INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	ARMAN MOHANTY
Roll Number	:	176106018
Programme of Study	:	Ph.D.

Thesis Title: Understanding the mechanism of action of cytochalasin D against TNBC cell line MDA-MB-231 and a nano-carrier based drug delivery system

Name of Thesis Supervisor(s)	:	Prof. Gurvinder Kaur Saini
Thesis Submitted to the Department	:	Biosciences and Bioengineering
Date of completion of Thesis Viva-Voce Exam	:	23/01/2025
Key words for description of Thesis Work	:	Cytochalasin D, MDA-MB-231, PLGA nanoparticles, Network pharmacology, MAPK signaling pathway, Apoptosis

SHORT ABSTRACT

Breast cancer remains a leading cause of mortality among women worldwide, with triple-negative breast cancer (TNBC) being one of the most aggressive subtypes. This thesis explores the therapeutic potential of cytochalasin D, a fungal secondary metabolite, against the TNBC cell line MDA-MB-231. The study employs a combination of network pharmacology, in vitro assays, and nano-carrier-based drug delivery systems to elucidate the mechanism of action and enhance the efficacy of cytochalasin D. Chapter 3 covers the *in-silico* approaches used to identify 278 potential protein targets of cytochalasin D using databases like DrugBank, BindingDB, and SwissTargetPrediction. The key pathways involved include the MAPK signaling pathway, PI3K-Akt signaling pathway, and pathways related to cancer and neurodegeneration. Molecular docking and MD simulations revealed stable interactions between cytochalasin D and MAPK family proteins (MAPK1, MAPK3, MAPK8, and MAPK14). Chapter 4 covers the *in vitro* therapeutic effects of cytochalasin D. Cytochalasin D exhibited significant cytotoxicity against MDA-MB-231 cells with an IC50 of 28.9 µg/mL. The compound also induced S-phase cell cycle arrest and inhibited cell migration. Depolarization of mitochondrial membrane due to elevated ROS levels and activation of caspase 8, hints apoptosis induction. Chapter 5 deals with the encapsulation of cytochalasin D in a suitable PLGA nanocarrier and further assays with the loaded nanoparticles. Developed cytochalasin D-loaded PLGA nanoparticles (NPs) had an average size of 54±21 nm and an entrapment efficiency of 60%. *In vitro* release studies showed a burst release in acidic conditions and sustained release in neutral pH. Cytochalasin D-loaded NPs demonstrated significant cytotoxicity with an IC50 of 1.056 mg/mL and increased ROS generation in MDA-MB-231 cells. To conclude, the study highlights the potential of cytochalasin D as a therapeutic agent for TNBC by targeting the MAPK signaling pathway and inducing apoptosis. The use of PLGA nanoparticles enhances the delivery and efficacy of cytochalasin D, making it a promising candidate for further preclinical and clinical development.