INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: Fabrication and evaluation of chemically modified chitosan and silk fibroin derived nanomaterials for anti-cancer agents

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SHORT ABSTRACT

The thesis is compiled into seven chapters, which comprises the introduction, review of literature, experimental findings, a summary of the work and future prospects.

Chapter 1 presents a brief introduction to the design and development of anti-cancer drug delivery systems based on biopolymers and their modified materials. It also showcases a brief review of biopolymer derived structures, including covalently conjugated systems, nanoparticles, and microparticles.

Chapter 2 presents the development of a photocleavable nanocarrier system where 5-fluorouracil (5-FU) is covalently conjugated to low molecular weight chitosan (LMWC) *via* a photocleavable linker. The conjugate was designed to be cleaved explicitly under UV-A radiations of wavelength 365 nm and release the drug in a dose-dependent manner. The conjugate was found to form hydrogel and organogel. The modified biopolymer was also fabricated into nanoparticles by ionic gelation technique for better cell penetration. The drug release study from the nanoparticles was done by irradiating it under a light of wavelength 365 nm.

Chapter 3 presents a method for antiproliferation of the cancer cells using a combination of 5-fluorocytosine (5-FC) loaded silver nanoparticles (AgNPs) prodrug and a non-mammalian enzyme Cytosine Deaminase (CD). 5-FC and 5-FU loaded AgNPs were synthesized using a green synthesis protocol using LMWC as the reducing and the stabilizing agent, and nanoparticles with size less than 25 nm were formed. CD activity study showed, it effectively hydrolyzes prodrug 5-FC in 5-FC loaded nanoparticles into 5-FU (active drug) but was inert to

blank nanoparticles and 5-FU loaded nanoparticles, thus proving its efficiency and specificity. The investigation in MDA-MB-468 cell lines manifested potent cytotoxicity for 5-FU nanoparticles compared to the 5-FC loaded nanoparticles without CD, thus showing the prodrug nature of 5-FC loaded nanoparticles.

Chapter 4 presents the synthesis of gold nanoparticles using LMWC, loaded with a model anti-cancer drug, doxorubicin (DOX), which was further coated with folic acid (FA) and fluorescein (FL) conjugated silk fibroin (SF). The SF coating helps in the sustained release of the drug and provides a binding domain for FA attachment to facilitate cell-targeting. The drug release from both the coated and uncoated nanoparticles was studied, where the coated one showed slow and sustained release compared to the uncoated ones. The cytotoxicity of coated nanoparticles in HeLa cell lines showed a maximum dose-dependent decrease in cell viability than the uncoated ones. The cellular uptake of coated and uncoated nanoparticles, as studied by confocal microscopy, showed increased uptake efficacy of the coated nanoparticles by the cells.

Chapter 5 presents the formulation of microparticles/beads from the synthesized DOX loaded gold nanoparticles in the previous chapter. Here, the beads were coated with FL coated SF for sustained drug release. The beads were synthesized by the ionic gelation technique using TPP, as the cross-linking agent. The drug release study from the coated beads showed slow and sustained release compared to the uncoated ones.

Chapter 6 presents the synthesis of biotin conjugated LMWC-SF based carbon dots (CS-dots) for targeted delivery of anti-cancer drugs and cell imaging. 5-FU is loaded to the conjugate as the model anti-cancer drug. LMWC and SF based Cdots possess a large number of free amino groups that can be utilized for functionalization. The LMWC-SF mixture based Cdots were 3±1.5 nm sized and showed increased fluorescence intensity and relative quantum yield compared to the pure LMWC and SF based Cdots. Biotin covalently conjugated to the free amino group of Cdots can provide target specificity to the nanocarrier.

Chapter 7 consists of the summary and the future prospects of the thesis work.