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pH-triggered pectin–silver nanogel as precision vehicle to 5-flourouracil for enhanced oral bioavailability and effective drug release in cancer therapy

A novel pectin hydrogel (Pec-Hgel) and silver nanogel (Pec-Ag-Ngel) material have been synthesized to enhance the bioavailability and therapeutic efficacy of 5-FU against cancer cells for progressive cancer therapy. Several techniques, such as UV-Vis spectroscopy, FT-IR spectroscopy, field-emission scanning electron microscopy (FE-SEM), and Energy dispersion X-ray Spectroscopy (EDX), are used to investigate the physicochemical features of Pec-Hgel and Pec-Ag-Ngel respectively. The synthesized Pec-Ag-Ngel material possess a higher encapsulation efficiency then Pec-Hgel. In-vitro drug release study demonstrates the gels' ability to provide controlled release of 5-FU at pH 2 and pH 5. Pec-Hgel and Pec-Ag-Ngel formulations exhibited excellent hemocompatibility, with hemolysis rates remaining below 5%. 5-FU alone exhibited a hemolysis rate of 17.98%. The cytocompatibility of the drug Pec-Ag-Ngel is assessed, and their in-vitro cytotoxicity is evaluated using the MTT assay on HepG2 cells. The results demonstrate that 5-FU loaded Pec-Ag-Ngel induce significant toxicity HepG2 cells. The LC50 values for 5FU and 5FU-Pec-Ag-Ngel, which were determined to be 0.35 µg/mL and 0.93 µg/mL respectively. This difference suggests that the nanogel formulation provides a controlled and sustained release of 5-FU, resulting in slower cellular uptake compared to the freely available pure compound. Acute oral toxicity studies were conducted on both the free drug and the drug-loaded nanogel formulation to evaluate and compare their in vivo safety profiles. The collective findings confirm the efficacy and suitability of Pec-Ag-Ngel for cancer treatment, underscoring its promise as an effective drug delivery platform. Nanogels, in general, present significant advantages for oral administration, including resistance to gastrointestinal degradation, enhanced solubility, improved absorption, and controlled drug release. This work demonstrates their therapeutic potential in cancer management and positions them as advanced oral nanocarriers in contemporary drug delivery strategies.

Key Words: Pectin Nanogel, HepG2 cells, drug delivery applications, in-vivo toxicity

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