Lipid polymer hybrid nanoparticles: a promising delivery system for siRNA-based gene therapy targeting breast cancer

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Background: Triple-negative breast cancer (TNBC) accounts for more than 15% of breast cancer patients. Despite recent advancements in chemotherapy, 40% of TNBC patients experience metastatic relapse and recurrence [1]. Previous research found that X-Box Protein-1 (XBP1) gene is overexpressed in 90% of breast tumors, including TNBC and responsible for chemoresistance and tumor cell survival [2]. siRNA therapy was developed and explored for genetic disorder and cancer treatment by knockdown the specific gene causing the disease [3]. However, naked siRNAs are negatively charged and hydrophilic in nature, resulting in inherent cytotoxicity to other healthy tissue and undesired changes in genomic processes [4]. Therefore, ideal nanocarriers that can safely deliver the siRNA to tumor sites with minimal side effects are still needed for the best therapeutic outcomes.

Methods and results: We developed siRNA-loaded lipid polymer hybrid nanoparticles using the double emulsion solvent evaporation method. The prepared nanoparticles had a mean particle size of 174.8 nm, a PDI of less than 0.1, and a positive surface charge. The entrapment efficiency of the formulation was determined using Ribogreen assay kit, and results showed that 72% of the siRNA had been encapsulated within the nanoparticles. The surface morphology of nanoparticles was studied using SEM, indicating that prepared nanoparticles are spherical in shape with homogenous size having a smooth surface. Cellular uptake of nanoparticles was studied using confocal microscopy and flow cytometry, which clearly show efficient binding and internalization of nanoparticles into MDA-MB-231 cells in 2 hr. *In-vitro* studies showed that our siRNA-loaded lipid polymer hybrid nanoparticles significantly reduced the expression of XBP1, thereby inhibiting cancer growth.

Conclusion: The current study provides a novel drug carrier that can deliver the siRNA safely to the target site with minimal toxicity, ultimately providing better therapeutic outcomes against cancer.

References

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