Formulation and Evaluation of Methotrexate-loaded Polymeric Nanoparticles in Breast Cancer Treatment

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BY

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CHAPTER 7

Summary & Future Scope

7.1 Summary of the work

In summary, Methotrexate (MTX) is an FDA-approved BSC class-IV drug used for breast cancer treatment. However, MTX is associated with various dose-limiting toxicities such as neutropenia, peripheral neuropathy, alopecia, constipation, diarrhea, nausea, and vomiting. To overcome these side effects while maintaining the drug's efficacy, there is a need for suitable carriers.

The successfully developed chitosan nanocarriers as a delivery system to enhance the effectiveness of MTX in breast cancer treatment. The nanocarriers were designed to encapsulate MTX and controlled release at the desired site. Compared to free MTX, the MTX-loaded chitosan nanoparticles demonstrated improved efficacy and reduced toxicity. These nanoparticles possess several advantages, including low toxicity and excellent biocompatibility. Toxicity evaluation using biochemical markers and histological examination indicated the biocompatibility of the nanoparticles. They also offer physical stability and protect labile drugs from degradation. Moreover, the chitosan nanocarriers showed excellent tolerability in the biological system. Further evaluate these MTX-loaded chitosan nanoparticles' pharmacokinetics, bio-distribution, and hemocompatibility. These studies will provide valuable insights into the behavior of the nanocarriers within the body and their interactions with the biological system. Furthermore, the study also focused on developing fluorescent calcium carbonate nanoparticles (@Cal-Nps) for drug delivery applications. @Cal-Nps are known for their

large specific surface area and excellent biocompatibility. However, their facile structure can lead to premature drug release, which requires modification for controlled delivery.

Chitosan (CS) was utilized to surface-functionalize @Cal-Nps through ionic gelation. The CS coating created a barrier that allowed for the controlled release of methotrexate over time. This modification effectively prevented the premature release of MTX from the @Cal-CS-MTX-Nps. The @Cal-CS-MTX-Nps demonstrated good biocompatibility with bioimaging capabilities. Furthermore, in a chemically-induced breast cancer rat model, the nanoparticles exhibited significant inhibition of tumor growth compared to free MTX, indicating their potential as an effective therapeutic approach for breast cancer treatment. They exhibited promising anticancer effects, indicating their potential as a drug delivery system for MTX.

Overall, the findings of this study highlight the potential of the developed chitosan nanocarriers and surface-modified calcium carbonate nanoparticles for enhancing the therapeutic efficacy of MTX in breast cancer treatment. These nanocarriers offer advantages such as improved drug delivery, controlled release properties, enhanced pharmacokinetics, and reduced toxicity.

7.2 Future Scope of the work

Here is a potential outline for a future work plan:

- Conduct large-scale genomic studies to identify any genetic changes related to breast cancer initiation, progression, and metastasis. Utilize next-generation sequencing technologies to analyse the genomic landscape of breast cancer.

- Investigate epigenetic modifications, such as DNA methylation and histone modifications, and their role in breast cancer development and progression.
- Use functional genomics approaches, such as CRISPR/Cas9-based gene editing and RNA interference, to validate the functional significance of identified genetic alterations.
- Investigate the role of altered genes in promoting invasion, metastasis, and drug resistance in breast cancer cells.
- Conduct mechanistic studies to elucidate the molecular pathways and signaling networks affected by genetic alterations.