An Efficient Topical Therapeutic for Atopic Dermatitis: Tacrolimus-loaded Chitosan-based Nanoparticles (TAC@CNP)

Enhancing Skin Permeability and Therapeutic Efficacy

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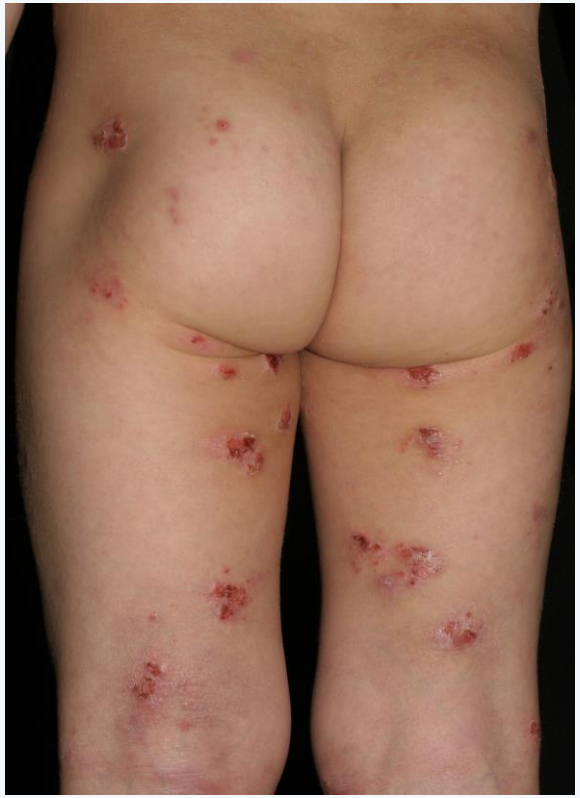
The Challenge with Atopic Dermatitis (AD)



Chronic inflammatory skin disease affecting up to 20% of children.

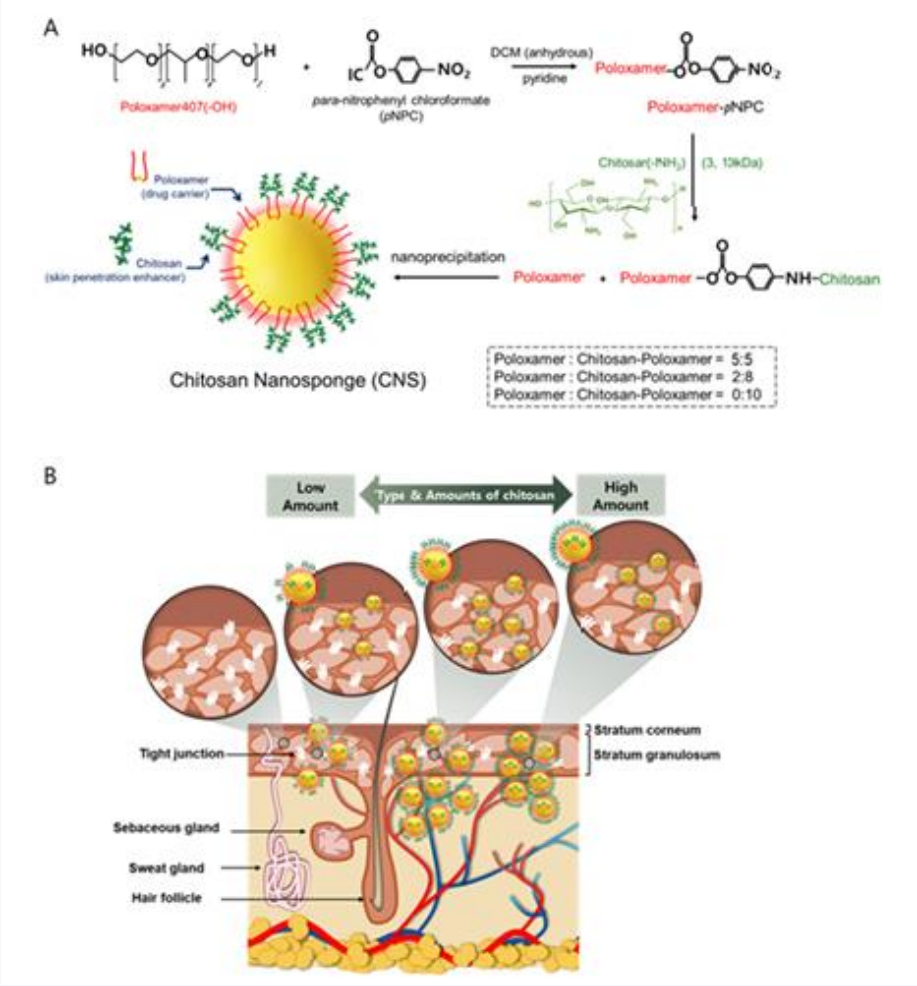
Current therapies rely on corticosteroids — limited by skin atrophy & side effects.

Tacrolimus (TAC): Effective calcineurin inhibitor, but poor skin penetration.

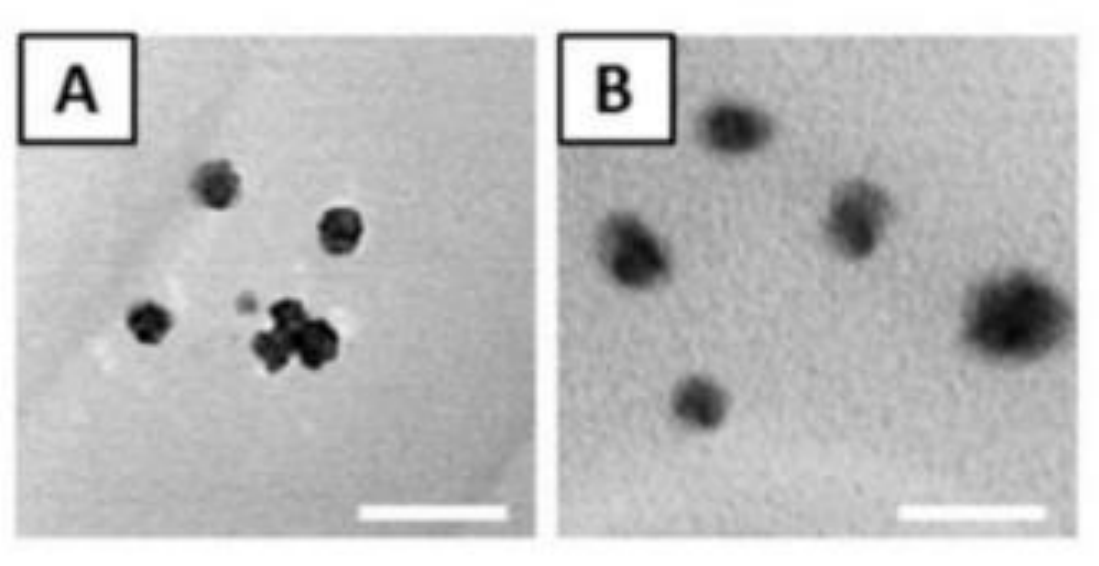
Hurdle: High molecular weight (822 Da) & low water solubility.

Our Objective

[Tacrolimus] → [Chitosan Nanoparticle] → [Enhanced Skin Delivery] → [Improved AD Treatment]



Formulation & Characterization of TAC@CNP



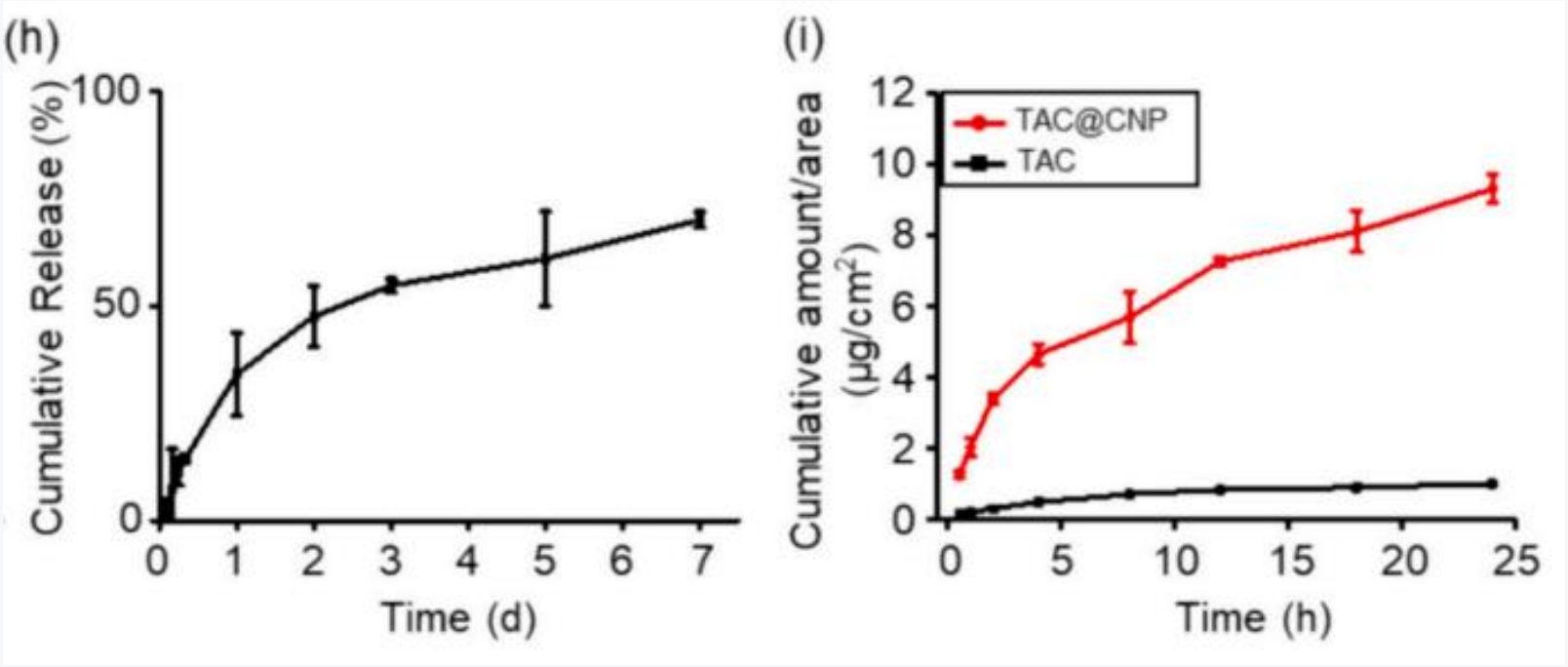
Size: 50–70 nm, monodisperse.

Zeta Potential: > +20 mV, strong skin adhesion.

Morphology: Spherical, confirmed by TEM.

Stability: 4-week colloidal stability (PBS, 37 °C).

Superior In Vitro Performance

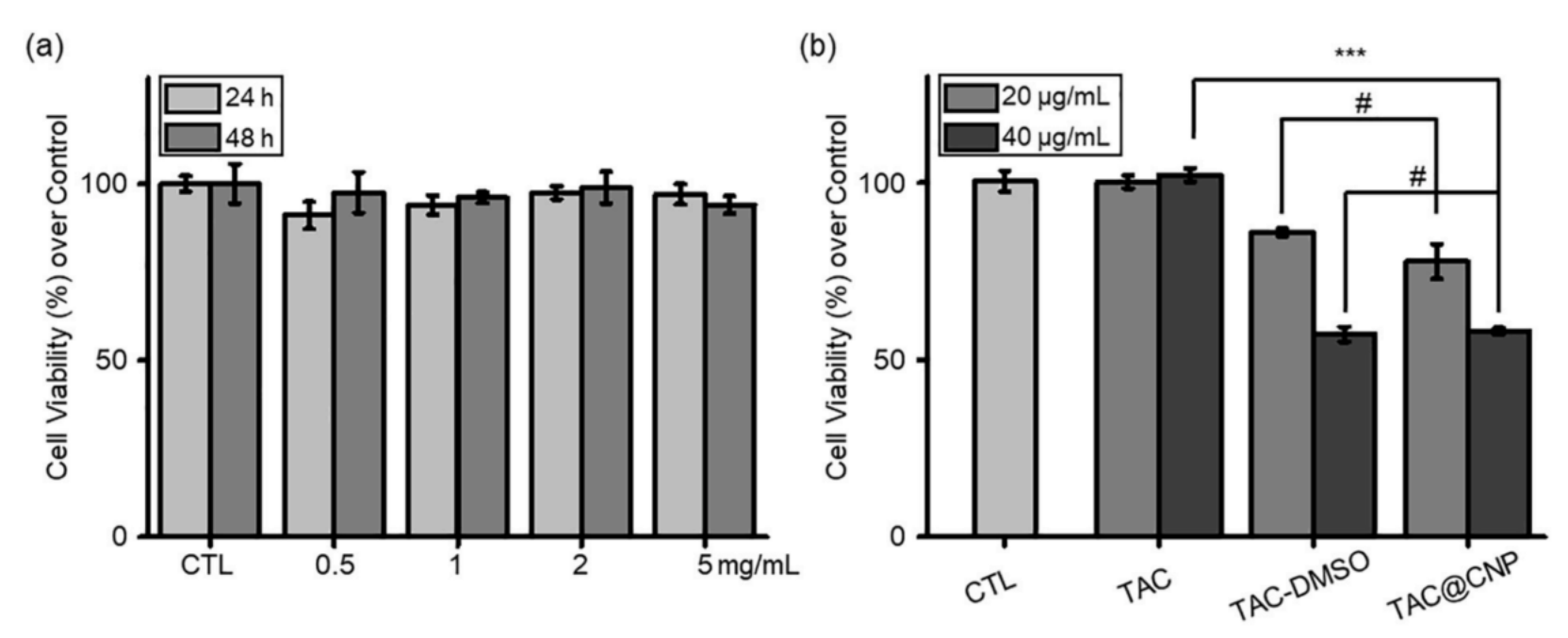


Sustained release: 70% released by day 7.

Enhanced penetration (TAC@CNP: 9.3 μg/cm² vs Free TAC: 1.0 μg/cm²).

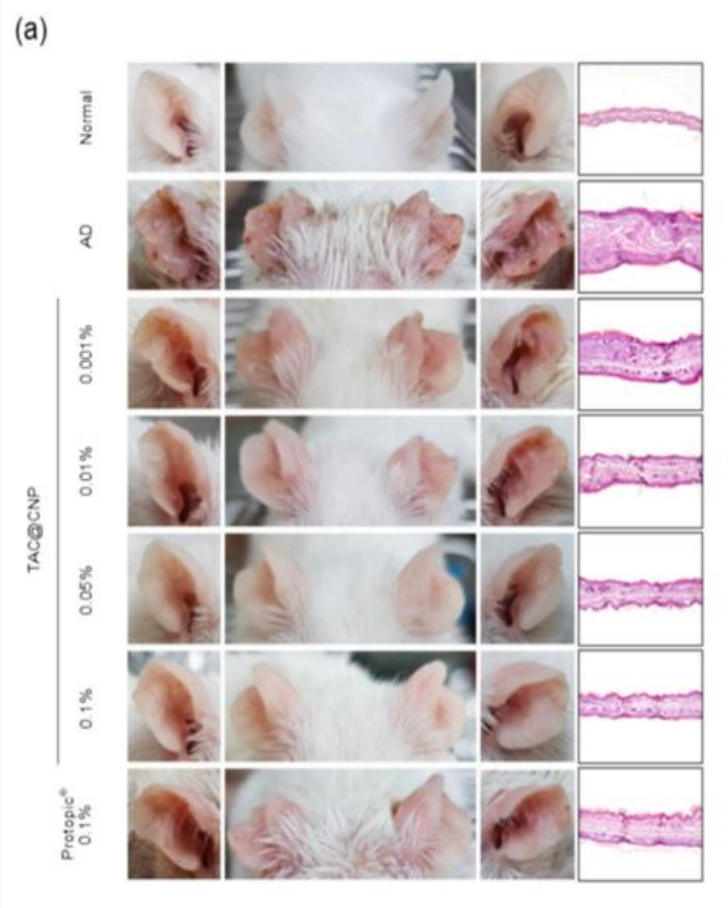
≈9× higher skin permeability confirmed via cadaver skin.

In Vitro Efficacy & Safety



CNP carrier: Non-toxic to HaCaT keratinocytes (>90% viability).
TAC@CNP inhibits keratinocyte proliferation (dose-dependent).
Equal efficacy to TAC-DMSO without solvent toxicity.

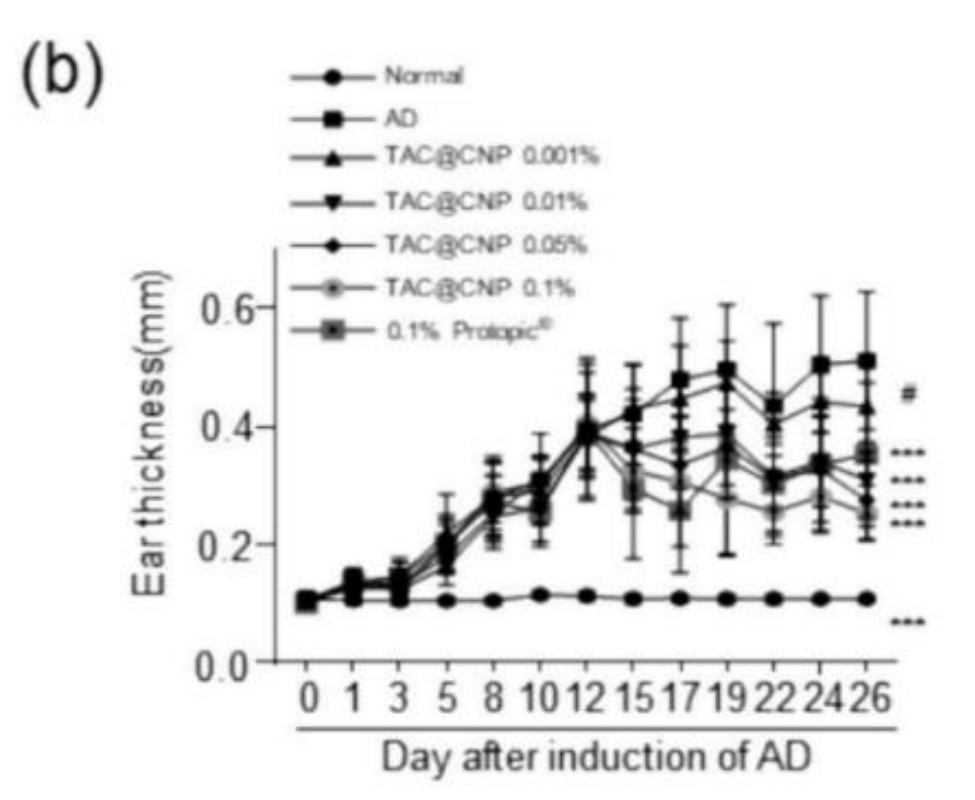
In Vivo Study: HDM-Induced AD Mouse Model

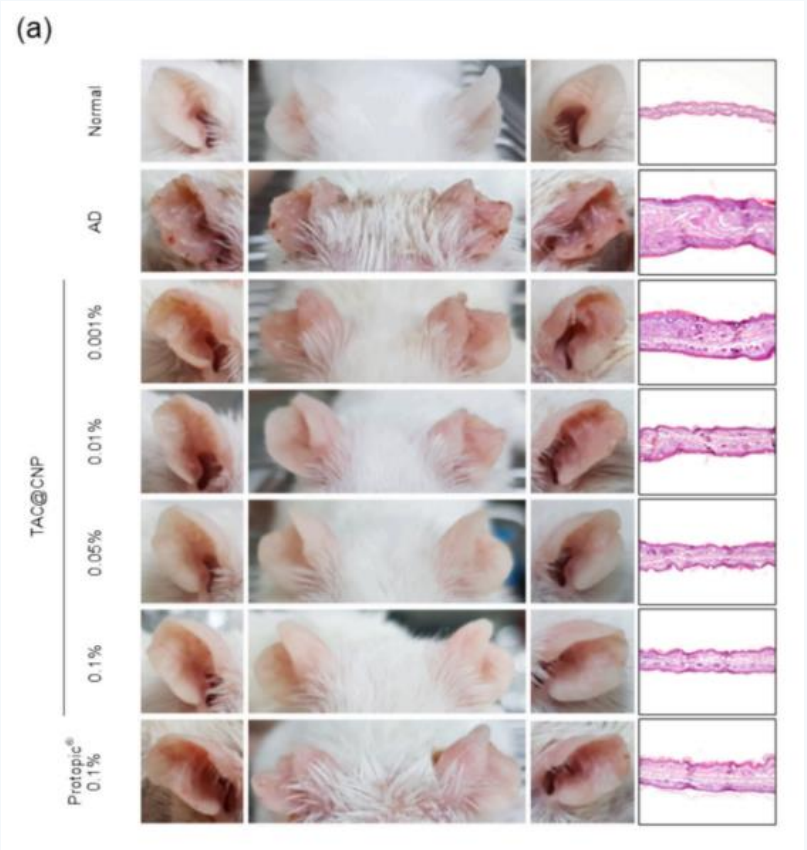


SDS (4%) 3h	Skin barrier disruption
HDM Cream 3×/week (4w)	AD induction
Treatment (2w)	TAC@CNP or Protopic®

Model: BALB/c mice, AD induced by House Dust Mite on ear skin.
Groups: Normal / AD / TAC@CNP (0.001–0.1%) / Protopic® 0.1%.
Regimen: Daily topical application for 2 weeks.

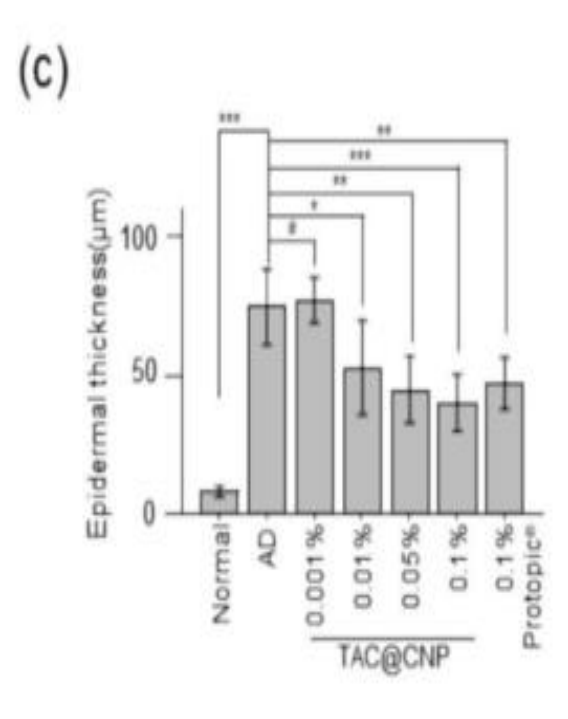
Significant Amelioration of AD Symptoms

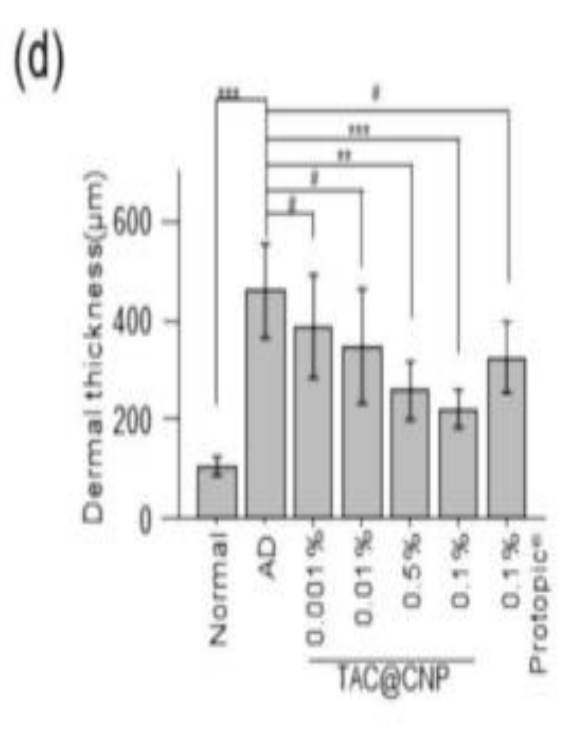


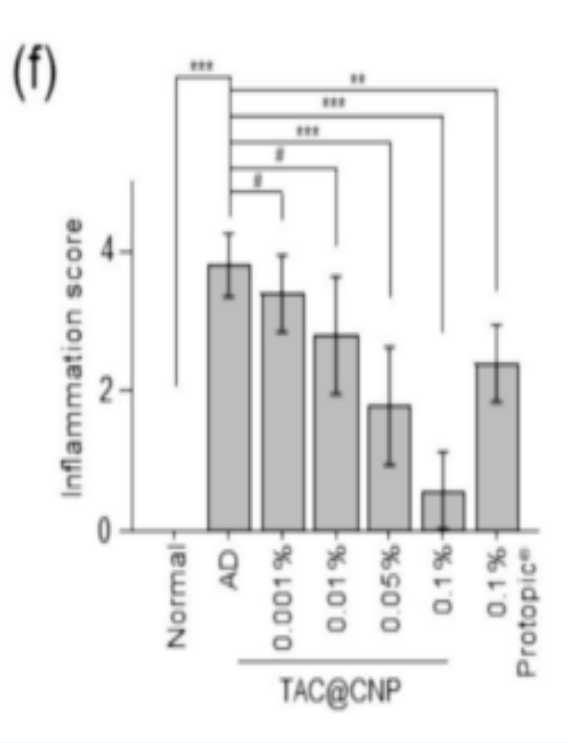


TAC@CNP reduced ear thickness, **erythema, edema**.
0.01% TAC@CNP ≈ 0.1% Protopic® efficacy.
10× dose reduction achieved with equivalent effect.

Histological Improvement

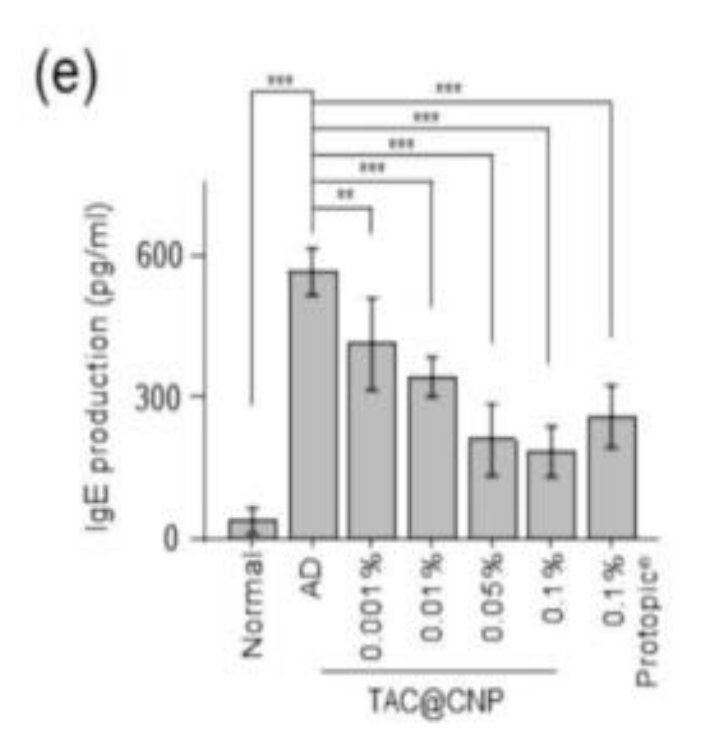


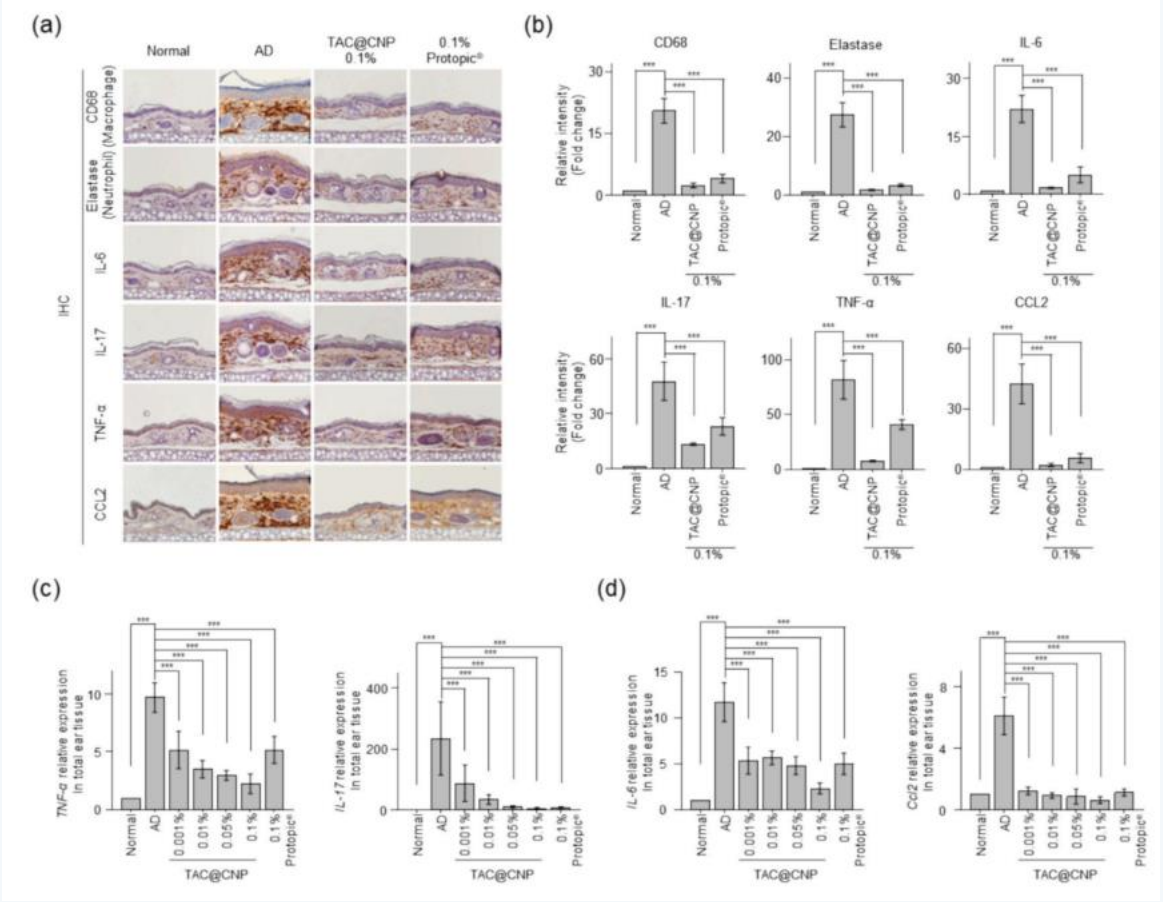




H&E staining: Reduced epidermal and dermal thickness.
Inflammation scores decreased dose-dependently.
Strong anti-inflammatory effect at tissue level.

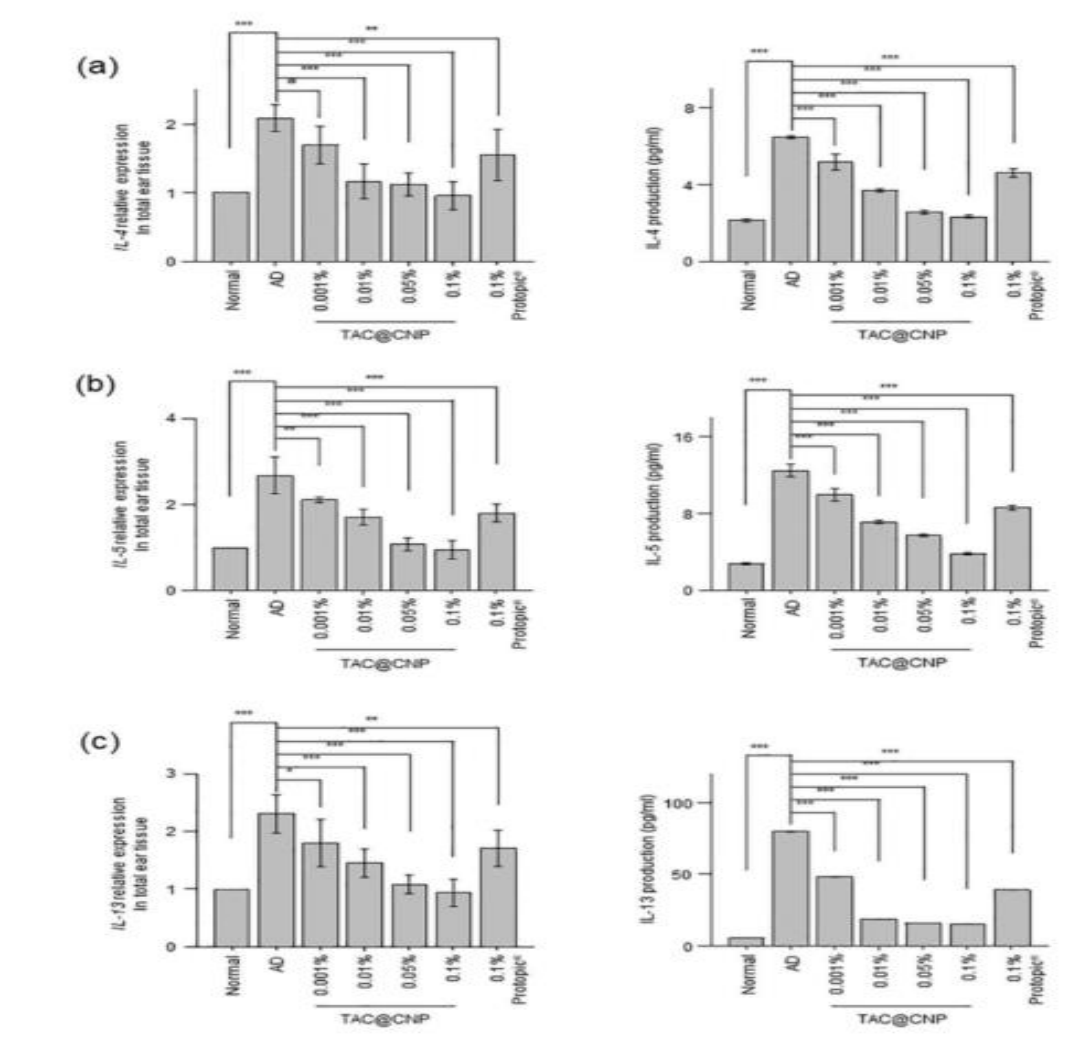
Suppression of Key Immune Markers

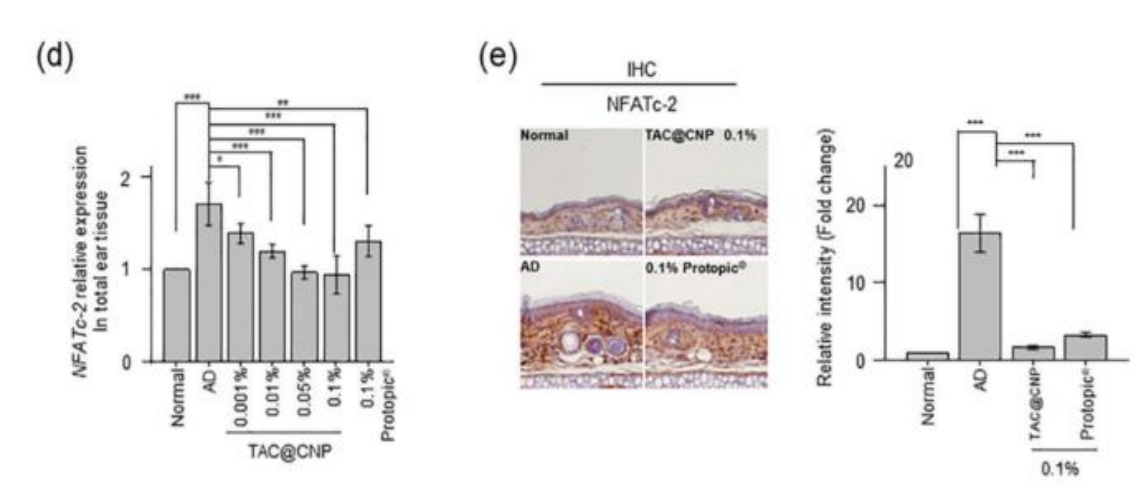




Serum **IgE reduced at ≥0.01%** TAC@CNP.
Decreased TNF-α, IL-6, IL-17, and CCL2 expression.
Enhanced immunomodulation compared to Protopic®.

Downregulation of Th2/NFATc-2 Pathway





Th2 cytokines (IL-4, IL-5, IL-13) downregulated.
NFATc-2 suppression confirmed (Tacrolimus target).
0.01% TAC@CNP = 0.1% Protopic® molecular efficacy.

Conclusion & Future Directions

Developed stable chitosan-based nanoparticle system for TAC.

Demonstrated enhanced skin permeability & efficacy.

Achieved 10-fold dose reduction with same therapeutic effect.

Next: Clinical translation of TAC@CNP for AD treatment.