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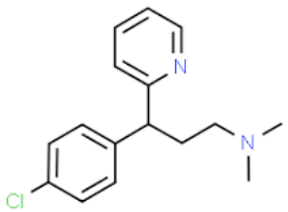
Paper 4204 - Organic Chemistry (Special Paper –V)

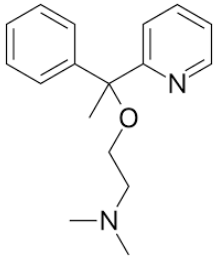
Course A: Medicinal Chemistry:

A. **Antihistamines:**

- Antihistamines are a class of drugs that stops release of Histamine from Histamine receptors.
- They are generally used to treat allergies such as fever, cold, and reaction to insect bites. Some time histamines are also used to treat insomnia.
- Antihistamines are generally classified into main groups; i) First generation of antihistamines and ii) Second generation of antihistamines.
- First generation antihistamines easily cross the blood brain barrier and act on histamine receptors (H-1 Receptors) in the central nervous system (CNS).
- H-1 receptors in the CNS help to regulate the body's sleep –wake cycle.
- They also act on muscarnic, alpha-adrenergic and serotonin receptors. The main side effects are sedation, headache, dry mouth, dizziness, blurred vision or double vision, abdominal pain, constipation, low blood pressure, rapid heart- beat and urinary problem.
- Some of the most important drugs are chlorphenamine, (including Piriton), hydroxyzine (Atarax, Vistaril), diphenhydramine (Benadryl), chlorpheniramine (Chlor-Trimeton), carbinoxamine (Clistin) clemastine (Tavist) doxylamine (Unisom) and promethazine.

Structure of some representative drugs:

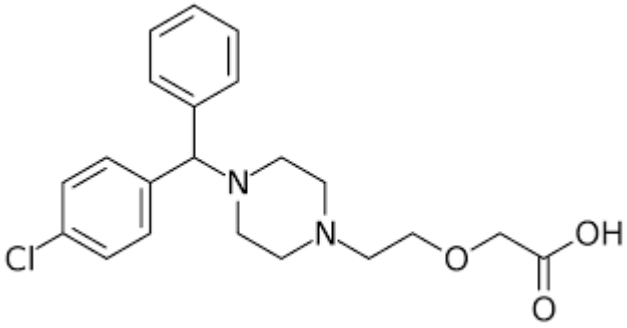




Chlorphenamine **Doxylamine**

- Second generation antihistamines act on histamine-1 receptors are less likely to cross the blood brain barrier, hence less sedative and have no significant affects on the CNS.
- The side effects include headache, nausea, fatigue, abdominal pain, dry mouth, feeling sick, drowsiness
- The common drugs are cetirizine, fexofenadine, and loratadine etc.

Structure of some representative drug:



Cetirizine

B. Anti-inflammatory and Anti-analgesic agents:

- Inflammation (from Latin word: inflammation) is a part of the complex biological response of the body tissue.
- Analgesic drugs are used to relieve pain, commonly known as pain killer or pain reliever
- Inflammation is a defence mechanism caused by tissue damage. It can be elicited by numerous stimuli including;

i) Infectious agents
ii) Antigen-antibodies interactions
iii) Ischemia
iv) Thermal and physical injury
v) Noxious chemicals
vi) Inflammation can be broadly classified into two category; Acute or Chronic inflammations. Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes (especially granulocytes) from the blood into the injured tissues. Prolonged inflammation results chronic inflammation

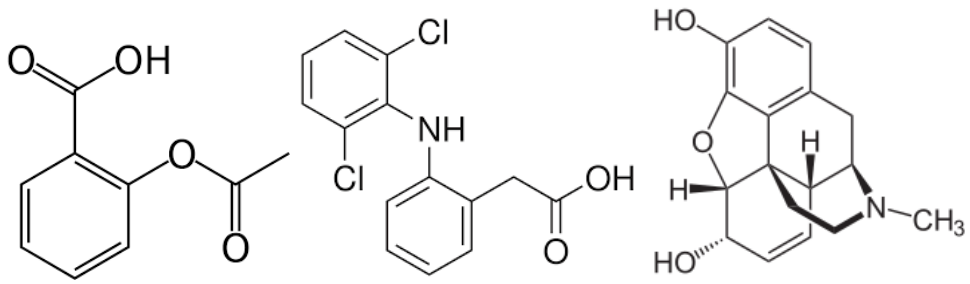
- There two types of drugs; Non-steroidal anti-inflammatory drugs (NSAIDs) and Opioid drugs. NSAID drugs relieve pain, fever, and reduce inflammation.
- Some of the common drugs are ;

i) Aspirin (single ingredient) or combination of other ingredients such as Anacin, Ascriptin, Bufferin, Excedrin)
ii) Ibuprofen (Mortin and Advil)
iii) Ketoprofen
iv) Diclofenac
v) Naproxen sodium (Aleve)

- NSAIDs block a specific group of enzymes called cyclo-oxygenase enzyme, often called COX-enzymes. These enzymes are responsible for production of prostaglandins. Prostaglandins are a group of complex molecules with hormone like effects that controls many different biological functions in the living organism such as inflammation, blood flow and blood clot etc.

- Moreover, the NSAIDs are frequently used to treat pain of rheumatoid arthritis (RA), osteoarthritis and tendonitis. They are also useful in treatment of muscle aches, backaches, dental pain, , and also in pain caused by gout, Bursitis, Menstrual cramps
- Opioid drugs such as Morphine(Duramorph) and Oxycodone (Oxaydo) Pro are used to treat moderate to several pain in patient.

Structure of some representative drugs:



Aspirin **Diclofenac** **Morphine**

C. Anti-hypertensive Agents:

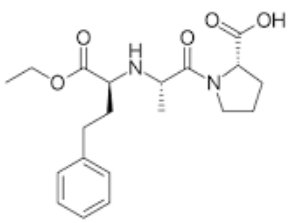
- Antihypertensive drugs are used to lower high blood pressure(hypertension)
- The treatment of high blood pressure prevents heart attack, stroke, and heart failure.
- Presently, almost 15% of patients have hypertension due to some specific reasons.
- Patients in whom no specific cause of hypertension referred as essential to primary hypertension.
- Patients with specific etiology are said to have secondary hypertension.
- Genetic factors, psychological stress, environmental and dietary factors as contributing to the development of hypertension. The heritability of essential hypertension is estimated to be said around 30%
- Classification of hypertension on the basis of blood pressure;

Systolic /Diastolic Pressure (mm/Hg)	**Category**
<120/80	Normal
120-135/80-89	Prehypertension
≥140/9	Hypertension
140-159/90-99	Stage I
≥160-/100	Stage II

- ACE inhibitors (Inhibitors of angiotension converting enzyme, decease activity of rennin angiotension system aldosterone)

  eg. : Captopril, Enalapril, Licinopril, Ramipril

Structure of some representative drugs:

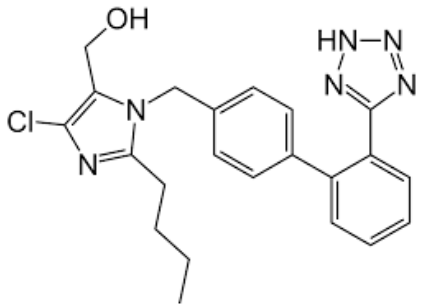


Enalapril

- Angiotensin (AT1 receptor) blockers

  eg. : Losartan, Valsartan, Telmisartan, Irbesartan

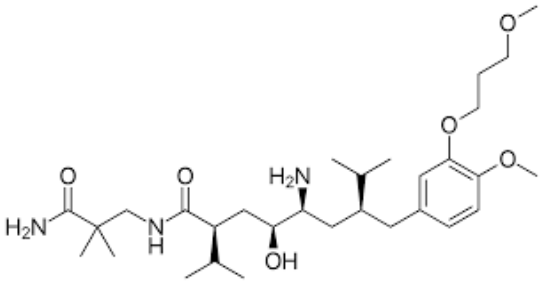
  Structure of some representative drugs :



Losartan

- Direct renin inhibitor

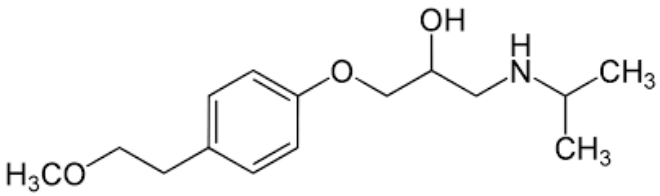
  eg. : Aliskiren



Aliskiren

- B-Andrenergic blockers:

  eg.: Metoprolol, Atenolol



Metoprolol

- $B^{+}\alpha$. Adrenergic blockers

  eg. : Labetalol, Carvedilol

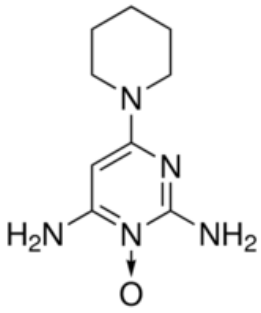
- A-Adrenergic blockers

  eg. : Prazosin, Terazosin, Doxazosin, Phenoxybenzamine

- Vasodilators

  -Arteriolar : eg.: Hydralazine, Minoxidil, and Diazoxide

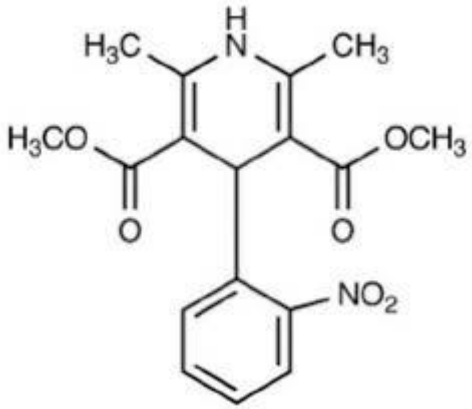
  -Arteriolar + venous : eg. : Sodium nitroprusside



Minoxidil

- Calcium channel blockers

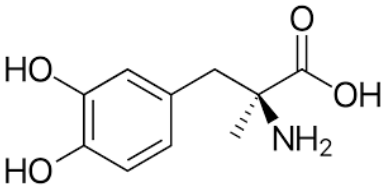
  eg.: Verapamil, Diltiazem, Nifedipine, Felodipine, Amlodipine , Lacidipine



Nifedipine

- Central sympatholytics;

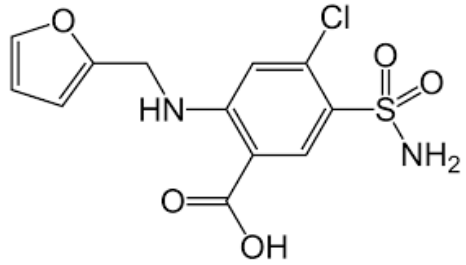
  eg.: Clonidine, Methyldopa.



Methyldopa

- Diuretics
  - Thiazides: eg.: Hydrochlorothiazide, Chlorthalidone,
  - High Ceiling: eg. : Furosemide, Torsemide,
  - K+ sparing : eg.: Spironolactone, Amiloride

Structure of representative drugs

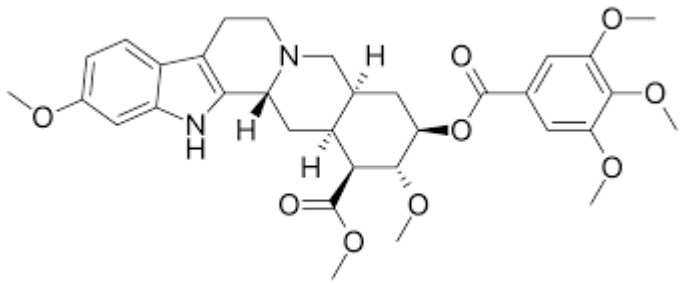


Furosemide

- Others:

  Andrenergic neurone blockers (eg. Reserpine, Guanethidine,), Ganglion blockers (Pentolinium)

Structure of representative drug



Reserpine

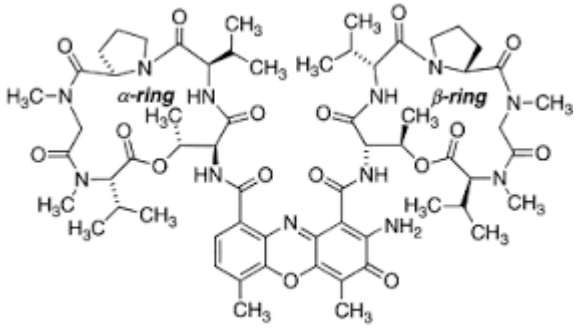
D. **Anticancer Drugs**:

- Cancer is defined as uncontrolled growth of cells due to loss of normal cell regulatory mechanism that control cell growth and multiplications.
- There are two types' cancers; benign cancer and malignant cancer.
- Benign cancer cells are localized and do not move in the other parts in the body.
- Malignant cancer cells invade new tissues to set up secondary tumours, a process known as

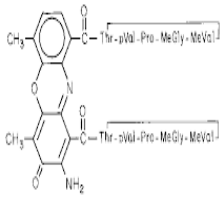
  Metastasis.
- Chemicals causing cancer are called mutagens**.**
- Cancer can be caused by chemicals, smoking, and viruses.

- Genes that are related to cause cancer are called oncogenes. Genes that become oncogenic upon mutation are called proto-oncogenes**.**
- Cancer cells are often called immortal since there seems to be no limit for how often they can divide.
- Life-time of normal cells is limited to 50-60 cell divisions. This is regulated By telomeres. The telomeres are at the 3' end of the chromosomes.
- After each replication about 50-100 base pairs are lost.
- At some point telomeres are too short to be effective and the DNA becomes unstable thereby limiting replication. Cancer cells possess an enzyme called telomerase which maintains the length of the telomeres and thereby allows more DNA replications.
  - **Various Anticancer drugs:**

i) Dactinomycin, (Intercalating agents)



Actinomycin D (dactinomycin)

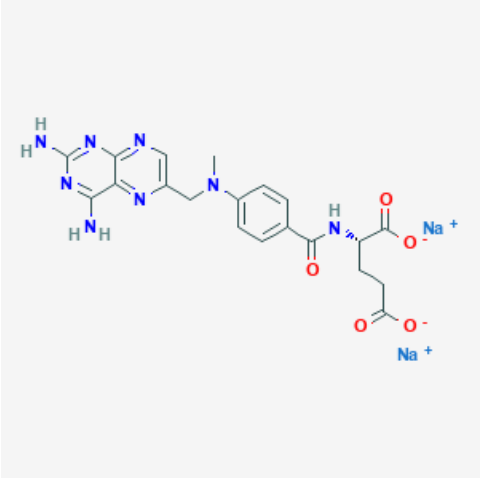


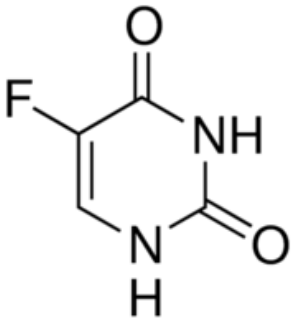
Dactinomycin

ii) Doxorubicin

Doxorubicin

ii) Methotrexate, 5- Flurouracil

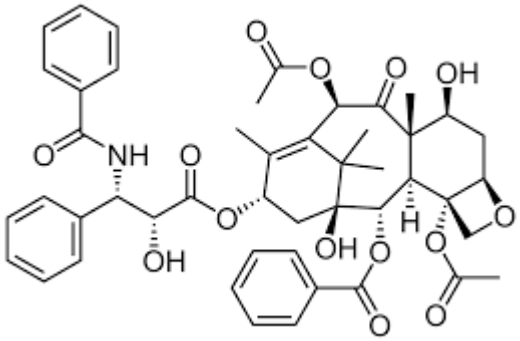




Methotrexate 5-Flurouracil

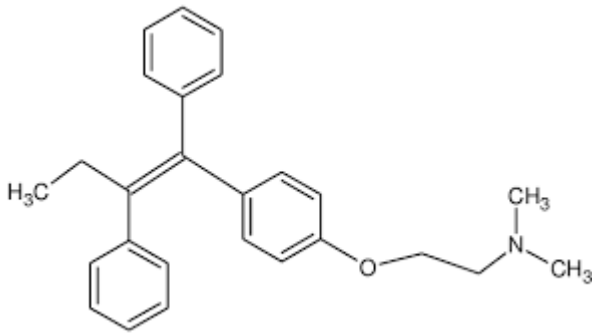
iii) Taxol (Mitosis inhibitors Target microtubules and associated proteins required in cell

division



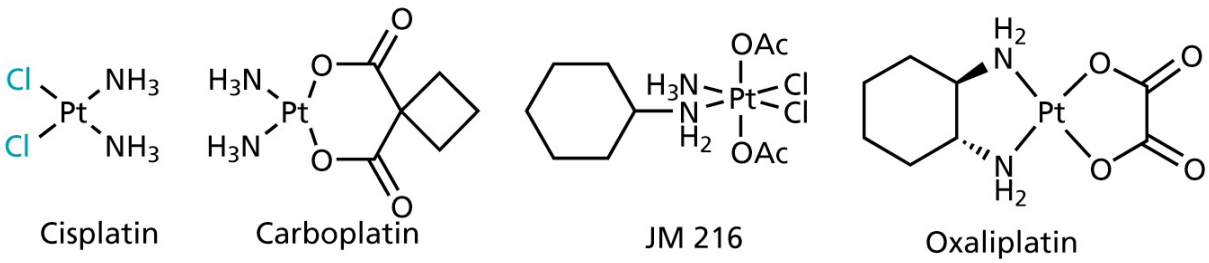
Taxol

iv) Tamoxifen, flutamide (Steroid hormones Block steroid- and hormone-dependent growth of certain tumors)



Tamoxifen

v) Cisplatin, Carboplatin , J M 216, Oxaliplatin (Alkylating/cross-linking agents Damage DNA and result in death of growing cells Endoxan)



Etoposide, doxorubicin (Antitumor antibiotics Bind DNA to prevent DNA and/or RNA synthesis)