

Ciências Farmacêuticas

X Congresso Iberoamericano



**Abrindo
Fronteiras**

**Abriendo
Fronteras**

**Opening
Borders**

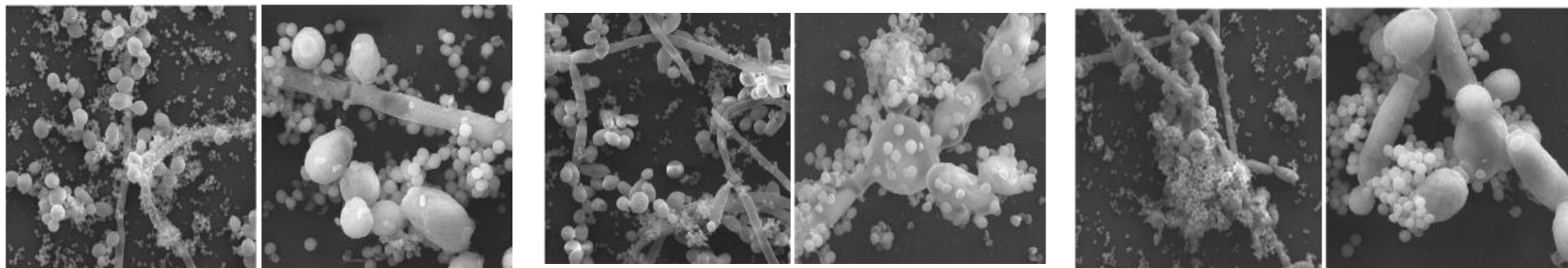
Poly(D,L-lactic acid) scaffolds as an innovative approach to the treatment of mixed *S. aureus*-*C. albicans* biofilms

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(a) iMed.Ulisboa (b) H&TRC (c) i3S (d) INEB (e) CQE (f) CDP2T (g) FEUP/DEMM

Problem

- ❖ Bone infections associated with polymicrobial biofilm formation
- ❖ Mixed bacterial-fungal biofilm infection
- ❖ *Staphylococcus aureus* and *Candida albicans* most described microbials



***S. aureus* – *C. albicans* mixed biofilm morphology and structure during 72 h of incubation.**

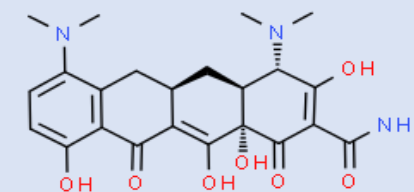
Zegre et al (2022) *Int J Pharm*

Willems et al (2016) *Curr Oral Heal Reports*

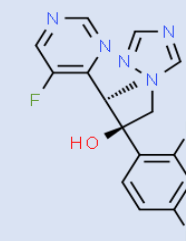
Strategy

- ❖ Local drug delivery scaffolds
- ❖ Development of poly-DL-lactic acid (PDLLA) scaffolds
- ❖ Co-delivery of antibacterial and antifungal drugs
- ❖ Minocycline and voriconazole as model drugs

Model drugs



Minocycline

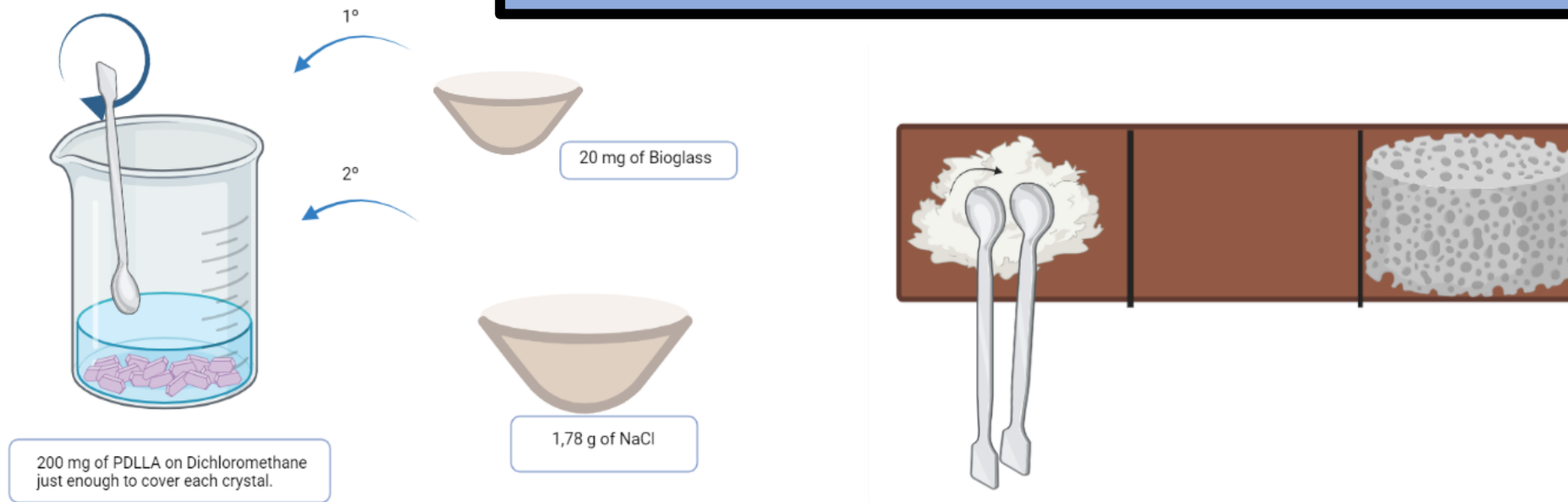


Voriconazole

Zegre et al (2022) *Int J Pharm*

Methods

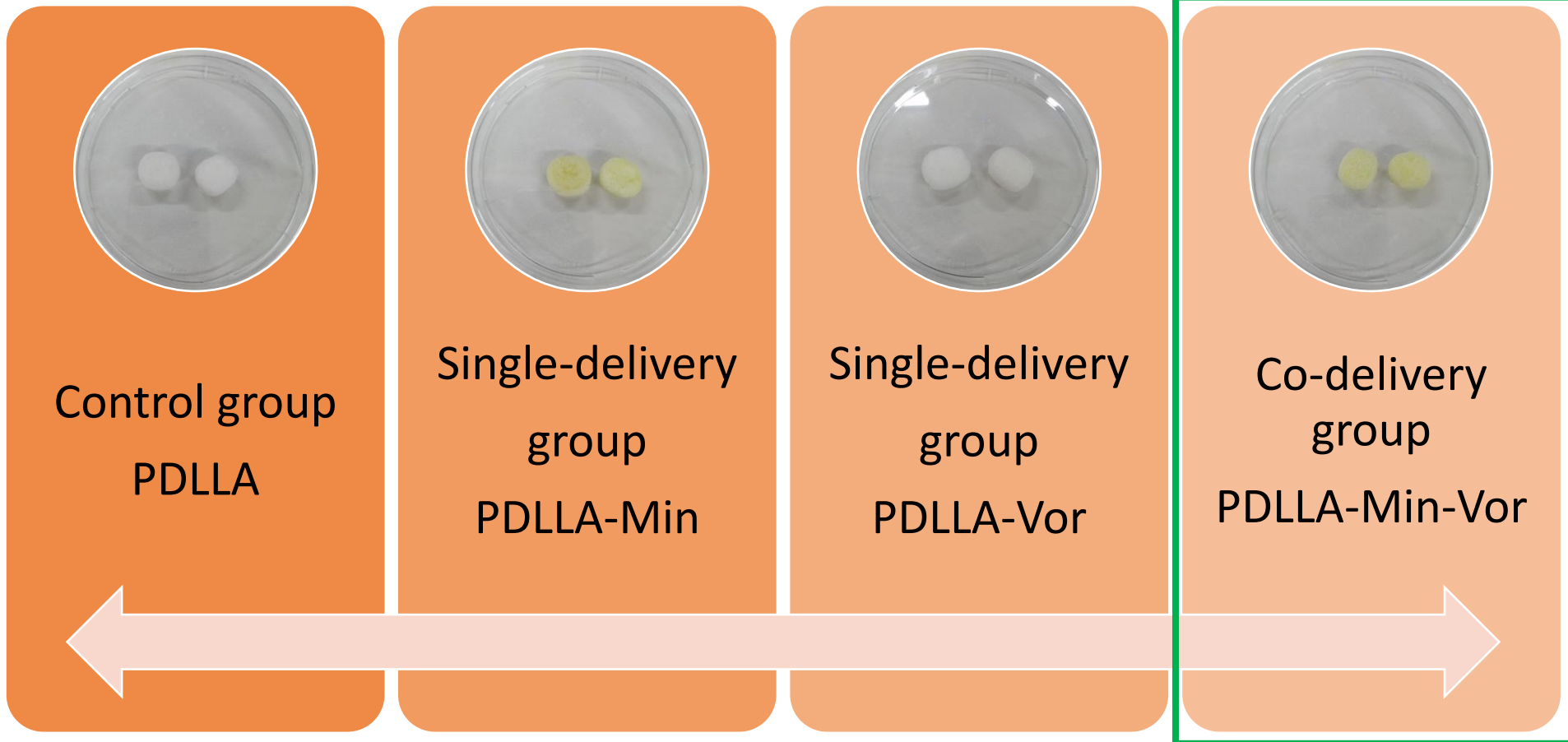
- ❖ Solvent casting/particulate leaching method
- ❖ Bioglass (osteoinductive) and NaCl (porogen)



PDLLA scaffolds preparation by solvent casting/particulate leaching method

Martin et al (2019) IEEE 6th Portuguese Meeting on Bioengineering

Methods



Different groups of scaffolds studied

Zegre et al (2022) Int J Pharm

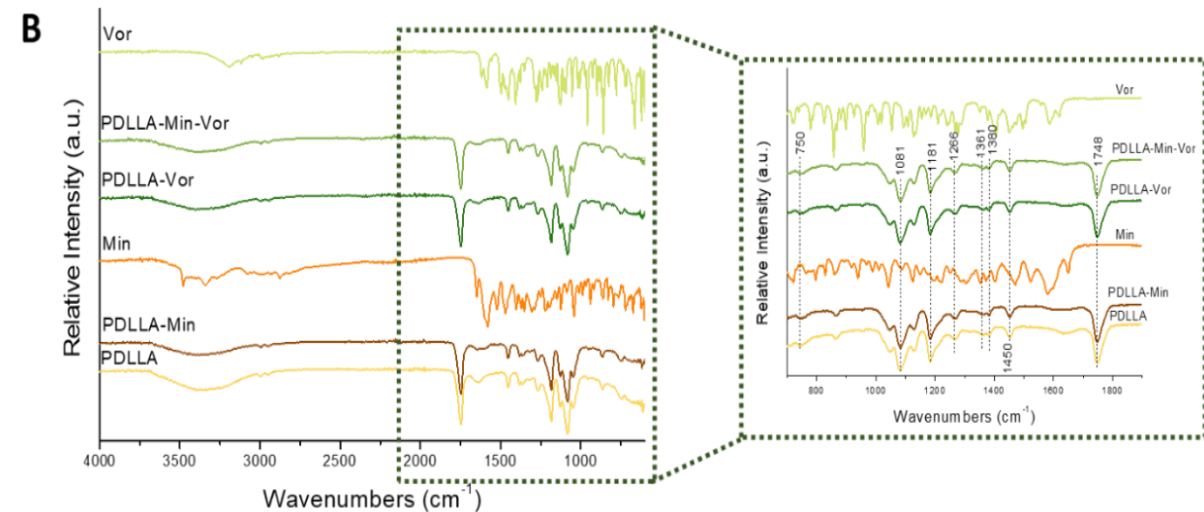
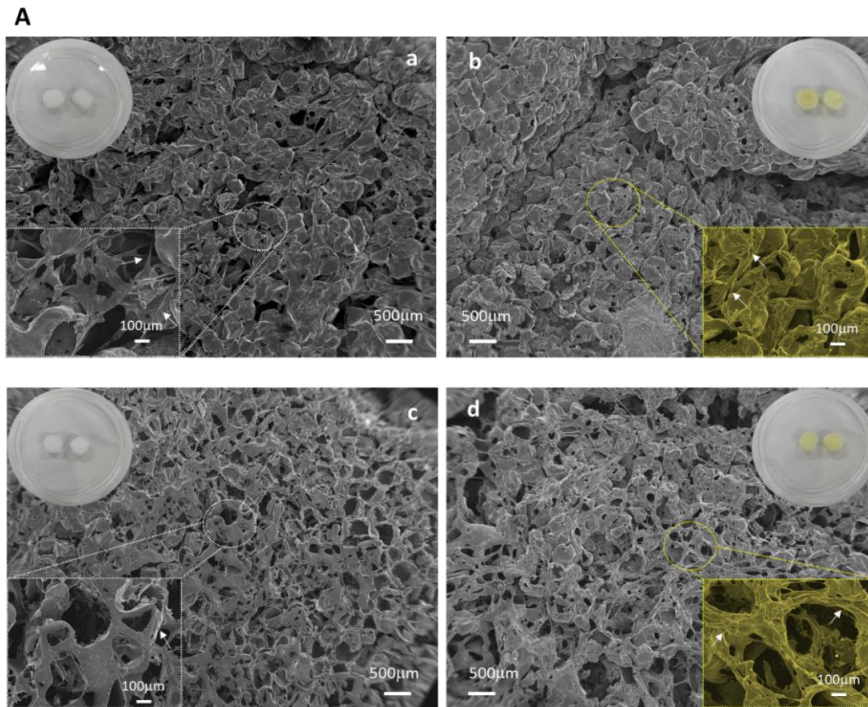
Methods

- ❖ Scaffolds characterization
 - ✓ Physical-chemical characterization (FEG-SEM*)
 - ✓ Chemical composition (FTIR-ATR**)
 - ✓ Drug loading and release studies
- ❖ Biofilm formation assays
- ❖ Cytocompatibility and functional activity testing

*FEG-SEM, field emission gun scanning electron microscopy **FTIR-ATR, *Fourier* transform infrared spectroscopy-attenuated total reflection

Zegre et al (2022) Int J Pharm

Results and Discussion – Scaffolds characterization

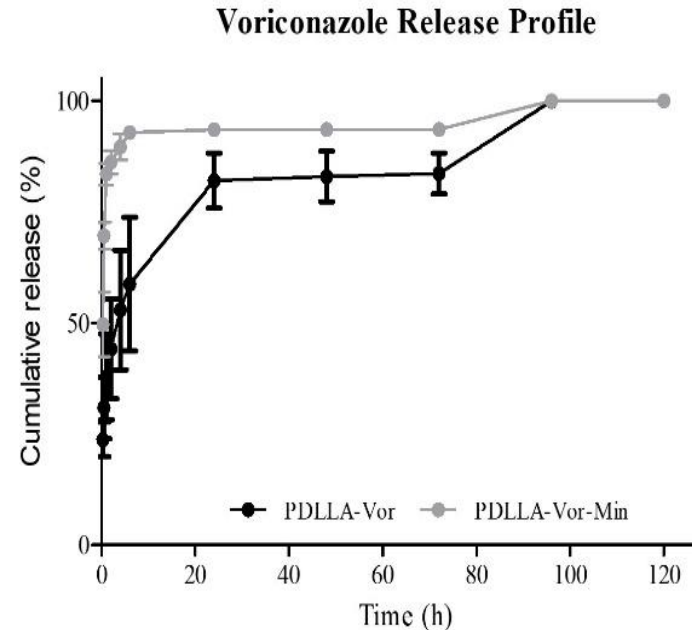
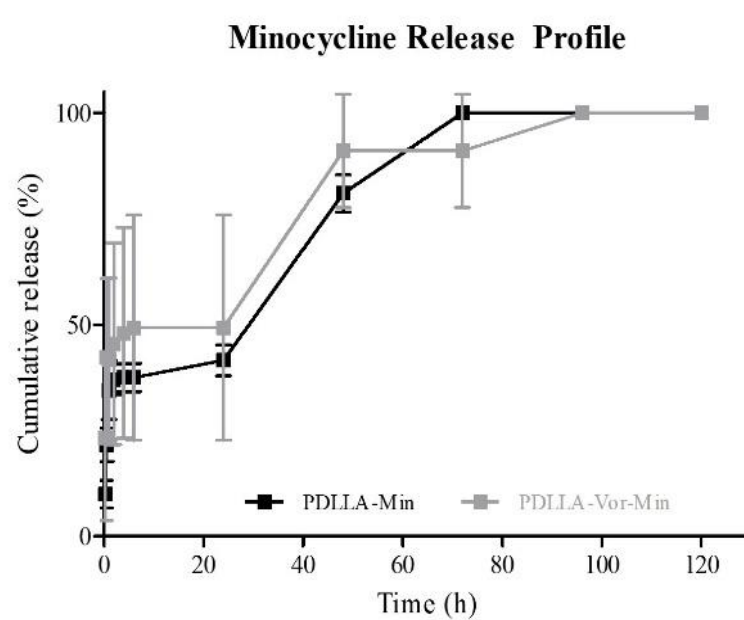


A - Representative optical images and SEM micrographs B – FTIR-ATR

❖ Physicochemical (pore architecture, surface) properties suitable for localized antimicrobial release

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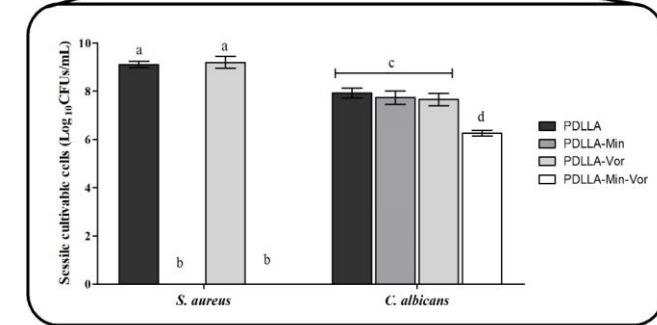
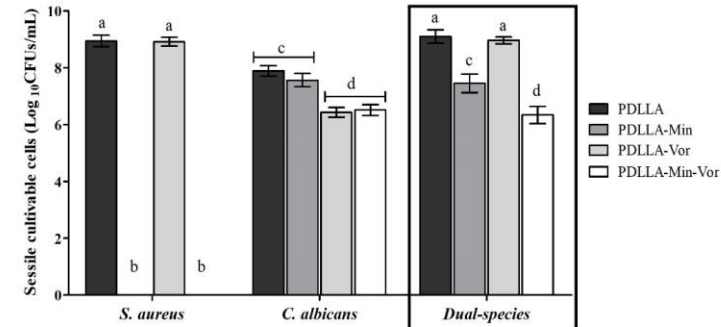
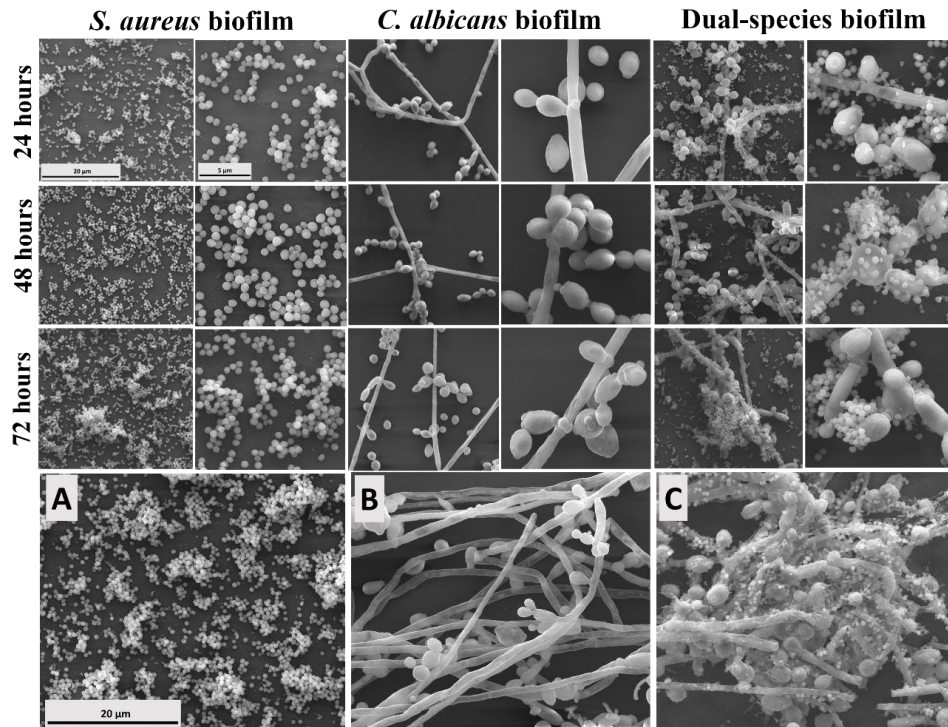
Results and Discussion – Release studies



Release studies and comparison of release profiles (single and co-delivery)

❖ “Burst phase” | Significant amount of drug released in the first 24 h (impact in infection control)

Results and Discussion – Biofilm formation assays



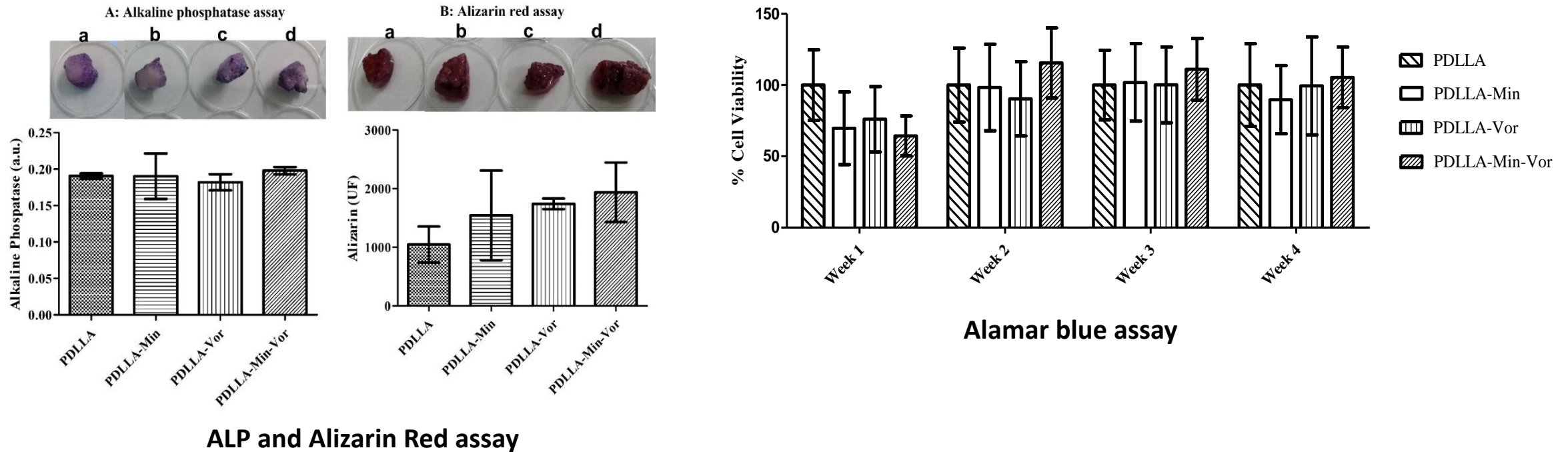
Scaffolds effect on mature biofilms – direct contact

Single and dual-species biofilm morphology and structure

❖ Synergistic relationship for biofilm formation | Promising antibiofilm activity results

Zegre et al (2022) Int J Pharm

Results and Discussion – Citocompatibility



❖ Released Min and Vor did not cause cytotoxicity and do not affect bone formation *in vitro*!

Conclusion

PDLLA scaffolds administrated locally, may emerge as a promising next generation co-delivery system for dual antimicrobial therapy, associated to *S. aureus* – *C. albicans* mixed bone infections.

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ACKNOWLEDGEMENTS

- H&TRC – Health and Technology Research Center (H&TRC)
- Research Institute for Medicines (iMed.Ulisboa)
- Faculdade de Farmácia da Universidade de Lisboa (FFUL)
- Fundação para a Ciência e a Tecnologia (FCT)

Projects UIDB/04138/2020 and UIDP/04138/2020 (iMed.Ulisboa), UIDB/00100/2020 (CQE), L. Gonçalves

Principal Researcher grant (CEECIND/03143/2017), UIDB/ 05608/2020 and UIDP/05608/2020 (H&TRC)

