Antifungal And Antibacterial Electrospun Wound Dressings For Complex Wounds

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Electrospun Dressings for Complex Wounds

- Management of open fractures wounds, diabetic ulcers, and military wounds frequently involve infections with G+ve and G-ve bacteria and in some cases invasive fungal infections which are linked to mycotic emboli and delays in reconstructive efforts or amputations[1].
- Topical anitbiotics and antifungals are recommended and local delivery of antimicrobials through beads or bead pouches along with a water impermeable dressing has been shown to be beneficial[1].
- ***HYPOTHESIS:*** Alternating electrospun (ES) polymeric membranes loaded with combination of antifungal (Amphotericin B, AmB) and antibacterial (Vancomycin, V) agents in clinically relevant concentrations on a fluid adsorbing layer can be used for the treatment of complex wounds.

Layer by layer assembly of ES Dressings

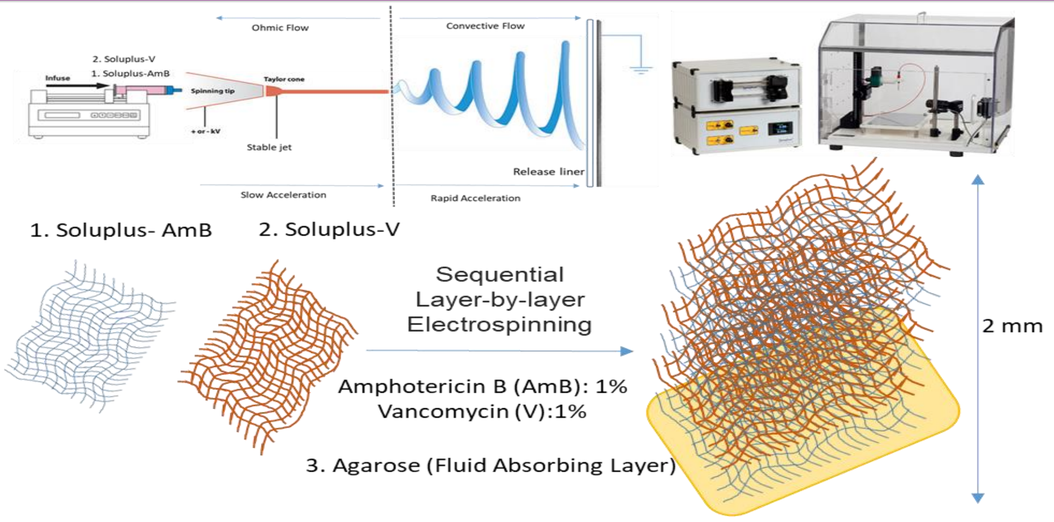


Figure 1. Schematic diagram of preparation of electrospun membranes on agarose hydrogels

1. Solid-State Characterisation

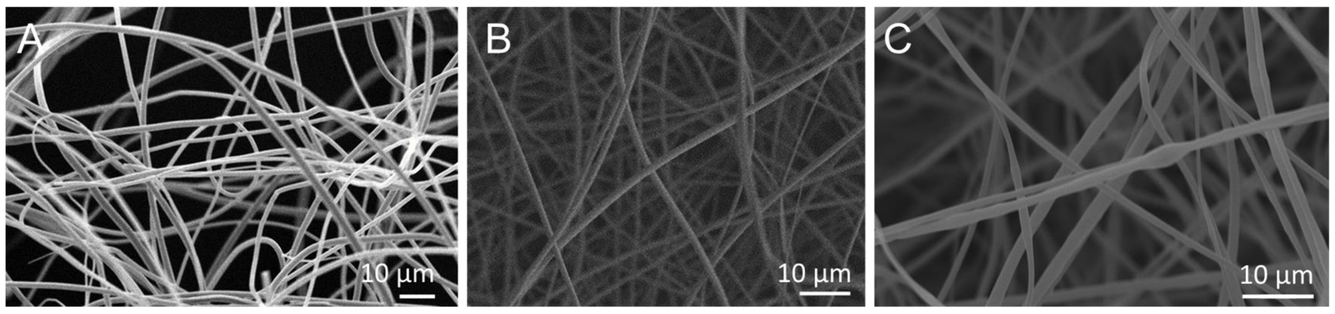


Figure 2. Scanning Electron Microscopy images; **A: AmB ES membranes (1%), B: ES membranes (Soluplus), C: Vancomycin ES membranes (1%)**, (Bar 10µm). ES membranes were produced using a Spraybase 30kV electrospinning kit attached to a syringe pump (NE-1000). Conditions; distance: 12.5 cm, Voltage: 15.5 kV, 8mL/h, co-axial electrospinning needle (~900 µm, Rame-hart Instrument Co).

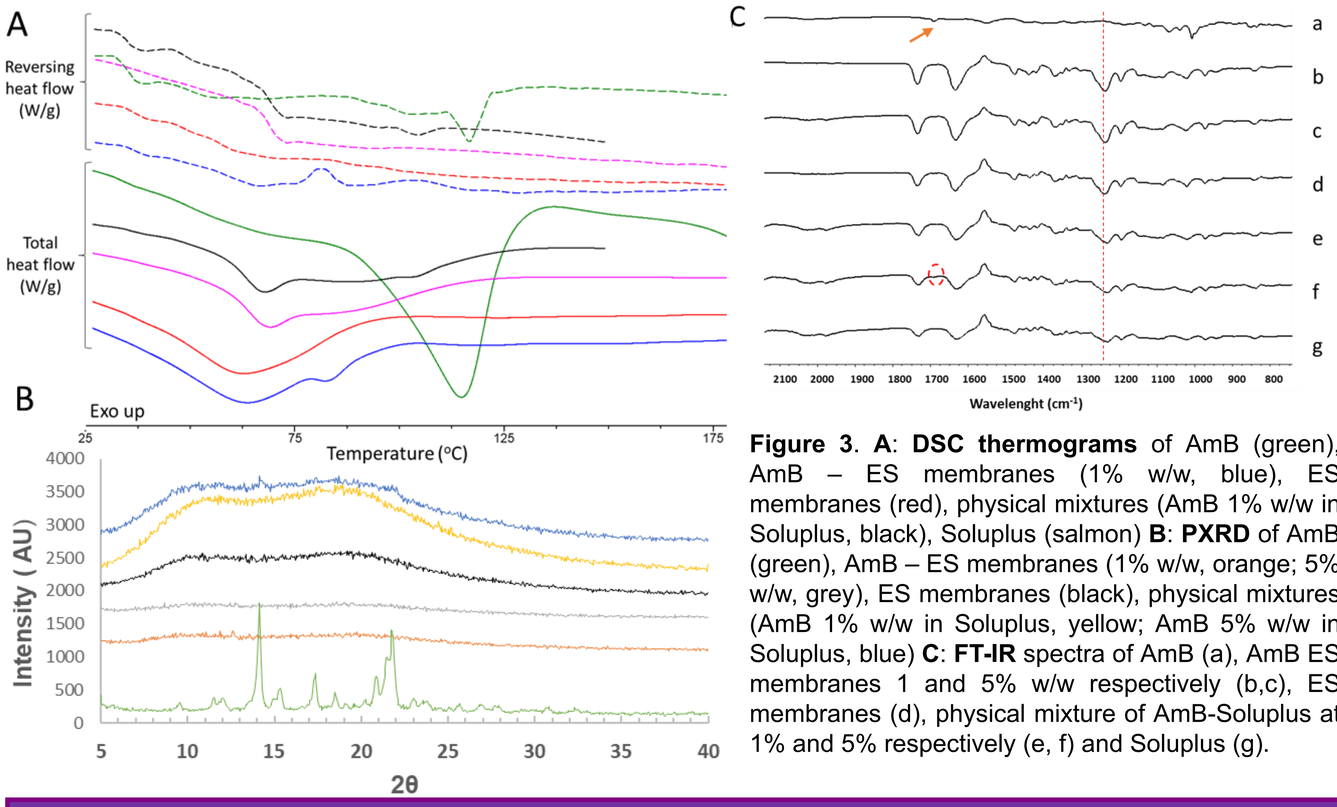


Figure 3. **A**: **DSC thermograms** of AmB (green), AmB – ES membranes (1% w/w, blue), ES membranes (red), physical mixtures (AmB 1% w/w in Soluplus, black), Soluplus (salmon) **B**: **PXRD** of AmB (green), AmB – ES membranes (1% w/w, orange; 5% w/w, grey), ES membranes (black), physical mixtures (AmB 1% w/w in Soluplus, yellow; AmB 5% w/w in Soluplus, blue) **C**: **FT-IR** spectra of AmB (a), AmB ES membranes 1 and 5% w/w respectively (b,c), ES membranes (d), physical mixture of AmB-Soluplus at 1% and 5% respectively (e, f) and Soluplus (g).

2. Release & Aggregation Studies

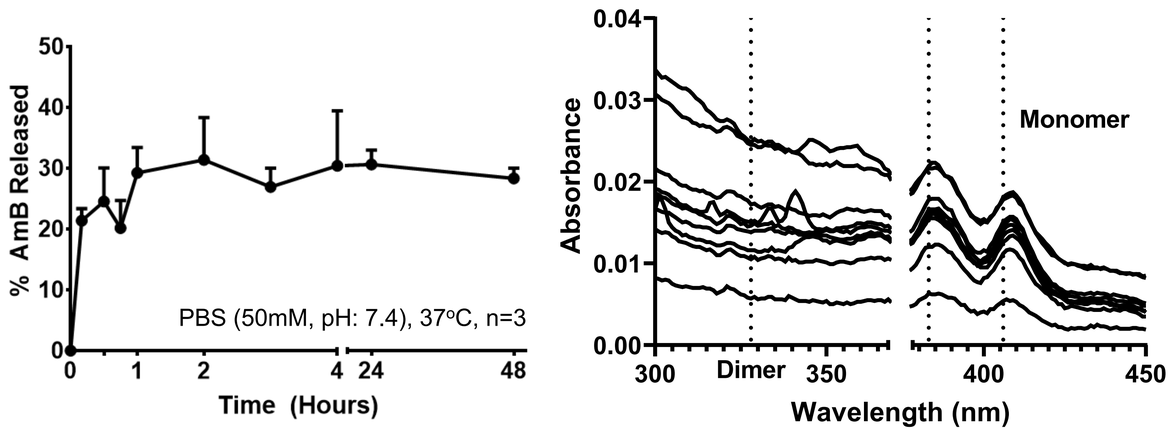
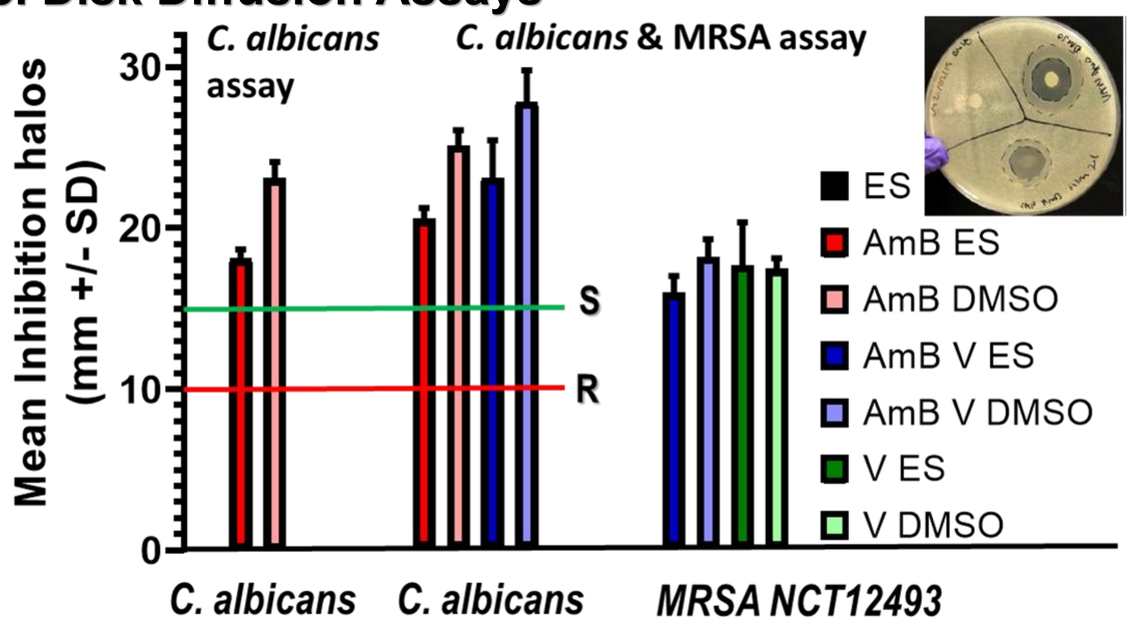


Figure 4. **AmB release from AmB ES membranes (A) and UV spectroscopy studies to assess the aggregation state of released AmB in media (B). Dimer peaks: 328nm, Monomer peaks: 383, 406 nm².**

3. Disk Diffusion Assays



ES Dressings Deliver Locally Sustained Levels of Antimicrobials to Complex Wounds

- AmB and V membanes contained near 100% AmB and V sprayed (9.85 ± 1.5 & 10.50 ± 0.89 mg/g respectively). Membanes demonstrated a fibrous morphology with higher curvature that unloaded membranes (Figure 2).
- Membranes were amorphous as shown by DSC, PXRD and FT-IR. Near 30% release was achieved after 1hour, while a controlled release profile was maintained over 2 days. Released AmB is present in monomeric form (UV).
- Inhibition halo of AmB membranes or AmB able to elicit AmB levels in which *C. albicans* is susceptible. Slightly smaller halos can be explained by partial release of AmB loaded in ES membranes as equivalent doses of AmB were used. V membanes were able to elicit comparable halos against MRSA.
- Prepared layer by layer ES membranes are currently under development in combination with agarose casted mats (main fluid absorbing layer). Release studies and *in vitro* activity studies are currently under way for producing dressings for the treatment of complex fungal infected wounds and able to avoid mycotic embolism.

Figure 5. ***In vitro*** **antifungal and antimicrobial activity[3]. Left; Disk Diffusion Assays - *C. albicans* WT CaTOK** (ES membranes, AmB ES membranes (%), AmB (DMSO, 10µg)**, Right: Disk Diffusion Assays – *C. albicans* WT CaTOK and MRSA (Methycilin resistant Staphylococcus Aureus) NCT12493** [ES membranes, AmB ES membranes (1%), AmB (DMSO, 10µg), AmB & V ES membranes (1% for both), AmB & V (DMSO, 10µg for both), V ES mebranes (1%), V (DMSO, 10µg)]. **The isolates were classified as susceptibile (S) and as resistant (R).**

References

1. Heller, SF (2017) Surgery 162 (6): 1330.
2. Serrano, DR (2015) Mol Pharm 12 (2):420
3. Serrano, DR (2019) Pharmaceutics; Under Review