ANTINEOPLASTIC AGENTS

Antineoplastic drus are the medications which are used in the treatment of cancer.

Cancer: The disease caused due to the uncontrolled division of abnormal cells in the part of body.

Anticancer drugs are used in the treatment of maliant diseases when surery is not possible OR prove ineffective.Antineoplastic aents are also known as the cytotoxic agents.They act to prevent OR inhibit the development of neoplasm.

Examples : mercaptopurine , melpalon

Classification

ANTINEOPLASTIC AGENTS

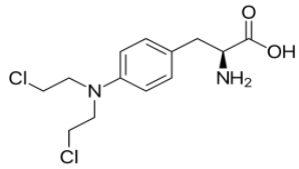
1) Alkylating agents
2) Antimetabolites
3) Antibiotics
4) Plant product
5) kinase inhibitor
6) Monoclonal Antibodies
7) Miscellaneous

1) Alkylating agents

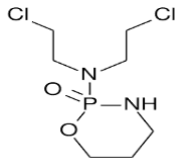
An alkylating antineoplastic agents are the alkylating agents used in te cancer treatment that attaches an alkyl roup to the DNA .The alkyl roup is attaced to gaunine base of DNA at seven no. nitrogen atom of purine ring .

1] Nitrogen mustard

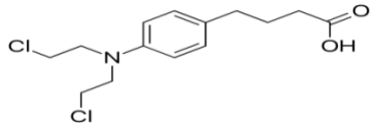
Examples : 1)Melpalan



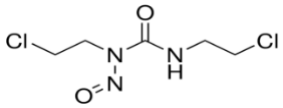
2)cyclophosphamide



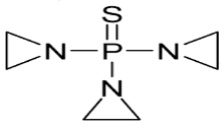
3)chlorambucil



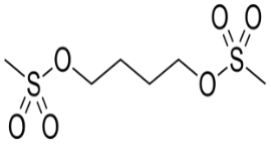
2] Nitrosource : E.g- Carmustine



3]Ethylenamine : E.g -Thiotepa

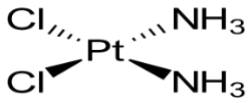


4] Alkyl sulfonte : E.g - Busulfan

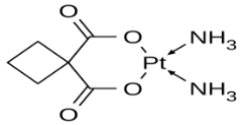


5]Triazine : E.g -dacarbazine

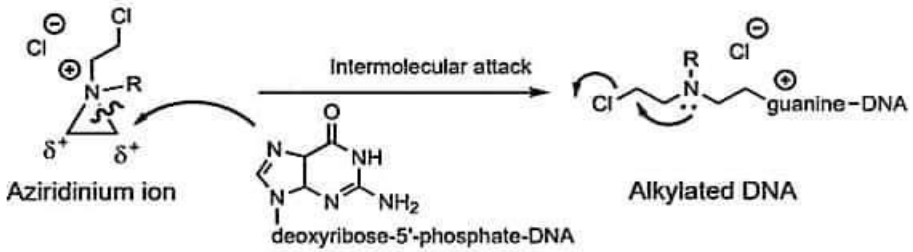
6]Metal Salts : E.g – 1)Cisplastin



2)carboplatin



Structure activity relationship



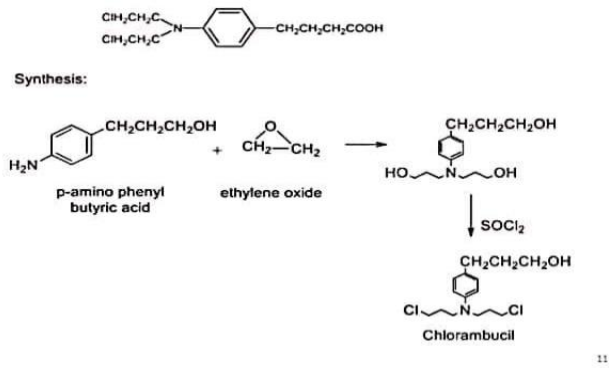
- The Bis (2chloroethyl group)is essential for activity.
- It is responsible for the formation of aziridine cation that alkylates the DNA.
- The aliphatic nitrogen mustard mechlorethamine is having reactivity. Mephalon and chlorambucil were developed that have phenylalanine and aminopenyl butyric acid in the structure.
- Nitrogen atom at 7^{th} position of guanine is suitable for the formation of the covalent bond with bifunctional alkylating agents. The presence of aromatic ring maintains the molecule more stable , enabling the better distribution of the drug .

Mechanism of action

Alkylating agents act by cross linkage strand of DNA, particularly at N-7position of guanine inhibiting the replication of DNA and the transcription of RNA.

Alkylating agents are reactive to DNA and cellular protein tey keep cell from reproducing(making copies of itself) by damaging the DNA

Synthesis of chlorambucil



Uses : It is used to treat cancer and work in all pases of cell cycle .

2) Antimetabolites

Antimetabolites are the class of anticancer drugs defined as the compounds structurally similar to natural purine OR pyrimidine base,nucleoside OR nucleotide , molecules needed to carry out the primary metabolic reactions that by virtue of their similarity act as analogues of normal metabolites , interfere with the normal metabolic processes within the cells and thus preventing the synthesis of DNA , RNA, and cell division.

Classification Of Antimetabolites

1) Float Antagonist

E.g.- methotrexate

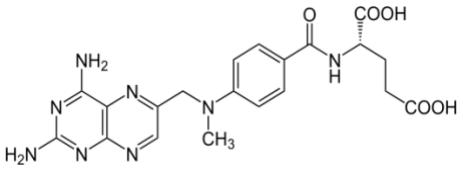
2) Purine Antagonist

E.g- mercaptopurine

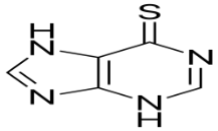
3) Pyridine Antagonist

E.g- flurouracil, cytarabine.

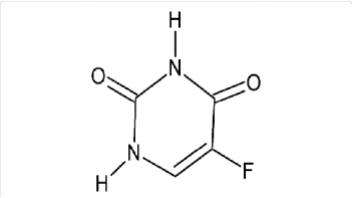
1] Folte Antagonist : E.g –methotrexate



2]Purine Antaonist : E.g – mercaptopurine



3]Pyridine Antagonist : E.g –flurouracil

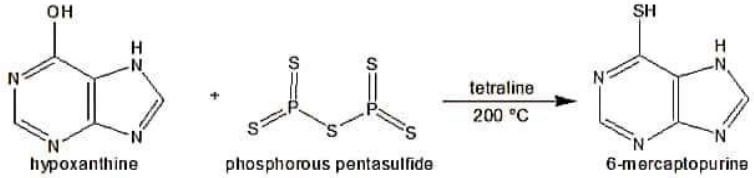


Mechanism of action

Antimetabolites are the drugs that are structurally related to naturally occuring compounds such as vitamin,amino acid,nucleotides.These drugscan compete for binding sites on enzymes or can themselves become incorporated into DNA or RNA and thus interfer with cell growth or proliferation. They work by mimicking the molecule cell needs.

Uses : It is used to treat cancer of breast, ovary, and intestinal tract. They work by slowing the growth of cancer cells and supress the immune system to reduce joint damage in rheumatoid arthritis.

Synthesis of mecaptopurine



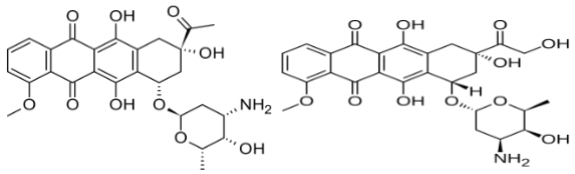
3) Antibiotics

Antineoplstic antibiotics also called as anticancer antibiotics or antitumor antibiotics that affect the DNA syntesis and replication by inserting into DNA or by donating electrone that result in the production of highly reactive oxyen compound (superoxide) that cause breakage of DNA strand.

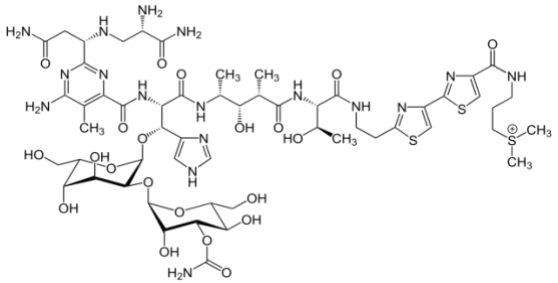
Examples : 1] Doxorubicin and Daunorubicin

2] Belomycin

1] Doxorubicin and Daunorubicin



2]Bleomycin



Mechanism of action

They are free radical genertor act by induction of DNA strand break

Uses : Doxorubicin and Daunorubicin are used in leukemias and oter solid tumors . Beomycin is used in squamous cell carcinoma and lymphoma.

Adverse Effect : Doxorubicin and Daunorubicin are dose dependent and causes nausea vomitting . Bleomycin causes pulmonary toxicity, fever etc.

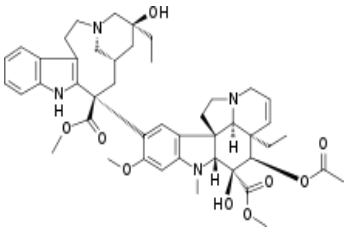
4) Plant products

1]Vinca Alkaloid : Vincristine , Vinblastin , and Vindesine ae the main vinca alkaloids used in the cancer cemoterapy. It is obtained from plant Vinca rosea.It inhibits mitosis.

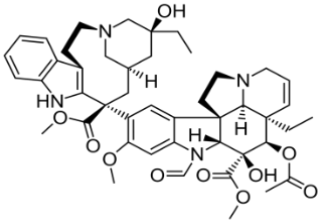
Mechanism of action

It binds to tubulin and inibit its polymerisation into microtubules ,preventing spindle formation in dividing cell and causing arrest at metaphase.

1)Vinblastine



2)Vincristine

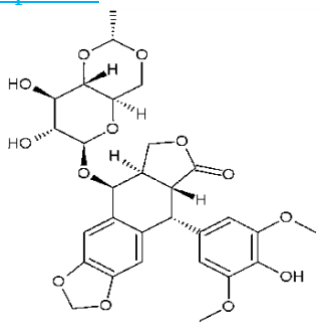


Uses : vincristine used in treatment of children leukemia and Vinblastine to treat hodgkins diseases.
Adverse Effect : Nausea , Vomitting ,Constipation , tiredness , loss of appetite.

2] Taxanes : They are obtained from western yew tree.It interfer with mitosis cell death, bind to tubulin and result in formation of microtubule .

3] Epipodopyllotoxin : It is semisyntetic derivative of podopyllotoxin obtained from podopyllum peltatum .It inhibit enzyme topoisomerase 2 ,leadingto DNA damage and block cell in SG2 phase of cell cycle.

1)Etoposide



Uses :

In combination with other medications to treat certain type of lung cancer(small cell lung cancer) and slows Or stop the growth of cancer cells.

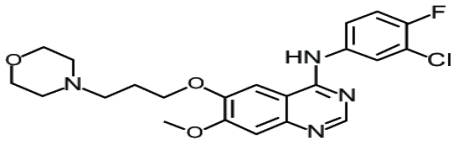
Adverse effect :

Nausea , Vomitting , Diarrhoea ,tiredness , weakness , loss of appetite.

5)Kinase Inhibitor

Antineoplastic tyrosine kinase inibitors are the type of targated therapy that identifies and attack specific type of cancer cell wile causing less damage to normal cell.

1)Gefitinib

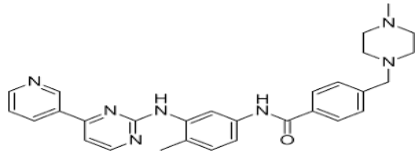


Mechanism of action

It inhibit intracellular phosphorylation of numerous tyrosine kinase associated with transmembrane cell suface receptor.

Uses : It is used to treat non –small cell lung cancer that has spred to another part of body in people with certain type of tumor.

2)Imatinib



uses : It is used to treat certain type of leukaemia and oter cancer and cell disorder.

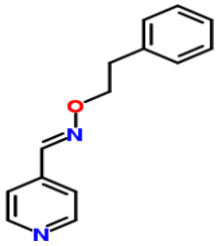
Adverse effect : upset stomach,Nausea.

6) Monoclonal Antibodies

They are created from the beta lymphocytes fused with the immortal beta lymphocyte tumor cell

The resulting hybrid cellcan be individually cloned and each clone will produce antibodies directed against the single antigen type.currently ,several monoclonal antibodies are available for the treatment of cancer.

1) Cetuximab



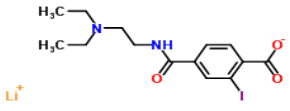
Mechanism of action

They act by inhibiting the growth and the survival of the epidermal growth factor expressing the tumor cell.

Uses : Treat certain type of cancer of the head and neck that has spread to nearby tissue or part of body.

Adverse Effect : Diarrhoea, Nausea,Vomittig,fatigue.

2) Bevacizumab



Mechanism of action

They act by selectively binding circulating vascular endothelial growth Factor terby inhibiting the binding of this factor to its cell surface receptor.

Uses : In combination with atezolizumab to treat eptocellular carcinoma that has spread or cannot be removed by surgery in people who have not previously received chemotherapy.

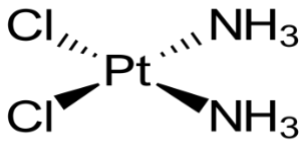
7) Miscellaneous

These agents include l-asparginase,cisplastin ,mitotane.

Antineoplastic or Anticancer drugs affect the growth and cell division that is are antiproliferative.

Examples : Cisplastin , Mitotane

1)Cisplastin



It is a square planar coordination complex (cis-[pt(NH3)2Cl2]).

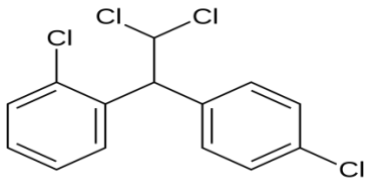
Mechanism of action

It induce its cytotoxic properties through binding to a nuclear DNA and subsequent interferance with normal transcription or DNA replication mecanism.

Uses :It is used to treat testicular , ovarian , bladder ,cervical cancer .

Adverse effect : Cough,drowsiness,burning,numbness

2)Mitotane



Mechanism of action

It modifies periperal metabolism of steroids and directly supress adrenal cortex

Uses: It is used to treat cancer of adrenal gland that cannot be treated by surgery.

Adverse Effect : Nausea, Diarroea,skin rashes.

Reference :

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2)Waman Pradnya Rajesh(66)

Class : Tird year B pharm(sem-6)

Subject : Medicinal chemistry 3

Academic year : 2021-22

Reference : 1)Foye's principle of medicinal chemistry.

2)Principle of medicinal chemistry by Kadam And mahadik