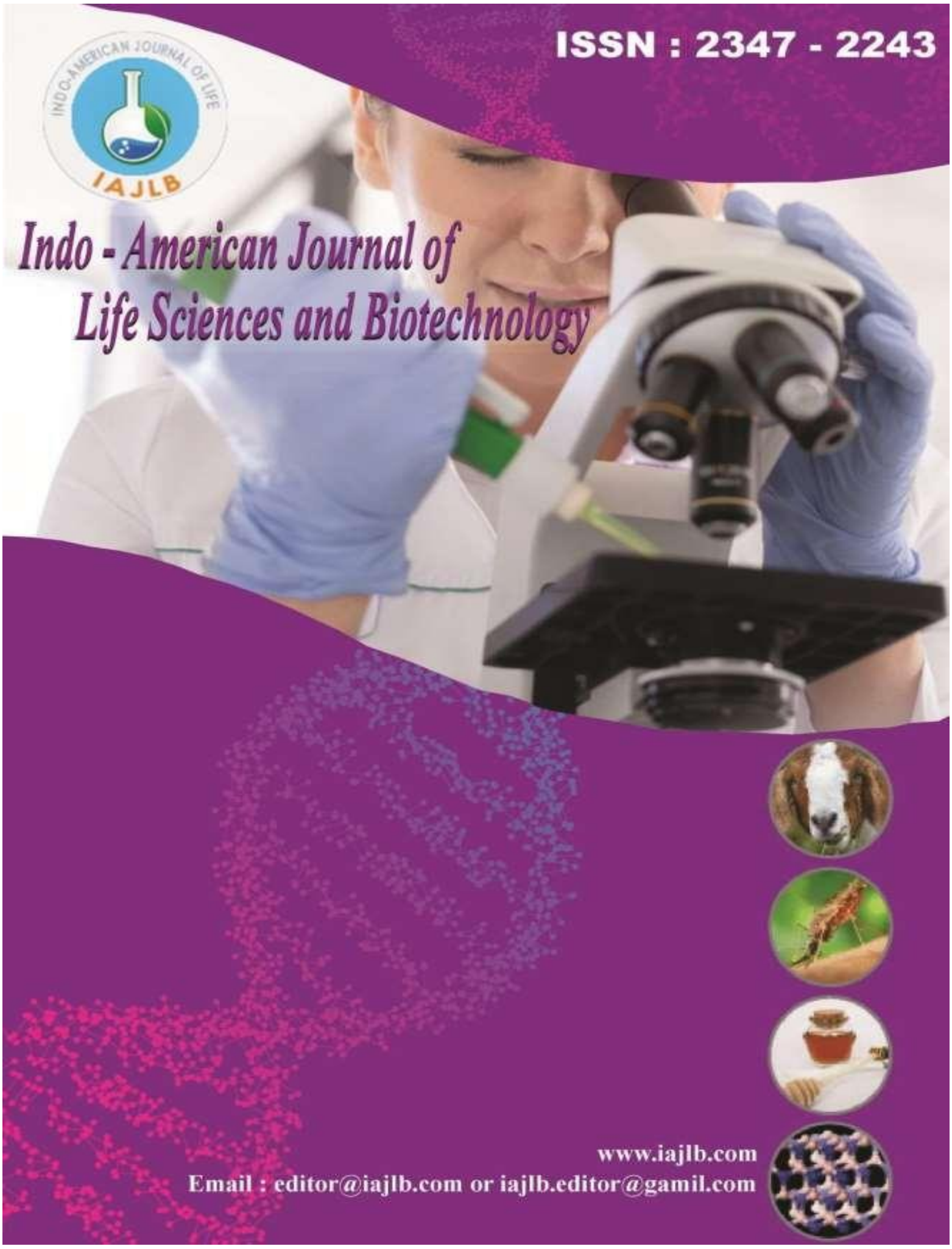
ISSN : 2347 - 2243
INDO-AMERICAN JOURNAL OF LIFE
IAJLB
Indo - American Journal of
Life Sciences and Biotechnology
www.iajlb.com
Email : editor@iajlb.com or iajlb.editor@gamil.com

ISSN 2347-2243 www.iajlb.com

Indo-Am. J. of LifeSc & Bt.,2023- Vol.20, Issue.4, Oct 2023

Indo-American Journal of Life Sciences and Biotechnology

MICRO ORGANISM MEDIATED CANCER THERAPY

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Abstract :

Globally, cancer is the primary cause of mortality. Today, cancer remains a very difficult and unsolvable problem. Despite the availability of conventional treatment, malignant cells were not entirely eradicated. Because of their high motility, carcinogenicity, tumor-specific target action, and ability to act as medication transporters, bacteria have become increasingly important in the treatment of cancer. Bacteria-mediated cancer therapy was first introduced in an attempt to treat cancer using a combination of dead microorganisms. Nowadays, a variety of bacteria are used to treat cancer in a targeted manner. Engineered microorganisms were used to develop therapeutic proteins.

key words: ***Microorganisms, Therapeutic proteins, Cancer, Carcinogenicity, Chemotherapy.***

Introduction:

Cancer is the fast emergence of aberrant cells that proliferate beyond their normal limits. These cells can then infect other body parts and move to other organs; this later process is known as metastasis.Precancerous lesions typically grow to malignant tumors, but cancer begins with the conversion of normal cells into cancereous cells. This multi-stage process is what causes cancer. These alterations arise from the interplay of an individual's genetic components.Engineered microorganisms were used to develop therapeutic proteins.

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Cancer treatment:

Biomarker Testing for Cancer Treatment : Biomarker testing is a way to blink about the genes, proteins, and other substances of the abnormalites (also called biomarkers or tumor markers) that can provide information regarding cancer. Biomarker testing can aid you and your doctor choose a cancer treatment. Germline genetic markers can also provide useful information regarding treatment options, in addition to providing cancer susceptibility information,[(1)] .

Chemotherapy : It is a type of cancer treatment which uses drugs to kill tumor cells. Learning about how chemotherapy works against cancer, why it causes side effects, and how it is used with other cancer treatments.

benefits :

- Chemotherapy can reduce the size of your cancer or slow down its growth, perhaps extending your life and alleviating your symptoms.
- Chemotherapy may be able to decrease the size of cancer in a tiny percentage of patients with cancer that is on the verge of being surgically removable.
- Having chemotherapy following surgery may lower the threatening of the cancer returning.

Demerits :

- Chemotherapy may have negative effects.
- Frequent hospital visits for treatment, examinations, and tests—possibly on various days—can be taxing.
- Each person responds to chemotherapy differently, and it might not be effective for certain individuals [(2)].

Hormone Therapy : Hormone therapy is a treatment that reduces or stops the growth of breast and prostate cancers that use hormones to grow. side effects that may happen and some side effects of hormone therapy;

- hot flushes
- loss of interest in or ability to have intercourse
- weakened bones
- diarrhea
- nausea
- enlarged and tender breasts
- fatigue

Hyperthermia : it is also called hyperthermy (or) hyperpyrexia. A form of therapy called hyperthermia involves heating bodily tissue to 113 °F in order to kill and destroy cancer cells while causing little to no damage to healthy tissue. Find out which tumors and precancers can be treated with hyperthermia, how it is administered, and what are the advantages and disadvantages of doing so.

To generate the heat , there are Different types of techniques for thperthermy. These techniques include:

- probes that make energy from microwaves
- radio waves (also called radiofrequency)
- Laser lights
- ultrasound
- heating fluids (called perfusion)
- placing the entire body in a heated chamber or hot water bath or wrapping within the heated blankets

Hyperthermy also enhances the performance of chemotherapy and radiation therapy, facilitates them to work better.

Immunotherapy : One kind of cancer treatment that increases your immune system's ability to fight itself against cancer is immunotherapy. In this we are discussing about immunotherapy kinds, its application in the fight against cancer, and what to anticipate from your course of treatment.In addition to identifying and eliminating aberrant cells, the immune system probably stops or slows the spread of many malignancies. For example, immune cells have been observed in and surrounding tumors on occasion. Tumor-infiltrating lymphocytes, known as TILs, are cells that states the response of tumor to the immune system. TIL-containing tumors typically have better predicts than those without them.Despite the immune system can prevent or slow cancer growth, cancer cells have ways to avoid destruction by the immune system. For example, cancer cells may:

- Have mutations that make them immune system gets weak.
- Have proteins on their surface that put off immune cells
- Modifies the normal cells around the tumor resulting in interfering with how the normal cells respond to the immune system.

Immunotherapy helps the immune system to better act against cancer[(3)].

Photodynamic Therapy : Photodynamic therapy,to kill cancer cells , uses a drug activated by light . Learn how photoradiation therapy works, about the types of cancer and premalignant it is used to treat, and the benefits and drawbacks of this treatment.it can only treat areas where light can reach.

Radiation Therapy : Radiation therapy is a type of cancer treatment that uses ionisation radiation to kill cancer cells and degrades tumors. Let us discuss about the what are the side effects and which side effects you might have, and more

PART OF BODY BEING TREATED	COMMON SIDE EFFECTS
Any part	Hair loss at treatment site , skin irritation at treatment site, fatigue
Head and neck	xerostomia, thickened saliva, pharyngitis, changes in the way food tastes, nausea, mouth ulcers, tooth decay
Chest	Difficulty swallowing, cough, shortness of breath
Abdomen	Nausea, vomiting, diarrhea
Pelvis	Bladder irritation, Diarrhea, Sexual dysfunction, Frequent urination.

Stem Cell Transplant : Stem cells that divide into blood cells are restored through stem cell transplant operations to individuals whose own stem cells were killed by severe doses of chemotherapy or radiation therapy. Find more about the many types of transplants, potential adverse effects, and the use of stem cell transplants in the treatment of cancer.Transplants of stem cells typically do not immediately reduce cancer. Rather, following treatment with extremely high doses of chemotherapy and possibly other treatments like radiation therapy that are designed to kill cancer cells, they restore your body's capacity to generate new blood cells.

Surgery : surgery is a procedure in which a surgeon eradicates cancer from the body of patient.

Targeted Therapy : Targeted therapy is a type of cancer treatment that centers the changes in tumour cells that help them grow, divide and spread.

Many properties of the bacteria make useful for cancer treatment: their unique form of motility allows them to easily penetrate cancer cells; they thrive in the hypoxic and immune-deficient environments of tumors; and they can deplete the tumor micro environment of nutrients necessary for cancer cell survival.On addition to these features an easy-to-modify genome and the power of inducing an immune response.

Microorganisms mediated cancer therapy

The bacteria is used as a vector to transfer the chemotherapeutic agent directly into the tumor, which allows the reduction of the side effects of treatment that usually co-exist in traditional chemotherapy[4].Inspite of other microorganisms such as *Neospora caninum* have also been observed to have antitumor properties, the present study has concentrated on the bacteria-based methods for cancer therapy[5].BCG vaccine is possibly the most famous bacterial based agent that used for cancer treatment. Caused by *Mycobacterium tuberculosis.Bacillus Calmette-Guérin* (BCG) vaccine, named after its inventors, is mainly injected into babies to prevent TB infection by intramuscular administration[6].Live strains of *Streptococci* and *Clostridia* were the first strains to be used for trials in cancer treatment. A variety of techniques can be used on bacteria with the aim to achieve tumor therapy . Bacteria species of *Pseudomonas*, *Caulobacter*, *Listeria*, *Proteus*, *Bifidobacteria*, and *Salmonellae* and others have been shown to have the capability to eradicate tumors through different mechanisms. Some of them may include the use of bacterial toxicity, synthesizing immunotherapic constituents, enzymes, biofilms, bacteriocins and capability to carry out RNA interference as well as prodrug cleavage.

Micro organisms used in cancer treatment :

- Clostridium
- Escherichia coli
- Streptococcus pyogenes
- Salmonella thyphimurium
- Bifidobacteria
- Lactic acid bacteria
- Bacteriocins
- Listeria monocytogenes

Clostridium

These are anaerobic in nature, which helps them to survive in a tumor site on the contrary to normal tissues. Various species of *Clostridium* have been used for antitumor therapy, such as *C. histolyticum*, *C. acetobutylicum*, *C. butyricum*, and *C. beijerinckii* . A bacterial metabolic substrate of *C. butyricum*, d-alanine (d-Ala) was linked to AIE photosensitizer (TPApy) to click through chemical reaction to produce d-Ala-TPApy. Engineered oncolytic *C. butyricum* was then synthesized by d-Ala-TPApy and then metabolically inserting it into bacterial peptidoglycan. Intratumoral injection of this bacteria could accumulate and proliferate in the tumor site, stimulate the immune TME, and ablate the hypoxia area.The PS on the C. butyricum might provide photodynamic effects under light irradiation after the tumor hypoxic region was ablationed, thereby eliminating the remaining tumor remnant.

Indo-American Journal of Life Sciences and Biotechnology

Escherichia Coli

E. coli are gram-negative anaerobic bacterium are the natural intestinal probiotic and has anti-inflammatory properties. *E. coli* has the capability to attack the low oxygen areas of a cancer lumps after intravenous administration, while bacteria are rapidly eradicated in normal tissue due to the sensitivity of lipopolysaccharide to serum on bacterial membrane. *E. coli* was genetically modified for catalyzing H2O2 decomposition in solid tumors. PS chlorin e6 (Ce6) was covered by PDA for attaching it to the surface of the bacteria, these are used for tumor-targeted delivery & for the combined treatment of PTT and PDT. Directly introducing particular therapeutic genes and proteins into tumor cells through bacteria for the cancer therapy has been popular.

Streptococcus pyogenes

By treating them with serum in an oxygenative environment, live streptococci (S-cocci) of the Su strain were produce H2O2. The resultant product was not viable and lost its erythrolytic activity.

Salmonella typhimurium

S. *typhimurium* makes up for the gap in chemotherapy and radiotherapy in oxygen deficiencient and necrotic regions. *S. typhimurium* provincially gets accumulated in tumors, thus resulting in the formation of normal tissue from tumors.

T. Bifidobacteria

Bifidobacterium have the capability to adjust to changes in growth and evolution. The intestinal *Bifidobacteria* is inhibited at the early stages of chemotherapy, but they may re-appear after adaptive changes & this may result in developing resistance to chemotherapeutic drugs.

Lactic acid bacteria

the antitumor characteristics of LAB can be described as hypoxia-triggered motility, which includes the synthesis of anticancer agents, stimulation of host immune responses & induction of cancer cell apoptosis. A fresh layout was developed by Yazdi et al in the year 2013 regarding selenium nanoparticles (SeNPs), the SeNP's are deposited on the LAB by the process of intracellular reduction which results in improving the immune response. Their study shows the level of some cytokines (e.g., IFN-γ and IL-17)relatively increased after the oral administration of SeNPs attached bacteria, resulting in better prediction in highly metastatic mouse mammary carcinoma[7,8].

Bacteriocins

The presence of microvilli leads to increase the capability of binding of bacteriocins.The binding and uptake of bacteriocins leads to the demise of cancer cells , mediated via lysis of the cell membrane .These bacteriocins can also induce apoptosis in cancer cells [9,10] .

Listeria monocytogenes

Recognisable because of its facultative anaerobic nature, Listeria monocytogenes is a frequently utilized vector in cancer immunotherapy.People can contract listeria infections, which can cause a variety of symptoms like meningitis, sepsis, and gastroenteritis. Nevertheless, the same traits that render Listeria pathogenic are also being developed for use in cancer therapeutic delivery platforms.Many techniques have been employed to design Listeria for the treatment of cancer, such as the initial discovery of fluorescent or bioluminescent gene-loaded nanoparticles that adhere to the surface of solid human tumors and efficiently express the Listeria gene [11,12].

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