International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

"Study of synthetic molecular medicine use in treatment of cancer "

Dr. Kaushal .K .Chandrul(Dean), Dr.Gurav Kumar Sharma(H.O.D), Keshav Krishna

Faculty Pharmaceutical Sciences, Mewar University
B.Pharmacy. 4th Year,8 Semester) MUR1700136

Guided By :Mr. Ravi Verma

Assistant professor Faculty Pharmaceutical Sciences MEWAR UNIVERSITY ,Chittorghar,(RAJASTHAN)

Date of Submission: 01-08-2021 Date of Acceptance: 11-08-2021

I. INTRODUCTION

Cancer is a hyperproliferative disease, and a cascade of events take place in order to cause a full blown disease. The major events include transformation, dysregulation of apoptosis, proliferation, invasion, angiogenesis, and metastasis. Meticulous research since the past few decades has yielded much information about the biology of cancer. Drugs used in the treatment of most cancers are those that can interfere with cell signalling, like growth factor signalling, prostaglandin production, inflammation, drug resistant gene products, cell cycle proteins, angiogenesis, invasion, antiapoptosis, cellular proliferation and many others (Aggarwal et al., 2006; Arora, 2010; Arora et al., 2010a,b,c). Herbals have been used in nearly every culture on earth for medicinal purposes. This method of medicine was practiced by various ancient civilizations thriving in Asia, Africa, Europe, and the Americas. As modern chemistry developed, chemicals and various constituents were isolated from medicinal herbs. These phytoconstituents have served either as drugs that are being used widely today or as starting materials for their synthesis. Many modern day drugs being used widely have been developed as a result of knowledge obtained from studying the mechanism of actions of various chemicals present in the herbal plants. Thus, we can easily infer that medicinal herbs have played a pivotal role in the expansion of modern medicine and continue to be widely used in their native form as well (Matthews et al., 1999; Sharma and Arora, 2006; Arora et al., 2008). Modern medicines derived from herbs are gaining attention throughout the world today. For example, the transformation of foxglove, a folk medicine, going through digitalis, eventually to a modern drug, digoxin, illustrates potential of modern pharmacology that has played a supportive role in making drugs safer and more effective

Cancer is one of the most serious health problems worldwide, affecting individuals from different sexes, ages, and races. It is a group of diseases, characterized by uncontrolled cellular growth with frequent cancer cells invasion to different body parts and spreading to other organs, a process referred to as Metastasis. Metastasis is the major cause of cancer related mortality. In 2005, cancer was the second leading cause of death among both men and women and accounted for 13% of the total 58 million deaths worldwide. In 2006, about 10.9 million new cancer cases are expected to be diagnosed worldwide and more than 7.8 million cancer patients may die. Cancer is also a problem of economical dimensions with a very high level of expenses associated to it. For example the National Institute of Health, USA estimates that an overall of $209.9 billion were invested worldwide in 2005, for the sake of cancer research and management. Cancer is a heterogeneous illness which can originate from many different organs of the human body. However, the most frequent cancer types in the world are lung, prostate, stomach, colorectal, and esophagus in men; and breast, lung, stomach, colorectal and cervical in women.

Prostate cancer is the most frequently diagnosed and the second leading cause of cancer death among men, with 234460 new cases estimated to occur in USA during 2006, and 27350 American men will die as a result of this disease(3). In Palestine, the mortality rate of prostate cancer was 1.4 per 100000 during the period from January, 1995 to December, 2002. Despite the fact there are several cell types in the

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

prostate, nearly all of the prostate cancers are adenocarcinoma, originating in the gland cells. Liver cancer ranks as the sixth most common type of cancer world wide. Many different liver related tumors are identified depending on the type of cells where they originate, from these types about 83% are hepatocellular carcinoma (HCC) that begin in the hepatocytes, the main type of liver cells.

Cervical cancer is the most common cause of cancer death among women in developing countries and the second most common caner in women worldwide. It is caused by a change in the epithelial cells, which line the wall of the cervix, and the most common risk factor for this type of cancer is the human Papillomavirus (HPV). In the last decades there were great advances in the diagnosis of cancer as well as in the field of molecular oncology. However, the cure rate of most cancers remains low. Several strategies have been used to cure cancer among which the most common are surgery, chemotherapy, radiotherapy, and immunotherapy. Other modern approaches such as hormonal and gene therapy were proposed by researchers to replace conventional cancer therapy, with variable degrees of success.

All of these therapies have undesired side effects, they are usually not available all the time and they are expensive. For instance, in surgery the immune system is compromised due to the large amount of cortisole **releas**ed subsequent to the surgery, which increase the probability of cancer relapse Moreover, the current use of chemotherapy is accompanied with difficult side effects. It inhibits bone marrow stem cells proliferation leading to immune suppression. Radiotherapy which is widely used in the world is also accompanied by a great deal of side effects. Lymphocytes are most readily affected by radiation resulting in prolonged T-cell suppression. Other side effects such as, bone necrosis, lung fibrosis, skin devascularization, ulceration, nausea, vomiting, and renal damage are also associated with all types of conventional therapies.

As the conventional cancer therapies failed to completely fulfill the criteria for a successful cancer therapy, the use of naturally developed anticancer agents has evolved as an alternative safe, low-cost and convenient one. Nontoxic chemoprevention agents from natural resources were proposed by researchers for this purpose.

1.2 What is cancer **?**

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. 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.

All tumor cells show the six hallmarks of cancer. These characteristics are required to produce a malignant tumor. 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[26]

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

Type of cancer ?

1 Bladder Cancer
2 Breast Cancer
3 Colon and Rectal Cancer
4 Endometrial Cancer
5 Kidney Cancer
6 Leukemia
7 Liver Cancer
8 Lung Cancer
9 Melanoma
10 Non-Hodgkin Lymphoma
11 Pancreatic Cancer
12 Prostate Cancer
13 Thyroid Cancer

What is oncology

Oncology is a branch of medicine that deals with the prevention, diagnosis, and treatment of cancer. A medical professional who practices oncology is an oncologist. The name's etymological origin is the Greek word ὄγκος (óngkos), meaning 1. "burden, volume, mass" and 2. "barb", and the Greek word λόγος (logos), meaning "study".

II. HISTORY

Cancer has existed for all of human history. The earliest written record regarding cancer is from circa 1600 BC in the Egyptian Edwin Smith Papyrus and describes breast cancer. Hippocrates (c. 460 BC – c. 370 BC) described several kinds of cancer, referring to them

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

with the Greek word καρκίνος karkinos (crab or crayfish). This name comes from the appearance of the cut surface of a solid malignant tumor, with "the veins stretched on all sides as the animal the crab has its feet, whence it derives its name". Galen stated that "cancer of the breast is so called because of the fancied resemblance to a crab given by the lateral prolongations of the tumor and the adjacent distended veins".:738 Celsus (c. 25 BC – 50 AD) translated karkinos into the Latin cancer, also meaning crab and recommended surgery as treatment. Galen (2nd century AD) disagreed with the use of surgery and recommended purgatives instead.These recommendations largely stood for 1000 years.

In the 15th, 16th and 17th centuries, it became acceptable for doctors to dissect bodies to discover the cause of death. The German professor Wilhelm Fabry believed that breast cancer was caused by a milk clot in a mammary duct. The Dutch professor Francois de la Boe Sylvius, a follower of Descartes, believed that all disease was the outcome of chemical processes and that acidic lymph fluid was the cause of cancer. His contemporary Nicolaes Tulp believed that cancer was a poison that slowly spreads and concluded that it was contagious.

III. CAUSES

The majority of cancers, some 90–95% of cases, are due to genetic mutations from environmental and lifestyle factors.The remaining 5–10% are due to inherited genetics.Environmental refers to any cause that is not inherited genetically, such as lifestyle, economic, and behavioral factors and not merely pollution. 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%), lack of physical activity, and pollution. Psychological stress does not appear to be a risk factor for the onset of cancer, though it may worsen outcomes in those who already have cancer.

3.1Chemicals

Exposure to particular substances have been linked to specific types of cancer. These substances are called carcinogens.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.

3.2 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.

3.3Infection

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. Viruses are the usual infectious agents that cause cancer but cancebacteria and parasites may also play a role.

Oncoviruses (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).

3.4 Radiation

Radiation exposure such as ultraviolet radiation and radioactive material is a risk factor for cancer. Many non-melanoma skin cancers are due to ultraviolet radiation, mostly from sunlight. Sources of ionizing radiation include medical imaging and radon gas.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

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.Radiation can cause cancer in most parts of the body, in all animals and at any age. Children are twice as likely to develop radiation-induced leukemia as adults; radiation exposure before birth has ten times the effect.

Medical use of ionizing radiation is a small but growing source of radiation-induced cancers. Ionizing radiation may be used to treat other cancers, but this may, in some cases, induce a second form of cancer. It is also used in some kinds of medical imaging.

3.5 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 population are carriers of a genetic mutation that has a large effect on cancer risk and these 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,[65] and hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome), which is present in about 3% of people with colorectal cancer, among others.

3.6 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. Other substances in this category, including both naturally occurring and synthetic asbestos-like fibers, such as wollastonite, attapulgite, glass wool and rock wool, are believed to have similar effects. Non-fibrous particulate materials that cause cancer include powdered metallic cobalt and nickel and crystalline silica (quartz, cristobalite and tridymite). Usually, physical carcinogens must get inside the body (such as through inhalation) and require years of exposure to produce cancer.

3.7 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.

3.8 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. However, the delay in diagnosis and initiation of a gluten-free diet seems to increase the risk of malignancies. Rates of gastrointestinal cancers are increased in people with Crohn's disease and ulcerative colitis, due to chronic inflammation. Also, immunomodulators and biologic agents used to treat these diseases may promote developing extra-intestinal malignancies.

IV. SYMPTOM AND COMPLICATION

When cancer begins, it produces no symptoms. Signs and symptoms appear as the mass grows or ulcerates. The findings that result depend on the cancer's type and location. Few symptoms are specific. Many frequently occur in individuals who have other conditions. Cancer can be difficult to diagnose and can be considered a "great imitator."

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

4.1 Local symptoms

Local symptoms may occur due to the mass of the tumor or its ulceration. For example, mass effects from lung 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 bowel, affecting bowel habits. Masses in breasts or testicles may produce observable lumps. Ulceration can cause bleeding that can lead to symptoms such as coughing up blood (lung cancer), anemia or rectal bleeding (colon cancer), blood in the urine (bladder cancer), or abnormal vaginal bleeding (endometrial or cervical cancer). Although localized pain may occur in advanced cancer, the initial tumor is usually painless. Some cancers can cause a buildup of fluid within the chest or abdomen.

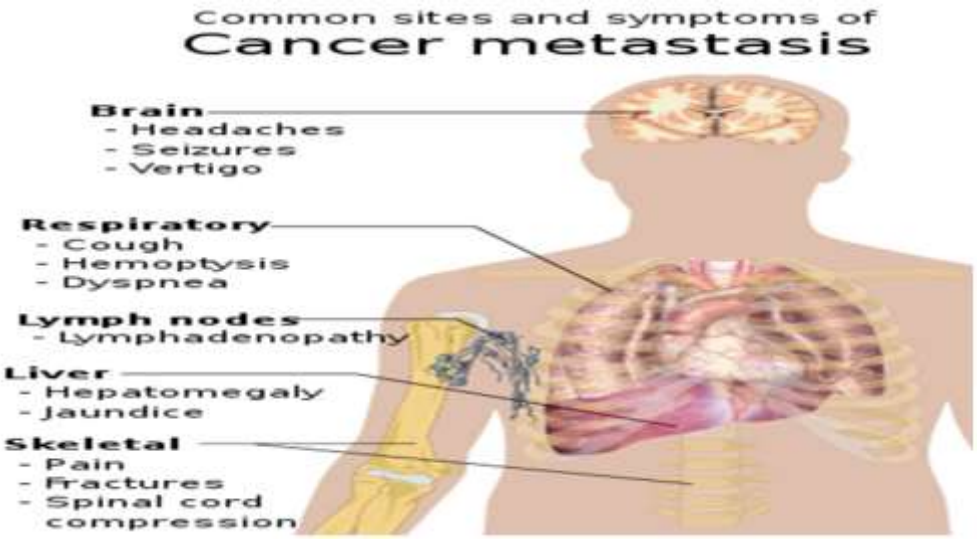
4.2 Systemic symptoms

Systemic symptoms may occur due to the body's response to the cancer. This may include fatigue, unintentional weight loss, or skin changes. Some cancers can cause a systemic inflammatory state that leads to ongoing muscle loss and weakness, known as cachexia. Some types of cancer such as Hodgkin disease, leukemias and cancers of the liver or kidney can cause a persistent fever.

Some systemic symptoms of cancer are caused by hormones or other molecules produced by the tumor, known as paraneoplastic syndromes. Common paraneoplastic syndromes include hypercalcemia which can cause altered mental state, constipation and dehydration, or hyponatremia that can also cause altered mental status, vomiting, headache or seizures.

4.3 Metastasis

Cancer can spread from its original site by local spread, lymphatic spread to regional lymph nodes or by hematogenous spread via the blood to distant sites, known as metastasis. When cancer spreads through the blood, it may spread through the body but is more likely to travel to certain areas depending on the cancer type. 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.



V. PREVATION

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. Thus, cancer is generally preventable. Between 70% and 90% of common cancers are due to environmental factors and therefore potentially preventable.

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. Not all environmental causes are controllable, such as

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

naturally occurring background radiation and cancers caused through hereditary genetic disorders and thus are not preventable via personal behavior.

5.1 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 found 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.

5.2 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%. COX-2 inhibitors may decrease the rate of polyp formation in people with familial adenomatous polyposis; however, it is associated with the same adverse effects as NSAIDs. 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.

5.3 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. 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 where resources allow.

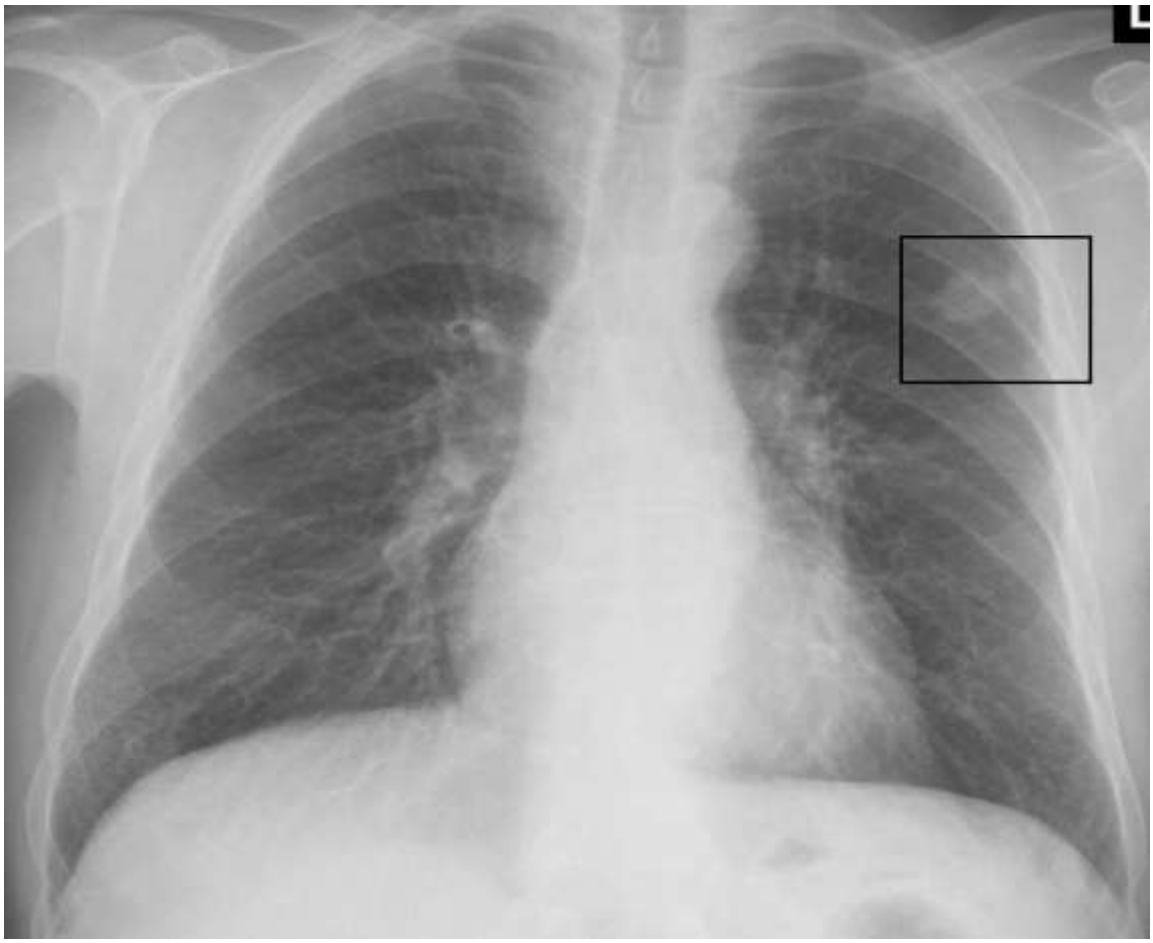
VI. DIAGNOSIS

Most cancers are initially recognized either because of the appearance of signs or symptoms or through screening. Neither of 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.

The tissue diagnosis from the biopsy indicates the type of cell that is proliferating, its histological grade, genetic abnormalities and other features. Together, this information is useful to evaluate the prognosis and to choose the best treatment.

Cytogenetics and immunohistochemistry a re other types of tissue tests. These tests provide information about molecular changes (such as mutations, fusion genes and numerical chromosome changes) and may thus also indicate the prognosis and best treatment.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



VII. MANAGEMENT

Many treatment options for cancer exist. 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

7.1 Chemotherapy

Chemotherapy is the treatment of cancer with one or more cytotoxic anti-neoplastic drugs (chemotherapeutic agents) as part of a standardized regimen. The term encompasses a variety of drugs, which are divided into broad categories such as alkylating agents and antimetabolites. Traditional chemotherapeutic agents act by killing cells that divide rapidly, a critical property of most cancer cells.

It was found that providing combined cytotoxic drugs is better than a single drug; a process called the combination therapy; which has an advantage in the statistics of survival and response to the tumor and in the progress of the disease. A Cochrane review concluded that combined therapy was more effective to treat metastasized breast cancer. However, generally it is not certain whether combination chemotherapy leads to better health outcomes, when both survival and toxicity are considered.

Targeted therapy is a form of chemotherapy that targets specific molecular differences between cancer and normal cells. The first targeted therapies blocked the estrogen receptor molecule, inhibiting the growth of breast cancer. Another common example is the class of Bcr-Abl inhibitors, which are used to treat chronic myelogenous leukemia (CML). Currently, targeted therapies exist for many of the most common cancer types, including bladder cancer, breast cancer, colorectal cancer, kidney cancer, leukemia, liver cancer, lung

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

cancer, lymphoma, pancreatic cancer, prostate cancer, skin cancer, and thyroid cancer as well as other cancer types.

7.2 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. As with chemotherapy, cancers vary in their response to radiation therapy.

Radiation therapy is used in about half of cases. The radiation can be either from internal sources (brachytherapy) or external sources. The radiation is most commonly low energy X-rays for treating skin cancers, while higher energy X-rays are used for cancers within the body. Radiation is typically used in addition to surgery and or chemotherapy. For certain types of cancer, such as early head and neck cancer, it may be used alone. For painful bone metastasis, it has been found to be effective in about 70% of patients.

7.3 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.

7.4 Palliative care

Palliative care is 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

7.5 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

7.6 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 are 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.

7.7 Alternative medicine

Complementary and alternative cancer treatments are a diverse group of therapies, practices and products that are not part of conventional medicine. "Complementary medicine" refers to methods and substances used along with conventional medicine, while "alternative medicine" refers to compounds used instead of conventional medicine. Most complementary and alternative medicines for cancer have not been studied or tested using conventional techniques such as clinical trials.

VIII. DRUGS USE IN TREATMENT OF CANCER

Theanticancer drugs either kill cancer cells or modify their growth. However, selectivity of majority of drugs is limited and they are one of the most toxic drugs used in therapy. Treatment of malignant diseases with drugs is a rather recent development—started after 1940 when nitrogen mustard was used, but progress has been rapid, both in revealing pathobiology of the diseases and in discovery of new drugs. The latest innovations target growth factors, specific signaling pathways, angiogenesis, tumour antigens, etc. to introduce a different spectrum of drugs. Inaddition, attempts have been made to define optimal combinations, treatment strategies and patient support measures.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

Cancer chemotherapy is now of established value and a highly specialized field to be handled by oncology specialists supported by a multidisciplinary team. Only the general principles and an outline will be presented here. In addition to their prominent role in leukaemias and lymphomas, drugs are used in conjunction with surgery, radiotherapy and

8.1 CLASSIFICATION OF DRUGS ARE USED IN CANCER

There is three classification of drugs are used in cancer diseases. Depend on the action of drugs

A. Cytotoxic drugs

1. Alkylating agents Mechlorethamine
Nitrogen mustards (Mustine HCl)
Cyclophosphamide,
Ifosfamide,
Chlorambucil,
Melphalan
Ethylenimine Thio-TEPA
Alkyl sulfonateBusulfan
Nitrosoureas Carmustine (BCNU),
Lomustine (CCNU)
TriazineDacarbazine (DTIC),
Temozolomide
Methylhydrazine Procarbazine

2. Platinum coordination Complexes: Cisplatin, Carboplatin, Oxaliplatin

3. Antimetabolites
Folate Antagonist: Methotrexate (Mtx), Pemetrexed
Purine AntagoAnist: 6-Mercaptopurine (6-MP), 6-Thioguanine (6-TG), Azathioprine, Fludarabin
Pyrimidine Antagonist: 5-Fluorouracil (5-FU), Capecitabine, Cytarabine (cytosine arabinoside)

4. Microtubule damaging agents: Vincristine (Oncovin), Vinblastine, Vinorelbine, Paclitaxel, Docetaxel, Estramustine

5. Topoisomerase-2 inhibitors: Etoposide

6. Topoisomerase-1 Inhibitors: Topotecan, Irinotecan

7.Antibiotics: Actinomycin D (Dactinomycin), Doxorubicin, Daunorubicin, (Rubidomycin) Epiribicin, Mitoxantrone, Bleomycins, Mitomycin C

8.Miscellaneous: Hydroxyurea, L-Asparaginase, Tretinoin, Arenic trioxide

B. Targeted drugs

BCR-ABL tyrosine Kinase inhibitors: Imatinib, Dasatinib, Nilotinib

EGF (HRE) receptor Inhibitors: Gefitinib, Erlotinib, Cetuximab, Trastuzumab, Lapatinib

Angiogenesis inhibitor: Bevacizumab, Sunitinib, Sorefenib

Proteasome inibitor: bortezomib

CD20 inhibitor: Rituximab

C. Hormonal drugs

Glucocorticoids: Prednisolane (other)

Estrogens: Ethinyl estradiol, Forfestrol

SERMs: Tamoxifen, Taremifene

SER-down regulator: Fulvestrant

Aromatase inhibitors: `Letrozole, Anastrozole, exemestane

Antiandrogens: Flutamide, Bicalutamide

5-a- reducatase inhibitors: Finasteride, Dutasteride

GnRH analogues: Nafsrelin, Leuperorelin, Triptorelin

Progestins: Hydroxy-progerone Acetate (other)

IX. SYNTHETIC MOLECULAR MEDICINES

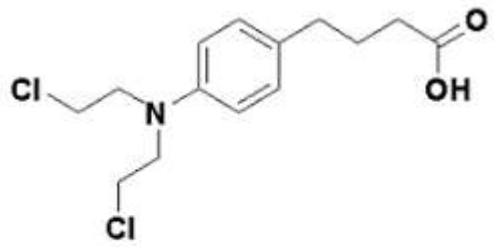
9.1 One nitrogen containing synthetic medicines

A Chlorambucil

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

is a nitrogen mustard alkylating agents (act as binding DNA) approved before 1984 for the treatment of Hodgkin and non-Hodgkin lymphoma, chronic lymphocytic leukemia, trophoblastic neoplasms, waldenström macroglobulinemia (a white blood cell carcinoma), polycythemia vera (formation of more red blood cell) and ovarian carcinoma with

side effects :- low white blood cells count, low platelet count, menstrual period stop, sperm reduction, hair loss etc.

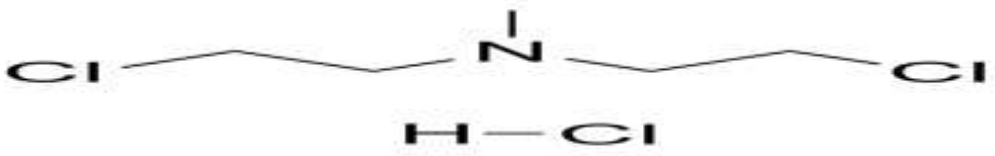


chlorambucil

B. Chlormethine

(mechlorethamine, mustine) is also nitrogen mustard alkylating agents and used to treatment of prostate cancer since 1946 with

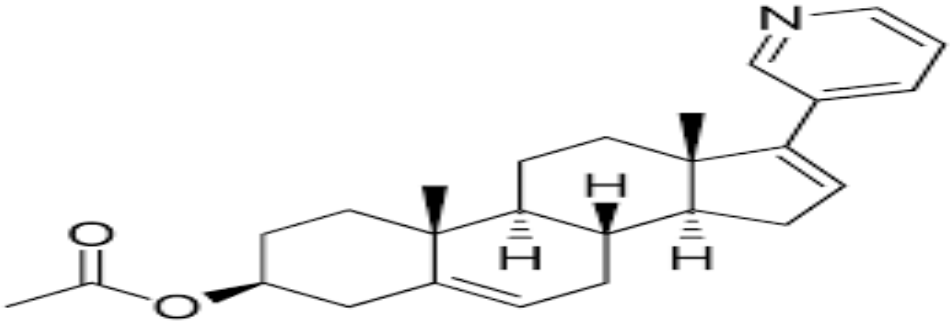
side effects :- low white blood cell count, low platelet count, anemia, nausea, vomiting, tasteless, low appetite, hair loss, longterm infertility etc



C. Abiraterone

It was approved to treatment of advanced prostate cancer in 2011 however. and works as 17 α-hydroxylase/C17, 20 lyase (CYP17A1) inhibitor with

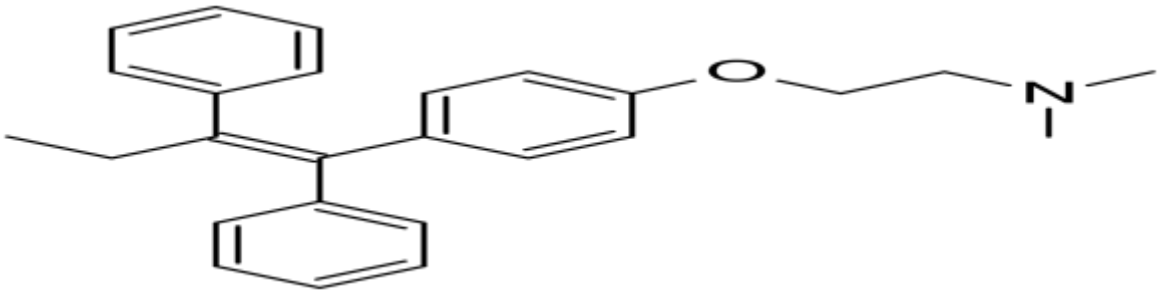
side effects:- joint pain, swelling, tiredness, muscle aches, low blood levels of potassium or phosphate, high cholesterol, anemia, low white blood cell count, abnormal blood test results, high blood sugar etc.



International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

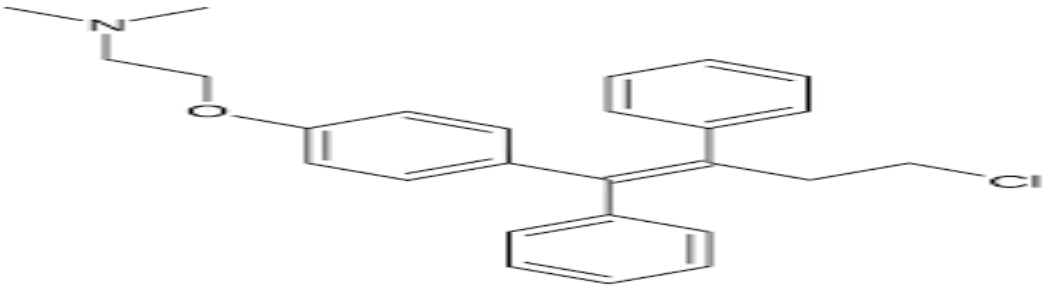
D. Tamoxifen

It is an essential medicine with very less side effects as comparison with other anticancer drugs and it is used to treatment of breast cance . It is a special type hormone prodrug, used as estrogen receptor and known as selective estrogen receptor modifier (SERM).



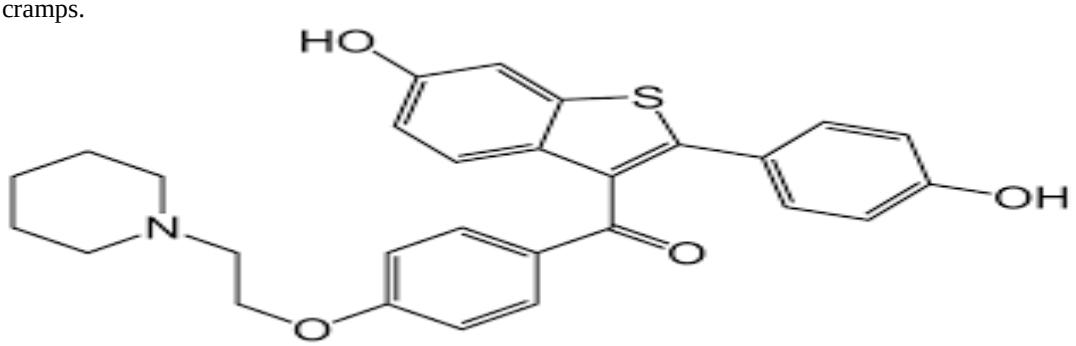
E. Toremifene

It was approved for the treatment of breast cancer in 1997 and also used for the treatment of prostate cancer and acts as selective estrogen receptor modifier (SERM) similar to tamoxifen.



F. Raloxifene

It is also a selective estrogen receptor modifier (SERM) and approved to treatment of breast cancer in 2007. Tamoxifen, toremifen and raloxifene were showing common side effects such as hot flashes, tiredness and leg cramps.



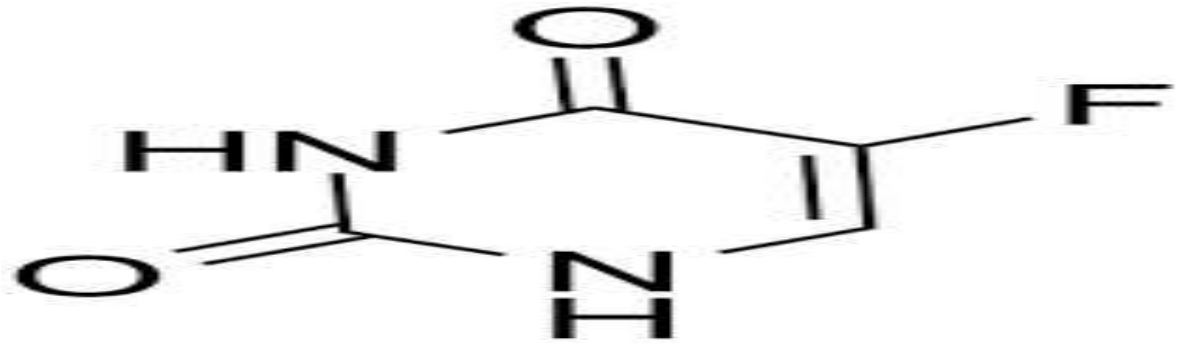
9.2 Two nitrogen containing synthetic medicines

A. Fluorouracil (5-FU)

It is an important essential drug of varies cancer treatment such as breast, anal, stomach, colorectal, pancreatic, skin and oesophageal. It acts as thymidylate synthase inhibitors

side effects :- nausea, headache, vomiting, hair loss, photosensitivity low white blood cell count, low platelet count, sores in mouth, brittle nails, dry skin etc.

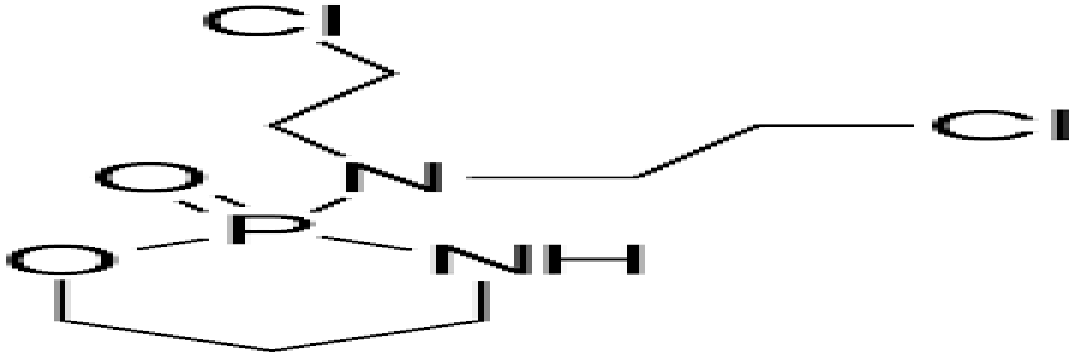
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



B. Cyclophosphamide

It is nitrogen alkylating agent which used for the treatment of lymphoma, multiple myeloma, leukemia, neuroblastoma, mycosis fungoides, retinoblastoma etc.

side effects:- hair loss, diarrhea, nausea, low white blood cell count, mouth sores, appetite loss, bleeding from bladder, vomiting etc.



C. Cisplatin (cis-diamminedichloroplatinu (II), cisplatinum)

It is a platinum containing anticancer drug which acts as cross linking of DNA (alkylating agents) of carcinoma cells and approved to treatment of ovarian, testicular, bladder, lung cancer.

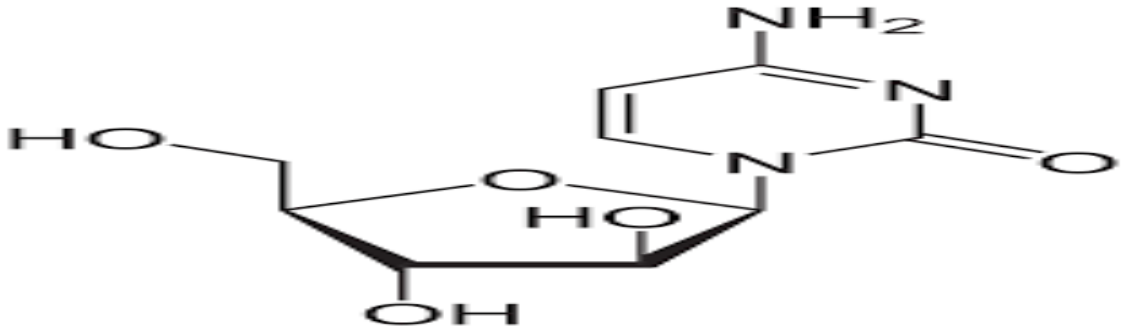
side effect:- kidney damage, decreased potassium, magnesium and calcium level in blood, vomiting, nausea, low white blood count, low platelet count, anemia, change in taste, numbness, swelling etc.

9.3 Three nitrogen containing synthetic medicines

A. Cytarabine

It is a most essential drug which is used to cure acute myeloid leukemia (a white blood cell cancer) and non-hodgkin lymphoma. Itacts as DNA synthesis inhibitors of carcinoma cell **side effects:-** nausea, vomiting, low blood cell count, low platelet count, stomach pain, tiredness, mouth sore etc.

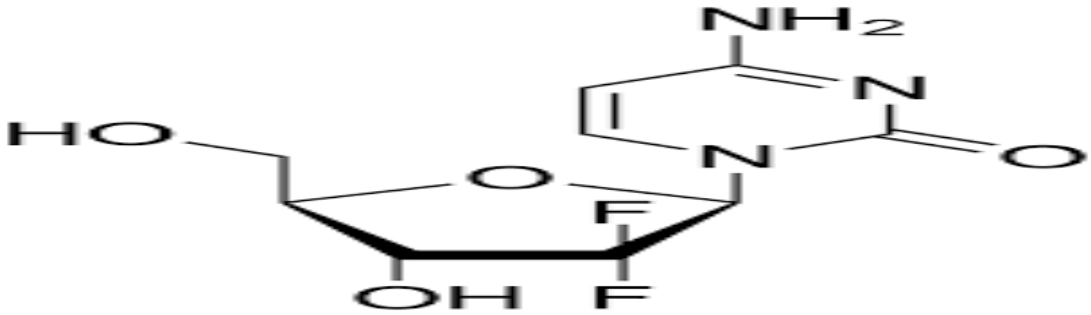
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



B. Gemcitabine

It is used to treatment of various type cancers such as pancreatic, lung [49], ovarian, breast cancers. It also acts as DNA synthesis inhibitors of carcinoma cells

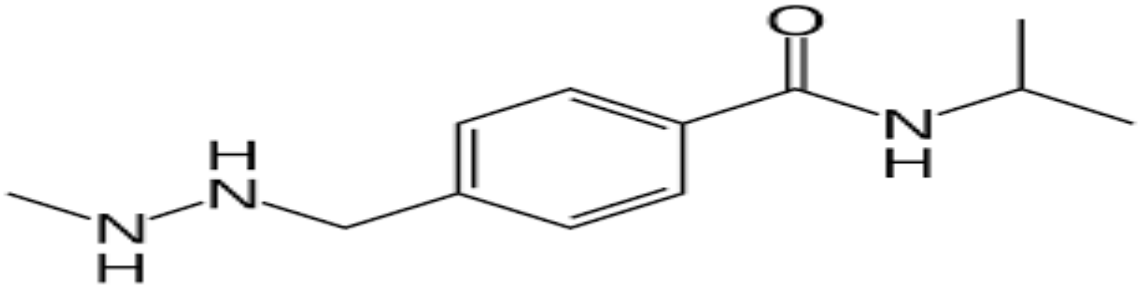
side effects:- such as fever, low white blood cell count, low platelet count, anemia, nausea, vomiting, tiredness, rash on skin, appetite loss etc.



C. Procarbazine

It is an alkylating agent and approved to treatment of Hodgkin's lymphoma and glioblastoma (brain cancer) in 1969 .

side effects:- low white blood cell count, low platelet count, depression, nausea, vomiting, felling nervousness, appetite loss, sleeping problems etc. It is used with combination of other anticancer medicines.



D. Bendamustine

It was approved to treatment of chronic lymphocytic leukemia and non Hodgkin lymphoma in 2008. It is a nitrogen mustard and acts as alkylating agents

side effects:- low white blood cell count, low platelet count, anemia, fever, nausea, vomiting, diarrhea, appetite loss, tiredness etc.

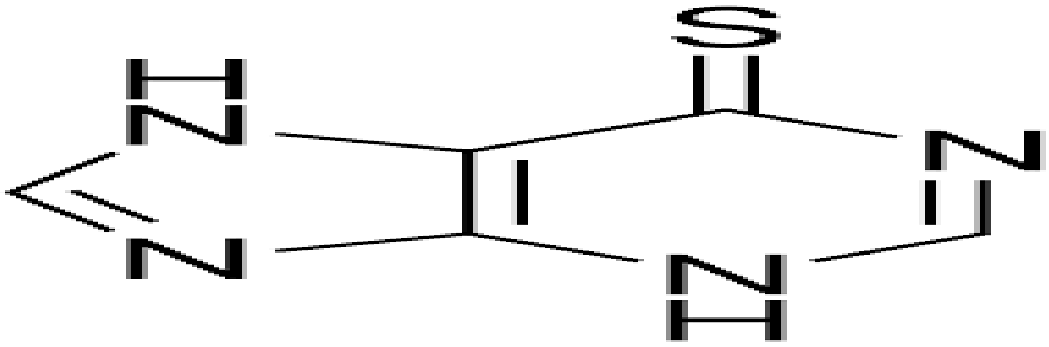
9.4 Four nitrogen containing synthetic medicines

A. Mercaptopurine (azathioprine)

It is used for the treatment of leukemia (a cancer of bone marrow). It acts as anti-metabolite.

side effects:- low white blood cell count, low blood platelet count and anemia etc.

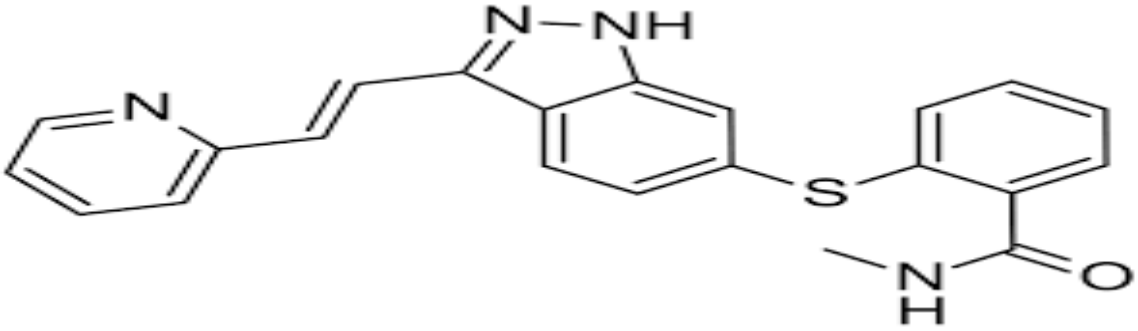
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



B. Axitinib

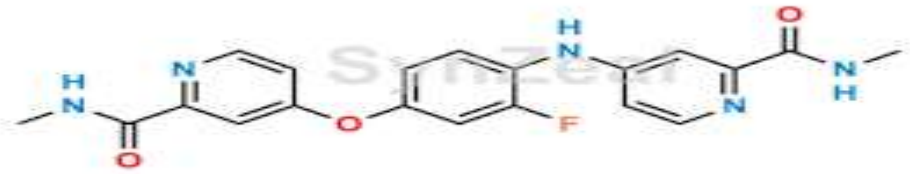
It was approved in 2012 for the treatment of renal cell carcinoma. It acts as vascular epidermal growth factor receptor (VEGFR) for a tyrosine kinase protein.

side effects:- such as skin rashes, diarrhea, nausea, low blood cell counts, tiredness, appetite loss, weight loss, swelling, numbness and pain in hand and high blood pressures etc.



C. Regorafenib

It was approved in 2012 for the treatment of metastatic colorectal and advanced gastrointestinal stromal tumors. It acts as oral receptor tyrosine kinase inhibitor with **side effects:-** fever, appetite loss, tiredness, weakness, diarrhea, infection, weight loss, moth's sores, rashes, high blood pressure, change in voice, bleeding etc.

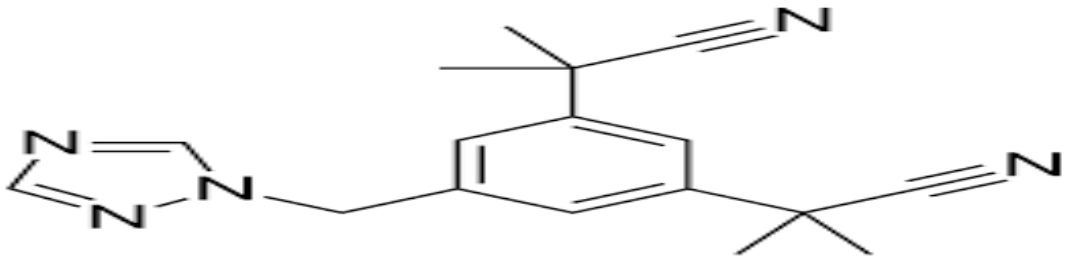


9.5Five nitrogen containing synthetic medicines

A. Anastrazole

It was approved in 1995 for the treatment of breast cancer. It acts as aromatase inhibitors (block aromatase which is necessary for the formation of estrogen) with **side effects :-** pain in joint and bones, hot flashes etc.

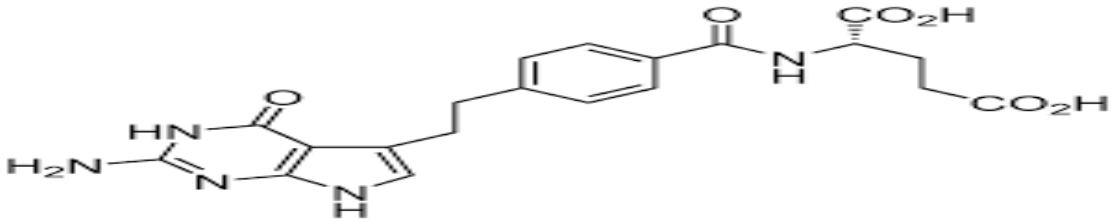
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



B. Pemetrexed

It was approved in 2004 and used for the treatment of malignant pleural mesothelioma (the lining of the chest cavity around the lungs cancer) and non small cell lung cancer. It acts as anti-metabolites.

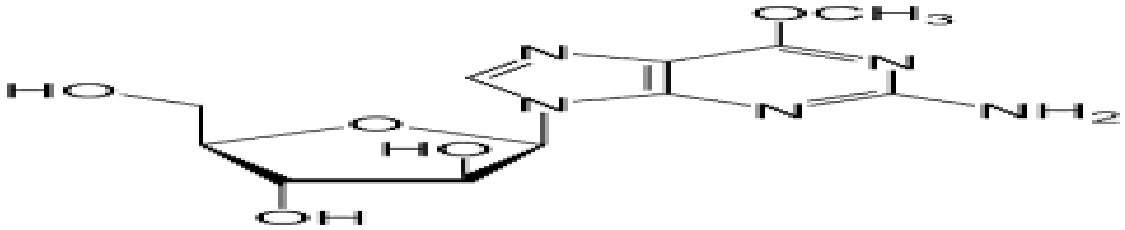
side effects :- breathing difficulty, tiredness, rashes, appetite loss, mouth sores, constipation, nausea, vomiting, low platelet count, low white blood cell count, anemia etc.



C. Nelarabine

It was approved in 2005 and used for the treatment of T-cell acute lymphoblastic leukemia (a white blood cell cancer). It also acts as anti-metabolites (block the formation of DNA and RNA of carcinoma cells).

side effects:- headache, tiredness, low platelet count, low white blood cell count, anemia etc.

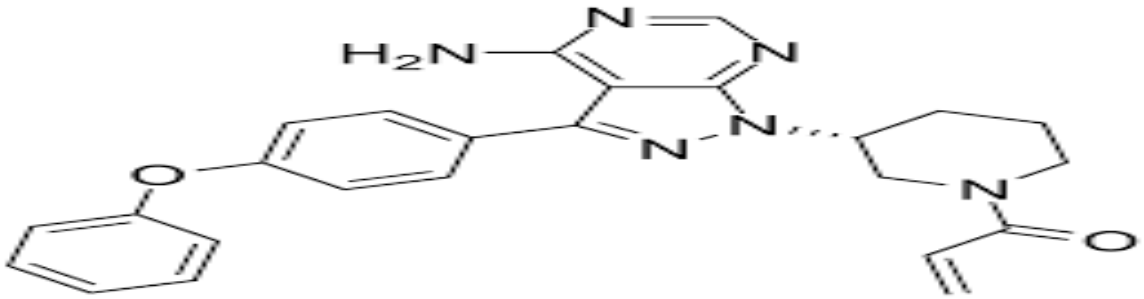


9.6 Six nitrogen containing synthetic medicines

A. Ibrutinib

It was approved in 2013 and used for the treatment of chronic lymphocytic leukemia and mantle cell lymphoma (a non-Hodgkin's lymphomas). It acts as tyrosine kinase inhibitor

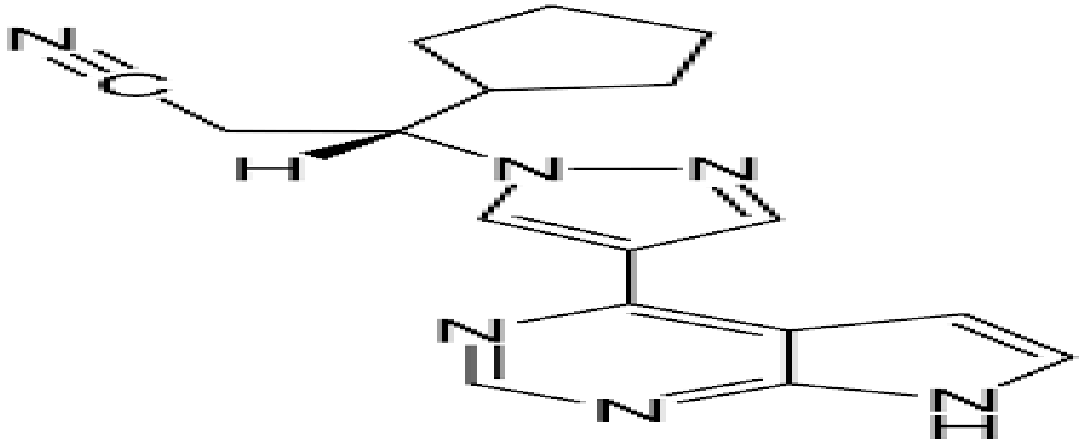
side effects:- nausea, vomiting, diarrhea, tiredness, pain in bone and muscles, cold, swelling, breath disorder, rashes in skin, constipation, abdominal pain, appetite loss, anemia, low platelet count etc.



International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

B. Ruxolitinib

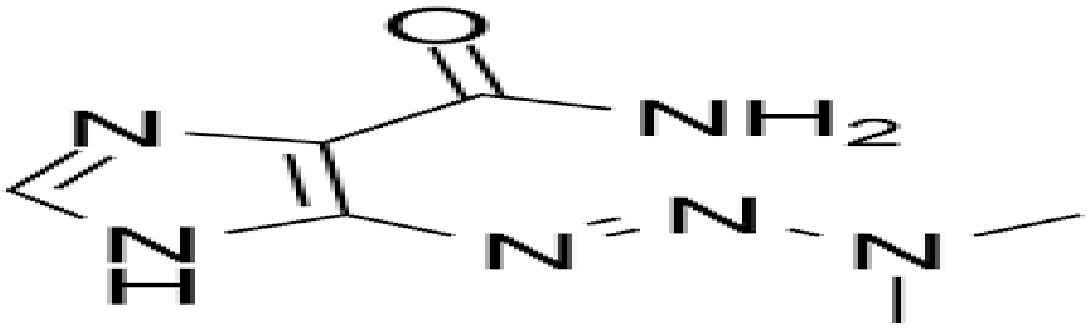
It was approved in 2011 and used for the treatment of myelofibrosis (a bone marrow carcinoma) and pancreatic carcinoma. It acts as Janus kinase inhibitor (JKI) **side effects**:- low blood platelet counts, fatigue, anemia, diarrhea, breath disorder, headache, nausea, dizziness etc.



C. Dacarbazine

It is an alkylating agents used for the treatment of Hodgkin lymphoma, malignant melanoma, islet cell carcinoma of the pancreas and sarcoma.

side effects:- low white blood cell count, low platelet count, vomiting, nausea, hair loss, appetite loss, tiredness, headache, fever etc.

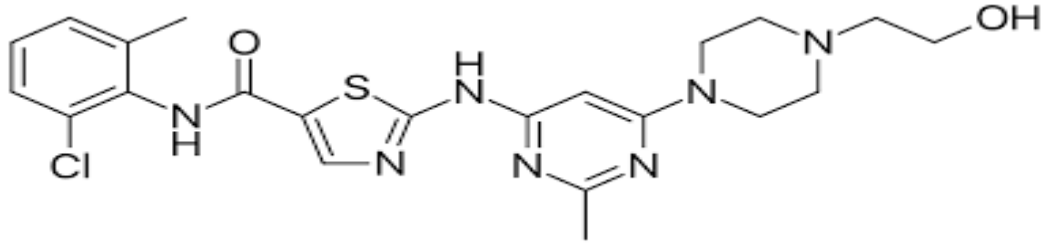


9.7 Seven nitrogen containing synthetic medicines

A. Dasatinib

It was approved in 2006 and used for the treatment of chronic myelogenous leukemia, acute lymphocytic leukemia and prostrate carcinoma. It acts a tyrosine kinase inhibitor.

side effects:- low white blood cell count, low blood platelet count, breath disorder, rashes in skin, pain in bone and muscle, headache, fever, tiredness, nausea, diarrhea, swelling etc.

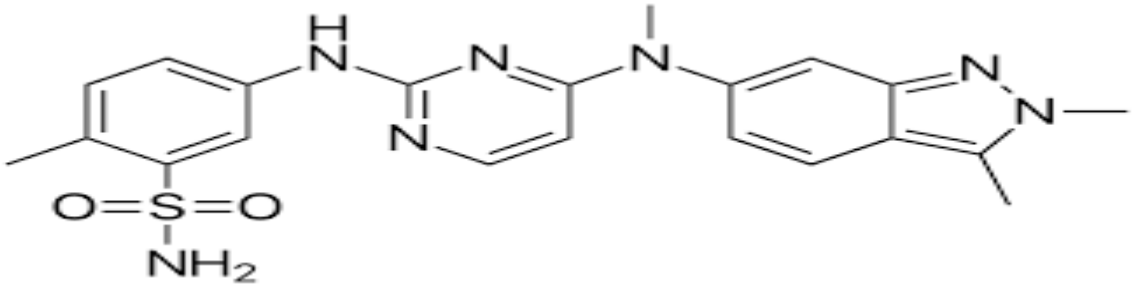


International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

B. Pazopanib

It was approved in 2009 and used for the treatment of renal cell carcinoma (kidney cancer) and soft tissue sarcoma (a connective tissue carcinoma). It acts as tyrosine kinase inhibitor.

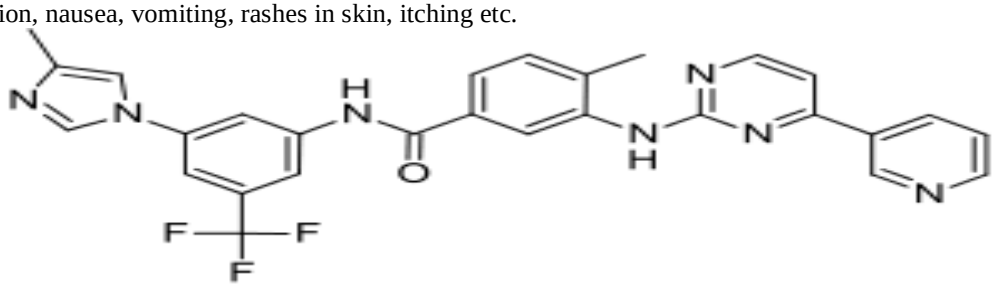
side effects:- slow heart beat, weight loss, pain in joint and muscles, abdomen pain, change in taste, appetite loss, tiredness, high blood pressure, headache, vomiting, diarrhea, nausea etc.



C. Nilotinib

It was approved in 2007 and used for the treatment of chronic myelogenous leukemia. It acts as tyrosine kinase inhibitor.

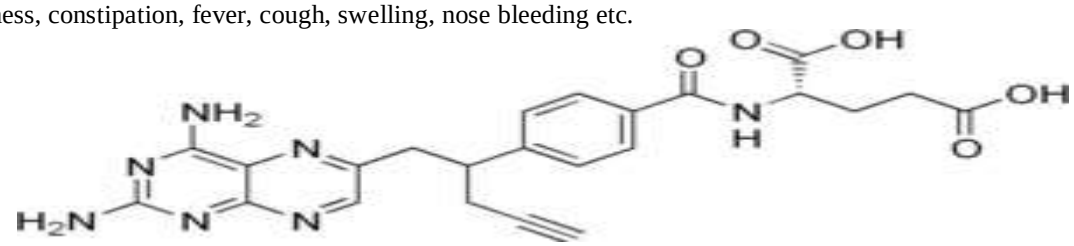
side effects:- low white blood cell count, low blood platelet count, tiredness, headache, fever, diarrhea, constipation, nausea, vomiting, rashes in skin, itching etc.



D.Pralatrexate

It was approved in 2009 and used for the treatment of peripheral T-cell lymphoma (a non-Hodgkin lymphoma). It acts as anti-metabolites.

side effects:- mouth sore, nausea, vomiting, diarrhea, anemia, low white blood cell count, low platelet count, tiredness, constipation, fever, cough, swelling, nose bleeding etc.



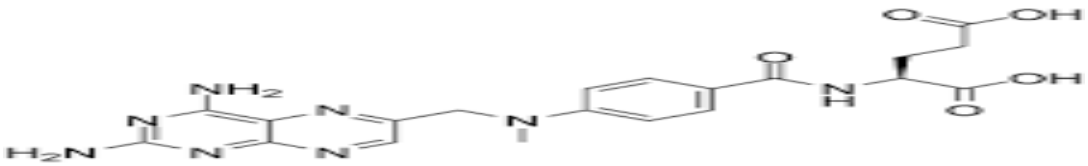
9.8 Eight nitrogen containing synthetic medicines

A. Methotrexate

It is used for the treatment of head and neck, breast, lymphoma, leukemia, osteosarcoma, lung, bladder and trophoblastic neoplasms carcinoma. It acts as anti-metabolites.

side effects:- mouth sores, diarrhea, vomiting, nausea, appetite loss, sunburn of skin, fever etc.

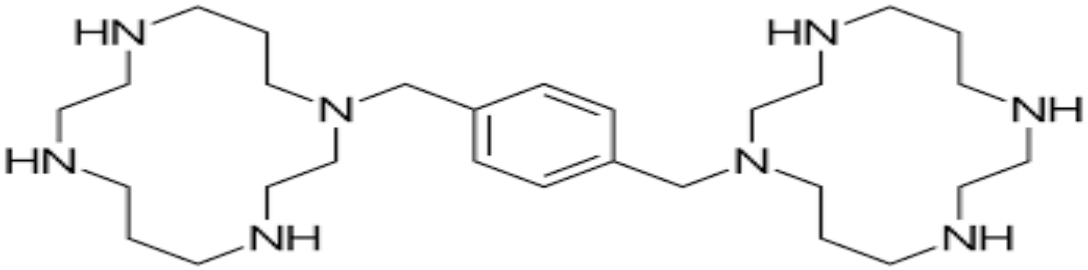
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



B.Plerixafor

It was approved in 2008 for the treatment of non-Hodgkin lymphoma and multiple myeloma. It acts as immunostimulant for mobilize hematopoietic stem cells in cancer patients.

side effects:- diarrhea, nausea, headache, pain in muscles, dizziness etc.

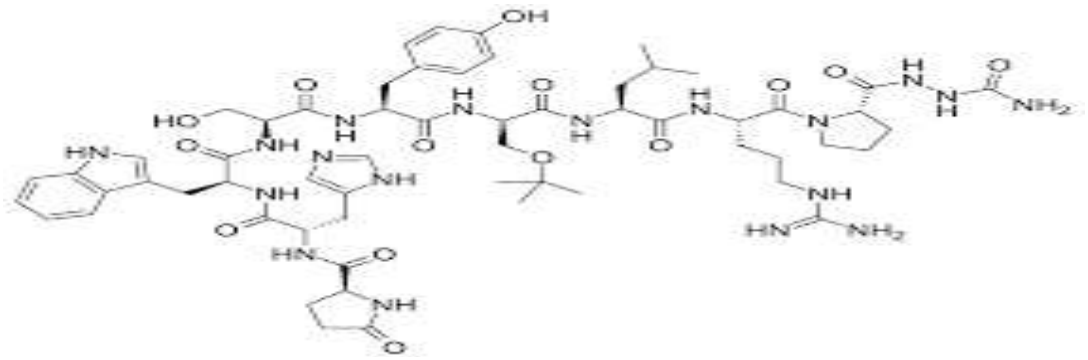


9.9 Multiple nitrogen containing synthetic medicines

A. Goserelin

It was approved in 1989 and used for the treatment of prostate and breast cancers. It is a decapeptide hormone also called luteinizing hormone releasing hormone (LHRH). It acts gonadotropin releasing hormone super agonist (block the formation of testosterone and estrogen).

side effects:- swelling, decease in breast size, skin disorder, depression, vaginal dryness, hot flashes, stooping menstrual period etc.

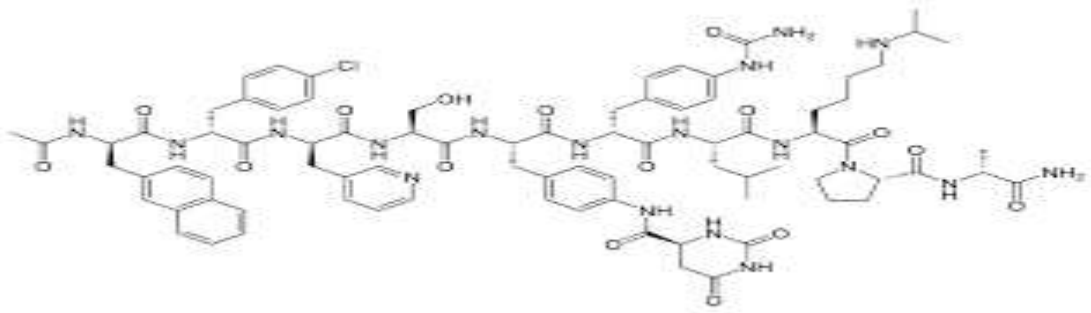


B. Degarelix

It was approved in 2008 and used for the treatment of prostate cancer. It is also a decapeptide hormone. It acts gonadotropin releasing hormone super agonist.

side effects:- sleeping disorder, hot flashes, breast enlargement, pain in breast, back pain, headache, constipation, tiredness, increase urination etc.

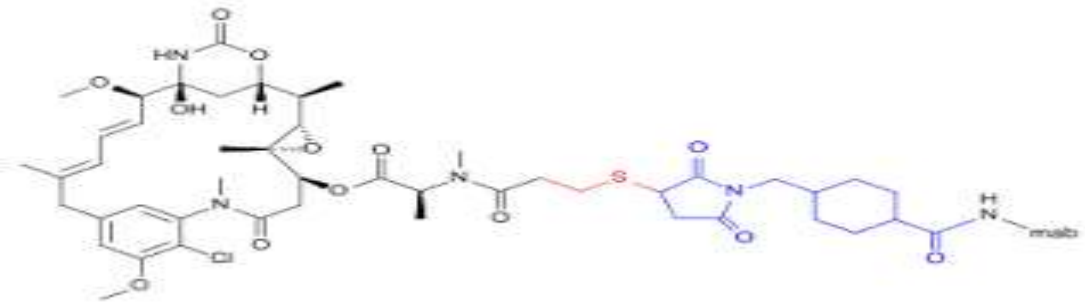
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



C. Trastuzumab Emtansine

It was approved in 2013 and used for the treatment of breast cancer. It contains monoclonal antibody part trastuzumab and second part is emtansine. Transtuzumab inhibit to grow cancer cell binding from HER2/neu receptor and emtansine bind with tubulin.

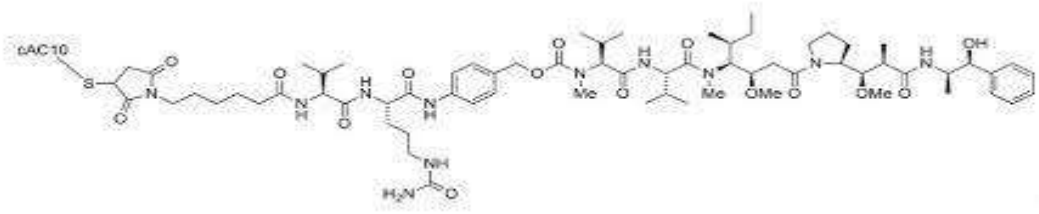
side effect:- nausea, tiredness, pain in joint, bone and muscles, diarrhea, constipation, headache, low blood platelet count, nose bleeding, numbness etc.



C.Brentuximab vedotin

It was approved in 2011 and used for the treatment of Hodgkin lymphoma and anaplastic large cell lymphoma (a non-Hodgkin lymphoma). It is also consist of two parts, first part is a monoclonal antibody which inhibit CD30 antigen of carcinoma cell and second part is monomethyl auristatin E (MMAE) which bind with microtubule of carcinoma cells.

side effects:- tiredness, rashes, cough, fever, nausea, vomiting, diarrhea, numbness in hands, abdomen pain etc.



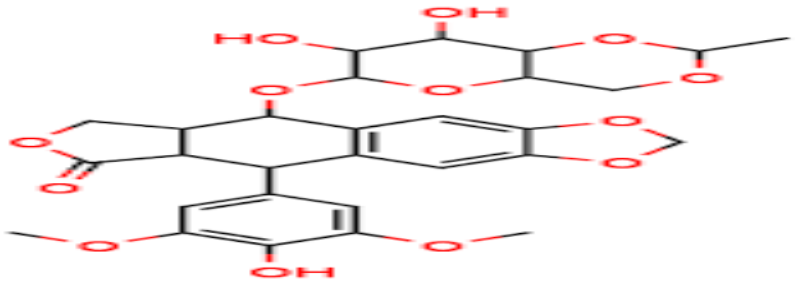
9.10. Without nitrogen containing synthetic medicines

A. Etoposide

It was approved in 1983 and used for the treatment of small cell lung and testicular cancer. It acts as topoisomerase II enzyme inhibitors.

side effects:- hair loss, appetite loss, vomiting, nausea, low white blood cell count, low blood platelet count etc.

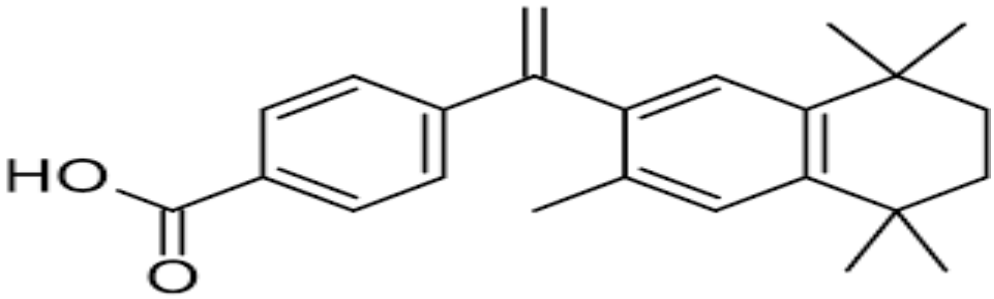
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781



B. Bexarotene

It was approved in 1999 and used for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma and also for lung and breast cancer. It is aretenoid and acts as retinoic acid receptors.

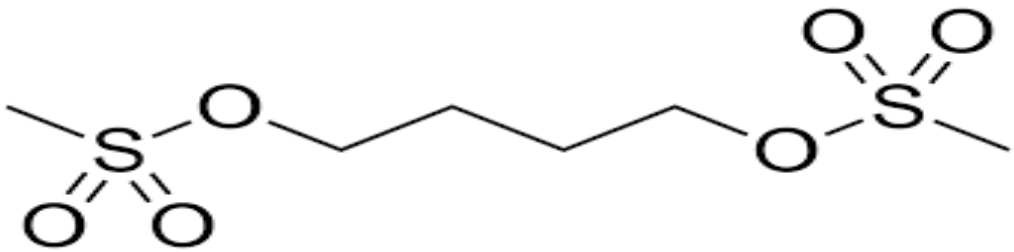
side effects:- diarrhea, headache, rashes, itching, low cholesterol disorder, high lipid levels, pain etc.



C. Busulfan

It was approved in 1999 and used for the treatment of chronic myelogenous leukemia (a white blood cell carcinoma). It acts as alkylating agents.

side effects:- low platelet count, low white blood cell count, anemia, hair loss, infertility disorder etc.



9.11.Steroidal medicines without nitrogen

Prednisone and dexamethasone

It is used for the treatment of leukemias and lymphomas as well as treatment of allergic reactions, treatment of nausea and vomiting, increase of appetite caused by various carcinoma drugs. It are a glucocorticosteroid hormone.

side effects:- sleeping disorder, stomach problem, weight gain, high blood glucose level etc.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

A. Megestrol

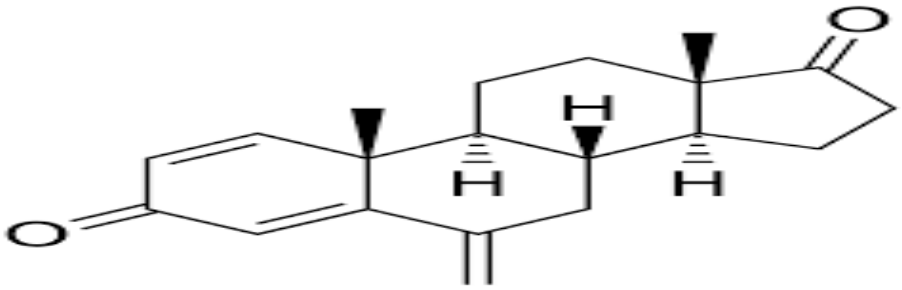
It is used for the treatment of breast and endometrial carcinoma. It acts as hormone antagonists.

side effects:- weight gain, increase in appetite, swelling in hands, legs and feet etc.

B. Exemestane

It was approved in 1999 and used for the treatment of breast cancer. It acts as aromatase inhibitors (block the formation of estrogen by inhibit aromatose) .

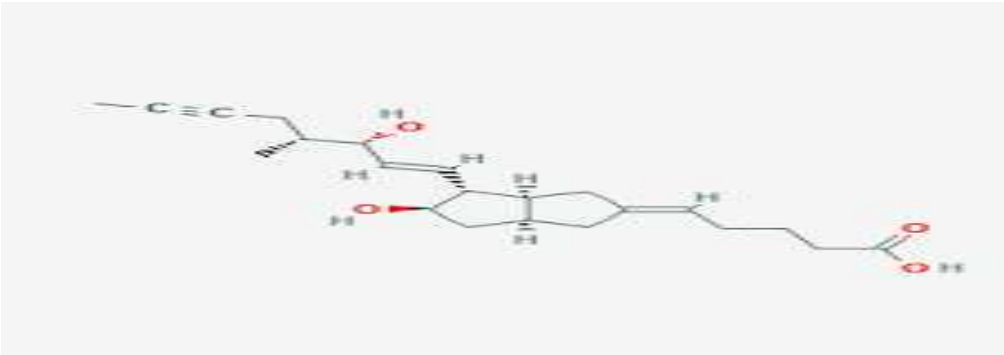
side effects:- pain in join and bone, hot flashes, tiredness, headache etc.



9.12.Other Protein, antibody and amino acids as anticancer medicines

A. Interleukin 2 (Aldesleukin) It was approved in 1992 and used for the treatment of skin melanomas and kidney carcinoma. It is an interleukin (a cytokine signaling molecule in the immune system). It belongs to cytokines protein group and acts as enhancement of immune system for the fight of cancers.

side effects:- fever, headache, pain in joint and muscles, low blood pressure, rashes, weakness, breath problem, confusion, itching in skin, nausea, vomiting, diarrhea etc.



B.Alemtuzumab

It was approved in 1992 and used for the treatment of chronic lymphocytic leukemia, cutaneous T-cell lymphoma, T-cell lymphoma, multiple sclerosis as lemtrada, regimens for bone marrow, kidney and islet cell transplantation. It is a monoclonal antibody and bind with CD52 protein of carcinoma cells.

side effects:- vomiting, fever, nausea, anemia, low white blood cell and platelet count, allergic reactions etc.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

C. Bevacizumab

It was approved in 2004 and used for the treatment of colon, cervical, kidney, breast, brain, non small cell lung cancer. It is also a human monoclonal antibody and acts as angiogenesis inhibitor which inhibit vascular endothelial growth factor (VEGF) protein of carcinoma cells.

side effects:- headache, mouth sores, diarrhea, tiredness, weaknes, back pain, skin dryness, appetite loss, nose bleeding, high blood pressure, bleeding form rectum, red and scaly skin etc.

D.Cetuximab

It was approved in 2004 and used for the treatment of head and neck cancer, metastatic colorectal cancer and metastatic non-small cell lung cancer. It is also a human monoclonal antibody and acts as angiogenesis inhibitor which inhibit vascular endothelial growth factor (VEGF) protein of carcinoma cells .

side effects:- itching, mouth sores, tiredness, weakness, rashes, fever etc.

9.13.Enzymes and Vaccine medicines

A.Recombinant Human Papillomavirus

It was approved in 2006 and used for prevent from cervical, anal, vaginal, vulvar (external genital organs of female) cancers. It is a virus-like particle which is not produce in human body.

B. Asparaginase (colaspase)

It is an enzyme that catalyzes the hydrolysis of asparagines (aspartic acid). Asparaginases are naturally occurringenzymes and produced by microorganisms Erwinia chrysanthemi.

C.Pegaspargase

It was approved in 2006 and used for the treatment of acute lymphoblastic leukemia. It is a pegylated E. coli L-asparagine amidohydrolase.

9.14.Inorganic medicines

A. Arsenic Trioxide (As_2O_3)

It was approved in 2000 and used for the treatment of leukemia.

side effects:- vomiting, nausea, appetite loss, abdomen pain, headache, tiredness, cough, fever, rashes etc.

B. Radium^{223}dichloride

It was approved in 2013 and used for the treatment of prostrate cancer. It is a radio pharma drug and its radiation damaged DNA of cancer cell in body.

side effects:- such as nausea, diarrhea, anemia, low white blood cell and platelet count etc.

9.15.Combined drugs

Due to several side effects of a single drug, resistant of drug, unavailability of drugs for advanced carcinona and for a better chemotherapy result combined drugs course are used for the treatment ofcancer. The combined drugs are ABVD (Adriamycin, Bleomycin, Vinblastine, Dacarbazine; used in Hodgkin lymphoma), ABVE (Adriamycin, Bleomycin, Vinblastine, Etopside, used in Hodgkin lymphoma of children), ABVE-PC (ABVE-Prednisone, Cyclophosphamide; used in Hodgkin lymphoma of children), AC (Adriamycin, Cyclophosphamide; used in breast cancer) AC-T(AC-Taxol; used in breast cancer), ADE (Cytarabine, Daunorubicin, Etopside; used for acute myeloid leukemia in children), BEACOPP(Bleomycin, Etopside, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone; used in Hodgkin lymphoma), BEP (Bleomycin, Etopside, Cisplatin, used in malignant tumor of ovaries and testis), CAF (Cyclophosphamide, Adriamycin, Fluorouracil; used in breast cancer), CAPOX (Capecitabine, Oxaliplatin; used in Colorectal cancer), CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone; used in non Hodgkin lymphoma), CMF (Cyclophosphamide, Methotrexate, Fluorouracil; used in breast cancer), COPP (Cyclophosphamide, Vincristine, Procarbazine, Prednisone; used in non Hodgkin lymphoma and Hodgkinlymphoma) COPP-ABV (COPP-Adriamycin, Bleomycin, Vinblastine; used in Hodgkin lymphoma), CVP (Cyclophosphamide, Vincristine, Prednisone; used in non Hodgkin lymphoma and Chronic lymphocytic leukemia), EPOCH (Etopside, Prednisone, Vincristine, Cyclophosphamide, Hydroxydaunomycin; used in non Hodgkin lymphoma), FEC (Fluorouracil, Epirubicin,Cyclophosphamide; used in breast cancer), FOLFIRI (Leucovorin, Fluorouracil, Irinotecan; used in colorectal cancer, FOLFOX (Leucovorin, Fluorouracil, Oxaliplatin; used in colorectal cancer), FU-LU (Fluorouracil, Leucovorin; used in colorectal cancer), ICE (Ifosfamide, Carboplatin, Etopside; used in non Hodgkin lymphoma and Hodgkin lymphoma), MOPP (Mechlorethamine, Vincristine, Procarbazine, Prednisone; used in Hodgkin lymphoma), OEPA (Vincristine, Etopside, Prednisone, Adriamycin; used in Hodgkin lymphoma), OFF (Oxaliplatin, Fluorouracil,

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

Leucovorin; used in pancreatic cancer), OPPA (Vincristine, Procarbazine, Prednisone, Adriamycin, Dexamethasone; used in multiple myloma), R-CHOP(Rituximab-CHOP; used in non Hodgkin lymphoma), R-CVP (Rituximab-CVP; used in non Hodgkin lymphoma), STANFORD V (Mechlorethamine, Doxorubicin, Vinblastine, Bleomycin, Etopside, Prednisone; used in Hodgkin lymphoma), TAC (Docetaxel, Adriamycin, Cyclophosphamide; used in breast cancer), TPF(Docetaxel, Cisplatin, Florouracil; used in gastric and squamous cell carcinoma of the head and neck), VAMP (Vincristine, Adriamycin, Methotrexate, Prednisone; used in Hodgkin lymphoma), XELOX (Capecitabine, Oxaliplatin; used in colorectal cancer).

X. CONCLUSION

This review have been covered anticancer drugs classified on the bases of present of nitrogen in the anticancer drugs with their structure, actions on cancer cell and side effects, the results are showing that these medicine are effecting cancer patient with a serious side effects. These side effects are itself a disease and several times these side effects became a main reason for a patient death. Thus, it needs new efforts with new thoughts to develop an anticancer medicine without side effects as well as cost effective medicine. Classification shown that four and three nitrogen containing anticancer are available in greater number as comparison of others.

REFERANCE

[1]. "Cancer Glossary". cancer.org. American Cancer Society. Archived from the original on 1 September 2013. Retrieved 11 September 2013.

[2]. "What is cancer?". cancer.gov. National Cancer Institute. 17 September 2007. Retrieved 28 March 2018.

[3]. Jump up to:[a b c d] Hanahan D, Weinberg RA (January 2000). "The hallmarks of cancer". Cell.

[4]. Jump up to:[a b] Hanahan D, Weinberg RA (March 2011). "Hallmarks of cancer: the next generation". Cell. **144** (5): 646–74. doi:10.1016/j.cell.2011.02.013. PMID 21376230.

[5]. Hajdu SI (March 2011). "A note from history: landmarks in history of cancer, part 1". Cancer. **117** (5): 1097–102. doi:10.1002/cncr.25553. PMID 20960499. S2CID 39667103.

[6]. ^ Paul of Aegina, 7th Century AD, quoted in Moss, Ralph W. (2004). "Galen on Cancer". CancerDecisions. Archived from the original on 16 July 2011. Referenced from Michael Shimkin, Contrary to Nature, Washington, DC: Superintendent of Document, DHEW Publication No. (NIH) 79–720, p. 35.

[7]. ^ Majno G, Joris I (12 August 2004). Cells, Tissues, and Disease : Principles of General Pathology: Principles of General Pathology. Oxford University Press. ISBN 978-0-19-974892-1. Retrieved 11 September 2013.

[8]. ^ Jump up to:[a b] Hajdu SI (June 2011). "A note from history: landmarks in history of cancer, part 2". Cancer. **117** (12): 2811–20. doi:10.1002/cncr.25825. PMID 21656759. S2CID 28148111.

[9]. ^ Yalom, Marilyn (1998). A history of the breast (1 ed.). New York: Ballantine Books. ISBN 978-0-679-43459-7.

[10]. ^ Hajdu SI (February 2012). "A note from history: landmarks in history of cancer, part 3". Cancer. **118** (4): 1155–68. doi:10.1002/cncr.26320. PMID 21751192.

[11]. ^ Grange JM, Stanford JL, Stanford CA (June 2002). "Campbell De Morgan's 'Observations on cancer', and their relevance today". Journal of the Royal Society of Medicine. **95** (6): 296–99. doi:10.1258/jrsm.95.6.296. PMC 1279913. PMID 12042378

[12]. Anguiano L, Mayer DK, Piven ML, Rosenstein D (July–August 2012). "A literature review of suicide in cancer patients". Cancer Nursing. **35** (4): E14–26. doi:10.1097/NCC.0b013e31822fc76c. PMID 21946906. S2CID 45874503.

[13]. ^ O'Dell, edited by Michael D. Stubblefield, Michael W. (2009). Cancer rehabilitation principles and practice. New York: Demos Medical. p. 983. ISBN 978-1-933864-33-4.

[14]. ^ Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. (May 2011). "Definition and classification of cancer cachexia: an international consensus". The Lancet. Oncology. **12** (5): 489–95. doi:10.1016/S1470-2045(10)70218-7. PMID 21296615.

[15]. ^ Dimitriadis GK, Angelousi A, Weickert MO, Randeva HS, Kaltsas G, Grossman A (June 2017). "Paraneoplastic endocrine

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

syndromes". Endocrine-Related Cancer. **24** (6): R173–R190. doi:10.1530/ERC-17-0036. PMID 28341725.

[16]. ^ "Share of cancer deaths attributed to tobacco". Our World in Data. Retrieved 5 March2020.

[17]. ^ Manton K, Akushevich I, Kravchenko J (28 December 2008). Cancer Mortality and Morbidity Patterns in the U.S. Population: An Interdisciplinary Approach. Springer Science & Business Media. ISBN 978-0-387-78193-8. The term environment refers not only to air, water, and soil but also to substances and conditions at home and at the workplace, including diet, smoking, alcohol, drugs, exposure to chemicals, sunlight, ionizing radiation, electromagnetic fields, infectious agents, etc. Lifestyle, economic and behavioral factors are all aspects of our environment.

[18]. ^ Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, McCullough ML, Patel AV, Ma J, Soerjomataram I, Flanders WD, Brawley OW, Gapstur SM, Jemal A (January 2018). "Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States". Ca. **68** (1): 31–54. doi:10.3322/caac.21440. PMID 29160902.

[19]. ^ Jump up to:[a] [b] Cohen S, Murphy ML, Prather AA (January 2019). "Ten Surprising Facts About Stressful Life Events and Disease Risk". Annual Review of Psychology. **70**: 577–597. doi:10.1146/annurev-psych-010418-102857. PMC 6996482. PMID 29949726. th e strongest conclusion derived from decades of research on stressors and cancer is that stressful events may be associated with decreased cancer survival but are probably not associated with disease incidence (Chida et al. 2008).

[20]. ^ Heikkilä K, Nyberg ST, Theorell T, Fransson EI, Alfredsson L, Bjorner JB, et al. (February 2013). "Work stress and risk of cancer: meta-analysis of 5700 incident cancer events in 116,000 European men and women". BMJ. **346**: f165. doi:10.1136/bmj.f165. PMC 3567204. PMID 23393080.

[21]. ^ Tolar J, Neglia JP (June 2003). "Transplacental and other routes of cancer transmission between individuals". Journal of Pediatric Hematology/Oncology. **25** (6): 430–4. doi:10.1097/00043426-200306000-00002. PMID 12794519. S2CID 34197973.

[22]. ^ Biesalski HK, Bueno de Mesquita B, Chesson A, Chytil F, Grimble R, Hermus RJ, Köhrle J, Lotan R, Norpoth K, Pastorino U, Thurnham D (1998). "European Consensus Statement on Lung Cancer: risk factors and prevention. Lung Cancer Panel". Ca. **48** (3): 167–76, discussion 164–66. doi:10.3322/canjclin.48.3.167. PMID 9594919.

[23]. ^ Kuper H, Boffetta P, Adami HO (September 2002). "Tobacco use and cancer causation: association by tumour type". Journal of Internal Medicine. **252** (3): 206–24. doi:10.1046/j.1365-2796.2002.01022.x. PMID 12270001. S2CID 6132726.

[24]. ^ Jump up to:[a] [b] Kuper H, Adami HO, Boffetta P (June 2002). "Tobacco use, cancer causation and public health impact". Journal of Internal Medicine. **251** (6): 455–66. doi:10.1046/j.1365-2796.2002.00993.x. PMID 12028500. S2CID 9172672.

[25]. http://www.medicalnewstoday.com

[26]. www.cancer.org

[27]. www.cancer.gov

[28]. Sigel RS, Ma J, Zou Z, Jemal A (2014) Cancer statistics, 2014. CA Cancer J Clin 64: 9-29.

[29]. World Health Organization report 2013, press release No 223, 12 December 2013.

[30]. Ali I, Wani WA, Saleem, K (2011) Cancer Scenario in India with Future Perspectives. Cancer therapy 8: 56-70.

[31]. Casinelli G, Orezzi P (1963) Daunomycin, a new antibiotic with cytostatic activity-isolation and properties. Giorn Microbiol 11: 167-174.

[32]. Arcamone F, Cassinelli G, Orezzi P, Franceschi G, Mondelli R (1964) Daunomycin-II. The structure and stereochemistry of daunosamine. J Am Chem Soc 86: 5335-5336.

[33]. Di Marco A, Gaetani M, Dorigotti L, Soldati M, Bellini, O (1964) Daunomycin-A new antibiotic with antitumor activity. Cancer Chemother Rep 38: 31-38.

[34]. Brayfield A ed. (2013) "Doxorubicin" Martindale: The Complete Drug Reference, Pharmaceutical Press, Retrieved 15 April 2014.
[35]. Tacar O, Sriamornsak P, Dass CR (2013) Doxorubicin: an update on anticancer molecular action, toxicity and novel drug delivery systems. J Pharmac Pharmaco 65: 157-170.
[36]. Bonfante V, Bonadonna G, Villani F, Martini A (1980) Preliminary clinical experience with 4-epidoxorubicin in advanced human neoplasia. Recent Results Cancer Res 74: 192-199.
[37]. Goodman J, Walsh V. (2001) The Story of Taxol: Nature and politics in the pursuit of an anti-cancer drug, Cambridge University Press: 179-182.
[38]. Lyseng-Williamson KA, Fenton C (2005) Docetaxel: a review of its use in metastatic breast cancer. Drugs 65: 2513-2531.
[39]. Galsky MD, Dritselis A, Kirkpatrick P, oh WK (2010) Cabazitaxel. Nat Rev Drug Discov 9: 677-678.
[40]. Ma WW, Jimeno A (2007) Temsirolimus. Drugs Today 43: 659-669.
[41]. Wachowska M, Muchowicz A, Firczuk M, Gabrysiak M, Winiarska M, et al. (2011) Aminolevulinic Acid (ALA) as a Prodrug in Photodynamic Therapy of Cancer. Molecules 16: 4140-4164.
[42]. Nashan B (2002) Review of the proliferation inhibitor everolimus. Expert Opin Investig Drugs11: 1845-1857.
[43]. Huyck TK, Gradishar W, Manuguid F, Kirkpatrick P (2011) Eribulin mesylate. Nat Rev Drug Discov 10: 173-174.
[44]. Wetzler M, Segal D (2011) Omacetaxine as an anticancer therapeutic: What is old is new again. Curr Pharm Design 17: 59-64.
[45]. Kim TD, Frick M, Coutre P le (2011) Omacetaxine mepesuccinate for the treatment of leukemia. Expert Opin Pharmaco 12: 2381-2392.
[46]. Conlin A, Fornier M, Hudis C, Kar S (2007) Ixabepilone. Nat Rev Drug Discov 6: 953-954.
[47]. 23.Johnson IS, Armstrong JG, Gorman M, Burnett JP (1963) The vinca alkaloids: a new class of oncolytic agents. Cancer Res 23: 1390-1427.
[48]. Li Q, Zu Y, Shi RZ, Yao, LP (2006) Review camptothecin: current perspectives. Curr Med Chem 13: 2021-2039.
[49]. Tomasz M (1995) Mitomycin C: small, fast and deadly (but very selective). Chem Biol 2: 575-579.
[50]. Bertino EM, Otterson GA, (2011) Romidepsin: a novel histone deacetylase inhibitor for cancer. Expert Opin Invest Drug. 20: 1151-1158.
[51]. Steele JM (2013) Carfilzomib: A new proteasome inhibitor for relapsed or refractory multiple myeloma. J Oncol Pharm Pract 19: 348-354.
[52]. Hollstein U (1974) Actinomycin. Chemistry and mechanism of action. Chem Rev 74 : 625-652.
[53]. Blum RH, Carter SK, Agre K (1973) A clinical review of bleomycin-a new antineoplastic agent. Cancer 31: 903-914.
[54]. Froudarakis M, Hatzimichael E, Kyriazopoulou L, Lagos K, Pappas P, et al. (2013) Revisiting bleomycin from pathophysiology to safe clinical use. Crit Rev Oncol Hematol 87: 90-100.
[55]. Rai KR, Peterson BL, Appelbaum FR, Kolitz J, Elias L, et al. (2000) Fludarabine compared with chlorambucil as primary therapy for chronic lymphocytic leukemia. N Engl J Med 343: 1750-1757.
[56]. Gilman A (1963) The initial clinical trial of nitrogen mustard. Am J Surg 105: 574-578.
[57]. Logothetis CJ, Efstathiou E, Manuguid F, Kirkpatrick P (2011) Abiraterone acetat. Nat Rev Drug Discov 10: 573-574.
[58]. Jordan VC (2006) Tamoxifen (ICI46,474) as a targeted therapy to treat and prevent breast cancer. Br J Pharmacol 147: 269-276.
[59]. Vogel CL, Johnston MA, Capers C, Braccia D (2014) Toremifene for breast cancer: A review of 20 years of data. Clin Breast Cancer 14: 1-9.
[60]. HansdÃ³ttir H (2008) Raloxifene for older women: a review of the literature. Clin Interv Aging 3: 45-50.
[61]. Sorrentino MF, Kim J, Foderaro AE, Truesdell AG (2012) 5-fluorouracil induced cardiotoxicity: review of the literature. Cardiol J 19: 453-458.
[62]. Likun Z, Xiang J, Yi B, Xin D, Tao ZL (2011) A systematic review and meta-analysis of intravenous palonosetron in the prevention of chemotherapy-induced nausea and vomiting in adults. Oncologist 16: 207-216.

[63]. Goa KL, Spencer CM. (1998) Bicalutamide in advanced prostate cancer. A review. Drug Aging 12: 401-422.
[64]. Dlugosz A, Agrawal S, Kirkpatrick P (2010) Vismodegib. Nat Rev Drug Discov 11: 437-438.
[65]. Stillwell TJ, Benson RC, (1988) Cyclophosphamide-induced hemorrhagic cystitis: A review of 100 patients. Cancer 61: 451-457.
[66]. Tascilar M, Loos WJ, Seynaeve C, Verweij J, Sleijfer S (2007) The pharmacologic basis of ifosfamide use in adult patients with advanced soft tissue sarcomas. Oncologist 12: 1351-1360.
[67]. Teni B, Maria V (2003) Cisplatin and platinum drugs at the molecular level (Review). Oncology 10: 1663-1682.
[68]. Misset JL, Bleiberg H, Sutherland W, Bekradda M, Cvitkovic E (2000) Oxaliplatin clinical activity: a review. Crc Cr Rev Oncol Hem 35: 75-93.
[69]. Go RS, Adjei AA (1999) Review of the comparative pharmacology and clinical activity of cisplatin and carboplatin. J Clin Oncol 17: 409-422.
[70]. Rajkumar SV, Witziq TE (2000) A review of angiogenesis and antiangiogenic therapy with thalidomide in multiple myeloma. Cancer Treat Rev 26: 351-362.
[71]. Grant S, Easley C, Kirkpatrick P (2007) Vorinostat. Nat Rev Drug Discov 6: 21-22.
[72]. Reese ND, Schiller GJ (2013) High-Dose Cytarabine (HD araC) in the Treatment of Leukemias: a Review. Curr Hematol Malig Rep 8: 141-148.
[73]. Noble S, Goa KL (1997) Gemcitabine. A review of its pharmacology and clinical potential in non-small cell lung cancer and pancreatic cancer. Drugs 54: 447-472.
[74]. Prados MD, Scott C, Curran Jr WJ, Nelson DF, Leibel S, et al. (1999) Procarbazine, Lomustine, and Vincristine (PCV) Chemotherapy for Anaplastic Astrocytoma: A Retrospective Review of Radiation Therapy Oncology Group Protocols Comparing Survival With Carmustine or PCV Adjuvant Chemotherapy. J Clini Oncol 17: 3389-3395.
[75]. Keating MJ, Bach C, Yasothan U, Kirkpatrick P (2008) Bendamustine Nat Rev Drug Discov 7: 473-474.
[76]. Nagilla M, Brown RL, Cohen, EEW (2012) Cabozantinib for the Treatment of Advanced Medullary Thyroid Cancer. Adv Ther 29: 925-934.
[77]. Walko CM, Lindley C (2005) Capecitabine: A review. Clin Ther 27: 23-44.
[78]. Tang PA, Tsao M-S, Moore MJ (2006) A review of erlotinib and its clinical use Expert Opin. Pharmaco 7: 177-193.
[79]. Bollag G, Tsai J, Zhang J, Zhang C, Ibrahim P, et al. (2012) Vemurafenib: the first drug approved for BRAF-mutant cancer. Nat Rev Drug Discov 11: 873-886.
[80]. Ahmad T, Gore M (2004) Review of the use of topotecan in ovarian carcinoma. Expert Opin Pharmaco 5: 2333-2340.
[81]. Weiss RB, Issell BF (1982) The nitrosoureas: carmustine (BCNU) and lomustine (CCNU) Cancer Treat. Rev. 9:313-310.
[82]. 458.Hideshima T, Raje N, Anderson KC (2008) A review of lenalidomide in combination with dexamethasone for the treatment of multiple myeloma. Ther Clin Risk Mang 4: 129-136.
[83]. Scott LJ (2014) Pomalidomide: a review of its use in patients with recurrent multiple myeloma. Drugs 74: 549-562.
[84]. Vismans JJ, BriÃ«t E, Meijer K, den Ottolander GJ (1980) Azathioprine and Subacute Myelomonocytic Leukemia. Acta Med Scand 207: 315-319.
[85]. Miller RL, Gerster, JF, Owens, ML, Slade HB, Tomai MA (1999) Review Article Imiquimod applied topically: a novel immune response modifier and new class of drug. International J Immunopharmacology 21: 1-14.
[86]. Derissen EJ, Beijnen JH, Schellens JH (2013) Concise drug review: azacitidine and decitabine. Oncologist 18: 619-624.
[87]. Curran MP (2013) Decitabine: A Review of its Use in older patients with acute myeloid leukaemia. Drugs Aging 30: 447-458.
[88]. Chen X, Liu Y, Qian Y, Guo R, Zhu L, et al. (2013) Gefitinib or Erlotinib as maintenance therapy in patients with advanced stage non-small cell lung Cancer: A systematic review. PLos One.
[89]. Moy B, Kirkpatrick P, Kar S, Goss P (2007) Lapatinib. Nat Rev Drug Discov 6: 431.
[90]. Karras S, Anagnostis P, Krassas GE (2014) Vandetanib for the treatment of thyroid cancer: an update Expert Opin Drug Met 10: 469-481.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

[91]. Van Geel RMJM, Beijnen JH, Schellens JHM (2012) Concise drug review: pazopanib and axitinib. Oncologist 17: 1081-1089.
[92]. Iyer R, Fetterly G, Lugade A, Thanavala Y (2010) Sorafenib: a clinical and pharmacologic review. Expert Opin Pharmaco 11: 1943-1955.
[93]. Davis SL, Eckhardt SG, Messersmith WA, Jimeno A (2013) The development of regorafenib and its current and potential future role in cancer therapy. Drugs Today 49: 105-115.
[94]. Motzer RJ, Hoosen S, Bello CL, Christensen JG (2006) Sunitinib malate for the treatment of solid tumors: a review of current clinical data. Expert Opin Investig Drugs 15: 553-561.
[95]. Dando TM, Perry CM (2004) Aprepitant: a review of its use in the prevention of chemotherapy-induced nausea and vomiting. Drugs 64: 777-794.
[96]. Bussel JB, Cheng G, Saleh MN, Psaila B, Kovaleva L, et al. (2007) Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. N Engl J Med 357: 2237-2247.
[97]. Richardson PG (2004) A review of the proteasome inhibitor bortezomib in multiple myeloma. Expert opin Pharmaco 5: 1321-1331.
[98]. CvetkoviÄ‡ RS, Scott LJ (2005) Dexrazoxane : a review of its use for cardioprotection during anthracycline chemotherapy. Drugs 65:1005.
[99]. Sanford M (2013) Enzalutamide: A review of its use in metastatic, castration-resistant prostate cancer. Drugs 73: 1723-1732.
[100]. Bhatnagar AS (2006) Review of the development of letrozole and its use in advanced breast cancer and in the neoadjuvant setting. Breast 15: 3-13.
[101]. Pazâ€• Ares L, Bezares S, Tabernero JM, Castellanos D (2003) Review of a promising new agent-pemetrexed disodium. Cancer 97: 2056-2063.
[102]. Dando TM, Perry CM (2004) Aprepitant: a review of its use in the prevention of chemotherapy-induced nausea and vomiting. Drugs 64: 777-794.
[103]. Gandhi V, Keating MJ, Bate G, Kirkpatrick P (2006) Nelarabine. Nat Rev Drug Discov 5:17-18.
[104]. Ricci F, Tedeschi A, Morra E, Montillo M (2009) Fludarabine in the treatment of chronic lymphocytic leukemia: a review. Ther Clin Risk Manag 5: 187-207./a>
[105]. Kline JP, Larson RA (2005) Clofarabine in the treatment of acute myeloid leukaemia and acute lymphoblastic leukaemia: a review. Expert Opin Pharmacother 6: 2711-2718.
[106]. Keating GM (2014) Afatinib: A review of its Use in the Treatment of Advanced Non-Small Cell Lung Cancer. Drugs 74: 207-221.
[107]. Rusconi F, Piazza R, Vagge E, Gambacorti-Passerini C (2014) Bosutinib: a review of preclinical and clinical studies in chronic myelogenous leukemia. Expert Opin Pharmaco 15: 701-710.
[108]. Davis JE, Anderson JE, Kim KB (2014) Dabrafenib therapy for advanced melanoma. Ann Pharmacother 48: 519-529.
[109]. Cooper MR, Chim H, Chan H, Durand, C (2014) Ceritinib a new tyrosine kinase inhibitor for NSCLC. Ann Pharmacother [Epub ahead of print].
[110]. Salama AKS, Kim KB (2013) Trametinib (GSK1120212) in the treatment of melanoma. Expert opin Pharmaco 14: 619-627.
[111]. Shaw AT, Yasothan U, Kirkpatrick P (2011) Crizotinib. Nat Rev Drug Discov 10: 897-898.
[112]. McDermott J, Jimeno A (2014) Ibrutinib for the treatment of chronic lymphocytic leukemia and mantle cell lymphoma. Drugs Today 50: 291-300.
[113]. Hoy SM (2014) Ponatinib: a review of its use in adults with chronic myeloid leukaemia or philadelphia chromosome-positive acute lymphoblastic leukaemia. Drugs 74: 793-806.
[114]. Swaim SJ (2014) Ruxolitinib for the treatment of primary myelofibrosis. Am J Health Syst Pharm 71: 453-462.
[115]. Wilson KS (2011) Ipilimumab plus dacarbazine in melanoma. N Engl J Med 365: 1256.
[116]. Newlands ES, Stevens MFG, Wedge SR, Wheelhouse RT, Brock C (1997) Temozolomide: a review of its discovery, chemical properties, pre-clinical development and clinical trials. Cancer Treat Rev 23: 35-61.

[117]. Kantarjian H, Jabbour E, Grimley J, Kirkpatrick P (2006) Dasatinib. Nat Rev Drug Discov 5: 717-718.
[118]. Bukowski RM, Yasothan U, Kirkpatrick P (2010) Pazopanib. Nat Rev Drug Discov 9:17-18.
[119]. Essat M, Cooper K (2011) Imatinib as adjuvant therapy for gastrointestinal stromal tumors: a systematic review. Int J Cancer 128: 2202-2214.
[120]. Plosker GL, Robinson DM (2008) Nilotinib. Drugs 68: 449-459.
[121]. Hong YS, Nam BH, Kim K, Kim JE, Park SJ, et al. (2014) Oxaliplatin, fluorouracil, and leucovorin versus fluorouracil and leucovorin as adjuvant chemotherapy for locally advanced rectal cancer after preoperative chemoradiotherapy (ADORE): an open-label, multicentre, phase 2, randomised controlled trial. Lancet 15: 1245-1253.
[122]. Dondi A, Bari A, Pozzi S, Ferri P, Sacchi F (2014) The potential of pralatrexate as a treatment of peripheral T-cell lymphoma. Expert Opin Invest Drug 23: 711-718.
[123]. Boulter PS (1967) Methotrexate in cancer. Br Med J. Mar 4: 553.
[124]. DiPersio JF, Uy GL, Yasothan U, Kirkpatrick P (2009) Plerixafor. Nat Rev Drug Discov 8: 105-106.
[125]. Perry CM, Brogden RN (1996) Goserelin. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in benign gynaecological disorders. Drugs 51: 319-346.
[126]. Mitchell MA (2005) Therapeutic review: Leuprolide acetate. Semin Avian Exot Pet Med 14: 153-155.
[127]. Carter NJ, Keam SJ (2014) Degarelix: a review of its use in patients with prostate cancer. Drugs 74: 699-712./a>
[128]. Gisselbrecht C, Bethge W, Duarte RF, Gianni AM, Glass B, et al. (2007) Current status and future perspectives for yttrium-90 (90Y)-ibritumomab tiuxetan in stem cell transplantation for non-Hodgkin's lymphoma. Bone marrow Transplant 40: 1007-1017.
[129]. Niculescu-Duvaz I (2010) Trastuzumab emtansine, an antibody-drug conjugate for the treatment of HER2+ metastatic breast cancer. Curr Opin Mol Ther 12 : 350-360.
[130]. Younes A, Yasothan U, Kirkpatrick P (2012) Brentuximab vedotin. Nat Rev Drug Discov 11: 19-20.
[131]. Katz J, Janik JE, Younes A (2011) Brentuximab vedotin (SGN-35). Clin Cancer Res.17: 6428-6436.
[132]. Hande KR (1998) Etoposide: four decades of development of a topoisomerase II inhibitor. Eur J Cancer 34: 1514-1521.
[133]. Gniadecki R, Assaf C, Bagot M, Dummer R, Duvic M, et al. (2007). The optimal use of bexarotene in cutaneous T-cell lymphoma. Br J Dermatol 157: 433-440.
[134]. Sostman HD, Putman CE, Gamsu G (1981) Review: diagnosis of chemotherapy lung. Am J Roentgenol 136: 33-40.
[135]. Shaw IC, Graham MI (1987) Mesna-a short review. Cancer Treat Rev 14: 67-86.
[136]. Wooldridge JE, Anderson CM, Perry MC (2001) Corticosteroids in advanced cancer. Oncology 15: 225-234.
[137]. Strang P (1996) The effect of megestrol acetate on anorexia, weight loss and cachexia in cancer and AIDS patients (review). Anticancer Res 17: 657-662.
[138]. Goss PE, Ingle JN, AlÃ©s-MartÃnez JE, Cheung AM, Chlebowski RT, et al. (2011) Exemestane for breast-cancer prevention in postmenopausal women. N Engl J Med 364: 2381.
[139]. Lee CI, Goodwin A, Freedman O, Clemons M, Wilcken N (2014) Fulvestrant for hormone-sensitive metastatic breast cancer. The Cochrane Library.
[140]. Rosenberg SA (1988) The development of new immunotherapies for the treatment of cancer using interleukin-2. A review. Ann Surg 208: 121-135.
[141]. O'Brien SM, Kantarjian HM, Thomas DA, Cortes J, Giles FJ, et al. (2003) Alemtuzumab as treatment for residual disease after chemotherapy in patients with chronic lymphocytic leukemia. Cancer 98: 2657-2663.
[142]. Cheson BD (2010) Ofatumumab, a Novel Anti-CD20 Monoclonal Antibody for the Treatment of B-Cell Malignancies. J Clin Oncol 28: 3525-3530.
[143]. Ferrara N, Hillan KJ, Gerber HP, Novotany W (2004) Discovery and development of bevacizumab, an anti-VEGF antibody for treating cancer. Nat Rev Drug Discov 3: 391-400.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1035-1063 www.ijprajournal.com ISSN: 2249-7781

[144]. Merlano M, Occelli M (2007) Review of cetuximab in the treatment of squamous cell carcinoma of the head and neck. Ther Clin Risk Manag 3: 871-876.
[145]. Walker T (2014) FDA approves advanced stomach cancer drug.
[146]. Prince HM, Newland KM (2014) Denileukin diftitox for the treatment of cutaneous T-cell lymphoma. Expert Opin. Orphan Drug 2: 625-634.
[147]. Henry DH, Costa L, Goldwasser F, Hirsh V, Hungria V, et al. (2011) Randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma. J Clin Oncol 29: 1125-1132.
[148]. Benesch M, Urban C (2008) Liposomal cytarabine for leukemic and lymphomatous meningitis: recent developments. Expert Opin Pharmacother 9: 301-309.
[149]. Lopez-Olivo MA, Pratt G, Palla SL, Salahudeen A (2013) Rasburicase in tumor lysis syndrome of the adult: a systematic review and meta-analysis. Am J Kidney Dis 62: 481-492.
[150]. Sourgens H, LefrÃ¨re F (2011) A systematic review of available clinical evidence-filgrastim compared with lenograstim. Int J Clin Pharmacol Ther 49: 510-518.
[151]. Illidge TM (2012) Obinutuzumab (GA101)-a different anti-CD20 antibody with great expectations. Expert opin Biol Ther 12: 543-545.
[152]. Kharfanâ€• Dabaja MA, Hamadani M, Reljic T, Pyngolil R, Komrokji RS, et al. (2013) Gemtuzumab ozogamicin for treatment of newly diagnosed acute myeloid leukaemia: a systematic review and meta-analysis. Brit J Haematol 163: 315-325.
[153]. Cada DJ, Demaris K, Levien TL, Baker DE (2012) Glucarpidase. Hosp Pharm 47: 463.
[154]. Kuter DJ, Rummel M, Boccia R, Macik BG, Pabinger I, et al. (2010) Romiplostim or Standard of Care in Patients with Immune Thrombocytopenia. Engl J Med 363: 1889-1899.
[155]. Eggermont AMM, Spatz A, Robert C (2014) Cutaneous melanoma. Lancet 383: 816-827.
[156]. GÃ¼rcan HM, Keskin DB, Stern JNH, Nitzberg MA, Shekhani H, et al. (2009) A review of the current use of rituximab in autoimmune diseases. Int Immunopharmacol 9: 10-25.
[157]. Markham A, Patel T (2014) Siltuximab: first global approval. Drugs 74: 1147-1152.
[158]. Tol J, Punt CJA (2010) Monoclonal antibodies in the treatment of metastatic colorectal cancer: A review. Clin Ther 32: 437-453.
[159]. Mitchell EP (2013) Targeted therapy for metastatic colorectal cancer: role of aflibercept. Clin colorectal can 12: 73-85.
[160]. Sondak VK, Smalley KSM, Kudchadkar R, Grippon S, Krikpatrick P (2011) Ipilimumab. Nat Rev Drug Discov 10: 411-412.
[161]. Beaven AW, Shea TC (2007) The effect of palifermin on chemotherapy and radiation therapy-induced mucositis: a review of the current literature. Support Cancer Ther 4: 188-197.
[162]. Quinn DI, Vaishampayan U, Higano CS, Lin DW, Shore ND, et al. (2014) Sequencing therapy in advanced prostate cancer: focus on sipuleucel-T. Expert rev anticanc Ther 14: 51-61.
[163]. Markowitz LE, Dunne EF, Saraiya M, Chesson HW, Curtis CR, et al. (2014) Human papillomavirus vaccination. Recommendations and Reports: Morbidity and Mortality Weekly Report. Recommendations and Reports. 63: 1-30.
[164]. Salzer WL, Asselin BL, Plourde PV, Corn T, Hunger SP (2014) Development of asparaginase Erwinia chrysanthemi for the treatment of acute lymphoblastic leukemia. Ann N Y Acad Sci 1329: 81-92.
[165]. Chang J, Zhang Y, Feng L, Zhong X, Wang L (2014) Treatment of Children with Advanced-Stage Lymphoblastic Lymphoma with Pegaspargase. Iran J Pediatr 24: 75-80.
[166]. Sanz MA, Fenaux P, Coco FL (2005) Arsenic trioxide in the treatment of acute promyelocytic leukemia. a review of current evidence