

Chapter 3

Objectives & Plan of Work

3 Objectives and Plan of Work

3.1 Objectives

Cancer remains a leading cause of mortality worldwide, necessitating the development of advanced therapeutic strategies to improve treatment outcomes. Traditional chemotherapeutics often face challenges such as poor aqueous solubility, limited penetration, and inadequate targeting potential, which hinder their therapeutic efficacy. To address these issues, this study aims to explore a few biopolymer-based targeted drug delivery platforms for more efficient delivery of chemotherapeutics. Here's how:

- Exploiting the role of over-expressed EGFR receptors in facilitating the intracellular delivery of chemotherapeutics selectively to cancer cells
- Leveraging the elevated redox levels in the tumor microenvironment to preferentially release the therapeutic payload in the tumor microenvironment
- Combining the two strategies mentioned above further to enhance the selective and targeted delivery of chemotherapeutics
- Exploring the viability of microneedles in delivering targeted nanoparticles locally to breast tumors

3.2 Plan of Work

3.2.1 Cetuximab functionalized chitosan/hyaluronic acid-based nanoparticles loaded with cabazitaxel for enhancing anti-tumor efficacy in DMBA-induced breast cancer model in rats through spatial targeting

3.2.1.1 Succinylation of D-alpha-tocopheryl succinate polyethylene glycol-1000 (TPGS-1000) to yield a carboxyl terminated molecule

- 3.2.1.2 *Characterization of the Succinylated TPGS-1000*
- 3.2.1.3 *Fabrication of chitosan oligosaccharide and hyaluronic acid-based nanoparticles via ionic gelation*
- 3.2.1.4 *Surface functionalization of the fabricated nanoparticles with Cetuximab*
- 3.2.1.5 *Characterization of the nanoparticles*
- 3.2.1.6 *Development of analytical and bioanalytical methods for estimation of Cabazitaxel using HPLC*
- 3.2.1.7 *Assessment of drug release at various pH*
- 3.2.1.8 *In vitro and in vivo assessment of efficacy and safety*
- 3.2.2 *Cabazitaxel-loaded redox-responsive nanocarrier based on D-alpha-tocopheryl-chitosan and hyaluronic acid loading for improved anti-tumor efficacy in DMBA-induced breast cancer model***
 - 3.2.2.1 *Conjugation of D-alpha-tocopheryl succinate on chitosan oligosaccharide chain to yield an amphiphilic chitosan derivative*
 - 3.2.2.2 *Characterization of the CSVE conjugate*
 - 3.2.2.3 *Fabrication of CSVE and hyaluronic acid-based hybrid nanoparticles crosslinked with DTPA*
 - 3.2.2.4 *Surface functionalization of the fabricated nanoparticles with Cetuximab*
 - 3.2.2.5 *Characterization of the nanoparticles*
 - 3.2.2.6 *Assessment of drug release at various pH and high glutathione concentrations*
 - 3.2.2.7 *In vitro and in vivo assessment of efficacy and safety*

3.2.3 *Hyaluronic acid-oleylamine and chitosan-oleic acid conjugate-based hybrid nanoparticle delivery via. dissolving microneedles for enhanced treatment efficacy in localized breast cancer*

3.2.3.1 *Synthesis of amphiphilic chitosan and hyaluronic acid conjugates with common hydrophobic fragments*

3.2.3.2 *Characterization of the synthesized conjugates*

3.2.3.3 *Fabrication of hyaluronic acid and chitosan-based self-assembled nanocarriers*

3.2.3.4 *Surface functionalization of the fabricated nanoparticles with Cetuximab to target overexpressed EGFR*

3.2.3.5 *Characterization of the nanoparticles and assessment of drug release at various complete it*

3.2.3.6 *In vitro evaluation of efficacy and targetability*

3.2.3.7 *Incorporation of fabricated nanoparticles in dissolving microneedle polymer blend*

3.2.3.8 *Fabrication of microneedle array using micro molding technique*

3.2.3.9 *Characterization of the fabricated microneedle array*

3.2.3.10 *In vivo assessment of efficacy and safety*