

CHAPTER-13

ANTI-NEOPLASTIC AGENTS

13.1 CANCER

- Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body.

13.1.1 Stages of Cancer

➤ Most cancers have four stages.

- The specific stage is determined by a few different factors, including the size and location of the tumor:

➤ **STAGE I**

- Cancer is localized to a small area and hasn't spread to lymph nodes or other tissues.

➤ **STAGE II**

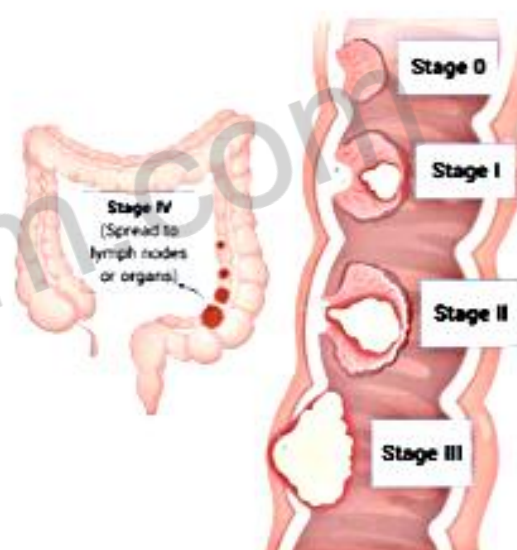
- Cancer has grown, but it hasn't spread.

➤ **STAGE III**

- Cancer has grown larger and has possibly spread to lymph nodes or other tissues.

➤ **STAGE IV**

- Cancer has spread to other organs or areas of your body. This stage is also referred to as metastatic or advanced cancer.



13.1.2 Types of Cancer

- There are five main types of cancer.

➤ **CARCINOMA**

- This type of cancer affects organs and glands, such as the lungs, breasts, pancreas and skin. Carcinoma is the most common type of cancer.



➤ **SARCOMA**

- This cancer affects soft or connective tissues, such as muscle, fat, bone, cartilage or blood vessels.

➤ **MELANOMA**

- Sometimes cancer can develop in the cells that pigment your skin. These cancers are called melanoma.

➤ **LYMPHOMA**

- This cancer affects your lymphocytes or white blood cells.

➤ **LEUKEMIA**

- This type of cancer affects the blood.

13.1.3 Causes of Cancer

➤ **Several factors contribute to the development of cancer in your body.**

- Smoking and using tobacco products is one of the main causes of
- Lung cancer
- Oral cancer
- Laryngeal cancer
- Esophageal cancer

➤ **An unhealthy lifestyle**

- Eating high-fat or high-sugar foods can increase your risk for many types of cancer. You're also more vulnerable to disease if you don't get enough exercise.

➤ **A toxic environment**

- Exposure to toxins in your environment, such as asbestos, pesticides and radon, can eventually lead to cancer.

➤ **Radiation exposure**

- Ultraviolet radiation from the sun significantly increases your risk for skin cancer. Over-exposure to radiation treatment can also be a risk factor.

➤ **Hormone therapy**

- Women who are taking hormone replacement therapy may have an increased risk for breast cancer and endometrial cancer.

13.1.4 Cancer is Treated by various method

➤ **CHEMOTHERAPY**

- One of the most common cancer treatments, chemotherapy uses powerful drugs to destroy cancer cells.

- Chemotherapy may be given through an IV or in pill form.



➤ RADIATION THERAPY

- This treatment kills cancer cells with high dosages of radiation.
- In some instances, radiation may be given at the same time as chemotherapy.

➤ SURGERY

- In some cases, your surgeon can surgically remove the tumour.

➤ HORMONE THERAPY

- Sometimes hormones can block other cancer-causing hormones
- For example, men with prostate cancer might be given hormones to keep testosterone (which contributes to prostate cancer) at bay.

➤ BIOLOGICAL RESPONSE MODIFIER THERAPY

- This treatment stimulates your immune system and helps it perform more effectively.
- It does this by changing your body's natural processes.

➤ IMMUNOTHERAPY

- Sometimes called biological therapy, immunotherapy treats disease by using the power of your body's immune system.
- It can target cancer cells while leaving healthy cells intact.

➤ BONE MARROW TRANSPLANT

- Also called stem cell transplantation, this treatment replaces damaged stem cells with healthy ones.
- Prior to transplantation, you'll undergo chemotherapy to prepare your body for the process.

13.2 ANTI-NEOPLASTIC AGENTS

- The drugs are used to inhibit abnormal cell growth or kill the cancer cells.

❖ **Classification of Anticancer Drugs (Cytotoxic Drugs)**

CLASSES	DRUGS
BCR-ABL tyrosine kinase inhibitors	Imatinib, Dasatinib, Nilotinib
EGF (HER) receptor inhibitors	Gefitinib, Erlotinib, Cetuximab, Trastuzumab, Lapatinib
Angiogenesis inhibitors	Bevacizumab, Sunitinib, Sorafenib
Proteasome inhibitors	Bortezomib
CD 20 inhibitors	Rituximab

❖ **Classification of Anticancer Drugs (Hormonal Drugs)**

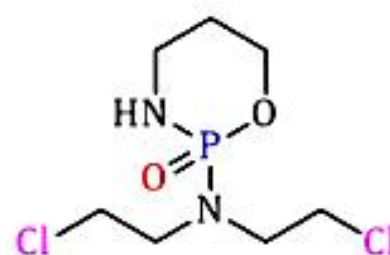
CLASSES	DRUGS
Glucocorticoids	Prednisolone, (others)
Estrogens	Fosfestrol, Ethinyl estradiol
Selective estrogen receptor modulators (SERMs)	Tamoxifen, Toremifene
Selective estrogen receptor down regulators	Fulvestrant
Aromatase inhibitors	Letrozole, Anastrozole, Exemestane
Antiandrogen	Flutamide, Bicalutamide
5- α reductase inhibitor	Finasteride, Dutasteride
GnRH analogues	Nafarelin, Triptorelin, Leuprorelin
Progestins	Hydroxyprogesterone acetate

13.2.1 ALKYLATING AGENTS

❑ **CYCLOPHOSPHAMIDE (CYTOPHOSPHANE)**

❖ **Chemical Formula** - $C_7H_{15}Cl_2N_2O_2P$

❖ **Structure**





❖ IUPAC Nomenclature

- (RS)-N,N-bis(2-chloroethyl)-1,3,2-oxazaphosphinan-2-amine 2-oxide

❖ Physiochemical Properties

- It occurs as a fine, white crystalline powder. It is odourless and has slight bitter taste. It is soluble in water, very soluble in alcohol but very slightly soluble in ether.
- It is having melting point in the range of 41-45°C.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of a tablet.

❖ Stability and storage

- It should be stored in a tightly closed container and protected from light.

❖ Popular Brand Names

- Lukeran
- Lyophilized cytoxan
- Endoxan

❖ Dose

- Initial adult dose of 40-50 mg per kg given intravenously in divided doses over 2-5 days and for children 2-8 mg per kg daily through IV injection.

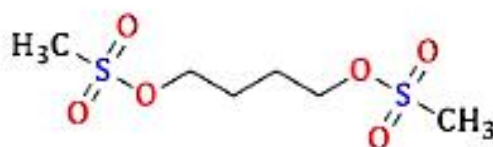
❖ Medicinal Uses

- It is used to treat ovarian cancer and breast cancer.
- It is also used in chronic lymphocytic leukemia and malignant lymphomas.

❑ **BUSULFAN**

- ❖ **Chemical Formula** $C_6H_{14}O_6S_2$

- ❖ **Structure**



❖ IUPAC Nomenclature

- Butane-1,4-diyl dimethanesulfonate

❖ Physiochemical Properties

- It appears as white crystals or powder, having melting point in the range of 114-118 °C.
- It is soluble in acetone, alcohol, practically insoluble in water but should be dissolved slowly otherwise hydrolysis will take place.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of a tablet.

❖ Stability and storage

- It is stored in a tightly closed light-resistant container.

❖ Popular Brand Names

- Myleran
- Busilvex
- Busulfex iv

❖ Dose

- For granulocytic leukemia, the daily oral dose is 60 µg/kg body weight, up to a maximum single daily dose of 4 mg, and to be continued till the white cell count falls between 15,000 and 25,000 per mm³

❖ Medicinal Uses

- It is used to treat chronic granulocytic leukemia and chronic myeloid leukemia.

13.2.2 ANTI-METABOLITES

❑ MERCAPTOPURINE (6-MERCAPTOPURINE [6-MP])

❖ Chemical Formula - C₅H₄N₄S

❖ Structure



❖ IUPAC Nomenclature

- 3,7-dihydropurine-6-thione

❖ **Physiochemical Properties**

- It is yellow crystalline powder. It is insoluble in water and soluble in alkaline solutions and ethanol.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of tablet.

❖ **Stability and storage**

- It is stored in a tightly closed light-resistant container.

❖ **Popular Brand Names**

- Purinethol
- Purixan
- Mepurine

❖ **Dose**

- The usual initial oral dose for children and adults is 2.5 mg per kg body weight daily, but the dose varies as per individual response and tolerance.

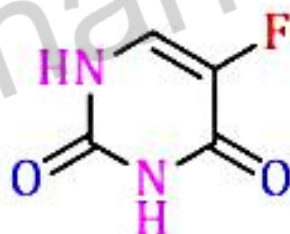
❖ **Medicinal Uses**

- It is used to treat acute lymphocytic leukemia, Crohn's disease, and ulcerative colitis.

❑ **FLUOROURACIL (5-FU)**

❖ **Chemical Formula** - $C_4H_3FN_2O_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 5-Fluoro-1H,3H-pyrimidine-2,4-dione

❖ **Physiochemical Properties**

- It is white to practically white crystalline powder, almost odourless, decomposes at 282- 283 °C.
- It is sparingly soluble in water and slightly soluble in alcohol.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of injection, cream and eye drops.

❖ **Stability and storage**

- It is stored in a tightly closed light-resistant container.

❖ Popular Brand Names

- Adrucil
- Carac
- Efudex

❖ Dose

- It is usually IV injected 1.2 mg/ kg body weight daily to a maximum of 1 gm daily for 3 or 4 days.

❖ Medicinal Uses

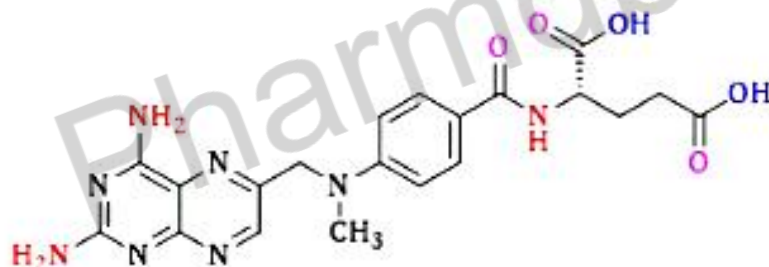
- Fluorouracil has been given systemically for anal, breast, colorectal, stomach, pancreatic and skin cancers (especially head and neck cancers).
- It has also been given topically (on the skin) for actinic keratosis, skin cancers and Bowen's disease.

❑ METHOTREXATE (MTX)

- It is a chemotherapy agent and immune-system suppressant and is used to treat cancer, autoimmune diseases, and ectopic pregnancies.

❖ Chemical Formula - $C_{20}H_{22}N_8O_5$

❖ Structure



❖ IUPAC Nomenclature

- (2S)-2-[[4-[[[(2,4-Diaminopteridin-6-yl) methyl] (methyl)amino] benzoyl] amino]pentanedioic acid

❖ Physicochemical Properties

- Methotrexate is a yellow or orange crystalline hygroscopic powder, practically insoluble in water, ethanol, and methylene chloride.
- It dissolves in dilute mineral acids and dilute solutions of alkali hydroxides and carbonates.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of injection, cream and tablet.

❖ Stability and storage

- It is stored in a tightly closed light-resistant container.

❖ Popular Brand Names

- Trexall
- Rheumatrex
- Otrexup

❖ Dose

- For the maintenance therapy of acute lymphoblastic leukaemia, the dose is 15-30 mg per m² body surface once or twice weekly either orally or intramuscularly, with other agents, such as mercaptopurine.

❖ Medicinal Uses

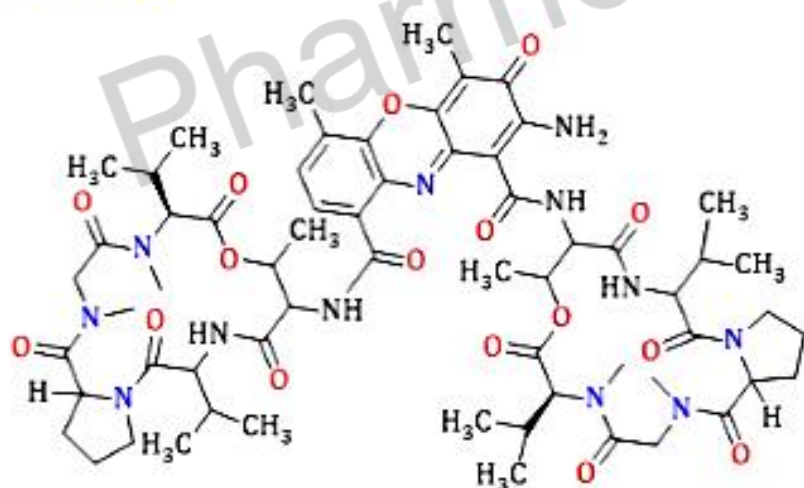
- It was originally developed and continues to be used for chemotherapy.
- It is effective for the treatment of a number of cancers, including solid tumors of the breast, head and neck, lung, and bladder, as well as acute lymphocytic leukemia's.

13.2.3 ANTI-BIOTICS

❑ DACTINOMYCIN (ACTINOMYCIN D)

❖ Chemical Formula - C₆₂H₈₆N₁₂O₁₆

❖ Structure



❖ IUPAC Nomenclature

- 2-Amino-N, N'- bis[(6S,9R,10S,13R,18aS)-6,13-diisopropyl-2,5,9-trimethyl-1,4,7,11,14-pentaoxohexadecahydro-1H-pyrrolo[2,1-i] [1,4,7,10,13] oxatetraazacyclohexadecin-10-yl]-4,6-dimethyl-3-oxo-3H-phenoxazine-1,9-dicarboxamide

❖ Physiochemical Properties

- It is obtained from the cultures of *Streptomyces antibioticus*.
- It consists of tricyclic phenoxazone ring in the quinone oxidation state and two identical polypeptides and intercalates into the double helical DNA.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of injection, cream and tablet.

❖ Stability and storage

- It is stored in a tightly closed light-resistant container.

❖ Popular Brand Names

- Cosmegen

❖ Dose

- Adults, IV, 0.01 mg (10 mcg) /kg body weight and Children: 0.015 mg/kg body weight for not more than 5 days.

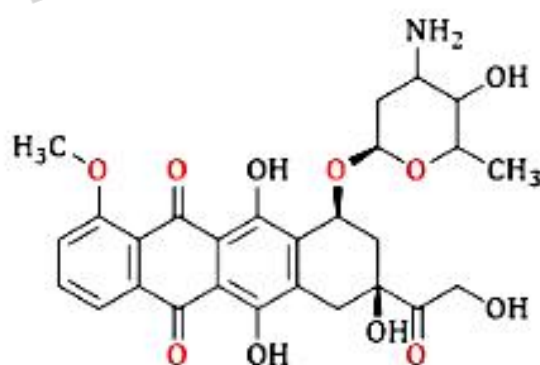
❖ Medicinal Uses

- It is used to treatment of Gestational trophoblastic neoplasia.
- Wilms' tumour.
- Rhabdomyosarcoma.
- Ewing's sarcoma.
- Malignant hydatid form mole.

❑ DOXORUBICIN HYDROCHLORIDE

❖ Chemical Formula - $C_{27}H_{29}NO_{11}$

❖ Structure



❖ IUPAC Nomenclature

- (7S,9S)-7-[(2R,4S,5S,6S)-4-Amino-5-hydroxy-6-methyloxan-2-yl]oxy-6,9,11-trihydroxy-9-(2-hydroxyacetyl)-4-methoxy-8,10-dihydro-7H-tetracene-5,12-dione

❖ Physiochemical Properties

- Doxorubicin hydrochloride is an orange-red crystalline hygroscopic powder, soluble in water, and slightly soluble in methanol.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of injection and capsule.

❖ Stability and storage

- It is stored in a tightly closed light-resistant container.

❖ Popular Brand Names

- Adriamycin
- Caelyx
- I-dox

❖ Dose

- It slowly injected 60-75 mg/m² in body surface area, every 3 weeks.

❖ Medicinal Uses

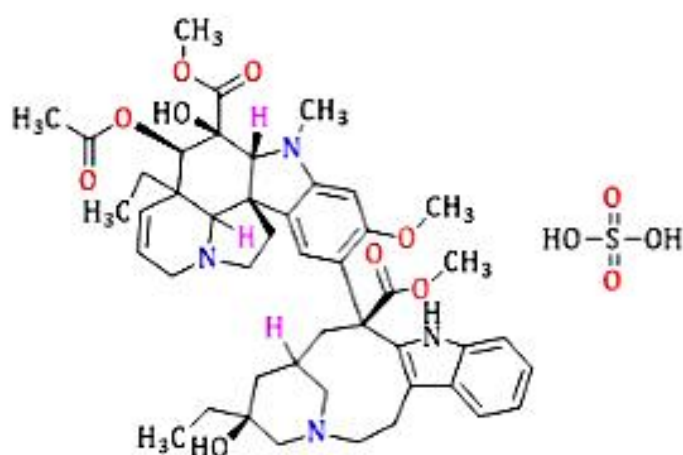
- It is used to treat breast cancer, ovarian cancer, and AIDS-related Kaposi's sarcoma
- It also used to treat leukaemia and Hodgkin's lymphoma, as well as cancers of the bladder, breast, stomach, lung, ovaries, thyroid, soft tissue sarcoma, multiple myeloma, and others.

13.2.4 MISCELLANEOUS COMPOUNDS

❑ VINBLASTINE SULPHATE

❖ **Chemical Formula** - C₄₆H₅₈N₄O₉

❖ **Structure**



❖ IUPAC Nomenclature

- dimethyl (2β,3β,4β,5α,12β,19α)-15-[[5S,9S]-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2H-3,7-methano aza cycloundecino[5,4-b]indol-9-yl]-3-hydroxy-16-methoxy-1-methyl-6,7-didehydroaspidospermidine-3,4-dicarboxylate

❖ **Physiochemical Properties**

- It is white to slightly yellow crystalline powder, with melting point in the range of 283- 285 °C.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of injection.

❖ **Stability and storage**

- It is stored in a tightly closed light-resistant container at 2-8°C temperature.

❖ **Popular Brand Names**

- Velban
- Velbe

❖ **Dose**

- Intravenously as a solution containing 1 mg per ml in sodium chloride injection

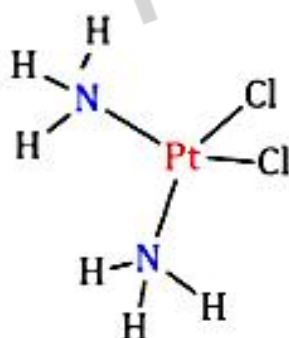
❖ **Medicinal Uses**

- Vinblastine is a component of a number of chemotherapy regimens, including ABVD for Hodgkin lymphoma.
- It is also used to treat histiocytosis according to the established protocols of the Histiocytosis Association.

❑ **CISPLATIN**

❖ **Chemical Formula** - $\text{Cl}_2\text{H}_6\text{N}_2\text{Pt}$

❖ **Structure**



❖ **IUPAC Nomenclature**

- Dichloroplatinum azane

❖ **Physiochemical Properties**

- Cisplatin is a yellow powder or yellow or orange-yellow crystals, slightly soluble in water, sparingly soluble in dimethylformamide, and practically insoluble in alcohol, used in testicular tumour.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of injection.

❖ **Stability and storage**

- It is stored in a tightly closed light-resistant container at 2-8°C temperature.

❖ **Popular Brand Names**

- Platinol
- Neoplatin
- Plastinex

❖ **Dose**

- Metastatic testicular tumors 20 mg/m² IV daily for five days, followed every 3 weeks for 3 courses.
- Metastatic ovarian tumors 50 mg/m² IV once every 3 weeks.

❖ **Medicinal Uses**

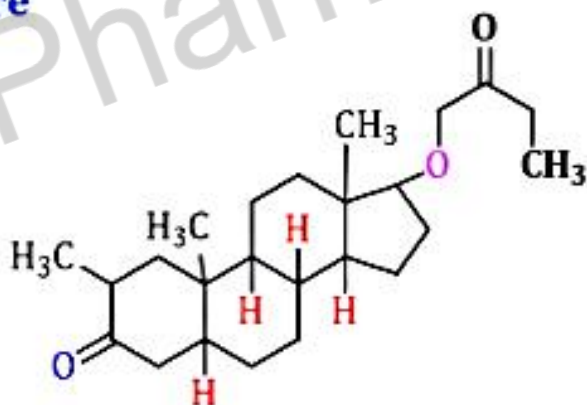
- It is used to treat various types of cancers, including sarcomas, carcinomas lymphomas, bladder cancer, cervical cancer and germ cell tumors.

❑ **DROMOSTANOLONE PROPIONATE**

- It is an androgen and anabolic steroid (AAS) medication which was used to treat breast cancer in women but is now no longer marketed.

❖ **Chemical Formula** - C₂₃H₃₆O₃

❖ **Structure**



❖ **IUPAC Nomenclature**

- 17-hydroxy-2,10,13-trimethyl-1,2,4,5,6,7,8,9,11,12,14,15,16,17-tetradecahydrocyclopenta[a]phenanthren-3-one

❖ **Physiochemical Properties**

- It is white to creamy white crystalline powder, having melting point of 128 °C.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of injection.