Poly(DL-lactic acid) scaffolds adsorbed with minocycline and voriconazole: a new pathway towards infection containment

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Purpose

✱ **Bone infection (osteomyelitis)**

Burden as a clinical complication of orthopaedic surgeries [1]

✱ **Controlled antimicrobial release systems**

Treat and prevent osteomyelitis

✱ **Biomaterials based on porous scaffolds**

Local administration of high concentration of drugs

No systemic toxicity

Extended time

✱ **Scaffolds in bone tissue engineering**

Combination of bioresorbable polymers with bioactive bioglasses

Present biodegradability and biosafety

Suitable microenvironment and structure

Favor osteogenic differentiation and cell growth [2]

✱ **Co-encapsulation of drugs**

Advantageous means for administration of drugs

Novel strategy directed to the co-delivery of two antimicrobials (voriconazole and minocycline)

Methods

➔ Poly(DL-lactic acid) (PDLLA) scaffolds prepared by solvent casting/particulate leaching [2]

➔ Release assays performed with HEPES buffer (37ºC)

➔ Aliquots of the supernatant collected and analyzed in triplicate

➔ Voriconazole quantified by HPLC

➔ Minocycline quantified by UV spectroscopy

➔ Antimicrobial activity against *S. aureus* (ATCC 25923) and *C. albicans* (ATCC 10231) assessed employing the agar diffusion method

➔ Four different groups of scaffolds were developed: PDLLA (without the antimicrobials), MH (with minocycline), Vor (with voriconazole) and MH-Vor (with both antimicrobials)

Acknowledgements

This work was supported by National Funds (Fundação para a Ciência e Tecnologia) through iMed.ULisboa (UIDB/04138/2020, UIDP/04138/2020) and Principal Researcher grant CEECIND/03143/2017 (L.Gonçalves).

References

[1] Matos, et al., *Int J Pharm,* 2015, **485**, 317-328.

[2] Martin, et al, 2019 IEEE 6th Portuguese Meeting on Bioengineering (ENBENG), 2019, 1-4.

[3] C. Vitorino, et al., *J Control Release*, 2013, **167**, 301.

Results

Scanning Electron Microscopy (SEM)

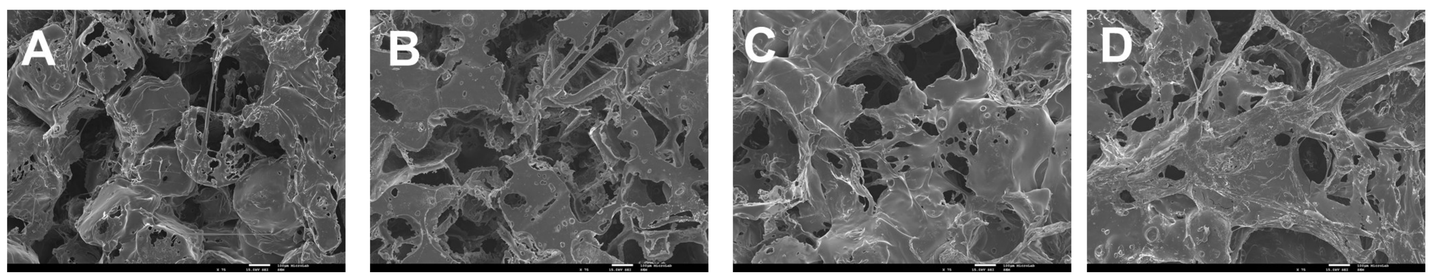

Fig. 1 - SEM analysis, 75 times magnification **A** - PDLLA scaffold **B** - MH scaffold **C** - Vor scaffold **D** - MH-Vor scaffold

- SEM analysis presented a rough and porous surface in all four samples
- Bioglass or salt particles cannot be noticed within the polymer matrix

Adsorption Efficiency and Drug Loading

Table 1 - Scaffolds adsorption efficiency (AE%) and drug loading (DL%)

	MH quantification		Vor quantification	
Scaffold	**AE (%)**	**DL (%)**	**AE (%)**	**DL (%)**
MH	81.788 ± 3.022	0.028 ± 0.009	-	-
Vor	-	-	18.365 ± 21.951	0.006 ± 0.007
MH-Vor	87.997 ± 3.593	0.029 ± 0.004	26.165 ± 2.115	0.009 ± 0.002

FT-IR / ATR analysis

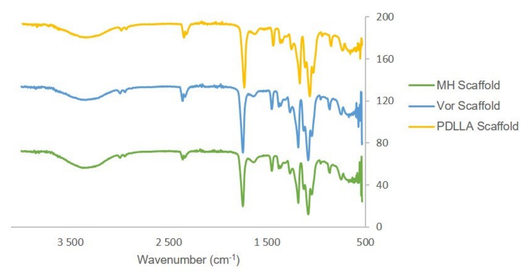

Fig. 2 - FT-IR / ATR spectra regarding PDLLA, MH and Vor scaffolds

- Better AE and DL related to minocycline than related to voriconazole
- MH and Vor inclusion did not change the scaffold composition

In vitro release studies

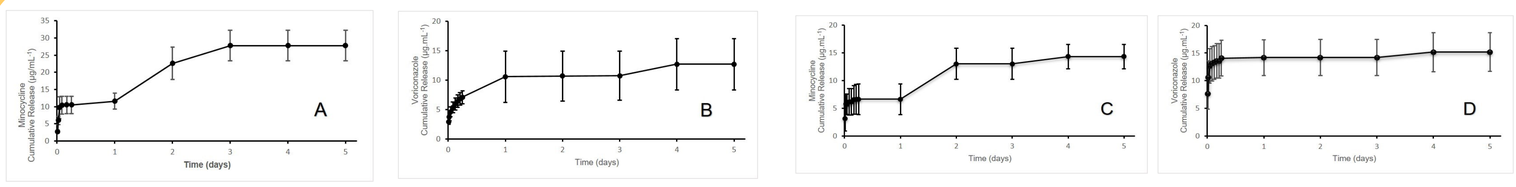

Fig. 3 - Cumulative release profiles of minocycline and voriconazole from MH (A), Vor (B) and MH-Vor scaffolds (C, D) over 5 days. Medium was changed after 72h.

- Both antimicrobials were bounded to the polymer
- Minocycline and voriconazole release is not affected by co-delivery

Antimicrobial activity

has

Table 2 - Results of drug inhibition of growth of *S. aureus* and *C. albicans* assays. Average ± SD

MH - minocycline, Vor - voriconazole, FCZ— fluconazole

		Inhibition zone diameter (mm)				
Organisms		**MH-Vor scaffold**	**MH-Vor disk**	**MH disk**	**Vor disk**	**FCZ disk**
S. aureus	**24 h**	27.5 ± 2.8	34.6 ± 0.7	33.1 ± 1.5	-	-
C. albicans	**24 h**	21.3 ± 2.1	32.6 ± 1.9	15.4 ± 1.5	25.0 ± 4.1	27.1 ± 1.6
	48 h	17.0 ± 2.6	29.4 ± 3.7	-	-	-

- Results propose that the scaffold combining voriconazole and minocycline has activity against both microorganisms

Conclusions

PDLLA scaffolds loaded with minocycline and voriconazole emerge as a promising co-delivery system for local antimicrobial therapy targeting osteomyelitis