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Design, Optimization and Characterization of Gemcitabine - Loaded Cubosomes for Treatment of Breast Cancer in MCF-7 Cell Lines

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SUMMARY. **Current research work aimed to design, characterize and optimize gemcitabine (GCB) cubosomes for the effective treatment of breast cancer. Cubosomes were developed by using solvent evaporation technique and optimized using 3^2 Factorial design to verify effect vesicle size and entrapment efficiency using poloxamer-407 (P-407) as emulsifier and glyceryl monooleate (GMO) as lipid. The optimized GCB cubosomes were characterized for morphology by transmission electron microscope (TEM), crystalline by X-ray diffraction (XRD), *in vitro* release, *in vitro* cytotoxicity, apoptotic potential, etc. Optimized GCB cubosomes have a mean vesicle size of 184.2±3 nm with PDI 0.230± 0.046, zeta potential -28.1±2.73 mV, and entrapped 94.48± 4.54 % of GCB. Furthermore, the GCB cubosomes demonstrated significantly ($p < 0.01$) higher *in vitro* cytotoxic and apoptotic activity against breast cancer (MCF-7) cells after 48 hr of incubation. Hence, the developed GCB cubosomes can be used as a competent alternative to systemic chemotherapy in the effective management of breast cancer.**

KEY WORDS: apoptosis, breast cancer, cubosomes, cytotoxicity, gemcitabine, Polaxomer-407.

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RESUMEN. El trabajo de investigación actual tiene como objetivo diseñar, caracterizar y optimizar los cubosomas de gemcitabina (GCB) para el tratamiento eficaz del cáncer de mama. Los cubosomas se desarrollaron utilizando la técnica de evaporación de solventes y se optimizaron utilizando un diseño factorial 32 para verificar el tamaño de las vesículas y la eficiencia de atrapamiento utilizando poloxámero-407 (P-407) como emulsionante y monooleato de glicerilo (GMO) como lípido. Los cubosomas GCB optimizados se caracterizaron por morfología mediante microscopio electrónico de transmisión (TEM), cristalino por difracción de rayos X (XRD), liberación *in vitro*, citotoxicidad *in vitro*, potencial apoptótico, etc. Los cubosomas GCB optimizados tienen un tamaño medio de vesícula de 184.2±3 nm con PDI 0.230± 0.046, potencial zeta -28.1±2.73 mV, y atrapado 94.48± 4.54 % de GCB. Además, los cubosomas GCB demostraron una actividad citotóxica y apoptótica *in vitro* significativamente mayor ($p < 0,01$) contra las células de cáncer de mama (MCF-7) después de 48 horas de incubación. Por lo tanto, los cubosomas GCB desarrollados se pueden utilizar como una alternativa competente a la quimioterapia sistémica en el tratamiento eficaz del cáncer de mama.