Abstract

Nearly one million cases of gastric cancer are diagnosed annually, making it the fourth most common cancer worldwide. It is also the second leading cause of cancer-related deaths, with approximately 700,000 fatalities each year. There is lack of early symptoms leading to delays diagnosis of gastric cancer, resulting in a five-year survival rate of just 15%.

Since 1994, *Helicobacter pylori* (*H. pylori*) has been perceived as a type I carcinogen for gastric cancer and is now observed as the most prominent etiologic source for cancer linked with infection, contributing to 5.5% of the cancer burden globally and 25% of all infection-associated cancers. *H. pylori* is responsible for 70-85% of gastric ulcers and 90-95% of duodenal ulcers. Nearly half of the world's population is having *H. pylori* infection, and while most infected individuals develop chronic inflammation, many do not exhibit any symptoms.

This work aimed towards developing a technology using a non-pathogenic strain of *H. pylori* coated with Iron-Oxide Nanoparticles (IONPs) to specifically target gastric cancer. The approach leverages hyperthermia-induced activation of the body's natural immune system. Given that *H. pylori* naturally infect the human stomach and duodenum, it can effectively deliver treatment to these tissues. IONPs serve as MRI sensitizers, allowing for the visualization of infected tissues, and they are responsive to Magnetic hyperthermia. After applying external high-frequency magnetic field, IONPs generate heat on the surface of the bacteria. This ruptures the bacterial membrane and in turn, spillage occurs in the tumor microenvironment, thereby activating the natural immunity. Further, this leads to the infiltration of immune cells like macrophages in the tumor microenvironment. These activated macrophages then cleanse the spillage along with the tumor cells. This proposed cancer treatment does not involve chemotherapeutic drugs, thereby avoiding the unsolicited aftereffects linked with chemotherapy.

The thesis entitled **"Iron-oxide Nanoparticles Coated on *Helicobacter pylori* for Gastric Cancer Treatment *via* Magnetic Hyperthermia"** represents the findings of the study and it is arranged into 5 chapters:

Chapter 1 gives a comprehensive introduction to gastric cancer and explores the existing literature on the subject, with a particular focus on the therapeutic approach of magnetic hyperthermia. This

chapter outlines the background, significance, and current understanding of gastric cancer, followed by a detailed review of studies and advancements linked with the utilization of magnetic hyperthermia for treating cancer.

Chapter 2 deals with the discussion of different kinds of terpenes derived from plants and their potential applications in gastric cancer treatment

Chapter 3 addresses protein-based iron oxide nanoparticles. This formulation aims to achieve targeted delivery of lactoferrin conjugated with iron oxide nanoparticles (LF-IONPs) to gastric tissue. When combined with hyperthermia, it is expected to offer enhanced efficacy in the treatment of gastric cancer.

Chapter 4 delves into the idea of immune activation through hyperthermia-treated *Helicobacter pylori* coated with iron oxide nanoparticles. It examines how this method employs the bacterium as a vehicle to deliver heat-sensitive therapeutic agents to a specific site in the body, with the goal of triggering the immune system to potentially achieve therapeutic effects.

Chapter 5 discusses a terpene-based nanoformulation involving artemisinin-loaded iron oxide nanoparticles. It explores the concept that delivering artemisinin conjugated with magnetic nanoparticles (ART-MNPs) into the gastric tissue, followed by hyperthermia treatment, could increase the effectiveness of gastric cancer therapy by overcoming tumor cell resistance to hyperthermia.

Chapter 6 summarizes the key findings, addressing how the research objectives were met and highlighting the study's contributions and limitations. It also outlines potential future research directions, suggesting areas for further exploration and practical applications of the findings to advance the field.