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**Review Article**

# A study on cancer and its drugs with their molecular structure and mechanism of action: A Review

Priyanka Sonker[1], Ashish Kumar Tewari[1], Shail Kumar Chaube[2], Ranjeet Kumar[1], Vishal Prasad Sharma[1], Akhilesh Sonker[1], Priyanka Yadav[1]

[1]Department of Chemistry, [2]Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi-221005, India

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## ABSTRACT

Cancer is a fatal disease that severely effects the human population. For treatment of cancer there is lots of demand of anticancerous drugs which every new anticancer drug or combination is evaluated for safety and efficacy before being approved. Anticancer therapy have urged scientist to discover new agents. As a result of growing spectrum of new targets and strategies and recent biological and biotechnological progresses, the mechanism of action of many anticancer agents such as tyrosine kinase inhibitors, epigenetic drugs, monoclonal antibodies have been reached to clinical trials. Addition to the traditional targets such as mitosis, DNA synthesis, repairing systems, tumor growth, apotosis tumor vasculature and cell signaling mechanism. Some other targets such as proteosome, heat shock protein ad epigenetics (HDACs, HATs, DNMT, PAD4, AID and Tet1) have been used to design as a new anticancer agent. In this review, recent approaches of the target based anticancer drug with molecular formula, molecular structure and mechanism of action have been highlighted to giving some examples from approved agents. In this review you can learn more about the known and possible causes of cancer, as well as general information about carcinogens and how genetics play a role in cancer.

**Keywords:** Apoptosis, Cytotoxicity, monoclonal antibodies, Thymidylatesynthase(TS), Dihydrofolatereductase (DHFR), Epigenetics, Deoxycytidine kinase, monoclonal antibodies, Causes, Symptoms,Therapy, Management

**Address for Correspondence:** Dr. A. K. Tewari ,Department of Chemistry (Center of Advanced Studies), Institute of Science, Banaras Hindu University, Varanasi, 221005, India. Email-tashish2002@yahoo.com

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## INTRODUCTION

Cancers are any one of large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissues .Cancers has ability to spread throughout the body. [1] They form a subset of neoplasms. A neoplasm or tumor is a group of cells that have undergone unregulated growth and will often form a mass or lump, but may be distributed diffusely. [2]

All tumor cells show the six hallmarks of cancer. These characteristics are required to produce a malignant tumor. [3] They include-

- Cell growth and division absent the proper signals
- Continuous growth and division even given contrary signals
- Avoidance of programmed cell death
- Limitless number of cell divisions
- Promoting blood vessel construction
- Invasion of tissue and formation of metastases[4]

The progression from normal cells to cells that can form a detectable mass to outright cancer involves multiple steps known as malignant progression. [5]

## SIGN AND SYMPTOMS

When cancer disease started, then it does not show produces any symptoms. After few days or years Signs and symptoms may appear forming a mass of cells or ulcerates. The findings of cancer disease that result depend on the cancer's type and location. Few symptoms are specific. Many frequently occur in individuals who have other conditions. [6]

## LOCAL SYMPTOMS

Local symptoms may occur due to the mass of the tumor or ulceration in body cells. For example, the mass of cells can affect to lungs cancer can block the bronchus resulting in cough or pneumonia; esophageal cancer can cause narrowing of the esophagus, making it difficult or painful to swallow; and colorectal cancer may lead to narrowing or blockages in the wall of colon, affecting bowel habits. Masses of breast cells or testicles may produce observable lumps. Ulceration can cause bleeding that, if it occurs in the lung, will lead to coughing with blood, in the bowels to anemia or rectal bleeding, in the bladder to blood in the urine and in the uterus to vaginal bleeding. Although localized pain may occur in advanced cancer, the initial swelling is usually painless. Some cancers can cause a buildup of fluid within the chest or abdomen. [6]

## SYSTEMIC SYMPTOMS

General symptoms are occurring due to effects that are not related to direct or metastatic spread. These may include: unintentional weight loss, fever, excessive fatigue and changes to the skin. Hodgkin disease, leukemias and cancers of the liver or kidney can cause a persistent fever.

## METASTASIS

The main reason that cancer is so serious is its ability to spread in the body. Cancer cells can spread locally by moving into nearby normal tissue. Cancer can also spread regionally, to nearby lymph nodes, tissues, or organs. So it is called metastasis and it can spread to distant parts of the body. When this happens, it is called metastatic cancer. For many types of cancer, it is also called stage IV (four) cancer. The process by which cancer cells spread to other parts of the body is called metastasis. The symptoms of metastatic cancers depend on the tumor location and can include enlarged lymph nodes (which can be felt or sometimes seen under the skin and are typically hard), enlarged liver or enlarged spleen, which can be felt in the abdomen, pain or fracture of affected bones and neurological symptoms.[7]

## CAUSES

Cancer is caused by changes (mutations) to the DNA within cells. The DNA inside a cell is packaged into a large number of individual genes, each of which contains a set of instructions telling the cell what functions to perform, as well as how to grow and divide. Errors in the instructions can cause the cell to stop its normal function and may allow a cell to become cancerous. [8]

The majority of cancers, some 90–95% of cases, are due to genetic mutations from environmental factors. The remaining 5–10% are due to inherited genetics.[3] *Environmental*, as used by cancer researchers, means any cause that is not inherited genetically, such as lifestyle, economic and behavioral factors and not merely pollution.[32] Common environmental factors that contribute to cancer death include tobacco (25–30%), diet and obesity (30–35%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity and pollution. [9]

It is not generally possible to prove what caused a particular cancer because the various causes do not have specific fingerprints. For example, if a person who uses tobacco heavily develops lung cancer, then it was probably caused by the tobacco use, but since everyone has a small chance of developing lung cancer as a result of air pollution or radiation,

the cancer may have developed for one of those reasons. Excepting the rare transmissions that occur with pregnancies and occasional organ donors, cancer is generally not a transmissible disease. [10]

## CHEMICALS

Exposure to particular substances has been linked to specific types of cancer. These substances are called *carcinogens*. [11] Tobacco smoke, for example, causes 90% of lung cancer. It also causes cancer in the larynx, head, neck, stomach, bladder, kidney, esophagus and pancreas. Tobacco smoke contains over fifty known carcinogens, including nitrosamines and polycyclic aromatic hydrocarbons. [12]

Tobacco is responsible for about one in five cancer deaths worldwide and about one in three in the developed world. Lung cancer death rates in the United States have mirrored smoking patterns, with increases in smoking followed by dramatic increases in lung cancer death rates and, more recently, decreases in smoking rates since the 1950s followed by decreases in lung cancer death rates in men since 1990.[13,14]

## DIET AND EXERCISE

Diet, physical inactivity and obesity are related to up to 30–35% of cancer deaths. In the United States excess body weight is associated with the development of many types of cancer and is a factor in 14–20% of cancer deaths. A UK study including data on over 5 million people showed higher body mass index to be related to at least 10 types of cancer and responsible for around 12,000 cases each year in that country. Physical inactivity is believed to contribute to cancer risk, not only through its effect on body weight but also through negative effects on the immune system and endocrine system. More than half of the effect from diet is due to overnutrition (eating too much), rather than from eating too few vegetables or other healthful foods. [15,16]

## INFECTION

Worldwide approximately 18% of cancer deaths are related to infectious diseases. This proportion ranges from a high of 25% in Africa to less than 10% in the developed world.[3]Viruses are the usual infectious agents that cause cancer but cancer bacteria and parasites may also play a role.[17] *Oncovirus*es (viruses that can cause cancer) include human papillomavirus (cervical cancer), Epstein–Barr virus (B-cell lymphoproliferative disease and nasopharyngeal carcinoma), Kaposi's sarcoma herpesvirus (Kaposi's sarcoma and primary effusion lymphomas), hepatitis B and hepatitis C viruses (hepatocellular carcinoma) and human T-cell leukemia virus-1(T-cell leukemias). Bacterial infection may also increase the risk of cancer, as seen in *Helicobacter pylori*-induced gastric carcinoma. Parasitic infections associated with cancer include *Schistosoma haematobium* (squamous cell carcinoma of the bladder) and the liver flukes, *Opisthorchis viverrini* and *Clonorchis sinensis* (cholangiocarcinoma).[18]

## RADIATION

Up to 10% of invasive cancers are related to radiation exposure, including both ionizing radiation and non-ionizing ultraviolet radiation. Additionally, the majority of non-invasive cancers are non-melanoma skin cancers caused by non-ionizing ultraviolet radiation, mostly from sunlight. Sources of ionizing radiation include medical imaging and radon gas. [19] Ionizing radiation is not a particularly strong mutagen. Residential exposure to radon gas, for example, has similar cancer risks as passive smoking. Radiation is a more potent source of cancer when combined with other cancer-causing agents, such as radon plus tobacco smoke.[52] Radiation can cause cancer in most parts of the body, in all animals and at any age. Children and adolescents are twice as likely to develop radiation-induced leukemia as adults; radiation exposure before birth has ten times the effect. [20, 21, 22] Non-ionizing radio frequency radiation from mobile phones, electric power transmission and other similar sources have been described as a possible carcinogen by the World Health Organization's International Agency for Research on Cancer. However, studies have not found a consistent link between mobile phone radiation and cancer risk. [23]

## HEREDITY

The vast majority of cancers are non-hereditary (sporadic). Hereditary cancers are primarily caused by an inherited genetic defect. Less than 0.3% of the populations are carriers of a genetic mutation that has a large effect on cancer risk and this cause less than 3–10% of cancer. Some of these syndromes include: certain inherited mutations in the genes *BRCA1* and *BRCA2* with a more than 75% risk of breast cancer and ovarian cancer, and hereditary non polyposis colorectal cancer (HNPCC or Lynch syndrome), which is present in about 3% of people with colorectal cancer, among others.[24] Statistically for cancers causing most mortality, the relative risk of developing colorectal cancer when a first-degree relative (parent, sibling or child) has been

diagnosed with it is about 2. The corresponding relative risk is 1.5 for lung cancer, and 1.9 for prostate cancer. For breast cancer, the relative risk is 1.8 with a first-degree relative having developed it at 50 years of age or older, and 3.3 when the relative developed it when being younger than 50 years of age. [25]

## PHYSICAL AGENTS

Some substances cause cancer primarily through their physical, rather than chemical, effects. A prominent example of this is prolonged exposure to asbestos, naturally occurring mineral fibers that are a major cause of mesothelioma (cancer of the serous membrane) usually the serous membrane surrounding the lungs. [26] Physical trauma resulting in cancer is relatively rare. Claims that breaking bones resulted in bone cancer, for example, have not been proven. Similarly, physical trauma is not accepted as a cause for cervical cancer, breast cancer or brain cancer. [27] One accepted source is frequent, long-term application of hot objects to the body. It is possible that repeated burns on the same part of the body, such as those produced by kanger and kairo heaters (charcoal hand warmers), may produce skin cancer, especially if carcinogenic chemicals are also present.[28] Frequent consumption of scalding hot tea may produce esophageal cancer. [29]

## HORMONES

Some hormones play a role in the development of cancer by promoting cell proliferation. Insulin-like growth factors and their binding proteins play a key role in cancer cell proliferation, differentiation and apoptosis, suggesting possible involvement in carcinogenesis. Hormones are important agents in sex-related cancers, such as cancer of the breast, endometrium, prostate, ovary and testis and also of thyroid cancer and bone cancer. For example, the daughters of women who have breast cancer have significantly higher levels of estrogen and progesterone than the daughters of women without breast cancer. These higher hormone levels may explain their higher risk of breast cancer, even in the absence of a breast-cancer gene. Similarly, men of African ancestry have significantly higher levels of testosterone than men of European ancestry and have a correspondingly higher level of prostate cancer. Men of Asian ancestry, with the lowest levels of testosterone-activating androstanediol glucuronide, have the lowest levels of prostate cancer. [30]

## AUTOIMMUNE DISEASES

There is an association between celiac disease and an increased risk of all cancers. People with untreated celiac disease have a higher risk, but this risk decreases with time after diagnosis and strict treatment, probably due to the adoption of a gluten-free diet, which seems to have a protective role against development of malignancy in people with celiac disease. [31] However, the delay in diagnosis and initiation of a gluten-free diet seems to increase the risk of malignancies. [32]

## PATHOPHYSIOLOGY

Cancers are caused by a series of mutations. Each mutation alters the behavior of the cell somewhat.

## GENETICS

Cancer is fundamentally a disease of tissue growth regulation. In order for a normal cell to transform into a cancer cell, the genes that regulate cell growth and differentiation must be altered. [33] The affected genes are divided into two broad categories. Oncogenes are genes that promote cell growth and reproduction. Tumor suppressor genes are genes that inhibit cell division and survival. Malignant transformation can occur through the formation of novel oncogenes, the inappropriate over-expression of normal oncogenes, or by the under-expression or disabling of tumor suppressor genes. Typically, changes in multiple genes are required to transform a normal cell into a cancer cell. [34]

Large-scale mutations involve the deletion or gain of a portion of a chromosome. Genomic amplification occurs when a cell gains copies (often 20 or more) of a small chromosomal locus, usually containing one or more oncogenes and adjacent genetic material. Translocation occurs when two separate chromosomal regions become abnormally fused, often at a characteristic location. A well-known example of this is the Philadelphia chromosome, or translocation of chromosomes 9 and 22, which occurs in chronic myelogenous leukemia and results in production of the BCR-ablfusion protein, an oncogenic tyrosine kinase. [35]

The errors that cause cancer are self-amplifying and compounding, for example:

- A mutation in the error-correcting machinery of a cell might cause that cell and its children to accumulate errors more rapidly.
- A further mutation in an oncogene might cause the cell to reproduce more rapidly and more frequently than its normal counterparts.
- A further mutation may cause loss of a tumor suppressor gene, disrupting the apoptosis signaling pathway and immortalizing the cell.
- A further mutation in the signaling machinery of the cell might send error-causing signals to nearby cells.[36]

Characteristic abilities developed by cancers are divided into categories, specifically evasion of apoptosis, self-sufficiency in growth signals, insensitivity to anti-growth signals, sustained angiogenesis, limitless replicative potential, metastasis, reprogramming of energy metabolism and evasion of immune destruction. [37]

## EPIGENETICS

The classical view of cancer is a set of diseases that are driven by progressive genetic abnormalities that include mutations in tumor-suppressor genes and oncogenes and chromosomal abnormalities. Later epigenetic alterations' role was identified. [38] Epigenetic alterations refer to functionally relevant modifications to the genome that do not change the nucleotide sequence. Examples of such modifications are changes in DNA methylation (hypermethylation and hypomethylation), histone modification[39] and changes in chromosomal architecture (caused by inappropriate expression of proteins such as HMGA2 or HMGA1). Each of these alterations regulates gene expression without altering the underlying DNA sequence. These changes may remain through cell divisions, last for multiple generations and can be considered to be epimutations (equivalent to mutation. [40,41]

## METASTASIS

Metastasis is the spread of cancer to other locations in the body. The dispersed tumors are called metastatic tumors, while the original is called the primary tumor. Almost all cancers can metastasize. Most cancer deaths are due to cancer that has metastasized.

Metastasis is common in the late stages of cancer and it can occur via the blood or the lymphatic system or both. The typical steps in metastasis are local invasion, intravasation into the blood or lymph, circulation through the body, extravasation into the new tissue, proliferation and angiogenesis. Different types of cancers tend to metastasize to particular organs, but overall the most common places for metastases to occur are the lungs, liver, brain and the bones. [42]

## DIAGNOSIS

Most cancers are initially recognized either because of the appearance of signs or symptoms or through screening. Neither of these leads to a definitive diagnosis, which requires the examination of a tissue sample by a pathologist. People with suspected cancer are investigated with medical tests. These commonly include blood tests, X-rays, (contrast) CT scans and endoscopy. [43]

## CLASSIFICATION

**Types of Cancers-**

1) **Cancers of Blood and Lymphatic Systems**

(a) Hodgkin's disease, (b) Leukemia's, (c) Lymphomas, d) Multiple myeloma, e) Waldenstrom's disease

**2) Skin Cancers**

a) Malignant Melanoma

**3) Cancers of Digestive Systems**

(a) Esophageal cancer (b) Stomach cancer (c) Cancer of pancreas (d) Liver cancer (e) Colon and Rectal cancer (f) Anal cancer

**4) Cancers of Urinary system**

(a) Kidney cancer (b) Bladder cancer (c) Testis cancer (d) Prostate cancer

**5) Cancers in women**

(a) Breast cancer (b) Ovarian cancer (c) Gynecological cancer (d) Choriocarcinoma

**6) Miscellaneous cancers**

(a) Brain cancer (b) Bone cancer (c) Characinoid cancer (d) Nasopharyngeal cancer (e) Retroperitoneal sarcomas (f) Soft tissue cancer (g) Thyroid cancer

Breast cancer is the most common form cancer in worldwide. Amongst South African women, breast cancer is likely to develop in one out of every 31 women in the country. Breast cancer in India is the second most common cancer in women after the cancer of uterine cervix. [44,45,46,]

## PREVENTION

Cancer prevention is defined as active measures to decrease cancer risk. The vast majority of cancer cases are due to environmental risk factors. Many of these environmental factors are controllable lifestyle choices.

Greater than 30% of cancer deaths could be prevented by avoiding risk factors including: tobacco, excess weight/obesity, poor diet, physical inactivity, alcohol, sexually transmitted infections and air pollution.[50] Not all environmental causes are controllable, such as naturally occurring background radiation and cancers caused through hereditary genetic disorders and thus are not preventable via personal behavior.[47]

## DIETARY

While many dietary recommendations have been proposed to reduce cancer risks, the evidence to support them is not definitive. The primary dietary factors that increase risk are obesity and alcohol consumption. Diets low in fruits and vegetables and high in red meat have been implicated but reviews and meta-analyses do not come to a consistent conclusion. A 2014 meta-analysis find no relationship between fruits and vegetables and cancer.Coffee is associated with a reduced risk of liver cancer. Studies have linked excess

consumption of red or processed meat to an increased risk of breast cancer, colon cancer and pancreatic cancer, a phenomenon that could be due to the presence of carcinogens in meats cooked at high temperatures. In 2015 the IARC reported that eating processed meat (e.g., bacon, ham, hot dogs, sausages) and, to a lesser degree, red meat was linked to some cancers.[48]

Dietary recommendations for cancer prevention typically include an emphasis on vegetables, fruit, whole grains and fish and an avoidance of processed and red meat (beef, pork, lamb), animal fats, pickled foods and refined carbohydrates.[49]

## MEDICATION

Medications can be used to prevent cancer in a few circumstances. In the general population, NSAIDs reduce the risk of colorectal cancer; however, due to cardiovascular and gastrointestinal side effects, they cause overall harm when used for prevention. Aspirin has been found to reduce the risk of death from cancer by about 7%. Daily use of tamoxifen or raloxifene reduce the risk of breast cancer in high-risk women. The benefit versus harm for 5-alpha-reductase inhibitor such as finasteride is not clear. [50]

Vitamin supplementation does not appear to be effective at preventing cancer. While low blood levels of vitamin D are correlated with increased cancer risk, whether this relationship is causal and vitamin D supplementation is protective is not determined. One 2014 review found that supplements had no significant effect on cancer risk. [51] Another 2014 review concluded that vitamin $D_3$ may decrease the risk of death from cancer (one fewer death in 150 people treated over 5 years), but concerns with the quality of the data were noted. [52]

Beta-carotene supplementation increases lung cancer rates in those who are high risk. Folic acid supplementation is not effective in preventing colon cancer and may increase colon polyps. It is unclear if selenium supplementation has an effect. [53]

## VACCINATION

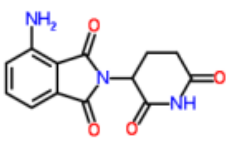
Vaccines have been developed that prevent infection by some carcinogenic viruses. Human papillomavirus vaccine (Gardasil and Cervarix) decrease the risk of developing cervical cancer.[54] The hepatitis B vaccine prevents infection with hepatitis B virus and thus decreases the risk of liver cancer. The administration of human papillomavirus and hepatitis B vaccinations is recommended when resources allow. [55]

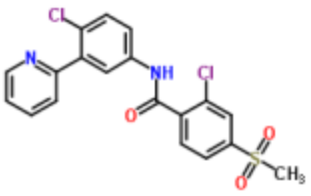
## MANAGEMENT

The primary ones include surgery, chemotherapy, radiation therapy, hormonal therapy, targeted therapy and palliative care. Which treatments are used depends on the type, location and grade of the cancer as well as the patient's health and preferences. The treatment intent may or may not be curative.[56]

## CHEMOTHERAPY

Chemotherapy is one of the most powerful tools we have to treat cancer, and research continues to find new chemotherapy drugs as well as new uses for existing ones. At the same time, newer types of drugs are being developed that work in different ways to attack cancer cells. These types of drugs include targeted therapy, which aims to more precisely identify cancer cells while doing less damage to normal cells, and immunotherapy, which uses the body's own immune system to help find and destroy cancer. This year, the US Food and Drug Administration (FDA) granted its first approvals for a type of immune therapy – or gene modification therapy – that changes a patient's own T cells in the lab to make them more effective against cancer.[57]

| DRUGS NAME | CHEMISTRY | MECHANISM OF ACTION |
|---|---|---|
| **Pomalidomide** | **Molecular Structure-$C_{13}H_{11}N_3O_4$**<br>  <br>*Chemsrc.com* | Its mechanism of action has pomalidomide appears to inhibit TNF-alpha production, enhance the activity of T cells and natural killer (NK) cells and enhance antibody-dependent cellular cytotoxicity(ADCC). Pomalidomide may also inhibit tumor angiogenesis, promote cell cycle arrest in susceptible tumor cell populations and stimulate erythropoeisis.[58] |
| **Vismodegib** | **Molecular formula- $C_{19}H_{14}Cl_2N_2O_3S$** | Vismodegib acts as cyclopamine |



competitive antagonist of smoothened receptor which is part of Vismodegib Acts as cyclopaminethe hedgehog signaling pathway. SMO inhibition causes the transcription factor GLI1 and GLI2 to remain inactive that prevents the expression of tumor mediating genes within the hedgehog pathway.[59]

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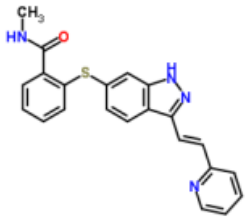
**Axitinib** **Molecular formula- $C_{22}H_{18}N_4OS$**



Its mechanism of action is thought to be vascular endothelial growth factor receptor 1-3, c-KIT and PDGFR inhibition, this, in turn, enables it to inhibit angiogenesis(the formation of new blood vessels by tumours).It was also proposed that it might act by inducing autophagy, it has also been shown to bind (in a different conformation from the VEGF binding) to the BCR-ABL fusion protein, specifically inhibiting the drug-resistant T315I mutant isoform.[60]

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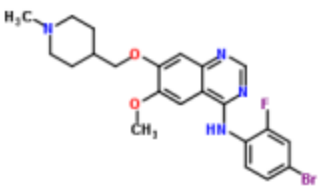
**Vandetanib** **Molecular Formula- $C_{22}H_{24}BrFNchemccchch$**



It is a potent and selective inhibitor of VEGFR (vascular endothelial growth factor receptor), EGFR (epidermal growth factor receptor) and RET (REarranged during Transfection) tyrosine kinases. VEGFR- and EGFR-dependent signalling are both clinically validated pathways in cancer, including non-small-cell lung cancer (NSCLC). RET activity is important in some types of thyroid cancer, and early data with vandetanib in medullary thyroid cancer.[61]

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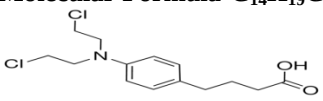
**Chlorambucil** **Molecular Formula-$C_{14}H_{19}Cl_2NO_2$**



The Drug Chlorambucil produces its anti-cancer effects by interfering with DNA replication and damaging the DNA in the cell. The DNA damage induces cell cycle arrest and cellular apoptosis via the accumulation of cytosolic p53 and subsequent activation of Bax, an apoptosis promoter.[62]

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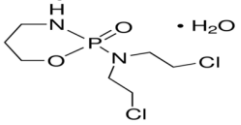
**Cyclophosphamide** **Molecular Formula - $C_7H_{15}Cl_2N_2O_2P$**



Cyclophosphamide form DNA crosslinks both between and within DNA strands at guanine N-7 positions (known as interstrand and intrastrand crosslinkages, respectively). This is irreversible and leads to cell apoptosis.[63]

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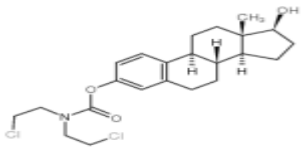
**Estramustine**

**Molecular Formula- $C_{23}H_{31}Cl_2NO_3$**



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Estramustine exert their cytotoxic effect by binding to tubulin and/or microtubule associated protein depolymerization and cellular metaphase arrest. Estramustine may also induce oxygen radicals damage cell membranes, promote DNA breakage and interference with DNA replication, and induce cellular apoptosis in cell lines.[64]

**Ifosfamide**

**Molecular Formula-$C_7H_{15}Cl_2N_2O_2P$**

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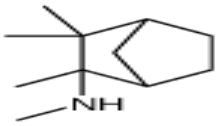
Ifosfamide is an oxazophosphorine alkylating agent. Following activation in the liver, ifosfamide interferes with DNA through formation of phosphotriesters and DNA-DNA crosslinks, thereby inhibiting protein synthesis and DNA synthesis.1,4 Ifosfamide is cell cycle-specific, but cell cycle phase non-specific.1,4 Ifosfamide is an immunosuppressive agent.[65]

**Mechlorethamine**

**Molecular Formula- $C_{11}H_{21}N$**



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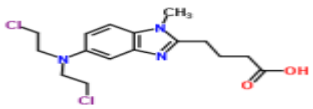
Mechlorethamine act by damaging the RNA and DNA that tells about the cell how to copy itself in division. If the the cells are not able to divide, they die. The faster the cells are dividing, the more likely it is that chemotherapy will kill the cancerous cells, causing the tumor to shrink. They also promote cell suicide (self-death or apoptosis).[66]

**Bendamustine**

**Molecular Formula- $C_{16}H_{21}Cl_2N_3O_2$**



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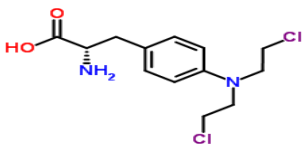
Bendamustine effects on DNA repair and cell cycle progression. Moreover, bendamustine can induce cell death through apoptotic and non apoptotic pathways, thereby retaining activity even in cells without a functional apoptotic pathway.[67]

**Melphalan**

**Molecular Formula- $C_{13}H_{18}Cl_2N_2O_2$**



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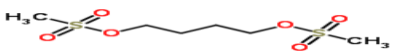
Melphalan chemically alters throgh through alkylation of the DNA nucleotide guanine, and causes linkages between strands of DNA. This chemical alteration inhibits DNA synthesis and RNA synthesis, functions necessary for cells to survive. These changes cause cytotoxicity in both dividing and non-dividing tumor cells.[68]

**Busulfan**

**Molecular Formula- $C_6H_{14}O_6S_2$**



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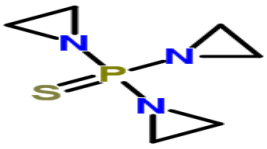
Busulfan is an alkylsulfonate. It is an alkylating agent that forms DNA-DNA intrastrand crosslinks between the DNA bases guanine and adenine and between guanine and guanine. This occurs through an SN2 reaction in which the relatively nucleophilic guanine N7 attacks the carbon adjacent to the mesylate leaving group. DNA crosslinking prevents DNA replication. Because the intrastrand DNA crosslinks cannot be repaired by cellular machinery, the cell undergoes apoptosis.[69]

**Thiotepa**

**Molecular Formula- $C_6H_{12}N_3PS$**

Thiotepa is attached to the guanine base of DNA, at the number 7 nitrogen atom of the imidazole ring.



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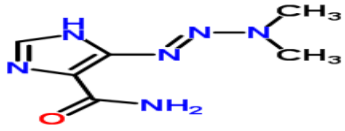
They stop tumor growth by cross linking guanine nucleobases in DNA double-helix strands, directly attacking DNA. This makes the strands unable to uncoil and separate. As this is necessary in DNA replication, the cells can no longer divide.[70]

**Dacarbazine**

**Molecular Formula- $C_6H_{10}N_6O$**



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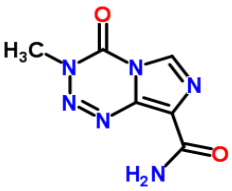
It actss by methylating guanine at the O-6 and N-7 positions. Guanine is one of the four nucleotides that makes up DNA. The methylated DNA strands stick together such that cell division becomes impossible. This affects cancer cells more than healthy cells because cancer cells divide faster. Unfortunately however, some of the healthy cells will still be damaged.[71]

**Temozolomide**

**Molecular Formula- $C_6H_6N_6O_2$**



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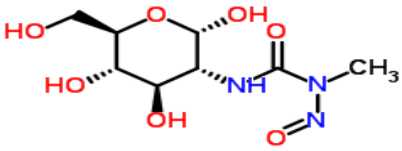
It depends on itability to alkylate/methylate DNA, which most often occurs at the N-7 or O-6 positions of guanine residues. This methylation damages the DNA and triggers the death of tumor cells. In some tumors, MGMT is epigenetic silencing gene which prevents the synthesis of this enzyme, and as a consequence such tumors are more sensitive to killing.[72]

**Streptozocin**

**Molecular Formula- $C_8H_{15}N_3O_7$**



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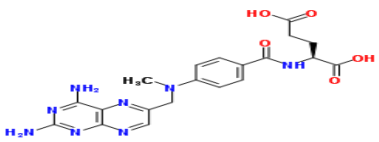
It is known to inhibit DNA synthesis, interfere with biochemical reactions of NAD and NADH, and inhibit some enzymes involved in gluconeogenesis. Its activity appears to occur as a result of formation of methylcarbonium ions, which alkylate or bind with many intracellular molecular structures including nucleic acids. Its cytotoxic action is probably due to cross-linking of strands of DNA, resulting in inhibition of DNA synthesis.[73]

**Methotrexate**

**Molecular Formula- $C_{20}H_{22}N_8O_5$**



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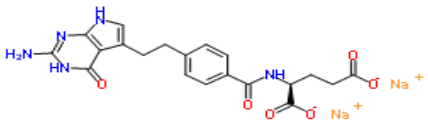
Methotrexate anti-tumor activity is a result of the inhibition of folic acid reductase, leading to inhibition of DNA synthesis and inhibition of cellular replication. DNA synthesis cannot proceed because the coenzymes needed for one-carbon transfer reactions are not produced from tetrahydrofolic acid because there is no tetrahydrofolic acid. Methotrexate selectively affects the most rapidly dividing cells (neoplastic and psoriatic cells).[74]

**Pemetrexed Disodium**

**Molecular Formula- $C_{20}H_{19}N_5Na_2O_6$**

It works by inhibiting three enzymes used in purine and pyrimidine synthesis—thymidylate synthase (TS), dihydrofolate reductase (DHFR) & glycinamide ribonucleotideformyltransferase (GARFT). By inhibiting the formation of precursor of purine and pyrimidine nucleotides, pemetrexed prevents the formation of DNA and RNA, which are required for the growth and survival of both normal cells and cancer cells.[75]



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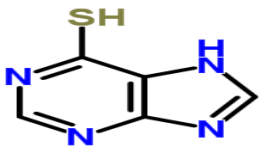
**Mercaptopurine** **Molecular Formula- $C_5H_4N_4S$**



Mercaptopurine competes with hypoxanthine and guanine for the enzyme hypoxanthine-guanine-phosphoribosyl-transferase (HGPRTase) and mercaptopurine itself converted to thioinosinic acid (TIMP). This intracellular nucleotide inhibits several reactions involving inosinic acid (IMP), including the conversion of IMP to xanthylic acid (XMP) and the conversion of IMP to adenylic acid (AMP) via adenylosuccinate.[76]

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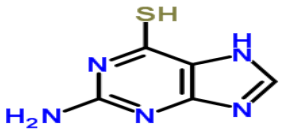
**Thioguanin** **Molecular Formula- $C_5H_5N_5S$**



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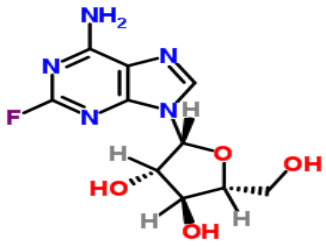
Thioguanine competes with hypoxanthine and guanine for the enzyme hypoxanthine-guanine-phosphoribosyltransferase (HGPRTase) and is itself converted to 6-thioguanilyic acid (TGMP), which reaches high intracellular concentrations at therapeutic doses. TGMP interferes with the synthesis of guanine nucleotides by its inhibition of purine biosynthesis by pseudofeedback inhibition of glutamine-5-phosphoribosyl-pyrophosphat-amidotransferase, Thioguanine nucleotides are incorporated into both the DNA and the RNA by phosphodiester linkages.[77]

**Fludarabine** **Molecular Formula- $C_{10}H_{12}FN_5O_4$**



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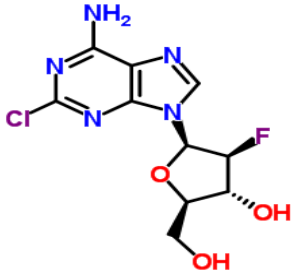
Fludarabine phosphate is rapidly dephosphorylated to 2-fluoro-ara-A and then phosphorylated intracellularly by deoxycytidine kinase to the active triphosphate, 2-fluoro-ara-ATP. This metabolite appears to act by inhibiting DNA polymerase alpha, ribonucleotide reductase and DNA primase, thus inhibiting DNA synthesis.[78]

**Clofarabine** **Molecular Formula- $C_{10}H_{11}ClFN_5O_3$**



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Clofarabine is metabolized intracellularly to the active 5'-monophosphate metabolite by deoxycytidine kinase and 5'-triphosphate metabolite by mono- and di-phospho-kinases. This metabolite inhibits DNA synthesis through an inhibitory action on ribonucleotide reductase, and by terminating DNA chain elongation and inhibiting repair through competitive inhibition of DNA polymerases. [79]

**Pentostatin** **Molecular Formula- $C_{11}H_{16}N_4O_4$**

It mimics the nucleoside adenosine and thus

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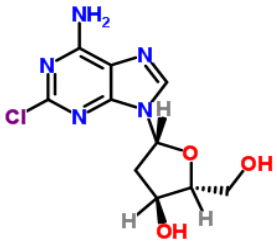
inhibits the enzyme adenosine deaminase, interfering with the cell's ability to process DNA. Cancer cells generally divide more often than healthy cells; DNA is highly involved in cell division (mitosis) and drugs which target DNA-related processes are therefore more toxic to cancer cells than healthy cells.[80]

**Cladribine** **Molecular Formula- $C_{10}H_{12}ClN_5O_3$**



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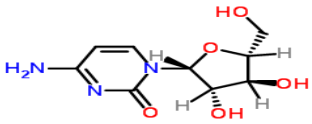
Cladribine is phosphorylated by deoxycytidine kinase to the nucleotide cladribine triphosphate (CdATP; 2-chloro-2′deoxyadenosine5′triphosphate), which accumulates and is incorporated into DNA in cells such as lymphocytes that contain high levels of deoxycytidine kinase and low levels of deoxynucleotidase, resulting in DNA strand breakage and inhibition of DNA synthesis and repair.[81]

**Cytarabine** **Molecular Formula- $C_9H_{13}N_3O_5$**



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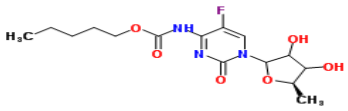
It acts through direct DNA damage and incorporation into DNA. It is cytotoxic to a wide variety of proliferating mammalian cells in culture. It exhibits cell phase specificity, primarily killing cells undergoing DNA synthesis (S-phase) and under certain conditions blocking the progression of cells from the G1 phase to the S-phase.[82]

**Capecitabine** **Molecular Formula- $C_{15}H_{22}FN_3O_6$**



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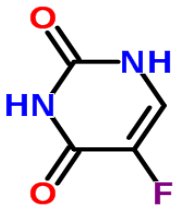
Capecitabine is metabolised to 5-FU which in turn is a thymidylate synthase inhibitor, thatswhy inhibiting the synthesis of thymidinemonophosphate (ThMP), the active form of thymidine which is required for the *de novo* synthesis of DNA.[83]

**Fluorouracil** **Molecular Formula- $C_4H_3FN_2O_2$**



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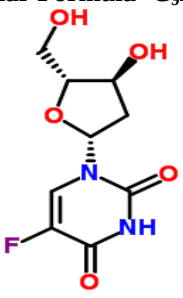
5-FU acts in several ways, but principally as a thymidylate synthase (TS) inhibitor. Interrupting the action of this enzyme blocks synthesis of the pyrimidine thymidine, which is a nucleoside required for DNA replication. Thymidylatesynthase methylates deoxyuridine monophosphate (dUMP) form thymidine monophosphate (dTMP). Administration of 5-FU causes a scarcity in dTMP, so rapidly dividing cancerous cells undergo cell death via thymineless death.[84]

**Floxuridine** **Molecular Formula- $C_9H_{11}FN_2O_5$**



The primary effect is interference with DNA synthesis and to a lesser extent, inhibition of RNA formation through the drug's incorporation into RNA, thus leading to the production of fraudulent RNA. As well, the monophosphate of floxuridine, 5-fluoro-2'-deoxyuridine-phosphate (FUDR-MP) inhibits the enzyme thymidylate synthetase. This leads to the inhibition of methylation of deoxyuridylicacid to thymidylic acid, thus interfering with DNA synthesis. [85]

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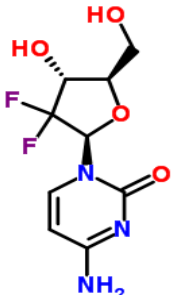
**Gemcitabine** **Molecular Formula- $C_9H_{11}F_2N_3O_4$**



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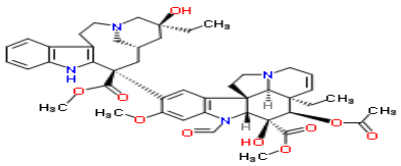
Gemcitabine once transported into the cell, must be phosphorylated by deoxycytidine kinase to an active form. Incorporation of dFdCTP into DNA is most likely the major mechanism by which gemcitabine causes cell death. After incorporation of gemcitabine nucleotide on the end of the elongating DNA strand, one more deoxynucleotide is added and thereafter, the DNA polymerases are unable to proceed. This action ("masked termination") apparently locks the drug into DNA as the proofreading enzymes are unable to remove gemcitabine from this position.[86]

**Vincristine** **Molecular Formula- $C_{46}H_{56}N_4O_{10}$**



The antitumor activity of Vincristine is thought to be due primarily to inhibition of mitosis at metaphase through its interaction with tubulin. Like other vinca alkaloids, Vincristine may also interfere with: 1) amino acid, cyclic AMP, and glutathione metabolism, 2) calmodulin-dependent $Ca^{2+}$-transport ATPase activity, 3) cellular respiration, and 4) nucleic acid and lipid biosynthesis.[87]

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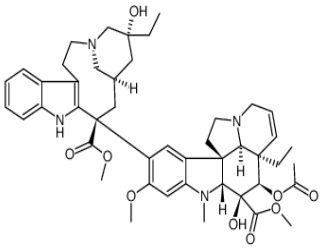
**Vinblastin** **Molecular Formula- $C_{46}H_{58}N_4O_9$**



The antitumor activity of vinblastine is thought to be due primarily to inhibition of mitosis at metaphase through its interaction with tubulin. Vinblastine binds to the microtubular proteins of the mitotic spindle, leading to crystallization of the microtubule and mitotic arrest or cell death.[88]

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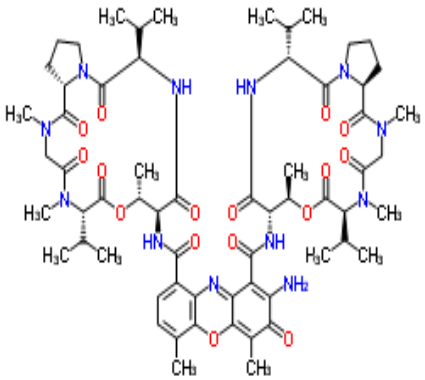
**Dactinomycin** **Molecular Formula- $C_{62}H_{86}N_{12}O_{16}$**



The binding of the Dactinomycin to DNA. The planar phenoxazone ring intercalates between adjacent guanine-cytosine base pairs of DNA, while the polypeptide chains extend along the minor groove of the helix. The summation of these interactions provides great stability to the dactinomycin-DNA complex and as a result of the binding of dactinomycin, the transcription of DNA by RNA polymerase is blocked. The DNA-dependent RNA polymerases are much more sensitive to the effects of dactinomycin than is the DNA polymerases. Dactinomycin cause single-strand breaks in DNA, possibly through a free-radical intermediate or as a result of the action of topoisomerase II.[89]

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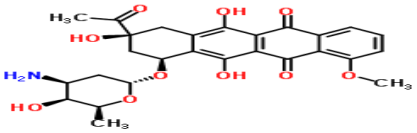
**Daunorubicin** **Molecular Formula- $C_{27}H_{29}NO_{10}$**

Daunorubicin has antimitotic and cytotoxic activity through a number of proposed mechanisms of action: Daunorubicin forms complexes with DNA by intercalation between base pairs, and it inhibits



topoisomerase II activity by stabilizing the DNA-topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzes.[90]

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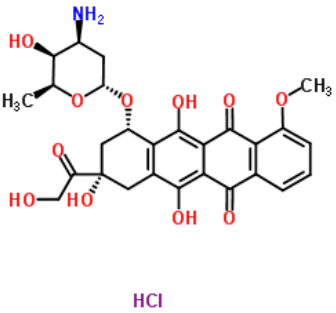
**Doxorubicin** **Molecular Formula- $C_{27}H_{30}ClNO_{11}$**



Doxorubicin has antiitotic and cytotoxic activity. It inhibits nucleic acid (DNA and RNA) and protein synthesis. Epirubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase II activity by stabilizing the DNA topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzs. It also interferes with DNA replication and transcription by inhibiting DNA helicase activity.[91]

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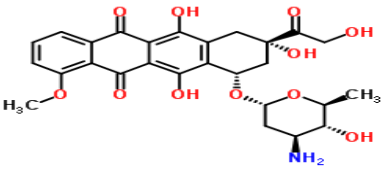
**Epirubicin** **Molecular Formula- $C_{27}H_{29}NO_{11}$**



Epirubicin has antiitotic and cytotoxic activity. It inhibits nucleic acid (DNA and RNA) and protein synthesis. Epirubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase II activity by stabilizing the DNA topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzs. It also interferes with DNA replication and transcription by inhibiting DNA helicase activity.[92]

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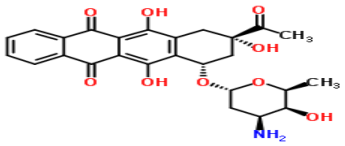
**Idarubicin** **Molecular Formula- $C_{26}H_{27}NO_9$**



Idarubicin has antimitotic and cytotoxic activity through a number of proposed mechanisms of action: Idarubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase- II activity by stabilizing the DNA-topoisomerase-II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzes.[93]

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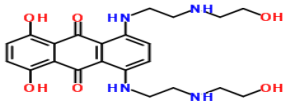
**Mitoxantrone** **Molecular Formula- $C_{22}H_{28}N_4O_6$**



It is a Type-II Topoisomerase inhibitor; it disrupts DNA synthesis and DNA repair in both healthy cells and cancer cells by intercalation between DNA bases.[94]

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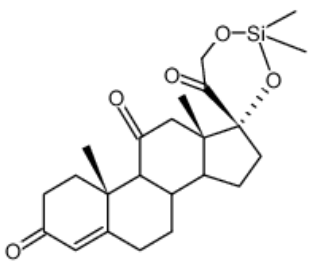
**Corticosteroid** **Molecular Formula- $C_{23}H_{32}O_5Si$**



Ligand binding induces a conformational change in the GR, which releases the receptor from its chaperones, containing hsp90 and other molecules. The release of these inhibitory molecules allows the GR to translocate to the nucleus, where it then binds to a GRE and acts as a modulator of transcription. Once bound to the appropriate response element, the GR regulates transcription of its target genes. Genes that are positively regulated by GR are characterized by responsive GR elements in their promoter regions.[95]

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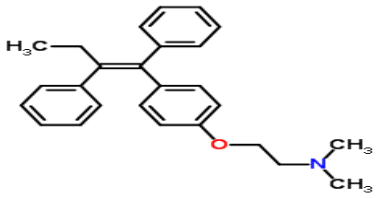
**Tamoxifene**

**Molecular Formula- $C_{26}H_{29}NO$**



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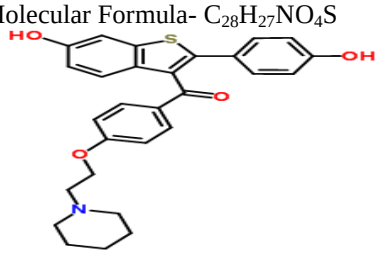
Tamoxifen (TAM) is known to have a dual mechanism of action: (1) to compete with 17β-estradiol ($E_2$) at the receptor site and to block the promotional role of $E_2$ in breast cancer; and (2) to bind DNA after metabolic activation and to initiate carcinogenesis. Recent large clinical trials indicate that TAM is also an effective chemopreventive agent against breast cancer.[96]

**Raloxifene**

Molecular Formula- $C_{28}H_{27}NO_4S$



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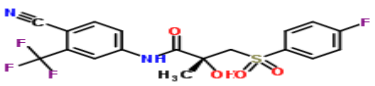
Raloxifene inhibits the estradiol-dependent proliferation of MCF-7 human mammary tumor cells in vitro.The drug's tissue-specific estrogen agonist or antagonist activity is related to the structural differences between the raloxifene-estrogen receptor complex (specifically the surface topography of AF-2) and the estrogen-estrogen receptor complex.[97]

**Bicalutamide**

**Molecular Formula- $C_{18}H_{14}F_4N_2O_4S$**



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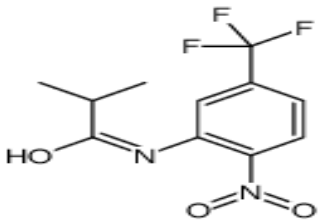
Bicalutamide competes with androgen for the binding of androgen receptors, consequently blocking the action of androgens of adrenal and testicular origin which stimulate the growth of normal and malignant prostatic tissue.[98]

**Flutamide**

**Molecular Formula- $C_{11}H_{11}F_3N_2O_3$**



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Flutamide is a nonsteroidal antiandrogen that blocks the action of both endogenous and exogenous testosterone by binding to the androgen receptor. In addition Flutamide is a potent inhibitor of testosterone-stimulated prostatic DNA synthesis. Moreover, it is capable of inhibiting prostatic nuclear uptake of androgen.[99]

**Altretamine**

**Molecular Formula- $C_9H_{18}N_6$**

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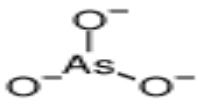
The precise mechanism by which altretamine exerts its cytotoxic effect is unknown although it is classified as an alkylating anti-neoplastic agent. Through this mechanism, the drug is metabolized into alkylating agents by N-demethylation. These alkylating species consequently damage tumor.[100]

**Arsenic Trioxide**

**Molecular Formula- $AsO_3$**



The mechanism of action of Arsenic Trioxide is not completely understood. Arsenic trioxide causes morphological changes and DNA fragmentation characteristic of apoptosis in NB4 human promyelocytic leukemia cells *in vitro*. Arsenic trioxide also causes damage or degradation of the fusion protein PML/RAR-alpha. It is suspected that arsenic trioxide induces cancer cells to undergo

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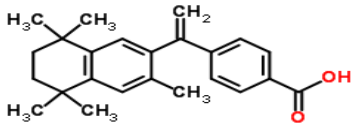
**Bexarotene** **Molecular Formula- $C_{24}H_{28}O_2$**



apoptosis.[101]

Bexarotene selectively binds with and activates retinoid X receptor subtypes. There are three subtypes in total: $RXR_{\alpha}$, $RXR_{\beta}$, $RXR_{\gamma}$. The exact mechanism of action of bexarotene in the treatment of CTCL is unknown but the drug has activity in all clinical stages of CTCL.[102]

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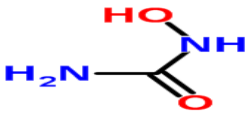
**Hydroxyurea** **Molecular Formula- $CH_4N_2O_2$**



Hydroxycarbamide decreases the production of deoxyribonucleotides. Via inhibition of the enzyme ribonucleotide reductase by scavenging tyrosyl free radicals as they are involved in the reduction of nucleoside diphosphates (NDPs).[103]

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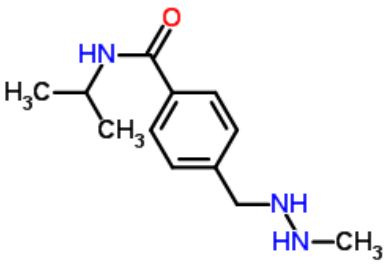
**Procarbazine** **Molecular Formula- $C_{12}H_{19}N_3O$**



Procarbazine may act by inhibition of protein, RNA and DNA synthesis. Studies have suggested that procarbazine may inhibit transmethylation of methyl groups of methionine into t-RNA. The absence of functional t-RNA could cause the cessation of protein synthesis and consequently DNA and RNA synthesis. In addition, procarbazine may directly damage DNA. Hydrogen peroxide, formed during the auto-oxidation of the drug, may attack protein sulfhydryl groups contained in residual protein which is tightly bound to DNA.[104]

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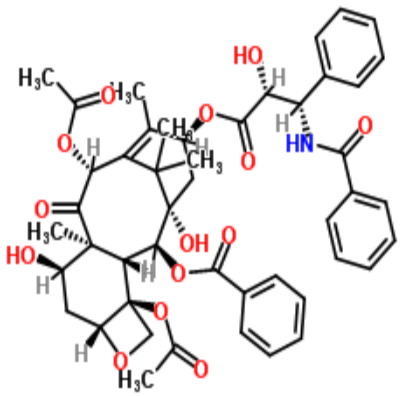
**Paclitaxel** **Molecular Formula- $C_{47}H_{51}NO_{14}$**



Paclitaxel-treated cells have defects in mitotic spindle assembly, chromosome segregation, and cell division. Unlike other tubulin-targeting drugs such as cholchicine inhibit microtubule assembly; paclitaxel stabilizes the microtubule polymer and protects it from disassembly. Chromosomes are thus unable to achieve a metaphase spindle configuration. This blocks the progression of mitosis and prolonged activation of the mitotic checkpoint triggers apoptosis or reversion to the G-phase of the cell cycle without cell division.[105]

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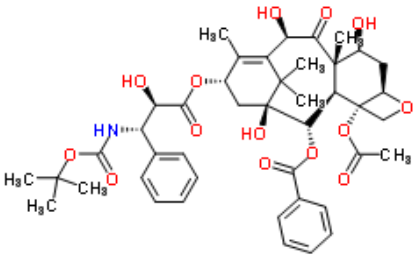
**Docetaxel** **Molecular Formula- $C_{43}H_{53}NO_{14}$**

Docetaxel interferes with the normal function of microtubule growth. Whereas drugs like colchicine causes the depolymerization of microtubules in vivo, docetaxel arrests their function by having the opposite effect; it hyper-stabilizes their structure. This destroys the cell's ability to use its cytoskeleton in a flexible manner. Specifically, docetaxel binds to



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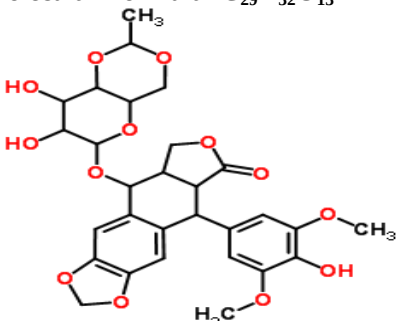
the β-subunit of tubulin. Tubulin is the "building block" of mictotubules, and the binding of docetaxel locks these building blocks in place. The resulting microtubule/docetaxel complex does not have the ability to disassemble. This adversely affects cell function because the shortening and lengthening of microtubules (termed dynamic instability) is necessary for their function as a transportation highway for the cell. Chromosomes, for example, rely upon this property of microtubules during mitosis. Further research has indicated that docetaxel induces programmed cell death (apoptosis) in cancer cells by binding to an apoptosis stopping protein called Bcl-2 (B-cell leukemia 2) and thus arresting its function.[106]

**Etoposide** **Molecular Formula- $C_{29}H_{32}O_{13}$**



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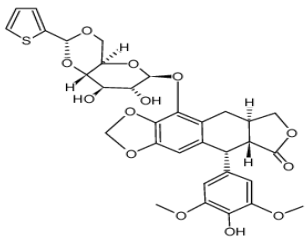
Etoposide forms a ternary complex with DNA and topoisomerase II enzyme (which aids in DNA unwinding), prevents re-ligation of the DNA strands, and by doing so causes DNA strands to break. Cancer cells rely on this enzyme more than healthy cells, since they divide more rapidly. Therefore, this causes errors in DNA synthesis and promotes apoptosis of the cancer cell.[107]

**Teniposide** **Molecular Formula- $C_{32}H_{32}O_{13}S$**



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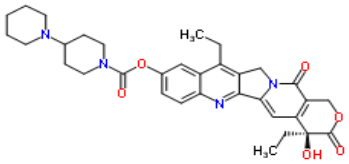
Teniposide causes dose-dependent single- and double-stranded breaks in DNA and DNA-protein cross-links. The substance has been found to act as an inhibitor of topoisomerase II (an enzyme that aids in DNA unwinding), since it does not intercalate into DNA or bind strongly to DNA. The cytotoxic effects of teniposide are related to the relative number of double-stranded DNA breaks produced in cells, which are a reflection of the stabilization of a topoisomerase II-DNA intermediate.[108]

**Irinotecan** **Molecular Formula- $C_{33}H_{38}N_4O_6$**



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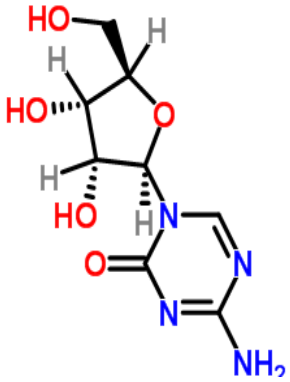
Irinotecan inhibits the action of topoisomerase I. Irinotecan prevents religation of the DNA strand by binding to topoisomerase I-DNA complex. The formation of this ternary complex interferes with the moving replication fork, which induces replication arrest and lethal double-stranded breaks in DNA. As a result, DNA damage is not efficiently repaired and apoptosis (programmed cell death) occurs.[109]

**Azacitidine** **Molecular Formula- $C_8H_{12}N_4O_5$**

Azacitidine is thought to induce antineoplastic activity via two mechanisms; inhibition of DNA methyltransferase at low doses, causing hypomethylation of DNA, and direct cytotoxicity in abnormal hematopoietic cells in the bone marrow through its incorporation into DNA and RNA at high doses, resulting in cell death. As azacitidine is a ribonucleoside, it incoporates into RNA to a larger



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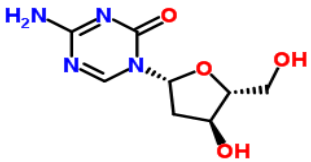
extent than into DNA. The incorporation into RNA leads to the dissembly of polyribosomes, defective methylation and acceptor function of transfer RNA, and inhibition of the production of protein.[110]

**Decitabin**

**Molecular Formula- $C_8H_{12}N_4O_4$**



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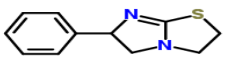
Decitabine is believed to exert its antineoplastic effects following its conversion to decitabine triphosphate, where the drug directly incorporates into DNA and inhibits DNA methyltransferase, the enzyme that is responsible for methylating newly synthesized DNA in mammalian cells. This results in hypomethylation of DNA and cellular differentiation or apoptosis. Decitabine inhibits DNA methylation in vitro, which is achieved at concentrations that do not cause major suppression of DNA synthesis.[111]

**Levamisole**

**Molecular Formula- $C_{11}H_{12}N_2S$**



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Levamisole act as an anticancer drug in combination with fluorouracil is unknown. The effects of levamisole on the immune system are complex. Levamisole can stimulate formation of antibodies to various antigens, enhance T-cell responses by stimulating T-cell activation and proliferation, potentiate monocyte and macrophage functions including phagocytosis and chemotaxis, and increase neutrophil mobility, adherence, and chemotaxis.[112]

## RADIATION

Radiation therapy involves the use of ionizing radiation in an attempt to either cure or improve symptoms. It works by damaging the DNA of cancerous tissue, killing it. To spare normal tissues (such as skin or organs, which radiation must pass through to treat the tumor), shaped radiation beams are aimed from multiple exposure angles to intersect at the tumor, providing a much larger dose there than in the surrounding, healthy tissue. [113]

## SURGERY

Surgery is the primary method of treatment for most isolated, solid cancers and may play a role in palliation and prolongation of survival. It is typically an important part of definitive diagnosis and staging of tumors, as biopsies are usually required. In localized cancer, surgery typically attempts to remove the entire mass along with, in certain cases, the lymph nodes in the area. For some types of cancer this is sufficient to eliminate the cancer. [114]

## PALLIATIVE CARE

Palliative care refers to treatment that attempts to help the patient feel better and may be combined with an attempt to treat the cancer. Palliative care includes action to reduce physical, emotional, spiritual and psycho-social distress. Unlike treatment that is aimed at directly killing cancer cells, the primary goal of palliative care is to improve quality of life. People at all stages of cancer treatment typically receive some kind of

palliative care. In some cases, medical specialty professional organizations recommend that patients and physicians respond to cancer only with palliative care. This applies to patients who:

1. display low performance status, implying limited ability to care for themselves
2. received no benefit from prior evidence-based treatments
3. are not eligible to participate in any appropriate clinical trial
4. no strong evidence implies that treatment would be effective[115]

## IMMUNOTHERAPY

A variety of therapies using immunotherapy, stimulating or helping the immune system to fight cancer, have come into use since 1997. Approaches include antibodies, checkpoint therapy and adoptive cell transfer. [116]

## LASER THERAPY

Laser therapy uses high-intensity light to treat cancer by shrinking or destroying tumors or precancerous growths. Lasers are most commonly used to treat superficial cancers that are on the surface of the body or the lining of internal organs. It is used to treat basal cell skin cancer and the very early stages of others like cervical, penile, vaginal, vulvar, and non-small cell lung cancer. It is often combined with other treatments, such as surgery, chemotherapy, or radiation therapy. Laser-induced interstitial thermotherapy (LITT), or interstitial laser photocoagulation, uses lasers to treat some cancers using hyperthermia, which uses heat to shrink tumors by damaging or killing cancer cells. Laser is more precise than surgery and cause less damage, pain, bleeding, swelling, and scarring. A disadvantage is surgeons must have specialized training. It may be more expensive than other treatments. [117]

## CONCLUSION

Naturally occurring anticancer drugs seem to play an important role in biochemical reactions in cells'metabolism. Their reactivity with cells and tissues makes the regulation of these molecules so tightly controlled that as a consequence any disturbance may be associated with pathological conditions.Therefore, the use of synthetic cyclic compounds as anticancer drugs tries to mimic natural ligands and substrates in order to disturb the delicate balance in cells. Heterocyclic compounds or heterocyclic fragments also play an important role in improving pharmacokinetics and pharmacodynamics properties of anticancer drugs by enhancing lipophilicity, polarity or other physicochemical features. Hence, Anticancer drugs play an important role in current drug design as they are present in the majority of marketed drugs. Only in 2018, about 60% of FDA-approved anticancer drugs have one or more cyclic rings containing nitrogen or oxygen. A correlation between heterocycle fragments' structure and potential families of targeted molecules seems to not be evidenced by any literature addressed. However, mechanisms of action of these compounds are being established and pass through interactions with major biomolecules or by intervening in metabolic pathways. Although changes in moiety of anticancer compounds improve pharmacokinetic and pharmacodynamics, it still faces many challenges such as lack of specific targeting. Therefore, it is imperative to search for a method to overcome these issues.

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