5 Summary and Future Prospects

Breast cancer is a prevalent and aggressive form of cancer affecting women worldwide. In the United States alone, it ranks as the second leading cause of female mortality, with approximately 250,000 new cases identified annually. The development of effective treatments, particularly targeted drug delivery systems, has been a focus of research to minimize non-specific cytotoxicity and improve therapeutic outcomes. Nanomedicine has emerged as a promising avenue for cancer treatment, offering the potential for targeted delivery of therapeutic agents to tumor sites while minimizing systemic side effects. Strategies such as passive and active targeting, along with the incorporation of imaging agents, have been explored to enhance the efficacy of cancer therapies.

One such advancement involves the development of chitosan NPs loaded with PLB, a chemotherapeutic agent used for advanced breast cancer treatment. These NPs are designed to target ER overexpressed breast cancer cells. The inclusion of chitosan, a biodegradable polymer, provides a stable matrix for drug delivery. Surface modification with estrone enhances the specificity of the NPs to ER-positive breast cancer cells. Furthermore, the addition of FA as a targeting moiety in the formulation leads to the development of dual-targeted NPs, capable of targeting both ER and FR overexpressed breast cancer cells. This approach aims to exploit the increased demand for FA in breast tumors, thereby enhancing the specificity of drug delivery. Incorporating UMN into the dual-targeted NPs enables simultaneous imaging and therapy of breast cancer. UMN serves as *in vivo* imaging agent with excellent biocompatibility, allowing for real-time visualization of tumor size, hypoxic regions, and vascularity during therapy.

Physicochemical characterization of the NPs, including particle size, surface charge, and drug entrapment efficiency, confirms their suitability for targeted drug delivery. *In vitro* studies demonstrate selective cellular uptake and cytotoxicity against ER and FR

overexpressed breast cancer cell lines, highlighting the efficacy of the formulations. *In vivo* pharmacokinetic studies in animal models reveal improved drug distribution and safety profiles compared to free drug administration. Histopathological evaluations demonstrate minimal toxicity to vital organs, supporting the biocompatibility of the NPs. Anticancer efficacy studies in breast cancer rat models show significant tumor regression and improved survival rates in animals treated with targeted NPs compared to conventional therapies. Imaging modalities such as ultrasound and photoacoustic imaging confirm the localization and therapeutic response of the NPs within the tumor microenvironment.

Overall, the developed nanomedicine and nanotheranostic NPs represent a significant advancement in breast cancer therapy. Their ability to selectively target ER and FR overexpressed breast cancer cells, coupled with simultaneous imaging capabilities, offers a promising approach for personalized cancer treatment. In conclusion, the integration of targeted drug delivery systems with imaging agents holds great potential for improving the diagnosis and treatment of breast cancer. Further research and clinical trials are warranted to validate these innovative formulations' clinical efficacy and safety in human patients.

Future research should focus on optimizing these single- and dual-targeted systems to improve their stability, biocompatibility, and targeted delivery capabilities. Additionally, incorporating advanced imaging agents such as UMN into these systems offers the potential for simultaneous diagnosis and therapy, enabling real-time monitoring of treatment efficacy and tumor progression. Clinical translation of these nanomedicine systems will require extensive evaluation in preclinical models and human trials to establish their safety, efficacy, and potential for personalized medicine. Furthermore, exploring the combination of these nanotherapeutics with other treatment modalities, such as immunotherapy, could provide synergistic effects and overcome drug resistance.