Utilizing bilosomes for buccal delivery of therapeutics

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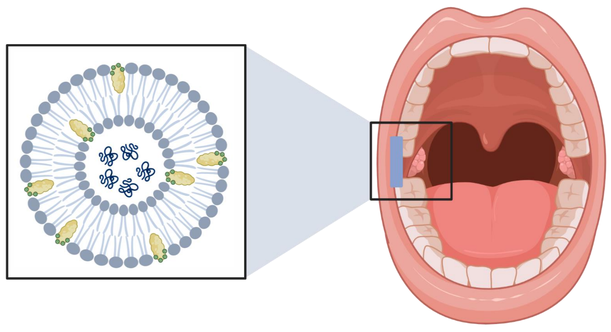
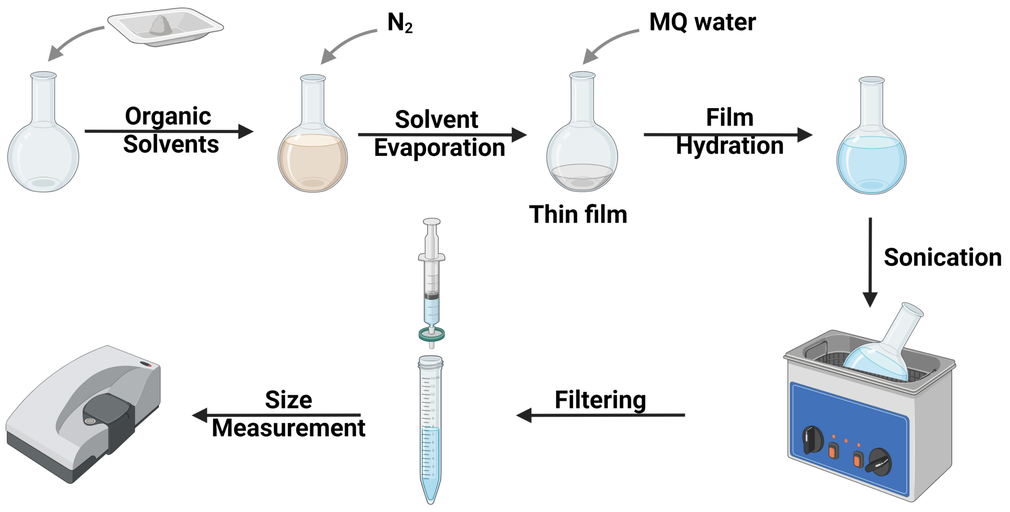
INTRODUCTION

- Therapeutics such as peptides face challenges in oral delivery due to degradation and poor absorption.
- Buccal drug administration bypasses degradation in the gastrointestinal tract and hepatic metabolism, improving patient compliance and enhancing bioavailability.
- The study aims to develop bilosomes (vesicular delivery systems encapsulating drugs within bile salts) as carriers for therapeutics and study their interaction with TR146 cells for mechanistic insights.



METHODS

Bilosomes were synthesized using a thin film hydration method.

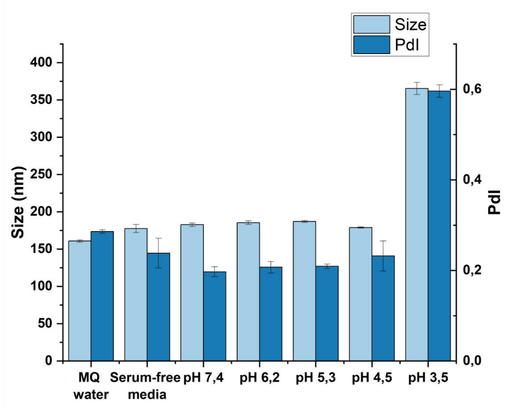


RESULTS

Bilosome preparation and characterization

- Freshly prepared bilosomes in Milli-Q water had a Z-average diameter of 160.8 ± 1.56 nm (PDI = 0.28).
- Size remained stable from pH 7.4 to 5.3, but at pH 3.5, it increased significantly (365.4 ± 8.20 nm, PDI = 0.596), indicating destabilization.
- Bilosomes in pH 4.5 showed signs of breakdown over 24 hours, while stability was maintained in serum-free DMEM and over four months of storage without agglomeration.

A)



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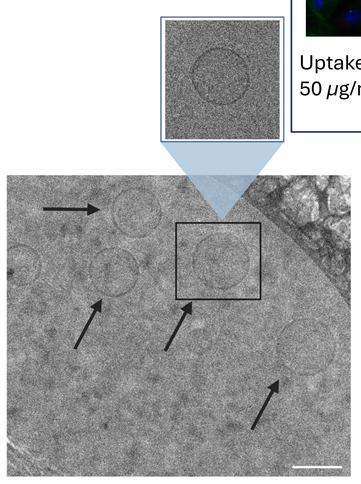

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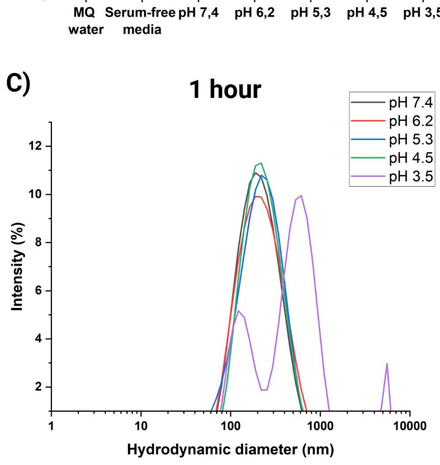
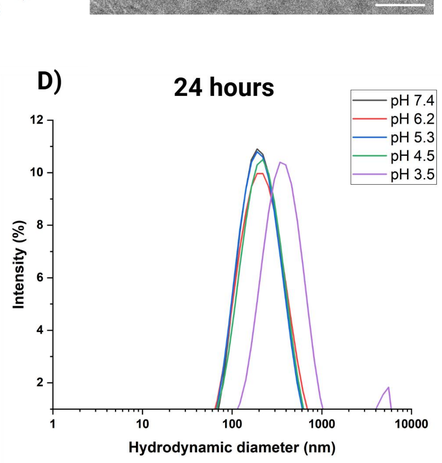
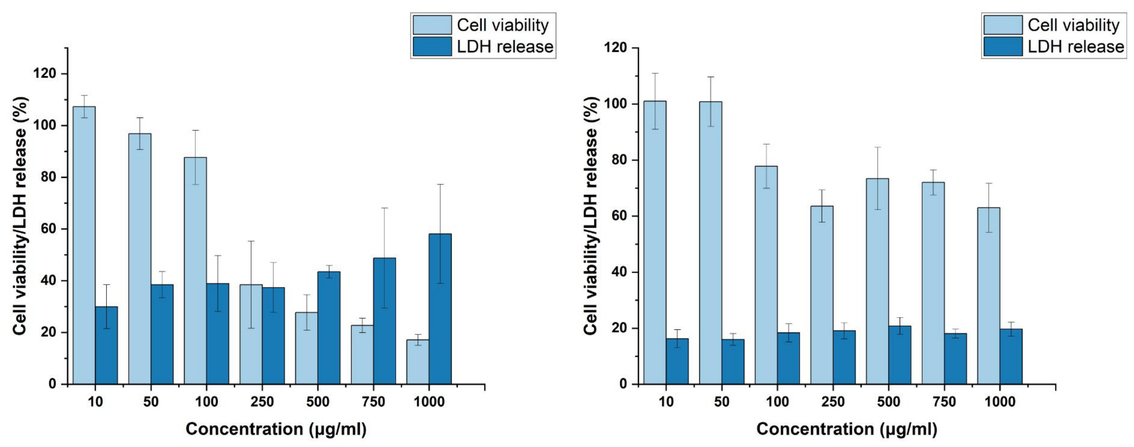


D)



TR146 Cell Viability After Bilosome Exposure

- Cells were incubated with bilosomes for 1 hour, and assays were performed immediately and after 24 hours in culture media.
- MTS assays showed that TR146 cell viability remained above 70% at 10 and 50 μg/mL, with LDH assays confirming low membrane damage (LDH release <30%), indicating no toxicity at these concentrations.



Uptake:

- Dose-dependent; 10 & 50 μg/mL showed no stress, while 100 μg/mL caused stress and minimal internalization.
- Cytoskeleton: Intact at lower doses; 100 μg/mL slightly disrupted integrity.

Uptake from TR146 cells (A: control) after incubation with 10 μg/mL (B), 50 μg/mL (C) and 100 μg/mL (D) bilosomes. Arrows indicate stress fibers.

Desmosome Opening:

- Bile salts: Open desmosomes but cause cell stress.
- Bilosomes: Open desmosomes in a concentration- & time-dependent manner (10 & 50 μg/mL, 1 & 3 h) with less stress.

Desmosome opening after incubation with 10 μg/ml, 1-hour (A), 50 μg/mL, 1-hour (B),10 μg/mL, 3 hours (C), 50 μg/mL 3 hours (D) bilosomes.

CONCLUSIONS

Bilosomes showed:

- Enhanced permeability: Formulated with bile salts for improved drug transport.
- pH-dependent stability: Stable at physiological pH, but breakdown occurs in acidic conditions.
- Efficient cellular uptake: Internalized by TR146 cells at concentrations ensuring high viability and low toxicity.
- Promising for drug delivery: Supports safe and effective transport across the buccal epithelium.

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