

# Dual-Crosslinked Alginate Hydrogel for Sustained Antioxidant Nanoparticles Delivery in Colon-Targeted Therapy

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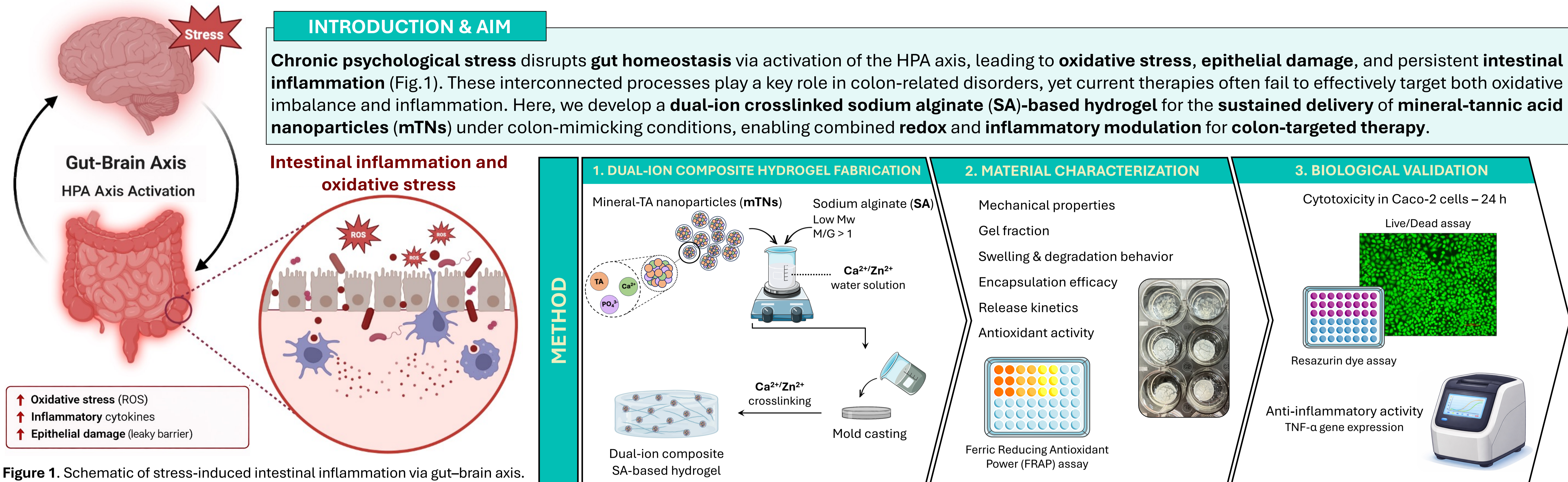


Figure 1. Schematic of stress-induced intestinal inflammation via gut-brain axis.

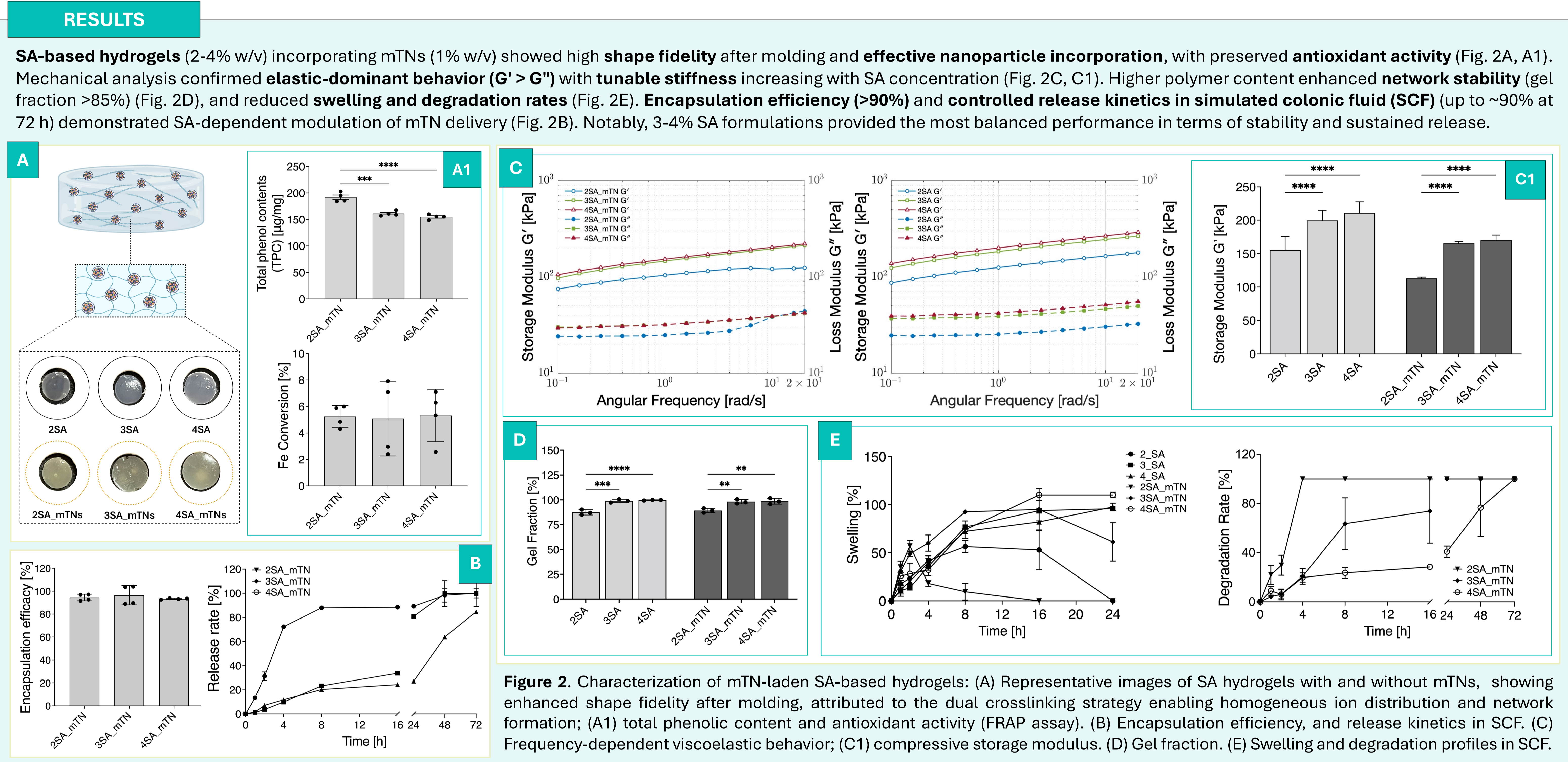


Figure 2. Characterization of mTN-laden SA-based hydrogels: (A) Representative images of SA hydrogels with and without mTNs, showing enhanced shape fidelity after molding, attributed to the dual crosslinking strategy enabling homogeneous ion distribution and network formation; (A1) total phenolic content and antioxidant activity (FRAP assay). (B) Encapsulation efficiency, and release kinetics in SCF. (C) Frequency-dependent viscoelastic behavior; (C1) compressive storage modulus. (D) Gel fraction. (E) Swelling and degradation profiles in SCF.

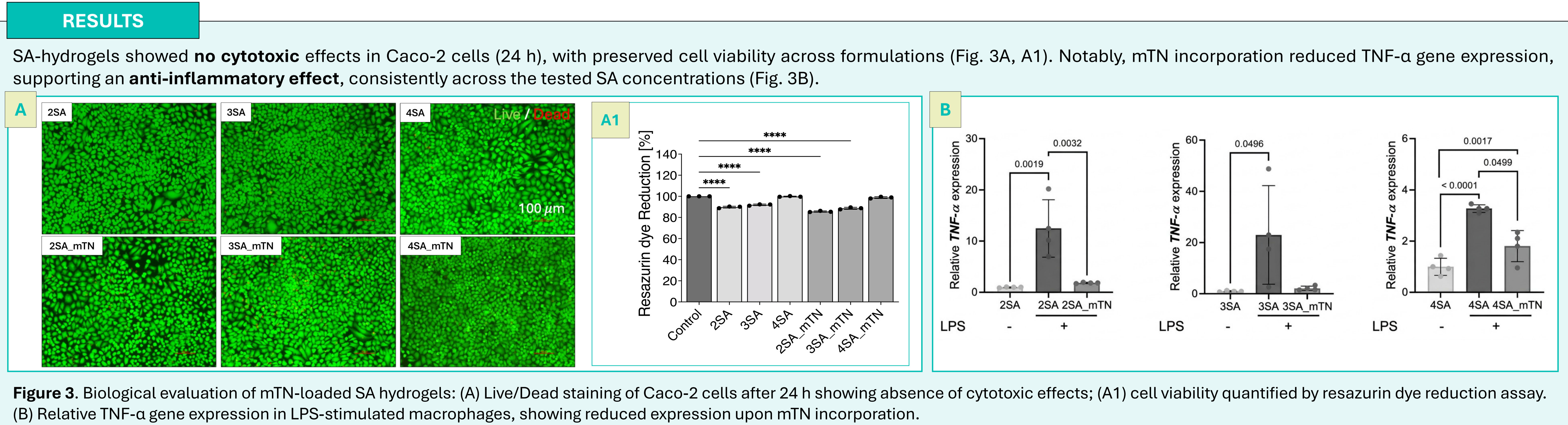


Figure 3. Biological evaluation of mTN-loaded SA hydrogels: (A) Live/Dead staining of Caco-2 cells after 24 h showing absence of cytotoxic effects; (A1) cell viability quantified by resazurin dye reduction assay. (B) Relative TNF- $\alpha$  gene expression in LPS-stimulated macrophages, showing reduced expression upon mTN incorporation.

**CONCLUSIONS**  
Dual-crosslinked SA hydrogels provide a tunable platform for sustained mTN delivery, combining structural stability and biological activity, with optimal performance observed in the 3-4% SA range. These systems hold strong potential for colon-targeted antioxidant and anti-inflammatory therapies.