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INFLUENCE OF DRUG-POLYMER INTERACTIONS ON RELEASE KINETICS OF PLGA AND PLA/PEG NPS

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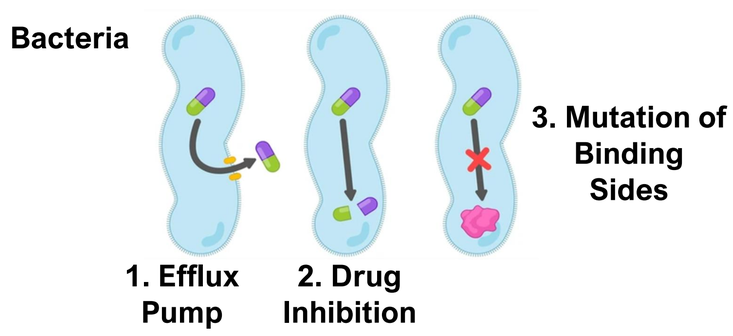
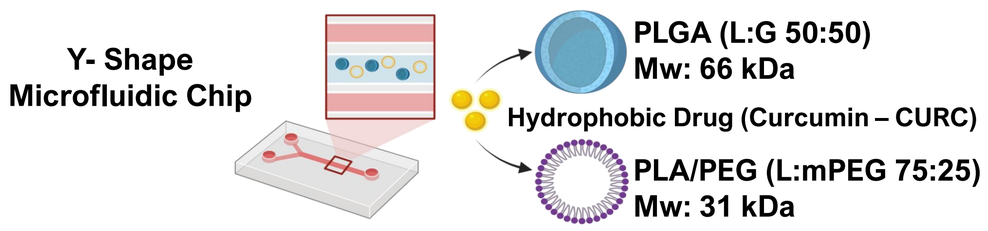
INTRODUCTION

Antimicrobial resistance (AMR) is a growing global health threat, requiring novel drug delivery strategies (1). Microfluidic-based synthesis of nano-sized carriers for drug delivery systems (NDDS) offers precise control over nanocarrier characteristics and improves encapsulation efficiency (2,3).

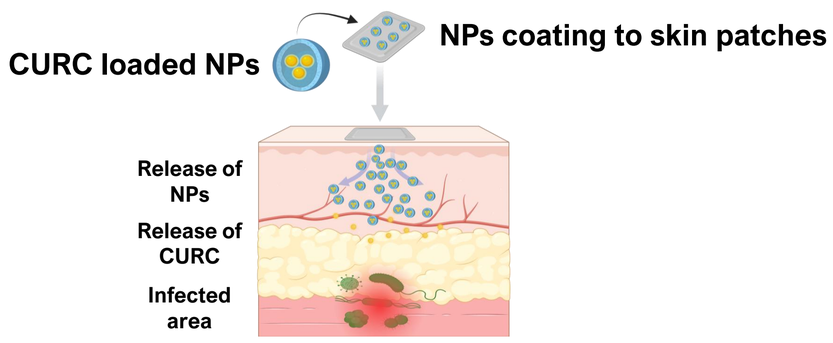
(1) ANTIMICROBIAL RESISTANCE



(2) NPs SYNTHESIS BY MICROFLUIDICS



(3) DRUG DELIVERY SYSTEM



METHODS

- An *ad hoc* custom-built device was used, comprising a pumping module with two syringe pumps and an infusion setup designed to place a **Passive Herringbone Mixer (PHBM) chip.**

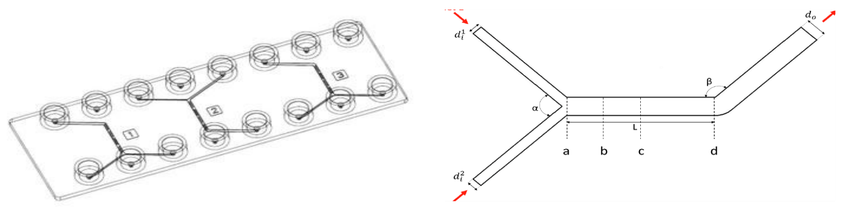


Figure 1: Representative scheme of a) outer and b) inner side of microfluidic chip (3).

Table 1: Drug loading into NPs and micelles.

	Type of Syringes	Final Volume (mL)	Total Flow Rate (TFR) (mL/min)	Flow Rate Ratio (FRR) (aqueous/ organic phase)
PLGA	Terumo 5 mL	2	8	4:1
NPs	Terumo 5 mL	2	8	4:1
PLA/PEG	Terumo 5 mL	2	3	3:1
NPs	Terumo 5 mL	2	3	3:1

RESULTS

1.Physical Properties of NPs

- NPs had uniform size distribution with PDI ≤ 0.2, consistent with TEM observations.

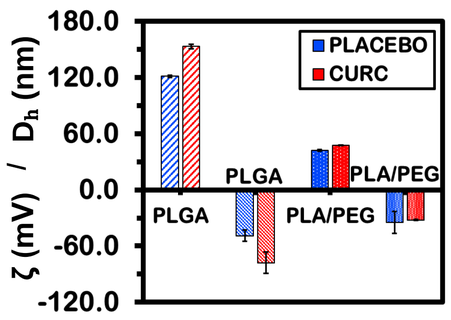


Figure 2: Physical features of PLGA NPs and PLA/PEG micelles.

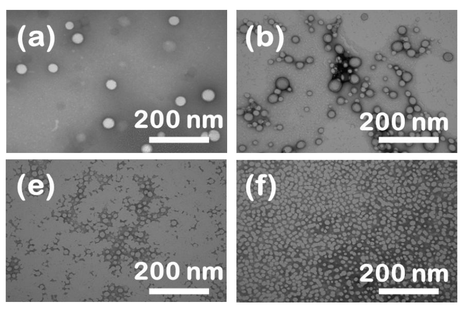


Figure 3: TEM images of a) PLGA NPs, b) CURC loaded PLGA NPs, c) PLA-PEG micelles, and d) CURC loaded PLA-PEG micelles.

2. Release Kinetics of NPs

Table 2: Drug loading into NPs and micelles.

	EE %	
Loading	**PLGA**	**PLA/PEG**
Curcumin	61.91 ± 1.86	13.74 ± 0.97
	Payload (% µg/mg)	
	2.81 ± 0.81	2.51 ± 0.57

Higher Encapsulation Efficiency (EE%)

Slower Release Rate

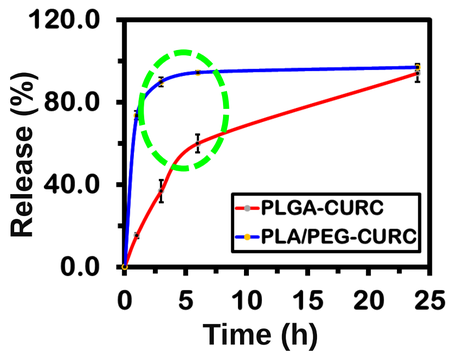


Figure 4: Release profiles of CURC from PLGA NPs and PLA/PEG micelles.

3. Cytotoxicity & Antimicrobial Activity

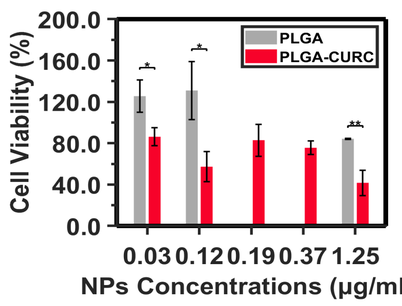


Figure 5: Cell viability (%) after 24 h treatment on NHDFs at a cell density of 3 × 10^8 cells/mL.

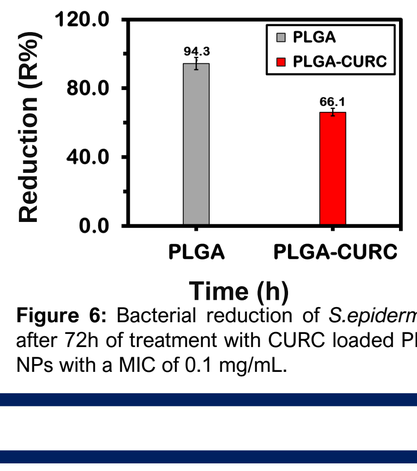


Figure 6: Bacterial reduction of *S.epidermidis* after 72h of treatment with CURC loaded PLGA NPs with a MIC of 0.1 mg/mL.

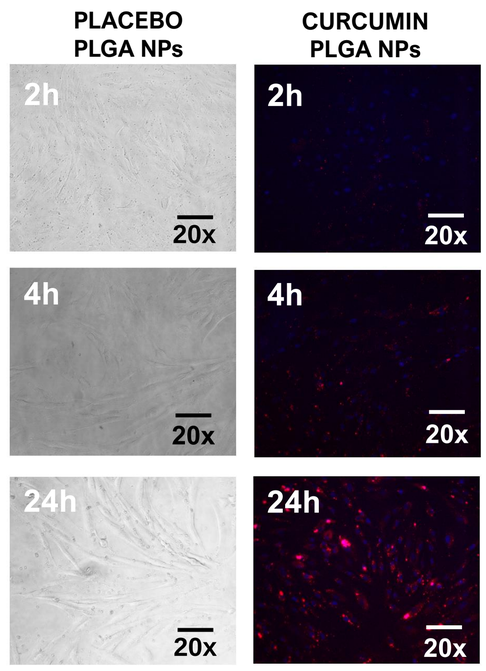


Figure 7: Fluorescence microscope images of placebo and CURC loaded PLGA NPs on NHDFs after 2, 4 and 24 h indicating cellular uptake.

CONCLUSION

- CURC loaded PLGA NPs were better candidates for controlled drug delivery due to **hydrophobic interactions between the drug and the polymer.**
- No or slight cytotoxic effect of CURC NPs was observed on NHDFs with **progressive cellular internalization of NPs**.
- The choice of **polymer composition** plays a key role in **drug-polymer interactions and release kinetics** to achieve **more controlled delivery and improved therapeutic efficacy** in regenerative medicine.

References
(1) Vega-Vásquez, P. et al. *Front. Bioeng. Biotechnol*. 2020, 8, 2296-4185.
(2) Fu, Y. S. et al. *Biomed. Pharmacother*. 2021, 141, 111888.
(3) Chiesa et al. ,International Journal of Pharmaceutics, Volume 629, 2022, 122368, ISSN 0378-5173.

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