PREPARATION OF POLYMERIC NANOPARTICLES BASED ON CHITOSAN MODIFIED WITH FOLIC ACID AND LOADED WITH ESSENTIAL OILS FOR THEIR POTENTIAL USE AS NANOCARRIERS OF ANTICANCER AGENTS

Ariadna Irais Gonzalez Nuñez[1], Héctor Iván Meléndez Ortiz[2], Roberto Espinosa Neira[3], Omar Felipe Fabela[4], Jose Manuel Martinez Lopez[5], Rebeca Betancourt Galindo[1]

[1]Centro de Investigación en Química Aplicada, Materiales Avanzados, Mexico. [2]CONAHCyT-CIQA, Materiales Avanzados, Mexico. [3]Centro de Investigación en Química Aplicada, Materiales Avanzados (Laboratorio de cultivo celular), Mexico. [4] CONAHCyT-CIQA, Química Macromolecular y Nanomateriales, Mexico. [5]Química Tech CD. Juárez Chihuahua, Microscopia, Mexico.

In this research, polymeric nanoparticles (NPs) based on folic acid-modified chitosan (CS) were developed as innovative nanocarriers for potential anticancer applications. The focus was on engineering a targeted delivery system that could leverage the overexpression of folate receptors in cancer cells, thus enhancing the selectivity and efficacy of the therapeutic agents. The NPs were synthesized using the ionic gelation method, a technique that allows to control the nanoparticle size. The CS was modified with different percentages of folic acid (10 and 20%), and the obtained NPs were loaded with essential oil of mint (AM) and clove (AC), both known for their therapeutic properties, along with the well-established anticancer drug methotrexate (MTX).

Comprehensive characterization of these NPs was performed using a suite of advanced analytical techniques, including Fourier Transform Infrared Spectroscopy (FTIR) to confirm chemical modifications, Nuclear Magnetic Resonance (NMR) for structural verification, Thermogravimetric Analysis (TGA) and Differential Scanning Calorimetry (DSC) to assess thermal stability, and X-Ray Diffraction (XRD) to understand the crystalline nature of NPs, Dynamic Light Scattering (DLS) for size distribution, and zeta potential analysis to evaluate surface charge and stability. These analyses confirmed stability and suitable physicochemical properties for drug delivery applications.
The nanoparticle formulations were further optimized by adjusting the concentration of sodium tripolyphosphate (TPP), a key crosslinking agent, and varying the amount of EO incorporated during preparation, to achieve optimal size, zeta potential, and encapsulation efficiency.

Cytotoxicity studies were conducted on two cancer cell lines: MDA-MB-231 (breast cancer) and A-549 (lung cancer). The results demonstrated a significant reduction in cell viability when treated with NPs loaded with AM-MTX, indicating the successful delivery and release of the therapeutic agents within the cancer cells. Additionally, fluorescence microscopy confirmed the efficient internalization of the NPs within A-549 cells, further highlighting their potential as effective and selective drug delivery systems tailored for targeted cancer therapy.

Keywords: folic acid-modified chitosan, nanocarriers, polymeric nanoparticles

Acknowledgment:

This work was supported by the Centro de Investigación en Química Aplicada (CIQA) and the Consejo Nacional de Humanidades, Ciencias y Tecnologías (CONAHCYT) (project 6703).

Presenting author's email: ariadna.gonzalez.m22@ciqa.edu.mx