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

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Colorectal cancer (CRC) is the second leading cause of cancer-related deaths worldwide, necessitating targeted therapeutic strategies. Curcumin, a natural compound, demonstrates anti-cancer properties but is limited by hydrophobicity and low bioavailability. This study develops a pH-responsive core-shell dual-layer chitosan-alginate nanogel (NG) to improve targeted curcumin delivery to the colon. NGs were synthesized using ionic gelation, in which deacetylated chitosan (CS) was cross-linked with sodium tripolyphosphate, incorporating solubilized curcumin. The sodium alginate (SA) outer-layer was applied through electrostatic interactions. Twenty systematic trials optimized solvent composition, pH of initial CS solution, and cross-linking RPM. Encapsulation efficiency (using UV-Vis spectroscopy) improved from 32% to a peak of 90.4% (final mean of 87% ± 2.2%). Structural characterization established successful single and dual-layer NG formation. SEM/TEM imaging showed uniform spherical morphology with diameters of 147 nm (single layer) increasing to 342 nm (dual-layer). Zeta potential reversal from +32.5 to -32.7 mV confirmed SA layering. FTIR verified the interactions among all components, and fluorescent microscopy validated curcumin internalization within the NG matrix. Drug release kinetics at simulated GI tract pHs was conducted for single and dual NGs. Dual-coated NGs achieved a significant 74% curcumin release at colonic pH. Biological validation in Drosophila melanogaster larvae demonstrated increased distal midgut fluorescence when fed dual NG versus single NG and free curcumin. This study establishes that dual-layer chitosan-alginate nanogels markedly improves the stability and targeted delivery of curcumin, increasing the therapeutic potential for CRC.

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