International Journal of New Findings in Health and Educational Sciences (IJHES)
ISSN 2980-0641
DOI: 10.63053/ijhes.123

Overview of Bacteria and Surfactins as Anticancer Agents

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ARTICLE INFO

Keywords:
Bacteria, Treatment, Cancer, Tumor, Surfactin

ABSTRACT

Cancer is one of the deadliest diseases worldwide. Late diagnosis of this disease leads to high mortality rates. Conventional treatments such as chemotherapy and radiation therapy have low survival rates. Bacteria are utilized in various ways in cancer treatment, primarily through their antitumor effects. Surfactins are recognized as anticancer agents; these surfactins are cyclic lipopeptides isolated from various Bacillus strains. The cytotoxic activities of surfactins against human chronic myelogenous leukemia cells, human colorectal cancer cells, and liver cancer cells are well-documented. Surfactins are targeted to cancer cells via nanocarriers or nanoformulations. The biosynthesis of surfactins is regulated by surfactin synthetase enzymes. These results position bacterial therapy as a promising treatment for cancer.

Introduction

The resistance to anticancer therapies in patients with advanced solid tumors highlights the need for new treatments. In an ideal treatment, cancer cells would be eradicated with minimal side effects. Bacteria are utilized in cancer treatment in various ways, either through direct antitumor effects or by delivering agents that have such effects. There are two methods for using bacteria as vectors: tumor-specific bacterial replication and intracellular plasmid delivery. Bacterial toxins act by killing cells and altering cellular processes that regulate proliferation, apoptosis, and differentiation associated with cancer. Another form of bacterial application is spores, which are highly resistant bacterial forms. Another application of bacteria is in the form of DNA vaccines, which engage the immune system against cancer cells by presenting tumor antigens (Siegel et al.2018).

2. Methodology:

To find relevant materials for the current study, keywords such as Bacteria, Treatment, Cancer, Tumor, Surfactin. were searched in databases like Science Direct, PubMed, Google Scholar, SID, and ELSEVIER. After reviewing the existing studies, approximately 45 articles were selected for examination. Following the removal of duplicates and screening, a total of 40 articles were reviewed as the most relevant. After eliminating duplicates, 37 articles remained for abstract and title review. Subsequently, 2 articles were discarded due to insufficient relevance and inadequate information. Ultimately, 35 of the most relevant articles were accepted and utilized after thorough screening and full-text review.

3. Findings:

Bacterial therapy refers to the therapeutic use of bacteria to treat diseases. Bacterial treatments involve live drugs, which may take the form of wild-type bacteria (often in the form of probiotics) or bacteria that have been genetically engineered to possess therapeutic properties administered to patients. Other examples of live drugs include cellular therapies (including immunotherapy) and phage therapy (Siegel et al.2019).

Biosurfactants are a class of organic molecules with surface activity produced by various microbes, utilized in various biomedical applications. Surfactin is a cyclic lipopeptide produced by Bacillus strains, which induces cytotoxicity against many types of cancers, including ascites, leukemia, hepatoma, breast cancer, and colorectal cancer. Surfactin treatment can prevent cancer progression by inhibiting growth, stopping the cell cycle, inducing apoptosis, and halting metastasis (Chauhan et al.2025).

Types of Bacterial Applications in Cancer Treatment:

1.Gene Therapy Vectors:

Gene delivery systems can be divided into two groups: non-biological (chemical and physical methods for delivering plasmid DNA to mammalian cells) and biological (viruses and bacteria). Similar to viruses, the inherent biological characteristics of bacteria allow for efficient DNA delivery to cells or tissues, but they are preferred over viral methods due to safety concerns. Currently (Marie & Scherman.2024).

CAR T-Cell Therapy:

CAR T-cells are chimeric antigen receptor T-cells that fight infections and diseases, modified in the laboratory to target and combat cancer. The goal of CAR T-cell therapy is to redesign our immune system to identify and eliminate cancer cells. These therapies hold promise for cancer treatment, with ongoing clinical trials aimed at developing additional CAR T-cell gene therapy products to target various cancers, including leukemia, lymphoma, lung, breast, and ovarian cancers in adults, as well as cancers in pediatric populations and other genetic disorders, such as severe combined immunodeficiency.

With the broader availability of this form of therapy, the diagnosis of interference from CAR T-cell products with HIV-1 NAAT testing in these patients is increasing (Hayati et al.2025).

2.Tumor-Specific Bacterial Replication:

An ideal antitumor treatment aims for selective tumor elimination with minimal negative effects on normal cells. Achieving this goal requires a thorough understanding of the characteristics that distinguish cancer cells from normal tissue. Initially, tumor-specific replication relates to the hypoxic nature of solid tumors. Necrotic regions provide nutrients such as purines and suitable conditions for the growth of anaerobic bacteria. Bacterial chemotaxis toward substances in necrotic areas, such as aspartate, serine, citrate, ribose, and galactose produced by cancer cells, has been observed (Curtis.2024).

3.Intracellular Plasmid Delivery:

The transfer of plasmid DNA into mammalian cells mediated by bacteria is a powerful tool for expressing heterologous proteins in various cells. The transfer of genetic material occurs through the complete entry of bacteria into target cells. Various bacteria, including *Salmonella*, *Listeria*, and *Escherichia coli*, have been studied for this purpose. Bacterial species used are categorized based on their location within the host cell: one group resides in the cytoplasm (*Listeria, Shigella*), another in vacuoles (*Salmonella*, *Yersinia*), and another in the extracellular space (*Agrobacterium*). Additionally, one common method for using bacteria as vectors involves targeted gene expression regulation in cancer cells. Gene expression is regulated at various levels, but transcriptional regulation is typically dominant. SLPI, a serine protease inhibitor, is significantly regulated at the transcriptional level, making its promoter a suitable candidate for targeted gene expression in lung cancer through bacterial plasmid application (Bai et al.2024)(Hirschhorn & Sarver.2021).

Drug Delivery:

Targeted drug delivery involves activities that lead to the accumulation of therapeutic agents in a specific area of the body. The primary advantage of targeted drug delivery is to enhance the therapeutic effects of drugs without inducing side effects on organelles, tissues, or healthy cells. Engineered microorganisms have the potential to function as biological thermostats, producing therapeutic agents only in response to demand. The use of genetically modified organisms (GMOs) is expected to become more widely accepted in medicine, especially for treating antibiotic resistance, cancer, and currently untreatable diseases. Furthermore, significant research is currently underway to explore the use of bacteria for drug delivery, showing promising results in both preclinical and clinical settings (Hayati. Denmark et al.2024).

4. Bacterial Toxins and Cancer Treatment:

The range of toxins produced by bacteria is extensive, including *tetanus, botulinum*, and *diphtheria* toxins. Cancer treatment with toxins can interfere with proliferation or, at lower levels, disrupt processes controlling proliferation, apoptosis, and differentiation. Bacterial toxins that invert the cell cycle are classified as cyclomodulins. Bacterial toxins act on cancer cells through two methods (Kamruzzaman et al.2021).

A. Tumor Surface Antigen-Binding Bacterial Toxins:

Diphtheria toxin (DT) binds to the surface of cells expressing EGF-HB precursor and enters via clathrin-mediated endocytosis. After several post-translational modifications, it becomes catalytically active, ultimately inhibiting protein synthesis, lysing cells, and inducing apoptosis (Trivanović et al.2021).

B. Ligand-Conjugated Bacterial Toxins:

Protein toxins such as pseudomonas exotoxin, diphtheria toxin, and ricin are highly lethal in cancer treatment. However, these toxins require specific binding sites on the surface of cancer cells for effective treatment. This issue can be resolved

by removing the receptor-binding portion of the toxin and conjugating it with monoclonal antibodies and growth factors that bind to cancer cells (Ijaz et al.2024).

5. Bacterial Spores in Cancer Treatment:

Most anaerobic bacteria exist as resistant spores in oxygen-rich conditions, although they lack the ability to grow and multiply. However, when placed in suitable conditions, such as necrotic regions within tumors, spores can germinate and grow. This spore characteristic enables targeted cancer treatment. Spores from genetically modified strains of *C. novyi-NT*, which lack lethal toxins and have targeted functions without side effects on normal cells, have shown significant tumor lysis in mice receiving *Clostridium histolyticum* spores via intratumoral injection and in mice receiving intravenous injections of *Clostridium* perfringens spores (Ahmed et al.2024).

6. Bacteria as Immune Agents:

Utilizing the immune system in cancer treatment is a promising approach. This therapeutic system involves stimulating the immune system to destroy cancer cells. The primary challenge of this method is the tumor's ability to evade the immune system and establish tolerance, as well as its weak immunogenicity. In some cases, the body perceives tumor antigens as self, prompting the use of bacteria to enhance the immunogenicity of cancer cells (Kwon et al.2024).

7. Bacteria and Cancer Diagnosis:

The ability to identify the location of colonizing bacteria is clinically significant, as it allows for the detection of obscure and metastatic tumors. Four strategies—bioluminescence (Mali.2024), fluorescence (Li et al.2024), magnetic resonance, and positron emission tomography (Udovicich et al.2024)—are employed to identify bacteria in tumors.

Surfactins:

Surfactins as Anticancer Agents:

Surfactins are cyclic lipopeptides isolated from various *Bacillus* strains. They are composed of heptapeptides and β-hydroxy fatty acids with variable carbon chain lengths. Therapeutically, they are known to inhibit the invasion, migration, and colony formation of human breast cancer cells. Surfactins also act as antiproliferative agents against human cancer cells by inducing apoptosis, halting the cell cycle, or suppressing survival signals. Their cytotoxic activity has been recognized against chronic myelogenous leukemia cells, human colorectal cancer cells, and liver cancer cells. Due to their wide range of targets, the molecular effects of surfactins vary across different cancer cells, making them promising candidates for chemotherapy. Surfactins are targeted to cancer cells through nano-carriers or nano-formulations. They are biosurfactants produced by various Bacillus strains during the stationary growth phase to survive under adverse conditions (Walvekar et al.2022).

They are synthesized non-ribosomally in bacterial cells with the help of non-ribosomal peptide synthetase (NRPS) enzymes, which recognize, activate, modify, and link amino acids to produce peptides (Kim et al.2023).

The biosynthesis process of surfactin is regulated by surfactin synthetase enzymes, which consist of four open reading frames: SrfA, SrfB, SrfC, and SrfD. SrfD initiates the first reaction of surfactin biosynthesis, followed by SrfA, SrfB, and SrfD to form seven modules that include twenty-four catalytic domains. Each domain works to incorporate a substrate into the developing heptapeptide chain. The acyl chain enters the peptide backbone through a liposomal reaction. The genes responsible for synthesizing NRPS enzymes are encoded by the Srf operon. Surfactins are amphipathic cyclic lipopeptides composed of heptapeptides and β-hydroxy fatty acids, with a carbonyl end that is esterified to the hydroxyl group of a fatty acid and linked to the terminal amino group of the heptapeptide (Kim et al.2023).

Natural Surfactins:

Isoforms of surfactins are biosynthesized in various *Bacillus* species, including *Bacillus subtilis*, *Bacillus amyloliquefaciens*, *Bacillus licheniformis*, and *Bacillus pumilus*. The standard structure of surfactin consists of a sequence of L-Glu-L-Leu-D-Leu-L-Val-L-Asp-D-Leu-L-Leu, with a β-hydroxy fatty acid containing 13, 14, or 15 carbon atoms. An isoform of surfactin, where L-valine replaces L-leucine at the seventh amino acid in the surfactin peptide chain, is referred to as Val-surfactin (Ijaz et al.2024) (Tank & Pandya.2022).

Another isoform of surfactin, which has L-isoleucine replacing L-valine at the seventh amino acid in the peptide chain, is named Ile-surfactin. In the standard structure of surfactin, aspartic acid is located at position 5, and di-leucine is at positions 3 and 6. However, lichenysin produced by *Bacillus licheniformis* differs from standard surfactin by having glutamine as the first amino acid instead of glutamic acid (Kim et al.2023).

Surfactins also exhibit diversity based on differences in their fatty acid chains. The fatty acid chain length varies from 12 to 17 carbon atoms, particularly at positions 14C and 15C. Fatty acid chain shapes can also differ in isometry, being linear, branched, iso, or ante-iso. Iso forms of fatty acids are found in all odd or even carbon chain lengths, while ante-iso forms are found in uneven carbon chain lengths (Tank & Pandya.2022).

Antiproliferative Properties and Mechanisms of Action of Surfactins on Human Cancer Cells:

Cyclic lipopeptides isolated from marine *Bacillus circulans* 2DMS- exhibit significant antiproliferative activity against human colorectal cancer cell lines 15HCT- and 29HT-. Biosurfactants produced by the fungus SK80 dermatitidis (*Dematiaceous Exophiala*) show antiproliferative activity against cervical cancer cells (Hella) and leukemia cells (937U). Growth inhibition of human breast cancer cells (7MCF-) was observed in a dose-dependent manner when treated with three isoforms of surfactin isolated from cultures of *Bacillus subtilis* strain *191CSY*(Kim et al.2021).

Cyclic lipopeptide Bacilomycin D produced by *Bacillus amyloliquefaciens* fiply 3A inhibits human cancer cell lines such as alveolar *adenocarcinoma* (549A), renal carcinoma (498A), and colon adenocarcinoma (HCT)-15 by inducing apoptosis. Pseudofactin II (PFII), a cyclic lipopeptide biosurfactant isolated from the polar strain *Pseudomonas fluorescens*, has the ability to induce apoptosis in melanoma cells (375A). Biosurfactants produced by *Bacillus safensis* 4 exhibit antitumor activity against breast cancer cells (T 47D) and mouse melanoma cells (10B16BF) (Kim et al.2021).

Five surfactin isoforms isolated from *Bacillus pumilus* strain 1HY have the potential to inhibit the proliferation of cancer cell lines (7MCF- and 2Caco-). Surfactins act by activating extracellular-related protein kinases and phosphoinositide-3-kinase or Akt to halt the cell cycle and induce pre-apoptotic processes in human colorectal cancer cells (LoVo) (Kim et al.2021)(Tank & Pandya.2022).

Bacteria as Antitumor Agents:

Human tumors are characterized by hypoxic, apoptotic, or dormant physiological conditions, which hinder the easy access of conventional drugs. Radiation therapy, which induces DNA damage through oxygen-dependent radicals, becomes ineffective in the hypoxic conditions prevailing in tumors. Initial evidence of temporary improvement in cancer patients following bacterial infections dates back to 1867. Researchers developing strategies to circumvent these challenges have been captivated by bacteria's ability to fill the human body and grow anaerobically, including within tumors. Possible mechanisms for controlling bacterial accumulation in tumors include: 1) entrapment in blood vessels, 2) entry into tumors following an inflammatory response, and 3) chemotactic attraction toward compounds. Given that cancer patients often have immune deficiencies, the tumor environment is conducive to the growth of bacteria that would otherwise be eliminated by macrophages and neutrophils. Coordinated studies have shown that certain bacteria can be utilized as anticancer agents (Mahdavi et al.2022).

***Clostridium*:**

Clostridium spp., including *C. novyi* and *C. sordellii*, are anaerobic and highly mobile, capable of rapidly and widely

disseminating in tumor areas with poor vascularization. Genetically modified *C. novyi* spores germinate effectively in avascular tumor regions and can efficiently eradicate tumors in mice. Non-toxic genetically modified *C. novyi* can produce redox proteins and secrete lipases even in a vegetative state, allowing the bacteria to survive exclusively in tumors. Furthermore, *C. novyi* induces tumor cell death by producing reactive oxygen species (ROS) (Xu et al.2023).

***Salmonella*:**

Salmonella, particularly the strain *S. typhimurium VNP 20009*, selectively targets tumor tissues in mice, leading to significant tumor reduction or elimination. *Salmonella* species are attracted to tumors via serine, aspartate, and ribose and can grow in the presence of nutrients from dying tumor cells, as observed in animal models. *S. enterica* has endogenous promoters, pflE and ansB, that are explicitly activated in human prostate tumors (3PC) and in tumor-free nude mice. *Salmonella* colonization in tumors induces an immune response, resulting in increased blood influx into tumors and elevated concentrations of tumor necrosis factor (TNF), which can disrupt antitumor activity (Badie et al.2021).

***Lactobacillus*:**

These bacteria are commonly found in fermented dairy products (such as yogurt and kefir). Species like *Lactobacillus acidophilus* and *Lactobacillus casei* can produce bioactive compounds such as bacteriocins and lactic acid. They can inhibit the growth of cancer cells by reducing the activity of carcinogenic enzymes in the gut, such as β-glucuronidase, and stimulating the immune system to recognize and eliminate cancer cells. Research has shown that *Lactobacillus* species can reduce the incidence of colorectal and stomach cancers (Garbacz.2022).

The use of probiotics has been investigated beyond the gastrointestinal tract, showing promising results in immune function, skin diseases, diabetes, cancer, liver diseases, hypertension, urogenital systems, and oral health. Overall, probiotics appear to be a promising and safe treatment; however, extensive studies are needed to establish their use as alternative therapies alongside conventional treatments (Hayati& Sadeghi.2022).

***Bifidobacterium*:**

Systematic screening of *Bifidobacterium* species has been conducted to expand the limitations of chemotherapy efficacy. Since this bacterium targets an anaerobic environment rather than specific tumor receptors, it can reach solid tumors in various tissues and locations. *Bifidobacterium bifidum* conjugated with folic acid can bind to their respective tumor receptors and serve as a means to deliver nanocrystals or quantum dots deep into tumor tissues. Using a similar approach, *Bifidobacterium* breve and *Clostridium difficile* have been designed as delivery systems for executing nanorods for imaging and tumor ablation (Faghfoori et al.2021).

The therapeutic effect of recombinant B. breve expressing IL-24 in head and neck tumor grafts in mice has been observed, indicating enhanced tumor growth inhibition and apoptosis induction. Despite the complexities of genetically modifying *Bifidobacterium*, a unique *Bifidobacterium* expression system (BEST) has been developed to enable the production and delivery of heterologous proteins to mucosal surfaces. Its functionality was confirmed by simulating 10IL- in mice, with a sevenfold increase in IL-10 secretion (Faghfoori et al.2021).

A newer approach, using high-intensity focused ultrasound (HIFU) for non-invasive cancer cell ablation, has been limited to preserving energy at low concentrations and short durations. The therapeutic efficacy of HIFU synergy has been enhanced using lipid nanoparticles attached to *Bifidobacterium* through electrostatic adsorption (Faghfoori et al.2021).

Bifidobacteria and *Lactobacillus* species have been identified as protective probiotics against the spread of colorectal cancer. It has been established that various bacterial species generally contribute to colorectal cancers, and the metabolism of certain food substances increases these tumors. Probiotics appear to prevent colorectal cancer through at least two mechanisms: (Hayati. BIOMEDICINE.2024).

Production of Protective Metabolites:

Butyrate, a common end product in the fermentation process, is recognized as a cancer-preventive agent. Therefore, it is generally believed that increasing butyrate levels in the colon is beneficial. However, it should be noted that *Lactobacillus* and *Bifidobacterium* do not produce butyrate. Butyrate producers in the colon are Clostridia and Eubacteria, and the proliferation of probiotics that enhance beneficial Eubacteria does not affect toxic *Clostridia*. (Hayati. BIOMEDICINE.2024).

Alteration of Gut Metabolism:

Distinct from lipid and protein metabolism, probiotics may create more beneficial end products due to changes in the bacterial metabolism of the colon. It is believed that lactic acid bacteria have inhibitory effects on various bacteria that produce carcinogenic enzymes (Hayati. BIOMEDICINE.2024).

Escherichia coli:

E. coli, expressing both LLO and the Wilms tumor gene 1 (WT1), an antigen associated with most adult leukemias, exhibits a strong antitumor effect against WT1-expressing tumors. The injection of the peptide NAPYLPSCL with *E. coli LLO* has been effective as an antitumor agent. The anticancer properties of *E. coli* strains 12K and DH5A have been evaluated, and they can be easily genetically modified and utilized (Nakkarach et al.2021).

***Actinobacteria*:**

The bioactive molecules produced by *Salinospora* and *Monashia flava*, *Microbacterium* mangrovi, have been studied for their anticancer properties against human cervical cancer *cells* (Hozzein et al.2021).

***Listeria*:**

Weak attenuated vaccines based on *L. monocytogenes (LM)* have demonstrated efficacy against F10 B16 melanomas and metastatic breast cancer. It has been shown that the short *LLO* expressed by *LM* and fragments of tumor-associated antigens (TAA) induce tumor cell death through elevated levels of reactive oxygen species (ROS). The activation of CD8 T cells by *Listeria*-derived antigens significantly reduces metastases in younger ages. The highly attenuated Listeria vector, LmddA, expressing the chimeric gene (neu2/Her2) (ChHer), effectively reduces immune tolerance, while the highly attenuated structure DXS-164-31 delays tumor growth in neu2/Her transgenic animals (Yu et al.2023).

***Lactococcus*:**

Bioactive compounds such as phenazine, isolated from *Lactococcus* species, have shown strong antifungal properties against *Aspergillus niger*, *Penicillium chrysogenum*, and *Fusarium oxysporum*. These compounds exhibit selective cytotoxicity against HeLa and 7MCF- cancer cell lines, with IC50 values of 24 and 20 micrograms per milliliter, respectively. It has been reported that phenazines act by interfering with topoisomerase I and II in cancer cells (Mahmoudi et al.2023).

Bacteriocins:

Eukaryotic hosts can sense pathogen invasion and activate defensive mechanisms. Free microbes produce toxins and antibacterial agents to attack other cells or resist antibacterial agents without estimating the extent of their attack. However, pathogenic microbes must evade host attacks and understand the host's ability to resist their invasion. At this stage, microbes only mount their counter-defenses after assessing the level of attack by the host immune system. This microbial mechanism

for communication and activation of specific virulence genes is known as quorum sensing (QS). In QS, these signaling molecules form a complex with receptors to transcribe virulence genes. To exploit QS and selectively kill tumor cells, bacteria that can target, attack, and effectively lyse tumor cells should be utilized. These organisms can be modified as improved anticancer agents that overcome the limitations of current cancer therapies. Natural toxins produced by QS can be used for cancer treatment. Bacteriocins such as colicin, nisin, pediocin, and pyocin produced by *Klebsiella*, *Pediococcus*, *Lactobacillus*, and *Pseudomonas* are biodegradable, non-immunogenic, and exhibit specific toxicity against cancer cells. Bacterial toxins like cytolysin A (ClyA) from E. coli strain 12K create pores in mammalian cell membranes and induce apoptosis. Various cytotoxic cytokines have been tested as treatments, including TRAIL, FAS ligand, and TNFα, all of which have shown efficacy against a range of cancers, including lung, breast, pancreatic, colorectal, prostate, bladder, kidney, brain, and ovarian cancers (Goh et al.2022)(Niamah et al.2024).

Microbiota:

A diverse range of bacteria exists in the human gut. Many gut bacterial communities are dysbiotic in various diseases, including colorectal cancer. *Helicobacter pylori* is widely recognized as a lethal infectious agent. However, it can also act as an anticancer agent, although its mechanism remains unknown. In eubiosis, the microbiota contributes to homeostasis through two mechanisms: a) the production of metabolites such as short-chain fatty acids (SCFAs), and b) participation in immune responses. Recently, two SCFA-producing strains in the gut microbiota, *Faecalibaculum rodentium* and *Holdemanella biformis*, have been reported to exhibit antitumor effects by inhibiting the activation of NFATc3 and calcineurin 1. The gut microbiota can also be utilized to overcome hypoxic conditions, promote invasion, and stimulate the innate immune system, thereby enhancing their efficacy as anticancer agents. The gut microbiome and human breast tissue are exposed to many infectious bacteria, including *Pseudomonas*, *Vibrio*, *Clostridium*, *Yersinia*, and *Streptococcus*. The QS signal from *Pseudomonas aeruginosa* blocks proliferation and induces apoptosis in human BC cell lines. Additionally, oxo-C12-HSL has been recorded to influence the survival of mammalian cells by reducing thymidylate synthase and decreasing growth in human colorectal cancer cells (630H). By increasing the activity of 5-fluorodeoxyuridine, taxol, and tomudex, which regulate tubulin expression, cancer growth is inhibited (Huang et al.2022).

4. Discussion and Conclusion:

Various applications of bacteria, including live and attenuated bacteria as anticancer agents and vectors for delivering therapeutic agents such as CAR T-cell processes, spores as environment-compatible agents, and bacterial toxins against cancer cells, have been explored (Yaghoubi et al.2016).

Huang, J. et al. (2022) reviewed the effect of the human microbiota as an exciting prospect for developing biomarkers to predict treatment outcomes and intervention approaches to enhance therapeutic effects. This review analyzed the interactions between gut microorganisms, host responses, and anticancer treatments (including cytotoxic chemotherapy and targeted therapies), emphasizing the immune-modulatory role of the microbiota that facilitates the efficacy of immune checkpoint inhibitors (Huang et al.2022).

Niamah, A.K. et al. (2024) concluded from their studies that *lactic acid bacteria (LAB)* have the potential to produce bacteriocins, which could serve as promising alternatives for cancer treatment, demonstrating effectiveness against cancer cells while having no impact on healthy cells (Niamah et al.2024).

Tank, J.G. et al. (2022) investigated the effects of surfactins through nano-carriers or nano-formulations on target cancer cells (Tank, et al. 2022).

Faghfoori, Z. et al. (2021) found that probiotic microorganisms exhibit anticancer effects, and recent studies have focused

on the apoptotic effects of certain *Bifidobacterium* species on colorectal cancer cell lines (Faghfoori et al. 2021).

These results position bacterial cancer therapy as a promising treatment for cancer. Furthermore, diverse applications of bacteria for cancer treatment are undergoing clinical trials based on foundational knowledge against cancer in Phase 1 cancer patients. Given the ineffectiveness of conventional treatments like chemotherapy and radiation therapy in advanced tumor stages, resistance to treatment, and the non-specificity of these therapeutic methods, it is hoped that advancements in this field will add a new dimension to cancer treatment (Yaghoubi et al.2016).

5. Future Recommendations:

We anticipate that future clinical and preclinical studies will highlight the significance of the human microbiome as a promising target for precision medicine in cancer treatments.

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