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Nanoparticle-enhanced postbiotics: Revolutionizing cancer therapy through effective delivery

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ABSTRACT

Aim: Gastric cancer contributes to cancer-related fatalities. Conventional chemotherapy faces challenges due to severe adverse effects, prompting recent research to focus on postbiotics, which are safer biomolecules derived from nonviable probiotics. Despite promising *in vitro* results, efficient *in vivo* delivery systems remain a challenge. This study aimed to design a potential nanoparticle (NP) formulation encapsulating the *Lacticaseibacillus paracasei* GMNL-133 (SGMNL-133) isolate to enhance its therapeutic efficacy in treating gastric cancer.
Main methods: We successfully isolated GMNL-133 (SGMNL-133) by optimizing the lysate extraction and column elution processes for L. *paracasei* GMNL-133, resulting in substantial enhancement of its capacity to inhibit the proliferation of gastric cancer cells. Additionally, we developed a potential NP utilizing arginine-chitosan and fucoidan encapsulating SGMNL-133.
Key findings: This innovative approach protected the SGMNL-133 from degradation by gastric acid, facilitated its penetration through the mucus layer, and enabled interaction with gastric cancer cells. Furthermore, *in vivo* experiments demonstrated that the encapsulation of SGMNL-133 in NPs significantly enhanced its efficacy in the treatment of orthotopic gastric tumors while simultaneously reducing tissue inflammation levels.
Significance: Recent research highlights postbiotics as a safe alternative, but *in vivo* delivery remains a challenge. Our study optimized the extraction of the lysate and column elution of GMNL-133, yielding SGMNL-133. We also developed NPs to protect SGMNL-133 from gastric acid, enhance mucus penetration, and improve the interaction with gastric cancer cells. This combination significantly enhanced drug delivery and anti-gastric tumor activity.

1. Introduction

Cancer of the gastric tract is a major global health concern and ranks fourth among the main causes of cancer-related mortality [1–3]. Its prevalence and poor prognosis continue to present substantial challenges in the realm of public health. Clinical strategies to address gastric cancer can be broadly categorized into three primary modalities: surgical resection, radiation therapy, and chemotherapy [4]. First-line chemotherapy typically uses combination regimens that incorporate fluoropyrimidine and platinum-based agents. However, the effectiveness of chemotherapy is often compromised by adverse side effects, which can include challenges in precise tumor targeting and systemic toxicity [5–7]. According to previous research, probiotics have demonstrated pro-apoptotic or antiproliferative effects against several cancer cells, including colon, gastric, breast, cervical, and myeloid leukemia cells. Their preventive and therapeutic potential in cancer management has been substantiated through various mechanisms, including modulation of the gut microbiota, degradation of potential carcinogens, and

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