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A Review - The Role of Chemotherapy of Cancer Treatment

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Abstract: ***Cancer is a chronic, multifactorial, and heterogeneous condition, comprising a group of diseases. Its high prevalence and complex interactions among risk factors mean that even subtle influences can lead to significant effects. Cancer happens when cells grow out of control and form harmful tumors, leading to millions of deaths every year. Cancer treatment involves various approaches, including surgery, radiation therapy, chemotherapy, immunotherapy, and stem cell transplantation, each tailored to the type, stage, and individual characteristics of the disease. The importance of chemotherapy in cancer treatment is steadily increasing, particularly when used as an adjuvant to local therapies such as surgery or radiation. Moreover, in advanced stages where the tumor has spread beyond its original site, chemotherapy plays a growing role in relieving cancer-related symptoms and extending patient survival.***

Keywords: Tumors, types of cancer, symptoms, treatment, role of chemotherapy

I. INTRODUCTION

Cancer encompasses a wide range of diseases characterized by the uncontrolled proliferation of abnormal cells, which possess the ability to invade surrounding tissues and disrupt normal physiological functions. Cancer can develop in any part of the body, and each type has its own distinct characteristics and behavior. Normally, cells receive signals to die so they can be replaced by new, healthy cells. But cancer cells ignore these signals and keep growing. They use up oxygen and nutrients, leaving less for healthy cells. Cancer cells also change their surroundings to help themselves grow, hide from the immune system, and take advantage of other cells in the body. Globally, cancer ranks as the second most common cause of mortality. In men, the most common types of cancer occur in the prostate, lungs and bronchi, colon and rectum, and urinary bladder, respectively. In women, the highest prevalence is observed in breast cancer, followed by cancers of the lungs and bronchi, colon and rectum, uterine corpus, and thyroid. This data highlights that prostate cancer in men and breast cancer in women represent a significant proportion of overall cancer cases. Among children, the most prevalent cancers are leukemia (blood cancer), followed by brain tumors and cancers affecting the lymph nodes.

A. Types of Cancer

Cancers are classified into several major types based on the origin of the cancerous cells:

1) Carcinomas

Origin: Begins in the epithelial tissue, which covers the skin, glands, and internal organ surfaces.
Tumor type: Typically forms solid tumors.
Examples: Breast cancer, Prostate cancer, Colorectal cancer, Lung cancer

2) Sarcomas

Origin: Develops in connective and supportive tissues of the body.
Possible locations: Nerves, tendons, joints, fat, blood vessels, bone, lymph vessels, muscles, cartilage.
Tumor type: Solid tumors

3) Leukaemias

Origin: Cancer of the blood-forming tissues, typically begins in the bone marrow.
Characteristics: Causes uncontrolled growth of abnormal blood cells.
Types: (i)Acute Myeloid Leukemia (AML)
(ii)Acute Lymphocytic Leukemia (ALL)
(iii)Chronic Myeloid Leukemia (CML)
(iv)Chronic Lymphocytic Leukemia (CLL)

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4) Lymphomas
   Origin: Begins in the lymphatic system, a part of the immune system.
   Function of lymphatic system: Helps the body fight infections.
   Types: (i)Hodgkin Lymphoma (ii)Non-Hodgkin Lymphoma
5) Central Nervous System (CNS) Cancers
   Origin: Starts in the brain or spinal cord tissues.
   Examples: Brain and spinal cord tumors, Primary CNS lymphomas,Vestibular schwannomas, Gliomas, Pituitary adenomas, Primitive neuroectodermal tumors (PNETs), Meningiomas
6) Multiple Myeloma
   Origin: Cancer of plasma cells, a type of white blood cell.
   Characteristics: Myeloma cells accumulate in the bone marrow, forming tumors in the bones.
   Other names: Plasma cell myeloma, Kahler disease
7) Melanoma
   Origin: Begins in melanocytes, the cells that produce melanin (skin pigment).
   Common locations: Mainly develops on the skin, but may also appear in other pigmented tissues.
8) Other Types of Tumors: (1) Germ Cell Tumors: These tumors originate in the cells that develop into eggs or sperm. Germ cell tumors can occur anywhere in the body and may be either benign (non-cancerous) or malignant (cancerous). (2) Neuroendocrine Tumors: These tumors form from specialized cells that release hormones into the bloodstream in response to signals from the nervous system. Neuroendocrine tumors may produce higher-than-normal levels of hormones, leading to a variety of symptoms. Like germ cell tumors, they can also be benign or malignant

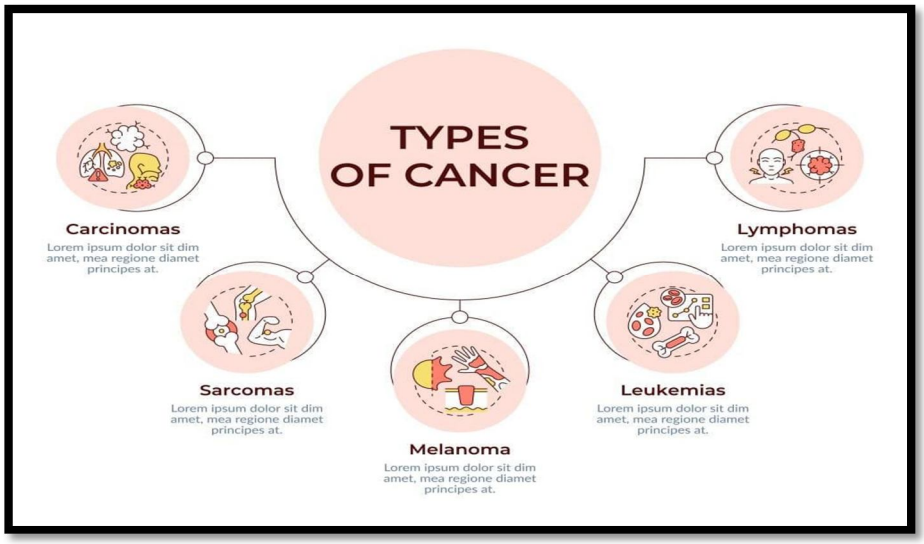


Fig No. 1 Types of cancer

II. SYMPTOMS

1) Fatigue or extreme tiredness that doesn't get better with rest (sometimes caused by anemia or a low red blood cell count)
2) Weight loss or gain of 10 pounds or more for no known reason
3) Eating problems such as not feeling hungry, trouble swallowing, belly pain, or nausea and vomiting
4) Swelling or lumps anywhere in the body
5) Thickening or lump in the breast or other part of the body
6) Pain, especially new or with no known reason, that doesn't go away or gets worse
7) Skin changes such as a lump that bleeds or turns scaly, a new mole or a change in a mole, a sore that does not heal, or a yellowish color to the skin or eyes (jaundice)
8) Cough or hoarseness that does not go away
9) Unusual bleeding or bruising for no known reason

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10) Change in bowel habits, such as constipation or diarrhea, that doesn't go away or a change in how your stools look
11) Blood in your stool
12) Bladder changes such as pain when urinating, blood in the urine, or needing to urinate more or less often
13) Fever or night sweats
14) Headaches
15) Vision or hearing problem
16) Mouth changes such as sores, bleeding, pain, or numbness

III. CANCER TREATMENT

1) Surgery: Surgery is the oldest form of cancer treatment. Until a few decades ago, it was the only method capable of curing patients, especially when the disease was localized.
2) Radiotherapy (RAPY): Radiotherapy treatment for invasive cancer uses ionizing radiation to deliver a lethal dose to a defined tumor volume. The radiation damages the DNA of cancer cells, leading to their death. particularly when they attempt mitosis while aiming to minimize damage to surrounding healthy tissue.
3) Chemotherapy: Chemotherapy is primarily used to control disseminated subclinical disease and to treat early (elementary) lesions.
4) Immunotherapy and Biological Therapy: Research has shown that immunologic mechanisms play a significant role in the development and growth of malignant tumors. Unlike chemotherapy, which follows first-order kinetics (the rate of cell killing depends on the number of tumor cells present), immunotherapy follows zero-order kinetics. A specific number of antibodies are required for the lysis of each tumor cell.

IV. CHEMOTHERAPY

Chemotherapy is one of the principal methods used in the treatment of cancer patients. Its origins date back to the late 1940s, when it was first applied to treat advanced lymphoma after observations from World War I revealed that mustard gas exposure caused leukopenia. Shortly after World War II, researchers discovered that folic acid stimulated the proliferation of acute lymphoblastic leukemia cells. This led to the development of folic acid antagonists first aminopterin, then amethopterin (now known as methotrexate which induced remission in children with acute lymphoblastic leukemia.

For nearly 30 years, chemotherapy's role in treating common epithelial malignancies was largely confined to palliative management of symptomatic metastatic disease. Today, however, cancer chemotherapy has three main applications:

1) Curative treatment for a limited number of malignancies, including childhood leukemia, Hodgkin's and non-Hodgkin's lymphoma, and germ cell tumors.
2) Palliative treatment for most metastatic epithelial malignancies.
3) Adjuvant treatment following surgical resection for several types of epithelial cancers.

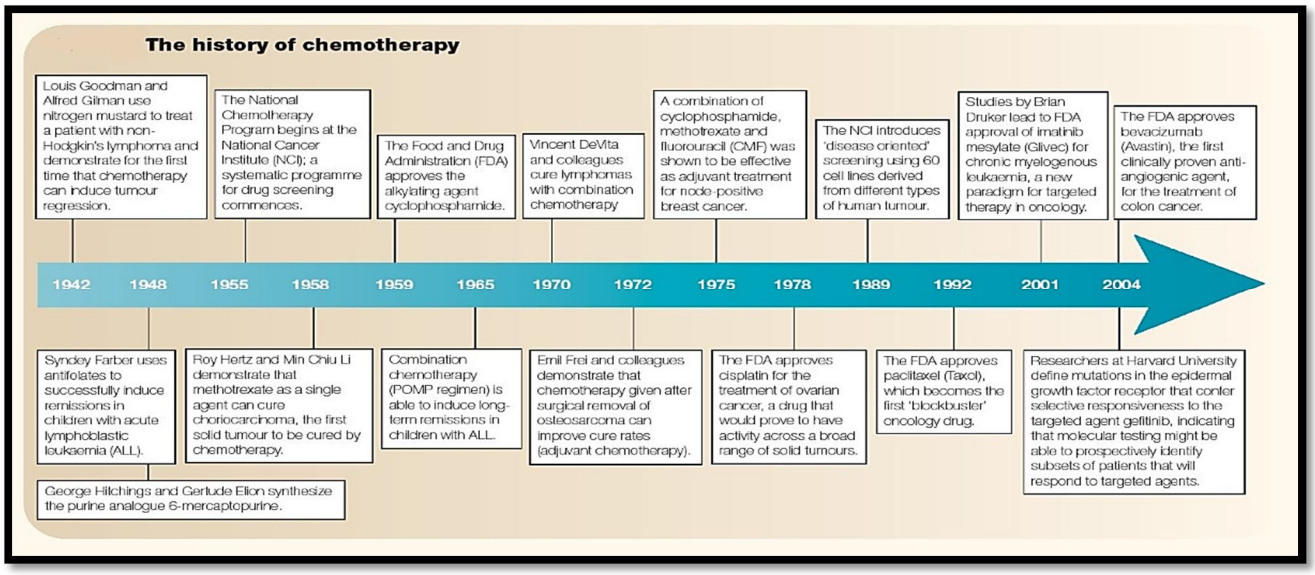


Fig No. 2 History of Chemotherapy

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A. Define of Chemotherapy

Chemotherapy uses drugs to kill cancer cells, working systemically throughout the body.
Anticancer drugs are classified by their mechanisms of action:
Alkylating agents – damage DNA.
Antimetabolites – mimic DNA/RNA building blocks.
Antibiotics – block enzymes needed for DNA replication.
Topoisomerase inhibitors – prevent DNA unwinding.
Mitotic inhibitors – stop cell division.
Corticosteroids – treat cancer and reduce drug side effects.

B. Mechanism of Action of Chemotherapeutic Drug

Class	Mechanism of Action	Primary Toxicities	Representative Drugs
Alkylating agents	Bind and cross-link DNA either inter-strand, intrastrand, or to proteins; pre-vents replication and transcription	Hemorrhagic cystitis, alopecia, nephrotoxicity	Cyclophosphamide, ifosfamide, melphalan
Alkylating-like agents	Cross-link DNA strands (interstrand)	Nephrotoxicity, neurotoxicity, myelosuppression	Cisplatin, carboplatin
Antibiotics	Interfere with DNA replication through free radical forma-tion and intercala-tion between bases	Variable	Bleomycin, actinomycin D
Antimetabolites	Block enzymes required for DNA synthesis	Gastrointestinal, myelosuppression, dermatologic, hepatotoxicity	Methotrexate, 5-fluorouracil
Plant (vinca) alkaloids	Inhibit microtubule assembly	Myelosuppression	Vincristine, vinblastine, paclitaxel
Topoisomerase inhibitors	Inhibit topoiso-merase, resulting in DNA strand breaks	Myelosuppression, alopecia, gastrointestinal	Etoposide, Topotecan

Fig No. 3 Mechanism of action of chemotherapeutic drug

C. Classification of Chemotherapeutic Agents

1) Alkylating agents: bind directly to DNA, preventing DNA replication and triggering cell death. They act in all phases of the cell cycle and are used to treat various cancers, including: Leukemia, Lymphoma, Hodgkin disease, Multiple myeloma, Sarcoma, Lung, breast, and ovarian cancers. Because they damage DNA, these drugs may cause long-term bone marrow suppression.

2) Antimetabolites: Antimetabolites are among the oldest families of anticancer drugs. They interfere with essential biosynthesis pathways by mimicking purines or pyrimidines. During the S phase, they incorporate into DNA, disrupting its synthesis and thereby halting cell growth and division.

3) Anti tumor antibiotics: Anti-tumor antibiotics are natural or synthetic compounds that specifically target cancer cells, unlike regular antibiotics used for bacterial infections. Sourced from bacteria, fungi, or marine organisms, they work by disrupting vital processes needed for cancer cell growth and survival.

4) Topoisomerase inhibitors: Topoisomerases are vital enzymes found in all living organisms that control the topology of DNA. They function by creating temporary breaks in the DNA strands—single-strand breaks in the case of type I topoisomerases and double-strand breaks in the case of type II topoisomerases. The DNA double helix must be unwound to allow processes like DNA replication and transcription to occur.

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5) Mitotic Inhibitors: Mitotic inhibitors targeting microtubules and their associated proteins disrupt the essential role these structures play in cell division. Since microtubules are often overexpressed in cancer cells, binding to or inhibiting them can interfere with mitosis, thereby slowing or completely halting the growth of cancer cells.
6) Corticosteroids: Corticosteroids are synthetic drugs widely used across medical specialties. They work by lowering inflammation through the suppression of certain chemical production. In higher doses, they can also decrease immune system activity.

Type	Examples
Antibiotics	Bleomycin, Mitomycin C
Alkylating agents	Cisplatin, Oxaloplatin, Chlorambucil, Melphalan
Antimetabolites	5-Fluorouracil, Gemcitabine
Anthracyclines	Doxorubicin, Daunorubicin, Mitoxanthrone
Nitrosoureas	Carmustine, Lomustine, Semustine
Topoisomerase Inhibitors	Etoposide, Irinotecan, Topotecan, Doxorubicin
CD-20 Binding Protein	Rituximab
EGFR Binding Protein	Cetuximab
VGEF Antibody	Bevacizumab
Tyrosine Kinase Inhibitors	Imatinib, Sunitinib, Erlotinib
Rapamycin (mTor) and proteasome Inhibitors	Bortezomib
Anti PD-1	Lambrolizumab, Nivolumab
Anti PDL-1	BMS-936559
CTLA-4	Ipilimumab

Fig No. 4 Chemotherapeutic Drug

D. Ideal Characteristics of a Chemotherapeutic Agent

An ideal chemotherapeutic agent should possess the following properties:

1) Selective toxicity – It should be more toxic to diseased cells or disease-causing microorganisms than to the healthy host cells.
2) Good solubility – It should be readily soluble in bodily fluids to ensure efficient transport to the target site.
3) Stable potency – Its activity should not be altered by food, other drugs, coexisting diseases, or physiological conditions such as pregnancy.
4) Non-allergenic – It should not trigger allergic reactions in the patient.
5) Chemical stability – It should remain stable in the body to maintain a consistent therapeutic concentration in blood and tissues.
6) Resistance prevention – It should not promote or lead to the development of resistance.
7) Long shelf life – It should be stable during storage, with minimal special requirements (e.g., refrigeration or light protection).
8) Affordability – It should be reasonably priced for accessibility to patients.

In practice, no chemotherapeutic agent meets all these criteria. A drug that achieves even 50% of these characteristics is considered highly effective.

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E. Administration Routes of Chemotherapy

Type	Route	Associated drug delivery system(s)	Examples of clinically used technology
Systemic	Intravenous	Micelles, liposomes, nanoparticles	Doxil®, DaunoXome®, Abraxane®, iMyocet®
	Oral	Sustained-release tablets, capsules, others	Gleevec®, Tarceva®, Xeloda®, Iressa®
	Subcutaneous/intramuscular	Micro- or nanoparticles, polymer implants	Eligard®, Zoladex®, DepoCyt®, Lupron Depot®, Sandostatin LAR®
Regional	Hepatic arterial infusion/trans-arterial embolization	Microparticles	Doxorubicin-eluting beads, Lipiodol-drug combination
	Intraperitoneal	Micro- or nanoparticles	Paclimer® (clinical trial)
	Convection-enhanced delivery	Liposomes, polymer nanoparticles	Liposomal gene therapy (clinical trials)*
Local	Intratumoral – adjuvant	Pre-formed and *in situ*-forming implants	Gliadel®
	Intratumoral – primary	Pre-formed and *in situ*-forming implants	OncoGel™

Fig No.5 Administration routes of chemotherapy

F. Role / work of Chemotherapy

1) Chemotherapy aims to inhibit cell proliferation and tumor growth, preventing invasion and metastasis. However, because it also affects normal cells, it can cause toxic side effects. Tumor growth inhibition can occur at various levels within the cell and its environment.

2) Traditional chemotherapy drugs mainly disrupt macromolecular synthesis and function in cancer cells by interfering with DNA, RNA, or protein production, or by impairing the function of existing molecules. When this interference is significant, it causes cell death—either directly or through apoptosis.

3) With these agents, cell death may be delayed, so repeated treatments are often needed. Cytotoxic drug toxicity is greatest during the S phase (DNA synthesis). Vinca alkaloids and Taxanes act in the M phase, blocking mitotic spindle formation.

4) Combination chemotherapy is often used to achieve better results and to prevent the emergence of drug-resistant cancer cell clones by targeting both resting and dividing cells

5) Chemotherapy targets cancer cells, stopping their uncontrolled growth and division. It can be used in different ways:

6) Adjuvant therapy: Given after surgery or radiation to destroy remaining cancer cells.

7) Curative therapy: Used alone or with other treatments (such as radiation or surgery) to eliminate cancer and prevent its return.

8) Neoadjuvant therapy: Given before surgery or radiation to shrink the tumor.

9) Palliative therapy: Reduces tumor size and relieves symptoms, but does not cure the cancer

G. Challenges in Chemotherapy

Despite its proven efficacy, chemotherapy presents several challenges. One of the most significant issues is drug resistance, in which cancer cells adapt and become unresponsive to chemotherapy, leading to treatment failure. Resistance can arise through various mechanisms, including alterations in drug metabolism, increased drug efflux, enhanced DNA repair, and changes in drug targets. Addressing this problem requires a multifaceted strategy such as developing novel agents, employing combination therapies, and tailoring treatments to the molecular profile of individual tumors.

H. Advantages of Chemotherapy

1) Kills cancer cells: Targets and destroys cancer cells, helping shrink tumors and prevent the spread of cancer.

2) Flexible use: Can be administered before or after surgery, or combined with treatments such as radiation therapy or immunotherapy.

3) Treats many cancers: Effective against various cancers, including lung cancer, breast cancer, leukemia, and lymphoma.

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I. Disadvantages of Chemotherapy

1) Side effects: May cause nausea, fatigue, hair loss, and increased infection risk, which can significantly affect quality of life.
2) Toxicity: Can damage healthy cells, potentially leading to long-term organ or tissue damage.
3) Limited effectiveness: May not kill all cancer cells, allowing the disease to return.
4) Long-Term Effects of Chemotherapy: While most chemotherapy side effects fade after treatment ends, some long-lasting effects may appear months or even years later, depending on the specific drugs used.
5) Emotional strain: Can lead to anxiety, depression, and emotional stress for patients and their families.

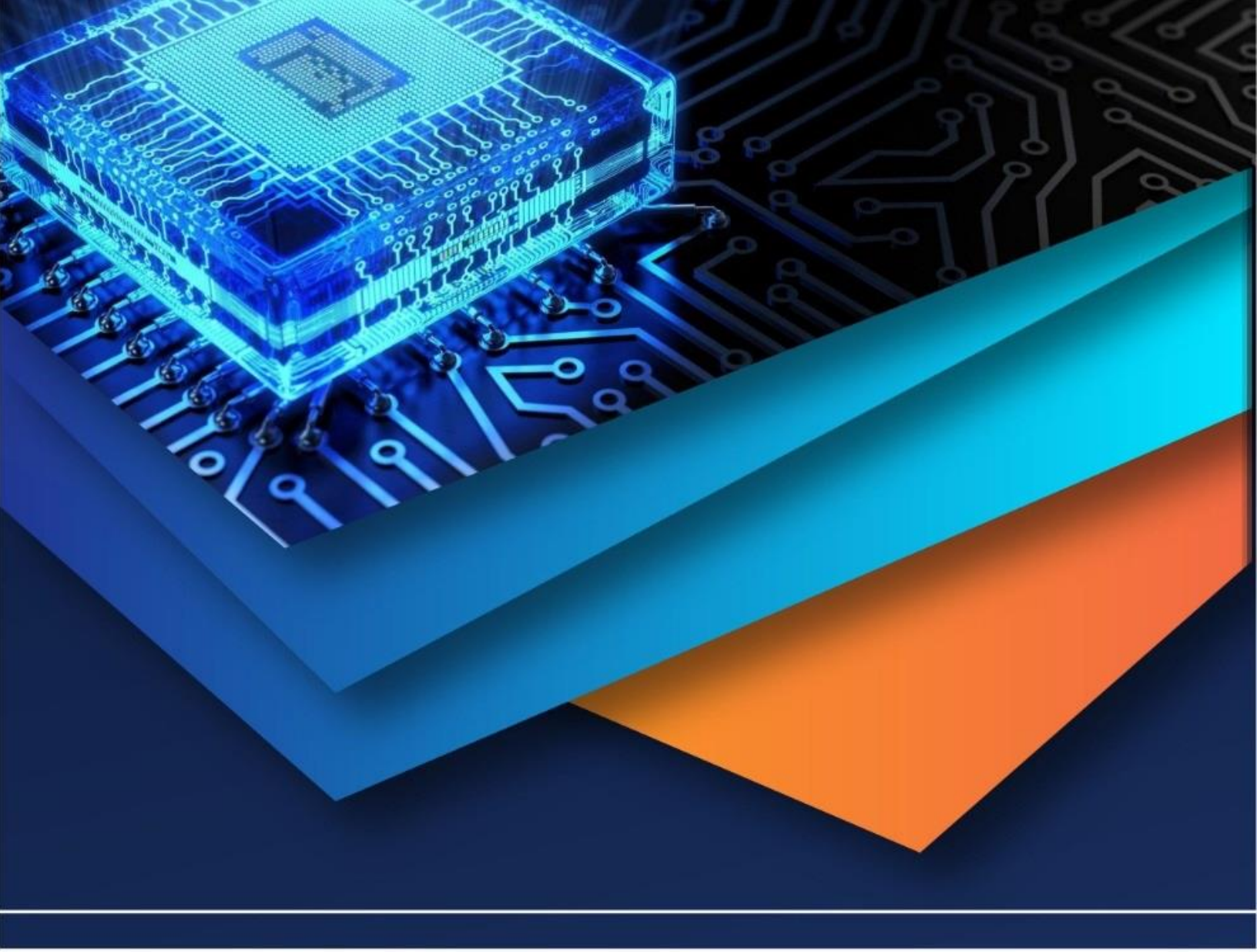
V. CONCLUSION

This review concisely summarize the chemotherapy in cancer treatment, considering their advantage and disadvantage. Cancer is a disease in which abnormal cells grow and divide without control. This uncontrolled growth is often caused by changes (mutations) in the signals that regulate the cell cycle. In healthy cells, tumor suppressor genes act like brakes to slow or stop cell division. Cancer cells bypass these controls, allowing them to avoid cell death and continue dividing indefinitely. Chemotherapy is one of several cancer treatment options, along with surgery, radiation therapy, and targeted molecular therapy. Although chemotherapy can be effective in treating certain types of cancer, its use is often limited by side effects. Some drugs produce toxic by-products that build up in the liver, causing liver damage (hepatotoxicity) and leading to symptoms such as loss of appetite, nausea, vomiting, diarrhea, abdominal cramps, constipation, anemia, tiredness, fever, and hair loss. Chemotherapy treatment hold a brighter future towards creating a cancer free world.

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