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Natural and Synthetic Molecular Medicine in Cancer Research: A Review

Review Article

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Abstract

This review presents the stimulating area of natural and synthetic anticancer drugs which are presently used for the cure of various type of cancer. In this review, twenty one naturally, semisynthetic naturally occurring and 109 synthetic anticancer drugs are reported. The emphasis of this review has described related structure, mechanism of action and major disadvantage of these drugs with the aims of providing an overview of anticancer drugs. This review will be provide current status of cancer drug and helpful to make strategy in the search of novel anticancer molecular medicine in future.

Keywords: Anticancer drugs; Chemotherapy; Cancer; Carcinoma; Tumor; Cancer medicine

Introduction

Cancer is a disease with abnormal cell growth of any part of our body. It is also called malignancy. Cancer's cells are divided uncontrollably and forms lumps. These lumps are called tumor and harms our body.

On the bases of part of our body more than hundred type carcinoma cells have been reported [1,2]. The most common cancer type are bladder cancer, lung cancer, breast cancer, melanoma (cancer of pigment making cells), colon and rectal cancer, non Hodgkin lymphoma (cancer of white blood cells), endometrial cancer (cancer of uterus), pancreatic cancer, kidney cancer, prostrate cancer, leukemia (cancer of blood forming tissue e.g. bone marrow), thyroid cancer etc [3].

For the treatment of these cancers, various methods were applied such as surgery (a method to remove tumors from body), radiation therapy (a method to destroy or damage carcinoma cell though applies the high wave radiation), targeted therapy (other substances or useing drugs to more accurately discover and attack carcinoma cells), immunotherapy (increase immune system to fight cancer cells), hyperthermia (using heat to treat cancer), Stem cell transplant (stem cells were transplant to treat cancer cells), photodynamic therapy (photosensitizing agents are a special drugs and used along with light to kill cancer cells), lasers in cancer treatment, blood product donation and transfusion, and most important tools chemotherapy (use of medicine to treat cancer) [2]. Cancer therapies are not secured to cure cancer completely. Some cases, it secure to cure cancer completely but it is much costly and maximum population cannot efforts such treatment. Thus maximum patients were died without proper treatment in world. In 2014, 1.66 million new case and 0.556 million deaths have been reported in USA [4], while 14.1 million new case and 8.2 million deaths were estimated in 2012. Cancer is second most common disease (0.806 million) [5] in world as well as in India [6]. These results showing that various therapy are not sufficient to cure this deadly disease.

The future of chemotherapy is only a way to control this disease. More than hundreds molecular medicines are available in market. Current review is a compilation of structures, type of cancer therapy,

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mechanism of action and major disadvantage of these drugs with the aims of providing an overview of anticancer drugs for further modification in the search of potent anticancer molecular medicine.

Molecular Medicines

However, various molecular medicines are containing nitrogen atoms; therefore, I have classified these medicines on the basis of nitrogen atoms present in drugs.

Natural and semi synthetic medicines

a) One nitrogen containing natural and semi synthetic medicines (Table 1-4)

Daunorubicin (daunomycin) is an anthracycline antibiotic which was isolated from *Streptomyces peucetius* [7-9]. It is used to treat acute lymphocytic and myelocytic leukemia since 1960 with the side effects such as hair loss, low white blood cells, vomiting, nausea, decrease platelet counts etc.

Doxorubicin (adriamycin) [10,11]is a semi synthetic medicine of daunorubicin. It is used to treat various type of cancer such as Hodgkin's lymphoma (a white blood cells' cancer), acute leukemia, multiple myeloma, Ewing sarcoma, Kaposi sarcoma, breast, ovary, lung, endometrium, adrenal cortex and other cancers with side effect cardiomyopathy (heart muscles disease) with heart failure, hair loss, low white blood cells, vomiting, nausea, decrease platelet counts etc.

Epirubicin [12] (an anthracycline analog) was synthesized from 13-dihydrodaunorubicine (13-daunorubicinol). It is used to treatment of breast cancer with the combination of other drugs and it has low side effects as comparison with doxorubicin.

Daunorubicin, doxorubicin and epirubicin acts as DNA cleavage of carcinoma cells by topoisomerase II inhibitor.

Paclitaxel (Taxol) [13] was isolated from the inner bark of *Taxus brevifolia* (Pacific yew tree) in 1967. It is used to treatment of long, breast, ovarian, neck, head, Kaposi (a tumor caused by herpes virus) carcinoma with the side effects such as hair loss, low white and red blood cells, vomiting, nausea, decrease platelet counts, diarrhea, numbness, pain in joint etc.

Docetaxel is a semi-synthetic medicine, synthesized from paclitaxel and used to treatment of breast [14], lung, prostate, stomach, head and neck cancers with the side effects such as fever, low white blood cell count, hair loss, diarrhea, nausea, tiredness, anemia, menstrual cycle abnormality in women, skin rash etc.

Cabazitaxel is also a semi-synthetic derivative of taxol and approved to cure prostate cancer [15] since 2010 with similar side effects as in docetaxel.

Table 1: One nitrogen containing natural and semi synthetic medicines.

S.N.	Drug	Isolated from/ Semi-synthetic of	Used for	Mechanism of action	Major side effects
1.	Daunorubicin (daunomycin)	*Streptomyces peucetius*	acute lymphocytic & myelocytic leukemia	topoisomerase II inhibitor	hair loss, low white blood cells, vomiting, nausea, decrease platelet counts etc
2.	Doxorubicin (adriamycin)	Semisynthetic of daunorubicin	Hodgkin's lymphoma, acute leukemia, multiple myeloma, Ewing sarcoma, Kaposi sarcoma, breast, ovary, lung, endometrium, adrenal cortex	topoisomerase II inhibitor	cardiomyopathy (heart muscles disease) with heart failure, hair loss, low white blood cells, vomiting, nausea, decrease platelet counts etc
3.	Epirubicin	Semisynthetic of 13-dihydrodaunorubicine	Breast cancer	topoisomerase II inhibitor	low white blood cells, vomiting, nausea, decrease platelet counts, mouth sores, hair loss etc

Table 2: One nitrogen containing natural and semi synthetic medicines.

S.N.	Drug	Isolated from/ Semisynthetic of	Used for	Mechanism of action	Major side effects
4.	Paclitaxel (Taxol)	*Taxus brevifolia*	long, breast, ovarian, neck, head, Kaposi carcinoma	microtubule inhibitors	as hair loss, low white and red blood cells, vomiting, nausea, decrease platelet counts, diarrhea, numbness, pain in joint
5.	*Docetaxel*	Semisynthetic of Paclitaxel	breast, lung, prostate, stomach, head and neck cancers	microtubule inhibitors	fever, low white blood cell count, hair loss, diarrhea, nausea, tiredness, anemia, menstrual cycle abnormality in women, skin rash
6.	Cabazitaxel	Semisynthetic of Paclitaxel	prostate cancer	microtubule inhibitors	fever, low white blood cell count, hair loss, diarrhea, nausea, tiredness, anemia, menstrual cycle abnormality in women, skin rash

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

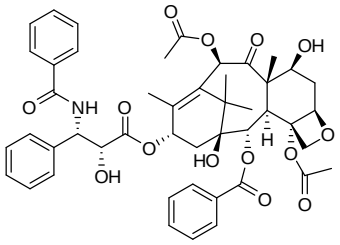
Table 3: One nitrogen containing natural and semi synthetic medicines.

S.N.	Drug	Isolated from/ Semisynthetic of	Used for	Mechanism of action	Major side effects
7.	Temsirolimus	Semisynthetic of rapamycin	renal cell carcinoma	mTOR inhibitors	skin rash, tiredness, mouth sores, nausea, swelling in hand, loss of appetite, anaemia, low white blood cell count, high blood sugar, high blood cholesterol
8.	Everolimus	Semisynthetic of rapamycin	renal cell carcinoma	mTOR inhibitors	skin rash, tiredness, mouth sores, nausea, swelling in hand, loss of appetite, anaemia, low white blood cell count, high blood sugar, high blood cholesterol
9.	5-Amino levulinic acid	Natural intermediate of porphyrin	detection of cancer, photodynamic therapy	fluorescent characteristic	swelling

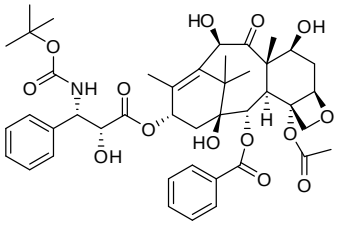
Table 4: One and two nitrogen containing natural and semi synthetic medicines.

S.N.	Drug	Isolated from/ Semisynthetic of	Used for	Mechanism of action	Major side effects
10.	*Eribulin*	*Halichondria okadai*	*metastatic breast cancer*	*microtubule inhibitor* inhibitors	*low white blood and red cell count, numbness, hair loss, tiredness, weakness, nausea, joint and muscle pain, weight loss, loss of appetite, constipation, fever*
11.	Omacetaxine	Semisynthetic of alkaloid cephalotaxine	chronic myelogenous leukemia	tyrosine kinase inhibitors	anemia, low blood platelet count, Low white blood cell count, diarrhea, nausea, pain, tiredness, fever, weakness
12.	Ixabepilone	*Sorangium cellulosum*	breast cancer	microtubule inhibitors	hair loss, diarrhea, mouth sores, vomiting, nausea, join and muscle pain, tiredness, numbness, low white blood cell count

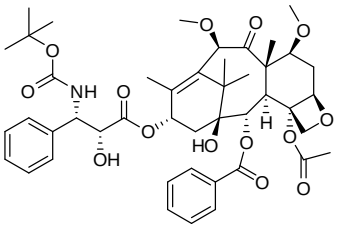
Paclitaxel, Docetaxel and Cabazitaxel are grouped as taxane and act as microtubule inhibitors (stop the formation of microtubule during the cancer's cell division).



Paclitaxel (Taxol)



Docetaxel



Cabazitaxel

Temsirolimus [16] is a semi synthetic medicine of sirolimus (also called rapamycin). Sirolimus was isolated from the soil bacteria *Streptomyces hygroscopicus*. Temsirolimus was approved to cure of renal cell carcinoma (kidney cancer) in 2007 with the side effects of skin rash, tiredness, mouth sores, nausea, swelling in hand, loss of appetite, anaemia, low white blood cell count, high blood sugar, high blood cholesterol etc.

Everolimus [17] is also a semi synthetic medicine of sirolimus and approved to cure renal cell carcinoma in 2009 with similar side effects as temsirolimus.

Temsirolimus and everolimus acts as mTOR inhibitors (mechanistic target of rapamycin). In which these drugs are interface the synthesis of proteins that control the proliferation, growth and survival of cancer cells.

5-Aminolevulinic acid [18] is a natural product intermediate in the formation of porphyrin and also found in insects, fungi, some bacteria, protozoans etc. Due to fluorescent characteristic, it is used detection of cancer and also as photodynamic therapy for various type cancers.

Table 5: Four nitrogen containing natural and semi synthetic medicines.

S.N.	Drug	Isolated from/ Semisynthetic of	Used for	Mechanism of action	Major side effects
13.	Vincristine (leurocristine)	*Catharanthus roseus*	leukemias, hodgkin's lymphomas & childhood cancers	mitotic inhibitors	constipation, tiredness, hair loss, pain etc
14.	Vinblastine	*Catharanthus roseus*	Hodking's lymphomas, breast, lung, testicular, head & neck cancers	mitotic inhibitors	mouth sores, tiredness, low blood platelet count, low white blood cell count
15.	Vinorelbine	Semisynthetic of *Catharanthus roseus*	non small cell lung & breast cancer	mitotic inhibitors	constipation, tiredness, weakness, vomiting, nausea, anemia, low white blood cell count

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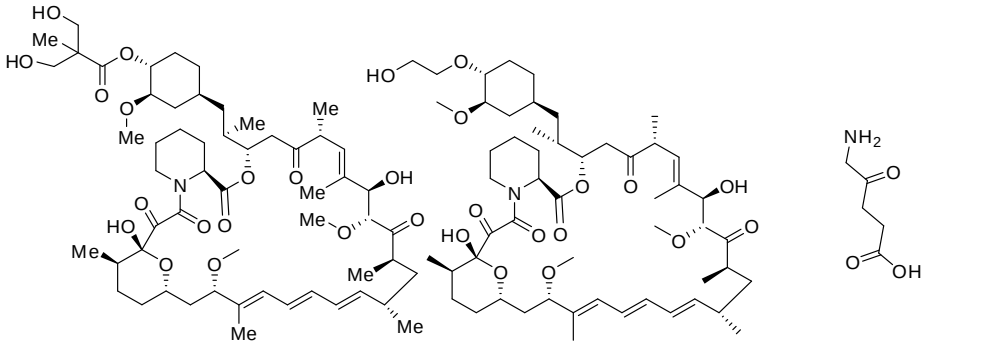
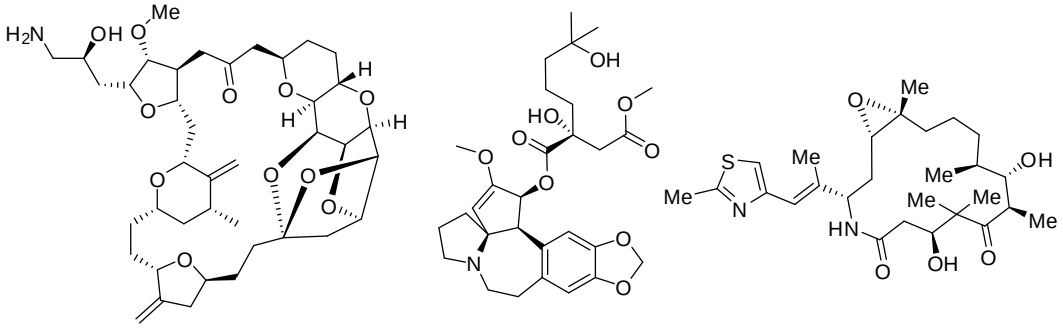


Temsirolimus Everolimus (Afinitor) Aminolevulinic Acid

Eribulin [19] is a synthetic analogue of natural product halichondrin B, which was isolated from the marine sponge *Halichondria okadai*. Eribulin was approved to treatment of metastatic breast cancer (4th state breast cancer) in 2010 with the side effects low white blood and red cell count, numbness, hair loss, tiredness, weakness, nausea, joint and muscle pain, weight loss, loss of appetite, constipation, fever etc. Eribulin acts as microtubule inhibitors of cancer cells.

Omacetaxine [20,21] is a semi synthetic derivative of the alkaloid cephalotaxine which was isolated from *Cephalotaxus harringtonia*. It is approved to treatment of chronic myelogenous (chronic granulocytic), leukemia (a white blood cell cancer) in 2012 with following side effects anemia, low blood platelet count, low white blood cell count, diarrhea, nausea, pain, tiredness, fever, weakness etc and it works as tyrosine kinase inhibitors.



Eribulin Omacetaxine Ixabepilone

b) Two nitrogen containing natural and semi synthetic medicines (Table 4)

Ixabepilone (azaepothilone B) is isolated by *Sorangium cellulosum* (a soil-dwelling gram-negative bacterium). Ixabepilone [22] had shown very high potential at very low concentration as microtubule inhibitors and approved to treatment of metastatic breast cancer in 2007 with side effects hair loss, diarrhea, mouth sores, vomiting, nausea, join and muscle pain, tiredness, numbness, low white blood cell count etc.

c) Four nitrogen containing natural and semi synthetic medicines (Table 5-6)

Vincristine (leurocristine) was isolated from the *Catharanthus roseus* (a vinca alkaloid) [23]. Vincristine is used to treatment of leukemias,

Table 6: Four nitrogen containing natural and semi synthetic medicines.

S.N.	Drug	Isolated from/ Semisynthetic of	Used for	Mechanism of action	Major side effects
16.	Irinoteca	Semisynthetic of camptothecin	colon and rectal cancer	topoisomerase I inhibitors	diarrhea, heir loss, appetite loss, nausea, vomiting, abdominal pain, weakness, low white blood cell count
17.	Mitomycins C	*Streptomyces caespitosus*	stomach, colon, rectal, pancreatic, breast, cervical, lung, head and neck cancers	alkylating agents	hair loss, tiredness, low white blood cell count, low platelet count
18.	Romidepsin	*Chromobacterium violaceum*	cutaneous T-cell lymphoma , peripheral T-cell lymphoma	histone deacetylase inhibitor	constipation, diarrhea, rashes on skin, other infection, increase blood sugar, anemia, low platelet count, low white blood cell count, appetite loss, tiredness, poor food taste, change in blood mineral level

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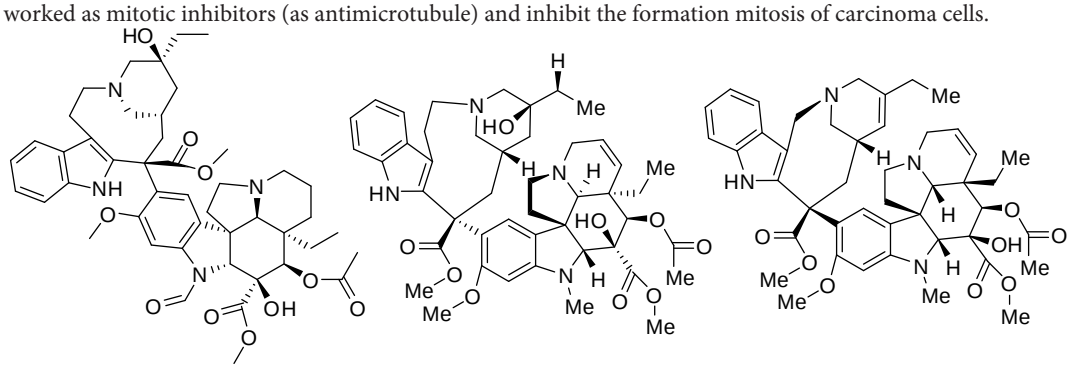
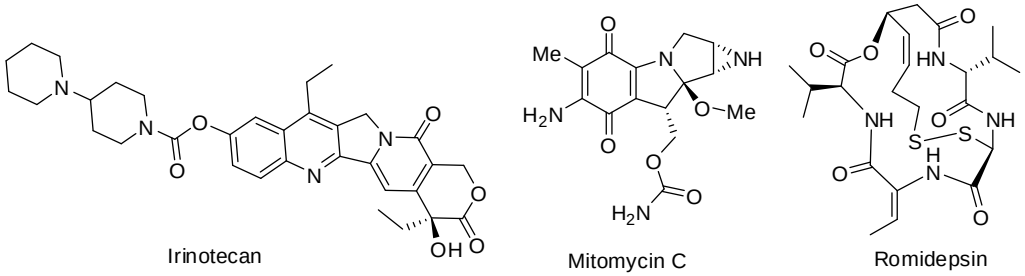
hodgkin's lymphomas and childhood cancers with side effects constipation, tiredness, hair loss, pain etc. Vinblastine was also obtained from *Catharanthus roseus* (vinca rosea, a madagascar periwinkle) and used to treatment of Hodking's lymphomas, breast, lung, testicular (a man reproductive system) head and neck cancers with side effects such as mouth sores, tiredness, low blood platelet count, low white blood cell count etc. Vinorelbine is a semi-synthetic vinca alkaloid and approved for the treatment of non small cell lung and breast cancer in 1989 with side effects constipation, tiredness, weakness, vomiting, nausea, anemia, low white blood cell count etc**.** Vincristine, vinblastine and vinorelbine are worked as mitotic inhibitors (as antimicrotubule) and inhibit the formation mitosis of carcinoma cells.



Vincristine Vinblastine Vinorelbine

Irinoteca is a semi-synthetic medicine of the natural alkaloid camptothecin [24] and approved to treatment of colon and rectal cancer which worked as topoisomerase I inhibitors with the side effects such as diarrhea, hair loss, appetite loss, nausea, vomiting, abdominal pain, weakness, low white blood cell count etc.

Mitomycins C [25] are a member of mitomycins natural products family, isolated from *Streptomyces caespitosus* or *Streptomyces lavendulae* and Mitomycins C is an antibiotics and worked as alkylating agents for the treatment of stomach, colon, rectal, pancreatic as well as breast, cervical, lung, head and neck cancers with the side effects such as hair loss, tiredness, low white blood cell count, low platelet count etc.



Irinotecan Mitomycin C Romidepsin

Romidepsin [26] (a depsipeptide) is a natural product obtained from the bacteria *Chromobacterium violaceum*. It is approved for the treatment for cutaneous T-cell lymphoma (a skin cancer), peripheral T-cell lymphoma in 2005 as histone deacetylase inhibitor with various side effects such as constipation, diarrhea, rashes on skin, other infection, increase blood sugar, anemia, low platelet count, low white blood cell count, appetite loss, tiredness, poor food taste, change in blood mineral level etc.

d) Five and more nitrogen containing natural and semi synthetic medicines (Table 7)

Carfilzomib (a tetrapeptide epoxyketones) is semisynthetic drug of a natural product epoxomicin. Carfilzomib [27] was approved for the

Table 7: Five or more nitrogen containing natural and semi synthetic medicines.

S.N.	Drug	Isolated from/ Semisynthetic of	Used for	Mechanism of action	Major side effects
19.	Carfilzomib	Semisynthetic of epoxomicin	multiple myeloma	proteasome inhibitors	fatigue, anemia, low platelet count, nausea, vomiting, shortness in breathing, fever, diarrhea, cold, cough, headache, diarrhea, swelling, back pain, constipation, low white blood cell count, increase of blood creatinine level
20.	Dactinomycin	*Streptomyces*	Wilms tumors, Ewings tumors of bone or soft tissues, testicular cancer, sarcomas	transcription inhibitors	radiation effects, hair loss, diarrhea, rash, skin darking, mouth sores, appetite loss, low platelet count, vomiting, nausea, low white blood cell count
21.	Bleomycin	*Streptomyces verticillus*	Hodgkin's sarcoma, lymphoma, squamous cell cancer of the head, neck, cervix, testicular cancer	DNA breaking of cancer cells	fever, chill, nausea, vomiting, appetite loss, hair loss, mouth sores, darkened skin

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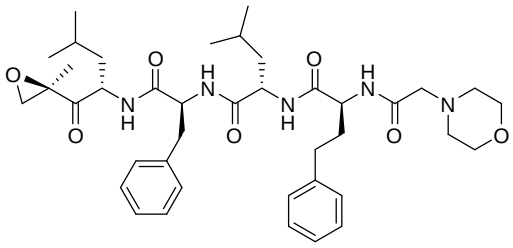
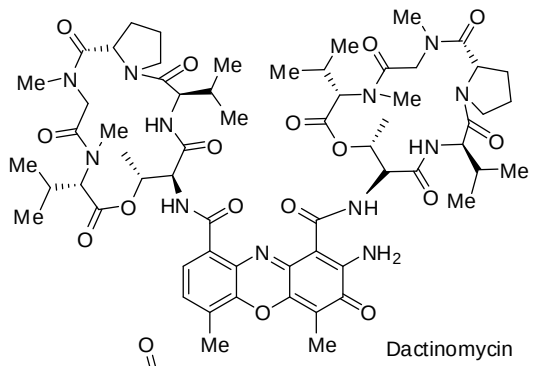
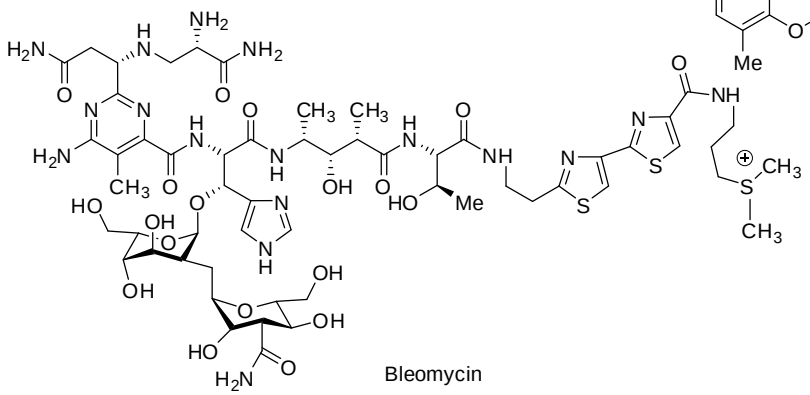
treatment of multiple myeloma (cancer of plasma cell) in 2012 and acts as proteasome inhibitors (block the action of proteasomes) with the side effects such as fatigue, anemia, low platelet count, nausea, vomiting, shortness in breathing, fever, diarrhea, cold, cough, headache, diarrhea, swelling, back pain, constipation, low white blood cell count, increase of blood creatinine level etc.



Carfilzomib



Dactinomycin



Bleomycin

Dactinomycin [28] (actinomycin D) is a polypeptide antibiotics which was isolated from soil bacteria of the genus *Streptomyces*. Dactinomycin was approved to treatment of Wilms tumors (a type of children's kidney tumors), Ewings tumors of bone or soft tissues, testicular cancer, sarcomas (in cartilage, fat, muscle or bone) in 1964 and acts as transcription inhibitors (stop cancer cells growing) with the side effects such as radiation effects, hair loss, diarrhea, rash, skin darking, mouth sores, appetite loss, low platelet count, vomiting, nausea, low white blood cell count.

Bleomycin (a glycopeptide) is an antibiotic which was isolated from the bacterium *Streptomyces verticillus*. Bleomycin [29,30] is used to treatment of Hodgkin's sarcoma, lymphoma, squamous cell cancer of the head, neck, cervix, testicular cancer etc and acting as DNA breaking of cancer cells with side effects such as fever, chill, nausea, vomiting, appetite loss, hair loss, mouth sores, darkened skin etc.

Synthetic molecular medicines

a) One nitrogen containing synthetic medicines (Table 8-9)

Chlorambucil [31] 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.

Table 8: One nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
22.	Chlorambucil	Hodgkin & non-Hodgkin lymphoma, chronic lymphocytic leukemia, trophoblastic neoplasms, waldenström macroglobulinemia polycythemia vera & ovarian carcinoma	alkylating agents	low white blood cells count, low platelet count, menstrual period stop, sperm reduction, hair loss
23.	Chlormethine	prostate cancer	alkylating agents	low white blood cell count, low platelet count, anemia, nausea, vomiting, tasteless, low appetite, hair loss, long-term infertility
24.	Abiraterone	prostate cancer	17 α-hydroxylase/ C17, 20 lyase inhibitor	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
25	Pamidronic acid	osteoporosis & multiple myeloma	-	bone pain, low calcium levels, nausea, dizziness

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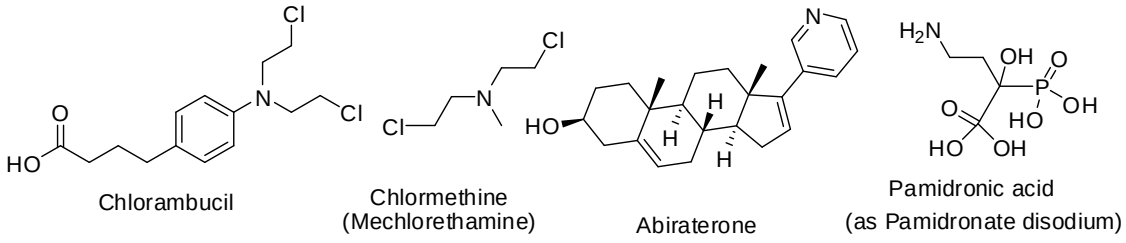
Table 9: One nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
26.	Tamoxifen	breast cancer	selective estrogen receptor modifier	hot flashes, tiredness and leg cramps
27.	Toremifene	breast, prostate cancer	selective estrogen receptor modifier	hot flashes, tiredness and leg cramps
28.	Raloxifene	breast cancer	selective estrogen receptor modifier	hot flashes, tiredness and leg cramps

Chlormethine (mechlorethamine, mustine) is also nitrogen mustard alkylating agents and used to treatment of prostate cancer since 1946 [32] with side effects such as low white blood cell count, low platelet count, anemia, nausea, vomiting, tasteless, low appetite, hair loss, long-term infertility etc.

Abiraterone was approved to treatment of advanced prostate cancer in 2011 however [33] and works as 17 α-hydroxylase/C17, 20 lyase (CYP17A1) inhibitor with side effects such as 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.

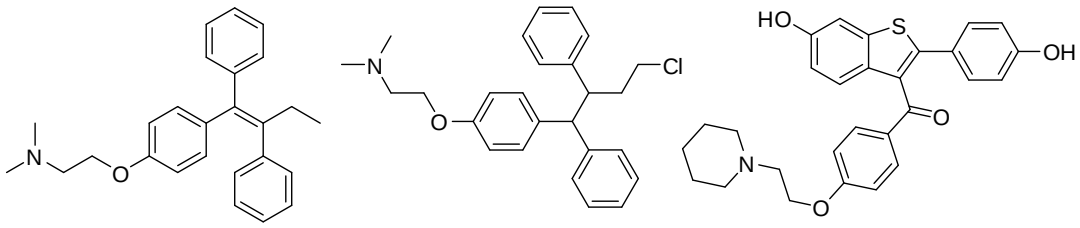
Pamidronic acid is a nitrogen containing bisphosphate used to treatment of osteoporosis and multiple myeloma and showing side effects such as bone pain, low calcium levels, nausea, dizziness etc.



Tamoxifen is an essential medicine with very less side effects as comparison with other anticancer drugs and it is used to treatment of breast cancer [34]. It is a special type hormone prodrug, used as estrogen receptor and known as selective estrogen receptor modifier (SERM).

Toremifene [35] 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.

Raloxifene [36] 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.



b) Two nitrogen containing synthetic medicines (Table 10-12)

Fluorouracil (5-FU) [37] 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 with side effects such as nausea, headache, vomiting, hair loss, photosensitivity low

Table 10: Two nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
29.	Fluorouracil	breast, anal, stomach, colorectal, pancreatic, skin, oesophageal cancer	thymidylate synthase inhibitors	nausea, headache, vomiting, hair loss, photosensitivity low white blood cell count, low platelet count, sores in mouth, brittle nails, dry skin
30.	Palonosetron	prevent vomiting and nausea after chemotherapy	anti-nausea $5HT_3$ antagonist	headache, constipation
31.	Bicalutamide	prostate cancer	androgen antagonist	swelling, hot flashes, pain in breast
32.	Vismodegib	basal cell carcinoma	hedgehog signaling pathway antagonist	hair loss, weight loss, nausea, muscle spam, tiredness, change in taste, diarrhea

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Table 11: Two nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
33.	Cyclophosphamide	lymphoma, multiple myeloma, leukemia, neuroblastoma, mycosis fungoides, retinoblastoma cancer	alkylating agent	hair loss, diarrhea, nausea, low white blood cell count, mouth sores, appetite loss, bleeding from bladder, vomiting
34.	Ifosfamide	breast, lung, cervical, testicular, ovarian, lymphoma &bone cancer	alkylating agent	breast cancer, lung cancer, cervical cancer, testicular cancer, ovarian cancer, lymphoma, bone cancer
35.	Cisplatin	ovarian, testicular, bladder, lung cancer	alkylating agent	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
36	Oxaliplatin	colorectal cancer	alkylating agents	vomiting, numbness, nauea, abdominal pain, mouth sores, tiredness, diarrhea
37	Carboplatin	ovarian, lung, head, neck etc carcinoma	alkylating agents	low white blood cell count, low platelet count, anemia, brittle hair, abnormal kidney function

Table 12: Two nitrogen containing synthetic medicines.

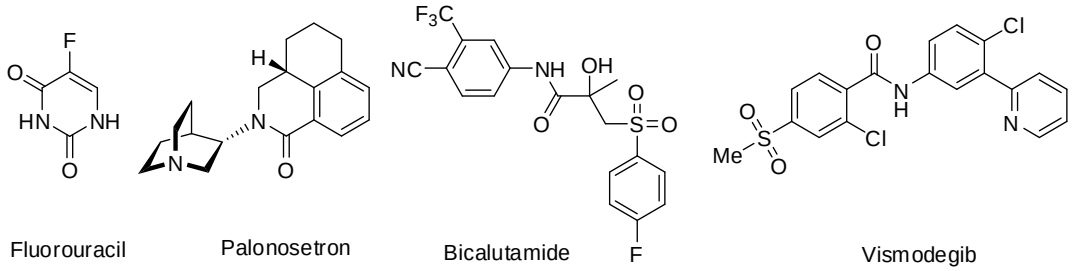
S.N.	Drug	Used for	Mechanism of action	Major side effects
38.	Thalidomide	multiple myeloma	immunomodulating agent	tiredness, rash, low white blood cell counts sleepiness, dizzy feeling
39.	Vorinostat	cutaneous T-cell lymphoma	histone deacetylase agent	tiredness, diarrhea, vomiting, nausea, appetite loss, weight loss, low blood platelet count, high blood sugar, muscle arches, food taste change
40	Zoledronic acid	bone spread cancers such prostrate and myloma cancer	bisphosphonate agents	fever, chills

white blood cell count, low platelet count, sores in mouth, brittle nails, dry skin etc.

Palonosetron [38] is an anti-nausea $5HT_3$ antagonist medicine which is used to prevent vomiting and nausea after chemotherapy.

Bicalutamide [39] is a hormone antagonist (block androgen male hormone) and approved to treatment of prostate cancer in 1995 with side effects swelling, hot flashes, pain in breast etc.

Vismodegib [40] was approved to treatment of basal cell carcinoma (a skin cancer) in 2012. It acts as hedgehog signaling pathway antagonist with side effects hair loss, weight loss, nausea, muscle spam, tiredness, change in taste, diarrhea etc.



Fluorouracil Palonosetron Bicalutamide Vismodegib

Cyclophosphamide [41] is nitrogen alkylating agent which used for the treatment of lymphoma, multiple myeloma, leukemia, neuroblastoma, mycosis fungoides, retinoblastoma etc with side effects hair loss, diarrhea, nausea, low white blood cell count, mouth sores, appetite loss, bleeding from bladder, vomiting etc.

Ifosfamide [42] is a nitrogen mustard alkylating agents and used for the treatment of breast cancer, lung cancer, cervical cancer, testicular cancer, ovarian cancer, lymphoma, bone cancer with side effects hair loss, diarrhea, nausea, low white blood cell count, mouth sores, appetite loss, bleeding from bladder, vomiting etc.

Cisplatin [43] (cis-diamminedichloroplatinum(II), cisplatinum) 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 with 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.

Oxaliplatin [44] is also a platinum containing drug which was approved to cure colorectal cancer in 2012 and acts cross linking of DNA (alkylating agents) of carcinoma cells with side effects such as vomiting, numbness, nauea, abdominal pain, mouth sores, tiredness, diarrhea etc.

Carboplatin [45] (a platinum containing drug) was approved to treatment of ovarian, lung, head, neck etc carcinoma in 1989. It acts as cross

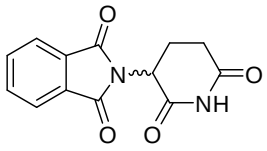
Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

linking of DNA (alkylating agents) of carcinoma cells with side effects such as low white blood cell count, low platelet count, anemia, brittle hair, abnormal kidney function etc.

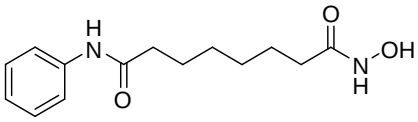
Thalidomide [46] was approved to treatment of multiple myeloma (bone marrow cancer) in 2006. It is an immunomodulating agents with various side effects tiredness, rash, low white blood cell counts sleepiness, dizzy feeling etc.

Vorinostat [47] was approved to treatment of cutaneous T-cell lymphoma (a skin cancer) in 2006 and acts as histone deacetylase inhibitors with side effect tiredness, diarrhea, vomiting, nausea, appetite loss, weight loss, low blood platelet count, high blood sugar, muscle arches, food taste change.

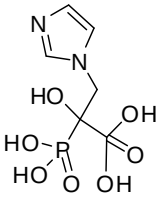
Zoledronic acid was approved in 2001 and used for the treatment of bone spread cancers such as prostrate and myloma cancer and acts as bisphosphonate with side effects fever, chills, etc.



Thalidomide



Vorinostat



Zoledronic Acid

c) Three nitrogen containing synthetic medicines (Table 13-15)

Cytarabine is a most essential drug which is used to cure acute myeloid leukemia (a white blood cell cancer) and non-hodgkin lymphoma. It acts as DNA synthesis inhibitors of carcinoma cell with a side effects such as nausea, vomiting, low blood cell count, low platelet count, stomach pain, tiredness, mouth sore etc [48].

Table 13: Three nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
41.	Cytarabine	acute myeloid leukemia & non-hodgkin lymphoma	DNA synthesis inhibitors	nausea, vomiting, low blood cell count, low platelet count, stomach pain, tiredness, mouth sore
42.	Gemcitabine	pancreatic, lung, ovarian, breast cancers	DNA synthesis inhibitors	fever, low white blood cell count, low platelet count, anemia, nausea, vomiting, tiredness, rash on skin, appetite loss
43.	Procarbazine	Hodgkin's lymphoma and glioblastoma	alkylating agent	low white blood cell count, low platelet count, depression, nausea, vomiting, felling nervousness, appetite loss, sleeping problems
44.	Bendamustine	chronic lymphocytic leukemia & non Hodgkin lymphoma	alkylating agent	low white blood cell count, low platelet count, anemia, fever, nausea, vomiting, diarrhea, appetite loss, tiredness

Table 14: Three nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
45.	Cabozantinib	modularly thyroid cancer	tyrosine kinase inhibitors	weight loss, diarrhea, mouth sores, nausea, appetite loss, weakness, abdomen pain, vomiting, high blood pressure, change in voice
46.	Capecitabine	breast cancer, colon, rectal	anti metabolized	fever hair loss, diarrhea, headache, nausea, appetite loss, weakness, abdomen pain, vomiting, eye irritations
47.	Erlotinib	pancreatic & lung cancer	tyrosine kinase inhibitors	skin rash, nausea, diarrhea, tiredness, appetite loss

Table 15: Three nitrogen containing synthetic medicines.

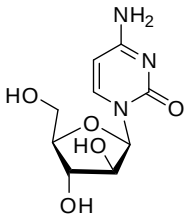
S.N.	Drug	Used for	Mechanism of action	Major side effects
48.	Vemurafenib	melanoma	B-raf enzymes inhibitors	hair loss, pain in joint, rash, warts, tiredness, headache, sunlight sensitivity, diarrhea, nausea
49.	Topotecan	ovarian, cervical, lung cancers	topoisomerase I inhibitors	nausea, vomiting, hair loss, low white blood cell count, low blood platelet count, anemia
50.	Lomustine	brain cancer	alkylating agents	vomiting, nausea, fatal disorder during pregnancy, low white blood cell count, low blood platelet count
51.	Lenalidomide	multiple myeloma	Immunomodulating agent	tiredness, rash, itching, diarrhea, low white blood cell count, low blood platelet count
52.	Pomalidomide	multiple myloma	angiogenesis inhibitors	tiredness, back pain, anemia, diarrhea, nausea, chest pain, appetite loss, pneumonia, breathing problem, rash, low white blood cell count, low blood platelet count

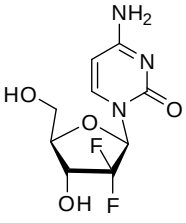
Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

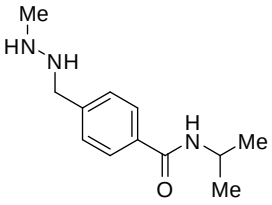
Gemcitabine is used to treatment of various type cancers such as pancreatic, lung [49], ovarian, breast cancers. It also acts as DNA synthesis inhibitors of carcinoma cells with side effects such as fever, low white blood cell count, low platelet count, anemia, nausea, vomiting, tiredness, rash on skin, appetite loss etc.

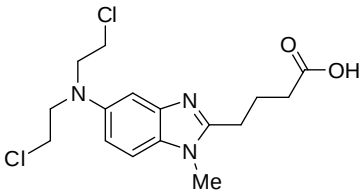
Procarbazine is an alkylating agent and approved to treatment of Hodgkin's lymphoma and glioblastoma (brain cancer) in 1969 with side effects low white blood cell count, low platelet count, depression, nausea, vomiting, felling nervousness, appetite loss, sleeping problems etc. It is used with combination of other anticancer medicines [50].

Bendamustine [51] was approved to treatment of chronic lymphocytic leukemia and non Hodgkin lymphoma in 2008. It is a nitrogen mustard and acts as alkylating agents with side effects low white blood cell count, low platelet count, anemia, fever, nausea, vomiting, diarrhea, appetite loss, tiredness etc.


Cytarabine


Gemcitabine

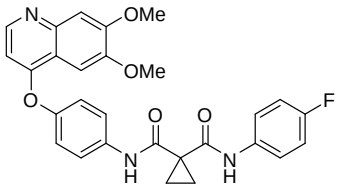

Procarbazine

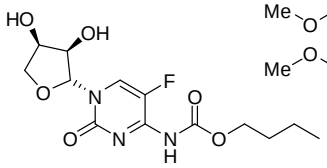

Bendamustine

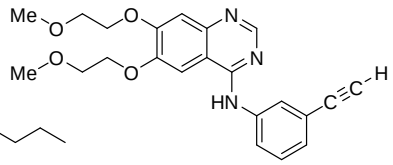
Cabozantinib [52] was recently approved (2012) for the treatment of modularly thyroid cancer. It acts as targeted tyrosine kinase inhibitors with side effects weight loss, diarrhea, mouth sores, nausea, appetite loss, weakness, abdomen pain, vomiting, high blood pressure, change in voice etc.

Capecitabine [53] was used to treatment of numerous type cancers such as breast cancer, colon, rectal etc. It acts as anti metabolized with side effects such as fever hair loss, diarrhea, headache, nausea, appetite loss, weakness, abdomen pain, vomiting, eye irritations.

Erlotinib [54] was approved to treatment of pancreatic and non small lung cancer in 2004. It acts as epidermal growth factor receptor (EGFR, a tyrosine kinase inhibitor) with side effects such as skin rash, nausea, diarrhea, tiredness, appetite loss.


Cabozantinib

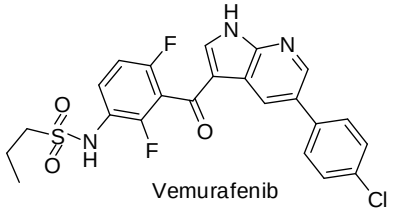

Capecitabine

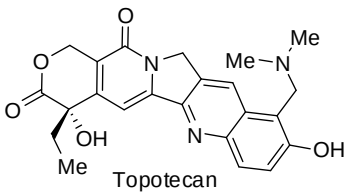

Erlotinib

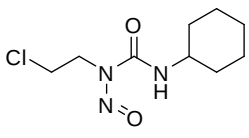
Vemurafenib [55] was approved to treatment of melanoma (a skin cancer) in 2011. It acts as B-raf enzymes inhibitors with side effects such as hair loss, pain in joint, rash, warts, tiredness, headache, sunlight sensitivity, diarrhea, nausea etc.

Topotecan [56] was approved for the treatment of ovarian, cervical and lung cancers in 1996. It acts as topoisomerase I inhibitors with side effects such as nausea, vomiting, hair loss, low white blood cell count, low blood platelet count, anemia etc.

Lomustine [57] was used to treatment of brain cancer due to high lipid solubility. It acts as alkylating agents with side effect such as vomiting, nausea, fatal disorder during pregnancy, low white blood cell count, low blood platelet count etc.

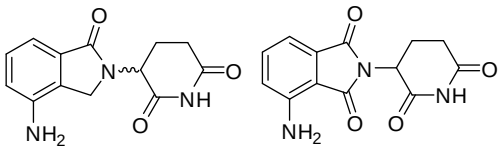

Vemurafenib


Topotecan


Lomustine

Lenalidomide [58] was approved to treatment of multiple myeloma in 2005 with side effects such as tiredness, rash, itching, diarrhea, low white blood cell count, low blood platelet count etc.

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.



Lenalidomide Pomalidomide

Pomalidomide [59] was approved to treatment of multiple myloma in 2013. Possible, it acts as angiogenesis inhibitors with side effects such as tiredness, back pain, anemia, diarrhea, nausea, chest pain, appetite loss, pneumonia, breathing problem, rash, low white blood cell count, low blood platelet count etc.

d) Four nitrogen containing synthetic medicines (Table 16-19)

Mercaptopurine (azathioprine) [60] is used for the treatment of leukemia (a cancer of bone marrow). It acts as anti-metabolite with side effects such as low white blood cell count, low blood platelet count and anemia etc.

Table 16: Four nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
53.	Mercaptopurine	leukemia	anti-metabolite	low white blood cell count, low blood platelet count, anemia
54.	Imiquimod	skin cancers	change of immune response	skin redness, sunburns, drying skin
55.	Azacitidine	myelodysplastic syndromes & chronic myelomonocytic leukemia	anti-metabolite	anemia, low platelet count, vomiting, fever, nausea, tiredness
56.	Decitabine	myelodysplastic syndromes	hypomethylating agents	anemia, low platelet count, low white blood cell count, vomiting, diarrhea, fever, nausea, pain in legs, tiredness

Table 17: Four nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
57.	Gefitinib	breast & lung cancer	tyrosine kinase inhibitor	skin rash and diarrhea
58.	Lapatinib	breast cancer	tyrosine kinase inhibitor	diarrhea, rashes, swelling, numbness and pain in hand and foot
59.	Vandetanib	thyroid cancers	kinase inhibitor	diarrhea, nausea, tiredness, appetite loss, abdomen pain, headache, high blood pressures, rashes

Table 18: Four nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
60.	Axitinib	renal cell carcinoma	*vascular* epidermal growth factor receptor	skin rashes, diarrhea, nausea, low blood cell counts, tiredness, appetite loss, weight loss, swelling, numbness and pain in hand and high blood pressures
61.	Sorafenib	renal and hepatocelluar carcinoma	tyrosine kinase inhibitor	tiredness, diarrhea, itching, rashes, swellings in hand and feet
62.	Regorafenib	metastatic colorectal and advanced gastrointestinal stromal tumors	tyrosine kinase inhibitor	fever, appetite loss, tiredness, weakness, diarrhea, infection, weight loss, moth's sores, rashes, high blood pressure, change in voice, bleeding
63.	Sunitinib	renal cell carcinoma and gastrointestinal carcinoma	tyrosine kinase inhibitor	low white blood cell count, nausea, vomiting, diarrhea, mouth sore, appetite loss, taste of food change, tiredness, weakness, and change in hair and skin color, high blood pressure, hair loss

Table 19: Four nitrogen containing synthetic medicines.

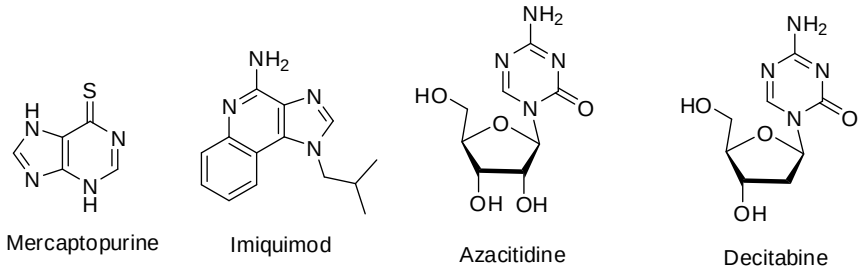
S.N.	Drug	Used for	Mechanism of action	Major side effects
64.	Aprepitant	nausea caused by anticancer drugs	-	diarrhea, itching, appetite loss
65.	Eltrombopag	low plate count caused by anticancer drugs	-	-
66.	Bortezomib	blood and bone marrow cancers	proteasome inhibitor	weakness, nausea, vomiting, tiredness, diarrhea, constipation
67.	Dexrazoxane	heart damage caused by anti-cancer drug	-	effect low white blood cell count and low blood platelet counts
68.	Enzalutamide	prostate cancer	androgen receptor antagonist	tiredness, weakness, diarrhoea, joint pain, hot flashes, swelling in head

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

Imiquimod [61] was approved in 1997 and it is used as cream for the treatment of skin cancers with the change of immune response and side effects such as skin redness, sunburns, drying skin etc.

Azacitidine [62] was first approved in 2004. It is used for the treatment of myelodysplastic syndromes and chronic myelomonocytic leukemia which act as anti-metabolite with side effects such as anemia, low platelet count, vomiting, fever, nausea and tiredness etc.

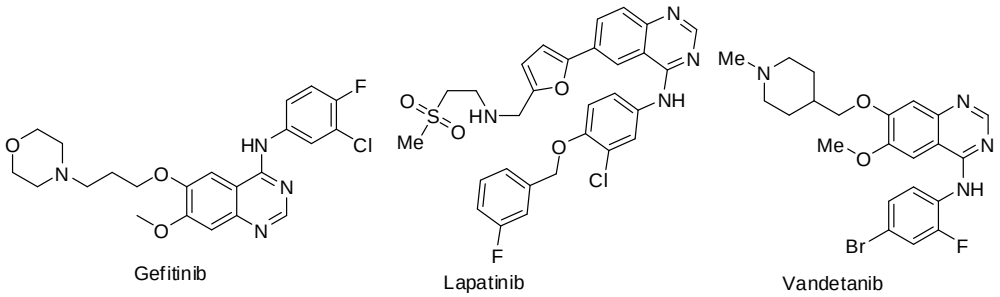
Decitabine [63] was approved in 2006 for the treatment of myelodysplastic syndromes and acts as hypomethylating agents with side effects such as anemia, low platelet count, low white blood cell count, vomiting, diarrhea, fever, nausea, pain in legs and tiredness etc.



Gefitinib [64] was approved in 2003. It used to treatment of breast and lung cancer. It acts as epidermal growth factor receptor (EGFR) for a tyrosine kinase protein with side effects such as skin rash and diarrhea etc.

Lapatinib [65] was approved to treatment of breast cancer. It acts as tyrosine kinase inhibitor with side effects diarrhea, rashes, swelling, numbness and pain in hand and foot.

Vandetanib [66] was approved in 2011 for the treatment of thyroid cancers. It acts as kinase inhibitor with side effects diarrhea, nausea, tiredness, appetite loss, abdomen pain, headache, high blood pressures, rashes etc.



Axitinib [67] 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 with 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.

Sorafenib [68] was approved in 2005 for the treatment of renal and hepatocelluar carcinoma. It also acts as oral receptor tyrosine kinase inhibitor with side effects tiredness, diarrhea, itching, rashes, swellings in hand and feet etc.

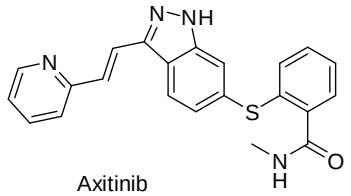
Regorafenib [69] was approved in 2012 for the treatment of metastatic colorectal and advanced gastrointestinal stromal tumors. It acts as oral receptor tyrosine kinase inhibitor with side effects fever, appetite loss, tiredness, weakness, diarrhea, infection, weight loss, moth's sores, rashes, high blood pressure, change in voice, bleeding etc.

Sunitinib [70] was approved in 2006 for the treatment of renal cell carcinoma and gastrointestinal carcinoma. It acts as tyrosine kinase receptor with side effects such as low white blood cell count, nausea, vomiting, diarrhea, mouth sore, appetite loss, taste of food change, tiredness, weakness, and change in hair and skin color, high blood pressure, hair loss etc.

Table 20: Five nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
69.	Anastrazole	breast cancer	aromatase inhibitors	pain in joint and bones, hot flashes
70.	Letrozole	breast cancer	aromatase inhibitors	weakness, pain in joint and bones, hot flashes
71.	Pemetrexed	malignant pleural mesothelioma & non small cell lung cancer	anti-metabolites	breathing difficulty, tiredness, rashes, appetite loss, mouth sores, constipation, nausea, vomiting, low platelet count, low white blood cell count, anemia

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.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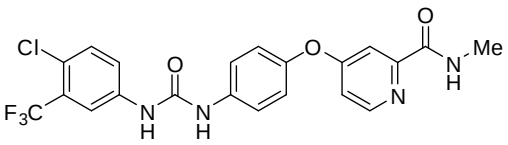
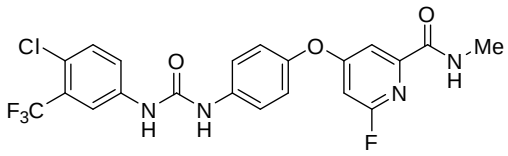
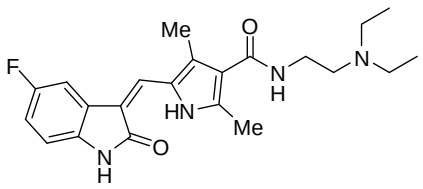

Sorafenib


Regorafenib


Sunitinib

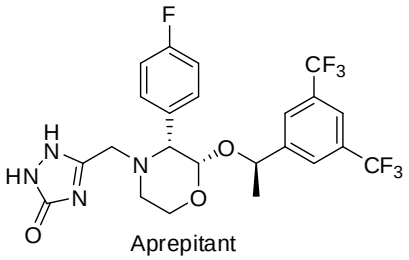
Aprepitant [71] was approved in 2003 for the treatment of nausea caused by various anticancer drugs with side effects such as diarrhea, itching, appetite loss etc.

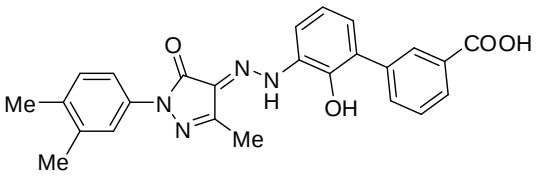
Eltrombopag [72] was approved in 2008 for the treatment of low plate count (thrombocytopenia) caused by various anticancer drugs.

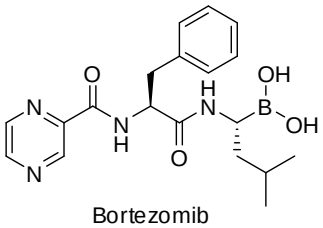
Bortezomib [73] was approved in 2003 for the treatment of blood and bone marrow (multiple myloma and mantle cell lymphoma) cancer. It acts as proteasome inhibitor with side effects such as weakness, nausea, vomiting, tiredness, diarrhea, constipation etc.

Dexrazoxane [74] was approved in 1995 to protect heart damage caused by anti-cancer drug doxorubicin with side effect low white blood cell count and low blood platelet counts.

Enzalutamide [75] was approved in 2012 for the treatment of prostate cancer. It acts an androgen receptor antagonist (blocking the male hormones androgens) with side effects such as tiredness, weakness, diarrhoea, joint pain, hot flashes, swelling in head etc.


Aprepitant


Eltrombopag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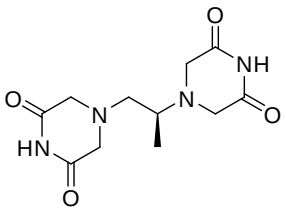
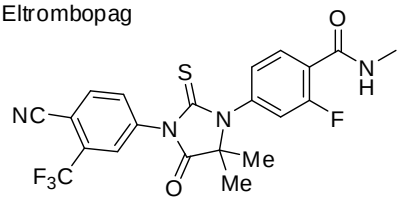

Dexrazoxane


Enzalutamide

e) Five nitrogen containing synthetic medicines (Table 20-23)

Anastrazole [76] was approved in 1995 for the treatment of breast cancer. It acts as aromatase inhibitors (block aromatase which is necessary

Table 21: Five nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
72.	Nelarabine	T-cell acute lymphoblastic leukemia	anti-metabolites	headache, tiredness, low platelet count, low white blood cell count, anemia
73.	Fludarabine	blood cells lymphomas & leukemias	anti-metabolites	tiredness, low platelet count, low white blood cell count, anemia, vomiting, nausea, infections, fever
74.	Clofarabine	acute lymphoblastic leukemia, acute myeloid leukaemia & juvenile myelomonocytic leukaemia	anti-metabolites	tiredness, low platelet count, low white blood cell count, anemia, vomiting, nausea, infections, fever

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

Table 22: Five nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
75.	Afatinib	non small cell lung carcinoma	tyrosine kinases inhibitors	scratchy and dry skin, appetite loss, infections in around nails skin, sores in mouth, rashes in skin, diarrhea
76.	Bosutinib	chronic myelogenous leukemia	chronic myelogenous leukemia	headache, cough, anemia, low white blood cell count, tiredness, fever, vomiting, nausea, diarrhea, rashes in skin, abdomen pain
77.	Dabrafenib	melanoma caused by changing in BRAF gene	kinase inhibitors	high blood sugar, fever, pain in joint, warts, hair loss, headache, skin thickness

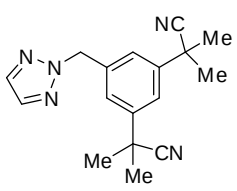
Table 23: Five nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
78.	Ceritinib	non small cell lung carcinoma	anaplastic lymphoma kinase inhibitors	anemia, low white blood cell count, constipation, tiredness, appetite loss, abdomen pain, diarrhea, nausea, vomiting
79.	Trametinib	melanoma caused by changing in BRAF gene	kinase inhibitors	anemia, low blood albumin level, rashes in skin, diarrhea, swelling
80.	Crizotinib	melanoma caused by changing in BRAF gene	anaplastic lymphoma kinase inhibitor	rashes in diarrhea, nausea, vomiting, vision disorder, constipation, appetite loss, breathing problem, cold, swelling, nerves disorders

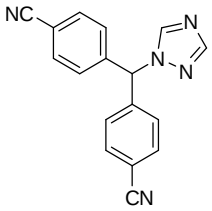
for the formation of estrogen) with side effects such as pain in joint and bones, hot flashes etc.

Letrozole [77] was approved in 1997 for the treatment of breast cancer. It also acts as aromatase inhibitors with side effects such as weakness, pain in joint and bones, hot flashes etc.

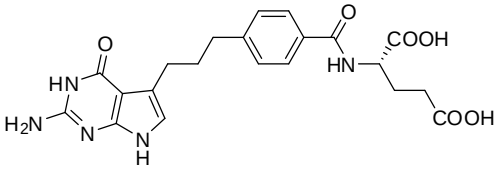
Pemetrexed [78] was approved in 2004 and used for the treatment of malignant pleural mesothelioma (the lining of the chest cavity around the lungs cancer) and non small cell lung cancer. It acts as anti-metabolites with side effects such as breathing difficulty, tiredness, rashes, appetite loss, mouth sores, constipation, nausea, vomiting, low platelet count, low white blood cell count, anemia etc.



Anastrozole



Letrozole

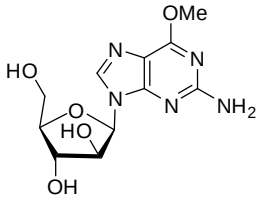


Pemetrexed

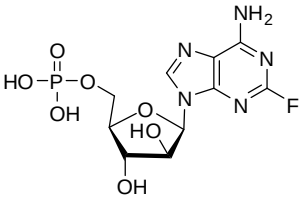
Nelarabine [79] was approved in 2005 and used for the treatment of T-cell acute lymphoblastic leukemia (a white blood cell cancer). It also acts as anti-metabolites (block the formation of DNA and RNA of carcinoma cells) with side effects such as headache, tiredness, low platelet count, low white blood cell count, anemia etc.

Fludarabine [80] was approved in 1991 and used for the treatment of cancers of blood cells lymphomas and leukemias (hematological malignancies). It also acts as anti-metabolites with side effects such as tiredness, low platelet count, low white blood cell count, anemia, vomiting, nausea, infections, fever etc.

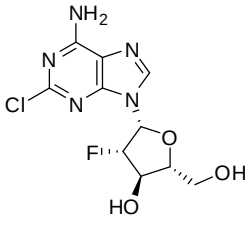
Clofarabine [81] was approved in 2004 and used for the treatment of acute lymphoblastic leukemia, acute myeloid leukaemia and juvenile myelomonocytic leukaemia. It acts a anti-metabolites with side effects such as tiredness, low platelet count, low white blood cell count, anemia, vomiting, nausea, infections, fever etc.



Nelarabine



Fludarabine



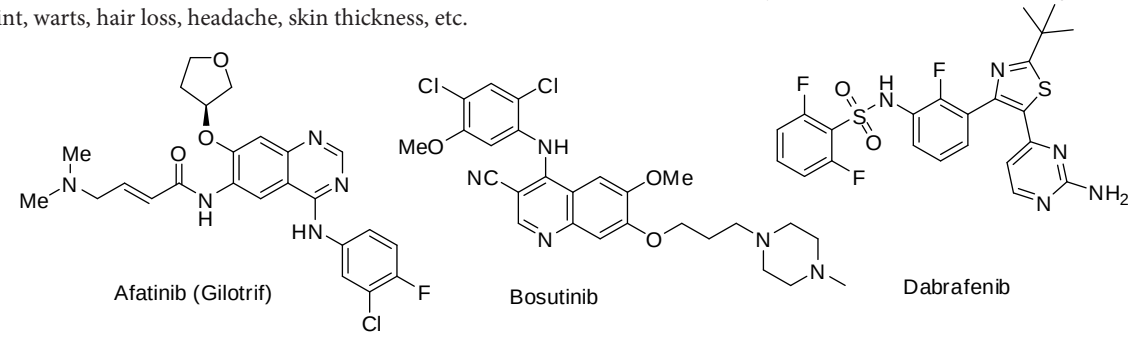
Clofarabine

Afatinib (Gilotrif) [82] was approved in 2013 and used for the treatment of non small cell lung carcinoma. It acts as tyrosine kinases inhibitors with side effects scratchy and dry skin, appetite loss, infections in around nails skin, sores in mouth, rashes in skin, diarrhea etc.

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

Bosutinib [83] was approved in 2012 and used for the treatment of chronic myelogenous leukemia (a white blood cell carcinoma). It also acts as tyrosine kinases inhibitors with side effects headache, cough, anemia, low white blood cell count, tiredness, fever, vomiting, nausea, diarrhea, rashes in skin, abdomen pain etc.

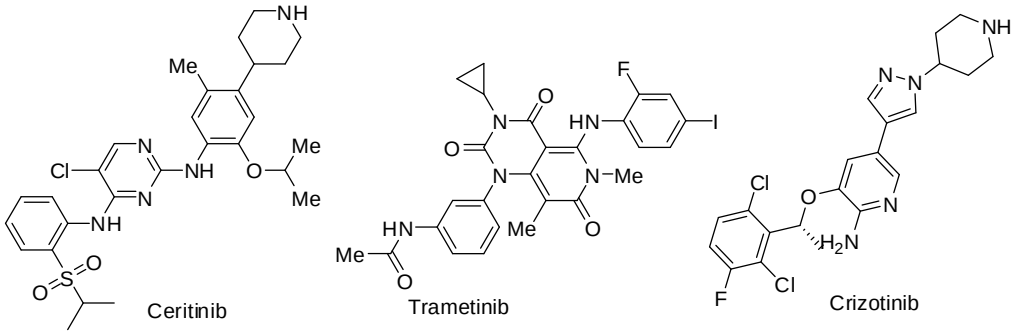
Dabrafenib [84] was approved in 2013 and used for the treatment of melanoma caused by changing in BRAF gene (a gene responsible for the formation of B-Raf protein). It acts as kinase inhibitors (inhibit associated enzyme B-Ref) with side effects high blood sugar, fever, pain in joint, warts, hair loss, headache, skin thickness, etc.



Ceritinib [85] was approved in 2014 and used for the treatment of non small cell lung carcinoma. It acts as anaplastic lymphoma kinase (ALK) inhibitor with side effects anemia, low white blood cell count, constipation, tiredness, appetite loss, abdomen pain, diarrhea, nausea, vomiting etc.

Trametinib [86] was approved in 2013 and used for the treatment of melanoma caused by changing in BRAF gene. It acts as kinase inhibitors with side effects anemia, low blood albumin level, rashes in skin, diarrhea, swelling etc

Crizotinib [87] was approved in 2011 and used for the treatment of non small lung cancer. It acts as anaplastic lymphoma kinase (ALK) inhibitor with side effects rashes in diarrhea, nausea, vomiting, vision disorder, constipation, appetite loss, breathing problem, cold, swelling, nerves disorders etc.



f) Six nitrogen containing synthetic medicines (Table 24)

Ibrutinib [88] was approved in 2013 and used for the treatment of chronic lymphocytic leukemia and mantle cell lymphoma (a non-

Table 24: Six nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
81.	Ibrutinib	chronic lymphocytic leukemia and mantle cell lymphoma	tyrosine kinase inhibitor	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
82.	Ponatinib	chronic myeloid leukemia & acute lymphoblastic leukemia	tyrosine kinase inhibitor	high blood pressure, heart attack disorder, dry skin, rashes in skin, abdomen pain, tiredness, weakness, headache, constipation, pain in joint and muscle, fever, nausea, low platelet count, low white blood cell count
83.	Ruxolitinib	myelofibrosis & pancreatic carcinoma	Janus kinase inhibitor	low blood platelet counts, fatigue, anemia, diarrhea, breath disorder, headache, nausea, dizziness
84.	Dacarbazine	Hodgkin lymphoma, malignant melanoma, islet cell carcinoma of the pancreas and sarcoma	alkylating agents	low white blood cell count, low platelet count, vomiting, nausea, hair loss, appetite loss, tiredness, headache, fever
85.	Temozolomide	glioblastoma multiforme & melanoma	alkylating agents	low white blood cell count, low platelet count, weakness, vomiting, nausea, hair loss, appetite loss, constipation, tiredness, headache, pain, itching

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

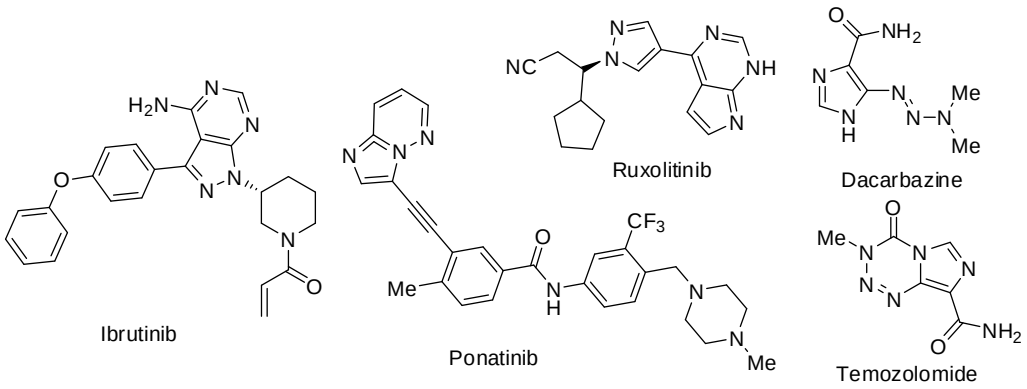
Hodgkin's lymphomas). It acts as tyrosine kinase inhibitor with side effects nausea, vomiting, diarrhea, tiredness, pain in bone and muscles, cold, swelling, breath disorder, rashes in skin, constipation, abdominal pain, appetite loss, anemia, low platelet count etc.

Ponatinib [89] was approved in 2012 and used for the treatment of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL). It acts tyrosine kinase inhibitor with side effects high blood pressure, heart attack disorder, dry skin, rashes in skin, abdomen pain, tiredness, weakness, headache, constipation, pain in joint and muscle, fever, nausea, low platelet count, low white blood cell count etc.

Ruxolitinib [90] 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) with side effects low blood platelet counts, fatigue, anemia, diarrhea, breath disorder, headache, nausea, dizziness etc.

Dacarbazine [91] is an alkylating agents used for the treatment of Hodgkin lymphoma, malignant melanoma, islet cell carcinoma of the pancreas and sarcoma with side effects low white blood cell count, low platelet count, vomiting, nausea, hair loss, appetite loss, tiredness, headache, fever etc.

Temozolomide [92] was approved in 1999 and used for the treatment of glioblastoma multiforme (brain tumor) and melanoma (skin cancer). It acts as alkylating agents with side effects low white blood cell count, low platelet count, weakness, vomiting, nausea, hair loss, appetite loss, constipation, tiredness, headache, pain, itching etc.



g) Seven nitrogen containing synthetic medicines (Table 25)

Dasatinib [93] 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 with 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.

Pazopanib [94] 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 with 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.

Table 25: Seven nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
86.	Dasatinib	chronic myelogenous leukemia, acute lymphocytic leukemia & prostrate carcinoma	tyrosine kinase inhibitor	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
87.	Pazopanib	renal cell carcinoma & soft tissue sarcoma	tyrosine kinase inhibitor	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
88.	Imatinib	chronic myelogenous leukemia and gastrointestinal stromal tumors	tyrosine kinase inhibitor	chronic myelogenous leukemia and gastrointestinal stromal tumors
89.	Nilotinib	chronic myelogenous leukemia	tyrosine kinase inhibitor	low white blood cell count, low blood platelet count, tiredness, headache, fever, diarrhea, constipation, nausea, vomiting, rashes in skin, itching
90.	Leucovorin	colorectal, head and neck carcinoma	thymidylate synthase inhibitor.	not known
91.	Pralatrexate	peripheral T-cell lymphoma	anti-metabolites	mouth sore, nausea, vomiting, diarrhea, anemia, low white blood cell count, low platelet count, tiredness, constipation, fever, cough, swelling, nose bleeding

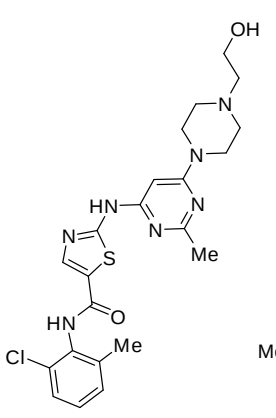
Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

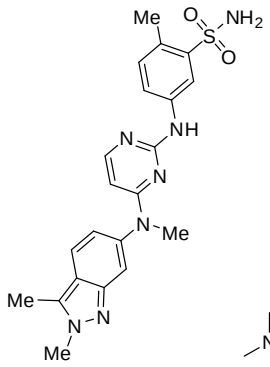
Imatinib [95] was approved in 2001 and used for the treatment of chronic myelogenous leukemia and gastrointestinal stromal tumors. It acts as tyrosine kinase inhibitor with similar side effects of pazopanib.

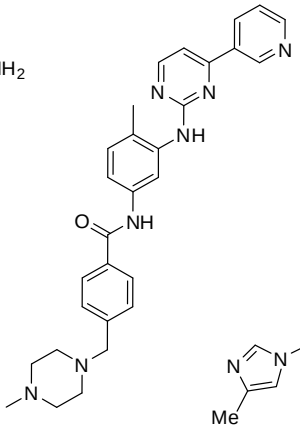
Nilotinib [96] was approved in 2007 and used for the treatment of chronic myelogenous leukemia. It acts as tyrosine kinase inhibitor with side effects low white blood cell count, low blood platelet count, tiredness, headache, fever, diarrhea, constipation, nausea, vomiting, rashes in skin, itching etc.

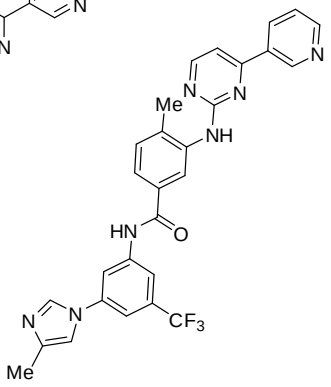
Leucovorin [97] is used as combinatorial chemotherapy drug with 5-fluorouracil for the better treatment of colorectal, head and neck carcinoma.

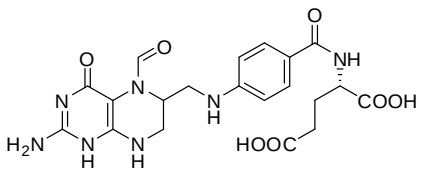
Pralatrexate [98] was approved in 2009 and used for the treatment of peripheral T-cell lymphoma (a non-Hodgkin lymphoma). It acts as anti-metabolites with side effects mouth sore, nausea, vomiting, diarrhea, anemia, low white blood cell count, low platelet count, tiredness, constipation, fever, cough, swelling, nose bleeding etc.

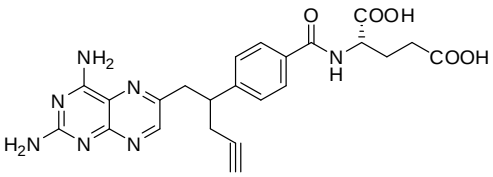

Dasatinib


Pazopanib


Imatinib


Nilotinib

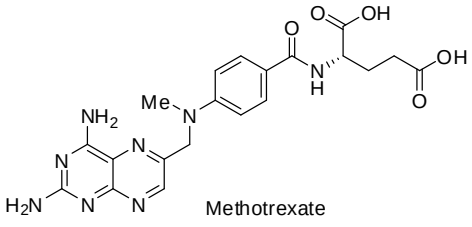

Leucovorin (Folinic acid)

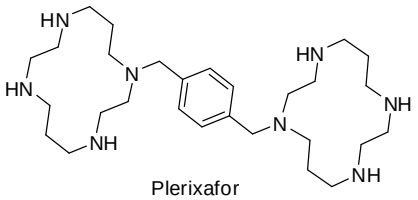

Pralatrexate

h) Eight nitrogen containing synthetic medicines (Table 26)

Methotrexate [99] is used for the treatment of head and neck, breast, lymphoma, leukemia, osteosarcoma, lung, bladder and trophoblastic neoplasms carcinoma. It acts as anti-metabolites with side effects mouth sores, diarrhea, vomiting, nausea, appetite loss, sunburn of skin, fever etc.

Plerixafor [100] 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 with side effects diarrhea, nausea, headache, pain in muscles, dizziness etc.


Methotrexate


Plerixafor

i) Multiple nitrogen containing synthetic medicines (Table 27)

Goserelin [101] 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

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

Table 26: Eight nitrogen containing synthetic medicines.

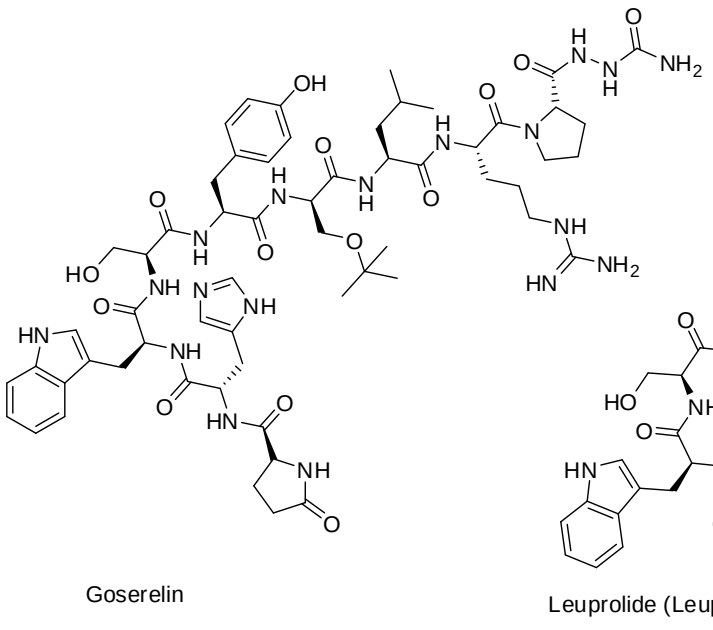
S.N.	Drug	Used for	Mechanism of action	Major side effects
92.	Methotrexate	head and neck, breast, lymphoma, leukemia, osteosarcoma, lung, bladder and trophoblastic neoplasms carcinoma	anti-metabolites	mouth sores, diarrhea, vomiting, nausea, appetite loss, sunburn of skin, fever
93.	Plerixafor	non-Hodgkin lymphoma and multiple myeloma	immunostimulant for mobilize hematopoietic stem cells	diarrhea, nausea, headache, pain in muscles, dizziness

Table 27: Multiple nitrogen containing synthetic medicines.

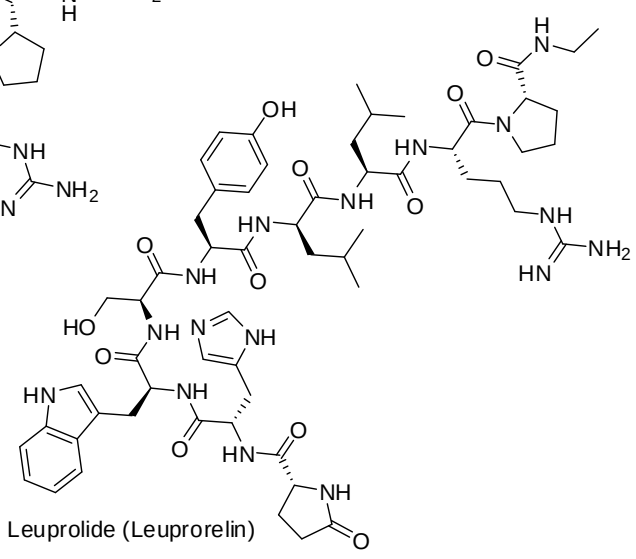
S.N.	Drug	Used for	Mechanism of action	Major side effects
94.	Goserelin	prostate & breast cancers	gonadotropin releasing hormone super agonist	swelling, decease in breast size, skin disorder, depression, vaginal dryness, hot flashes, stooping menstrual period
95.	Leuprolide	prostate cancer	gonadotropin releasing hormone super agonist	swelling, decease in breast size, skin disorder, depression, vaginal dryness, hot flashes, stooping menstrual period
96.	Degarelix	prostate cancer	gonadotropin releasing hormone super agonist	sleeping disorder, hot flashes, breast enlargement, pain in breast, back pain, headache, constipation, tiredness, increase urination
97.	Ibritumomab tiuxetan	follicular B-cell non-Hodgkin's lymphoma	CD20 antigen inhibitor	nausea, tiredness, fever, low white blood cell count, low platelet count, low red blood cell count
98.	Trastuzumab Emtansine	breast cancer	HER2/neu receptor & tubline inhibitor.	nausea, tiredness, pain in joint, bone and muscles, diarrhea, constipation, headache, low blood platelet count, nose bleeding, numbness
99.	Brentuximab vedotin	Hodgkin lymphoma and anaplastic large cell lymphoma	CD30 antigen inhibitor	effects tiredness, rashes, cough, fever, nausea, vomiting, diarrhea, numbness in hands, abdomen pain

and estrogen) with side effects swelling, decease in breast size, skin disorder, depression, vaginal dryness, hot flashes, stooping menstrual period etc.

Leuprolide [102] was approved in 1985 and used for the treatment of prostate cancer. It is also decapeptide hormone (a luteinizing hormone releasing hormone). It also acts similar to goserelin as well as similar side effects.



Goserelin

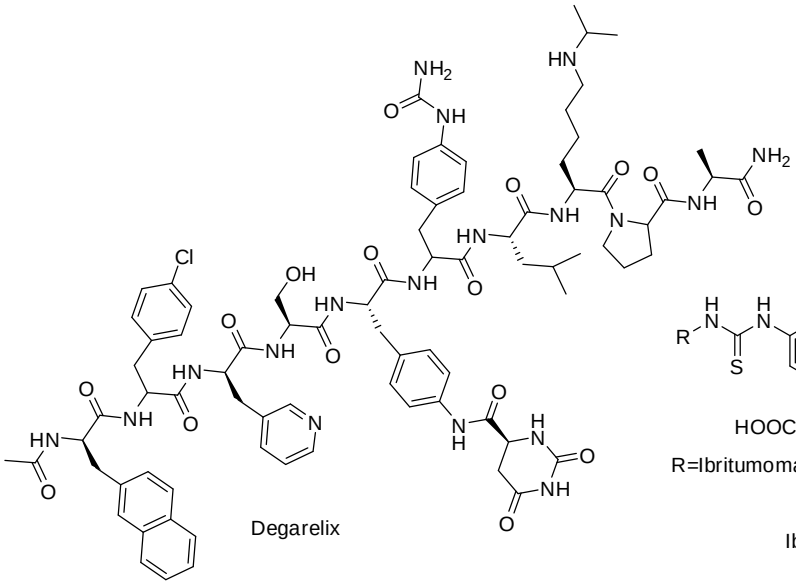


Leuprolide (Leuprorelin)

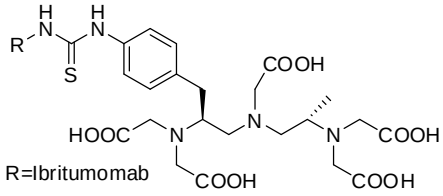
Degarelix [103] was approved in 2008 and used for the treatment of prostate cancer. It is also a decapeptide hormone. It acts gonadotropin releasing hormone super agonist with side effects sleeping disorder, hot flashes, breast enlargement, pain in breast, back pain, headache, constipation, tiredness, increase urination etc.

Ibritumomab tiuxetan [104] was approved in 2002 and used for the treatment of follicular B-cell non-Hodgkin's lymphoma. It is a monoclonal antibody drugs. It acts as CD20 antigen inhibitor with side effects nausea, tiredness, fever, low white blood cell count, low platelet count, low red blood cell count.

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.



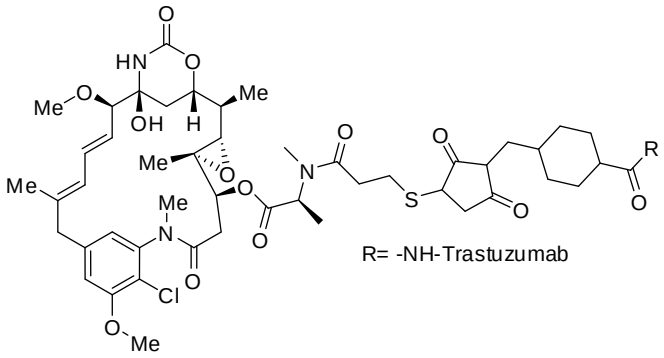
Degarelix



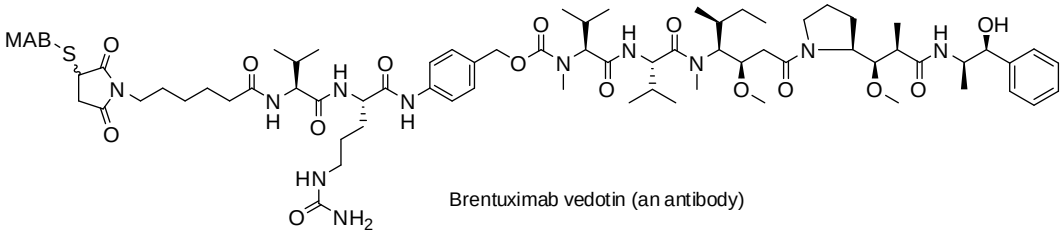
Ibritumomab tiuxetan

Trastuzumab Emtansine [105] 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. It has found side effect nausea, tiredness, pain in joint, bone and muscles, diarrhea, constipation, headache, low blood platelet count, nose bleeding, numbness etc.

Brentuximab vedotin [106,107] 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. It has shown side effects tiredness, rashes, cough, fever, nausea, vomiting, diarrhea, numbness in hands, abdomen pain etc.



Ado-Trastuzumab Emtansine



Brentuximab vedotin (an antibody)

Without nitrogen containing synthetic medicines (Table 28)

Etoposide [108] was approved in 1983 and used for the treatment of small cell lung and testicular cancer. It acts as topoisomerase II enzyme inhibitors with side effects hair loss, appetite loss, vomiting, nausea, low white blood cell count, low blood platelet count etc.

Bexarotene [109] was approved in 1999 and used for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma and also for

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

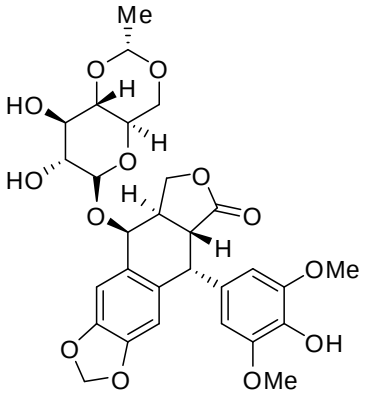
Table 28: Without nitrogen containing synthetic medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
100.	Etoposide	small cell lung & testicular cancer	topoisomerase II enzyme inhibitors	hair loss, appetite loss, vomiting, nausea, low white blood cell count, low blood platelet count
101	Bexarotene	cutaneous manifestations of cutaneous T-cell lymphoma, lung & breast cancer	retinoic acid receptors	diarrhea, headache, rashes, itching, low cholesterol disorder, high lipid levels, pain
102	Busulfan	chronic myelogenous leukemia	alkylating agents	low platelet count, low white blood cell count, anemia, hair loss, infertility disorder
103	Mesna	risk reduction of bladder damage during chemotherapy drugs treatment	-	-

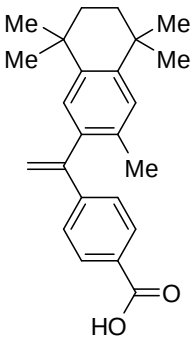
lung and breast cancer. It is aretenoid and acts as retinoic acid receptors with side effects diarrhea, headache, rashes, itching, low cholesterol disorder, high lipid levels, pain etc.

Busulfan [110] was approved in 1999 and used for the treatment of chronic myelogenous leukemia (a white blood cell carcinoma). It acts as alkylating agents with side effects low platelet count, low white blood cell count, anemia, hair loss, infertility disorder etc.

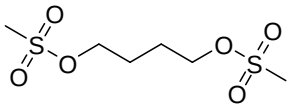
Mesna [111] was approved in 1988 and used for the risk reduction of bladder damage during chemotherapy drugs treatment of patients.



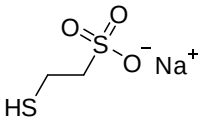
Etoposide



Bexarotene



Busulfan



Mesna

Steroidal medicines without nitrogen (Table 29)

Prednisone and dexamethasone [112] 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 hormones and have shown side effects sleeping disorder, stomach problem, weight gain, high blood glucose level etc.

Megestrol [113] is used for the treatment of breast and endometrial carcinoma. It acts as hormone antagonists with side effects such as weight gain, increase in appetite, swelling in hands, legs and feet etc.

Table 29: Steroidal medicine without nitrogen.

S.N.	Drug	Used for	Mechanism of action	Major side effects
104.	Prednisone	leukemias & lymphomas, allergic reactions nausea, vomiting, increase of appetite caused by carcinoma drugs	-	sleeping disorder, stomach problem, weight gain, high blood glucose level
105.	dexamethasone	leukemias & lymphomas, allergic reactions nausea, vomiting, increase of appetite caused by carcinoma drugs	-	sleeping disorder, stomach problem, weight gain, high blood glucose level
106.	Megestrol	breast and endometrial carcinoma	hormone antagonists	weight gain, increase in appetite, swelling in hands, legs and feet
107.	Exemestane	breast cancer	aromatase inhibitors	pain in join and bone, hot flashes, tiredness, headache
108.	Fulvestrant	metastatic breast cancer	estrogen receptor antagonist	nausea, weight gain, tiredness, vomiting

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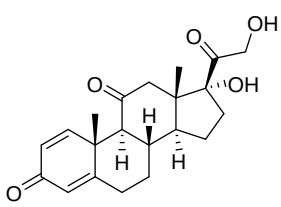
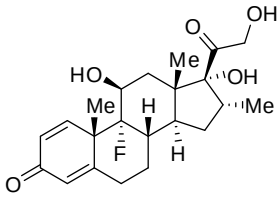
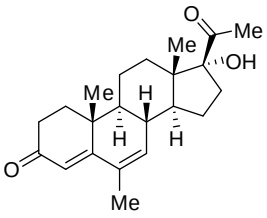


Prednisone



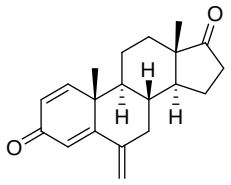
Dexamethasone



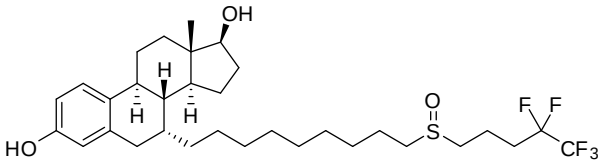
Megestrol

Exemestane [114] 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) with a side effects such as pain in join and bone, hot flashes, tiredness, headache etc.

Fulvestrant [115] was approved in 2002 and used for the treatment of metastatic breast cancer. It acts as estrogen receptor antagonist with side effects nausea, weight gain, tiredness, vomiting etc.



Exemestane



Fulvestrant

Other Protein, antibody and amino acids as anticancer medicines (Table 30)

Interleukin 2 (Aldesleukin) [116] 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 with side effects fever, headache, pain in joint and muscles, low blood pressure, rashes, weakness, breath problem, confusion, itching in skin, nausea, vomiting, diarrhea etc.

Table 30: Other Protein, antibody and amino acids as anticancer medicines.

S.N.	Drug	Used for	Mechanism of action	Major side effects
109.	Interleukin 2	skin melanomas and kidney carcinoma	immune system enhancer	fever, headache, pain in joint and muscles, low blood pressure, rashes, weakness, breath problem, confusion, itching in skin, nausea, vomiting, diarrhea
110.	Alemtuzumab	chronic lymphocytic leukemia, cutaneous T-cell lymphoma, T-cell lymphoma etc.	CD52 protein inhibitor	vomiting, fever, nausea, anemia, low white blood cell and platelet count, allergic reactions
111.	Ofatumumab	chronic lymphocytic leukemia	CD20 protein inhibitor	fever, low white blood cell count, lung infection, allergies, tiredness
112.	Bevacizumab	colon, cervical, kidney, breast, brain, non small cell lung cancer	vascular endothelial growth factor inhibitor	headache, mouth sores, diarrhea, tiredness, weaknes, back pain, skin dryness, appetite loss, nose bleeding, high blood pressure, bleeding form rectum, red and scaly skin
113.	Cetuximab	head and neck cancer, metastatic colorectal cancer and metastatic non-small cell lung cancer	vascular endothelial growth factor inhibitor	itching, mouth sores, tiredness, weakness, rashes, fever
114.	Ramucirumab	stomach cancer	vascular endothelial growth factor inhibitor	High blood pressure, head pain, diarrhea
115.	Denileukin diftitox	non-Hodgkin lymphoma	CD25 protein & diphtheria toxin inhibiter	chills, fever, rashes, weakness, appetite loss, vomiting, nausea, low blood pressure
116.	Denosumab	multiple myeloma in bones	osteoclasts inhibitor	diarrhea, nausea, weakness, tiredness, breathe disorder
117.	Liposomal cytarabine	lymphoma which spread from brain or spinal card	anti-metabolites	fever, nausea, vomiting, diarrhea, headache, back pain, sleepiness, weakness
118.	Rasburicase	tumor lysis syndrome	urate oxidase	fever, mouth sores, diarrhea, headache
119.	Filgrastim	neutropenia (increase white blood cell) in cancer patients	granulocyte colony-stimulating factor	-

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

120.	Obinutuzumab	chronic lymphocytic leukemia	CD20 protein inhibitor	low white blood cell count, fever
121.	Gemtuzumab ozogamicin	acute myelogenous leukemia	CD33 protein inhibitor	fever, swelling, pain in stomach, chest etc.
122.	Glucarpidase	toxic plasma methotrexate in cancer patients	-	-
123.	Romiplostim	blood platelet regulation	-	-
124.	Peginterferon alfa-2b	melanoma	interferon-alpha receptor	abdominal pain, chills, fever, cough, depression, nausea, vomiting
125.	Rituximab	chronic lymphocytic leukemia	CD20 protein inhibitor	headache, fever, nausea
126.	Siltuximab	prostrate, renal cancer	interleukin-6 protein inhibitor	rashes, weight gain, infections in respiratory system
127.	Panitumumab	colorectal cancer	epidermal growth factor receptor	diarrhea, tiredness, abdomen pain, constipation
128.	Ziv-Aflibercept	colorectal cancer	epidermal growth factor receptor	weight loss, diarrhea, mouth sores, low white blood cell count, appetite loss, tiredness, weakness, low blood platelet count
129.	Ipilimumab	melanoma	CTLA-4 protein inhibitor	tiredness, itching, rashes, diarrhea
130.	Palifermin	mouth sores of cancer patients	keratinocyte growth factor	-
131.	Sipuleucel-T	prostate cancer	increase immune system	fever, chill, nausea, weakness, back pain

Alemtuzumab [117] 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. It has shown side effects vomiting, fever, nausea, anemia, low white blood cell and platelet count, allergic reactions etc.

Ofatumumab [118] was approved in 2009 and used for the treatment of chronic lymphocytic leukemia. It is a fully human monoclonal antibody and bind with CD20 protein of carcinoma cells to inhibit early-stage B lymphocyte activation with side effects fever, low white blood cell count, lung infection, allergies, tiredness etc.

Bevacizumab [119] 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 with 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.

Cetuximab [120] 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 with side effects itching, mouth sores, tiredness, weakness, rashes, fever etc

Ramucirumab [121] was approved in 2014 and used for the treatment of stomach cancer. It is also a human monoclonal antibody and acts as angiogenesis inhibitor which inhibits vascular endothelial growth factor (VEGF) protein of carcinoma cells.

Denileukin diftitox [122] was approved in 1999 and used for the treatment of non-Hodgkin lymphoma (cutaneous T-cell lymphoma). It is a combined 2 fusion protein of diphtheria toxin and interleukin-2 and acts CD25 (IL 2 receptor protein) inhibiter and diphtheria toxin inhibit the formation of new carcinoma cell with side effects chills, fever, rashes, weakness, appetite loss, vomiting, nausea, low blood pressure etc.

Denosumab [123] was approved in 2010 and used for the treatment of multiple myeloma in bones. It is also a human monoclonal antibody and acts as osteoclasts inhibitor with side effects diarrhea, nausea, weakness, tiredness, breathe disorder etc.

Liposomal cytarabine [124] was approved in 1999 and used for the treatment of lymphoma which spread from brain or spinal card. It is a form of cytarabine contained liposomes. It acts as anti-metabolites with side effects fever, nausea, vomiting, diarrhea, headache, back pain, sleepiness, weakness etc.

Rasburicase [125] was approved in 1999 and used for the treatment of tumor lysis syndrome (a metabolic complication after treatment of cancer drugs). It is a tetrameric protein and acts as urate oxidase (metabolizes uric acid to allantoin) with side effects fever, mouth sores, diarrhea, headache etc.

Filgrastim [126] was approved in 1999 and used for the treatment of neutropenia (increase white blood cell) in cancer patients. It is a protein called granulocyte colony-stimulating factor (G-CSF).

Obinutuzumab [127] was approved in 1999 and used for the treatment of chronic lymphocytic leukemia. It is a humanized monoclonal antibody and bind with CD20 protein of carcinoma cells and inhibits B-cell (B lymphocytes) with side effects low white blood cell count, fever etc.

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

Gemtuzumab ozogamicin [128] was approved for 2000-2010 and used for the treatment of acute myelogenous leukemia. It is a monoclonal antibody and bind with CD33 protein of carcinoma cells.

Glucarpidase [129] was approved in 2012 and used for the treatment of toxic plasma methotrexate in cancer patients.

Romiplostim [130] was approved in 2003 and used for the treatment of blood platelet regulation. It is a fusion protein hormone analog of thromboprotein.

Peginterferon alfa-2b [131] was approved in 2011 and used for the treatment of melanoma with side effects such as abdominal pain, chills, fever, cough, depression, nausea, vomiting, etc.

Rituximab [132] was approved in 1997 and used for the treatment of chronic lymphocytic leukemia**.** It is a chimeric (fusion of human and mouse antibody) monoclonal antibody and bind with CD20 protein of carcinoma cells with side effect headache, fever, nausea, etc.

Siltuximab [133,134] was approved in 2014 and used for the treatment of prostrate cancer, renal cancer and Castleman disease. It is a chimeric (fusion of more than one gene of separated proteins) monoclonal antibody and bind with interleukin-6 protein of carcinoma cells with side effect rashes, weight gain, infections in respiratory system, etc.

Panitumumab [134] was approved in 2006 and used for the treatment of colorectal cancer. It is a fully human monoclonal antibody and bind with epidermal growth factor receptor (EGFR) protein of carcinoma cells with side effect diarrhea, tiredness, abdomen pain, constipation, etc.

Ziv-Aflibercept [135] was approved in 2012 and used for the treatment of colorectal cancer. It is a recombinant fusion protein and bind with epidermal growth factor receptor (EGFR) protein of carcinoma cells with side effects weight loss, diarrhea, mouth sores, low white blood cell count, appetite loss, tiredness, weakness, low blood platelet count etc.

Ipilimumab [136] was approved in 2011 and used for the treatment of melanoma. It is a is a monoclonal antibody and block CTLA-4 protein of carcinoma cells and increase immune efficacy with side effects tiredness, itching, rashes, diarrhea etc.

Palifermin [137] was approved in 2004 and used for the treatment of mouth sores of cancer patients. It is produced in *Escherichia coli* and acts as keratinocyte growth factor (KGF) for enhancement damaged epithelial cells of mouth and throat of cancer patient.

Sipuleucel-T [138] was approved in 2010 and used for the treatment of prostate cancer. It is a protein subunit and increase immune system of patient with side effects fever, chill, nausea, weakness, back pain etc.

Enzymes and Vaccine medicines (Table 31)

Recombinant Human Papillomavirus [139] 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.

Asparaginase Erwinia chrysanthemi [140] was approved in 2011 and used for the treatment of acute lymphoblastic leukemia. Asparaginase (colaspase) is an enzyme that catalyzes the hydrolysis of asparagines (aspartic acid). Asparaginases are naturally occurring enzymes and produced by microorganisms *Erwinia chrysanthemi*.

Pegaspargase [141] was approved in 2006 and used for the treatment of acute lymphoblastic leukemia. It is a pegylated *E. coli* L-asparagine amidohydrolase.

Inorganic medicines (Table 32)

Arsenic Trioxide (As_2O_3) [142] was approved in 2000 and used for the treatment of leukemia with side effects vomiting, nausea, appetite loss, abdomen pain, headache, tiredness, cough, fever, rashes etc.

Radium^{223}dichloride [143] 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 with side effects such as nausea, diarrhea, anemia, low white blood cell and platelet count etc.

Combined drugs (Table 33)

Due to several side effects of a single drug, resistant of drug, unavailability of drugs for advanced carcinona and for a better chemotherapy

Table 31: Enzymes and Vaccine medicines.

S.N.	Drug	Used for	produced by
132.	Recombinant Human Papillomavirus	cervical, anal, vaginal, vulva carcinoma	-
133.	Asparaginase Erwinia chrysanthemi	acute lymphoblastic leukemia	*Erwinia chrysanthemi*
134.	Pegaspargase	acute lymphoblastic leukemia	*E. coli*

Citation: Maurya HK. Natural and Synthetic Molecular Medicine in Cancer Research: A Review. J Cancer Res Molecul Med. 2014;1(1): 101.

Table 32: Inorganic medicines.

S.N.	Drug	Used for	Side effects
135.	Arsenic Trioxide	leukemia	vomiting, nausea, appetite loss, abdomen pain, headache, tiredness, cough, fever, rashes
136.	Radium^{223}dichloride	prostrate cancer	nausea, diarrhea, anemia, low white blood cell and platelet count

Table 33: Combined drugs.

S.N.	Drug	Combination	Used for
137.	ABVD	Adriamycin, Bleomycin, Vinblastine, Dacarbazine	Hodgkin lymphoma
138.	ABVE	Adriamycin, Bleomycin, Vinblastine, Etopside	Hodgkin lymphoma of children
139.	ABVE-PC	ABVE-Prednisone, Cyclophosphamide	Hodgkin lymphoma of children
140.	AC	Adriamycin, Cyclophosphamide	breast cancer
141.	AC-T	AC-Taxol	breast cancer
142.	ADE	Cytarabine, Daunorubicin, Etopside	acute myeloid leukemia in children
143.	BEACOPP	Bleomycin, Etopside, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone	Hodgkin lymphoma
144.	BEP	Bleomycin, Etopside, Cisplatin	malignant tumor of ovaries and testis
145.	BEACOPP	Bleomycin, Etopside, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone	Hodgkin lymphoma
146.	BEP	Bleomycin, Etopside, Cisplatin	malignant tumor of ovaries and testis
147.	CAF	Cyclophosphamide, Adriamycin, Fluorouracil	breast cancer
148.	CAPOX	Capecitabine, Oxaliplatin	Colorectal cancer
149.	CHOP	Cyclophosphamide, Doxorubicin, Vincristine, Prednisone	non Hodgkin lymphoma
150.	CMF	Cyclophosphamide, Methotrexate, Fluorouracil	breast cancer
151.	COPP	Cyclophosphamide, Vincristine, Procarbazine, Prednisone	non Hodgkin lymphoma and Hodgkin lymphoma
152.	COPP-ABV	COPP- Adriamycin, Bleomycin, Vinblastine	Hodgkin lymphoma
153.	CVP	Cyclophosphamide, Vincristine, Prednisone	Hodgkin lymphoma and Chronic lymphocytic leukemia
154.	EPOCH	Etopside, Prednisone, Vincristine, Cyclophosphamide, Hydroxydaunomycin	non Hodgkin lymphoma
155.	FEC	Fluorouracil, Epirubicin, Cyclophosphamide	breast cancer
156.	FOLFIRI	Leucovorin, Fluorouracil, Irinotecan	colorectal cancer
157.	FOLFOX	Leucovorin, Fluorouracil, Oxaliplatin	colorectal cancer
158.	FU-LU	Fluorouracil, Leucovorin	colorectal cancer
159.	ICE	Ifosfamide, Carboplatin, Etopside	non Hodgkin lymphoma and Hodgkin lymphoma
160.	MOPP	Mechlorethamine, Vincristine, Procarbazine, Prednisone	Hodgkin lymphoma
161.	OEPA	Vincristine, Etopside, Prednisone, Adriamycin	Hodgkin lymphoma
162.	OFF	Oxaliplatin, Fluorouracil, Leucovorin	pancreatic cancer
163.	OPPA	Vincristine, Procarbazine, Prednisone, Adriamycin	Hodgkin lymphoma
164.	PAD	Bortezomib, Adriamycin, Dexamethasone	multiple myloma
165.	R-CHOP	Rituximab-CHOP	non Hodgkin lymphoma
166.	R-CVP	Rituximab-CVP	non Hodgkin lymphoma
167.	STANFORD V	Mechlorethamine, Doxorubicin, Vinblastine, Bleomycin, Etopside, Prednisone	Hodgkin lymphoma
168.	TAC	Docetaxel, Adriamycin, Cyclophosphamide	Breast cancer
169.	TPF	Docetaxel, Cisplatin, Florouracil	Gastric,squamous cell carcinoma of the head and neck
170.	VAMP	Vincristine, Adriamycin, Methotrexate, Prednisone	Hodgkin lymphoma
171.	XELOX	Capecitabine, Oxaliplatin	colorectal cancer

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result combined drugs course are used for the treatment of cancer. 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 Hodgkin lymphoma) 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, Leucovorin; used in pancreatic cancer), OPPA (Vincristine, Procarbazine, Prednisone, Adriamycin; used in Hodgkin lymphoma), PAD (Bortezomib, 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).

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.

Acknowledgement

This review is dedicated to my maternal grandfather (Let. Sohan Lal), his elder brother, my favorite teacher and an aunt. They were died after suffering from deadly side effects of cancer drugs for more than six month treatment. I am also acknowledged DST, New Delhi, India for the awarded of DST fast track young scientist fellowship.

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