ANTINEOPLASTICS-(BP 501)

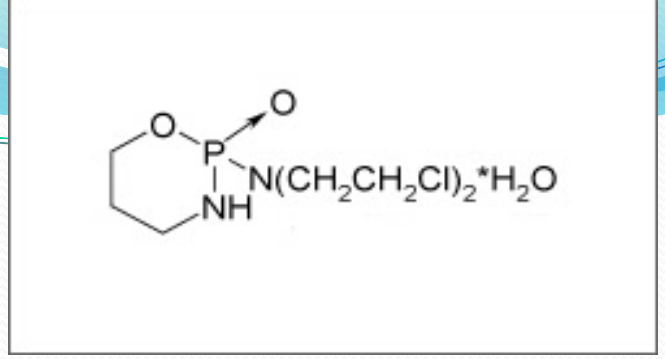
- **ALKYLATING AGENTS**: They are highly reactive compounds capable of form co valent bond with nucleophile region of intracellular macromolecules contains –***OH, -NH2, -SH –COOH*** groups

- Busulphan
- Chlorambucil
- **Cyclophosphamide**
- **MECHLORETHAMINE**
- **Melphalan**
- Thiotepa

OFFICIAL DRUGS

DRUGS	DRUGS
ALKYLATING AGENTS: 1. Busulphan 2. Chlorambucil 3. Cyclophosphamide 4. MECHLORETHAMINE 5. Melphalan 6. Thiotepa	

1. Cyclophosphamide (Cyclostine, Neosar)



CATEGORY: : It is an alkylating agent/cytotoxic agent

NOMENCLATURE:

(RS)-2-bis (2-chloroethyl)amino-perhydro-1,3,2-oxazaphosphorinane-2-oxide mono hydrate

PROPERTIES: white or almost white crystalline powder; freely soluble in ethanol; slightly soluble in ether, soluble in water. Stored in well closed container in a cool place and avoid long exposure to temperature above 30 degree C

USES: Used to chronic lymphatic leukemia; multiple myeloma, cancer in breast, neck and ovaries ***(alopecia is the major toxicity)***

DOSE: orally 100-150mg daily

PREPARATIONS: INJECTION **IP , contain 100 parts cyclophosphamide and 45 parts sodium chloride;, Tablets 10 and 50 mg**

Mechlorethamine synthesis:

Reaction with methylamine and ethylene oxide subsequent treatment with thionyl chloride yields final product

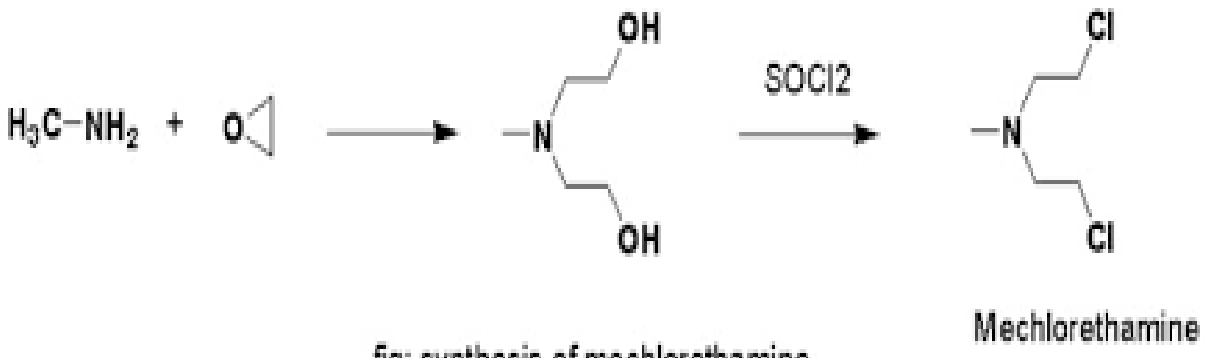
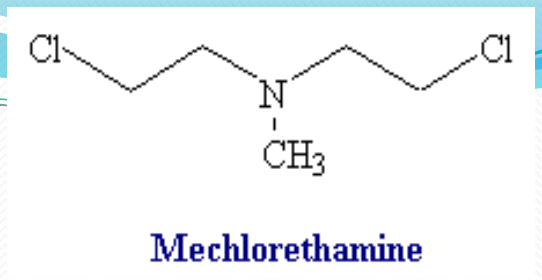


fig: synthesis of mechlorethamine

2. MECHLORETHAMINE (Chlorethamine, Mustargen)



Mechlorethamine

CATEGORY: Alkylating agent/Cytotoxic

NOMENCLATURE:

Bis-2-chloroethyl)methylamine

PROPERTIES: White , odorless , powder , hygroscopic powder; soluble in water and in ethanol, it should be stored in well closed container;

It is a prototype series of alkylating agent called as nitrogen mustard, used in combination with other drugs VINCRISTINE (**ONCOVIR**),PROCARBAZINE, PREDNISONE- ***MOPP.***

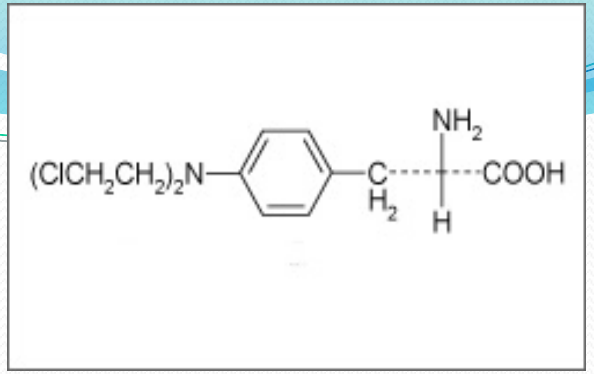
USES: Widely used in lymphosarcoma, in leukemia, in bronchogenic carcinoma, also used as an immunosuppressive agents also in ulcerative colitis

DOSE: Given along with other drugs , as single dose 400 MCG/kg body wt.

PREPARATIONS: HCL salt as Injection BP (1mg/ml in Na cl)

3. Melphalan

(ALKERAN)



CATEGORY: CYTOTOXC/alkylating agent

NOMENCLATURE:

4-bis(2-chloroethyl) amino-L-Phenylalanine

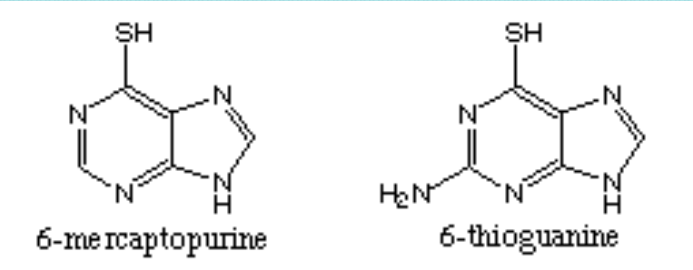
PROPERTIES: white powder odorless; slightly soluble in methanol and in ethanol; practically in soluble in water, chloroform and in ether. Stored in well closed light resistant container

USES: Used in lymphatic leukemia; multiple myeloma, cancer in breast, neck and ovaries

DOSE: Usual dose of 2-4mg daily for 4-6 days ; by injection 50 mg

PREPARATIONS: Melphalan injection 50mg **tablets 2mg and 5mg**

A. THIOGUANINE Tabloid, (6TG)



CATEGORY: CYTOTOXC/antimetabolite-purine

NOMENCLATURE: ***2-aminopurine-6(1H)-thione***

PROPERTIES: pale yellow crystalline powder odorless; practically in soluble in water, soluble in alkali hydroxides

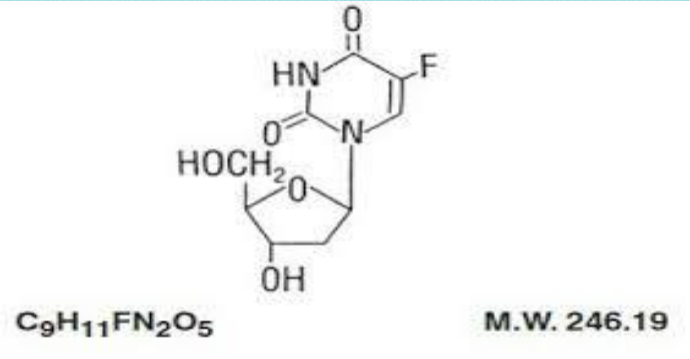
MOA similar to Mercaptopurin (inhibit nucleic acid synthesis)

USES: Used in myelose leukemia; chronic myeloid leukemia, lymphoblastic leukemia

DOSE: Usual dose of 2-2.5mg /per kg body wt. daily for conditions of the patient

REPARATIONS: Thioguanine **tablets BP**

B. FLOXURIDINE (FUDR)



CATEGORY: CYTOTOXC/antimetabolite-PYRIMIDINE

NOMENCLATURE: 5-floro-1-(2-deoxyfuranosyl) (1H, 3H)pyrimidine-2,4 dione

PROPERTIES: white powder odorless; slightly soluble in methanol and in ethanol; practically in soluble in water, chloroform and in ether. Stored in well closed light resistant container

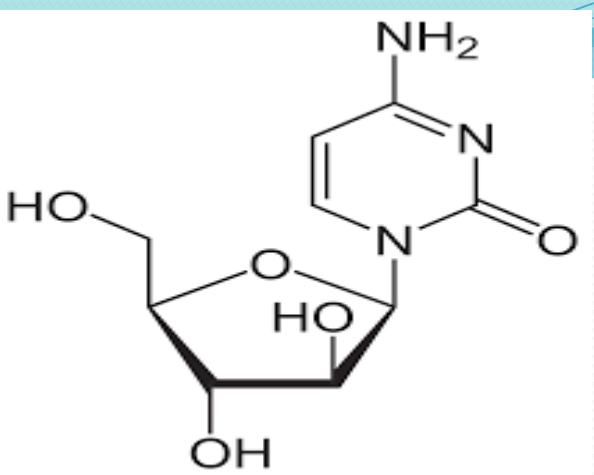
MOA: it's a prodrug metabolized to 5f-dump (deoxy uridine monophosphate)-active form in multiple steps

USES: Used in the palliative treatment of ***GI adeno carcinoma, can't managed by surgery and colorectal cancer***

DOSE: Usual dose of 2-4mg daily for 4-6 days ; by injection 50 mg

PREPARATIONS: Floxuridine (arterial as infusion)

C. CYTARABINE (CYTOSAR, ARACYTIN)



CATEGORY: cytotoxic/antimetabolite –**PYRIMDINE nucleoside**

NOMENCLATURE:

4-amino-1-b-arabinofurannosyl-1,2-dihydro-pyrimidine-2-one; 1-beta-o-arabinofuranosylcytocine; also known as b-cytosine arabinoside

PROPERTIES: white crystalline powder . Freely soluble in water; very slightly soluble in ethanol and in dichloromethane. Stored in well closed light resistant container

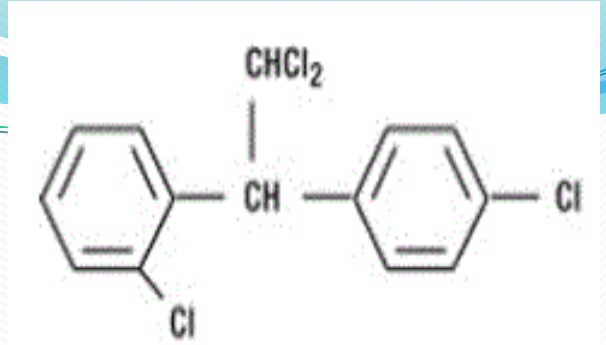
MOA: Inhibit DNA synthesis and cell death,***(it is very poisonous compound)***

USES: Used in acute granulocytic leukemia; it is more effective when combined with Thioguanine and Daunarubicin

DOSE: Usual dose of 2mg per kg body wt., parenterally for 10days

PREPARATIONS: Cytarabine injection IP (100mg)

D.MITOTANE



CATEGORY: cytotoxic/ derivative of DDT

NOMENCLATURE: O,P-DDD;

1-(2-chlorophenyl)-1-(4-chlorophenyl)-2,2dichloroethane

PROPERTIES: White granular solid, clear colorless crystals with slightly aromatic peasant odor. Stored in well closed light resistant container; soluble in ethanol

MOA: act as a selective cholesterol side chain cleavage enzyme inhibitor ***,(it is very TOXIC compound)***

USES: Used in the treatment of Adrenal cortex carcinoma-(***inoperable functional or non functional), Cushing's syndrom***

DOSE: orally 2-6 gram TID

PREPARATIONS: MITOTANE as LYSODREN tablets (500mg)

Anti Cancer Antibiotics:

OFFICIAL DRUGS=4

1.Bleomycin 2.Dactinomycin 3.Daunarubicin 4.Doxorubicin.

I. Bleomycins: Heterocyclic antibiotic Pyrimidine:

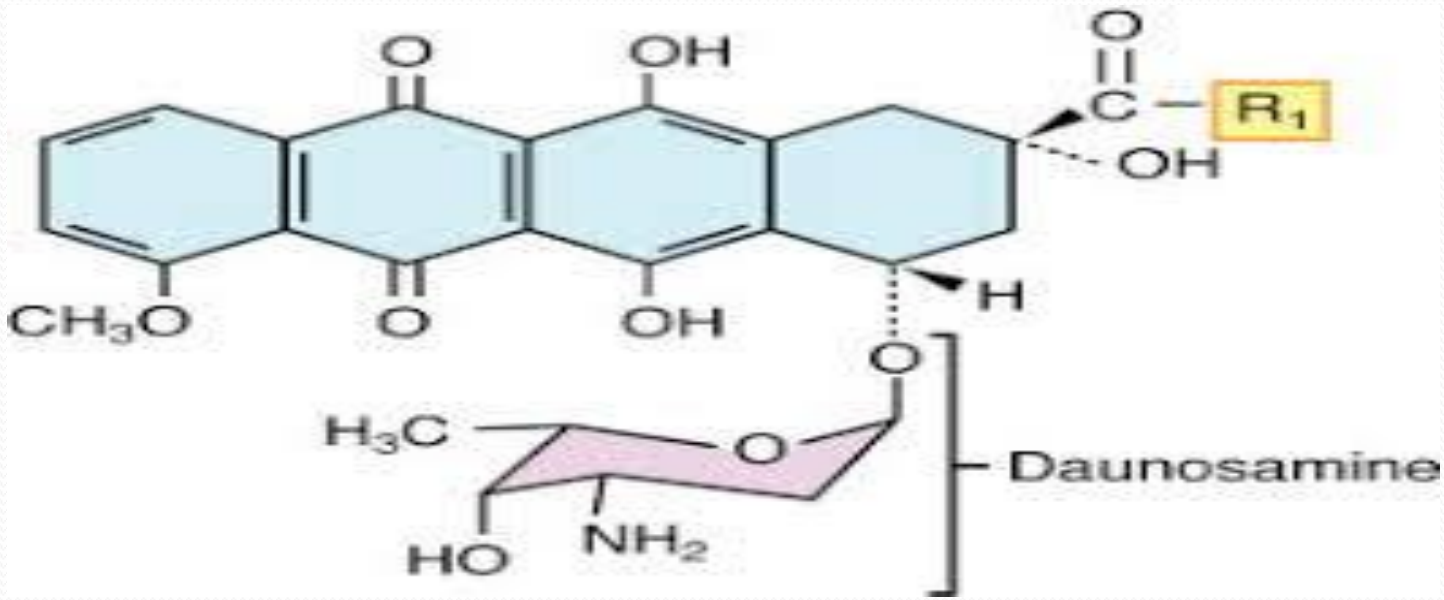
II. Actinomycins: Dactinomycin (Actinomycin-D)

III. Anthracyclines are class of antibiotics derived from strains of ***'Streptomyces bacterium'***

Examples: A-Daunarubicin, B-Doxorubicin

A : R1=CH3

B: R1=OH

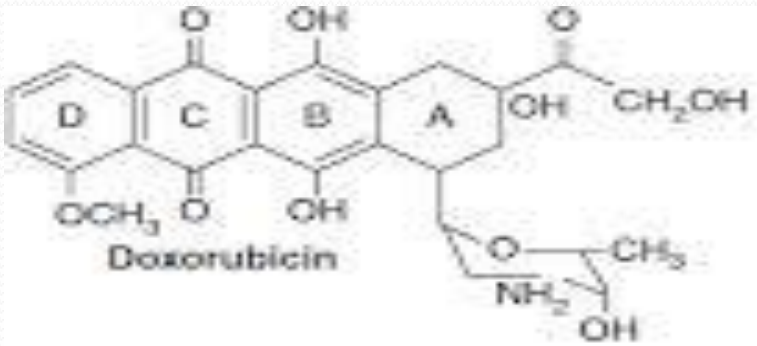


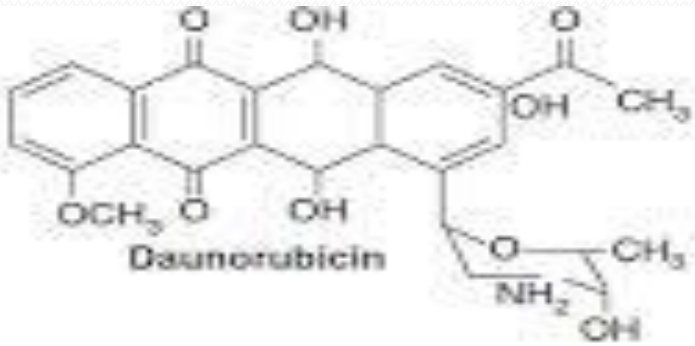
Structure &Mechanism

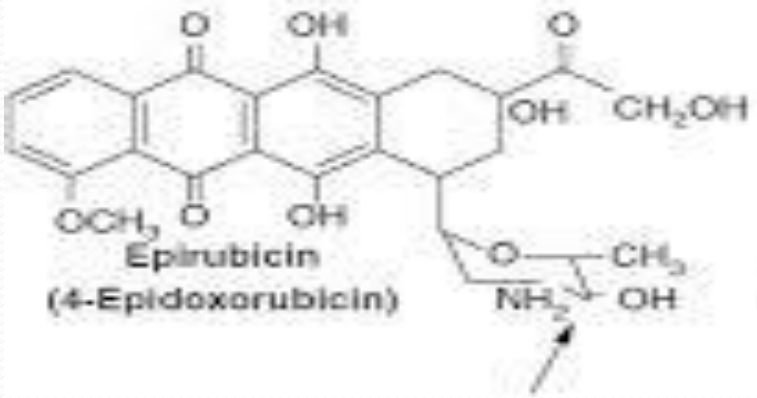
Mechanism of Action

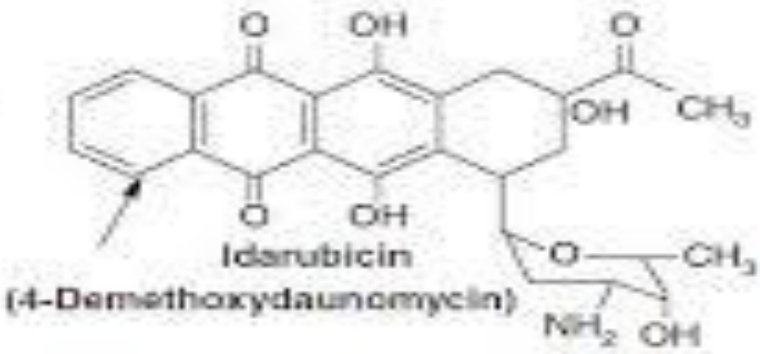
- Cell cycle nonspecific (predominant action on G2/S phase) of cell cycle.
- Various mechanisms are implicated for its cytotoxicity:
  - DNA intercalation.
  - Inhibition of topoisomerase II
  - Formation of cytotoxic oxygen free radical.

- Anthracyclines



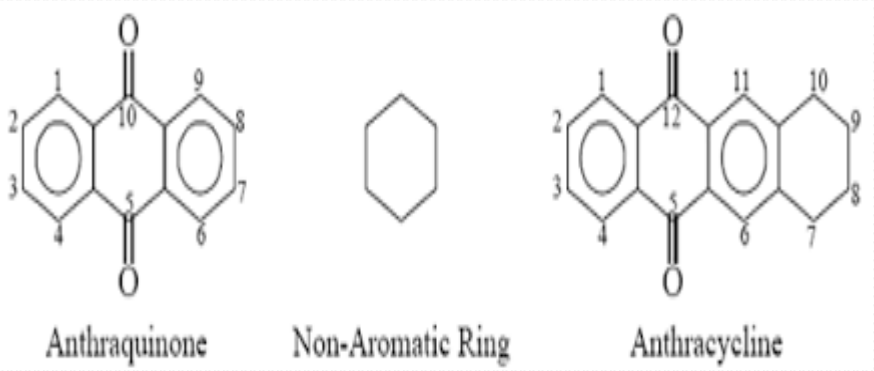




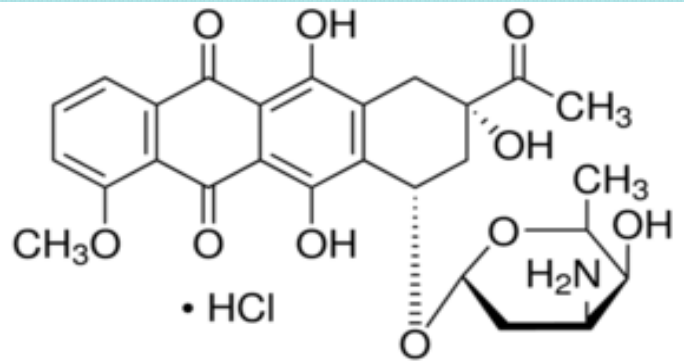


Anthracyclines nomenclature

- numbering



1.DAUNARUBICIN
(Rubidomycin, NORUBIN)



CATEGORY: cytotoxic antibiotic from ***Streptomyces Coeruleo rubidus*** , ***S. Peucetius***

NOMENCLATURE: 8-acetyl-10-[(3-amino-2,3,6-trideoxy-a-lyxo-hexopyranosyl)]-oxy-6,8,11-trihydroxy-1-methoxy ***7,8,9,10-Tetrahydronaphthacene-5,12-dione***

PROPERTIES: orange-red hygroscopic crystalline powder;

Stored in well closed light resistant container; freely soluble in water

MOA: act as a selective cytotoxic to tumor cells and topoisomerase II enzyme inhibitors

USES: Used to induce remission of acute lymphoblastic leukemia

DOSE: parenterally30-45mg/sq. m body surface daily for 2-3 days

PREPARATIONS: HCL salt as intravenous injection

2. Doxorubicin (Adriamycin; Doxil)

CATEGORY: cytotoxic/ Anthracycline-Antibitic

NOMENCLATURE: 10-[(3-amino-2,3,6-trideoxy-a-Llyxo-hexopyranosyl)]-oxy-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy 7,8,9,10-Tetrahydronaphthacene-5,12-dione

PROPERTIES: orange-red hygroscopic crystalline powder

Stored in well closed light resistant container; soluble in water

MOA: similar to ***Daunarubicin***

USES: Used in the treatment of acute leukemia, Hodgkin & non Hodgkin's disease; bone and soft tissue carcinoma, neuroblastoma, neoplasm of bladder, breast, lung, overy and thyroid.

DOSE: Parenterally 60-75mg/sq. m body surface area or 1.2-2.4mg/kg body wt. as single dose every 3 weeks

PREPARATIONS: HCL salt as Intravenous injection IP, BP