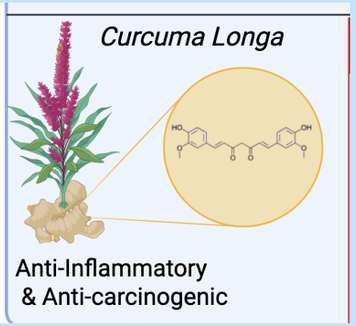
Synthesis and Characterization of Novel pH-Responsive Dual-Layer Chitosan-Alginate Smart Nanogels for Curcumin Delivery with Relevance to Colorectal Cancer and Biological Validation in *Drosophila melanogaster*

Research Question

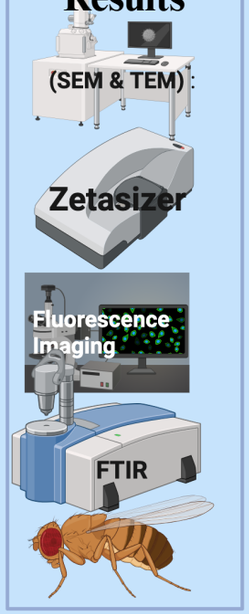
Colorectal Cancer (**CRC**): 2nd leading cause of cancer-related deaths but current treatment have off target side effects. Curcumin (**CUR**) has anti-cancer properties but poor solubility and stability.



Research Question:
Can optimized Dual-coated Nanogels (NGs) safely delivery and trigger pH-responsive release of CUR in the colon?

Hypothesis: Dual layer Chitosan (CS)-Alginate (Alg) NGs will achieve >70% encapsulation efficiency (EE%) and superior delivery

Results



SEM/TEM: Confirmed spherical NGs, dual-layer, and core-shell structure (PDI < 0.1) Single NG size - 147 & Dual Ng-342 nm

Zeta Potential: +32.5 to -32.7 mv charge reversal confirmed second coating

FTIR: CS-CUR-NH-bending (C=O shift 1647 → 1637cm^{-1}),

Alg shell confirmed in dual NG via COO− stretches (1566 & 1407 cm^{-1})

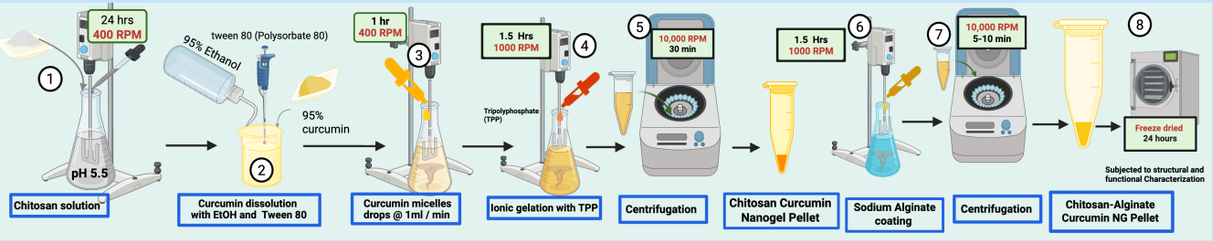
UV-Vis: Mean Encapsulation Efficiency (EE%) was 87.6%

Fluorescence: Showed CUR encapsulation and solubilization

***In vitro* Drug Release Kinetics :** Dual NG released 74% in colon compared to 8% by single NG.

Drosophila Model: Dual-layer structure decreased CUR gastric release from 92% to 9% and increased CUR colonic release from 8% to 73%

Methods & Procedure



- **Process Optimization:** Evaluated multiple synthesis variables including: solvent type, pH, stirring RPM for cross-linking, and composition ratios. Testing was conducted across 20 trials (12 exploratory, 8 confirmatory) to standardize the protocol.
- **In Vitro Drug Release Kinetics**: pH-responsive CUR release kinetics at gastric pH (1.2), small intestine pH (6.8), and colon pH (7.4)
- **In Vivo Validation:** *Drosophila melanogaster* gut model for targeted drug delivery confirmation

Discussion & Conclusions

- To attain high EE % optimization of three key parameters include EtOH and Tween 80 as a solvent for CUR, initial pH of 5.5 of CS solution and higher cross-linking RPM all played a major role in achieving our synthesis of smart NGs
- Drug Release Kinetics: Analyzed using Korsmeyer-Peppas model and confirmed Super Case ll transporter, proving that release is regulated by polymer swelling and relaxation by pH-responsiveness
- Dual-layer Chitosan Alginate NGs successfully enhances targeted delivery of CUR to the colon.
- Alginate shell protected the payload under gastric conditions while chitosan core enabled controlled swelling and release at colonic pH.
- *In vivo* Drosophila validation confirmed this trend