OFFICE: BUILDING No. 3/314, OFFICE-1, GAUSHALA ROAD, SHAMLI DISTRICT SHAMLI (U.P.) – 247776
Mobile: +91-9719638415
Email: arvindrkgit@gmail.com

Course Name	**: D. Pharm**
Year	**: First Year**
Subject Name	**: Pharmaceutical Chemistry**
Topic Name	**: Antineoplastic Agents**

Ch – 19

Antineoplastic Agents

The antineoplastic agents or anticancer drugs represent a large and diverse class of medications that inhibit or prevent the proliferation of neoplasms. These are a group of specialized drugs used primarily to treat cancer. Antineoplastic drugs are also called anticancer, cytotoxic or hazardous drugs.

Cancer is an extremely common disease, which impacts an untold number of people (and animals) each year. The abnormal cell division caused by cancers can impact virtually any body system, unlike other diseases that may only impact a single organ. In many cases, multiple systems are impacted at the same time.

Antineoplastic agents can be administered to patients alone or in combination with other antineoplastic drugs. They can also be given before, during or after a patient receives surgery or radiation therapy.

Classification of Antineoplastic Agents:

1. **Alkylating Agents: E.g.:** Busulfan, Chlorambucil, Cyclophosphamide, Dacarbazine, Melphalan, Procarbazine, Thiotepa
   a. **Nitrosoureas: E.g.:** Carmustine,
   b. **Platinum Coordination Complexes: E.g.:** Carboplatin, Cisplatin
2. **Antibiotics: E.g.:** Bleomycin, Daunorubicin, Doxorubicin
3. **Antimetabolites:**
   a. **Antifolates: E.g.:** Methotrexate, Pemetrexed
   b. **Purine Analogues: E.g.:** Azathioprine, Mercaptopurine
   c. **Pyrimidine Analogues: E.g.:** Cytarabine, Floxuridine, Fluorouracil, Trifluridine
4. **Biologic Response Modifiers: E.g.:** Aldesleukin (IL-2)
5. **Histone Deacetylase Inhibitors: E.g.:** Belinostat
6. **Hormonal Agents**
   a. **Antiandrogens: E.g.:** Cyproterone
   b. **Antiestrogens (including Aromatase Inhibitors): E.g.:** Anastrozole
   c. **Gonadotropin Releasing Hormone Analogues: E.g.:** Goserelin
   d. **Peptide Hormones: E.g.:** Lanreotide,
7. **Monoclonal Antibodies: E.g.:** Cetuximab
8. **Protein Kinase Inhibitors: E.g.:** Abemaciclib
9. **Topoisomerase Inhibitors: E.g.:** Etoposide, Topotecan
10. **Vinca Alkaloids: E.g.:** Vinblastine, Vincristine
11. **Miscellaneous: E.g.:** Asparaginase

1. ALKYLATING AGENTS

Alkylating agents are a class of antineoplastic or anticancer drugs which act by inhibiting the transcription of DNA into RNA.

MOA:

Classic alkylating agents interfere with DNA replication by crosslinking DNA strands, DNA strand breaking, and abnormal pairing of base pairs. They exert their lethal effects on cells throughout the cellcycle but tend to be more effective against rapidly dividing cells.

Because alkylating agents are active against cells in G0, they can be used to debulk tumours, causing resting cells to be recruited into active division. At this point, those cells are vulnerable to thecell cycle-specific agents.

Therapeutic uses:

These agents are active against lymphomas, Hodgkin's disease, breast cancer, and multiple myeloma.

Toxicity:

Major toxicities occur in the hematopoietic, gastrointestinal and reproductive systems. Individuals treated with these agents are also placed at a higher risk of developing secondary malignancies.

Classification:

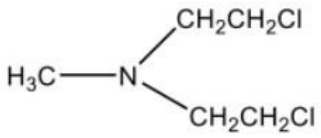
1. Nitrosoureas

The nitrosoureas are a subgroup of the alkylating agents. They also interfere with DNA replication and repair. They are highly lipid soluble and readily cross the blood-brain barrier. An example is Carmustine.

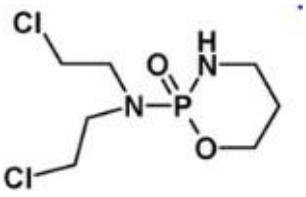
2. Platinum-containing compounds

Another subgroup of alkylators called Platinum-containing compounds include agents such as Cisplatin, Carboplatin and Oxaliplatin. Their cytotoxic properties also extend to alteration of the cell membrane transport systems and suppression of mitochondrial function.

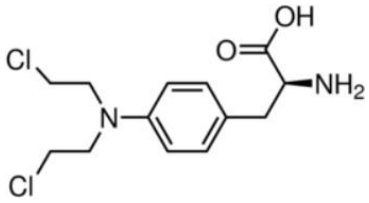
MECLORETHAMINE



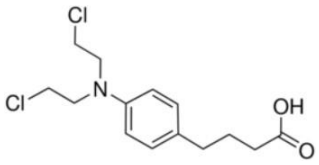
CYCLOPHOSPHAMIDE



MELPHALAN



CHLORAMBUCIL



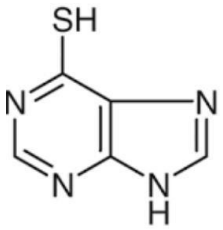
BUSULFAN

2. ANTIMETABOLITES

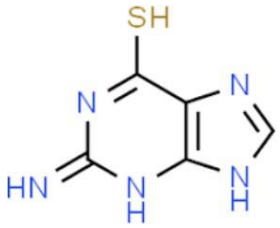
They interfere with DNA and RNA synthesis by acting as false metabolites, which are incorporated into the DNA strand or block essential enzymes, so that DNA synthesis is prevented. Most agents are cell cycle phase specific for S phase. These agents are most effective when used against rapidly cycling cell populations and are consequently more effective against fast-growing tumors than slow-growing tumors. Major toxicities occur in the hematopoietic and gastrointestinal systems.

E.g.: Methotrexate, 5-Fluorourocil and Cytosine Arabinoside.

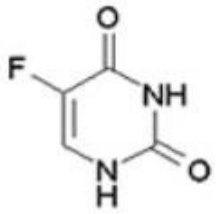
MERCAPTOPURINE



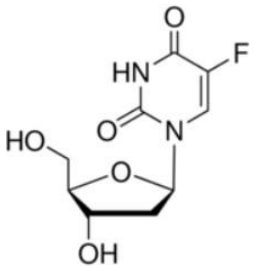
THIOGUANINE



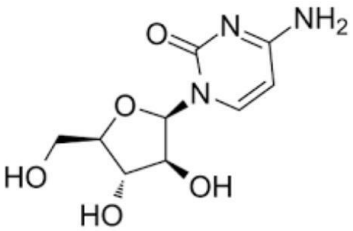
FLUORO URACIL



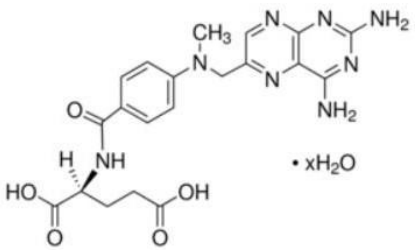
FLOXURIDINE



CYTARABINE



METHOTREXATE

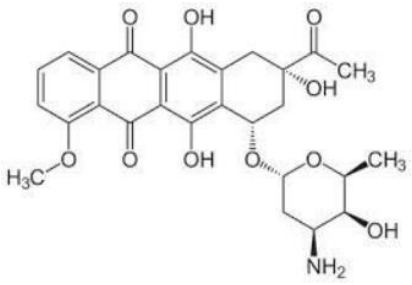


3. ANTITUMOR ANTIBIOTICS (also called Anthracyclines)

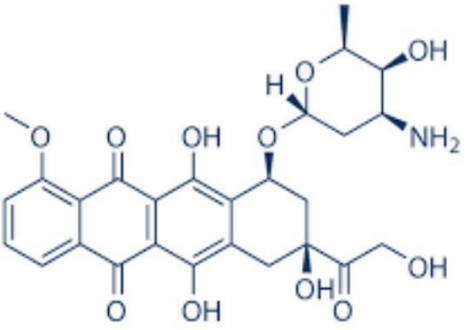
These interfere with RNA and DNA synthesis. Most drugs are cell cycle non-specific. Major toxicities occur in the haematopoietic, gastrointestinal, cardiac and reproductive systems. Cardiac toxicity may be manifested as acute changes in the electrocardiograph (ECG) and arrhythmias. Individuals with pre-existing heart disease are most at risk.

E.g.: include Bleomycin, Daunorubicin, and Doxorubicin.

DAUNORUBICIN



DOXORUBICIN

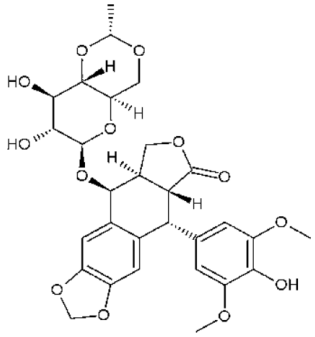


4. PLANT ALKALOIDS

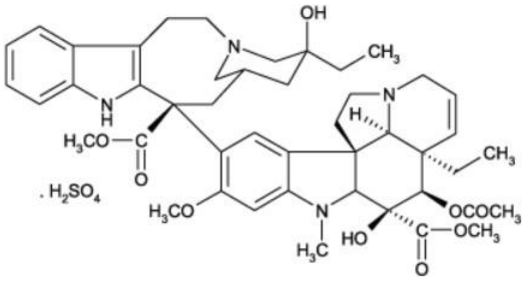
They bind to microtubule proteins during metaphase, causing mitotic arrest. The cell cannot divide and dies. This group is mainly cell cycle phase specific for M phase. Major toxicities occur in the haematopoietic, integumentary, neurologic and reproductive systems. Hypersensitivity reactions also may occur during administration of these agents. This group contains three subgroups:

- Vinca alkaloids e.g. vincristine and vinblastine
- Epipodophyllotoxins e.g. etoposide and teniposide
- Taxanes e.g. paclitaxel and docetaxel.

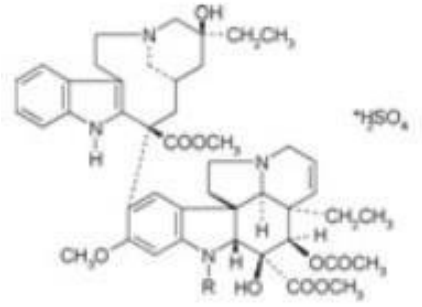
ETOPOSIDE



VINBLASTINE



VINCRISTINE



R is CHO

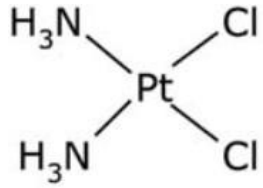
5. MISCELLANEOUS AGENTS

They differ from any of the major classes of cytotoxic agents. Common miscellaneous agents are asparaginase and hydroxyurea.

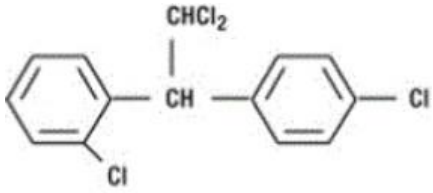
Topoisomerase inhibitors prevent realigning of DNA strands and maintain single-strand breaks. Majortoxicities occur in the haematopoietic and gastrointestinal systems.

E.g.: Irinotecan and topotecan.

CISPLATIN



MITOTANE



6. HORMONAL AGENTS alter the internal / extracellular environment.

Most agents are cell cycle phase non-specific. Breast, thyroid, prostate and uterine cancers are examples of tumours that are sensitive to hormonal manipulation. With these diseases, the action of hormones or hormone antagonists depends on the presence of hormone receptors in the tumours themselves (i.e. oestrogen receptors in breast cancers). There are individual classifications of hormonal agents:

- adrenocorticoids, eg. prednisone
- androgens, eg. testosterone propionate
- oestrogens, eg. diethylstilboestrol
- selective oestrogen receptor modulators, eg. tamoxifen citrate
- selective aromatase inhibitors, eg. anastrozole
- progesterones, eg. megestrol acetate
- antitestosterone, eg. flutamide