Amphotericin B Nanocrystals-in-Nanofibres films for the Topical Treatment of Cutaneous Leishmaniasis

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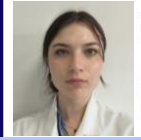
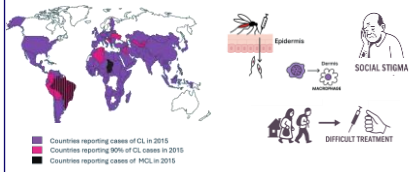


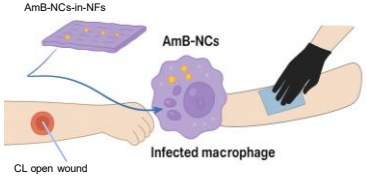
INTRODUCTION

Cutaneous leishmaniasis (CL) is a **neglected** parasitic skin disease transmitted by sandfly bites, affecting up to **1 million people annually** and leaving disfiguring scars, especially in low-income regions [1]. Current treatments are toxic, expensive, and **poorly accessible** [2]. Although Amphotericin B (AmB) is effective, its use is limited by poor solubility and systemic toxicity. **Nanocrystals (NCs)** improve solubility [3] and may enhance **macrophage uptake** [4], while **nanofibres (NFs)** adhere to skin and enable controlled drug release. Embedding **AmB-NCs into NFs** offers a promising, localised strategy for this overlooked disease.



AIM OF WORK

To develop a dissolvable **NFs** patch loaded with **AmB NCs** for **topical, self-administered** treatment for CL.

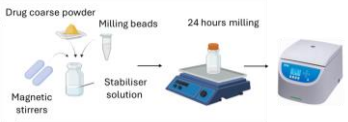


AmB-NCs will act as **'Trojan horses'**, being phagocytosed by infected macrophages and releasing the drug intracellularly to combat the parasite while limiting systemic toxicity.

METHODS

1-NCs PREPARATION

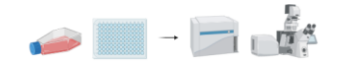
Media Milling and washing process



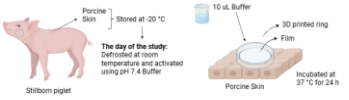
Electrospinning

Characterisation

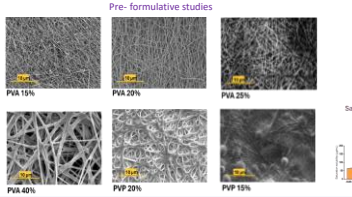
3- *IN VITRO*: CELLS STUDIES



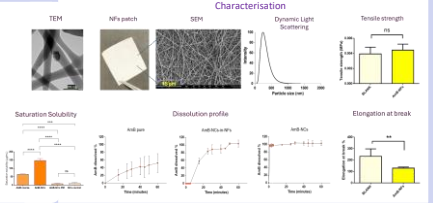
4- *EX VIVO*: SKIN DEPOSITION



Pre- formulative studies

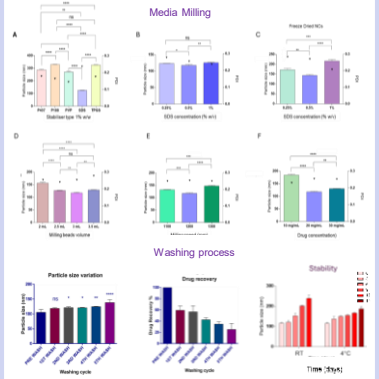


Characterisation



RESULTS

1-NCs PREPARATION

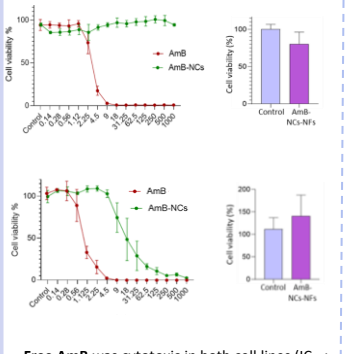


AmB NCs (**~120 nm**) successfully produced via wet media milling and purified from the SDS excess

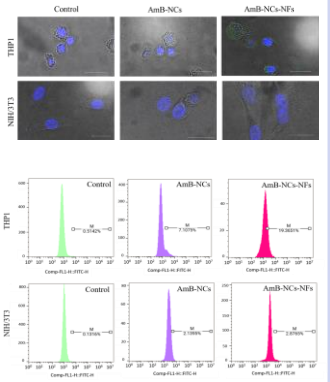
2-NFs PREPARATION

AmB-NCs **were effectively embedded into uniform NFs** with suitable mechanical properties, maintaining particle size **below 200 nm**. TEM confirmed the NCs-in-NFs architecture. The NCs formulation markedly **improved saturation solubility** compared to the coarse AmB powder while AmB-NCs-in-NFs **delayed the dissolution profile** of the AmB-NCs.

3- *IN VITRO*: CELLS STUDIES

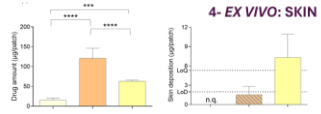


Free AmB was cytotoxic in both cell lines (IC_{50}: 2.96 µg/mL in THP-1; 0.9 µg/mL in NIH/3T3); **AmB-NCs preserved cell viability** in both lines; **NF formulations**, with or without AmB-NCs (~30 µg/well), showed **no significant cytotoxicity**, confirming **system biocompatibility**.



Fluorescence quantification by flow cytometry confirmed increased **AmB-NCs-in-NFs uptake** by human monocytes *vs* untreated controls.

4- *EX VIVO*: SKIN DEPOSITION



Only the **AmB-NCs-in-NFs** system enabled **~11%** transdermal delivery in 24 h, combining NC-enhanced solubility with NFs-mediated skin retention.

CONCLUSIONS

AmB-NCs-in-NFs patches were developed, combining NCs that **enhanced solubility, dissolution rate, and uptake by human monocytes,** with electrospun PVA NFs that ensured skin adhesion and **delayed NCs dissolution**. This biocompatible, **self-applicable** patch achieved **~11% transdermal delivery** across intact skin in **24 hours** and offers a **practical, safer alternative to systemic therapy,** holding strong promise for accessible, community-level treatment of CL in resource-limited settings.