**Development Of Olaparib-Loaded Nanomedicine Using Nanoparticle Albumin-BoundTM Technology**

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**Background and aims.** Olaparib, a PARP inhibitor, has demonstrated clinical efficacy in BRCA-mutated breast cancers, including a subset of triple-negative breast cancer (TNBC) patients. However, its broader application in unselected TNBC populations is limited by poor aqueous solubility and suboptimal tumor delivery. This study aims to improve the therapeutic potential of olaparib by developing albumin-bound nanoparticulate formulations using nanoparticle albumin-boundTM (NabTM) technology to enhance drug solubility, stability, and tumor-targeted delivery.

**Methods.** Olaparib-loaded human serum albumin (OLA-HSA) nanoparticles were prepared using a high-pressure homogenization-based NabTM process. A systematic optimization screened injectable plant-based oils and non-ionic surfactants to produce nanoparticles with uniform size, low polydispersity, and suitable zeta potential. Key process parameters included the organic/aqueous phase ratio, HSA concentration, homogenization pressure. The physicochemical characteristics, stability under physiological conditions, and drug release kinetics were evaluated, while in vitro cellular uptake and cytotoxicity assays were conducted in MDA-MB-231 cells.

**Results.** The optimized OLA-HSA nanoparticles exhibited a mean diameter of 108.5 ± 1.1 nm, narrow size distribution (PDI 0.154 ± 0.022), and stable negative zeta potential. Stability was maintained in biologic media at various temperatures, and in vitro release studies revealed controlled olaparib release (~60% over 24 hr at pH 7.4). Nanoparticles displayed superior cellular uptake and induced greater cytotoxicity and apoptosis in MDA-MB-231 cells compared to free olaparib, highlighting improved antitumor efficacy.

**Conclusion/Discussion.** NabTM-based OLA-HSA nanoparticles improve olaparib’s delivery and cytotoxic potency in TNBC models via enhanced solubility, tumor accumulation, and cellular uptake. This nanotechnology-driven approach may offer a promising strategy for advancing PARP inhibitor therapies against TNBC. Further preclinical investigations are warranted to confirm in vivo efficacy.

**References:**

(1) Vysyaraju, N.R. et al. (2022) Journal of Drug Targeting, 1–18

(2) Shrestha, S. et al. (2025) J. Pharm. Investig. 55, 1–14

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