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PHARMACOKINETIC SOLUBILITY AND DISSOLUTION PROFILE OF ANTI-CANCER DRUGS

Achhrish goel[*1] , shivani saini[2] , Vicky chowdhry[3], syed azeem haider[1], robin kumar singh[1]
1.Teerthankar mahaveer college of pharmacy,Teerthankar mahaveer university,Moradabad
2.Guru Jambheshwar University of Science and Technology, Hisar, Haryana
3.Shoolini university,solan

Abstract
Pharmacokinetic data, Solubility Profile and Dissolution profile of drugs are the basic requirement of any researcher, for selecting an appropriate drug for any kind of formulation development. To get such data of all drugs of any category at one place is very difficult task; we by our review article have tried to give all such data of anticancer drugs at one place.

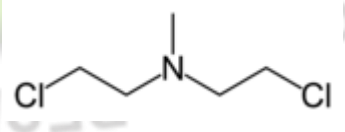
Keywords: - Solubility profile, pharmacokinetic parameters, Dissolution profile, Anticancer drugs.

Introduction
Classification: -
A. Drugs acting directly on cells (cytotoxic drugs)
1.Alkylating agent- Nitrogen mustards:- mechlorethamine cyclophosphamide, ifosamide, chlorabucil, melphalanethylenimine- thio-TEPA, alkyl sulfonate- busulfan, nitrosoureas- carmustine (BCNU), lomustine (CCNU), triazine- dacarbazine (DTIC)
2. Antimetabolites: Folate antagonist- methotrexate (Mtx)
Purineantagonist- 6-mercaptopurine, 6-thioguanine, azathioprine, fludarabine.
Pyrimidine antagonist- 5-flurouracil, cytarabine
3. Vinca alkaloid- vincristine, vinblastine
4. Taxane- paclitaxel, docetaxel
5. Epipodophyllo toxin-etoposide.
6. Camptothecin analogues- topotecan, irinotecan
7.Antibiotics- actinomycin D, doxorubicin, daunorubicin, mitoxantrone, belomycins, mitomycin C.
8. Miscellaneous-hydroxyurea, procarbazine, L-asparginase, cisplatin, carboplatin, imatinib.

Correspondence Address:
Achhrish goel
Teerthankar mahaveer college of pharmacy
Teerthankar mahaveer university,moradabad
Phone no: +91-9412367363
E-mail- achhrishgoel@yahoo.com

B. Drugs altering hormonal milieu
1. Glucocorticoids- prednisolone and others
2. Estrogens-fosfestrol, ethylinylestradiol
3. Selective estrogen receptor modulators- tamoxifen, toremifene.
4. Selective estrogen receptor down regulators- fulvestrant
5. Aromatase inhibitor- Letrozole, anastrozole, exemestane
6**. Antiandrogen-** flutamide, bicultamide
7.5-alpha reductase inhibitor - finasteride, dutasteride
8. GnRHanalogues- nafareline, triporelin
9. Progestins-hydroxyprogesterone acetate.(1)

Mechlorethamine[2]



Systematic (IUPAC) name: - 2-chloro-N-(2-chloroethyl)-N-methyl-ethanamine
Chemical Data: -
Molecular formula: - C5H11Cl2N**. [3]**
Molecular Weight: - 172.053 g/mol. **[4]**
Boiling Point: - 110.3°C at 760 mmHg**. [5]**
Melting point: - 108-111°C**. [6]**
Description: It is a light yellow brown, crystalline, hygroscopic *powder***.** ***[7]***
Solubility profile*:* - very soluble in water and also *soluble* in alcohol**. [8]**

Mechanism of Action: **-** Alkylating agents work by three different mechanisms: 1) attachment of alkyl groups to DNA bases, resulting in the DNA being fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA, 2) DNA damage via the formation of cross-links (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription, and 3) the induction of mispairing of the nucleotides leading to mutations. Mechlorethamine is cell cycle phase-nonspecific**. [9]**

Pharmacokinetic data: -

Bioavailability: - variable, with 20-50 per cent being excreted in the stool**. [10]**

Metabolism: - Rapid hydrolysis and demethylation, possibly in plasma

Half-life: - < 1 minute

Excretion: - Urine (50% as metabolites, <0.01% as unchanged drug)

LogP*:* - 0.91**. [11]**

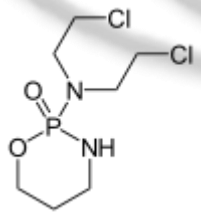
pKa: - 6.1**.[12]**

Nature: - Hydrophobic**. [13]**

Uses: - It has been derivatized into the estrogen analogue estramustine, used to treat prostate cancer.It can also be used in chemical warfare where it has the code-name HN2. This chemical is a form of nitrogen mustard gas and a powerful vesicant. [2]

Dissolution profile: - Not available.

Cyclophosphamide. [14]



Systematic (IUPAC) name: - *N*,*N*-bis(2-chloroethyl)-1,3,2-oxazaphosphinan-2-amine2-oxide

Chemical data: -

Formula: - C7H15Cl2N2O2P**.** ***[15]***

Molecular Weight*:* - 261.088 g/mol**. [16]**

Boiling point*:* - 407.5°C at 760 mmHg. **[17]**

Melting point: - (monohydrate) 41-45°C**. [18]**

Description: - white colored powder which makes a colorless solution when dissolved**. [19]**

Solubility profile: - Soluble in water and in alcohol**. [20][USP]**

Solubility profile: - Free soluble in ethanol (95%), soluble in water, slightly soluble in ether**. [21][IP]**

Mechanism of action: - Alkylating agents work by three different mechanisms: 1) attachment of alkyl groups to DNA bases, resulting in the DNA being fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA, 2) DNA damage via the formation of cross-links (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription, and 3) the induction of mispairing of the nucleotides leading to mutations**. [22]**

Pharmacokinetic data

Bioavailability: - >75% (oral)

Protein binding: - >60%

Metabolism: - Hepatic

Half-life: - 3-12 hours

Excretion: - Renal

***log P*: -** 1.5**. [23]**

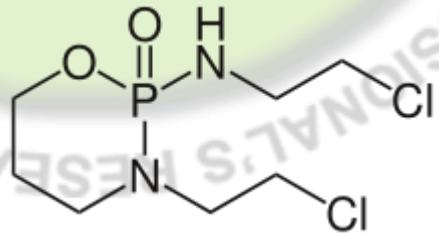
pKa: - 6.4**. [24]**

Nature: - Hydrophillic**. [25]**

Uses: - treat various types of cancer. It is a chemotherapy drug that works by slowing or stopping cell growth.Cyclophosphamide also works by decreasing your immune system's response to various diseases. It is used to treat a certain type of kidney disease in children after other treatments have not worked**. [26]**

Dissolution profile: - Not available.

Ifosfamide. [27]



Systematic (IUPAC) name: - *N*-3-*bis*(2-chloroethyl)-1,3,2-oxazaphosphinan-2-amide-2-oxide.

Chemical data: -

Molecular weight*:* - 261.1**. [28]**

Molecular formula: - C7H15Cl2N2O2P**. [29]**

Boiling Point*:* - 336.1 °C at 760 mmHg **... [30]**

Melting point: - 39 - 41 C**. [31]**

Description: - white crystalline *powder***. [32]**

Solubility profile: - Freely soluble in water, very soluble in alcohol, in ethyl acetate, in isopropyl alcohol, in methanol,in

ethylene chloride, very slightly soluble in hexane**. [33][USP]**

Mechanism of action: - The exact mechanism of ifosfamide has not been determined, but appears to be similar to other alkylating agents. Ifosfamide requires biotransformation in the liver by mixed-function oxidases (cytochrome P450 system) before it becomes active. After metabolic activation, active metabolites of ifosfamide alkylate or bind with many intracellular molecular structures, including nucleic acids. The cytotoxic action is primarily through the alkylation of DNA, done by attaching the N-7 position of guanine to its reactive electrophilic groups. The formation of inter and intra strand cross-links in the DNA results in cell death. **[34]**

Pharmacokinetic data

Bioavailability: - 100%**. [27]**

Metabolism: - Hepatic**. [27]**

Half-life: - 60-80% in 72 hours**. [27]**

Excretion: - Renal**. [27]**

Log p: **-** 0.28**. [35]**

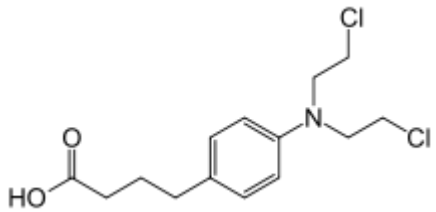
Pka: - 4.75**. [36]**

Nature: - *Hydrophobic. [37]*

Uses: **-** Ifosfamide is used to treat various cancers (such as testicular cancer). It works by slowing or stopping the growth of cancer cells. OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional. This drug may also be used to treat other types of cancer (such as sarcomas, lung cancer)**. [38]**

Dissolution profile: - Not available.

Chlorambucil. [39]



Systematic (IUPAC) name: - 4-[bis(2-chlorethyl)amino]benzenebutanoic acid.

Chemical data: -

Molecular mass**: -** 304.2. 1.2. **[40]**

Molecular formula**: -** *C14H19Cl2NO2***.** ***[41]***

Boiling Point: - 460.1 °C at 760 mmHg**. [42]**

Melting point: - 64℃**. [43]**

Description: - off-white, slightly granular *powder***.** ***[44]***

Solubility profile: - Very slightly soluble in water, freely soluble in acetone, soluble in dilute alkali. **[45][USP]**

Soubility profile: - Freely soluble in ethanol(95%), in acetone and in chloroform. Practically insoluble in water. **[46][IP]**

Mechanism of action: - Alkylating agents work by three different mechanisms: 1) attachment of alkyl groups to DNA bases, resulting in the DNA being fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA, 2) DNA damage via the formation of cross-links (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription, and 3) the induction of mispairing of the nucleotides leading to mutations**. [47]**

Pharmacokinetic data

Bioavailability: - ?

Metabolism: - Hepatic

Half-life: - 1.5 hours

Excretion: - N/A

pKa: **-** 5.8**. [48]**

LogP**: -** 3.25**. [49]**

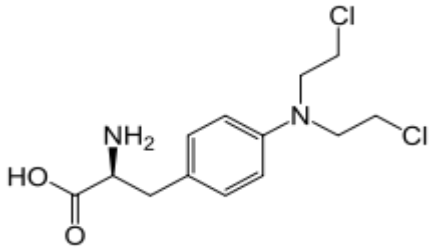
Nature: - Hydrophillic**. [50]**

Uses: - It is used to treat cancer of the blood and lymph system. It may also be used to treat other kinds of cancer, as determined by your doctor.

Chlorambucil interferes with the growth of cancer cells, which are eventually destroyed. Since the growth of normal body cells may also be affected by chlorambucil, other effects will also occur. Some of these may be serious and must be reported to your doctor. Other effects may not be serious but may cause concern. Some effects may not occur for months or years after the medicine is used**. [51]**

Dissloution profile; - Not available.

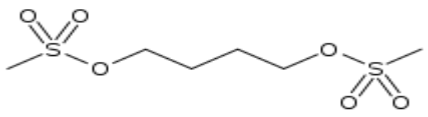
Melphalan. [52]



Systematic (IUPAC) name: - 4-[bis (chloroethyl) amino]phenylalanine

Chemical data: -
Molecular weight : - 305.20. **[53]**
Molecular weight: - 305.20. **[54]**
Boiling Point: - 473.1°Cat760mmHg**. [55]**
Melting point: - 177 ºC**. [56]**
Description: - white, to light yellow- ish white, crystalline powder**. [57]**
Solubility profile: - Practically insoluble in water, in chloroform and in ether, soluble in dilute mineral acid, slightly soluble in alcohol and in methanol. **[58][USP]**
Mechanism of action: - Alkylating agents work by three different mechanisms: 1) attachment of alkyl groups to DNA bases (primarily at the N-7 position of guanine and to a lesser extent, at the N-3 position of adenine), forming monoadducts and resulting in the DNA being fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA, 2) DNA damage via the formation of cross-links (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription, and 3) the induction of mispairing of the nucleotides leading to mutations**. [59]**
Pharmacokinetic data
Bioavailability: - 25% to 89%
Metabolism: - hydrolysis
Half-life: - 1.5 ± 0.8 hours
Excretion: - Renal, significantly metabolized
Log P: - 0.73**. [60]**
pKa (pH 7.4): - 1.83**. [61]**
Nature: - highly hydrophobic**. [62]**
Uses: - This medication is used to treat certain types of cancer (multiple myeloma, ovarian cancer). Melphalan belongs to a class of drugs known as alkylating agents. It works by slowing or stopping the growth of cancer cells**. [63]**
Dissolution Profile: - [64]
Medium: - 0.1 N hydrochloric acid, 900ml
Apparatus: - 2
RPM: - 50
Time: - 30

Busulfan. [65]

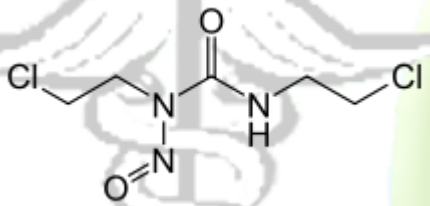


Systematic (IUPAC) name: - butane-1,4-diyl dimethanesulfonate
Chemical data: -
Molecular mass: - 246.3. 1.2**. [66]**
Molecular formula: -C6H14O6S2**. [67]**
Boiling point: - 464 °C at 760 mmHg**. [68]**
Melting Point: - 115~118º C**. [69]**
Description: - yellow powder**. [70]**
Solubility profile: - Freely soluble in acetone, in chloroform and in acetonitrile, very slightly soluble in water, in ethanol and in ether. **[71][IP]**
Solubility profile: - very slightly soluble in water, sparingly soluble in acetone , slightly soluble in alcohol**. [72][USP]**
Mechanism of action: - Busulfan is an alkylating agent that contains 2 labile methanesulfonate groups attached to opposite ends of a 4-carbon alkyl chain. Once busulfan is hydrolyzed, the methanesulfonate groups are released and carbonium ions are produced. These carbonium ions alkylate DNA, which results in the interference of DNA replication and RNA transcription, ultimately leading to the disruption of nucleic acid function. Specifically, its mechanism of action through alkylation produces guanine-adenine intrastrand crosslinks. This occurs through an SN2 reaction in which the relatively nucleophilic guanine N7 attacks the carbon adjacent to the mesylate leaving group. This kind of damage cannot be repaired by cellular machinery and thus the cell undergoes apoptosis. **[73]**
Pharmacokinetic data
Bioavailability: - 80% (oral)
Protein binding: - 32.4%
Metabolism: -Hepatic
Half-life : - .5 hours
Excretion: - Following administration of 14C- labeled busulfan to humans, approximately 30% of the radioactivity was excreted into the urine over 48 hours; negligible amounts were recovered in feces. **[74]**
Pka: - 3.8. **[75]**
Log p: - 0.39. **[76]**
Nature: - hydrophilic. **[76]**
Uses: - Busulfan can be used for the treatment of cancers of the blood cells (leukaemias) and to treat certain blood problems, such as polycythaemia vera.
Busulfan is also used in high doses to treat people who are going to have a bone marrow transplant (also called a stem cell transplant). Stem cells are blood cells at their earliest stage of development. Stem cells in the bone marrow mature into different cell types and are then released into the bloodstream. A stem cell transplant is used as a treatment for certain types of cancers involving the blood cells. Busulfan

is given before a stem cell transplant to destroy the existing stem cells and blood cells in the bone marrow and any remaining cancer cells. Other chemotherapy medicines are used as well. Busulfan is usually given every six hours for four days, starting seven days before the transplant. After the chemotherapy, the next step is to give an infusion of stem cells to replace the ones that have been destroyed. These stem cells find their way into the bone marrow, where they will then mature into new red blood cells, white blood cells and platelets. **[77]**

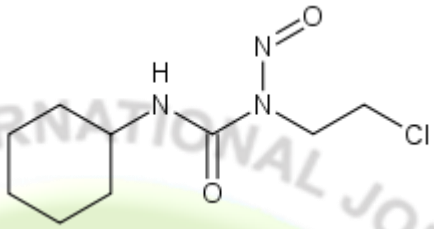
Dissolution Profile: - [78]
Medium: - Water, 500ml
Apparatus: - 2
RPM: - 50
Time: - 5,10,15,30

Carmustine. [79]



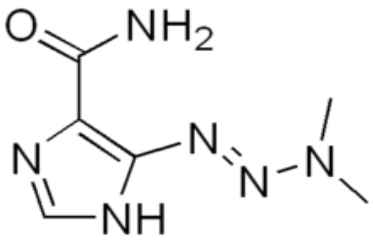
Systematic (IUPAC) name: -N,N′-bis(2-chloroethyl)-*N*-nitroso-urea
Chemical data: -
Molecular Weight: - 214.05**. [80]**
Molecular Formula: - C5H9Cl2N3O2**. [81]**
Boiling Point: - 404**. [82]**
Melting point: - 29.5-32°C**. [83]**
Description: - light yellow powder**. [84]**
Solubility profile: - very soluble in methylene chloride, freely *soluble* in ethanol, Soluble in water**. [85,86]**
Mechanism of action: - Carmustine causes cross-links in DNA and RNA, leading to the inhibition of DNA synthesis, RNA production and RNA translation (protein synthesis). Carmustine also binds to and modifies (carbamoylates) glutathione reductase. This leads to cell death**. [87]**
Pharmacokinetic data
Bioavailability: - 5 to 28% (oral)
Protein binding: -80%
Metabolism: -Hepatic (CYP1 A2-mediated)
Half-life: - 15 to 30 min
Pka value: - 1.5. **[88]**
log value: - 0.75. **[89]**
Nature: - Hydrophilic**. [90]**
Uses: - Carmustine is used to treat Hodgkin and non-Hodgkin lymphoma, multiple myeloma, and other types of cancer. The implantable wafer that contains Carmustine is used to treat gliomas, which are a type of brain tumor.

Lomustine. [91]



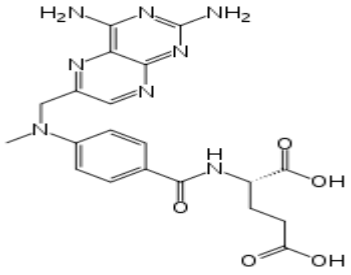
Systematic (IUPAC) name: - N-(2-chloroethyl)-*N′*-cyclohexyl-*N*-nitrosourea.
Chemical data: -
Molecular Weight: - 233.695 g/mol**. [92]**
Molecular Formula: - C9H16ClN3O2**. [93]**
Boiling Point: °C: - 760 mmHg**. [94]**
Melting Point: - 88-90 oC**. [95]**
Description: - yellow powder**. [96]**
Solubility profile: - Soluble in 10% ethanol (0.05 mg per mL) and in absolute alcohol (70 mg per mL), very slightly soluble *in* water**. [97, 98]**
Mechanism of action: - Lomustine is a highly lipophilic nitrosourea compound which undergoes hydrolysis in vivo to form reactive metabolites. These metabolites cause alkylation and cross-linking of DNA (at the O6 position of guanine-containing bases) and RNA, thus inducing cytotoxicity. Other biologic effects include inhibition of DNA synthesis and some cell cycle phase specificity. Nitrosureas generally lack cross-resistance with other alkylating agents. As lomustine is a nitrosurea, it may also inhibit several key processes such as carbamoylation and modification of cellular proteins**. [99]**
Pharmacokinetic data
Protein binding: - 50%
Half life: - 16 hours**. [100]**
Bioavailability: - 100%**. [101]**
Excretion: - Urine , Kidney**. [102]**
pKa: - 3.4. **[103]**
Log P: - 0.14**. [104]**
Uses: - This medication is used to treat various types of cancer. Lomustine belongs to a class of drugs known as alkylating agents. It works by slowing or stopping the growth of cancer cells. **[105]**
Dissolution profile: - Not available.

Dacarbazine. [106]



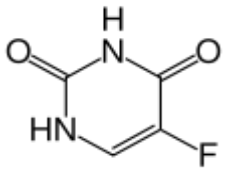
Systematic (IUPAC) name: - 5-(3,3-Dimethyl-1-triazenyl)imidazole-4-carboxamide.
Chemical data: -
Molecular Weight: - 182.18**. [107]**
Molecular formula: - C6H10N6O**. [108]**
Boiling Point: - 456.253 °C at 760**. [109]**
Melting point: - 205°C**. [110]**
Description: - White , toxic, light-sensitive powder**. [111][112]**
Solubility: - slightly soluble in ethanol and water**. [113]**
Mechanism of action: - The mechanism of action is not known, but appears to exert cytotoxic effects via its action as an alkylating agent. Other theories include DNA synthesis inhibition by its action as a purine analog, and interaction with SH groups. Dacarbazine is not cell cycle-phase specific**. [114]**
Pharmacokinetic data
Bioavailability: - 100%. **[115]**
Metabolism: - recombinant human CYP1A1, CYP1A2, and CYP2E1**. [116]**
Half-life: - 5 hours
Excretion: - 40% renal (unchanged)
pKa*:* - 4.42**. [117]**
LogP: - 1.938**. [118]**
Nature: - Hydrophillic**. [119]**
USES: Dacarbazine is used to treat certain types of cancer, such as skin cancer that has spread (metastatic malignant melanoma) and Hodgkin's disease. It is a cancer chemotherapy drug that is used alone or with other medications to slow or stop cancer cell growth**. [120]**
Dissolution profile: - Not available.

Methotrexate. [121]



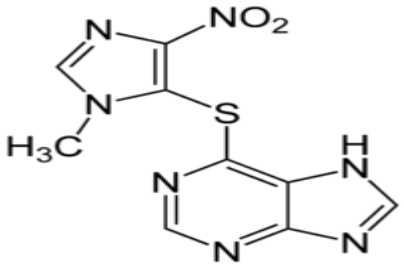
Systematic (IUPAC) name: - (2*S*)-2-[(4-{[(2,4-diaminopteridin-6-yl)methyl](methyl)amino}benzoyl)amino]pentanedioic acid.
Chemical data: -
Molecular weight: - 454.4444**. [122]**
Molecular formula: - C20H22N8O5**. [123]**
Boiling point: - 931.3 °C at 760 mmHg**. [124]**
Melting point: - 185-204°C**. [125]**
Description: - Yellow to orange brown crystalline powder**. [126]**
Solubility profile: - Practically insoluble in water, in alcohol, in chloroform and in ether, freely soluble in dilute solution of alkali hydroxides and carbonates, slightly soluble in 6N-hydrochloric acid**. [127][USP]**
Solubility profile: - Practically insoluble in water, 1,2 dichloro ethane, in ethanol and in ether. It dissolve in dilute solution of mineral acids and in dilute solution of alkali hydroxides and in carbonates. **[128][IP]**
Mechanism of action: - Methotrexate anti-tumor activity is a result of the inhibition of folic acid reductase, leading to inhibition of DNA synthesis and inhibition of cellular replication. The mechanism involved in its activity against rheumatoid arthritis is not known**. [129]**
Pharmacokinetic data
Bioavailability: - 17–90%
Metabolism: - hepatic
Half-life: -3–15hours (dose dependent)
Excretion: - renal48–100%
Pka value: - 3.8, 4.8, and 5.6**. [130]**
Log p: - 1.5-2.760**. [131]**
Nature: - Hydrophobic**. [132]**
Use: - Methotrexate is commonly used to treat neoplastic diseases, rheumatoid arthritis, and psoriasis. Methotrexate is also used to treat ectopic pregnancies, Crohn's disease, systemic lupus, and severe asthma and also used to treat in cancer**. [133]**
Dissolution Profile: - Methotrexate tablet. [134]
Medium: - 0.1 N hydrochloric acid, 900ml
Apparatus: - 2
RPM: - 50
Time: - 45

Fluorouracil. [135]



Systematic (IUPAC) name: - 5-fluoro-1*H*-pyrimidine-2,4-dione.
Chemical data: -
Molecular weight: - 130.08**. [136]**
Molecular formula: - C4H3FN2O2**. [137]**
Boiling Point: - 401.4 °C at 760 mmHg**. [138]**
Melting Point: - 282-283 °C**. [139]**
Description: - off-white to White powder**,** odorless crystalline powder. **[140]**
Solubility profile: - sparingly soluble in water, slightly soluble in alcohol practically insoluble in chloroform and in ether**. [141][USP]**
Solubility profile: - sparingly soluble in water, slightly soluble in ethanol, practically insoluble in chloroform and in ether. **[142][IP]**
Pharmacokinetic data
Bioavailability: - 28 to 100%
Protein binding: -8 to 12%
Metabolism: - Intracellular and hepatic (CYP-mediated)
Half-life: - 10 to 20 minutes
Excretion: - Renal
pKa: - 7.5**. [143]**
Log p: - 0.96 and 2.63**. [144]**
Nature: - Hydrophilic**. [145]**
Mechanism of action: - The precise mechanism of action has not been fully determined, but the main mechanism of fluorouracil is thought to be the binding of the deoxyribonucleotide of the drug (FdUMP) and the folate cofactor, N5–10-methylenetetrahydrofolate, to thymidylate synthase (TS) to form a covalently bound ternary complex. This results in the inhibition of the formation of thymidylate from uracil, which leads to the inhibition of DNA and RNA synthesis and cell death. Fluorouracil can also be incorporated into RNA in place of uridine triphosphate (UTP), producing a fraudulent RNA and interfering with RNA processing and protein synthesis. **[146]**
USES: This medication is used on the skin to treat pre-cancerous and cancerous skin growths. Fluorouracil belongs to a class of medications known as anti-metabolites. It works by blocking the growth of abnormal cells that cause the skin condition**. [147]**
Disslotion profile: - Not available.

Azathioprine. [148]

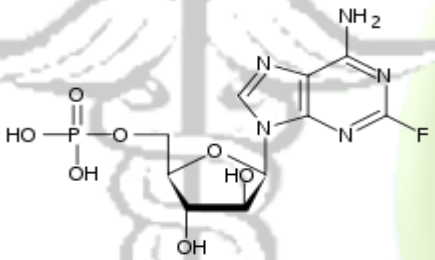


Systematic (IUPAC) name: - 6-[(1-methyl-4-nitro-1*H*-imidazol-5-yl)sulfanyl]-7*H*-purine
Chemical daa: -
Molecular Weight: - 277.26**. [149]**
Molecular formula: - C9H7N7O2S. [**150]**
Boiling Point: - 685.7 °C at 760 mmHg**. [151]**
Melting point*:* - 244 C**. [152]**
Description: - Pale yellow odorless powder**. [153]**
Solubility profile: - Insoluble in water, soluble in dilute solution of alkai hydroxides, sparingly soluble in dilute mineral acid, very slightly soluble in dilute alcohol and in chloroform**. [154][USP]**
Solubility profile: - practically insoluble in water and in ethanol, it is soluble in solution of alkali hydroxides and springly soluble in dilute mineral acid**. [155][IP]**
Mechanism of action; - Azathioprine antagonizes purine metabolism and may inhibit synthesis of DNA, RNA, and proteins. It may also interfere with cellular metabolism and inhibit mitosis. Its mechanism of action is likely due to incorporation of thiopurine analogues into the DNA structure, causing chain termination and cytotoxicity**. [156]**
Pharmacokinetic data
Bioavailability: - Well absorbed
Metabolism: - By xanthine oxidase
Half-life: - 3 hours
Excretion: - Renal, minimally
pKa: - 8.2. **[157]**
logP: - 1.17**. [158]**
Nature: - Hydrphillic. **[159]**
USES; - Azathioprine is used with other medications to prevent rejection of a kidney transplant. It works by weakening your body's defense system (immune system) to help your body accept the new kidney as if it were your own. This medication belongs to a class of drugs known as immunosuppressants.Azathioprine is also used to treat patients with severe rheumatoid arthritis who have not responded to other medications (e.g., nonsteroidal anti-inflammatory drugs/NSAIDs such as ibuprofen). Rheumatoid arthritis is thought to be caused by the immune system attacking the joints. Early treatment of rheumatoid arthritis with more aggressive therapy such as azathioprine helps to reduce further joint damage and to preserve joint

function.Talk to the doctor about the risks and benefits of azathioprine, especially when used in children and young adults.OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional.This medication may also be used to prevent rejection of other transplanted organs, to treat a certain type of bowel condition (Crohn's disease) that is not responsive to usual treatment, and to treat other immune system problems (autoimmune diseases) as determined by your doctor**. [160]**

Dissolution profile: - not available.

Fludarabine. [161]



Systematic (IUPAC) name: - [(2*R*,3*R*,4*S*,5*R*)-5-(6-amino-2-fluoro-purin-9-yl)- 3,4-dihydroxy-oxolan-2-yl]methoxyphosphonic.

Chemical daa: -

Molecular Weight: - 285.23**. [162]**

Molecular formula: - C10H13FN5O7P**. [163]**

Boiling Point: 864.2 °C at 760 mmHg**. [164]**

Melting Point: - 253.5 - 255°C**. [165]**

Description: -white or almost white powder**. [166]**

Solubility Profile: - Freely soluble in dimethyl formamide, slightly soluble in water and in 0.1 M hydrochloric acid, practically insoluble in ethanol**. [167][USP]**

Mechanism of action: - Fludarabine phosphate is rapidly dephosphorylated to 2-fluoro-ara-A and then phosphorylated intracellularly by deoxycytidine kinase to the active triphosphate, 2-fluoro-ara-ATP. This metabolite appears to act by inhibiting DNA polymerase alpha, ribonucleotide reductase and DNA primase, thus inhibiting DNA synthesis. The mechanism of action of this antimetabolite is not completely characterized and may be multi-faceted**. [168]**

Pharmacokinetic data

Bioavailability: - 55%

Protein binding: - 19 to 29%

Half-life: - 20 hours

Excretion: - Renal

Pka: - 3.2 ± 0.1**. [169]**

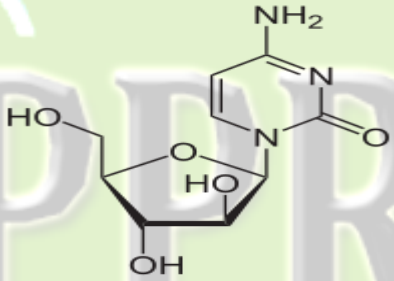
logP*:* - -3.97**. [168]**

Nature: - Hydrophiilic**. [170]**

Use: - Fludarabine interferes with the growth of cancer cells, which are eventually destroyed. Since the growth of normal body cells may also be affected by fludarabine, other effects will also occur. Some of these may be serious and must be reported to your doctor. Other effects may not be serious but may cause concern. Some effects may not occur for months or years after the medicine is used. **[171]**

Dissolution profile: - Not available.

Cytarabine. [172]



Systematic (IUPAC) name; - 4-amino-1-[(2R,3S,4R,5R)-3,4-dihydroxy-5- (hydroxymethyl)oxolan-2-yl] pyrimidin-2-one

Chemical data: -

Molecular Weight: - 243.22. **[173]**

Molecular formula: - C9H13N3O5**. [174]**

Boiling Point: - 545.7 °C at 760 mmHg**. [175]**

Melting point: - 212-213oC. **[176]**

Description: - odorless, white to off-white, crystalline powder**. [177]**

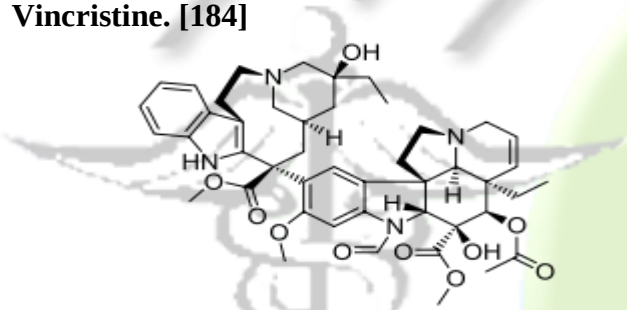
Solubility profile: - Freely soluble in water, slightly soluble in alcohol and in chloroform**. [178][USP]**

Solubility profile: - Freely soluble in wate, very slightly solble in ethnol and in dichloromethane**. [179][IP]**

Mechanism of action: - Cytarabine acts through direct DNA damage and incorporation into DNA. Cytarabine is cytotoxic to a wide variety of proliferating mammalian cells in culture. It exhibits cell phase specificity, primarily killing cells undergoing DNA synthesis (S-phase) and under certain conditions blocking the progression of cells from the G1 phase to the S-phase. Although the mechanism of action is not completely understood, it appears that cytarabine acts through the inhibition of DNA polymerase. A limited, but significant, incorporation of cytarabine into both DNA and

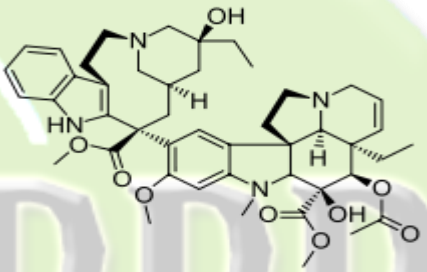
RNA has also been reported**. [180]**
Pharmacokinetic data
Bioavailability: - 20% oral
Protein binding; - 13%
Metabolism: - Liver
Half-life biphasic: - 10 min, 1-3 hr
Excretion: - Renal
Pka: - 4.2**. [181]**
log P: - −2.15**. [182]**
USES: - Cytarabine is used alone or with other medications to treat various types of cancer. It is a chemotherapy drug that works by slowing or stopping cancer cell growth**. [183]**
Dissolution profile: - Not available.

Vincristine. [184]



Systematic (IUPAC) name: - methyl (1*R*,9*R*,10*S*,11*R*,12*R*,19*R*)- 11-(acetyloxy).
Chemical data: -
Molecular weight: - 923.04**. [185]**
Molecular formula: - C46H56N4O10**. [186]**
Boiling Point: - 100 C (212 F**. [187]**
Melting point: - 284 ~ 285 ℃**. [188]**
Description: - white to off–white powder**. [189]**
Solubility profile: - Freely soluble in water, soluble in methanol, slightly soluble in alcohol**. [190][USP]**
Solubility profile: - Freely soluble in water, soluble in methanol, slightly soluble in ethanol and insoluble in water**. [191][IP]**
Mechanism of action: - The antitumor activity of Vincristine is thought to be due primarily to inhibition of mitosis at metaphase through its interaction with tubulin. Like other vinca alkaloids, Vincristine may also interfere with: 1) amino acid, cyclic AMP, and glutathione metabolism, 2) calmodulin-dependent Ca^{2+}-transport ATPase activity, 3) cellular respiration, and 4) nucleic acid and lipid biosynthesis**. [192]**
Pharmacokinetic data
Bioavailability: - n/a
Protein binding : - 75%
Metabolism; - Hepatic
Half-life: - 19 to 155 hours
Excretion: - Mostly biliary, 10% in urine
pK: - 7.4**. [193]**
Log p: - 2.14**. [194]**
Nature: - Hydrophillic**. [195]**
USES: - Vincristine is used to treat various types of cancer. It is a cancer chemotherapy drug that is usually used with other chemotherapy drugs to slow or stop cancer cell growth**. [196]**
Dissolution profile: - Not available**.**

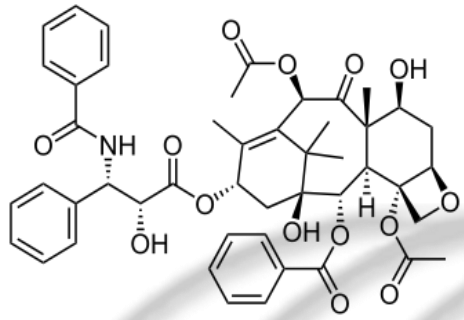
Vinblastine. [197]



Systematic (IUPAC) name dimethyl: - (2β,3β,4β,5α,12β,19α)- 15-[(5*S*,9*S*)- 5-ethyl- 5-hydroxy- 9-(methoxycarbonyl).
Chemical data: -
Molecular formula: - C46H58N4O9**. [198]**
Molecular weight: - 811**. [199]**
Boiling point: - Not available
Melting point: - 267**. [200]**
Description: - white to off-white powder**. [201]**
Solubility profile: - Freely soluble in water**. [202][USP]**
Solubility profile: - Freely soluble in wate, soluble in methanol, practically insoluble in ethaol ad in ether**. [203][IP]**
Mechanism of action: - The antitumor activity of vinblastine is thought to be due primarily to inhibition of mitosis at metaphase through its interaction with tubulin. Vinblastine binds to the microtubular proteins of the mitotic spindle, leading to crystallization of the microtubule and mitotic arrest or cell death**. [204]**
Pharmacokinetic data
Bioavailabilit: - n/a
Metabolism: - Hepatic (CYP3A4-mediated)
Half-life: - 24.8 hours (terminal)
Excretion: - Biliary and renal
Pka: - 7.9**. [205]**
Log p: - 3.51**. [206]**
Nature: - Hydrophilic**. [207]**

USES: - Vinblastine is used to treat cancer. It works by slowing or stopping the growth of cancer cells**. [208]**

Paclitaxel. [209]



Systematic (IUPAC) name: - (2α,4α,5β,7β,10β,13α)-4,10-bis(acetyloxy)-13-{[(2*R*,3*S*)- 3-(benzoylamino)-2-hydroxy-3-phenylpropanoyl]oxy}- 1,7-dihydroxy-9-oxo-5,20-epoxytax-11-en-2-yl benzoate.

Chemical Data: -

Molecular weight: - 853.9**. [210]**

Molecular formula: - C47H51NO14**. [211]**

Boiling point: - 979.829 °C**. [212]**

Melting point: - 213 - 216 C**. [213]**

Description: - white to off-white crystalline powder**. [214]**

Solubility profile: - insoluble in water and soluble in alcohol**. [215][USP]**

Solubility profile: - Insoluble in water and soluble in ethanol**. [216][IP]**

Mechanism of action: - Paclitaxel interferes with the normal function of microtubule growth. Whereas drugs like colchicine cause the depolymerization of microtubules in vivo, paclitaxel arrests their function by having the opposite effect; it hyper-stabilizes their structure. This destroys the cell's ability to use its cytoskeleton in a flexible manner. Specifically, paclitaxel binds to the β subunit of tubulin. Tubulin is the "building block" of mictotubules, and the binding of paclitaxel locks these building blocks in place. The resulting microtubule/paclitaxel complex does not have the ability to disassemble. This adversely affects cell function because the shortening and lengthening of microtubules (termed dynamic instability) is necessary for their function as a transportation highway for the cell. Chromosomes, for example, rely upon this property of microtubules during mitosis. Further research has indicated that paclitaxel induces programmed cell death (apoptosis) in cancer cells by binding to an apoptosis stopping protein called Bcl-2 (B-cell leukemia 2) and thus arresting its function**. [217]**

Pharmacokinetic data

Bioavailability: - 6.5% (oral)

Protein binding: - 89 to 98%

Metabolism: - Hepatic (CYP2C8 and CYP3A4)

Half-life: - 5.8 hours

Excretion: - Fecal and urinary

Pka: - 13.1**. [218]**

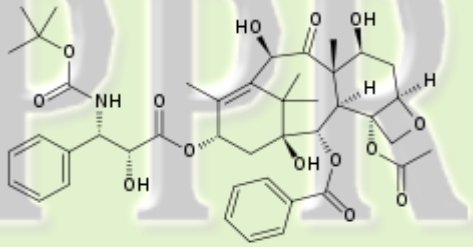
Log p: - 3.1**. [219]**

Nature: - Hydrophillic**. [220]**

USES: - Paclitaxel is used to treat various types of cancer. It is a cancer chemotherapy drug that works by slowing or stopping cancer cell growth**. [221]**

Dissolution profile: - Not available.

Docetaxel. [222]



Systematic (IUPAC) name: - 1,7β,10β-trihydroxy-9-oxo-5β,20-epoxytax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-{(2*R*,3*S*)-3-[(*tert*-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoate}

Chemical Data: -

Molecular weight: - 807.88**. [223]**

Molecular formula: - C43H53NO14**. [224]**

Boiling point: - 900.5**. [225]**

Melting point: - 232 oC**. [226]**

Description: - white to off-white crystalline powder**. [227]**

Solubility profile: - Soluble in ethanol, methanol, chloroform, Hardly *soluble* in water**. [228]**

Mechanism of action: - Docetaxel interferes with the normal function of microtubule growth. Whereas drugs like colchicine cause the depolymerization of microtubules in vivo, docetaxel arrests their function by having the opposite effect; it hyper-stabilizes their structure. This destroys the cell's ability to use its cytoskeleton in a flexible manner. Specifically, docetaxel binds to the β-subunit of tubulin. Tubulin is the "building block" of mictotubules, and the binding of docetaxel locks these building blocks in place. The resulting microtubule/docetaxel complex does not have

the ability to disassemble. This adversely affects cell function because the shortening and lengthening of microtubules (termed dynamic instability) is necessary for their function as a transportation highway for the cell. Chromosomes, for example, rely upon this property of microtubules during mitosis. Further research has indicated that docetaxel induces programmed cell death (apoptosis) in cancer cells by binding to an apoptosis stopping protein called Bcl-2 (B-cell leukemia 2) and thus arresting its function**. [229]**

Pharmacokinetic data

Bioavailability: - NA

Protein binding : - >98%

Metabolism: - Hepatic

Half-life: - 86 hours

Excretion: - Biliary

Pka: - 7.14**. [230]**

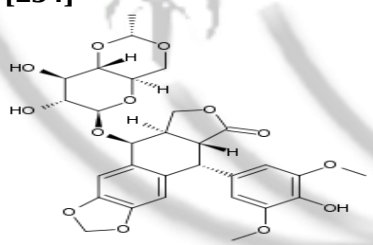
Log p: - 3.9**. [231]**

Nature: - Hydrophilic**. [232]**

USES: - This medication is used to treat cancer (such as breast, lung, prostate, stomach, and head/neck cancer). Docetaxel is a member of a family of drugs called taxanes. This drug works by slowing cell growth**. [233]**

Dissolution profile: - Not available**.**

Etoposide. [234]



Systematic (IUPAC) name: - 4'-demethyl-epipodophyllotoxin 9-[4,6-O-(*R*)-ethylidene-beta-D-glucopyranoside], 4' -(dihydrogen phosphate)

Chemical Data: -

Molecular weight: - 588.6**. [235]**

Molecular formula: - C29 H32 O13**. [236]**

Boiling point: - 798.1 °C at 760 mmHg**. [237]**

Melting point: - 236-251°C**. [238]**

Description: - White to yellow-brown crystal- line *powder*; white to off-white crystalline**. [239]**

Solubility profile: - Slightly soluble in water, slightly soluble in alcohol and chloroform,in ethyl acetate, in methylene chloride, sparingly soluble in methanol**. [240][USP]**

Solubility profile: - Practically insoluble in water, sparingly soluble in methanol, slightly soluble in ethanol and in methylene chloride.**[241][IP]**

Mechanism of action: - Etoposide inhibits DNA topoisomerase II, thereby inhibiting DNA re-ligation. This causes critical errors in DNA synthesis at the premitotic stage of cell division and can lead to apoptosis of the cancer cell.. Etoposide is cell cycle dependent and phase specific, affecting mainly the S and G2 phases of cell division**. [242]**

Pharmacokinetic data

Bioavailability: - Highly variable, 25 to 75%

Protein binding: - 97%

Metabolism: - Hepatic (CYP3A4 involved)

Half-life: - Oral: 6 h., IV: 6-12 h., IV in children: 3 h.

Excretion: - Renal and fecal

Pka: - 9.8**. [243]**

logP: - 1.16**.[242]**

Nature: - Hydrophilic**. [244]**

USES: Etoposide is used alone or in combination with other chemotherapies to treat testicular cancer that has not responded to other treatment and small cell lung cancer. Etoposide works by slowing cancer cell growth. It is also commonly known as VP-16.OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional.This drug may also be used to treat certain childhood cancers that have not responded to other treatment, certain types of leukemias, lymphomas, liver cancer, ovarian cancer, esophageal cancer, another type of lung cancer (non-small cell type), and a certain type of prostate cancer**. [245]**

Dissolution Profile: - Etoposide capsule. [246]

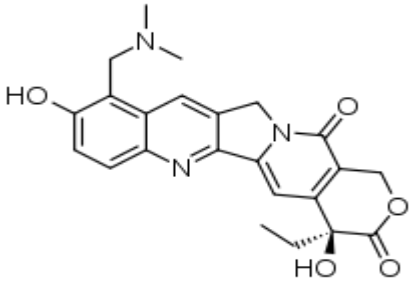
Medium: - ph4.5 acetate buffer, 900ml

Apparatus: - 2

RPM: - 50

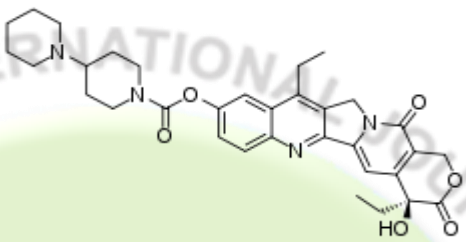
Time: - 30

Topotecan. [247]



Systematic (IUPAC) name: - (*S*)-10-[(dimethylamino)methyl]-4-ethyl-4,9- dihydroxy-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*] quinoline-3,14(4*H*,12*H*)-dione monohydrochloride
Chemical Data: -
Molecular weight: - 457.9**. [248]**
Molecular formula: - C23H23N3O5. **[249]**
Boiling point: - 782.9 °C at 760 mmHg. **[250]**
Melting point: - 213-218 °C. **[251]**
Description: - yellow to green powder. **[252]**
Solubility profile: - Soluble in water. **[253][IP]**
Mechanism of action: - Topotecan has the same mechanism of action as irinotecan and is believed to exert its cytotoxic effects during the S-phase of DNA synthesis. Topoisomerase I relieves torsional strain in DNA by inducing reversible single strand breaks. Topotecan binds to the topoisomerase I-DNA complex and prevents religation of these single strand breaks. This ternary complex interferes with the moving replication fork, which leads to the induction of replication arrest and lethal double-stranded breaks in DNA. As mammalian cells cannot efficiently repair these double strand breaks, the formation of this ternary complex eventually leads to apoptosis (programmed cell death). Topotecan mimics a DNA base pair and binds at the site of DNA cleavage by intercalating between the upstream (−1) and downstream (+1) base pairs. Intercalation displaces the downstream DNA, thus preventing religation of the cleaved strand. By specifically binding to the enzyme–substrate complex, Topotecan acts as an uncompetitive inhibitor.**[254]**
Pharmacokinetic data
Bioavailability: - 31.4 % in humans
Protein binding: - 35%
Metabolism: - Hepatic
Half-life: -2-3 hours
Excretion: - Renal
Pka: - 10.50. [**255]**
Log p: - 0.033. **[256]**
Nature: - Hydrophilic**. [257]**
Uses: - This medication is used to treat cancer of the ovaries or lungs when other treatments have not been successful. It is also used with another medication (cisplatin) to treat cancer of the cervix.OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional.This medication may also be used to treat other types of cancer (such as bone cancer).**[258]**
Dissolution profile: - Not available.

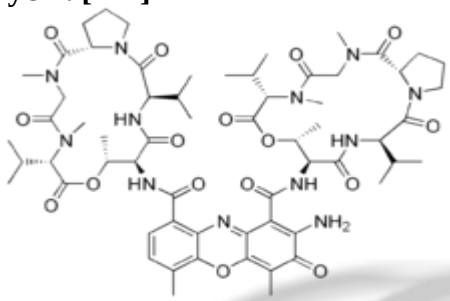
Irinotecan. [259]



Systemic IUPAC name: - (*S*)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy- 3,14-dioxo1*H*-pyrano[3',4':6,7]-indolizino[1,2-b]quinolin-
Chemical Data: -
Molecular weight: - 677.19. **[260]**
Molecular formula: - C33H39ClN4O6. **[261]**
Boiling point: - 873.4 °C at 760 mmHg. **[262]**
Melting point: - 222-223 oC. **[263]**
Description: - pale yellow to yellow crystalline powder. **[264]**
Solubility profile: - soluble in water. **[265][IP]**
Mechanism of action: - Irinotecan inhibits the action of topoisomerase I. Irinotecan prevents religation of the DNA strand by binding to topoisomerase I-DNA complex. The formation of this ternary complex interferes with the moving replication fork, which induces replication arrest and lethal double-stranded breaks in DNA. As a result, DNA damage is not efficiently repaired and apoptosis (programmed cell death) occurs. **[266]**
Pharmacokinetic data
Bioavailability: - NA
Metabolism: - Hepatic glucuronidation
Half-life: - 6 to 12 hours
Excretion: - Biliary and renal
Pka: - 8.79. [**267]**
Log p: - 4.37. **[268]**
Nature: - Hydrophobic. **[269]**
Uses: - This medication is used to treat cancer of the colon and rectum.OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional.This drug may also be used to treat other

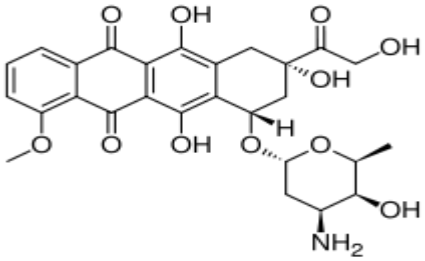
types of cancer (such as lung, bone cancer). **[270]**
Dissolution profile: - Not available.

Actinomycin. [271]



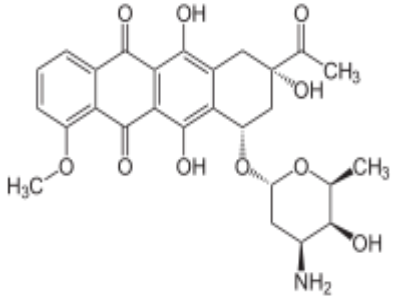
Systematic (IUPAC) name: - 2-amino-*N*,*N*′-bis[(6*S*,9*R*,10*S*,13*R*,18a*S*)- 6,13-diisopropyl- 2,5,9-trimethyl- 1,4,7,11,14-pentaoxohexadecahydro-1*H*-pyrrolo[2,1-*i*] [1,4,7,10,13] oxatetraazacyclohexadecin- 10-yl]- 4,6-dimethyl-3-oxo- 3*H*-phenoxazine- 1,9-dicarboxamide
Chemical Data: -
Molecular weight: - 1255.42**. [272]**
Molecular formula: - C62H86N12O16**. [273]**
Boiling point: - 1392.8°Cat760mmHg. **[274]**
Melting point: - 245°-252°C**. [275]**
Description: - red, highly hygroscopic crystallic powder**. [276]**
Solubility profile: - Soluble in ethanol, methanol, DMF or DMSO. Slightly *soluble* in water. **[277]**
Mechanism of action: - Good evidence exists that this drug bind strongly, but reversibly, to DNA, interfering with synthesis of RNA (prevention of RNA polymerase elongation) and, consequently, with protein synthesis**. [278]**
Pharmacokinetic data
Protein binding: - 5%
Half-life: - 36 hours
Pka: - 5-10 × 106. M. **[279]**
Log p: - 2.9. **[280]**
Nature: - Hydrophobic**. [281]**
Use: - Actinomycin D is an antineoplastic antibiotic that inhibits cell proliferation. It is a cytotoxic inducer of apoptosis against tumor cells. The compound inhibits the proliferation of cells in a nonspecific way by forming a stable complex with double-stranded DNA (via deoxyguanosine residues), thus inhibiting DNA-primed RNA synthesis. It also causes single-strand breaks in DNA. **[282]**
Disolution profile: - Not available.

Doxorubicin. [283]



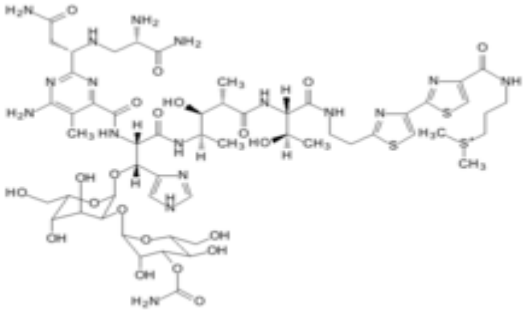
Systemic IUPAC name: - (7S,9S)-7-[(2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyloxan-2-yl]oxy-6,9,11-trihydroxy-9-(2-hydroxyacetyl)-4-methoxy-8,10-dihydro-7H-tetracene-5,12-dione.
Chemical Data: -
Molecular weight: - 579.98**. [284]**
Molecular formula: - C27H29NO11**. [285]**
Boiling point: - 810.3 °C at 760 mmHg. **[286]**
Melting point: - 204 - 205oC. **[287]**
Description: - sterile red-orange lyophilized powder. **[288]**
Solubility profile: - soluble in water, isotonic sodium chloride solution nad in methanol, practically insoluble in chloroform, in ether and in other organic solvents. **[289][USP]**
Solubility profile: - soluble in water, slightly soluble in methanol and practically insoluble in chloroform, in ether and in other organic solvents. **[290][IP]**
Mechanism of action: - Doxorubicin has antimitotic and cytotoxic activity through a number of proposed mechanisms of action: Doxorubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase II activity by stabilizing the DNA-topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzes. **[291]**
Pharmacokinetic data
Bioavailability: - 5% (Oral)
Metabolism: - CYP3A4
Half-life: - 12–18.5 hours when released from liposomes
Excretion: - Biliary and fecal
Pka: - 7.6. **[292]**
Log p: - 1.5. **[293]**
Nature: - Hydrophillic. **[294]**
Use: -It cause a decrease in the number of blood cells in your bone marrow. Prolonged use of doxorubicin can also cause severe heart damage, even years after you have stopped taking doxorubicin. The risk of heart damage after stopping doxorubicin is higher in children. **[295]**
Dissolution profile: - Not available.

Daunorubicin. [296]



Systematic (IUPAC) name: - (8*S*,10*S*)-8-acetyl-10-[(2*S*,4*S*,5*S*,6*S*)- 4-amino-5-hydroxy-6-methyl-oxan- 2-yl]oxy-6,8,11-trihydroxy-1-methoxy- 9,10-dihydro-7*H*-tetracene-5,12-dione.
Chemical Data: -
Molecular weight: - 563.99. **[297]**
Molecular formula: - C27H29NO10. [**298]**
Boiling point: - 770 °C at 760 mmHg. **[299]**
Melting point: - 190. **[300]**
Description: - hygroscopic, crystalline, orange-red powder. **[301]**
Solubility profile: - Freely soluble in water and in methanol, slightly soluble in alcohol, very slightly soluble in alcohol, practically insoluble in acetone**. [302][USP]**
Mechanism of action: - Daunorubicin has antimitotic and cytotoxic activity through a number of proposed mechanisms of action: Daunorubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase II activity by stabilizing the DNA-topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzes. **[303]**
Pharmacokinetic data
Metabolism: - Hepatic
Half-life: - 26.7 hours (metabolite)
Excretion: - Biliary and urinary
Pka: - 10.3. **[304]**
Log p: - 1.26. **[303]**
Nature: - Hydrophillic. **[305]**
Use: - Daunorubicin is used to treat leukemia and other cancers. It belongs to a class of drugs known as anthracyclines and works by slowing or stopping the growth of cancer cells. **[306]**
Dissolution profile: - Not available.

Bleomycin. [307]

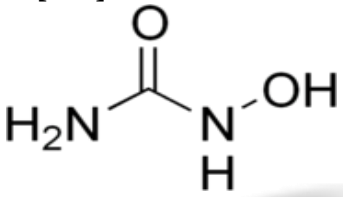


Systematic (IUPAC) name: - (3-{[(2'-{(5*S*,8*S*,9*S*,10*R*,13*S*)-15-{6-amino-2- [(1*S*)-3-amino-1-{[(2*S*)-2,3-diamino-3-oxopropyl]amino}-3-oxopropyl] -5-methylpyrimidin-4-yl}-13-[{[(2*R*,3*S*,4*S*,5*S*,6*S*)-3- {[(2*R*,3*S*,4*S*,5*R*,6*R*)-4-(carbamoyloxy)-3,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy} -4,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy} (1*H*-imidazol-5-yl)methyl]-9-hydroxy-5-[(1*R*)-1-hydroxyethyl]-8,10-dimethyl-4,7,12,15-
Chemical Data: -
Molecular weight: - 1414. **[308]**
Molecular formula: - : C55H84N17O21S3. **[309]**
Boiling point: - 810.3°Cat760mmHg. **[310]**
Melting point: - 71oC. **[311]**
Description: - Creamed colored amorphous powder. **[312][USP]**
Solubility profile: - Very soluble in water. **[312][USP]**
Solubility profile: - very soluble in water. **[313][IP]**
Mechanism of action: - Although the exact mechanism of action of bleomycin is unknown, available evidence would seem to indicate that the main mode of action is the inhibition of DNA synthesis with some evidence of lesser inhibition of RNA and protein synthesis. DNA cleavage by bleomycin depends on oxygen and metal ions, at least in vitro. It is believed that bleomycin chelates metal ions (primarily iron) producing a pseudoenzyme that reacts with oxygen to produce superoxide and hydroxide free radicals that cleave DNA. **[314]**
Pharmacokinetic data
Bioavailability well absorbed
Metabolism: - Tissue. **[315]**
Half-life 2 hours
Excretion renal (60-70%)
Pka: - 7.3. **[316]**
Log p: - -3.62. **[317]**
Nature: - Hydrophobic. **[318]**
Uses: - Bleomycin is used to treat cancer. It works by slowing or stopping the growth of cancer cells.This medication may also be used to control the build-up of fluid around the lungs (pleural effusion) caused by tumors that

have spread to the lungs. For this condition, bleomycin is placed in the space around the lungs through a chest tube. **[319]**

Dissloution profile: - Not available.

Hydroxyurea. [320]



Systematic (IUPAC) name: - hydroxyurea.

Chemical Data: -

Molecular weight: - 76.05. **[321]**

Molecular formula: - CH4N2O2. **[322]**

Boiling point: - 350.8 ºC at760mmHg. **[323]**

Melting point: - 142-146 ºC. **[324]**

Description: - white crystalline powder. **[325]**

Solubility profile: - Free soluble in water aned in alcohol. **[326][USP]**

Mechanism of action: - Hydroxyurea is converted to a free radical nitroxide (NO) in vivo, and transported by diffusion into cells where it quenches the tyrosyl free radical at the active site of the M2 protein subunit of ribonucleotide reductase, inactivating the enzyme. The entire replicase complex, including ribonucleotide reductase, is inactivated and DNA synthesis is selectively inhibited, producing cell death in S phase and synchronization of the fraction of cells that survive. Repair of DNA damaged by chemicals or irradiation is also inhibited by hydroxyurea, offering potential synergy between hydroxyurea and radiation or alkylating agents. Hydroxyurea also increases the level of fetal hemoglobin, leading to a reduction in the incidence of vasoocclusive crises in sickle cell anemia. Levels of fetal hemoglobin increase in response to activation of soluble guanylyl cyclase (sGC) by hydroxyurea-derived NO. **[327]**

Pharmacokinetic data

Metabolism: - Liver

Half-life: - 3-4 hours

Excretion: - Renal and lungs

Protein binding: - 75% and 80%. **[328]**

Pka: - 10.65. **[329]**

Log p: - -2.46. **[330]**

Nature: - Hydrophillic. **[331]**

USES: This medication is used in people with sickle cell anemia to reduce the number of painful crises caused by the disease and to reduce the need for blood transfusions. It is also used to treat several types of cancer (such as melanoma, chronic myelogenous leukemia, squamous cell carcinomas).OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional.This drug may also be used to treat polycythaemia vera and thrombocythemia. **[332]**

Dissolution Profile: - Hydroxyurea. [333]

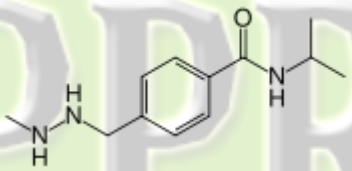
Medium: - water, 500ml

Apparatus: - 2

RPM: - 50

Time: - 30

Procarbazine. [334]



Systematic (IUPAC) name: - *N*-isopropyl-4-[(2-methylhydrazino)methyl]benzamide

Chemical Data: -

Molecular weight: - 257.76. **[335]**

Molecular formula: - C12H19N3O. **[336]**

Boiling point: - 384.6 °C at 760 mmHg. **[337]**

Melting point: - *223* oC. **[338]**

Description: - white to pale yellow crystalline powder. **[339]**

Solubility profile: - soluble in water, methanol, chloroform, and diethyl ether and is sensitive to oxidation. **[340]**

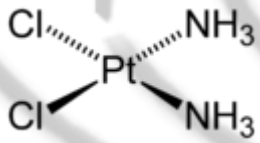
Mechanism of action: - The precise mode of cytotoxic action of procarbazine has not been clearly defined. There is evidence that the drug may act by inhibition of protein, RNA and DNA synthesis. Studies have suggested that procarbazine may inhibit transmethylation of methyl groups of methionine into t-RNA. The absence of functional t-RNA could cause the cessation of protein synthesis and consequently DNA and RNA synthesis. In addition, procarbazine may directly damage DNA. Hydrogen peroxide, formed during the auto-oxidation of the drug, may attack protein sulfhydryl groups contained in residual protein which is tightly bound to DNA. **[341]**

Pharmacokinetic data

Bioavailability: - 100%**. [342]**

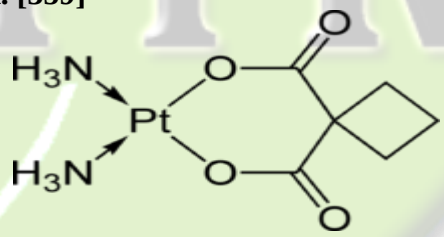
Metabolism: - Hepatic, Renal. **[334]**
Half-life: - 10 minutes. . **[334]**
Excretion: - Renal. . **[334]**
Pka: - 9.0. **[343]**
Log p: - .50. **[344]**
Nature: - Hydrophobic. **[345]**
Uses: - Procarbazine is an alkylating chemotherapy drug used along with other chemotherapy drugs to treat Hodgkin's disease (also known as Hodgkin's lymphoma). It works by preventing cancer cells from growing and from creating new cancer cells. Because procarbazine also affects the growth of normal body cells, you will most likely experience side effects while using this drug.Procarbazine also acts as a monoamine oxidase inhibitor. (See also Drug Interactions for cautions regarding use of procarbazine with other drugs and the need to limit the amount of tyramine in your diet.)OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional.This drug may also be used to treat other cancers such as brain tumors. **[346]**
Dissolution profile: - Not available.

Cisplatin. [347]



Systematic (IUPAC) name: - (*SP*-4-2)-diamminedichloridoplatinum.
Chemical Data: -
Molecular weight: - 300.1 **[348]**
Molecular formula: - PtCl2H6N2. **[349]**
Boiling point: - 483.3. **[350]**
Melting point: - 270°. **[351]**
Description: - white to light yellow lyophilized powder. **[352]**
Solubility profile: - Sparingly soluble in dimethylformamide, slightly soluble in water, practically insoluble in ethanol. **[353][IP]**
Mechanism of action: - Alkylating agents work by three different mechanisms: 1) attachment of alkyl groups to DNA bases, resulting in the DNA being fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA, 2) DNA damage via the formation of cross-links (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription, and 3) the induction of mispairing of the nucleotides leading to mutations. **[354]**
Pharmacokinetic data
Bioavailability: - complete
Protein binding: - > 95%
Metabolism: - 56
Half-life: - 30-100 hours
Excretion: - Renal
pKa: - 6.56. **[355]**
log P: - 2.17. **[356]**
Nature: - Hydrophillic. **[357]**
Uses: - Cisplatin may cause severe kidney problems or very serious allergic reactions. Hearing loss (more common in children), bleeding problems, a decrease in your body's ability to fight infections (bone marrow suppression), and severe nausea and vomiting may occur as well. Your risk of these problems increases with higher doses or longer treatment with cisplatin. **[358]**
Dissolution profile: - not available.

Carboplatin. [359]



Systematic (IUPAC) name: - cis-diammine(cyclobutane-1,1-dicarboxylate-*O*,*O'*)platinum(II)
Chemical Data: -
Molecular weight: - 371.24848 g/mol. **[360]**
Molecular formula: - C6H12N2O4Pt. **[361]**
Boiling point: - 383C. **[362]**
Melting point: - 228-230 °C. **[363]**
Description: - yellow crystalline powder. **[364]**
Solubility profile: - sparingly soluble in water, very slightly soluble in alcohol. **[365]**
Mechanism of action: - Alkylating agents work by three different mechanisms: 1) attachment of alkyl groups to DNA bases, resulting in the DNA being fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA, 2) DNA damage via the formation of cross-links (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription, and

3) the induction of mispairing of the nucleotides leading to mutations. **[366]**

Pharmacokinetic data

Bioavailability: - complete

Protein binding: - Very low

Half-life: -1.1-2 hours

Excretion: - hepatic

Pka: - 6.56. **[367]**

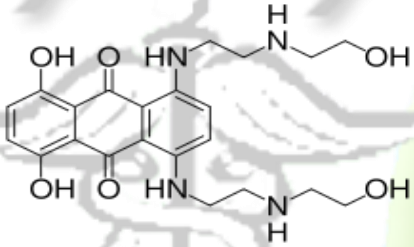
Log p: - 7.2. **[368]**

Nature: - Hydrophobic. **[369]**

Uses: Carboplatin is used to treat advanced-stage breast cancer and usually is given in combination with other chemotherapy medicines. **[370]**

Dissolution profile: - Not available.

Mitoxantrone. [371]



Systematic IUPAC name: - 1,4-dihydroxy-5,8-bis[2-(2-hydroxyethylamino) ethylamino]-anthracene-9,10-dione.

Chemical Data: -

Molecular weight: - 517.41. **[372]**

Molecular formula: - C22H28N4O6. **[373]**

Boiling point: - 805.7 °C at 760 mmHg. **[374]**

Melting point: - 60–162 °C. **[375]**

Description: - dark-blue, electrostatic, hygroscopic powder. **[376]**

Solubility profile: - Sparingly soluble in water, slightly soluble in methanol, practically insoluble in acetone, in acetonitrile and in chloroform. **[377]**

Mechanism of action: - Mitoxantrone, a DNA-reactive agent that intercalates into deoxyribonucleic acid (DNA) through hydrogen bonding, causes crosslinks and strand breaks. Mitoxantrone also interferes with ribonucleic acid (RNA) and is a potent inhibitor of topoisomerase II, an enzyme responsible for uncoiling and repairing damaged DNA. It has a cytocidal effect on both proliferating and nonproliferating cultured human cells, suggesting lack of cell cycle phase specificity. **[378]**

Pharmacokinetic data

Bioavailability: - Good. **[379]**

Protein binding: - 78%

Metabolism: - Hepatic (CYP2E1)

Half-life: - 75 hours Excretion Renal

Pka: - 5.99. **[380]**

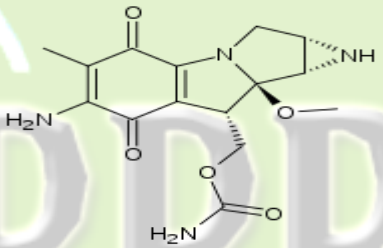
Log p: - 0.034. **[381]**

Nature: - Hydrophillic. **[382]**

Uses: - Mitoxantrone is used to treat leukemia and other cancers. It is also used to treat multiple sclerosis. It belongs to a class of drugs known as anthracenediones and works by slowing or stopping the growth of certain cells (including cancer cells and cells that affect the body's natural defenses). **[383]**

Dissolution profile: - Not available.

Mitomycin. [384]



IUPAC name: - [6-Amino-8a-methoxy-5-methyl-4,7-dioxo-1,1a,2,4,7,8,8a,8boctahydroazireno[2',3':3,4]pyrrolo[1,2-*a*]indol-8-yl]methyl carbamate.

Chemical Data: -

Molecular weight: - 334.33. **[385]**

Molecular formula: - C15H18N4O5. **[386]**

Boiling point: - 581.8°C at 760 mmHg. **[387]**

Melting point: - 159-161°C. **[388]**

Description: - blue-purple crystals or crystalline powder. **[389]**

Solubility profile: - Slightly soluble in water, soluble in acetone, in methanol , in butylacetate and in cyclohexanone. **[390][USP]**

Mechanism of action: - Mitomycin is activated in vivo to a bifunctional and trifunctional alkylating agent. Binding to DNA leads to cross-linking and inhibition of DNA synthesis and function. Mitomycin is cell cycle phase-nonspecific. **[391]**

Pharmacokinetic data: -

Metabolism: - Hepatic

Elimination half-life: - 8-48 min.

Pka: - 3.2. **[392]**

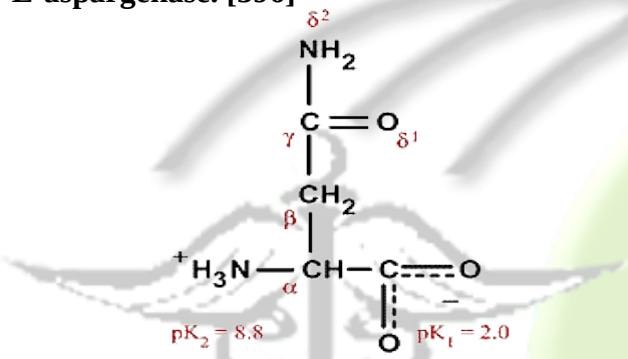
Log p: - -. 0.49. **[393]**

Nature: - Hydrophobic. **[394]**

Uses: - Mitomycin is used with other drugs to treat various types of cancer (such as stomach/pancreas cancer). It works

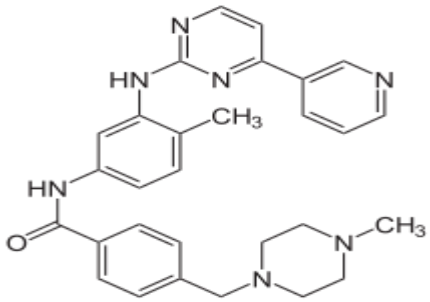
by slowing or stopping the growth of cancer cells. OTHER This section contains uses of this drug that are not listed in the approved professional labeling for the drug but that may be prescribed by your health care professional. Use this drug for a condition that is listed in this section only if it has been so prescribed by your health care professional.This drug may also be used to treat other types of cancers (such as lung cancer). **[395]**
Dissolution profile: - Not available.

L-aspargenase. [396]



Systematic (IUPAC) name: - E. coli L-asparagine amidohydrolase**. [397]**
Chemical Data: -
Molecular weight: - 171000 to 180000. **[398]**
Molecular formula: - Not available.
Boiling point: - 438.029 °C at 760 mmHg. **[399]**
Melting point: - 233-235 ° C. **[400]**
Description: - white lyophilized powder. **[401]**
Solubility profile: - Soluble in water, practically insoluble in alcohol and in ether, its solution are acids to litmus. **[402][USP]**
Mechanism of action: - Asparagine used for protein synthesis is generated from aspartate by asparagine synthase; asparagine outside the cell is converted to aspartate by L-ASPARAGINASE before being pumped into the cell and converted back to asparagines. **[403]**
Pharmacokinetic data
Half-life: - 8-30 hrs
Pka: - 6.58. **[404]**
Log p: - 0.289. **[405]**
Nature: - Hydrophillic. **[406]**
Uses: - Introduced into Erythrocytes for the Treatment of Leukaemia. **[407]**
Disslotion profile: - Not available.

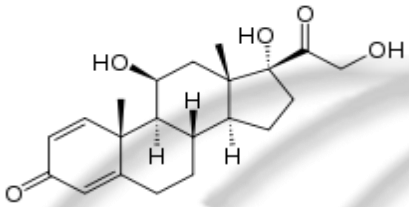
Imatinib. [408]



Systematic (IUPAC) name: - 4-[(4-methylpiperazin-1-yl)methyl]-*N*-(4-methyl-3-{[4-(pyridin-3-yl)pyrimidin-2-yl]amino}phenyl)benzamide.
Chemical Data: -
Molecular weight: - 493.60274 [g/mol]. **[409]**
Molecular formula: - C29H31N7O. **[410]**
Boiling point: - 754.9 °C at 760 mmHg. **[411]**
Melting point: - 226. **[412]**
Description: - white to off-white to brownish or yellowish tinged crystalline powder. **[413]**
Solubility profile: - soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, poorly soluble in water. **[414][415]**
Mechanism of action: - Imatinib mesylate is a protein-tyrosine kinase inhibitor that inhibits the Bcr-Abl tyrosine kinase, the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in chronic myeloid leukemia (CML). It inhibits proliferation and induces apoptosis in Bcr-Abl positive cell lines as well as fresh leukemic cells from Philadelphia chromosome positive chronic myeloid leukemia. Imatinib also inhibits the receptor tyrosine kinases for platelet derived growth factor (PDGF) and stem cell factor (SCF) - called c-kit. Imatinib was identified in the late 1990s by Dr Brian J. Druker. Its development is an excellent example of rational drug design. Soon after identification of the bcr-abl target, the search for an inhibitor began. Chemists used a high-throughput screen of chemical libraries to identify the molecule 2-phenylaminopyrimidine. This lead compound was then tested and modified by the introduction of methyl and benzamide groups to give it enhanced binding properties, resulting in imatinib. **[416]**
Pharmacokinetic data
Bioavailability: - 98%
Protein binding: - 95%
Metabolism: - Hepatic (mainly CYP3A4-mediated)
Half-life: - 18 hours (imatinib) 40 hours (active metabolite)
Excretion: - Fecal (68%) and renal (13%)
Pka: - 1.52-8.07. **[417]**
logP: - 1.267 at 37°C. **[418]**

Nature: - Hydrophillic. **[419]**
Use: - Treat chronic myeloid leukaemia. NICE has recommended that imatinib should be the first treatment considered for an adult with the Philadelphia-chromosome type of CML in the chronic phase. **[420]**
Dissolution profile: - Not available.

Predinisolone. **[421]**



Systematic (IUPAC) name: - (11β)-11,17,21-trihydroxypregna-1,4-diene-3,20-dione.
Chemical Data: -
Molecular weight: - 358.43. **[422]**
Molecular formula: - C21H28O5. **[423]**
Boiling point: - 674.8 ºC at 760 mmHg. **[424]**
Melting point: - 233 - 235 C. **[425]**
Description: - White to practically white, odorless, crystalline powder. **[426]**
Solubility profile: - Very soluble in water, soluble in methanol and in dioxane, sparingly soluble in acetone and in alcohol, slightly soluble in chloroform. **[427][USP]**
Prednisolone Hemisuccinate: - Fine creamy white powder with friable lumps, practically odorless, very slightly soluble in water , freely soluble in alcohol, soluble in acetone.
Prednisolone Acetate: - white to practically white odorless powder, practically insoluble in water, slightly soluble in acetone , in alcohol, in chloroform.
Prednisolone Sodium Phosphate: - White or slightly yellow crystalline granules, is odorless and has a slightly odor, is slightly hygroscopic and soluble in water, soluble in methanol and slightly soluble in chloroform, very slightly soluble in acetone and in dioxane.
Prednisolone Sodium Succinate for injection: - Cream white powder with friable lumps, having a slight odor.

- **Prednisolone Tebutate: -** White to slightly yellow free flowing powder which may show more soft lumps. Is odorless and not characteristic smell. Is hygroscopic and slightly soluble in water, freely soluble in water and dioxane and soluble in acetone, sparingly soluble in methanol and in alcohol.

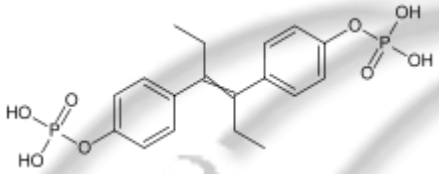
Solubility profile: - Soluble in ethanol and in methanol, dimethyl formamide and in dimethylacetamide. Veru slightly soluble in water. **[IP][428]**
Mechanism of action: - Glucocorticoids such as Prednisolone can inhibit leukocyte infiltration at the site of inflammation, interfere with mediators of inflammatory response, and suppress humoral immune responses. The antiinflammatory actions of glucocorticoids are thought to involve phospholipase A2 inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes. Prednisolone reduces inflammatory reaction by limiting the capillary dilatation and permeability of the vascular structures. These compounds restrict the accumulation of polymorphonuclear leukocytes and macrophages and reduce the release of vasoactive kinins. Recent research suggests that corticosteroids may inhibit the release of arachidonic acid from phospholipids, thereby reducing the formation of prostaglandins. Prednisolone is a glucocorticoid receptor agonist. On binding, the corticoreceptor-ligand complex translocates itself into the cell nucleus, where it binds to many glucocorticoid response elements (GRE) in the promoter region of the target genes. The DNA bound receptor then interacts with basic transcription factors, causing an increase or decrease in expression of specific target genes, including suppression of IL2 (interleukin 2) expression. **[429]**
Pharmacokinetic data
Half-life: - 2-3 hours
Excretion: - Prednisolone is excreted via urine
Pka: - 13.86
Log p: - 3.21. **[430]**
Nature: - Hydrophillic. **[431]**
Use: - Anti-inflammatory (especially for joint pain and itchy skin). **[432]**

- Immune-suppression (treatment of conditions where the immune system is destructively hyperactive. Higher doses are required to suppress the immune system).
- Cancer chemotherapy (especially in the treatment of lymphoma and mast cell tumors.)
- Central nervous system disorders (usually after trauma or after a disc episode to relieve swelling in the brain or spinal cord or more chronically in the event of a brain tumor.)
- Shock (steroids seem to help improve circulation).

more than a Blood calcium reduction (in medical conditions where blood calcium is dangerously high and treatment is needed to reduce levels to normal).

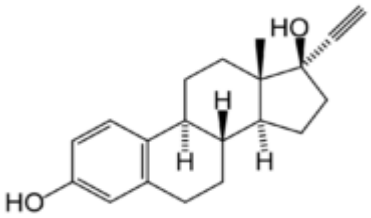
Dissolution Profile: - [433]
Medium: - Water, 900ml
Apparatus: - 2
RPM: - 50
Time: - 30

Fostestrol. [434]



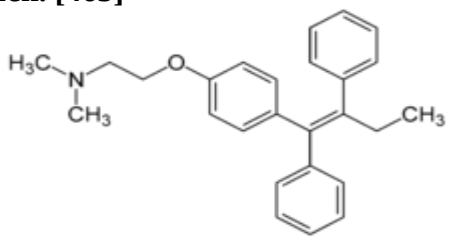
Systematic (IUPAC) name: - [4-[4-(4-phosphonooxyphenyl)hex-3-en-3-yl]phenoxy]phosphonic acid.
Chemical Data: -
Molecular weight: - 516.24**. [435]**
Molecular formula: - C18H18Na4O8P2. **[436]**
Boiling point: - 648.7 °C at 760 mmHg. **[437]**
Melting point: - 234°C. **[438]**
Description: - off-white, odourless, crystalline powder. **[439]**
Solubility profile: - Freely *soluble* in water; practically insoluble in dehydrated alcohol and in ether. **[440]**
Mechanism of action: - At the cellular level, estrogens increase the synthesis of DNA, RNA, and various proteins in target tissues . Pituitary mass is also increased. Estrogens reduce the release of gonadotropin-releasing hormone from the hypothalamus, leading to a reduction in release of follicle-stimulating hormone and luteinizing hormone from the pituitary. **[441]**
Pharmacokinetic data
Half life: - 15 to 25 days. **[442]**
Bioavailability: - 70-80%. **[443]**
Excretion: - Liver. **[444]**
Pka: - Not available.
Log p: - 0.035. **[445]**
Protein binding: - Very high. **[446]**
Nature: - Hydrophillic. **[447]**
Use: - In the treatment of advanced prostate cancer. **[448]**
Dissolution profile: - Not available.

Ethinyl estradiol. [449]



Systematic (IUPAC) name: - 19-Nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol
Chemical Data: -
Molecular weight: - 296.4. **[450]**
Molecular formula: - C20H24O2. **[451]**
Boiling point: - 457.2°Cat760mmHg. **[452]**
Melting point: - 141 to 146°C. **[453]**
Description: - white to pale yellow crystals or crystalline *powder*. It is odorless. **[454]**
Solubility profile: - Insoluble in water, soluble in alcohol and in chloroform, in ether, in vegitable oils and in solution of fixed alkali hydroxides. **[455][USP]**
Solubility profile: - Freely soluble in ethanol and in ether, sparingly soluble in chloroform, practically insoluble in water. **[456][USP]**
Mechanism of action: - Estrogens diffuse into their target cells and interact with a protein receptor. Target cells include the female reproductive tract, the mammary gland, the hypothalamus, and the pituitary. Estrogens increase the hepatic synthesis of sex hormone binding globulin (SHBG), thyroid-binding globulin (TBG), and other serum proteins and suppress follicle-stimulating hormone (FSH) from the anterior pituitary. This cascade is initiated by initially binding to the estrogen receptors. The combination of an estrogen with a progestin suppresses the hypothalamic-pituitary system, decreasing the secretion of gonadotropin-releasing hormone (GnRH). **[457]**
Pharmacokinetic data
Bioavailability: - 97% is bound
Metabolism: - Liver
Half-life: - 36±13 hours
Excretion: - Feces and Urine
Pka: - 7.2. **[458]**
***log* P: -** 3.67. **[459]**
Nature: - Hydrophillic. **[460]**
Use: - Used as oral contraceptive. **[461]**
Dissolution Profile: - [462]
Medium: - polysorbate 80
Apparatus: - 2
RPM: - 75
Time: - 60

Tamoxifen. [463]



Systematic (IUPAC) name: - (*Z*)-2-[4-(1,2-diphenylbut-1-enyl)phenoxy]-*N*,*N*-dimethylethanamine

Chemical Data: -

Molecular weight: - 371.51. **[464]**

Molecular formula: - C26H29NO. **[465]**

Boiling point: - 665.9 °C at 760 mmHg. **[466]**

Melting point: - 143 - 146 C. **[467]**

Description: - fine, white, essentially odorless, crystalline powder. **[468]**

Solubility profile: - Very slightly soluble in water, in acetone, in chloroform and in alcohol, soluble in methanol. **[469][USP]**

Solubility profile: - Soluble in methanol, very slightly soluble in water, in chloroform and in ethanol. **[470][IP]**

Mechanism of action: - Tamoxifen binds to estrogen receptors (ER), inducing a conformational change in the receptor. This results in a blockage or change in the expression of estrogen dependent genes. The prolonged binding of tamoxifen to the nuclear chromatin of these results in reduced DNA polymerase activity, impaired thymidine utilization, blockade of estradiol uptake, and decreased estrogen response. It is likely that tamoxifen interacts with other coactivators or corepressors in the tissue and binds with different estrogen receptors, ER-alpha or ER-beta, producing both estrogenic and antiestrogenic effects. **[471]**

Pharmacokinetic data

Metabolism: - Hepatic (CYP3A4, 2C9 and 2D6)

Half-life: - 5–7 days

Excretion: - Fecal

Protein binding: - 23, 28, 29. **[472]**

Pka: - 8.85. **[473]**

LogP: - 7.87+/-0.75. **[474]**

Nature: - Hydrophillic. **[475]**

Use: - Tamoxifen has been used for more than 30 years to treat breast cancer in women and men. Tamoxifen is used to treat patients with early-stage in the tumor. Toremifene may also inhibit tumor growth through breast cancer, as well as those with metastatic breast cancer (cancer that has spread to other parts of the body). As adjuvant therapy (treatment given after the primary treatment to increase the chances of a cure), tamoxifen helps prevent the original breast cancer from returning and also helps prevent the development of new cancers in the other breast. As treatment for metastatic breast cancer, the drug slows or stops the growth of cancer cells that are present in the body. Tamoxifen has been used for almost 10 years to reduce the risk of breast cancer in women who are at increased risk of developing breast cancer. Tamoxifen is also used to treat women with ductal carcinoma in situ (DCIS), a noninvasive condition that sometimes leads to invasive breast cancer. **[476]**

Dissolution Profile: - [477][Tamoxifen citrate tablet]

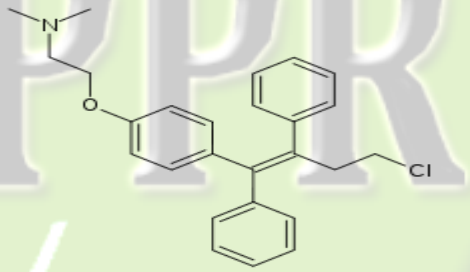
Medium: - 0.2 N hydrochloric acid, 1000ml

Apparatus: - 1

RPM: - 100

Time: - 30

Toremifene. [478]



Systematic (IUPAC) name: - 2-{4-[(1*Z*)-4-chloro-1,2-diphenyl-but-1-en-1-yl]phenoxy}-*N*,*N*-dimethylethanamine.

Chemical Data: -

Molecular weight: - 598.10. **[479]**

Molecular formula: - C26H28CINO • C6H8O7. **[480]**

Boiling point: - 535.1 ºC at 760 mmHg. **[481]**

Melting point: - 158-164℃. **[482]**

Description: - white or almost white crystalline powder. **[483]**

Solubility profile: - Sparingly soluble in methanol, slightly soluble in ethanol, sparingly water soluble. **[484][485]**

Mechanism of action: - Toremifene is a nonsteroidal triphenylethylene derivative. Toremifene binds to estrogen receptors and may exert estrogenic, antiestrogenic, or both activities, depending upon the duration of treatment, animal species, gender, target organ, or endpoint selected. The antitumor effect of toremifene in breast cancer is believed to be mainly due to its antiestrogenic effects, in other words, its ability to compete with estrogen for binding sites in the cancer, blocking the growth-stimulating effects of estrogen

other mechanisms, such as induction of apoptosis, regulation of oncogene expression, and growth factors. **[486]**

Pharmacokinetic data

Protein binding: - 99.5%

Half-life: - 5 days

Metabolized: - Liver. **[487]**

Pka: - 8.0. **[488]**

LogP: - 3.3. **[489]**

Nature: - Hydrophobic. **[490]**

USES: - Toremifene is used in postmenopausal women to treat breast cancer that has spread to other parts of the body (metastatic breast cancer). It is usually used to treat cancer that needs estrogen, a female hormone, in order to grow (estrogen-receptor positive). Toremifene is a nonsteroidal antiestrogen that blocks the effects of estrogen in the breast tissue, thereby slowing or stopping the growth of cancer. **[491]**

Dissolution Profile: - [492]

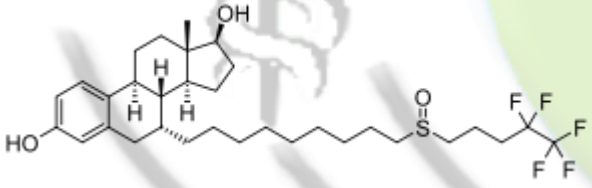
Medium: - 0.02 N hydrochloric acid, 1000ml

Apparatus: - 2

RPM: - 50

Time: - 30

Fulvestrant. [493]



Systematic (IUPAC) name: - (7α,17β)-7-{9-[(4,4,5,5,5-pentafluoropentyl)sulfinyl]nonyl}estra-1,3,5(10)-triene-3,17-diol

Chemical Data: -

Molecular weight: - 606.77**.[494]**

Molecular formula: - C32H47F5O3S**. [495]**

Boiling point: - 674.8°C at 760 mmHg. **[496]**

Melting point: - 106~109℃. **[497]**

Description: - white crystalline solid powder. **[498]**

Solubility profile: - Freely soluble in alcohol, low water solubility. **[499][500]**

Mechanism of action: - Fulvestrant competitively and reversibly binds to estrogen receptors present in cancer cells and achieves its anti-estrogen effects through two separate mechanisms. First, fulvestrant binds to the receptors and downregulates them so that estrogen is no longer able to bind to these no receptors. Second, fulvestrant degrades the estrogen receptors to which it is bound. Both of these mechanisms inhibit the growth of tamoxifen-resistant as well as estrogen-sensitive human breast cancer cell lines. **[501]**

Pharmacokinetic data

Protein binding: - 99%

Half-life: - 40 days

Pka: - 19.38. **[501]**

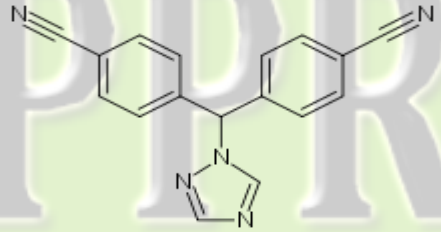
Log p: - 7.848. **[502]**

Nature: - hydrophilic. **[503]**

USES: Fulvestrant is used to treat breast cancer that has spread to other areas of the body in women who have gone through "the change of life" (menopause). It is used in patients who have not responded well to other medications (e.g., tamoxifen). Breast cancer cells need the hormone estrogen in order to grow. Fulvestrant works by blocking the effect of estrogen, slowing tumor cell growth. **[504]**

Dissolution Profile: - Not available.

Letrozole. [505]



Systematic (IUPAC) name: - 4,4'-(1,2,4-triazol-1-ylmethyl)dibenzonitrile

Chemical Data: -

Molecular weight: - 285.31. **[506]**

Molecular formula: - C17H11N5. **[507]**

Boiling point: - 563.5 °C at 760 mmHg. **[508]**

Melting point: - 181-183 oC. **[509]**

Description: - white to yellowish crystalline *powder*, practically odorless. **[510]**

Solubility profile: - Freely *soluble* in dichloromethane, slightly *soluble* in ethanol, and practically insoluble in water. **[511]**

Mechanism of action: - Letrozole is a nonsteroidal competitive inhibitor of the aromatase enzyme system; it inhibits the conversion of androgens to estrogens. In adult nontumor- and tumorbearing female animals, letrozole is as effective as ovariectomy in reducing uterine weight, elevating serum Leuteinizing hormone (LH), and causing the regression of estrogen-dependent tumors. In contrast to ovariectomy, treatment with letrozole does not lead to an increase in serum (folicile stimulating hormone (FSH). Letrozole selectively inhibits gonadal steroidogenesis but has

significant effect on adrenal mineralocorticoid or glucocorticoid synthesis. **[512]**

Pharmacokinetic data

Bioavailability: - 99.9%

Protein binding: - 60%, mainly to albumin

Metabolism: - pharmacologically-inactive carbinol metabolite (4,4´-methanol-bisbenzonitrile)

Half-life: - 2 days

Excretion: - Kidneys

Pka: - Not available.

Log p: - 0.175. **[513]**

Nature: - hydrophilic. **[514]**

USES: - This medication is used to treat certain types of breast cancer (such as hormone-receptor-positive breast cancer) in women after menopause. Letrozole is also used to help prevent the cancer from returning. Some breast cancers are made to grow faster by a natural hormone called estrogen. Letrozole decreases the amount of estrogen the body makes and helps to slow or reverse the growth of these breast cancers.Letrozole is usually not used in women of childbearing age. **[515]**

Dissolution Profile: - [516]

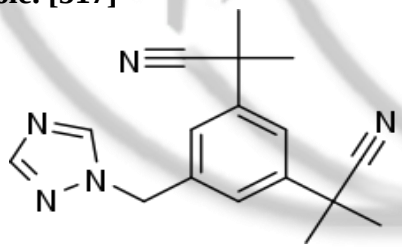
Medium: - 0.1 N hydrochloric acid, 900ml

Apparatus: - 2

RPM: - 75

Time: - 30

Anastrozole. [517]



Systematic (IUPAC) name: - 2,2'-[5-(1H-1,2,4-triazol-1-ylmethyl)-1,3-phenylene]bis(2-methylpropanenitrile).

Chemical Data: -

Molecular weight: - 293.4. **[518]**

Molecular formula: - C17H19N5. **[519]**

Boiling point: - 469.7 °C at 760 mmHg. **[520]**

Melting point: - 81-82 ºC. **[521]**

Description: - Off-white crystalline powder. **[522]**

Solubility profile: - freely soluble in methanol, acetone, ethanol, and tetrahydrofuran, moderate aqueous solubility. **[523][524]**

Mechanism of action: - Anastrozole selectively inhibits aromatase. The principal source of circulating estrogen (primarily estradiol) is conversion of adrenally-generated androstenedione to estrone by aromatase in peripheral tissues. Therefore, aromatase inhibition leads to a decrease in serum and tumor concentration of estrogen, leading to a decreased tumor mass or delayed progression of tumor growth in some women. Anastrozole has no detectable effect on synthesis of adrenal corticosteroids, aldosterone, and thyroid hormone. **[525]**

Pharmacokinetic data

Bioavailability: - 83-85%

Protein binding: - 40%

Metabolism: - 85% hepatic

Half-life: - 46.8 h

Excretion: - 11% renal

Pka: - 8. 85. **[526]**

Log p: - 0.2184, 0.3577. **[527]**

Nature: - Hydrophillic. **[528]**

USES: This medication is used to treat breast cancer in women who have gone through "the change of life" (menopause). Anastrozole works by lowering estrogen hormone levels to help shrink tumors and slow their growth. **[529]**

Dissolution Profile: - [530]

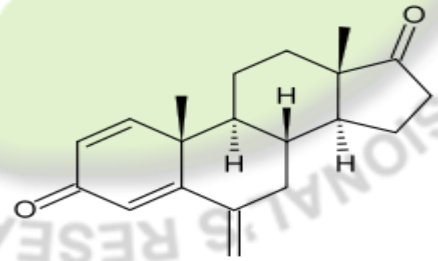
Medium: - water, 900ml

Apparatus: - 2

RPM: - 50

Time: - 30

Exemestane.[531]



Systematic (IUPAC) name: - 6-methylideneandrosta-1,4-diene-3,17-dione.

Chemical Data: -

Molecular weight: - 296.40. **[532]**

Molecular formula: - C20H24O2. **[533]**

Boiling point: - 453.7 °C at 760 mmHg. **[534]**

Melting point: - 188-191. **[535]**

Description: - White crystalline powder. **[536]**

Solubility profile: - Practically insoluble in water, soluble in ethanol and slightly soluble in n-hexane. **[537][538]**

Mechanism of action: - Breast cancer cell growth may be estrogen-dependent. Aromatase (exemestane) is the principal enzyme that converts androgens to estrogens both in pre- and postmenopausal women. While the main source of estrogen (primarily estradiol) is the ovary in premenopausal women, the principal source of circulating estrogens in postmenopausal women is from conversion of adrenal and ovarian androgens (androstenedione and testosterone) to estrogens (estrone and estradiol) by the aromatase enzyme in peripheral tissues. Estrogen deprivation through aromatase inhibition is an effective and selective treatment for some postmenopausal patients with hormone-dependent breast cancer. Exemestane is an irreversible, steroidal aromatase inactivator, structurally related to the natural substrate androstenedione. It acts as a false substrate for the aromatase enzyme, and is processed to an intermediate that binds irreversibly to the active site of the enzyme causing its inactivation, an effect also known as "suicide inhibition". Exemestane significantly lowers circulating estrogen concentrations in postmenopausal women, but has no detectable effect on the adrenal biosynthesis of corticosteroids or aldosterone. This reduction in serum and tumor concentrations of estrogen delays tumor growth and disease progression. Exemestane has no effect on other enzymes involved in the steroidogenic pathway up to a concentration at least 600 times higher than that inhibiting the aromatase enzyme. **[539]**

Pharmacokinetic data

Bioavailability: - 60%

Protein binding: - 90%

Half-life: - 27 hours

Pka: - 6.5. **[540]**

Log p: - 3.87. **[539]**

Nature: - Hydrophillic. **[541]**

USES: This medication is used to treat certain types of breast cancer (such as hormone-receptor-positive breast cancer) in women after menopause. Exemestane is also used to help prevent the cancer from returning. Some breast cancers are made to grow faster by a natural hormone called estrogen. Exemestane decreases the amount of estrogen the body makes and helps to slow or reverse the growth of these breast cancers.Exemestane is usually not used in women of childbearing age. **[542]**

Dissolution Profile: - [543]

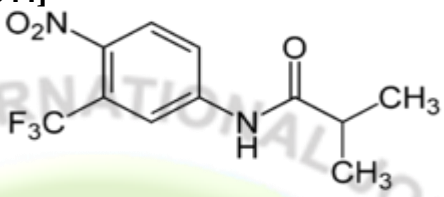
Medium: - 0.5%(w/v) SLS Solution , 900ml

Apparatus: - 1

RPM: - 100

Time: - 30

Flutamide.[544]



Systematic (IUPAC) name: -2-methyl-*N*-[4-nitro-3-(trifluoromethyl)phenyl]-propanamide.

Chemical Data: -

Molecular weight: - 276.212 g/mol. **[545]**

Molecular formula: - C11H11F3N2O3. **[546]**

Boiling point: - 400.3 °C at 760 mmHg.**[547]**

Melting point: - 111-113 oC. **[548]**

Description: - buff to yellow powder.**[549]**

Solubility profile: - Freely soluble in acetone, in ethyl acetate and in methanol, soluble in acetonitrile, practically insoluble in water, optically inactive. **[550][USP]**

Mechanism of action: - Flutamide is a nonsteroidal antiandrogen that blocks the action of both endogenous and exogenous testosterone by binding to the androgen receptor. In addition Flutamide is a potent inhibitor of testosterone-stimulated prostatic DNA synthesis. Moreover, it is capable of inhibiting prostatic nuclear uptake of androgen. **[551]**

Pharmacokinetic data

Bioavailability: - >90%

Protein binding: - 94 to 96%

Excretion: - >90% via urine

Half life: - 5-hour to 6-hour. **[552]**

Pka: - 4.83. **[553]**

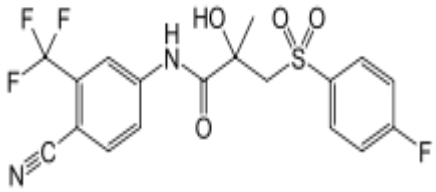
Log p: - 2.6. **[554]**

Nature: - Hydrophobic. **[555]**

USES: This medication is used to treat men with prostate cancer, and is used with other medications and sometimes with radiation treatments. Flutamide belongs to a class of drugs known as anti-androgens (anti-testosterone). Testosterone, a natural hormone, helps prostate cancer to grow and spread. Flutamide works by blocking the effects of testosterone, thereby slowing the growth and spread of prostate cancer. **[556]**

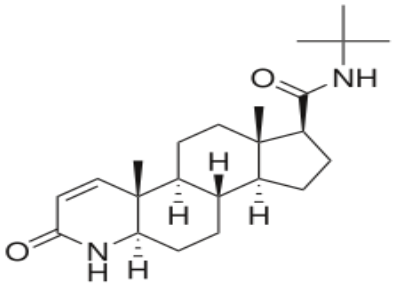
Dissolution Profile: - Not available.

Bicalutamide. [557]



Systematic (IUPAC) name: - *N*-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methylpropanamide
Chemical Data: -
Molecular weight: - 430.37. **[558]**
Molecular formula: - C18H14F4N2O4S. **[559]**
Boiling point: - 650.3 °C at 760 mmHg. **[560]**
Melting point: - 191-193 ºC.**[561]**
Description: - off-white powder. **[562]**
Solubility profile: - freely soluble in tetrahydrofuran and in acetone, soluble in acetonitrile, sparingly soluble in methanol, slightly soluble in alcohol. **[563][USP]**
Mechanism of action: - Bicalutamide competes with androgen for the binding of androgen receptors, consequently blocking the action of androgens of adrenal and testicular origin which stimulate the growth of normal and malignant prostatic tissue. **[564]**
Pharmacokinetic data
Bioavailability: - well absorbed
Protein binding: - 96%
Metabolism: - hepatic
Half-life: - 5.8 days.
Pka: - 4.94, 9.44 and 11.49. **[565]**
Log p: - 2.92. **[566]**
Nature: - Hydrophillic. **[567]**
USES: Bicalutamide is used to treat prostate cancer that has spread to other areas of the body. It is used in combination with hormone treatment. This medication works by blocking the action of male hormones in the prostate, slowing growth of the tumors.This medication should not be used in women or children. **[568]**
Dissolution Profile: - [569]
Medium: - 1% SLS in water, 100ml
Apparatus: - 2
RPM: - 50
Time: - 30

Finasteride. [570]



Systematic (IUPAC) name: - *N*-(1,1-dimethylethyl)-3-oxo-(5α,17β)-4-azaandrost-1-ene-17carboxamide.
Chemical Data: -
Molecular weight: - 372.55. **[571]**
Molecular formula: - C23H36N2O2. **[572]**
Boiling point: - 576.6 °C at 760. **[573]**
Melting point: - near 250°C. **[574]**
Description: - white powder. **[575]**
Solubility profile: - Practically insoluble in water, freely *soluble* in ethanol and methylene chloride. **[576]**
Mechanism of action: - The mechanism of action of Finasteride is based on its preferential inhibition of Type II 5a-reductase through the formation of a stable complex with the enzyme. Inhibition of Type II 5a-reductase blocks the peripheral conversion of testosterone to DHT, resulting in significant decreases in serum and tissue DHT concentrations, minimal to moderate increase in serum testosterone concentrations, and substantial increases in prostatic testosterone concetrations. As DHT appears to be the principal androgen responsible for stimulation of prostatic growth, a decrease in DHT concentrations will result in a decrease in prostatic volume (approximately 20-30% after 6-24 months of continued therapy). In men with androgenic alopecia, the mechanism of action has not been fully determined, but finasteride has shown to decrease scalp DHT concentration to the levels found in hairy scalp, reduce serum DHT, increase hair regrowth, and slow hair loss. **[577]**
Pharmacokinetic data
Bioavailability: - 63%
Metabolism: - Hepatic
Half-life: - Elderly: 8 hours
Adults: 6 hours
Excretion: - Feces (57%) and urine (39%) as metabolites
Pka: - 8.1. **[578]**
Log P: - 1.9. **[579]**
Nature: - Hydrophillic. **[580]**
USES: Finasteride is used to shrink an enlarged prostate (benign prostatic hyperplasia or BPH) in adult men. It may be used alone or taken in combination with other medications to reduce symptoms of BPH and may also

reduce the need for surgery.Finasteride may improve symptoms of BPH and provide benefits such as decreased urge to urinate, better urine flow with less straining, less of a feeling that the bladder is not completely emptied, and decreased nighttime urination.This medication works by decreasing the amount of a natural body hormone (DHT) that causes growth of the prostate.Women and children should not use this medication. **[581]**

Dissolution Profile: - [582]

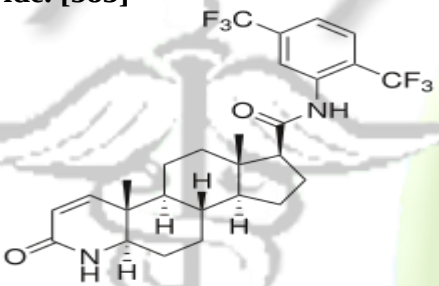
Medium: - water, 900ml

Apparatus: - 2

RPM: - 50

Time: - 30

Dutasteride. [583]



Systematic (IUPAC) name: - (5α, 17β)-*N*-{2,5 bis(trifluoromethyl) phenyl}-3-oxo-4-azaandrost-1-ene-17-carboxamide

Chemical Data: -

Molecular weight: - *528.53* g/mol. **[584]**

Molecular formula: - C27H30F6N2O2. **[585]**

Boiling point: - 620.313°C at 760 mmHg. **[586]**

Melting point: - 242-250. **[587]**

Description: - white to pale yellow powder. **[588]**

Solubility profile: - soluble in ethanol , methanol, insoluble in water **[589][590]**

Mechanism of action: - Dutasteride inhibits the conversion of testosterone to 5 alpha-dihydrotestosterone (DHT), which is the androgen primarily responsible for the initial development and subsequent enlargement of the prostate gland. Testosterone is converted to DHT by the enzyme 5 alpha-reductase, which exists as 2 isoforms, type 1 and type 2. Dutasteride is a competitive and specific inhibitor of both type 1 and type 2 5 alpha-reductase isoenzymes, with which it forms a stable enzyme complex. Dissociation from this complex has been evaluated under *in vitro* and *in vivo* conditions and is extremely slow. Dutasteride does not bind to the human androgen receptor. **[591]**

Pharmacokinetic data

Bioavailability: - 60%

Protein binding: - 99%

Metabolism: - Hepatic (CYP3A4-mediated)

Half-life: - 5 weeks

Excretion: - Fecal

Pka: - 9.87. **[592]**

LogP: - 3.98. **[593]**

Nature: - Hydrophillic. **[594]**

Use: - Dutasteride is an oral medication that blocks the conversion of testosterone to dihydrotestosterone (DHT), the hormone largely responsible for prostate enlargement and for male pattern baldness. It does this by inhibiting the action of both types (Type I and II) 5-alpha reductase enzyme. In contrast, Finasteride, the FDA approved medication for hair loss, inhibits only the Type II enzyme, the enzyme that is present in highest concentrations in and around the hair follicles.

Both dutasteride and finasteride produce a rapid decrease in serum DHT concentration. Lowering DHT appears to inhibit the miniaturization (shrinking) of affected hair follicles and helps restore miniaturized hair follicles to re-grow visible hair.

Dutasteride (Avodart) inhibits both type I and type II, 5?-reductase. At the 0.5-mg dose it is about 3 times as potent as finasteride at inhibiting type II, 5?-reductase enzyme and more than 100 times as potent at inhibiting the type I 5?-reductase enzyme. Type I receptors inhibited by dutasteride are present in other organs of the body besides the skin, including the liver and kidneys. **[595]**

Dissolution Profile: - Capsule[596]

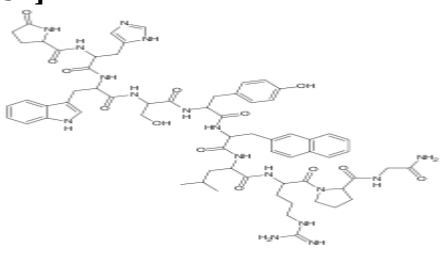
Medium: - Tier I: Dissolution Medium: 0.1 N HCI with 2% (w/v) sodium dodecyl sulfate (SDS) (900 mL) Tier II: Dissolution Medium: 0.1 N HCI with pepsin (as per USP) (450 mL) for the first 25 minutes, followed by addition of 0.1 N HCI with SDS (4% w/v) (450 mL) for the remainder of the dissolution test. , 900ml

Apparatus: - 2

RPM: - 50

Time: - 30

Nafarelin. [597]



Systematic (IUPAC) name: - (2*R*)-*N*-[(2*R*)-5-carbamimidamido-1-[(2*S*)-2-[(carbamoylmethyl) carbamoyl]pyrrolidin-1-yl]-1-oxopentan-2-yl]-2-[(2*R*)-2-[(2*R*)-2-[(2*R*)-3-hydroxy-2-[(2*S*)-2-[(2*S*)-3-(1*H*-imidazol-4-yl)-2-{[(2*R*)-5-oxopyrrolidin-2-yl] formamido}propanamido]-3-(1*H*-indol-3-yl) propanamido]propanamido]-3-(4-hydroxyphenyl) propanamido]-3-(naphthalen-2-yl)propanamido]-4-methylpentanamide

Chemical Data: -

Molecular weight: - 1322.48. **[598]**

Molecular formula: - Sn(C8H12O2)2. **[599]**

Boiling point: - 1840.1°C at 760 mmHg. **[600]**

Melting point: - 195-199 °C. **[601]**

Description: - fine white to off-white amorphous powder. **[602]**

Solubility profile: - soluble in water, very slightly *soluble* in 0.02M phosphate buffer (pH 7.58). **[603]**

Mechanism of action: - Like GnRH, initial or intermittent administration of nafarelin stimulates release of the gonadotropins luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the pituitary gland, which in turn transiently increases production of estradiol in females and testosterone in both sexes. However, with continuous daily administration, nafarelin continuously occupies the GnRH receptor, leading to a reversible down-regulation of the GnRH receptors in the pituitary gland and desensitization of the pituitary gonadotropes. This causes a significant and sustained decline in the production of LH and FSH. A decline in gonadotropin production and release causes a dramatic reversible decrease in synthesis of estradiol, progesterone, and testosterone by the ovaries or testes. Like normal endometrium, endometriotic implants contain estrogen receptors. Estrogen stimulates the growth of endometrium. Use of nafarelin induces anovulation and amenorrhea and decreases serum concentrations of estradiol to the postmenopausal range, which induces atrophy of endometriotic implants. However, nafarelin does not abolish the underlying pathophysiology of endometriosis. In children with central precocious puberty receiving nafarelin, serum LH, testosterone, and estradiol concentrations return to prepubertal levels. This results in the supression of secondary sexual characteristics and decrased rate of linear growth and skeletal maturation. Following disconinuation nafarelin, the effects of the drug is reversed, meaning FSH and LH concentrations usually return to pretreatment levels. **[604]**

Pharmacokinetic data

Half-life: - 2.6 to 4 hours

Excretion: - renal

Protein binding: - 80%. **[605]**

Pka: - 10.2. **[606]**

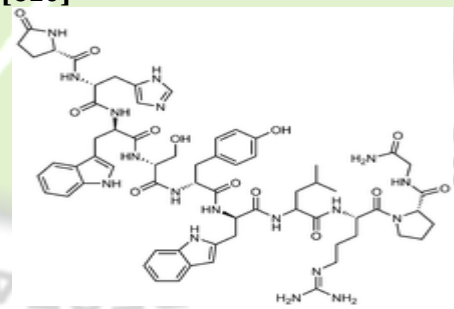
Log p: - 13.4 +/- 1.9. **[607]**

Nature: - Hydrophobic. **[608]**

USES: Nafarelin is used in women to treat a condition in which the tissue that normally lines the inside of the uterus grows in the wrong place (endometriosis). This medication helps to decrease the abnormal tissue and also the symptoms of endometriosis (e.g., pelvic pain, painful menstrual cramps, and pain during/after sex).This medication is also used in children to treat a certain type of early puberty (central precocious puberty, gonadotropin-dependent). It helps to slow the bone aging and height growth rate so that it is near normal and to stop or reverse signs of early puberty (e.g., breast growth in girls, growth of sexual organs in boys).Nafarelin is a man-made hormone that is similar to a natural hormone made by the body (gonadotropin-releasing hormone-GnRH). It works by decreasing the testosterone hormones in boys and estrogen hormones in women and girls. **[609]**

Dissolution Profile: - Not available.

Piperazine. [610]



Systematic (IUPAC) name: - 5-oxo-D-prolyl-L-histidyl-Ltryptophyl-L-seryl-Ltyrosyl-3-(1*H*-indol-2-yl)-L-alanylleucyl-L-arginyl-L-prolylglycinamide

Chemical Data: -

Molecular weight: - 1311.46. **[611]**

Molecular formula: - C64H82. **[612]**

Boiling point: - 1533.3 °C at760mmHg. **[613]**

Melting point: - 107~110℃. **[614]**

Description: - White to off-white powder. **[615]**

Solubility profile: - SOLUBILITY IN WATER, Soluble (Soluble in acetic acid). **[616]**

Mechanism of action: - Triptorelin is a potent repressor of

gonadotropin secretion when given continuously and in therapeutic doses. Following the first administration, there is a transient surge in circulating levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and estradiol. After chronic and continuous administration, usually 2 to 4 weeks after initiation of therapy, a sustained decrease in LH and FSH secretion and marked reduction of testicular and ovarian steroidogenesis is observed. In men, a reduction of serum testosterone concentration to a level typically seen in surgically castrated men is obtained. Consequently, the result is that tissues and function that depend on these hormones for maintenance become quiescent. These effects are usually reversible after cessation of therapy. **[617]**

Pharmacokinetic data

Excretion:- Renal

Half life: - 7.5 hours. **[618]**

Protein binding: - clinically relevant concentrations. **[619]**

Pka: - 7.2. **[620]**

Log P: - 0.088. **[621]**

Nature: - Hydrophillic. **[622]**

USES: - Triptorelin is used to treat advanced prostate cancer in men. It is not a cure. Most types of prostate cancer need the male hormone testosterone to grow and spread. Triptorelin is similar to a natural hormone made by the body (luteinizing hormone releasing hormone-LHRH). It works by reducing the amount of testosterone that the body makes. This effect helps slow or stop the growth of cancer cells and helps relieve symptoms such as painful/difficult urination. **[623]**

Dissolution Profile: - [624][injectable]

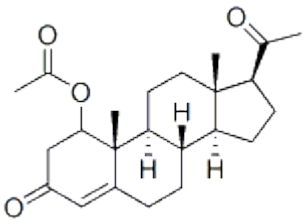
Medium: - Water-Methanol (95:5); Reconstitute vial in 2 mL Water for Injection, add to 500 mL medium at 37°C, 500ml

Apparatus: - 2

RPM: - 200

Time: - 30

Hydroxyprogestroneacetate.[625]



Systemic IUPAC name: - 17A-hydroxyprogesterone 17-acetate;17-(acetyloxy)-pregn-4-ene-20-dione;17-ap;20-dione ,17-hydroxy-pregn-4-ene-acetate; acetoxyprogesterone; prodoxacetate;u5533;17a-hydroxyprogesterone 17-acetate vetra

Chemical Data: -

Molecular weight: - 372.5. **[626]**

Molecular formula: - C23H32O4. **[626]**

Boiling point: - 490 °C at 760 mmHg, **[627]**

Melting point: - 249-250 ºC. **[628]**

Description: - White Or Almost White Crystalline Powder. **[629]**

Solubility profile: - Insoluble in water; *soluble* in ether; slightly *soluble* in benzene. **[630]**

Mechanism of action: - Not available.

Pharmacokinetic parameter:- Not available.

Dissolution Profile: - Not available

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