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ANTICANCER AGENTS

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ABSTRACT

Cancer is a frightful disease and represents one of the biggest healthcare issue for human race and demands a proactive strategy for cure . Cancer is a condition marked by irregular and unregulated cellular proliferation . Oncology is a branch of a science that deal with the tumors and cancer .cancer maybe benign and malignant . Anti cancer drug are pharmacological agent designed to target and inhibit the growth of the cancer cell .they can be work by interfering with the various aspects of a cancer cells life cycle including cell division ,DNA replication and signaling pathways .Anti cancer agent have a different mode of action and their effect depend upon cytotoxic action which is selective for the benign cells. cancer can be treated by many ways including chemotherapy ,surgery , radiation therapy and neoplastic agent . This article discuss about cancer and their development and anti cancer drug with their classification ,action for understanding treatment of cancer by anti cancer drugs.

Keywords :- Cancer , uncontrolled cell division, Oncology, Anti-cancer drug, Cytotoxic action, Chemotherapy, surgery , radiation therapy

INTRODUCTION

Cancer is a disease characterized by uncontrolled growth and spread of abnormal cells in the body. These abnormal cells can form tumors or invade other parts of the body, leading to serious health problems and even death. There are many various types of cancer, including breast cancer, lung cancer, colon cancer, and prostate cancer. The development of cancer is a complex process that involves changes in the DNA of cells. These changes can be caused by a variety of factors, including genetic mutations, exposure to environmental toxins, and lifestyle choices such as smoking and poor diet.

Anticancer drugs are medications used to treat cancer by killing or slowing the growth of cancer cells. Therapies aim to target particular molecules or pathways linked to cancer development and progression. There are several different categories of anticancer drugs, including chemotherapy, targeted therapy, and immunotherapy.

Chemotherapy drugs, which are often alkylating agents, work by damaging the DNA of cancer cells, preventing them from dividing and growing. They can also damage healthy cells, leading to side effects such as nausea, vomiting, hair loss, and fatigue.

Antimetabolites are another type of chemotherapy drug that work by interfering with the metabolism of cancer cells. They mimic the building blocks of DNA and RNA, preventing the cancer cells from replicating and dividing. Side effects of antimetabolites can include nausea, vomiting, diarrhea, and mouth sores.

Natural products are another category of anticancer drugs that are derived from natural sources such as plants or bacteria. Antibiotics are a type of natural product that can be used to treat cancer by inhibiting the growth of cancer cells. Side effects of antibiotics are nausea, vomiting, diarrhea, and damage to the liver or kidneys.

Anticancer drugs play a crucial role in treating cancer by targeting specific molecules or pathways involved in the development and progression of cancer cells. Alkylating agents, antimetabolites, and natural products such as antibiotics are all important categories of anticancer drugs with different mechanisms of action and side effect profiles. The future development of anticancer drugs is focused on improving their effectiveness and reducing side effects through new drug development and innovative treatment approaches.

CANCER

The word “cancer” finds its roots in ancient Greece, attributed to the renowned physician Hippocrates (460-370 BC), often hailed as the “Father of Medicine.” Hippocrates employed the terms “carcinos” and “carcinoma” to distinguish tumors that did not form ulcers from those that did. Cancer is defined by the uncontrollable proliferation and dissemination of abnormal cells within the body. Oncology, the medical discipline devoted to exploring, diagnosing, treating, and preventing cancer, delves into this complex field. Cancer may affect people at all ages, even fetuses, but the risk of most varieties increase with age. When cells at particular site starts to grow out of control, they may become cancerous. The growth of cancer cells deviates from the typical pattern of normal cell growth. Instead of dying, cancer cells continue to grow and form new abnormal cells. Cancer may be benign and malignant. A benign tumor Is an abnormal but noncancerous collection of cells. A benign tumor is not malignant. Malignant growths consist of cells that proliferate uncontrollably and can spread either locally or to distant locations. Malignant tumors are cancerous .

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Type of cancer tumor

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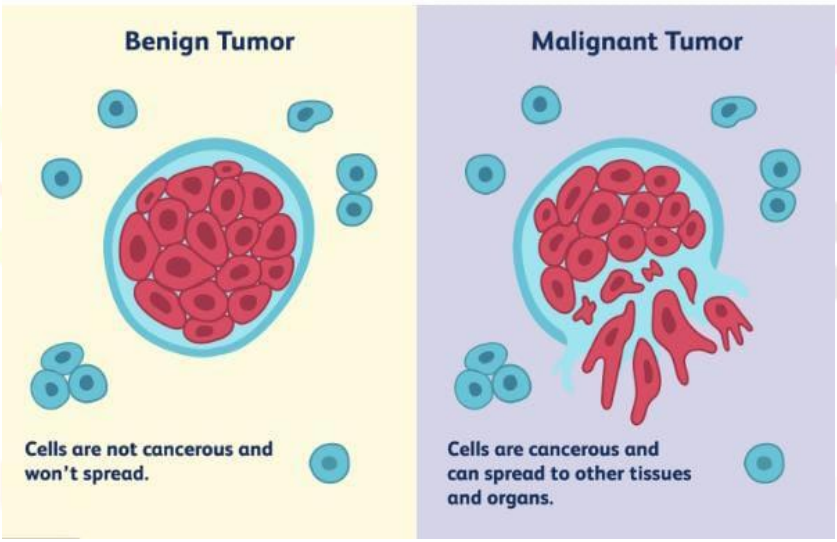

HOW CANCER DEVELOPS

Carcinogenesis or oncogenesis is the process in which normal Cells transform into cancerous, or malignant cells. Development of cancer is a complex process. The development of cancer is often attributed to the widely accepted three-stage theory of carcinogenesis. This theory divides cancer development into three stages: initiation, promotion, and progression.

- **Initiation** :- The first phase, initiation, marks the onset of cellular mutations. This stage encompasses various spontaneous changes or alterations induced by exposure to carcinogens. These changes forms a potential for the affected cell and its daughter cells to develop into a cancer cell. A disruption in the cell development Cycle can be caused by a response to the activation of cellular Genes known as oncogenes, the portion of deoxyribonucleic acid that regulates normal cell growth and repair. Conversely, inactivation is the mechanism through which Tumor suppressor genes, responsible for regulating the normal cell cycle, undergo modification. These genes, integral to DNA, act as inhibitors, halting or suppressing cell division. Mutations in both oncogenes and tumor suppressor genes enable cells to surpass the typical requirements of the body. New cell clones resulting from cellular changes usually exhibit a selective and reproductive advantage over the original cells. Consequently, these new cells undergo uncontrolled division and lack apoptosis, commonly known as programmed cell death. Apoptotic genes, also DNA components, govern cell death, and mutations in these genes empower cancer cells to evade programmed cell death.

- **Promotion** :- Promotion is the second stage where the transformed (or initiated) cells are stimulated to divide. Cancer development is influenced by both the intracellular (within the cell) and extracellular (outside the cell) environment. The progression to malignancy often entails multiple stages and necessitates repeated encounters with promoting agents. A notable example of a tumor promoter is estrogen, a naturally occurring hormone that, on its own, does not serve as a cancer initiator. However, estrogen can stimulate the proliferation of a mutated breast cell.
- **Progression** :- Progression is the third stage in the three-stage theory of cancer causation. During progression, tumor cells compete with one another to survive, leading to more mutations that make the cells more aggressive. As the tumor expands, additional mutations occur, resulting in heightened genetic diversity within the tumor. Heterogeneity denotes the presence of various genetic variants of the mutated or transformed cell. The growing heterogeneity among cancer cells within a mass can lead to variations in appearance and behavior, posing challenges in diagnosis and treatment.

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CHARACTERISTICS OF NORMAL CELL AND CANCER CELL

Parameters	Normal cell	Cancer cell
Shape	Regular	Irregular
Nucleus	Proportionate size	Larger , darker
Growth	In control, systematic	Out of control
Maturation	Mature (Cell differentiation)	Immature - Doesn't mature
Communication	Communicates	Doesn't communicate
Visibility	Visible to immune cells,with ID	Invisible to immature cells
Blood supply	Angiogenesis during repair	Tumor angiogenesis
Oxygen	Requires Oxygen	Doesn't like or require oxygen
Glucose	Requires some glucose	Loves, craves glucose
Energy Efficiency	Very high (95%)	Very low (5%)
Amount of ATP	36 units of ATP	2 units of ATP
Cell Environment	Alkaline	Acidic
Nutrient preference	Fat, ketone, Glucose	Glucose

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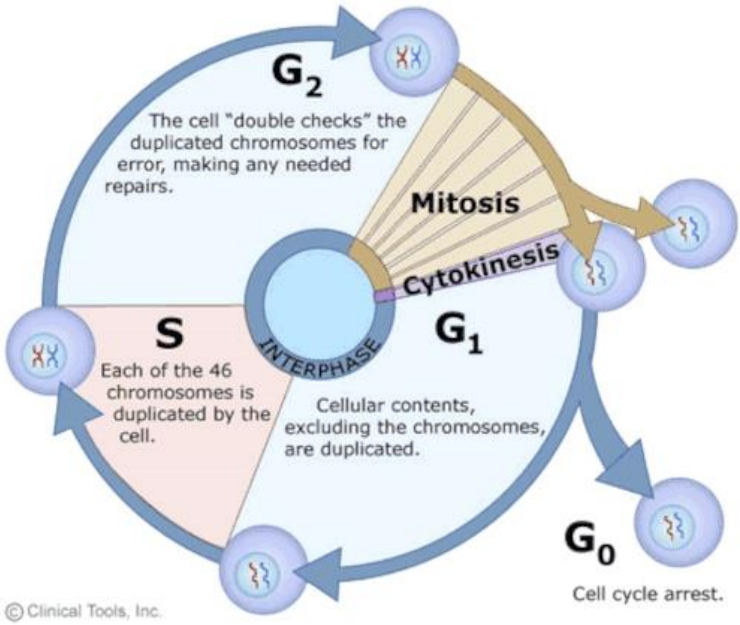
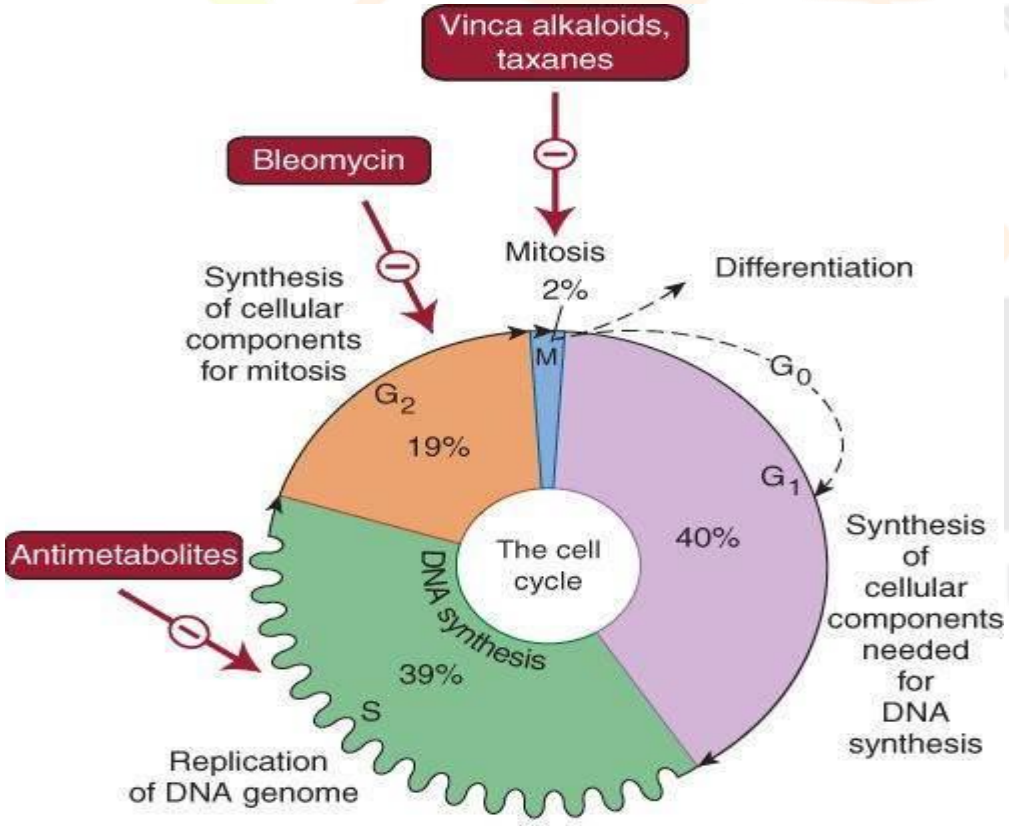
NORMAL CELL CYCLE



CANCER CELL CYCLE



TYPE OF CANCER

Cancer types can be grouped into broader categories. Based on tissue types, cancer can be classified into five major categories.

1) **Carcinoma** :- Carcinoma are the most common type of cancer. This cancer originates from the epithelial layers of cell that form the lining of external parts of the body or the internal lining of organ within the body. There are many subtypes of carcinoma like adenocarcinoma, besal cell carcinoma ,squamous cell carcinoma and transitional cell carcinoma.

2) **Sarcoma** :- Sarcoma cancer that form in bone and soft tissues, including muscle ,fat blood vessels, lymph vessel and fibrous tissue. Osteosarcoma is the most common cancer of a bone.The most common type of soft tissue sarcoma are leiomyosarcoma, Kaposi sarcoma.

3) **Leukemia** :- Cancers that being in the blood forming tissue of the bone marrow are called leukemia. These cancer affect the bone marrow which is the site for the blood cell production. The bone marrow begins to produce excessive immature WBC that failed to perform their usual action and the patient is often prone to infection.

4) **Lymphoma** :- These are the cancer of lymphatic system. These are diseases fighting WBC that are the part of the immune system. In cases of lymphoma, there is an accumulation of abnormal lymphocytes in lymph nodes, lymph vessels, and various organs throughout the body. Lymphoma are solid cancers. There are two main type of lymphoma :- a) Hodgkin lymphoma b) Non- Hodgkin lymphoma.

5) **Multiple myeloma** :- Multiple myeloma is a cancer that begins in plasma cell , another type of immune cell .The abnormal plasma cell called myeloma cells, build up in bone all through the body. Multiple myeloma is called plasma cell myeloma and Kahler disease.

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CAUSES OF CANCER

1. Mutation or changes in DNA cells
2. tobacco use
3. high alcohol consumption
4. A diet characterized by the consumption of red and processed meat, sugary drinks, salty snacks, starchy foods, and refined carbohydrates, including sugars and processed items, is associated with an increased risk of cancer.
5. a lack of physical activity
6. exposure to air pollution
7. exposure to radiation
8. unprotected exposure to UV light, such as sunlight
9. infection by certain viruses including H. pylori, human papillomavirus (HPV), hepatitis B, hepatitis C, HIV, and human herpesvirus 4.

TREATMENT FOR CANCER

- Chemotherapy
- Hormone therapy
- Hyperthermia
- Immunotherapy
- Photodynamic therapy
- Radiation therapy
- Steam cell transplant
- Surgery
- Targeted therapy

ANTI CANCER AGENT

Anti-cancer drugs are medications used to treat cancer. Other names for anti-cancer drugs are antineoplastic , chemotherapy, chemo, cytotoxic, or hazardous drugs. The anticancer agents are specialized drugs used primarily to treat cancer. The first anticancer agents were used in,1940s, which were made naturally or synthetically . anticancer agents can be used alone or in combination with other anticancer drugs. These drugs destroy the cancer cells but have less side effects like, nausea, hair loss, mouth ulcer and lowering of the blood anti-cancer/ antineoplastic agents have different mode of action and their depend upon cytotoxic action which is selective for benign cells i.e. rapidly dividing cells. Anticancer or chemotherapy drugs have the ability to disrupt the growth of cancer cells by causing them to undergo denaturation. While these drugs primarily target dividing cancer cells, normal cells are inevitably impacted during the process. There are over 100 different chemo drugs .Treatment approaches for cancers vary, with some responding to a single chemotherapy drug, while others necessitate a combination involving surgery and/or radiation.

❖ **The main goal of chemotherapy is to:**

- Eliminate cancer cells
- Shrink the tumor
- Prevent cancer from spreading
- Relieve symptoms from cancer

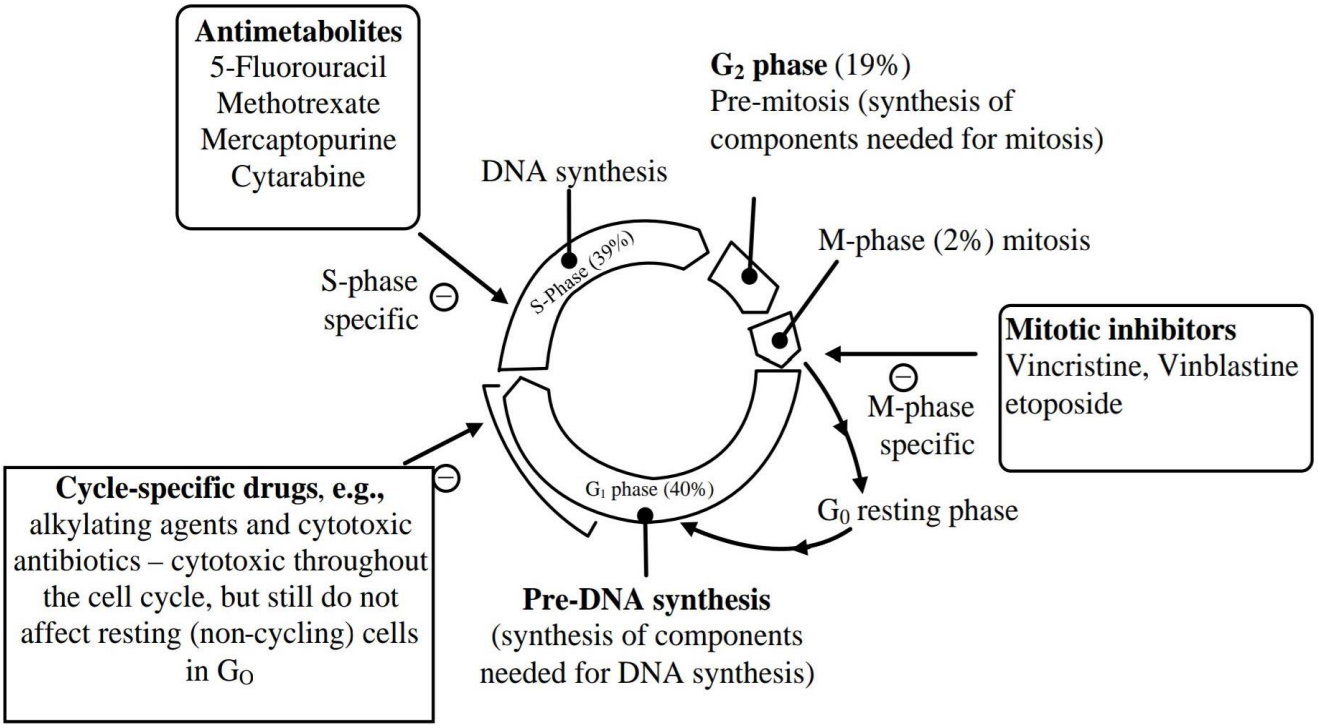
❖ **Chemotherapy can be given through**

- Intravenous (IV)

- By mouth (pill or liquid),
- Injection
- Rubbed into the skin as a cream.

Mechanism of Action

Cytotoxic drugs primarily impact DNA synthesis and cell division, with their effectiveness contingent on the site of action during the cancer cell's DNA synthesis process. These drugs prove most potent against actively cycling/proliferating cells, both normal and malignant, and exhibit lesser efficacy against non-dividing cells.



Distinct drugs excel at targeting cycling cells during specific phases of the cell cycle; these are termed phase-specific drugs . Some other drugs like alkylating agents, are cytotoxic towards the cycling cells in the cell cycle ; these drugs are called cycle-specific drugs.

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CLASSIFICATION OF ANTI-CANCER AGENT

The anti-neoplastic/ anti-cancer agents are classified as follows:

1) Alkylating agents:-

- Nitrogen mustards:-Mechlorethamine (Mustine HCl) , Ifosfamide, cyclophosphamide, Chlorambucil, and Melphalan
- Ethylenimine :-Thiotepa
- Alkyl sulfonate :-Busulfan
- Nitrosoureas:- Carmustine (BCNU) and Lomustine (CCNU)
- Triazine:- Dacarbazine (DTIC)

2) Antimetabolites:-

- Folate antagonist :-Methotrexate (Mtx)
- Purine antagonist :-6-Mercaptopurine (6 -MP), 6-Thioguanine (6 -TG), and Azathioprine
- Pyrimidine antagonist:- 5-Fluorouracil (5 -FU) and Cytarabine (cytosine arabinoside)

3) Natural Products:-

- Vinca alkaloids:- Vincristine (Oncovin) and Vinblastine
- Taxanes:-Paclitaxel and Docetaxel
- Epipodophyllo toxin:- Etoposide
- Camptothecin analogues :- Topotecan and Irinotecan

4) Antibiotics:- Actinomycin D, Dactinomycin, Doxorubicin, Daunorubicin, Rubidomycin, Mitoxantrone, Bleomycin, Mitomycin C, and Mithramycin

5) Enzymes:- Asparaginase (Elspar)

6) Miscellaneous:-Hydroxyurea, Procarbazine, L -Asparaginase, Cisplatin, and Carboplatin

7) Hormones:-

- Glucocorticoids :- Prednisolone
- Estrogens:- Fosfestrol and Ethinylestradiol
- Antiestrogen :- Tamoxifen
- Antiandrogen:- Flutamide
- 5-alpha reductase inhibitor:- Finasteride
- GnRH analogues:-Nafarelin and Goserelin
- Progestins:-Hydroxyprogesterone Acetate, etc.

8) Radioactive Isotopes:- Sodium phosphate, Sodium iodide , and Radio gold solution

ALKYLATING AGENTS

Alkylating agents exert cytotoxic and radiomimetic actions. Several of these substances influence both dividing and resting cells,making them cell cycle -non-specific. Certain agents show CNS stimulant and cholinergic properties. Alkylating agents are chemically reactive compounds. It combines most easily with nucleophilic centres, and a fully saturated carbon atom of the alkylating group attaches to the nucleophile. The expression “alkylating agent” refers to a compound that, through covalent bonding, reacts with a substance and induces alkylation. Any antineoplastic agent that acts by such a mechanism is an alkylating agent. Alkylating agents chemically bound to nucleic acid and bring about the changes in DNA and RNA of cells. This include cross-linking between strands of DNA which results in breaking of the nucleic acid which will not be replicated. This altered DNA unable the functioning of the cell, resulting in cell death. Normal cells may also be affected. Alkylating agents are the derivatives of nitrogen mustards. Advancements in nitrogen mustard led to the discovery of new alkylating agents with cytotoxic effects against cancer.

MECHANISM OF ACTION

Alkylating agents shows three different mechanisms:

1. These alkyl groups attach to DNA bases, prompting repair enzymes to attempt the replacement of alkylated bases. This process inhibits DNA synthesis and RNA production.
2. Cross-links, which are bonds between atoms within the DNA, are established, preventing the DNA from separating during synthesis or transcription, consequently causing harm to the DNA.
3. Mis-pairing of nucleotides occurs that causes mutations.

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DRUGS OF ALKYLATING AGENTS

DRUG NAME	MECHLORETHAMINE	CYCLOPHOSPHAMIDE
INTRODUCTION	Mechlorethamine is the first nitrogen mustard. Administered intravenously, it is highly reactive.	Cyclophosphamide serves as a precursor to alkylating nitrogen mustard, functioning as an antineoplastic and immunosuppressive agent.
MOA	Attachment of alkyl groups to DNA bases ⬇ Prevents DNA synthesis and RNA transcription ⬇ Damages DNA via cross linking	active metabolite of cyclophosphamide i.e. phosphoramide mustard forms DNA cross links between and within DNA strands at guanine N-7 positions. ⬇ This is irreversible and leads to cell death.
BRAND NAME	Mustargen	Cytoxan®
USES	Used for the treatment of metastatic carcinoma. Used for the treatment of Hodgkin' s disease, lymphosarcoma, chronic myelocytic or chronic lymphocytic leukaemia,	used in the treatment of malignant lymphomas, multiple myeloma, leukaemia used in various non-neoplastic autoimmune diseases
SIDE EFFECTS	loss of appetite, Diarrhea, dizziness, painful, swollen joints.	Diarrhea, Hair loss , sores on the mouth or tongue, changes in skin color.

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DRUG NAME	THIOTEPA	BUSULFAN
INTRODUCTION	Thiotepa, a member of the alkylating agent group in cancer chemotherapy.	Busulfan is a bifunctional alkylating agent. It is not a structural analogue of nitrogen mustards
MOA	It acts on 7" position of guanine base of DNA ⬇ stop tumor growth by cross linking with DNA double helix strands ⬇ cells can no longer divide.	It interacts with the thiols groups of proteins and nucleic acids and forms DNA-protein and DNA -DNA cross-links. ⬇ cross -linkages prevent the synthesis and function of DNA.
BRAND NAME	Tepadina	Busulfex
USES	Used for treating breast, ovarian and bladder cancer. Used as conditioning for bone marrow transplantation.	It is combined with cyclophosphamide as part of a conditioning regimen before allogeneic hematopoietic progenitor cell transplantation for chronic conditions.
SIDE EFFECTS	Bleeding gums , Blood in the urine, Blurred or double vision, Coughing up blood, cracked lips.	Sudden weakness or unusual fatigue, persistent cough, congestion, or shortness of breath; flank, stomach or joint pain

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DRUG NAME	CARMUSTINE	DACARBAZINE
INTRODUCTION	Carmustine is a type of chemotherapy drug. It is also known as BCNU.	Dacarbazine is a chemotherapy drug. It is also called DTIC
MOA	It causes cross-links in DNA and RNA, leading to the inhibition of DNA synthesis, RNA production and RNA translation . ↓ It also binds to and modifies (carbamoylates) glutathione reductase. ↓ This leads to cell death.	The mechanism of action is not known, but appears to exert cytotoxic effects via its action as an alkylating agent. ↓ Other theories include DNA synthesis inhibition by its action as a purine analog, and interaction with SH groups. Dacarbazine is not cell cycle-phase specific.
BRAND NAME	BiCNU	DTIC Dome
USES	It is employed in the treatment of brain tumors, non-Hodgkin's lymphoma, and Hodgkin's lymphoma.	Utilized for treating cancers of the lymphatic system and malignant melanoma (a form of skin cancer).
SIDE EFFECTS	Leukopenia, thrombocytopenia, nausea.	Hair thinning, headaches changes to your eye sight feeling confused

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ANTIMETABOLITES

Antimetabolites are one of the oldest and most common types of chemotherapy drugs. An antimetabolite is a substance that hinders the normal cellular metabolic function by either replacing or inhibiting a specific metabolite, which serves as an intermediate or product of metabolism. In other words, antimetabolites prevent the biosynthesis and utilization of normal cellular metabolites. This category of substances shares a structural resemblance with metabolites. So, due to its structure similarity, antimetabolites readily incorporated into DNA or RNA and interfere with cellular function. For e.g. antifolate competitively inhibit the folic acid and produce toxic effects on cells i.e. they stop cell growth and cell division. Antimetabolites show interference with the availability of normal purine or pyrimidine nucleotide precursors either by inhibiting their synthesis, or by competing with them in DNA or RNA synthesis. These drugs stand as the initial effective chemotherapeutic agents. These drugs has low molecular weighed analogues of folic acid, pyrimidine or purine. Their structures are identical to those of naturally occurring molecules involved in nucleic acid (DNA and RNA) synthesis. Antimetabolites are similar to the chemicals required for normal biochemical activity. Nevertheless, their structures are distinctive enough to disrupt normal cell functioning.

MECHANISM OF ACTION

Antimetabolites are structurally same as normal metabolic constituents, like folic acid, pyrimidines, or purines. Antimetabolites operate by impeding the enzymes essential for the regeneration of folic acid or the activation of pyrimidine or purine in DNA or RNA synthesis within neoplastic cells. Typically, antimetabolites induce cell death during the S phase by impeding the DNA replication machinery, either through the integration of chemically altered nucleotides or by depleting the supply of deoxynucleotides essential for DNA replication and cell proliferation.

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DRUGS OF ANTIMETABOLITES

DRUG NAME	METHOTREXATE	6- MERCAPTOPURINE
INTRODUCTION	Methotrexate (MTX) is an antineoplastic antimetabolite with immunosuppressant properties.	Mercaptopurine is an an timetabolite antineoplastic drug having immunosuppressant properties.
MOA	Methotrexate inhibits the enzyme dihydrofolate reductase thus prevents the formation of THF ⬇ Synthesis of DNA And RNA is inhibited	Mercaptopurine is metabolised into 6-MPMP (6-Thioinosinate) by HGPRT. ⬇ This 6-Thioinosinate inhibits conversion of inosinic acid to adenylic acid and xanthylic acid ⬇ prevent the purine biosynthesis.
BRAND NAME	ONCOTREX	Purinethol
USES	It is effectively used with other drugs in acute lymphocytic leukaemia, choriocarcinoma, Burkitt lymphoma in children, breast cancer, and head and neck carcinomas.	Mercaptopurine is used in treatment of leukaemia, usually with other agents.
SIDE EFFECTS	feeling sick, Headaches, Vomiting, Diarrhoea shortness of breath, mouth ulcers	Vomiting, Darkening of the skin, hair loss, Rash, swelling in the legs, ankles, or feet unusual bruising or bleeding

DRUG NAME	5- FLUOROURACIL	6- THIOGUANINE
INTRODUCTION	Fluorouracil is a pyrimidine analogue which is an antineoplastic antimetabolite	Thioguanine, functioning as an antineoplastic compound with antimetabolite action, is employed in the treatment of acute leukemia
MOA	It is activated to fluorodeoxyuridine monophosphate (FdUmp) ⬇ This interferes with DNA Synthesis and function by inhibiting Hymidylate Synthetase enzyme	Like 6-MP, 6-TG is converted intracellularly to TGMP (6-thioguanylic acid) by the enzyme Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) ⬇ TGMP is further converted to the di- and triphosphates, thioguanosine diphosphate and thioguanosine triphosphate ⬇ which inhibits the biosynthesis of purines and also the phosphorylation of GMP to guanosine diphosphate
BRAND NAME	Efudex	TABLOID
USES	It is used in acute lymphocytic leukaemia , Crohn's disease , and ulcerative colitis. On topical application, it is effective in superficial basal cell carcinomas.	It is used for remission induction and remission consolidation treatment of acute non-lymphocytic leukaemia.
SIDE EFFECTS	Skin irritation, burning, redness, dryness, pain, swelling, tenderness, or changes in skin color may occur at the site of application. Eye irritation	Black, tarry stools, Blood in the urine or stools, hoarseness. joint pain, stiffness, or swelling, lower back, side, or stomach pain, pinpoint red spots on the skin.

NATURAL PRODUCTS

Over the years, natural products have proven to be a valuable and practical reservoir of anticancer agents. Numerous compounds have been derived from natural products through structural modifications or by incorporating naturally occurring compounds as building blocks in the synthesis of various compounds. These applications span diverse fields such as biology, medicine, and engineering. People suffering from cancer used herbal medicines as the most commonly used complementary and Alternative methods. Medicinal plants alleviate and address cancer by utilizing compounds that possess antioxidant and anticancer properties, facilitating the elimination of carcinogenic cells. Certain plants inherently possess properties that impede the spread or potential development of various types of cancer.

MECHANISM OF ACTION

Medicinal herbs combat cancer by engaging in the following mechanisms:

1) Disruption in Cell Signal Transduction Pathways: Cancer is related to defects in signal transduction proteins that cause uncontrolled or abnormal cell growth. The herbal drugs impede signal transduction in cancer patients through various pathways.:

i) Nuclear Factor (NF -kB) Pathways with Activator Protein -1 (Ap-1):Nuclear factor with activator protein-1 is a transcription factor diverse gene expressions related to oncogenesis, apoptosis, and more, responding to extracellular signals. This protein complex oversees DNA transcription, cytokine production, and cell survival. Dysregulated NF-kB is linked to cancer, inflammatory conditions, and autoimmune diseases. Plant products block the growth of cancer ous cells by this mechanism; for example, botanical extract of mountain ginseng blocks the growth of lung cancer cells through regulating NF-kB signalling pathway.

ii) Protein Tyrosine Kinase (PTK) Pathways: PTK enzyme ,transfers a phosphate group to a protein in the cell. It may function as an active and in active form in various cellular reactions. It causes growth in signal transduction to cells.

2) Modification in Cell Cycle: Natural and constant balance of cell cycle safeguards standard cell escalation. A tumor arises as a result of any alteration in the cell cycle. The cell cycle elongates due to the existence in the control points in G1 and G2 phases. Neoplastic cells cannot prevent cell division at the control Points (G1/S and G2/M), and thus cell proliferation becomes deregulated.

3) Mitogen-Activated Protein Kinase (MAPK) Signal Pathways: MAPK signaling pathway induces signals for cell division. Therefore, carcinogenesis occurs due to the deregulation of MAPK signal pathways. These methods are employed to trigger apoptosis.

4) Cyclooxygenase (Cox-2) Pathways: Prostaglandin synthesis is facilitated by Cox-2 inhibitors. Its inhibition blocks cell proliferation, thus affects the growth of tumor cells.

5) Intervention with Microtubules: These tubules are microscopically small and found in the cell cytoplasm. These compounds hinder the proper alignment of daughter chromosomes, halting mitosis at anaphase, ultimately leading to apoptosis. Phytochemicals from herbaceous plants, such as vinca alkaloids (vincristine and vinblastine) and taxanes, play a crucial role as microtubulin-binding agents.

6) Topoisomerase Inhibitor: Herbal drugs play crucial role in cancer
Treatment with balancing capacity of topoisomerases. Camptothecins block
Topoisomerase-I, and epipodophyllotoxins blocks topoisomerase II.

DRUGS OF NATURAL PRODUCTS

DRUG NAME	VINCRISTINE/ VINBLASTINE	PACLITAXEL
INTRODUCTION	Vinblastine and vincristine are derived from the periwinkle plant. They are CCS agents and act during M phase of cell cycle.	Paclitaxel is a taxane derived from the bark of the Western yew tree. Docetaxel is a newer taxane.
MOA	Vinblastine and vincristine ↓ Bind to B-tubulin (Drug-tubulin complex) ↓ Inhibits its -polymerization into microtubules ↓ No intact Mitotic spindle ↓ Cell division arrested in metaphase	Paclitaxel ↓ Binds to B-tubulin ↓ Stabilizes microtubules ↓ Formation of abnormal microtubules ↓ Inhibits mitosis
BRAND NAME	Oncovin Velban	Taxol
USES	Vincristine and Vinblastine are used in the treatment of carcinoma of the breast, Hodgkin's disease. Used in the treatment of lymphocytic leukaemia.	Useful in advanced breast, ovarian, lung, oesophageal and bladder cancer
SIDE EFFECTS	Feeling or being sick, Constipation. Fever or chills, nausea	Bone marrow suppression, peripheral neuropathy, myalgia and hypersensitivity reactions

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DRUG NAME	ETOPOSIDE	TOPOTECAN
INTRODUCTION	Etoposide is a semi -synthetic derivative of podophyllotoxin.	Topotecan is a type of chemotherapy drug called a topoisomerase 1 inhibitor.
MOA	Etoposide ↓ Form complex with -DNA and topoisomerase II (Drug-DNA-topoisomerase II) ↓ Prevent resealing of broken DNA strand ↓ Cell death	Topotecan prevents topoisomerase from religating cleaved DNA strand and subsequently DNA damage occurs. ↓ Inactivation of topoisomerase ↓ results in apoptosis and cell death.
BRAND NAME	Vepesid	hycamtin
USES	Etoposide is employed in combination with other cytotoxic drugs for testicular and lung cancers, demonstrating effectiveness in non-Hodgkin's lymphoma and AIDS-related Kaposi's sarcoma.	Topotecan injection is administered to patients with metastatic cancer and is also indicated for treating a specific type of lung cancer known as small cell lung cancer.
SIDE EFFECTS	Bone marrow suppression, Gl side effects such as nausea, vomiting and diarrhoea	Bone marrow suppression.

ANTIBIOTICS

Antineoplastic antibiotics, also known as anticancer or antitumor antibiotics, function similarly to quinolones. The key distinction lies in their target cells: antibiotics act on bacterial cells, while antineoplastic antibiotics act on tumorous or cancerous cells within the human body. Antibiotics, recognized as a significant class of antineoplastic agents. Hence, the production of antineoplastic agents necessitates meticulous strain selection and regulated microbial fermentation conditions to enhance the targeted development of a specific component within an antibiotic mixture. They are secondary metabolites produced by microorganisms (including bacteria, fungi, and actinomycetes) or higher animals and plants during their lifespan, displaying activities such as anti-pathogenic effects and can interfere with the development of other living cells. Research indicates that antibiotics have the potential to induce cancer apoptosis, impede cancer growth, and deter cancer metastasis. Consequently, antibiotics are increasingly employed to aid in cancer treatment.

MECHANISM OF ANTIBIOTICS

Anticancer antibiotics are medications that impact DNA synthesis and replication by integrating into DNA or providing electrons, leading to the generation of highly reactive superoxide (oxygen compounds). These compounds induce the breakage of DNA strands. Many of the antineoplastic antibiotics are obtained from fungus streptomyces include bleomycin, mito- mycin, dactinomycin and doxorubicin. These compounds also having antibacterial activity but because of their high toxicity these are not used as antibiotics.

Antineoplastic antibiotics operate through various mechanisms, such as intercalation, alkylation, and strand breakage. Intercalation is a mechanism in which a planar molecule of suitable size inserts itself between adjacent base pairs of DNA, causing local unwinding and disrupting the template function of DNA. Apart from that intercalation may also inhibit the topoisomerase enzymes (responsible for transcription process).

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DRUGS OF ANTIBIOTICS

DRUG NAME	DACTINOMYCIN	BELOMYCIN
INTRODUCTION	Dactinomycin, a high molecular weight antineoplastic antibiotic, is sourced from Streptomyces parvulus.	Bleomycin is a combination of interconnected glycopeptide antibiotics extracted from Streptomyces verticillus, encompassing bleomycin A2 and B2.
MOA	Dactinomycin, bind to DNA through intercalation between adjoining nucleotide pairs on the same strand of DNA and block transcription of DNA ⬇ Causes DNA damage	Bleomycin binds to DNA, produces free radicals which cause DNA damage.
BRAND NAME	Cosmegen	Bleocip
USES	used as a part of combination chemotherapy and/or multi-modality treatment regimen for treating Wilms' tumo ur, childhood rhabdomyosarcoma, Ewing's sarcoma and metastatic, non-seminomatous testicular cancer	It is used in the treatment of testicular and ovarian tumours and in Hodgkin's lymphoma (ABVP regimen).
SIDE EFFECTS	Cough, Diarrhea (continuing) difficulty with swallowing. Fever, heartburn.	Hyperpigmentation of the skin and pulmonary fibrosis. There is very little bone marrow suppression (spares bone marrow).

DRUG NAME	DOXORUBICIN	DAUNORUBICIN
INTRODUCTION	Doxorubicin is a cytotoxic anthracycline antibiotic. It is obtained from cultures of Streptomyces peucetius var. caesius.	Daunorubicin is a toxic anthracycline aminoglycoside antineoplastic obtained from Streptomyces peucetius
MOA	Doxorubicin exerts its antimitotic and cytotoxic activity by formingcomplexes with DNA through intercalation between bas e pair. ⬇ It blocks the activity of topoisomerase II by stabilising DNA - topoisomerase II complex,inhibiting the religation portion of the ligation-religation reaction catalysed by topoisomerase II.	It blocks the activity of topoisomerase II by stabilising DNA-topoisomerase II complex, inhibiting the religation portion of the ligation-religation reaction catalysed by topoisomerase II.
BRAND NAME	Caelyx	Cerubidine
USES	It is employed to induce regression in widespread neoplastic conditions, including acute lymphoblastic leukemia, acute myeloblastic leukemia, Wilms' tumor, neuroblastoma, soft tissue and bone sarcomas, breast carcinoma, ovarian carcinoma, transitional cell bladder carcinoma, and thyroid carcinoma.	Daunorubicin is effective in acute leukaemias; doxorubicin is active against solid tumours
SIDE EFFECTS	Hair loss, bone marrow suppression, vomiting, rash,anaphylaxis, heart damage, tissue damage at the site of injection	Bone marrow suppression. Gl disturbances and cardiomyopathy with CCF, hypotension or arrhythmias

ENZYMES

Anticancer enzymes catalyse specific amino acid and convert it into an unavailable form to the cells leading to starvation condition. Normal cells remain unaffected by this state of deprivation , because they have the ability to convert the product obtained by the action of anticancer enzyme into the required form for it growth. L-Asparaginase, L-Glutaminase, L-Argininase, L-methioninase are some of the examples of anticancer enzymes.

HORMONES

Some cancers use hormones to grow or develop. This indicates that the cancer is responsive to hormones or reliant on hormones. In cancer treatment, hormone therapy involves the use of medications to obstruct or reduce the levels of hormones in the body, thereby halting or decelerating the cancer's growth. Hormone therapy either halts the production of hormones or hinders hormones from promoting the growth and division of cancer cells. It does not work for all cancers. Prednisolone , Fosfestrol and Ethinylestradiol, Tamoxifen, Flutamide, Finasteride ,Nafarelin and Goserelin are the example of hormones.

RADIOACTIVE ISOTOPE

Radioisotopes are radioactive isotopes of a particular chemical element on the periodic table.Radioisotope therapy uses radioisotopes to destroy cancer cells . Depending on which type of cancer is present, different radioactive isotopes will be used . Sodium phosphate, Sodium iodide , and Radio gold Solution are the example of radioactive isotope.

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DRUG NAME	CISPLATIN	L- ASPARAGINASE
INTRODUCTION	Cisplatin, cisplatinum or cis - diamminedichloroplatinum (II) (CDDP) is a platinum based chemotherapy drug	It is an enzyme sourced from E. coli bacteria. Asparagine is an amino acid which is necessary for protein synthesis.
MOA	Cisplatin ↓ Forms highly reactive platinum complexes ↓ Reacts with DNA ↓ (Forms both intrastrand and interstrand cross-links) DNA damage	L-Asparaginase degrades asparagine to aspartic acid. Hence, Depriving neoplastic cells of asparagine leads to their death.
BRAND NAME	Platinol	Elspar
USES	Cisplatin is highly effective in the treatment of testicular, ovarian, endometrial and bladder cancer. It is also used in lung and oesophageal cancer.	L-asparaginase is used to treat acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL)
SIDE EFFECTS	Nephrotoxicity, peripheral neuropathy, severe nausea and vomiting	Hypersensitivity reaction with skin rashes itching, urticaria,Headache, Hallucinations, confusion and coma

ADVERSE EFFECTS OF ANTI-CANCER DRUGS

The acute effects of antineoplastic / Anticancer drugs often include Nausea and vomiting, sometimes extremely severe. Moreover, numerous of these substances exhibit irritant or vesicant properties, causing localized pain, irritation, and inflammation at the site of administration. Extravasation has the potential to result in ulceration and necrosis. Hypersensitivity reactions may also occur.

The effects may not manifest for days or weeks, depending both on the drugs used and the rate of division in the tissue concerned, and may sometimes be cumulative. Perhaps the most common serious effect, and one which has often limited the doses that can be given, is bonemarrow depression. Because of their effects on the various types of white blood cell many antineoplastics also cause profound suppression of normal immunity, and patients may be at greatly increased risk of severe and disseminated infection.

The rapid destruction of large numbers of cells during antineoplastic therapy of certain highly sensitive tumour, and the consequent release of breakdown products, may also lead to problems with hyperuricaemia and acute renal failure due to uric acid nephropathy (the 'tumour lysis syndrome').

TOXICITY OF ANTICANCER

As anticancer drugs target cancer cells, they also impact rapidly dividing normal cells. Bone marrow, skin, hair, gastrointestinal mucosa, RE system, gonads, fetus, etc. are most severely affected.

Bone marrow suppression: It manifests as leukopenia, agranulocytosis, thrombocytopenia and aplastic anaemia. In such patients, infection and bleeding are common.

(a) Platelet transfusion.
(b) Granulocyte colony-stimulating factor (G-CSF).
(c) Erythropoietin (iv) Bone marrow transplantation.
(d) Using bone marrow-sparing drugs if possible (eg. L-asparaginase, bleomycin, cisplatin And vincristine).

Immunosuppression: Decreased lymphocytes results in immunosuppression. Such patients are Prone for opportunistic infections with fungi, bacteria, viruses, parasites .

Skin and hair: Hair follicles undergo damage, leading to alopecia (hair loss). Alopecia is umally reversible on stoppage of therapy. Dermatitis and skin rashes may manifest as side effects.

Fetus: The use of cytotoxic drugs during pregnancy typically results in abortion or teratogenic effects.

Nephrotoxicity with cisplatin: Saline infusion and mannitol decreases the incidence of nephrotoxicity

Neuropathy with vincristine and paclitaxel.

Pulmonary fibrosis and pigmentation of skin with busulphan and bleomycin.

Carcinogenicity (Secondary malignancy): These drugs may rarely cause secondary cancers in some patients, eg, development of leukaemia in patients with prolonged use of alkylating agents.

CONCLUSION

In conclusion, this study on anticancer drugs provides a comprehensive overview of the various pharmaceutical agents employed in the fight against cancer. From traditional chemotherapy to targeted therapies and immunotherapies, each class of drugs plays a crucial role in disrupting cancer cell growth and progression. Advances in chemotherapy have definitely proved that anticancer drugs can cure cancer if they will combine with other treatment options like radiation therapy and surgical therapy. The primary obstacles to the clinical efficacy of chemotherapy have been the toxicity to the normal tissues of the body. The sites where tissues multiply rapidly such as bone marrow. All anticancer drugs are interfere with DNA or RNA synthesis . Anticancer drugs are almost never used alone, but are used in combination Drugs are highly toxic, cause myelosuppression, mucositis and alopoecia . Must use high dose, intermittent therapy. Overall, this study highlights the significant strides made in anticancer drug development and the ongoing pursuit of more effective and targeted treatment options.

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