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Title: Optimization and Formulation of Fucoxanthin-Loaded Microsphere (F-LM) Using Response Surface Methodology (RSM) and Analysis of Its Fucoxanthin Release Profile

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Abstract: Fucoxanthin has interesting anticancer activity, but is insoluble in water, hindering its use as a drug. Microencapsulation is used as a technique for improving drug delivery. This study aimed to formulate fucoxanthin-loaded microspheres (F-LM) for anticancer treatment of H1299 cancer cell lines and optimize particle size (PS) and encapsulation efficiency (EE). Using response surface methodology (RSM), a face centered central composite design (FCCCD) was designed with three factors: Polyvinylalcohol (PVA), poly(D,L-lactic-co-glycolic acid) (PLGA), and fucoxanthin concentration. F-LM was produced using a modified double-emulsion solvent evaporation method. The F-LM were characterized for release profile, release kinetics, and degradation pattern. Optimal F-LM PS and EE of 9.18 mu m and 33.09%, respectively, with good surface morphology, were achieved from a 0.5% (w/v) PVA, 6.0% (w/v) PLGA, 200 mu g/mL fucoxanthin formulation at a homogenization speed of 20,500 rpm. PVA concentration was the most significant factor ($p < 0.05$) affecting PS. Meanwhile, EE was significantly affected by interaction between the three factors: PVA, PLGA, and fucoxanthin. In vitro release curve showed fucoxanthin had a high burst release (38.3%) at the first hour, followed by a sustained release stage reaching (79.1%) within 2 months. Release kinetics followed a diffusion pattern predominantly controlled by the Higuchi model. Biodegradability studies based on surface morphology changes on the surface of the F-LM, show that morphology changed within the first hour, and F-LM completely degraded within 2 months. RSM under FCCCD design improved the difference between the lowest and highest responses, with good correlation between observed and predicted values for PS and EE of F-LM.

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