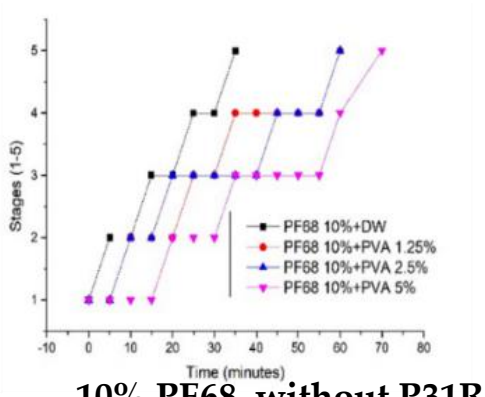
2.5% PF68, with P31R1



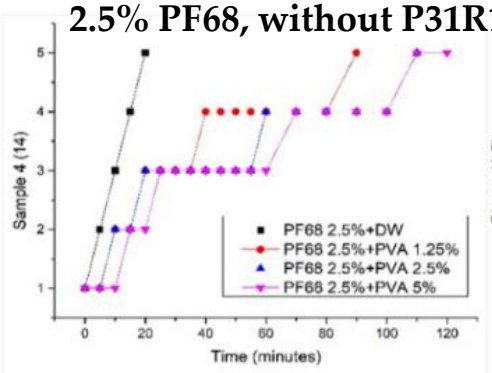
5% PF68, with P31R1



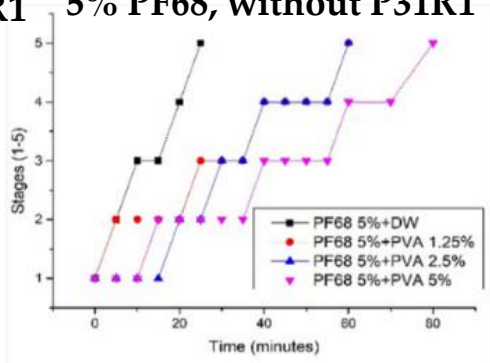
10% PF68, with P31R1



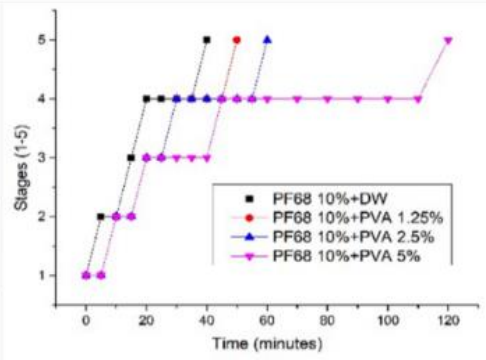
2.5% PF68, without P31R1



5% PF68, without P31R1



10% PF68, without P31R1



Stability of the emulsion notably increased when both polymers were used together. Presence of the P31R1 seems to improve the stability of the emulsion, however, only in the presence of other surfactants (PF68 and PVA).

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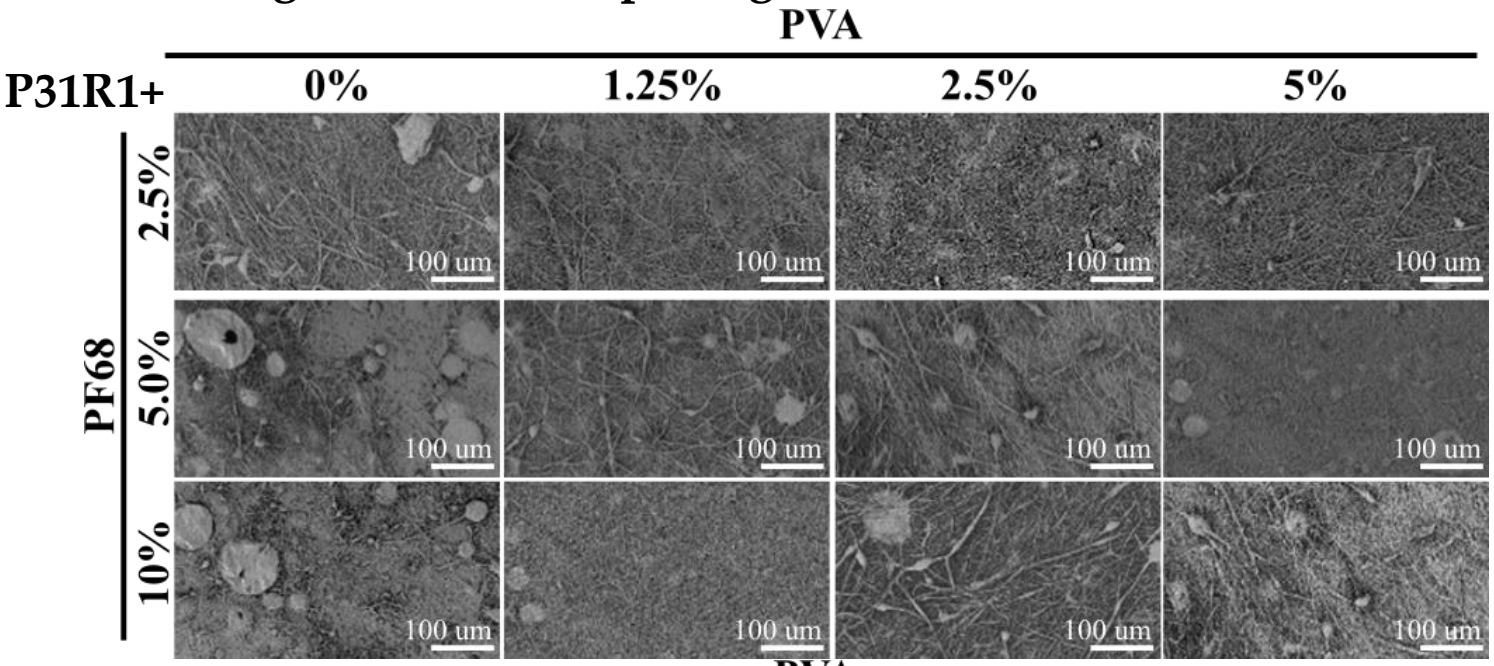
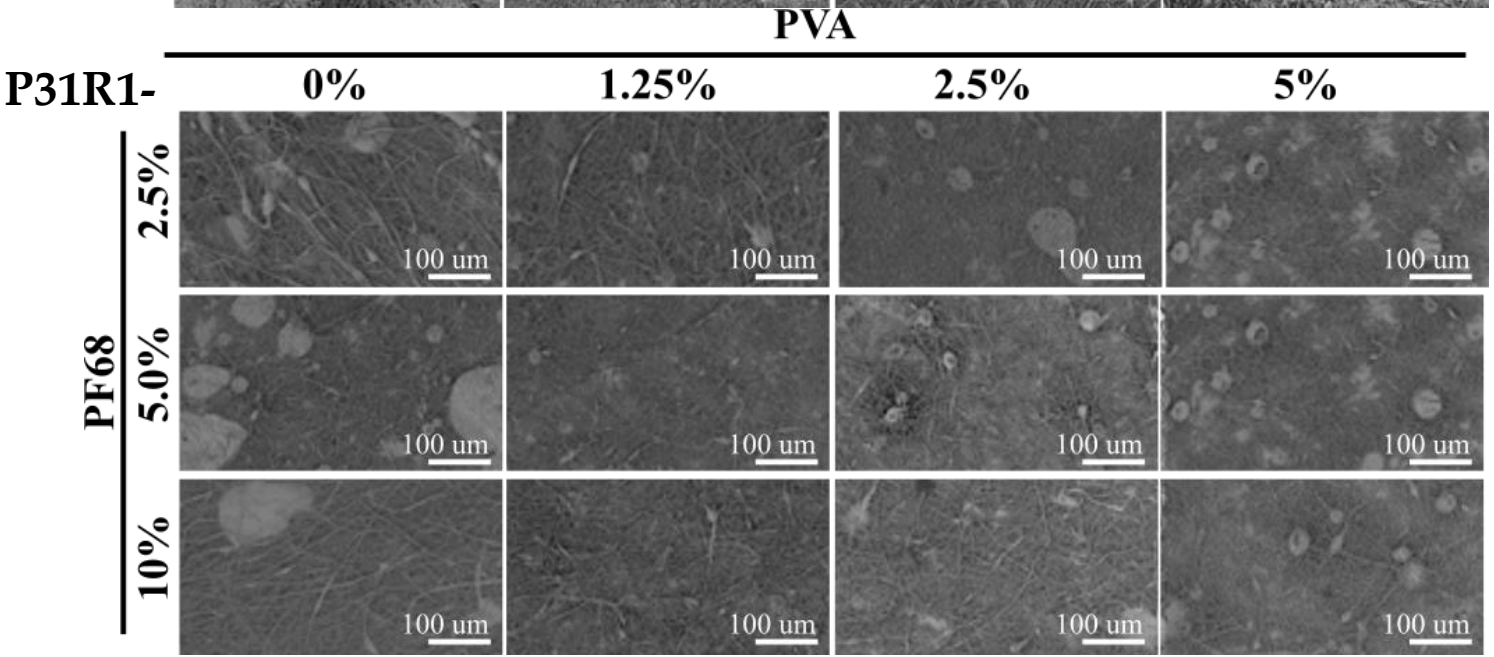
Results

SEM images of fibre morphologies





- The best electrospinning results- P31R1 + and low amounts of PF68.
- For all PVA concentrations nearly no large defects.
- Improvement in fibre morphology with PVA presence, but not concentration increase.

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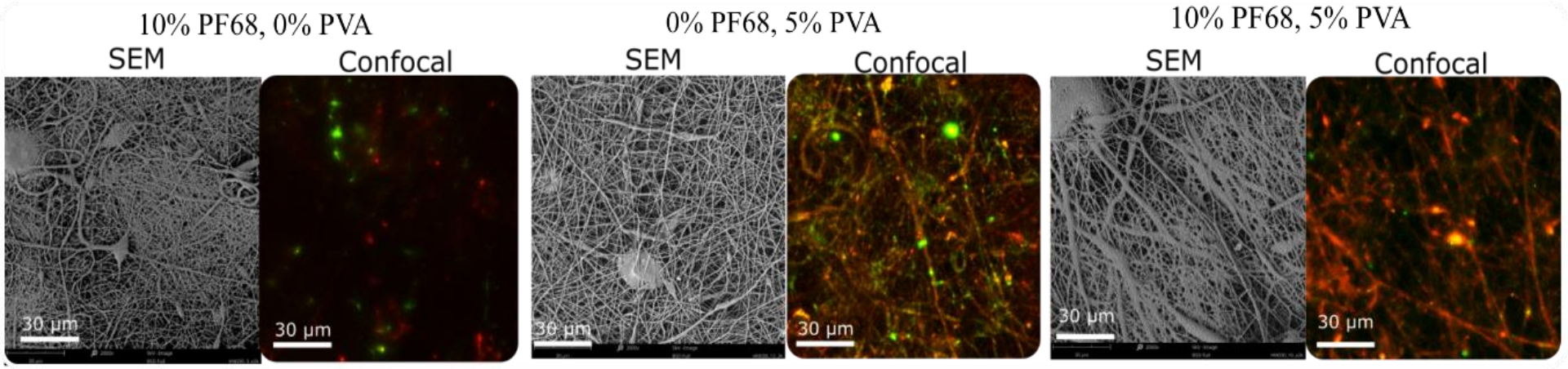
Results

Comparison of SEM and confocal images



- PF68 only: separated instances of fluorophores are seen.
- PVA only: continuous core structure + traces of both fluorescent dyes possibly due to insufficient water phase mixing
- PF68 & PVA: continuous core

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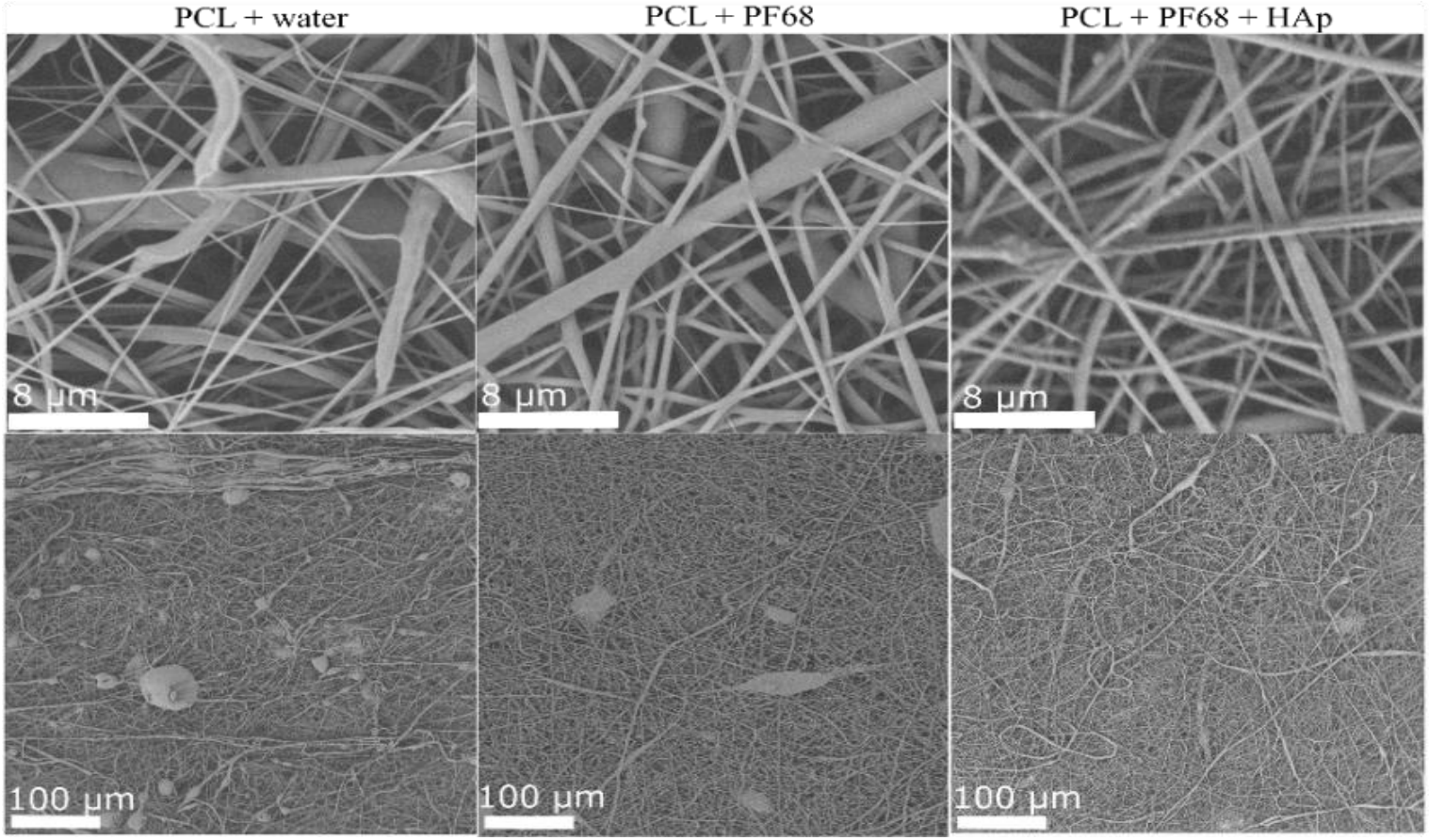
Results

Comparison between 3 compositions



Fibres made with HAp appear to be more rough, clusters of HAp can also be observed showing that HAp was successfully incorporated. Moreover, the improvement in morphology is clearly visible in from PCL+water to PCL+PF68+HAp, where the best morphology was obtained with incorporated HAp.

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Conclusions

- Emulsions with surfactant combinations and defined stabilities made for high-throughput electrospinning.
- Presence of PVA (but not concentration increase) in the water phase improves the stability and quality of obtained fibres.
- Emulsion stability is not necessarily correlated with morphology fibres.
- Proved possibility of protein encapsulation.

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Acknowledgments

This work was supported by European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreements No. 823981 (actiTOX) and No. 824007 (iP-Osteo). H.N. has received support from the Erasmus+ traineeship programme for the research activities at InoCure s.r.o.

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