



Newer Anticancer Drugs (Approved by FDA 2019)

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Abstract Cancer is one of the most common and widespread diseases in the human population and has been reported to be the second major cause of death globally. The World Health Organisation states that about 200 different types of cancers have been identified worldwide, each of which requires unique approaches for treatment. It also records that 1 in every 6 deaths in the world are due to cancer which clearly evidences for the inevitable necessity for the control and cure of cancer. Unlike normal cells, cancer cells undergo uncontrollable cell division and each division leads to multiple mutations in a continuous fashion. There are various strategies towards targeting cancerous cells. With the advent of conventional therapies, various chemical derivatives are being used as anticancer drugs. This article reviews on the various approaches put forth in the fight against cancer through cancer therapies and drug designing by identifying potent targets. Here we will be discussing about the history of cancer and its advances towards development of anticancer drugs from tip to toe.

Keywords Cancer; Anticancer Drugs

Introduction

Definitions

Cancers are a large family of diseases that involve abnormal cell growth with the potential to invade or spread to other parts of the body [1,2]. 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 [3, 4].

All tumor cells show the six hallmarks of cancer. These characteristics are required to produce a malignant tumor. They include [5].

- 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
- The progression from normal cells to cells that can form a detectable mass to outright cancer involves multiple steps known as malignant progression [6].



What is cancer?

- Cancer describes a range of diseases that can affect different organs and any part of the body.

Types of Tumor

- **Benign tumour**

Cells are confined to one area and are not able to spread to other parts of the body. This is not cancer.

- **Malignant tumour**

This is made up of cancerous cells, which have the ability to spread by travelling through the bloodstream or lymphatic system (lymph fluid).

Aim and Objective

Aim: This study is based on the overview on cancer & Newer anti- cancer drugs.

Objective: This study is carried to perform brief description about cancer and newer cancer drugs that have anticancer activity. Study reviewed of cancer, Newer anticancer drugs in treatment or/and chemoprevention of cancer.

Types of Cancer

There are more than 100 types of cancer. Types of cancer are usually named for the organs or tissues where the cancers form. For example, lung cancer starts in cells of the lung, and brain cancer starts in cells of the brain. Cancers also may be described by the type of cell that formed them, such as an epithelial cell or a squamous cell [7].

Carcinoma

Carcinomas are the most common type of cancer. They are formed by epithelial cells, which are the cells that cover the inside and outside surfaces of the body.

There are many types of epithelial cells, which often have a column-like shape when viewed under a microscope.

Leukemia

Cancers that begin in the blood-forming tissue of the bone marrow are called leukemias. These cancers do not form solid tumors. Instead, large numbers of abnormal white blood cells (leukemia cells and leukemic blast cells) build up in the blood and bone marrow, crowding out normal blood cells. The low level of normal blood cells can make it harder for the body to get oxygen to its tissues, control bleeding, or fight infections. There are four common types of leukemia, which are grouped based on how quickly the disease gets worse (acute or chronic) and on the type of blood cell the cancer starts in (lymphoblastic or myeloid).

Sarcoma

Sarcomas are cancers that form in bone and soft tissues, including muscle, fat, blood vessels, lymph vessels, and fibrous tissue (such as tendons and ligaments). Osteosarcoma is the most common cancer of bone. There are four common types of leukemia, which are grouped based on how quickly the disease gets worse (acute or chronic) and on the type of blood cell the cancer starts in (lymphoblastic or myeloid).

Lymphoma

Lymphoma is cancer that begins in lymphocytes (T cells or B cells). These are disease-fighting white blood cells that are part of the immune system. In lymphoma, abnormal lymphocytes build up in lymph nodes and lymph vessels, as well as in other organs of the body.

There are two main types of lymphoma:

Hodgkin lymphoma – People with this disease have abnormal lymphocytes that are called Reed-Sternberg cells. These cells usually form from B cells.



Non-Hodgkin lymphoma – This is a large group of cancers that start in lymphocytes. The cancers can grow quickly or slowly and can form from B cells or T cells.

Multiple Myeloma

Multiple myeloma is cancer that begins in plasma cells, another type of immune cell. The abnormal plasma cells, called myeloma cells, build up in the bone marrow and form tumors in bones all through the body. Multiple myeloma is also called plasma cell myeloma and Kahler disease.

Melanoma

Melanoma is cancer that begins in cells that become melanocytes, which are specialized cells that make melanin (the pigment that gives skin its color). Most melanomas form on the skin, but melanomas can also form in other pigmented tissues, such as the eye.

Brain and Spinal Cord Tumors

There are different types of brain and spinal cord tumors. These tumors are named based on the type of cell in which they formed and where the tumor first formed in the central nervous system. For example, an astrocytic tumor begins in star-shaped brain cells called astrocytes, which help keep nerve cells healthy. Brain tumors can be benign (not cancer) or malignant (cancer).

Common Cancer Types

- **Bladder Cancer**

The most common type of bladder cancer is transitional cell carcinoma, also called urothelial carcinoma. Smoking is a major risk factor for bladder cancer.

- **Breast Cancer**

Breast cancer is the second most common cancer in women after skin cancer. Mammograms can detect breast cancer early, possibly before it has spread [8,9].

- **Colon and Rectal Cancer**

Colorectal cancer often begins as a growth called a polyp inside the colon or rectum.

- **Endometrial Cancer**

Uterine cancers can be of two types: endometrial cancer (common) and uterine sarcoma (rare). Endometrial cancer can often be cured. Uterine sarcoma is often more aggressive and harder to treat.

- **Kidney Cancer**

Kidney cancer can develop in adults and children. The main types of kidney cancer are renal cell cancer, transitional cell cancer, and Wilms tumor.

- **Leukemia**

Leukemia is a broad term for cancers of the blood cells.

- **Liver Cancer**

Liver cancer includes hepatocellular carcinoma (HCC) and bile duct cancer (cholangio carcinoma).

- **Lung Cancer**

Lung cancer includes two main types: non-small cell lung cancer and small cell lung cancer.



- **Melanoma**

Melanoma is much less common than the other types but much more likely to invade nearby tissue and spread to other parts of the body.

- **Non-Hodgkin Lymphoma**

Lymphoma is a broad term for cancer that begins in cells of the lymph system. The two main types are Hodgkin lymphoma and non-Hodgkin lymphoma (NHL).

- **Pancreatic Cancer**

Pancreatic cancer can develop from two kinds of cells in the pancreas: exocrine cells and neuroendocrine cells, such as islet cells.

- **Prostate Cancer**

Prostate cancer usually grows very slowly, and finding and treating it before symptoms occur may not improve men's health or help them live longer.

- **Thyroid Cancer**

There are four main types of thyroid cancer. These are papillary, follicular, medullary, and anaplastic. Papillary is the most common type.

How Cancer Arises

Cancer is caused by certain changes to genes, the basic physical units of inheritance. Genes are arranged in long strands of tightly packed DNA called chromosomes.

Cancer is a genetic disease that is, it is caused by changes to genes that control the way our cells function, especially how they grow and divide [10].

Genetic changes that cause cancer can be inherited from our parents. They can also arise during a person's lifetime as a result of errors that occur as cells divide or because of damage to DNA caused by certain environmental exposures. Cancer-causing environmental exposures include substances, such as the chemicals in tobacco smoke, and radiation, such as ultraviolet rays from the sun.

Pathophysiology

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-abl fusion protein, an oncogenic tyrosine kinase.

Small-scale mutations include point mutations, deletions, and insertions, which may occur in the promoter region of a gene and affect its expression, or may occur in the gene's coding sequence and alter the function or stability of its protein product. Disruption of a single gene may also result from integration of genomic material from a DNA virus or retrovirus, leading to the expression of viral oncogenes in the affected cell and its descendants.

Replication of the data contained within the DNA of living cells will probabilistically result in some errors (mutations). Complex error correction and prevention is built into the process and safeguards the cell against cancer. If a significant error occurs, the damaged cell can self destruct through programmed cell death, termed apoptosis. If the error control processes fail then the mutations will survive and be passed along to daughter cells.

Some environments make errors more likely to arise and propagate. Such environments can include the presence of disruptive substances called carcinogens, repeated physical injury, heat, ionising radiation or hypoxia [11].



What are the risk factors?

- smoking tobacco/passive smoking
- exposure to UV radiation (e.g. from sunlight)
- alcohol consumption
- diet
- physical inactivity and obesity
- chronic infections, including the human papillomavirus (HPV) and hepatitis B or C
- family history and genetic susceptibility
- hormonal factors

How is cancer treated?

The most common types of cancer treatment are surgery, chemotherapy and radiotherapy.

Main types of cancer treatments**• Surgery**

Surgery is the primary method of treatment for most isolated, solid cancers and may play a role in palliation and prolongation of survival.

• Chemotherapy

Chemotherapy is the treatment of cancer with one or more cytotoxic anti-neoplastic drugs (chemotherapeutic agents) as part of a standardized regimen.

• Radiotherapy

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.

• Hormone (endocrine) therapy

Hormone therapy uses synthetic hormones to block the effect of the body's natural hormones that help some cancers to grow. The treatment may be given as tablets or injections.

• Targeted therapy

Targeted therapy attacks specific genetic changes (mutations) within cells that allow cancers to grow and spread, while minimizing harm to healthy cells. They are generally administered in tablet form (orally).

• 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.

Side effects of treatment

- Anemia
- Appetite Loss
- Bleeding and Bruising (Thrombocytopenia)
- Constipation
- Delirium
- Diarrhea
- Edema (Swelling)
- Fatigue



- Fertility Issues in Boys and Men
- Fertility Issues in Girls and Women
- Flu-Like Symptoms
- Hair Loss (Alopecia)
- Infection and Neutropenia
- Lymphedema
- Memory or Concentration Problems
- Mouth and Throat Problems
- Nausea and Vomiting
- Nerve Problems (Peripheral Neuropathy)
- Organ-Related Inflammation and Immuno therapy
- Pain
- Sexual Health Issues in Men
- Sexual Health Issues in Women
- Skin and Nail Changes
- Sleep Problems
- Urinary and Bladder Problems

Anticancer drug

Anticancer drug, also called antineoplastic drug, any drug that is effective in the treatment of malignant, or cancerous, disease. There are several major classes of anticancer drugs; these include alkylating agents, antimetabolites, natural products, and hormones. In addition, there are a number of drugs that do not fall within those classes but that demonstrate anticancer activity and thus are used in the treatment of malignant disease. The term chemotherapy frequently is equated with the use of anticancer drugs, although it more accurately refers to the use of chemical compounds to treat disease generally.

Anti-Cancer Drugs is an international medical journal, which aims to promote and encourage research on anti-cancer agents. It was first published in 1990 and it includes reports on clinical and experimental research results, from conventional cytotoxic chemotherapy to hormonal or biological response modalities [12].

Examples:

- Tamoxifen.
- Imatinib.
- Letrozole.
- Antineoplastic antibiotic.
- Dactinomycin.
- Bleomycin.
- Vinblastine.

Newer Anticancer Drugs Approved by FDA in 2019

- Enzalutamid
- Atezolizumab
- Acalabrutinib
- Givosiran
- Crizanlizumab
- Zanubrutinib
- Niraparib



- Daratumumab
- Apalutamide
- Pexidartinib
- Entrectinib
- Darolutamide
- Pembrolizumab
- Venetoclax
- Ramucirumab
- Ivosidenib
- Erdafitinib
- Trifluridine/tipiracil
- Cabozantinib

Conclusion

HDAC inhibitors represent a promising class of anticancer agents, with three of them now approved for cutaneous and/or peripheral T-cell lymphoma. Many HDAC inhibitors are in different stages of clinical trials for various haematological and solid tumors. While HDAC inhibitors alone have displayed anticancer activities in various cancers, a growing number of studies have demonstrated more efficient and tumor specific anticancer activities of HDAC inhibitors when they are given in combination with other drugs. Even though vorinostat, romidepsin and belinostat are approved for cutaneous and/or peripheral T-cell lymphoma, these drugs are still being studied in clinical trials for other types of cancers, either as single agents or in combination with other drugs. This clearly underscore the potential of HDAC inhibitors in cancer treatment. Besides the promising effects on anticancer activities, the use of HDAC inhibitors in other diseases, such as intestinal fibrosis, autoimmune, inflammatory diseases, metabolic disorders and many more, is also growing.

Computer modeling has emerged as a powerful complement to the experimental approach to finding more potent and specific HDAC inhibitors. As such, clinical studies in combination with basic biological research and computer modeling should enable us to discover a greater variety of HDAC inhibitors specific for a given target, and also to develop tumor specific HDAC inhibitors. This review highlights the interplay between computer modeling based research and experimental research that is essential for the development of novel HDAC inhibitors as anticancer agents.

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