INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study	:	Ph.D.

Thesis Title:
Designing Nano-Therapeutic Carrier Embedded Multifunctional Injectable Silk Hydrogels for Localized Targeted Cancer Treatment

Name of Thesis Supervisor(s)	:	Prof. Biman B Mandal
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SHORT ABSTRACT

Cancer is a chronic disease that requires long-term interaction with chemo drugs for efficacious therapeutic effects. Chemotherapy is the most fundamental treatment option as it is prescribed to each cancer patient at some stage of their therapy. However, the conventional systemic (intravenous) route of chemo delivery causes various undesired side effects such as vomiting, infertility, hair loss, anemia, fatigue, weakness, loss of appetite, fertility issues, etc. For cancer therapy, various potential chemotherapeutics have been synthesized so far; however, their inability to discriminate between healthy and cancerous tissue, loss of action in blood serum, and burst release limits their use. Additionally, their delivery is also an issue due to lack of solubility in water.

The current need for an injectable hydrogel system that could on-demand release the anticancer drug post its implantation in a minimally invasive way locally at near/intratumor was the motivation behind this thesis. A thorough literature survey suggested various natural/synthetic nanocomposite smart materials for drug delivery applications. However, these studies were restricted to employ a single external stimulus for spatiotemporally controlled release of drug at the tumor site. Also, the use of synthetic materials in these studies may produce toxic by-

products on their degradation. These limitations have opened a considerable scope to develop a natural silk based nanocomposite smart material that would be responsive to multiple stimuli and produce nontoxic, resorbable by-products on their degradation. This system could also provide the flexibility to select and embed various types of anticancer drug-loaded nanoparticles for the therapy of different kinds of cancer. Moreover, there is no 3D culture system available that can be used to accurately study the interaction/functionality of biomolecule releasing out from injectable hydrogel with cancer cells. This further leads to the design of a scaffold prototype that can support the growth of the cancer cells and provide a space for the injectable hydrogels at the same time to study the long term interaction between cells and the hydrogel.

Overall, the thesis dealt with the preparation, modification, and characterization of two types of nanoparticles (carbon nanotube and *B. mori* silk fibroin nanoparticle) and silk based injectable hydrogel. The nanoparticles were loaded with anticancer drugs (doxorubicin or cisplatin) before embedding them into silk hydrogel. The resultant nanocomposite silk hydrogel was studied for sustained and on-demand drug release. The functional assessment of therapeutics release was conducted by *in vitro* biological tests (both 2D and 3D) using three types of cancer cells: oral cancer, lung cancer, and stomach cancer. Moreover, one nanocomposite hydrogel with excellent properties (SWCNT-FA/DOX loaded silk hydrogel) was assessed further *in vivo* for small animal tumor regression studies. The hydrogel formulation showed drastic tumor regression in the mice model at a very shallow dose without requiring multiple cycles of injections.