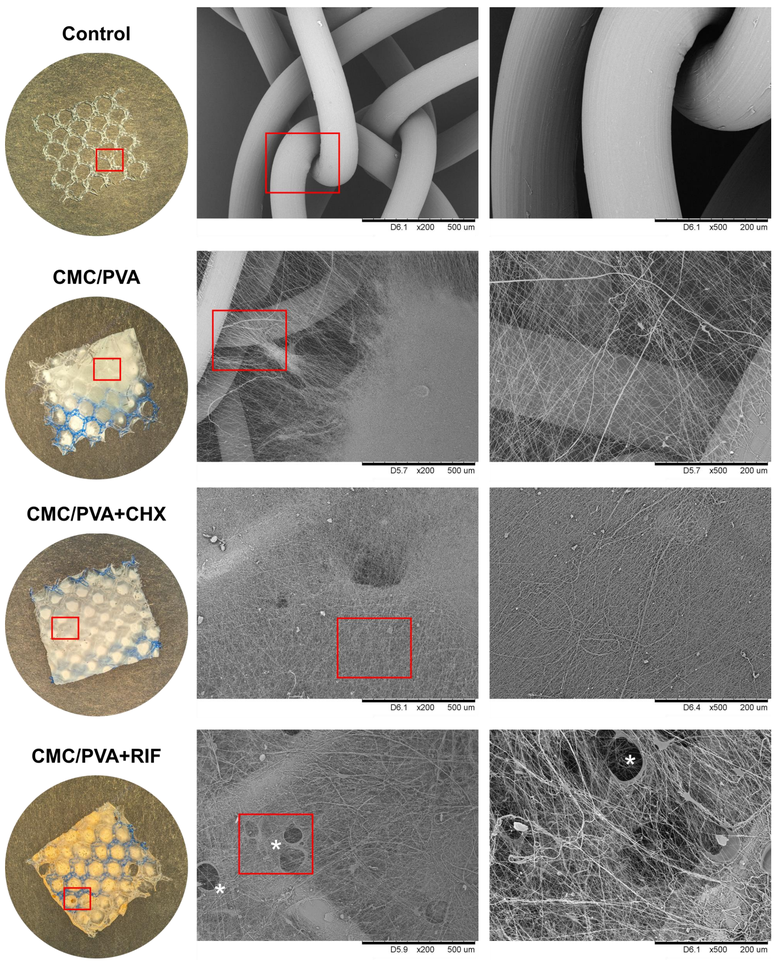
Endowing polypropylene meshes with advanced antibacterial drug-releasing coatings to prevent device-related infections

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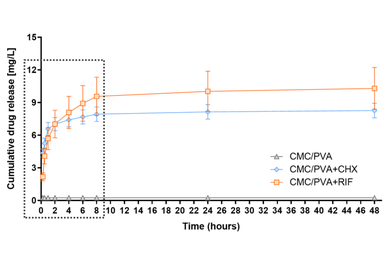
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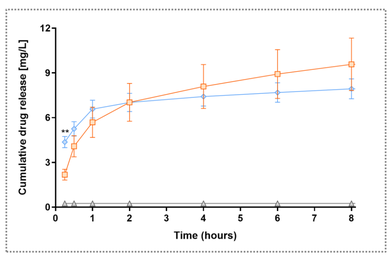
Aim and objective. Postoperative infection remains a major complication in hernia repair, often requiring reintervention and prolonged antibiotic treatment. Functionalizing polypropylene meshes with drug-releasing coatings offers a cutting-edge strategy to deliver antibacterial agents locally while preserving the mechanical performance of the implant. This study evaluates two novel electrospun antibacterial coatings for polypropylene meshes, assessing their performance through *in vitro* and *in vivo* assays.

Materials and methodology. Carboxymethylcellulose/polyvinyl alcohol (CMC/PVA) microfibers (0.5% w/v), loaded with chlorhexidine (CHX) or rifampicin (RIF), were electrospun on both sides of the mesh, establishing four groups: uncoated (control), CMC/PVA, CMC/PVA+CHX, and CMC/PVA+RIF *(Fig. 1)*. *In vitro* assays (mesh size: 1 cm^2) included drug release (high performance liquid chromatography, HPLC), antibacterial activity against *Staphylococcus aureus* (10^6 CFU/mL), and cytotoxicity on rabbit fibroblasts. Preclinical evaluation was conducted in a rabbit model of prosthetic hernia repair under *S. aureus* infection (n=6/group; mesh size: 5x2 cm). Antibacterial performance and biocompatibility were assessed 14 days postoperatively through macroscopic analysis, sonication, histology (hematoxylin-eosin HE; Masson´s trichome MT), light/scanning electron microscopy (SEM), and macrophage immunolabeling (RAM-11).



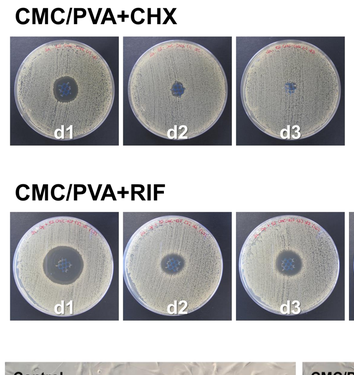
▶***Fig.1.*** *Macroscopic (10x) and SEM (200x, 500x) images of control, CMC/PVA, CMC/PVA+CHX, and CMC/PVA+RIF meshes showing uniform electrospun microfiber distribution and discrete micropores (*) in the antibiotic-loaded coatings.*



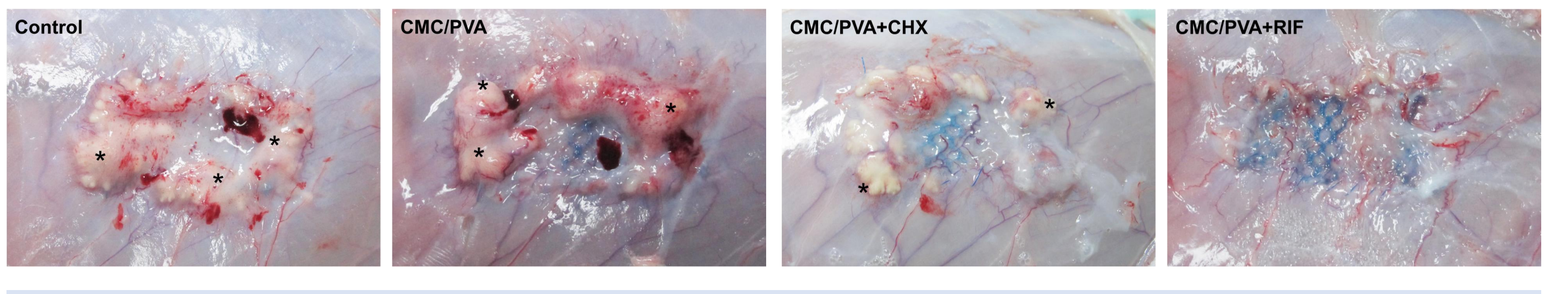


◀***Fig.2.*** *Cumulative release of CHX and RIF measured by HPLC over time (mean ± SEM; n=6). Initial burst release (dashed line box), was significantly higher in CHX at 15 minutes (**p<0.01).*

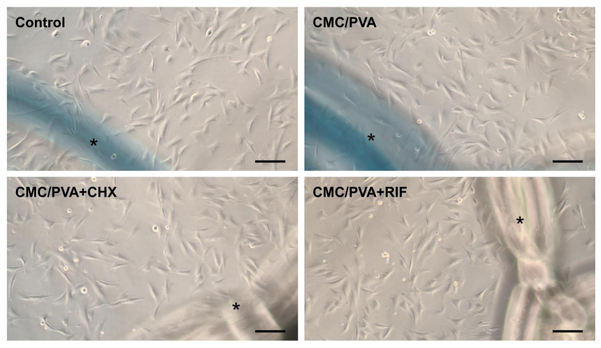
Results. RIF-functionalized meshes showed sustained release *(Fig. 2)*, complete bacterial clearance, and optimal tissue integration without exerting cytotoxicity or excessive inflammation. Contrary, CHX-based coatings exhibited mild cell toxicity (p<0.001) and limited antibacterial efficacy (p<0.05) *(Figs. 3-4)* which was corroborated preclinically by residual infectious niches found in areas of the implants adjacent to sutures *(Fig. 5)*. Regardless of the drug, electrospinning enabled uniform coating deposition and rapid biodegradation without compromising host response *(Figs. 6-8)*.



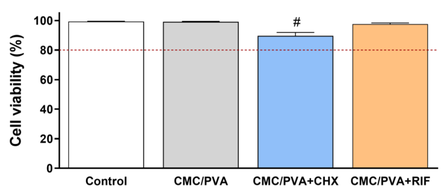
◀▼***Fig.3.*** *Sequential agar diffusion showing inhibition zone diameters over time for CMC/PVA+CHX and CMC/PVA+RIF. Larger halos were recorded in RIF group at days 1 (*p<0.05), 3 (**p<0.01), 4 (p<0.05).*

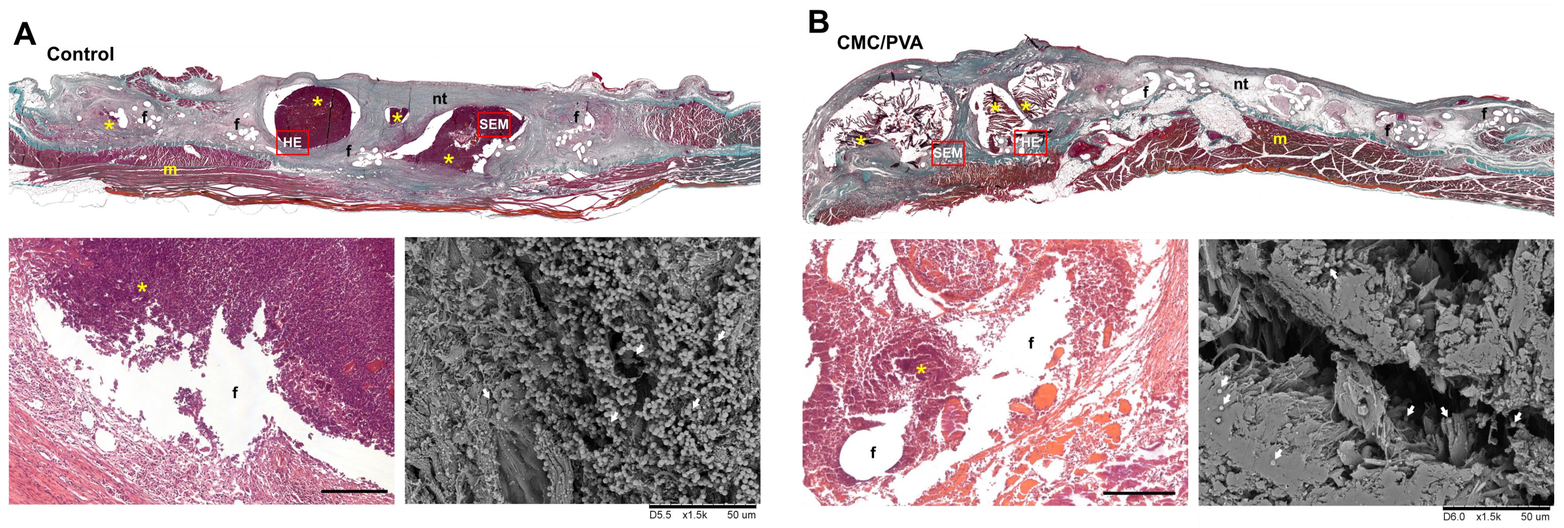


▲***Fig.5.*** *Macroscopic implant area showing abscesses of different sizes (*) developed in control, CMC/PVA, and CMC/PVA+CHX groups, but none in CMC/PVA+RIF. Mild neovascularization was observed near abscesses.*

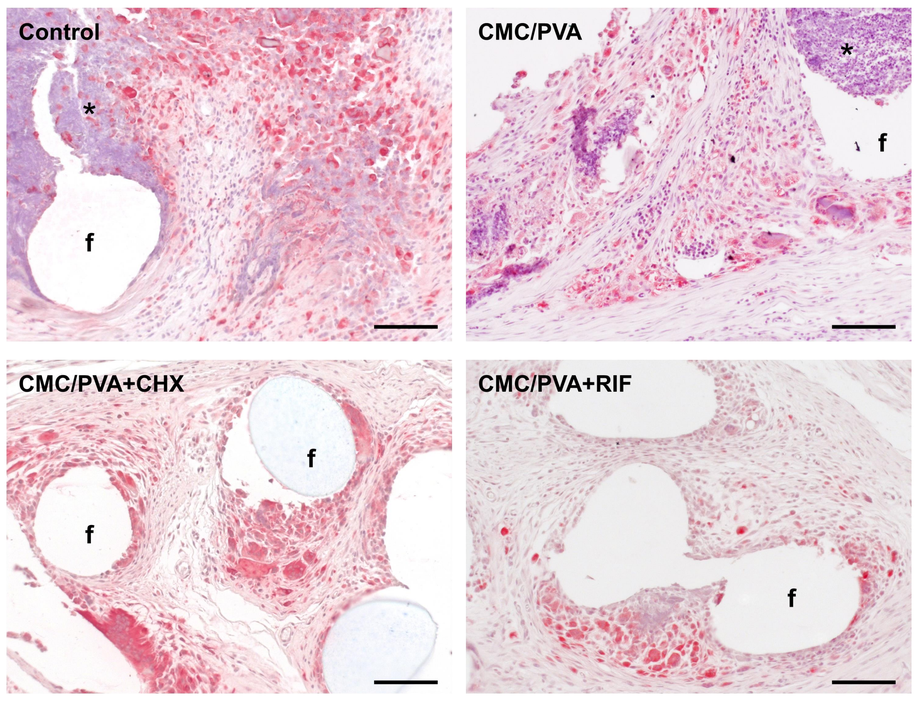


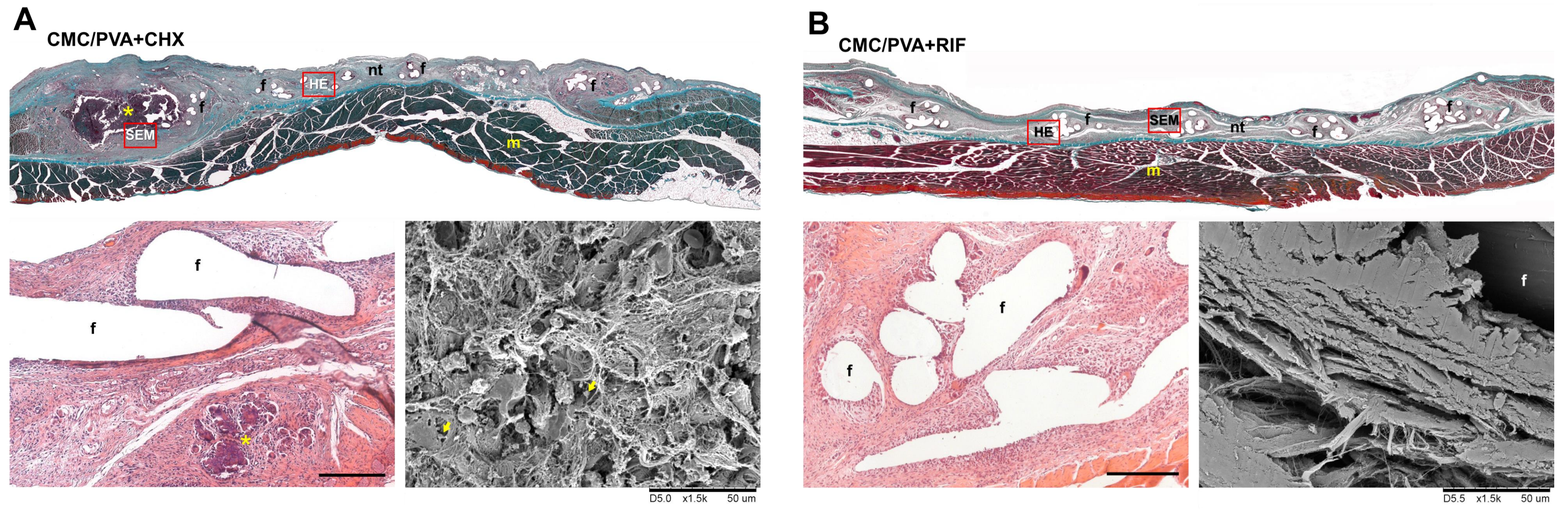
◀***Fig.4.*** *Representative micrographs (100x, scales: 100 µm) of cultured fibroblasts after a 24-hour exposure to uncoated control, CMC/PVA, CMC/PVA+CHX and CMC/PVA+RIF meshes (*). Quantification of the alamarBlue test showed reduced viability in CMC/PVA+CHX compared to the rest of groups (#: ***p<0.001). The toxicity threshold was set at 80% (red dashed line).*



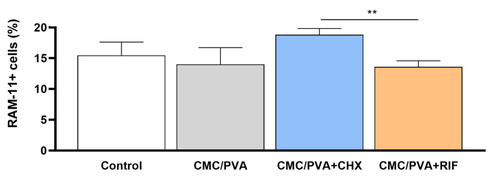


▲***Fig.6.*** *Histological evaluation of **(A)** control and **(B)** CMC/PVA implants. Representative panoramic transversal view of the implants are shown (MT staining, composition pictures taken at 50x. Boxed areas were magnified by light microscopy (HE staining, 100x, scales 200 µm) and SEM (1,500x, scales 50 µm). Legends: neoformed connective tissue (nt), abscesses (*), bacteria (→), mesh filaments (f), abdominal muscle (m).*





▲▶***Fig.8.*** *Immunolabeling of macrophages (200x, scales: 100 µm), and quantification of the percentage RAM-11+ cells per light microscopy field, with significant difference found between CMC/PVA+CHX and CMC/PVA+RIF (**p<0.01).*



▲***Fig.7.*** *Histological evaluation of **(A)** CMC/PVA+CHX and **(B)** CMC/PVA+RIF implants. Representative panoramic transversal view of the implants are shown (MT staining, composition pictures taken at 50x. Boxed areas were magnified by light microscopy (HE staining, 100x, scales 200 µm) and SEM (1,500x, scales 50 µm). Legends: neoformed connective tissue (nt), abscesses (*), bacteria (→), mesh filaments (f), abdominal muscle (m).*

Conclusion. CMC/PVA+RIF coatings provide a robust strategy for infection prevention in hernia repair, outperforming CHX-based formulations and supporting their translational relevance. This electrospun microfiber platform represents a versatile approach to endow polypropylene meshes (and potentially other biomedical implants) with a local, effective antibacterial functionality.

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