International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252

A Review on Antineoplastic Agent

Sharma Anupam* Ankalgi Amar Deep, Devi Arti, Ashawat Mahindra Singh

Department of pa&qa of laureate institute of pharmacy kathog jawala ji
Corresponding author: Sharma Anupam

Date of Submission: 30-08-2020 Date of Acceptance: 12-09-2020

ABSTRACT: - Antineoplastic agents are used to prevent, inhibit or halt the development of a neoplasm (a tumor). Cancer is a diseases characterized by uncontrolled multiplication and spread of abnormal forms of the body's own cells. Most drugs on the market are designed to kill only a specific type of bacteria or virus, but antineoplastic drugs have to target a wide range of cells over sometimes multiple body systems. As a result, anti cancer drugs often harm healthy cells in an attempt to kill the cancer cells. Cancer or neoplastic disease is a genomic disorder of the body's own cells which start to proliferate and metastasize in an uncontrolled fashion that is ultimately detrimental to the individual. Antineoplastic agents are used in conjunction with surgery and radiopathy to restrain that growth with curative or palliative intention. The different classifications have different mechanism of action and their adverse effect. The primary objective of antineoplastic agents is to eliminate the cancer cells without affecting normal tissues.

Keywords: - Anticancer drugs, Mechanism of Action, Chemotherapy, ADR

I. INTRODUCTION: -

Antineoplastic agents are the drugs used for the treatment of cancer. Cancer or neoplasm (Greek neo = new); plasm = formation) refers to a group of diseases caused by a several agents viz. chemical compound, radiant energy**.** The primary objective of antineoplastic agents is to eliminate the cancer cells without affecting normal tissues. In reality, all the cytotoxic drugs impact normal tissues as well as malignancies –aim for a favorable therapeutic index (aka therapeutic ratio). Cancer is characterized by an abnormal and uncontrolled division of cells exhibiting varying degrees of malignancy which produced tumors and invade adjacent normal tissue. [(1)] Often cancer cells separate themselves from the primary tumors and carried by the lymphatic system, reach distant sites of the organism, where they divide and form secondary tumors **(metastasis)**.Not all the tumors are malignant; benign tumors do not attack neighboring tissues and do not spread all through the body. The main characteristics of malignant tumors are, therefore,

(a) Autonomous growth, incentive to the normal control mechanism that limits cell growth and division in differentiated tissues and

(b) Invasiveness of adjacent capillaries and lymph channels.

Types of Tumors:-

- Not all tumors are malignant; tumors can be benign or malignant.
- **Benign tumors** are not cancerous. They can frequently be evacuated, and, in most cases, they don't return. Cells in benign tumors don't spread to different parts of body.
- **Malignant tumors** are cancerous. Cells in these tumors can attack nearby tissues and spread to different pieces of the body. The spread of malignancy from one parts of body to another is called metastasis.

Types of Cancer:-

Categorized based on the functions/locations of the cells from which they originate: [(2), (3)]

1. Carcinoma – skin or in tissues that line or spread inner organs. e.g., epithelial cells. 80-90 % revealed cases are carcinomas.

2. Sarcoma – bone, cartilage, fat, muscle, blood vessels,or other connective or supportive tissue.

3. Leukemia – White blood cells and their precursor cells such as the bonemarrow cells, causes large numbers of abnormal blood cells to be produced and enter the blood.

4. Lymphoma – cells of the immune system that affect lymphatic system.

5. Myeloma – B-cells that produce antibodies – spreads through lymphatic system.

International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252

6. Central nervous system cancers – cancers that begin in the tissues of the brain and spinal cord.

Cancer Therapeutic Modalities (classical)

1. Surgery 1/3 of patients without metastasis

Respond to surgery and radiation

2. Radiation If diagnosed at early stage,

Close to 50% cancer could be cured.

3. Chemotherapy 50% patients will undergo chemotherapy

to remove micro metastasis. However, chemotherapy

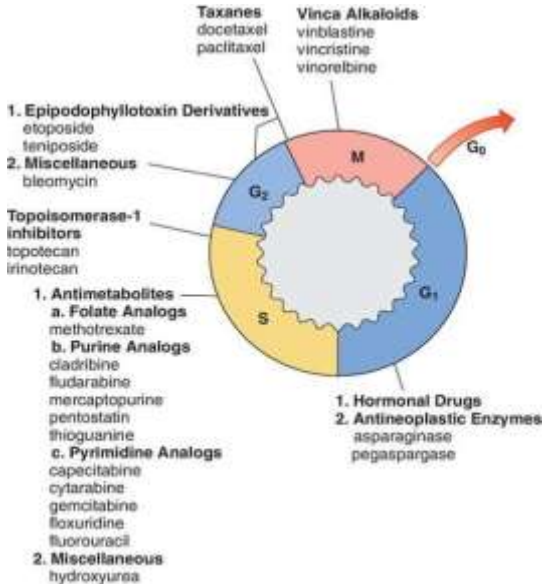
is able to cure just around 10-15%of all cancer patients. [7], [8], [10]

Two major classes of Antineoplastic agent

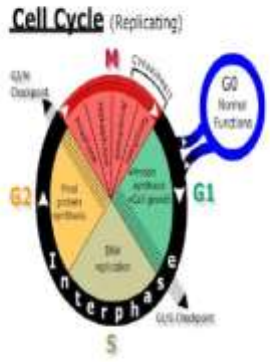
Cell Cycle Specific (CCS)Agent	**Cell Cycle Non – Specific (CCNS)Agents**
• Plant alkaloids and Antimetabolites	• Alkylating agents and some natural products
• Plant alkaloid G_2-M phase • DNA synthesis inhibitors(S-phase)	• Any phase of the cell cycle. • Cross linking and gene silencing
• Only proliferating cells are killed.	• Both proliferating and non-proliferating cells are killed.
• Schedule dependent • (duration and timing rather than dose)	• Dose dependent (total dose rather than schedule)

Drugs Based on Cell Cycle

- **CCNS:Nitrogenmustard, yclophosphamide, Chlorambucil,Carmustine,dacarbazine, busulfan,L-asparginase,cisplatin,procarbazine,and actinomycin D**
- **CCS:**



Cell Cycle Phases



• G1 phase (gap 1): Cell develops in size and prepares to copy its DNA in response to various growth factors

• S phase (synthesis): Replication of DNA, duplicating of the chromosome. [6], [43]

• G2 phase (gap 2): Ready for cell division. Check repeated DNA and fix harmed copies.

• M phase (mitosis): Formation of the mitotic spindle, and partition into two individual cells (cell division).

New types of cancer treatment

Hormonal Treatments:-These medication are intended to prevent malignant growth cell development by keeping the cells from accepting signals essential for their continued growth and

International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252

division.e.g; Breast cancer –tamoxifen after surgery and radiation. [5]

Specific Inhibitors:-Drug targeting specific proteins and processes that are limited primarily to cancer cells or that are much more prevalent in cancer cells.

Antibodies:-The antibodies are used in the treatment of cancer have been manufactured for use as a drug. e.g.; Herceptin, avastin.

Biological Response Modifiers:-The use of natural occurring, normal proteins to stimulate the body's own defenses against cancer.e.g; Abciximab, Rituximab

Vaccines:-Stimulate the body's defenses against cancer. Vaccines usually contain proteins found on or delivered by diseases cells. By administering these proteins, the treatment means to expand the reaction of the body against the malignancy cells.

Diagnosis of Cancer:-

Biopsy:-involves historical examination by a pathologist of a piece of tissue. [4]

Imaging techniques:-

- CT scan
- MRI

Laboratory test:-

Tumor markers (produced by cancer)

Example:

- CA15-3 ——Breast cancer.
- CA19-9 ———Gastrointestinal tumors.
- CA-125 ———Ovarian cancers
- PSA ————Prostate cancers.

Risk Factors of cancer:

Tobacco
Sunlight
Ionization radiation
Chemicals and other substances
Certain hormones
Family history of cancer
Alcohol

The Goal of Cancer Treatments:-

- **Curative**
  - Total irradication of cancer cells
  - Curable cancers include testicular tumors ,Wills tumor
- **Palliative**
  - Alleviation of symptoms
  - Avoidance of life-threatening toxicity
  - Increased survival and improved quality of life
- **Adjuvant therapy**
  - Attempt to eradicate microscopic cancer after surgery
  - e.g. breast cancer &colorectal cancer

Cancer Chemotherapy (Background)

A. The majority of the continuous advancement using antineoplastic treatment relies upon:

1. Advancement of new combination treatment of utilizing existing medications.
2. Better understanding of the mechanism of antitumor activity.
3. Development of chemotherapeutic approaches to destroying micro metastases.
4. Understanding the molecular component concerning the commencement of tumor development and metastasis.
5. Recognition of the heterogeneity of tumors. [20], [21]

B. Recently developed principles which have helped guide the treatment of neoplastic diseases

1. A single clonogenic cell can create enough progeny to murder the host.
2. Unless few malignant cells are present, host immune mechanisms do not play a significant role in therapy of neoplastic diseases.
3. A given treatment brings about decimation of a consistent rate instead of a constant number of cells; in this way cell kill follows first order kinetics.

C. Maligancies which respond favorably to chemotherapy:

1. Choriocarcinoma,
2. Acute leukemia,
3. Hodgkin's disease,
4. Burkitt's lymphoma,
5. Wilms tumor,
6. Testicular carcinoma,
7. Ewing's sarcoma,
8. Retinoblastoma in children,
9. Diffuse histiocytic lymphoma
10. Rhabdomyosarcoma

D. Antineoplastic medications are most effective against rapidly dividing tumor cells. [24], [25]

E. The main objective of Antineoplastic Agents is to eliminate the cancer cells without influencing normal tissues (the idea of differential sensitivity).In reality; every single cytotoxic medication influence normal tissues as well as malignancies-aim for a favorable therapeutic index.

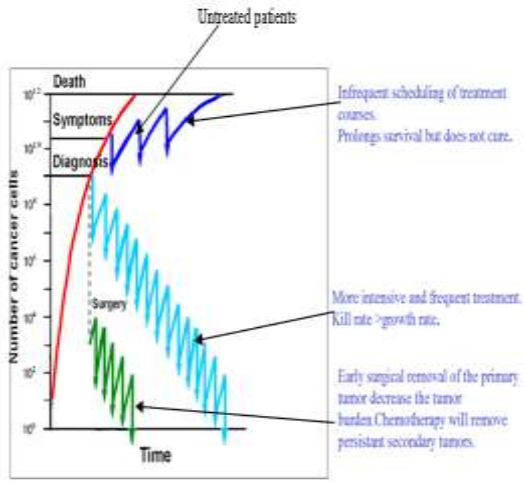
Therapeutic index = LD50 /ED50

A therapeutic index is the lethal portion of a medication for 50% of the population (LD50)

Divided by the minimum viable dose for 50%of the population (ED50)

F. The effect of tumor burden, scheduling, dosing, and initiation /duration of treatment on patient survival.

International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252



G. Goals of cancer chemotherapy

1. Selectively destroy cancer cells
2. Minimize toxicity to normal cells [12], [13]

H. Adverse effects of chemotherapeutic drugs (Table -1) [19]

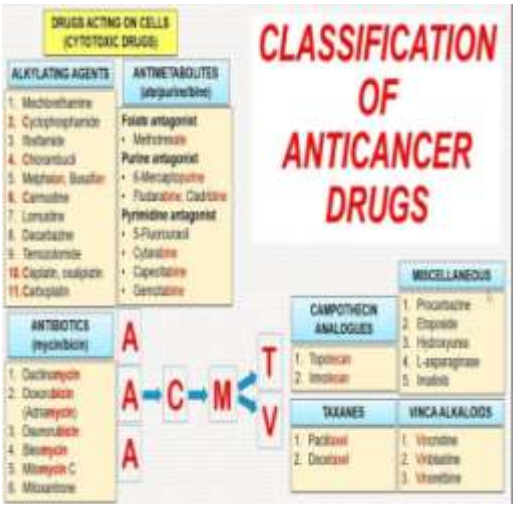
1. Individual drugs have "signature" adverse effects
2. Common shared adverse effects

TABLE 1 :- Therapeutic Uses and Adverse Effects of Selected Drugs Used in Cancer Chemotherapy

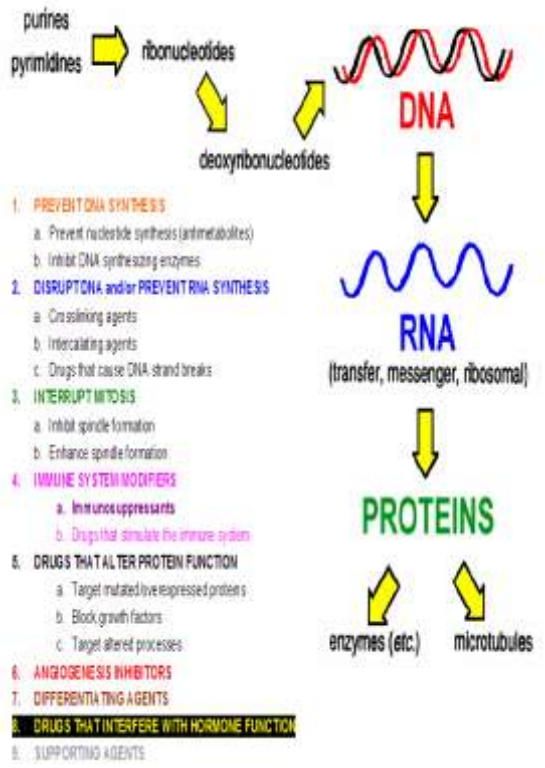
Drug	Use: Type(s) of Cancer	Important Adverse Effect(s)
Aminoglutethimide	Breast, prostate	Adrenal suppression, dizziness, rash
Anastrozole	Breast	Hot flashes
Bleomycin	Testicular, ovarian, cervical, thyroid	Pulmonary fibrosis; very little bone marrow toxicity
Busulfan	CML, polycythemia vera	Interstitial pulmonary fibrosis
Carmustine/lomustine	Brain	Leukopenia, thrombocytopenia, hepatotoxicity
Cisplatin	Head and neck, lung, testicular, cervical, thyroid, Ovarian	Ototoxicity, severe nephrotoxicity, mild bone marrow suppression
Cyclophosphamide	Leukemias/lymphomas	Hemorrhagic cystitis, alopecia
Cytarabine	Leukemias	Bone marrow suppression, CNS toxicity, immunosuppression
Dactinomycin	Wilms' tumor	Hepatotoxicity
Daunorubicin/doxorubicin	Acute leukemia, Hodgkin's disease, breast and lung	Cardiomyopathy (daunorubicin)
Etoposide	Lung, testicular	Bone marrow suppression
Imatinib	CML, gastrointestinal stromal tumors	Fluid retention
Irinotecan	Colon	Bone marrow suppression
Leuprolide	Prostate, breast	Hot flashes
Melphalan	Multiple myeloma	Bone marrow suppression
6-Mercaptopurine	Leukemias	Bone marrow suppression
Methotrexate	Wilms' tumor, choriocarcinoma, leukemias	Bone marrow suppression, oral and GI tract ulceration, diarrhea, Hepatotoxicity
Paclitaxel	Breast, ovarian	Bone marrow suppression
Procarbazine	Hodgkin's disease	Secondary malignancies, teratogenic
Tamoxifen	Breast	Hot flashes
Trastuzumab	Breast	Fever and chills
Vinblastine	Lymphomas	Bone marrow suppression
Vincristine	Acute lymphocytic leukemia	Neurotoxicity/peripheral neuropathy, low bone

International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252

		marrow suppression



Mechanism of Action of Antineoplastic



Alkylating Agent:-

Mechanism of Action

- Nitrogen mustards restrain cell proliferation by binding irreversibly with the nucleic acid (DNA).The specific type of chemical holding included is alkylation. [44), (45)]
- After alkylation, DNA is unable to duplicate and accordingly can no longer synthesize proteins and other fundamental cell metabolites.
- Consequently, cell reproduction is inhibited and the cell eventually dies from the inability to maintain its metabolic functions. [(31)]

Classification of alkylating agent

- Bis Chloroethyl Amine: Cyclophosphamide, Chlotmethine, Chlorambucil, Sarcolysine
- Nitrosoureas: Carmustine, Lomustine
- Ethyeneammonium or Aziridines:Thiotepa, triethylene melamine
- Alkysulfonates:Busulfan

Resistance of Alkylating Agents:-

Resistance to alkylating agents has several causes:

- Membrane transport may be decreased.
- The medication may be bound by glutathione(GSH) by means of GSH-S-transferase or metallothioneins in the cytoplasm and inactivated
- The medication may be metabolized to inactive species.

Adverse Effects of Alkylating Agents:-

- Myelosuppression is the dose –limiting adverse unfavorable impact for alkylating agents.
- Nausea and vomiting are basic as are teratogenesis and gonadal atrophy, in spite of the fact that in the last cases these are variable, according to the drug, its schedule, and route of administration.
- Treatment likewise conveys a significant danger of leukemogenesis and carcinogenesis.

Cyclophosphamide

- It is a prodrug and is activated by the P-450 enzymes to its active form phosphoamide mustard
- The active medication alkylates nucleophilic groups on DNA bases. Especially at the N-7 position of guanine
- This leads to cross linking of bases,abnormal base pairing and DNA strand breakage

Indication:-

- It is used in the treatment of chronic lymphocytic leukemia, non-Hodgkin's lymphomas, breast and ovarian cancer, and a variety of other cancers.
- It is also a potent immunosuppressant; it is used in the management of rheumatoid disorders and autoimmune nephritis.

International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252

Adverse effect:-

- Alopecia, nausea, vomiting, myleosuppression, and hemorrhagic cystitis.

Nitrosoureas

Carmustine, Lomustine, Semustine

Pharmacokinetics:-

- Nitrosoureas are more lipophilic and arrive at cerebrospinal fluid concentrations that are about 30% of plasma concentrations.

Indications:-

- Because of their excellent CNS penetration, carmustine and lamustine have been used to treat brain tumors.

Phenylalanine Nitrogen Mustard

- Melphalan is nitrogen mustard that is primarily used to treat multiple myeloma (plasma cell myeloma), breast cancer, and ovarian cancer.

Alkysulfonates

Busulfan

Indication:-

- Busulfan is administered orally to treat cronic granulocytic leukemia and other myeloproliferative disorders.

Adverse Effects:-

- Busulfan produces adverse effects related to myelosuppression.It only occasionally produces nausea and vomiting. In high doses, it creates an uncommon however in some cases fatal pulmonary fibrosis,"busulfan lung".

Thiotepa

- Thiotepa is changed over quickly by liver mixed function oxidases to its dynamic metabolite triethylenephosphoramide (TEPA); it is active in bladder diseases.

Antimetabolites

General characteristics:-

- Antimetabolites are S phase –specific drugs that are structural analogues of essential metabolites and that interfere with DNA synthesis.
- Myelosuppression is the dose-limiting toxicity for all drugs in this class.

Classification of Antimetabolites

- Folic acid Antagonists: Methotrexate
- Purine Antagonists: 6 Mercapapurine
- Pyrimidine Antagonists: 5Fluorouracil

Folic Acid Antagonist

Methotrexate (MTX)

Mechanism of Action:

- The stracture of MTX and folic acid are similar.MTX is actively transported into mammalian cells and inhibits dihydrofolate reductase, the enzyme that normally converts dietary folate to the tetrahydrofolate form required for thymidine and purine synthesis.

Indication:-

- The utilization of MTX in the treatment of choriocarinoma, a trophoblastic tumor, was main showing of curative chemotherapy.
- It is particularly successful for treating acute lymphocytic leukemia and for treating the meningeal metastases of a wide scope of tumors.

Adverse Effects:-

- MTX is myelosuppressive, producing severe leucopenia, bone marrow aplasia,and thrombocytopenia.
- This agent may produce severe gastrointestinal disturbances.
- Renal toxicity may occure because of precipitation (crystalluria) of the 7-OH metabolite of MTX.

Purine Antagonists

6-Mercaptopurine:-

The drugs are believed to act similarly to inhibit purine base synthesis, although their exact mechanism of action are still uncertain.

Indication:-

- Mercaptopurine is utilized basically for the maintenance of remission in patients with acute lymphocytic leukemia and is given in combination with MTX for this raason.

Adverse Effect:-

- Well tolerate.
- Myelosuppression is generally mid with thioguanine.Long –term mercaptopurine use may cause hepatotoxicity.

Pyrimidine Antagonists

5-Fluorouracil (5-FU)

Mechanism of Action:-

- Flurouracil is an analogue of thymine in which the methyl group is replaced by a fluorine atom. It has two dynamic metabolites: 5-FdUMP and 5-FdUTP .5-FdUMP inhibits thymidylate synthetases and prvent the combination of thymidine, a significant stracture square of DNA.5-FdUTP is fused into RNA by RNA polymerase and interferes with RNA function. [48],[49]

Indication:-

- Fluorouracil is only used to treat solid tumors, particularly breast, colorectal, and gastric tumors and squamous cell tumors of the head and neck.

Adverse Effects:-

International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252

- Flurouracil may cause nausea and vomiting, myelosuppression, and oral and gastrointestinal ulceration. Nausea and vomiting are usually mild.
- With fluorouracil, myelosuppression is progressively risky after bolus an injection, through mucosal harm is dose limiting with continuous infusions.

Cytarabine:-

Indication:-

- Cytarabine has a restricted clinical range and is essentially utilized in the combination with daunorubicin or thioguanine for the treatment of intense non lymphocytic leukemia.

Adverse Effects:-

- High dose of cytarabine can damage the liver, heart, and other organs.

Antibiotics

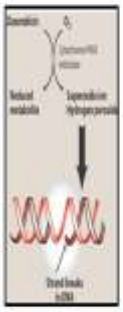
- Anthracyclines:

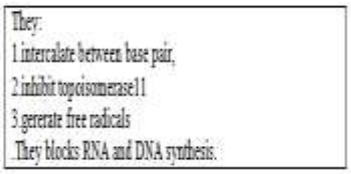
-Doxorubicine (Adriamycine)

-Daunorubicine

- Bleomycin
- Dactinomycin
- Mitomycin

Doxorubicine &Daunorubicine





ADR:-

- Cardiac harmfulness (due to generation of free radicals)
- Acute form:arrthymias,ECG changes , pericarditis,myocardities
- Chronic form: Dilated cardiomyopathy, heart failure
- ***Rx with dexrazoxane

-This is an inhibitor of iron mediated free radical generation

- Bone marrow depression ,Total alopecia
- Radiation recall reaction

Mitomycin C:-

Mechanism:-

- Mitomycin C is an antineoplastic antibiotic that alkylates DNA and consequently causes strand breakage and restraint of DNA synthesis.

Indications:-

- It is primarily used in the combination with vinvristine as salvage therapy for breast cancer.[28]

Adverse Effects:-

- Mitomycin produces delays and prolonged myelosuppression that specially influences platelets and leukocytes.

Actinomycin D:-

- Actinomycin D intercalates DNA and thereby prevents DNA transcription and messenger RNA synthesis.[40],[41]
- The medicine is given interavenously, and its clinical use is restricted to the treatment of trophoblastic (gestational) tumors and the treatment of pediatric tumors, for example, Wilm's tumors and Ewing's sarcoma.

Bleomycin:-

Mechanism:-

- The medication has its greatest impact on neoplastic cell in the G_2phase of the cell replication cycle. Altough bleomycin intercalates DNA; the significant cytotoxicity is accepted to result from iron catalyzed free radical formation and DNA strand breakage.[39]

Indication:-

- It is helpful in Hodgkin's and non-Hodgkin's lymphomas, testicular cancer, and a few other solid tumors.

Uses:-

- Epidermoid causes of skin, oral cavity, genitourinary tract, esophagus
- Testicular tumors
- Hodgkins lymphoma

Adverse Effects:-

- Bleomycin delivers almost myelosuppression. The most genuine toxicities of bleomycin are pulmonary and mucocutaneous responses.
- Hyper pigmentation
- Spares bone marrow

Anti-Cancer Plant Alkaloid

Tubulin-Binding Agents [26], [27]

Vinca Alkaloids:-The cellular movement of vinca alkaloids is the shirking of microtubules get together, making cell to catch in the late G2 stage

by preventing formation of mitotic fibers for nuclear and cell division [30]
Vinblastine, vincristin, vindesine and vinorelbine are on the whole alkaloids got from the periwinkle plant (vinca rosea).
Indications:-

- Vinblastine is utilized in combination with bleomycin and Cisplatin for metastatic testicular tumors.
- Vincristine is utilized in combination with prednisone to induce remission in childhood leukemia.
- Vinorelbine is utilized to treat non-small-cell lung cancer and breast cancer.

ADR:-

- Severe neurotoxicity

-Paresthesias
-Loss of reflexes
-Foot drop
-Ataxia

Paclitaxel &Docetaxel (Taxans)

- These drugs act by meddling with mitotic spindle
- They prevent microtubule disassembly into tubulin monomers.

Therapeutic Uses:-
Docetaxel and paclitaxel have become central components of regimens fortreating metastatic ovarian, breast, lungs, head and neck cancers.
ADR:-

- Neutropenia
- Peripheral neuropathy

Cisplatin:-
Mechanism of Action :- [46), (47)]
Cisplatin binds to guanne in DNA and RNA, and the interaction is stabilized by hydrogen bonding. The molecular mechanism of action is unwinding and shortening of the DNA helix.
Indications:-

- Ciaplatin has efficacy against a wide range of neoplasms.It is given intravenously as a first-line drug for testicular ovarian and bladder cancer,and it is also useful in the treatment of melanoma and a number of other solid tumors.

Adverse Effects:-

- Cisplatin creates generally little myelosuppression but can cause extreme nausea, vomiting, and nephrotoxicity.

Carboplatin
Indication:-

- Carboplatin has asimilar spectrum of activity, but it is approved only as a second-line drug for ovarian cancer.

Miscellaneous agents:-

- Asparaginase imatinib,interferons, monoclonal antibodies Asparaginase
- L-Asparaginase catalyzes the deamination of asparagine to aspartic acid and ammonia salt.
- L-Asparaginase is utilized in combination treatment to treat childhood intense lymphocytic leukemia
- Its mechanism of action is based on the fact that some neoplastic cells require an external source of asparagines because of their limited capacity to synthesize sufficient amount of that amino acid to support growth and function
- L-Asparaginase hydrolyzes blood asparagines and thus, deprivesthe the tumor cells of this amino acid, which is needed for protein synthesis.

ADR:-
Acute pancreatitis

Imatinib:-

- Example of a drug, whose development was guided by knowledge of specific oncogene.
- Used for the treatment of interminable myeloid leukemia
- Act by inhibiting tyrosine kinase activity of the protein product of the Bcr-Abl oncogene.

Treatment Protocols:-

- Combination is more effective than monotherapy without increasing toxicity.[29]
- Also decrease possibility of development of resistance.
- Higher responsive rate due to both additive cytotoxic effects and non –overlapping host toxicities.

Important drug combinations are:

REGIMEN	CANCER	DRUGS
MOPP	Hodgkins	Mechlorethamine,oncovin,prednisolone,procarbazine
ABVD	Hodgkins	Doxorubicin,bleomycin,vinblastine,dacarbazine
CMF	Breast	Cyclophosphamide, methotrexate,5-FU
CAF	Breast	Cyclophosphamide, doxorubicine,5-FU
	ALL	Vincristine,prednisolone,asparginе,daunorubicin
	AML	Cytarabine,methotrexate
	CML	Hydroxyurea,interferon

International Journal of Advances in Engineering and Management (IJAEM)
Volume 2, Issue 5, pp: 827-838 www.ijaem.net ISSN: 2395-5252

	Wilms	Actinomycin,vincristine,doxorubicin

Principles of administering antineoplastic agents
Occupational health and safety guidelines, and local policy and procedures must be adhered to throughout the administration process. [(11), (14) ,(17)] Antineoplastic agents can be administered via various routes including:

Intravenous	• Peripheral venous access • Central venous access – percutaneous lines – peripherally inserted central catheters (PICC) – implantable devices (Port-a-caths) – Tunnelled venous access devices (Hickman catheter).
Oral	• Enables shorter treatment time, more noteworthy autonomy of the individual and improved tolerability. Disadvantages are that the individual is not checked as seriously, there is a danger of noncompliance, possibility of under- or over-dosing, and irregularity of absorption from the gastrointestinal tract.
Intrathecal/ Intraventricular	• Antineoplastic agents are controlled legitimately into the cerebrospinal fluid, as a rules as prophylaxis in leukaemia or lymphoma.
Intraperitoneal	• Direct administration of antineoplastic specialists into the peritoneal cavity
Intrapleural	• To treat malignant emission, complications various malignant growths, including lung, breast, prostate, gastrointestinal and ovarian.
	• Administration of antineoplastic agents
Intravesical	directly into the bladder to treat superficial cancer of the bladder.
Topical	• Made up as ointments; normally used to treat sun cancers.
Subcutaneous and intramuscular	• Very not many antineoplastic agents may be administered by these routes as the medications are typically aggravating or might be a vesicant.

Prevention / management of cancer chemotherapy induced ADR :- [(22), (23)]

- Nausea and Vomiting: 5-HT 3 antagonist(ondansetron)
- Bone marrow suppression:Filgrastim,Sargromastim (colony stimulating factors)
- MTX toxicity:Leucovorin
- Cyclophosphamide toxicity:MESNA
- Cisplatin toxicity:Amifostine
- Anthracycline toxicity; Dexaroxazone

II. CONCLUSION:

Recent advancement in cancer treatments has dramatically altered the nature and progression of cancer .The main goal of antineoplastic agents is to eliminate the cancer cells without affecting normal tissues.

Consequently more than 1 million Americans and in excess of 10 million individual worldwide are expected to be diagnosed with cancer, a disease commonly believed to be preventable. Only 5-10% of all cancer causes can be attributed to genetic defect, whereas the remaining 90-95% has their roots in the environment and lifestyle. The proof demonstrate that all the anticancer –related deaths, just about 25-30% are because of tobacco, and numerous as 30-35% are connected to diet, about 15-20% are because of contaminations, and the remainder of the rate are because of various part like radiation, stress, physical activity, environmental pollutants etc. These drugs are completely effective for the treatment of cancer.

REFERENCE:-

[1]. Aranda S, Yates P. Competency appraisal apparatus for antineoplastic operator organition . Canberra: The National Cancer Nursing Education Project (EdCaN), Cancer Australia; 2009.

[2]. Dougherty L, Bailey C. Chemotherapy. In: Corner J, Bailey C, editors. Diseases nursing: care in setting 2nd ed. Malden MA: Blackwell Publishing Ltd; 2009.
[3]. Otto SE. Chemotherapy. In: Langhorne ME, Fulton JS, Otto SE, editors. Oncology nursing. 5th ed. St Louis: Elsevier Mosby.; 2007.
[4]. Polovich M, Whitford J, Olsen N, editors. Chemotherapy and biotherapy rules and suggestion for training . 3rd ed. Philadelphia: Oncology Nursing Society; 2009.
[5]. Priestman T. Disease's chemotherapy in clinical practice. London: Springer London Ltd; 2008.
[6]. Barton-Burke M, Wilkes G. Diseases chemotherapy and cell cycle energy. In: Barton-Burke M, Wilkes GM, editors. Diseases treatment. Massachusetts: Jones & Bartlett Publishers; 2006.
[7]. Tortorice PT. Cytotoxic chemotherapy: standards of treatment. In: Yarbro CH, Holmes Gobel B, Wujcik D, editors. Diseases Nursing standard and practice. 7th ed. Sudbury: Jones and Bartlett Publishers; 2011.
[8]. Wilkes GM, Barton-Burke M. Oncology Nursing Drug Handbook. Boston: Jones and Bartlett Publishers; 2010.
[9]. Temple SV, Poniatowski B. Nursing ramifications of antineoplastic treatment. In: Itano J, Taoka K, editors. Core curriculum for oncology nursing. 4th ed. Philadelphia: Elsevier Saun ders; 2005.
[10]. Wilkes G, Barton-Burke M. Standard of chemotherapy. In: Gates R, Fink R, editors. Oncology nursing mysteries: your oncology questions replied by specialists you trust. 3rd ed. Missouri: Mosby Elsevier; 2008.
[11]. Levin VA, Groves M, Forman A. Intraventricular and intrathecal therapy. In: Perry M, editor. The chemotherapy source book. 4th ed. Philadelphia: Wolters Kluwer; 2008.
[12]. Tervit S, Phillips K. Chemotherapy. In: Grundy M, editor. Nursing in haematological oncology. Edinburgh: Elsevier Baillière Tindall; 2006.
[13]. Carrington C, Stone L, Koczwara B, Searle C, Siderov J, Stevenson B, et al. The Clinical Oncological Society of Australia (COSA) rule for the safiely recommending, apportioning and organization of malignancy chemotherapy. Asia-Pacific Journal of Clinical Oncology. 2010; 6(3):220-37.
[14]. Wall A, Hansen G. Tips for controlling chemotherapy. In: Gates R, Fink R, editors. Oncology nursing insider facts: your oncology questions replied by specialists you trust. 3rd ed. Missouri: Mosby Elsevier; 2008.
[15]. Goodman M. Chemotherapy: standards of administration. In: Yarbro CH, Wujcik D, Holmes Gobel B, editors. Diseases nursing standards and practice. Sudbury: Jones and Bartlett Publishers; 2011.
[16]. Multinational Association of Supportive Care in Cancer (MASCC). MASCC Antiemesis Tool (MAT). 2011; Available from: http://www.mascc.org/mat.
[17]. Tipton JM, McDaniel RW, Barbour L, Johnston MP, Kayne M, LeRoy P, et al.Trying Evidence: Evidence-based intercessions to forestall, oversee, and treat chemotherapy-actuated queasiness and spewing. Clinical Journal of Oncology Nursing. 2007;11(1).
[18]. Multinational Association of Supportive Care in Cancer (MASCC). Mucositis Guidelines. 2012.
[19]. National Comprehensive Cancer Network. NCCN Guidelines Version 1.2013 Cancer- and Chemotherapy-Induced Anemia. 2012; Available from: http:// www.nccn.org/ professionals/ physician_gls/PDF/anemia.pdf.
[20]. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloid development factors. 2012 [02.11.11]; Available from: http://www.nccn.org/ professionals/ physician_gls/PDF/myeloid_growth.pdf.
[21]. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: prevention and treatment of malignant growth related contaminations, version 2. 2011 [17.02.2012]; Available from: http://www.nccn.org/professionals/physician gls/pdf/infections.pdf.
[22]. Woolery M, Bisanz A, Lyons H, Gaido L, Yenulevich M, Fulton S, et al. Trying Evidence Into Practice: Evidence-Based Interventions for the Prevention and Management of Constipation in Patients With Cancer. Clinical Journal of Oncology Nursing. 2008;12(2):317-37.
[23]. Mitchell S, Beck S, and Hood L, Moore K, Tanner E. Trying Evidence: Evidence-Based Interventions for Fatigue During and

Following Cancer and Its Treatment. Clinical Journal of Oncology Nursing. 2007; 11(1):99-113.

[24]. Rehwaldt M, Wickham R, Purl S, Tariman J, Blendowski C, Shott S, et al. Self-Care Strategies to Cope with Taste Changes After Chemotherapy. Oncology Nursing Forum 2009; 36(2):E47-E56.

[25]. National Cancer Institute. Overview of Nutrition in Cancer Care. 2011 [17/9/12]; Availablefrom: http://www.cancer.gov/cancertopics/pdq/supportivecare/nutrition/Patient.

[26]. Visovsky C, Workman ML, Collins M, Abbott L, Aschenbrenner J, Hart C. Putting evidence into practice: Evidence Based interventions for chemotherapy-initiated fringe neuropathy. Clinical Journal of Oncology Nursing. 2007; 11(6):901-13.

[27]. Dalton LK, Demerac S, Elmes BC, Loder JW, Swan JM, Teitei T. (1967) Synthesis of the tumor-inhibitory alkaloids, ellipticine, 9-methoxyellipticine, and related pyrido-[4,3-b]carbazoles. Aust J Chem 20, 2715–2727.

[28]. Rouesse JG, Le Chevalier T, Caille F, Mondesir JM., SanchoGamier H., May-Levin F Spielman M, DeJager R, Amiel JL.(1985) Phase II investigation of ellipticinium in cutting edge bosom malignant growth . Malignant growth Treat Rep 69, 707–708.

[29]. Mathe G, Triana K, Pontiggia P, Blanquet D, Hallard M, Morette C. (1998) Data of pre-clinical and early clinical preliminaries of acriflavine and hydroxy-methyl-ellipticine reviewed, enriched by the experience of their use for 18 months to 6 years in combination with other HIV1 virostatic. Biomed Pharmacother 52, 391–396.

[30]. Goodwin S, Smith AF, Horning EC. (1959) Alkaloids of Ochrosia elliptica Labill. J Am Chem Soc 81, 1903–1908.

[31]. Auclair C. (1987) Multimodal action of antitumor specialist on DNA: The ellipticine series. Arch Biochem Biophys 259, 1–14.

[32]. Boyd MR. (1989) Status of the NCI preclinical antitumor medication discovery screen: Implications for choice of new agents for clinical trials. In: DeVita VT Jr, Hellman S and Rosenburg S, Editors. Cancer: Principles and Practice of Oncology Updates. vol. 3, Philadelphia: Lippincott, p. 1–12.

[33]. Boyd MR. (1993) the eventual fate of medication development. In: Niederhuber JE, Editor. Current Therapy in Oncology. Philadephia: B.C. Decker, p. 11–22.

[34]. Acton EM, Narayanan VL, Risbood PA, Shoemaker PH, Vistica DT, Boyd MR. (1994) anticancer particularly of some ellipticinium salts against human mind tumors in vitro. J Med Chem 37, 2185–2189.

[35]. DeMarini DM, Abu-Shakra A, Gupta R, Hendee LJ, Levine JG. (1992) Molecular examination of mutations induced by the intercalating agent ellipticine at the hisD3052 allele of Salmonella typhimurium TA98. Environ Mol Mutagenesis 20, 12–18.

[36]. Singh MP, Hill GC, Peoc'h D, Rayner B, Inabach JL, Lown JW. (1994) High-field NMR and restrained molecular modeling studies on a DNA heteroduplex containing an adjusted apurinic abasic site as covalently linked 9-aminoellipticine. Biochemistry 33, 10271–10285.

[37]. Chu Y, Hsu MT. (1992) Ellipticine expand the superhelical thickness of intracellular SV40 DNA by intercalation. Nucleic Acids Res 20, 4033–4038.

[38]. Monnot M, Mauffret O, Simon V, Lescot E, Psaume B, Saucier JM, Charra M, Belehradek JJr, Fermandjian S. (1991) DNA-drug acknowledgment and effects on topoisomerase II-mediated cytotoxicity. A three-mode binding model for ellipticine derivatives. J Biol Chem 25, 1820–1829.

[39]. Fossé P, René B, Charra M, Paoletti C, Saucier JM. (1992) Stimulation of topoisomerase II-intervented DNA cleavage by ellipticine derivatives: structure-activity relationships. Mol Pharmacol 42, 590–595.

[40]. Peng Y, Li C, Chen L, Sebti S, Chen J. (2003) Rescue of mutant p53 transcription capacity of ellipticine. Oncogene 22, 4478–4487.

[41]. Sugikawa E, Hosoi T, Yazaki N, Gamanuma N, Nakanishi N, Ohashi M. (1999) Mutant p53 mediated induction of cell cycle capture and apoptosis at G1 phase by 9-hydroxyellipticine. Anticancer Res 19, 3099–3108.

[42]. Ohashi M, Sugikawa E, and Nakanishi N. (1995) Inhibition of p53 protein phosphorylation by 9-hydroxyellipticine: A potential anticancer instruments. Jpn J Cancer Res 86, 819–829.

[43]. Kuo PL, Hsu Y, Chang C, Lin C. (2005) the instrumentof ellipticine-initiated apoptosis and cell cycle capture in human breast MCF-7 cancer cells. Cancer Lett 223, 293–301.

[44]. Schwaller MA, Allard B, Lescot E and Moreau F. (1995) Protonophoric action of ellipticine and isomers over the energy-transducing membrane of mitochondria. J Biol Chem 270, 22709–22713.
[45]. Hagg M, Berndtsson M, Mandic A, Zhou R, Shoshan MC, Linder S. (2004) Induction of endoplasmic reticulum worry by ellipticine plant alkaloids. Mol Cancer Ther 3, 489–497.
[46]. Stiborová M, Bieler CA, Wiessler M, Frei E. (2001) the anticancer specialist ellipticine on initiation by cytochrome P450 forms covalent DNA adducts. Biochem Pharmacol 62, 675–684.
[47]. Frei E, Bieler CA, Arlt VM, Wiessler M, Stiborová M. (2002) Covalent official of the anticancer medication ellipticine to DNA in V79 cells transfected with human cytochrome P450 enzymes. Biochem Pharmacol 64, 289–295.